American Journal of Ophthalmology

Prevalence and Risk Factors of Open Angle Glaucoma in an Adult Chinese American Population: The Chinese American Eye Study

--Manuscript Draft--

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	Rohit Varma, MD, MPH
Abstract:	Purpose: To estimate the prevalence of and identify risk factors associated with open angle glaucoma (OAG) among adult Chinese Americans. Design: Population-based, cross-sectional study Participants: 4,582 Chinese Americans aged 50 years and older residing in Monterey Park, CA Methods: Participants from the Chinese American Eye Study underwent a comprehensive interview, eye examination, and ophthalmic testing. Open-angle glaucoma (OAG) was defined by characteristic optic nerve head changes with or without corresponding visual field loss, as determined by a panel of glaucoma specialists and required at gonioscopic confirmation of least 2 quadrants of visible pigmented trabecular meshwork. Candidate risk factors comprised demographic, clinical, and ocular characteristics. Multivariable logistic regression analysis was used to identify independent risk factors associated with OAG. Main Outcome Measures: Prevalence of and independent risk factors associated with OAG. Results: Of the 4,310 participants with complete data, the prevalence of OAG was 4.8% (207/4310), ranging from 2.8% among those aged 50-59 years to 14.8% among those 80 years and older. Of those with OAG, 68.5% were previously undiagnosed or untreated, and 88.5% had intraocular pressure (IOP) < 21 mmHg. Independent risk factors for OAG, adjusting for sex, were older age (odds ratio [confidence interval] = 1.06 [1.05,1.08], per year); higher IOP (1.12 [1.08,1.17], per mmHg); longer axial length (AL; 1.36 [1.25,1.47], per mm); family history of glaucoma (1.88 [1.19,2.97]); and diabetes mellitus (1.49 [1.05,2.11]). Conclusions: The prevalence of OAG among Chinese Americans may be higher than that reported in U.S. populations of European descent and in Asia-based Chinese populations, but lower than that observed in Latinos in Los Angeles and individuals of African Caribbean descent. More than two thirds of OAG cases in our study were previously undiagnosed or untreated, with a majority presenting with IOP <21 mmHg. These findings highlight the importance of identifying high-risk individuals based on age, IOP, axial length, family history and diabetes mellitus. Given the high prevalence of myopia, future research should evaluate whether interventions to prevent myopia

	could help reduce risk for developing OAG.
Suggested Reviewers:	
Opposed Reviewers:	
Response to Reviewers:	Thank you for the opportunity to revise the manuscript entitled “Prevalence and Risk Factors of Open Angle Glaucoma in an Adult Chinese American Population: The Chinese American Eye Study." All coauthors have seen and agree with each of the revisions made to the manuscript. Please see our responses below. Reviewer #1: General Comments This is the first population-based study on Chinese American population providing with information on prevalence and risk factors on OAG. Overall, the study was well conducted, and the authors used a robust glaucoma definition. Although still with inherent limitations, one needs to congratulate the authors for the glaucoma definition used which although may overlap with the ISGEO definition is not identical. The ISGEO definition aims in standardizing epidemiology studies glaucoma definition using cut offs on optic disc structure measurements which is again the nature of the disease and the well-known variability of the optic disc morphology leading inherently to misclassification. In this study the definition used still has limitations related to variability among observers in assessing optic disc but this goes with the nature of the disease and on the other hand the definition used is consistent with other large population-based studies like Los Angeles Latino Eye Study and Blue Mountains Eye Study. 1. Although this is a study on open angle glaucoma one would expect that in a Chinese origin population narrow angle will present with significant prevalence. The authors could provide the information on what was the percentage in the population having narrow angle and the overall prevalence of open angle glaucoma, just to have the magnitude of the overall glaucoma problem in this population. Response: We thank the reviewer for this suggestion. We have now included the prevalence of angle closure in the introduction section to provide a more complete understanding of disease burden. (Introduction section, Page 3). 2. In line 51, it should be better written "in populations with high prevalence of myopia". Response: Thank you for this suggestion. We revised the sentence to read “in populations with high myopia prevalence” (Introduction section, Page 2). 3. In what % of those myopia (high axial length) optic nerve findings were matched with visual field findings. In myopic eyes relying glaucoma diagnosis only on disc findings may lead to over diagnosis glaucoma. Response: We thank the reviewer for this comment. Among 76 OAG cases with axial length ≥ 25mm, 82% had abnormal glaucomatous visual fields, highlighting that structural findings were often confirmed with functional loss even in myopic eyes. Also at the end of the third discussion paragraph, we report: “Even excluding “pre-perimetric” glaucoma cases, our prevalence remained 3.76% - still higher than any other previously studied Chinese population from Asia.” (Discussion section, Page 13) 4. Regarding the area Monterey Park, California, how this specific area was chosen and how Chinese living in this area are representative of Chinese American population in socioeconomic and demographic terms. Response: We thank the reviewer for this comment. The study area of 15 census tracts within Monterey Park California was chosen because a high proportion of Chinese Americans reside in this area, the population was large enough to obtain robust prevalence estimates, there was strong support and encouragement from community leaders, the nearby LAC/USC Medical Center was available to provide necessary emergency care and the demographic characteristics of the population were similar to those of Chinese American populations in Los Angeles County, the state of California, and the United States. This is detailed in the reference “Varma R, Hsu C, Wang D, Torres M, Azen SP; Chinese American Eye Study Group. The Chinese American Eye Study: Design and methods. Ophthalmic Epidemiol 2013;20(6):335-47,” which is cited in this paper.

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Response: Thank you for this question. Since this was not a clinical trial but rather an observational epidemiology study, it was not registered.

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Response: We thank the reviewer for this suggestion. This edit has been made (Abstract, Conclusion section).

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Response: We thank the reviewer for this comment. A comprehensive eye exam is described in the second paragraph of the methods section, and additional details have been added as requested. (Methods section, Page 4).

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Response: We thank the reviewer for this important comment. It is true that myopic eyes can have larger cup-disc ratios. Our glaucoma specialists were not assessing cup-disc ratio alone as a way to diagnose glaucoma but rather focusing on the neuroretinal rim including features such as diffuse thinning, focal notching, peripapillary hemorrhage, and cup-disc ratio asymmetry between the 2 eyes. They also evaluated visual fields. The diagnosis of glaucoma had to be agreed upon by 2 glaucoma specialists and used two adjudicators when necessary. At the end of the third discussion paragraph, we state, “Even excluding “pre-perimetric” glaucoma cases, our prevalence remained 3.76% - still higher than any other previously studied Chinese population from Asia.” We hope this demonstrates that even in those cases with a glaucomatous appearing optic nerve determined by the panel of glaucoma specialists, if we exclude those with normal VF, the prevalence in our population is still higher than any other studied Chinese population from Asia.

22. Were the examiners performing tonometry masked to the applanation reading?
Response: We thank the reviewer for this question. The examiners were not masked to the applanation reading.

23. In the third line of the results, what was the standard deviation of the ages?
Response: We thank the reviewer for this question. This has now been added (Results section, Page 8).

24. The authors define ocular hypertension as an IOP > 21 mm Hg, yet the OHTS study, which is well accepted, defines OHTS as an IOP ≥ 24 mm HG. Might the authors kindly describe why they chose a different definition and change the definition and numbers in their results?
Response: We thank the reviewer for this question. The definition of ocular hypertension used in our study was defined as above so that it could be directly comparable to other studies, which used the same definition and has identical study methodology. However, we have now added the prevalence of OHTN based on OHTS as well: “If OHTN is defined as an IOP ≥ 24mmHg, open angles ≥ 180°, and absence of glaucoma (per the Ocular Hypertension Treatment Study), the prevalence was 0.5% in females, 1.1% in males, and 0.7% overall)” (Results section, Page 9).

25. Line 20 of the discussion uses reference 25. I believe this might be the incorrect reference.
Response: Thank you for noticing this error. The correct reference has now been included (Discussion, page 11).

26. The authors discuss their "younger" study population within the discussion, yet their study population is older than those in most other prevalence studies.
Response: We thank the reviewer for this comment. We clarified that “younger” refers to participants being younger than non-participants in the same community and not in comparison to other study populations (Discussion section, Page 13).

27. The authors describe a higher education level and greater near work. This as a causative factor is speculation and I would delete.
Response: We thank the reviewer for this comment. We agree this was speculative and have removed the sentence linking education level and near work to glaucoma risk. (Discussion section, Page 15).

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Response: We thank the reviewer for this comment. We have revised the comparison to focus exclusively on Chinese populations and removed ethnically unrelated

	references. (Discussion section, Page 15). 29. The sentence, "Prevention efforts, such as ..." should be deleted. Response: We thank the reviewer for this comment. As suggested, the sentence regarding prevention efforts has been deleted. 30. Subjects had larger eyes. They may therefore have larger scleral canals and therefore larger cups. These physiologic larger cups might account for an increased glaucoma diagnosis by cup appearance". Response: We thank the reviewer for this comment. Please refer to our response to item 21 regarding the evaluation of optic nerve head and visual field data in diagnosing glaucoma. 31. Might the authors change IOP to screening IOP in parts of the discussion? Response: We thank the reviewer this suggestion. IOP has been replaced with screening IOP in relevant sections of the discussion (Discussion section, Page 15).

Abstract

Purpose: To estimate the prevalence of and identify risk factors associated with open angle glaucoma (OAG) among adult Chinese Americans.

Design: Population-based, cross-sectional study

Participants: 4,582 Chinese Americans aged 50 years and older residing in Monterey Park, CA

Methods: Participants from the Chinese American Eye Study underwent a comprehensive interview, eye examination, and ophthalmic testing. Open-angle glaucoma (OAG) was defined by characteristic optic nerve head changes with or without corresponding visual field loss, as determined by a panel of glaucoma specialists and required at gonioscopic confirmation of least 2 quadrants of visible pigmented trabecular meshwork. Candidate risk factors comprised demographic, clinical, and ocular characteristics. Multivariable logistic regression analysis was used to identify independent risk factors associated with OAG.

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Conclusions: The prevalence of OAG among Chinese Americans may be higher than that reported in U.S. populations of European descent and in Asia-based Chinese populations, but lower than that observed in Latinos in Los Angeles and individuals of African Caribbean descent. More than two thirds of OAG cases in our study were previously undiagnosed or untreated, with a majority presenting with IOP $\leq$21 mmHg.These findings highlight the importance of identifying high-risk individuals based on age, IOP, axial length, family history and diabetes mellitus. Given the high prevalence of myopia, future research should evaluate whether interventions to prevent myopia could help reduce risk for developing OAG.

SCEI SOUTHERN CALIFORNIA EYE INSTITUTE

July 28, 2025

Re: Manuscript **AJO-25-1216**
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Dear Dr. Parrish,

Thank you for the opportunity to revise the manuscript entitled **"Prevalence and Risk Factors of Open Angle Glaucoma in an Adult Chinese American Population: The Chinese American Eye Study."** All coauthors have seen and agree with each of the revisions made to the manuscript.

Please see our responses below.

Reviewer #1: General Comments
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Response: We thank the reviewer for this question. The examiners were not masked to the applanation reading.

23. In the third line of the results, what was the standard deviation of the ages?

Response: We thank the reviewer for this question. This has now been added (Results section, Page 8).

24. The authors define ocular hypertension as an IOP > 21 mm Hg, yet the OHTS study, which is well accepted, defines OHTS as an IOP ≥ 24 mm HG. Might the authors kindly describe why they chose a different definition and change the definition and numbers in their results?

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Response: We thank the reviewer for this question. The definition of ocular hypertension used in our study was defined as above so that it could be directly comparable to other studies, which used the same definition and has identical study methodology. However, we have now added the prevalence of OHTN based on OHTS as well: "If OHTN is defined as an IOP ≥ 24mmHg, open angles ≥ 180°, and absence of glaucoma (per the Ocular Hypertension Treatment Study), the prevalence was 0.5% in females, 1.1% in males, and 0.7% overall)" (Results section, Page 9).

25. Line 20 of the discussion uses reference 25. I believe this might be the incorrect reference.

Response: Thank you for noticing this error. The correct reference has now been included (Discussion, page 11).

26. The authors discuss their "younger" study population within the discussion, yet their study population is older than those in most other prevalence studies.

Response: We thank the reviewer for this comment. We clarified that "younger" refers to participants being younger than non-participants in the same community and not in comparison to other study populations (Discussion section, Page 13).

27. The authors describe a higher education level and greater near work. This as a causative factor is speculation and I would delete.

Response: We thank the reviewer for this comment. We agree this was speculative and have removed the sentence linking education level and near work to glaucoma risk. (Discussion section, Page 15).

28. The authors compare their results to the Chennai eye study. Tamils who populate Chennai, have a totally different ethnicity.

Response: We thank the reviewer for this comment. We have revised the comparison to focus exclusively on Chinese populations and removed ethnically unrelated references. (Discussion section, Page 15).

29. The sentence, "Prevention efforts, such as ..." should be deleted.

Response: We thank the reviewer for this comment. As suggested, the sentence regarding prevention efforts has been deleted.

30. Subjects had larger eyes. They may therefore have larger scleral canals and therefore larger cups. These physiologic larger cups might account for an increased glaucoma diagnosis by cup appearance".

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Response: We thank the reviewer for this comment. Please refer to our response to item 21 regarding the evaluation of optic nerve head and visual field data in diagnosing glaucoma.

31. Might the authors change IOP to screening IOP in parts of the discussion?

Response: We thank the reviewer this suggestion. IOP has been replaced with screening IOP in relevant sections of the discussion (Discussion section, Page 15).

Sincerely,

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Prevalence and Risk Factors of Open Angle Glaucoma in an Adult Chinese American Population: The Chinese American Eye Study

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Short Title: Prevalence of Open Angle Glaucoma in Chinese Americans

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Key Words: open angle glaucoma, prevalence Chinese Americans, ocular epidemiology

Introduction

Open angle glaucoma (OAG) is a progressive optic neuropathy leading to irreversible vision loss and represents a leading cause of blindness worldwide.[1] The mainstay of glaucoma treatment is intraocular pressure (IOP) reduction, which effectively slows progressive glaucomatous optic nerve damage and prevents blindness.[2] Early in its course, OAG remains asymptomatic and can progress without patients detecting vision changes. Therefore, identifying effective approaches for early OAG detection is critical to prevent avoidable vision loss and blindness. Understanding the disease in specific populations and associated risk factors can guide targeted detection and management strategies.

Chinese Americans represent part of the fastest growing minority population in the United States over the past decade.[3] Due to the high prevalence of myopia in Chinese Americans[4,5], this population may experience a disproportionately higher burden of myopia-related diseases, including myopic macular degeneration, retinal detachment, cataract, and open angle glaucoma.[6,7] A recent meta-analysis of 14 population-based studies demonstrated a significant association between even mild myopia (> -3 D) and OAG, with this association strengthening for moderate to high myopia (≤ -3 D).[6] Some studies have also demonstrated an association between progressive glaucomatous visual field loss and myopia.[8-10] However, additional research is needed to understand the burden and characteristics of glaucoma in populations with high myopia prevalence such as Chinese Americans.

While several epidemiological studies have examined OAG in urban and rural Asia-based populations of Chinese descent[11-14], no comparable data exist for persons

of Chinese descent residing in the US. The Chinese American Eye Study (CHES) represents the first such investigation conducted in the US. We recently reported on the prevalence of primary angle closure suspects, primary angle closure, and primary angle closure glaucoma (8.1%, 3.1%, 1.1%, respectively), in this population.[15] The current study provides the opportunity to determine OAG prevalence and identify associated risk factors in this specific US population.

Methods:

Study Population and Data Collection

The study design of CHES has been detailed elsewhere.[16] Briefly, self-identified Chinese Americans, aged 50 years and older and residing in 10 census tracts in Monterey Park, California, were invited to participate. Of the 5782 eligible Chinese American adults, 4582 (79.2%) underwent interview and comprehensive eye examination from 2010-2013. The institutional review boards from the University of Southern California, Los Angeles, and the University of Illinois at Chicago approved the study protocol. All patients provided informed consent, and the study adhered to the tenets of the Declaration of Helsinki.

A detailed in-home interview obtained demographic characteristics and ocular and medical histories. A complete eye examination was performed at a local eye examination center by a comprehensive ophthalmologist. Visual acuity was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts and the Lea symbol charts for illiterate participants. Lensometry verified participant's eyeglass prescriptions. Automated refraction with a Humphrey Automatic Refractor (Carl Zeiss

Meditec, Dublin, CA) was performed if the presenting visual acuity was not 20/20 in either eye. Subjective refraction was performed if participants achieved less than 20/20 vision on the automated refraction. IOP was measured twice using Goldman applanation tonometry (Haag-Streit, Mason, OH) and averaged for analyses. Visual field evaluation utilized the Swedish Interactive Threshold Algorithm (SITA) Standard C24-2 test (Carl Zeiss Humphrey Field Analyzer II 750). Slitlamp examination included manual gonioscopy, performed by a trained ophthalmologist masked to other exam findings, under standardized dark conditions (<1 lux illumination) at a slit lamp (Model BM900, Haag-Streit, Bern, Switzerland) using a four-mirror gonioprism (Ocular Instruments, Bellevue, WA, USA). A 1x1mm slit beam was used to avoid having light fall on the pupil. Each quadrant of the angle was evaluated, and the presence of the pigmented trabecular meshwork and the presence and circumferential extent of peripheral anterior synechiae were recorded. In addition to documenting a dilated fundus exam, stereoscopic disc photography was performed using an optic nerve camera (Nidek 3DX, Nidek Inc., Fremont, CA). Three measurements were obtained using A-scan ultrasonography (4000B A-Scan/Pachymeter; DGH Technology, Exton, PA) for axial length (AL), anterior chamber depth (ACD), central corneal thickness (CCT), and lens thickness (LT). Vitreous chamber depth was calculated by subtracting CCT, ACD, and LT from AL.

Glaucoma Diagnosis

Glaucoma was defined based on characteristic optic nerve head and/or visual field changes, which was established previously for the Los Angeles Latino Eye Study

(LALES)[17], and consistent with other major epidemiological studies such as the Beaver Dam Eye Study and Melbourne Vision Impairment Study[18,19]. The definition largely overlaps with criteria established by the International Society of Geographical and Epidemiological Ophthalmology (ISGEO)[20]. Glaucoma was defined as: 1) characteristic or compatible glaucomatous visual field abnormality and/or evidence of characteristic or compatible glaucomatous optic disc damage in at least one eye after ophthalmologic exclusion of other possible causes; or 2) end-stage disease with visual acuity of ≤20/200 and a cup-to-disc ratio of 1.0. Glaucoma cases were further categorized as "definite" or "probable" based on the degree of correlation between optic disc and visual field changes **(Supplemental Table)**. Intraocular pressure was not considered in the definition of open-angle glaucoma.

Glaucoma diagnosis was initially determined for each eye by 2 fellowship-trained graders who reviewed participants' clinical history, examination findings, stereoscopic optic disc photographs and visual fields. Cases in which at least one grader diagnosed glaucoma were adjudicated by a third glaucoma fellowship-trained grader. When both initial graders diagnosed glaucoma, but the adjudicating grader did not, the case was then adjudicated by a senior glaucoma fellowship-trained grader who provided the final diagnosis for a given eye.

Open-angle glaucoma required an open angle on manual gonioscopy, defined as visible pigmented trabecular meshwork in at least 2 quadrants (≥180°). Primary angle closure disease, including primary angle closure, primary angle closure suspect, primary angle closure glaucoma, and suspected primary angle closure glaucoma in the Chinese American Eye Study is discussed in detail elsewhere.[15]

OAG diagnosis was assigned at the participant level for prevalence assessments, where OAG was present in 1 or both eyes. In 7 cases where angle closure glaucoma was diagnosed in one eye and OAG in the contralateral eye, the participant-level diagnosis was assigned as angle closure glaucoma rather than OAG due to six of seven eyes being pseudophakic in the OAG eye. For eye-level variables, data were obtained from the glaucomatous eye or the worse eye (based on mean deviation on VF testing) when both were glaucomatous, or from the worse eye when both were non-glaucomatous.

Statistical Analysis

Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC). Overall and sex-and age-stratified OAG prevalence estimates were calculated as the ratio of subjects with OAG to total study subjects in each category. 95% Wald confidence intervals (CIs) were constructed for each prevalence estimate. Variables significantly associated with OAG were identified using chi-square tests (for binary variables) and t-tests (for continuous variables), with two-sided tests at an alpha of 0.05. Multivariable logistic regression identified independent risk factors associated with OAG. For comparison with other studies, we obtained age- and sex-specific prevalence data from published reports and performed direct age standardization using the age and sex distribution of the Asian population in the 2010 US Census.[21] This standardization allows prevalence comparison between studies with different age and sex distributions.

Candidate risk factors for open angle glaucoma comprised demographic, clinical, and ocular characteristics. These included age, sex, diabetes mellitus type 2 (defined as

self-reported history or hemoglobin A1c $\geq$ 6.5%), history or presence of hypertension (defined as self-reported history or systolic blood pressure > 140 mmHg, or diastolic blood pressure >90 mmHg), systolic blood pressure, diastolic blood pressure, history of ever smoking, history of hypercholesterolemia, height, weight, body mass index category (underweight/normal = less than 25 kg/m^2, overweight=25.0-29.9 kg/m^2, obese= 30 or higher kg/m^2), family history of glaucoma (in any blood relative), cortical lens opacities, nuclear lens opacities, posterior subcapsular lens opacities, pseudophakia, IOP, spherical equivalent, axial length, central corneal thickness, anterior chamber depth, lens thickness, vertical cup/disc ratio, and visual field mean deviation. Variables univariately associated with OAG at the 0.15 significance level were entered into separate multivariable models designed to identify demographic, clinical or ocular risk factors, respectively, controlling for other variables in the same category. Variables retained in each of these models were then entered into a final multivariable logistic regression model in which variables having beta estimates significant at the α = .05 level were retained to yield a final model. 95% CIs were built around each beta using the Wald method. Due to prior literature on the interaction of AL and IOP in OAG,[22] this interaction was investigated in our dataset but was not found to be significant.

Results

Among the 5782 eligible adults, 4582 (79.2%) participated and completed an in-clinic eye examination. Compared to nonparticipants, participants were similar in age (mean age, 61.3$\pm$8.9 versus 69.1$\pm$13.3 years), less likely to be current smokers (0.6% versus

12.1%, P<0.001), and more likely to have 12 or more years of education (67.4% versus 57.9%; P<0.001). There were no differences in health insurance or vision coverage, income, percentage born outside the United States, or self-reported history of diabetes, high blood pressure, macular degeneration, or cataracts.

Among 4582 participants receiving complete in-clinic eye exams, 272 (5.9%) participants had missing or inconclusive glaucoma grades related to: 1) missing gonioscopy grades (*N* = 57; 1.2%); 2) missing visual fields and/or fundus photos (*N* = 129; 2.8%); or 3) inability by both clinician graders to establish or exclude glaucoma (*N* = 86; 1.9%). Excluded participants were significantly older, had a higher pattern standard deviation, and a more negative mean deviation. No significant differences existed in sex distribution, mean IOP, or CCT.

The final analysis included 4310 participants with complete data. The mean age of participants was 61.4 years (±8.9 years), and 36.7% (1583) were males. Seventeen percent of participants had diabetes mellitus, and 41.9% had hypertension. The mean AL was 23.9 mm (±1.4 mm). Seven percent of all eyes included in the study were pseudophakic. In phakic eyes, the mean spherical equivalent (SE) was -0.54 D (±2.98 D), with a SE of -0.53 D (± 3.01 D) for females and -0.58 D (± 2.92 D) for males. The mean central corneal thickness was 559 ± 4 microns. The mean IOP was 15.3± 3.29 mm Hg. 12.3% of the population completed grade school or less, 48.4% completed some or all of high school, 33.1% completed some or all college, and 6.2% completed some or all post-graduate studies. Education level had no association with POAG status (p=0.146) but had a strong positive association with AL (p<0.001). Among those diagnosed with open angle glaucoma (n=207), 91.3% had at least 1 visual field and

99.5% had a gradable disc photography (**Table 1**). Ninety five persons (2.2%) had ocular hypertension (OHTN), defined as IOP greater than 21 mmHg, open angles ≥ 180°, and absence of glaucoma (as defined in the Los Angeles Latino Eye Study[17]) . The prevalence of OHTN was 2.1% (43/2092) for ages 50-59; 3.1% (38/1484) for ages 60-69; 2.0% (10/504) for ages 70-79; and 1.7% (4/230) for ages 80 and over. Females and males had similar OHTN (2.20% vs. 2.21%). If the definition of OHTN includes those with any type of angle (IOP greater than 21 mmHg and absence of glaucoma, with any gonioscopy grading), the overall prevalence was 3.2%, ranging from 2.7% among those in their 50s, 3.8% among those in their 60s, 4.1% among those in their 70s, to 2.2% among those 80 and over, with no significant overall difference between females and males. If OHTN is defined as an IOP ≥ 24mmHg, open angles ≥ 180°, and absence of glaucoma (per the Ocular Hypertension Treatment Study[23]), the prevalence was 0.5% in females, 1.1% in males, and 0.7% overall. The overall prevalence of OAG was 4.8% (207/4310) in Chinese Americans ages 50 years and older. Age-specific prevalence ranged from ranged from 2.8% (58/2092) among those aged 50-59 years to 14.8% (34/230) among those aged 80 years and older (**Table 2**). The overall prevalence of OAG was lower among women [3.85% (105/2727)], than among men [6.4% (102/1583), P=.0002]. The lower prevalence among females was seen mostly in younger participants. Among those aged 80 years and older, the prevalence among women and men was 16.7% (20/120) and 12.7% (14/110) respectively (P=0.4593).

Participants with OAG (mean age, 66 years) were significantly older than those without OAG (61 years). Participants with OAG had a mean IOP of 17.0 mmHg with 13.5% having an IOP >21 mmHg. Compared to those without OAG, participants with

OAG had significantly longer AL (24.58mm vs 23.83mm), more negative mean deviation (-8.16 vs. -2.35 dB), greater pattern standard deviation (6.44 vs. 2.81 dB) and larger cup-disc ratios (0.7 vs. 0.4) (**Table 3**).

A notable finding was that 68.5% of CHES participants with OAG had previously undiagnosed disease. Of the 31.5% with OAG and prior glaucoma history and available treatment information available, 94% were treated with eye drops, 15% had prior laser trabeculoplasty, 13% had glaucoma surgery, 20% had laser peripheral iridotomy, and 43% had prior cataract surgery. Among the 122 participants who were previously undiagnosed and untreated, 88.5% (108) had an untreated IOP of 21 mmHg or less. Mean IOP in this group was 16.8 $\pm$ 3.24 mm Hg (range 10-24.7 mm Hg) (**Table 4**).

Independent risk factors for OAG in the final multivariable model, controlling for sex, included: older age (odds ratio [95% confidence interval] = 1.06 [1.05,1.08], per year); higher IOP (1.12 [1.08,1.17], per mm Hg); longer axial length (1.36 [1.25,1.47], per mm); family history of glaucoma (1.88 [1.19,2.97]); and diabetes mellitus (1.49 [1.05,2.11]) (**Table 5**).

Age standardized comparisons using 2010 US Census data for the Asian population demonstrated that the prevalence of OAG in Chinese Americans was higher than previously studied Asia-based Chinese populations [11-14], non-Hispanic White populations, and Latinos in Proyecto VER (who had higher Native American genetic admixture than Los Angeles Latinos)).[17,18,19, 24] The prevalence was comparable to Japanese population in the Kumejima Eye Study [25] and Indians in the Chennai Glaucoma Study,[26] lower than Los Angeles Latinos in LALES [17] and African populations

in Barbados Eye Study[27] but similar to African Americans in the Baltimore Eye Survey[28](**Table 6**).

Discussion

The overall prevalence of OAG among Chinese Americans was 4.8%. Independent risk factors for OAG in Chinese Americans included longer AL, older age, higher IOP, family history of glaucoma, and diabetes mellitus.

When compared to other populations, Chinese Americans demonstrated higher OAG prevalence than previously studied Asia-based Chinese[11-14] and Caucasian populations.[18,19] (**Table 6**). Several factors may explain this finding.

First, disease definitions vary across studies. Several studies used the International Society of Geographical and Epidemiological Ophthalmology (ISGEO)[20] glaucoma criteria, which required specific cup/disc ratio thresholds (vertical cup/disc ratio in the ≥97.5 percentile) with corresponding visual field defects; or a vertical cup/disc ratio of ≥ 99.5 percentile if visual field was not available or an intraocular pressure ≥ 99.5% and vision of less than 3/60 if both vertical cup/disc ratio and visual field were not available. [20] Our definition based on conventions from the Beaver Dam Eye Study[18] and the Melbourne Visual Impairment Project[19], allowed glaucoma diagnosis based on expert consensus of characteristic optic nerve changes with or without visual field abnormality.. A similar consensus approach has been used in the Ocular Hypertension Treatment Study and other clinical trials. This approach addresses inherent limitations of 24-2 visual field testing, which may fail to detect early glaucomatous optic nerve damage,[29] as structural optic nerve damage can precede

detectable visual field loss. In addition, a specific cup disc ratio (a criteria used in the ISGEO definition) may not define whether glaucomatous optic nerve damage has occurred or not. Even excluding “pre-perimetric” glaucoma cases, our prevalence remained 3.76% - still higher than any other previously studied Chinese population from Asia.

Second, risk factor burden may differ across Chinese populations. We investigated whether these differences could be related to axial length differences. The risk of having OAG was 36% higher for every 1mm longer axial length. Prior studies from China have reported longer AL among those living in urban areas and also among the younger populations.[30,31] In fact, there is now a well-established epidemic of myopia and high myopia, due to increases in near work and less outdoor time among children especially in East and Southeast Asia but also across several other populations worldwide.[32,33] The mean AL among CHES participants was 23.9 ±1.4 mm, which was among the longest compared to most other studies of Chinese descent individuals. In comparison, mean AL was 22.8± 0.9 mm in the Handan Eye Study,[14] 22.82 mm in the Yunnan Eye Study,[34] 23.25±1.14 mm in the Beijing Eye Study,[35]and 24.0 (±1.32) mm in the Singapore Chinese Eye Study.[36] Axial elongation and associated thinning of the lamina cribrosa may compromise biomechanical support for the retinal ganglion cell axons[37] and reduce structural support for the retinal ganglion cell microvasculature.[38]

Third, environmental differences may alter risk for OAG across Chinese populations. One example is air pollution, which is poorly studied but suspected to increase glaucoma risk.[39] Additional research is needed to investigate this and other potential environmental influences.

Age represented a major risk factor, with 79% higher risk per decade of aging. The OAG prevalence in CHES in those aged 80 years and older was five times higher than prevalence in those aged 50-59 years. Age-related changes including increased scleral thinning and stiffness and reduced vascular health contribute to age-related glaucoma risk.[37,40] With rapid global population aging, glaucoma cases are projected to reach 111.8 million by 2040, disproportionately affecting Asia and Africa.[1]

A prominent feature of our study was that 68.5% were previously undiagnosed with 88.5% having a screening IOP of 21 mmHg or less. This high proportion of undiagnosed glaucoma highlights the importance of improving screening strategies. The predominance of “normotensive” glaucoma emphasizes major limitations of IOP based screening. This finding is consistent with other Asia-based studies reporting high proportions of normal tension OAG: 92.3% in Japan, 84.6% in Singapore, 83.6% in northern China, 82% in south India, and 79.3% in southern China.[14,26,41-43] This contrasts with non-Asian populations showing lower proportions: 31.7% in U.S. Caucasians, 31.5% in Iceland, and 30% in Italy.[18,44-48] Mounting evidence suggests that vascular health, oxidative stress, and endothelial dysfunction interact with IOP and contribute to glaucoma pathogenesis.[41]

Despite most new cases having screening IOP $\leq$ 21 mmHg, higher IOP remained an independent risk factor. Each 1mm Hg higher IOP conferred 12% higher risk. This matches findings from the Ocular Hypertension Treatment Study showing 10% higher risk per mm Hg of IOP.[23] Elevated IOP causes progressive retinal ganglion cell axons damage at the lamina cribrosa, reduces retinal blood flow and increase cytokine expression.[49-51]

Interestingly, CCT was not an independent risk factor in our study, contrasting with other populations.[54] Similarly, the Beijing Eye Study found no CCT-glaucoma association in a mainland Chinese population.[13,53] Wang et al previously demonstrated that CCT explained a significant glaucoma risk among Black and Hispanic individuals, but not among Asians in a large multiethnic population.[54] They also reported that average CCT was 6 to 13 microns thicker among Chinese, Japanese, and Koreans compared to Southeast Asians, Filipinos, and Pacific Islanders. This highlights differences within Asian populations; therefore, our Chinese American findings may not generalize to other Asian groups.[56]

Family history of glaucoma (in any blood relative) conferred 88% higher OAG risk. Complex inheritance predominates in adult-onset OAG with many unknowns regarding glaucoma inheritance patterns.[55] Recent genome-wide association studies have identified POAG loci, and other efforts continue refining specific genetic influences.[55] Mars et al recently demonstrated that high polygenic risk scores and family history have equal but largely independent effects for glaucoma[56], suggesting substantial gaps remain in understanding genetic risk or environmental exposures common within families. Self-reported family history is subject to recall, selection, and survival bias and community under-diagnosis limitations.[57] A recent Nepalese study demonstrated that screening of first degree relatives of POAG patients identified remarkable numbers of previously undiagnosed glaucoma cases.[58] Future screening efforts targeting family members of OAG patients would likely represent a high yield approach for detecting undiagnosed glaucoma.

Diabetes mellitus conferred 49% higher OAG risk in CHES participants. Prior studies and meta-analyses supported this association.[59-61] Diabetes causes microvascular damage and vascular dysregulation of the retina and optic disc, increasing optic nerve susceptibility to glaucomatous damage.[62,63] The African American Eye Disease Study, which utilized optical coherence tomography angiography, recently demonstrated associations between diabetes duration and reduced peripapillary retinal vessel density among non-glaucomatous subjects.[64] Optical coherence tomography (OCT) studies showed reduced retinal nerve fiber layer (RNFL) and ganglion cell layer thickness associated with diabetes duration in non-glaucoma subjects.[65,66] This supports the concept that diabetes compromises the peripapillary neurovascular bundle before clinically detectable glaucoma onset.

Our findings suggest several important clinical considerations. The high prevalence of undiagnosed normal tension glaucoma emphasizes the need for improved screening strategies beyond IOP measurement alone. Targeting high-risk populations including family members of glaucoma patients and individuals with high myopia may enhance screening efficiency. The strong association between longer axial length and glaucoma risk suggests that myopia prevention strategies in childhood warrant investigation as potential glaucoma prevention approaches.

Several limitations of our study merit consideration. One limitation is that our study population may not fully represent the broader Chinese American community, as participants were more frequently female, more educated and less likely to smoke than non-participants. Second the definition of glaucoma lacks a universal “gold standard” and varies between experts, representing a common source of debate.[67] However, our

consensus approach using a glaucoma expert panel may represent the most robust definition currently available. Third longitudinal data are needed to validate identified risk factors and their relative contributions to OAG development in Chinese Americans.

Chinese Americans demonstrate a high prevalence of OAG (4.8%) approaching that of other racial minority populations in the United States. Independent risk factors including longer axial length, older age, higher IOP, family history of glaucoma and diabetes mellitus. The finding that over two thirds of OAG cases were previously undiagnosed, with approximately 88% having “normal” IOP, highlights substantial opportunities for improved early disease detection and underscores the need for enhanced education among patients and eye care providers. Future research investigating alternative prevention strategies and targeted screening approaches for high-risk individuals may help reduce the burden of preventable vision loss from OAG in this population.

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Chinese American Eye Study Data Monitoring and Oversight Committee: Alfred Sommer, MD, MHS (chair); Anne Coleman, MD, PhD; Dennis Han, MD; Craig Hanis, PhD; Louise Wideroff, PhD; and Terri Young, MD.

All persons provided permission to be acknowledged.

References

1. Tham YC, Li X, Wong TY, Quigley H, Aung T, Cheng C-Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology 2014;121(11):2081-90.
2. Heijl, A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, Early Manifest Glaucoma Trial. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120(1):1268-79.
3. Hoeffel, E., Rastogi, S., Kim, MO., Shahid, H. 2010 Census Briefs. Washington, DC: U.S. Census Bureau; 2012. The Asian population: 2010. 20. Pew Research Center. The Rise of Asian Americans. 2012. http://www.pewsocialtrends.org/files/2012/06/SDT-The-Rise-of-Asian-Americans-Full-Report.pdf.
4. Varma R, Torres M, Mckean-Cowdin R, Rong F, Hsu C, Jiang X. Prevalence and risk factors for refractive error in adult Chinese Americans: The Chinese American Eye Study. Am J Ophthalmol 2017:175:201-212.
5. Pan C-W, Klein BEK, Cotch MF, Shrager S, Klein R, Folsom A, Kronmal R, Shea SJ, Burke GL, Saw S-M, Wong TY. Racial variations in the prevalence of refractive errors in the United States: The Multi-Ethnic Study of Atherosclerosis. Am J Ophthalmol 2013;155(6):1129-1138.
6. Haarman AEG, Enthoven CA, Tiderman MWL, Tedja MS, Verhoeven VJM, Klaver CW. Complications of myopia: A review and meta-analysis. Invest Ophthalmol Vis Sci 2020;61(4):49.

7. Choudhury F, Meuer SM, Klein R, Wang D, Torres M, Jiang X, McKean-Cowdin R, Varma R. Prevalence and characteristics of myopic degeneration in an adult Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2018;187:34-42.
8. Ohno-Matsui K, Shimada N, Yasuzumi K, et al. Long-term development of significant visual field defects in highly myopic eyes. Am J Ophthalmol. 2011;152:256–265.e1.
9. Perdicchi A, Iester M, Scuderi G, Amodeo S, Medori EM, Recupero SM. Visual field damage and progression in glaucomatous myopic eyes. Eur J Ophthalmol. 2007;17:534– 537.
10. Lee YA, Shih YF, Lin LL, Huang JY, Wang TH. Association between high myopia and progression of visual field loss in primary open-angle glaucoma. J Formos Med Assoc. 2008;107:952–957.
11. Baskaran M, Foo RC, Cheng C-Y, Narayanaswamy AK, Zheng Y-F, Wu R, Saw S-M, Foster PJ, Wong T-Y, Aung T. The prevalence and types of glaucoma in an urban Chinese population: The Singapore Chinese Eye Study. JAMA Ophthalmol 2015;133(8):874-880.
12. Pan C-W. Zhao C-H. Yu M-B. Cun Q, Chen Q, Shen W, Li J, Xu J-G. Yuan Y. Zhong H. Prevalence, types and awareness of glaucoma in a multi-ethnic population in rural China: the Yunnan Minority Eye Study. Ophthalmic Physiol Opt 2016, 36: 664-670.
13. Wang YX, Xu L, Yang H, Jonas JB. Prevalence of glaucoma in north China: The Beijing Eye Study. Am J Ophthalmol 2010;150:917-924.

14. Liang YB, Friedman DS, Zhou Q, Yang X, Sun LP, Guo LX, Tao QS, Chang DS, Wang NL. Prevalence of primary open angle glaucoma in a rural adult Chinese population: The Handan Eye Study. Invest Ophthalmol Vis Sci 2011;52:8250-8257.
15. Xu BY, Richter GM, Burkemper BS, Wang D, Jiang X, Torres M, McKean-Cowdin R, Dhablania N, Varma R. Prevalence and risk factors of primary angle closure disease in an adult Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2025;274:32-41.
16. Varma R, Hsu C, Wang D, Torres M, Azen SP; Chinese American Eye Study Group. The Chinese American Eye Study: Design and methods. Ophthalmic Epidemiol 2013;20(6):335-47.
17. Varma R, Ying-Lai M, Francis BA, Nguyen BB-T, Deneen J, Wilson MR, Azen SP. Prevalence of open-angle glaucoma and ocular hypertension in Latinos. Ophthalmology 2004;111:1439-1448.
18. Klein BEK, Klein R, Sonsel WE, Franke T, Cantor LB, Martone J, Menage MJ. Prevalence of glaucoma: The Beaver Dam Eye Study. Ophthalmology 1992;99:1499-1504.
19. Wensor MD, McCarty CA, Stanislavsky YL, Livingston PM, Taylor HR. The prevalence of glaucoma in the Melbourne Visual Impairment Project. Ophthalmology 1998;105(4):733-9.
20. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002;86(2):238-242.

21. 2019 Population Estimates by Age, Sex, Race and Hispanic Origin. June 25, 2020. United States Census Bureau. https://www.census.gov/newsroom/press-kits/2020/population-estimates-detailed.html
22. Tham Y-C, Aung T, Fan Q, et al. Joint effects of intraocular pressure and myopia on risk of primary open-angle glaucoma: The Singapore epidemiology of eye diseases study. Sci Rep. 2016;6(1):1–7.
23. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Philip Miller J, Parrish RK, Roy Wilson M, Kass MA. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120(6):714-720.
24. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. Arch Ophthalmol 2001;119:1819-1826.
25. Yamamoto S, Sawaguchi S, Iwase A, Yamamoto T, Abe H, Tomita G, Tomidokoro A, Araie M. Primary open-angle glaucoma in a population associated with high prevalence of primary angle-closure glaucoma: The Kumejima Study. Ophthalmology 2014;121:1558-1565.
26. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai glaucoma study. Ophthalmology 2008;115(4):848-54.e1.
27. Leske MC, Connel AMS, Schachat AP, Hyman L. The Barbados Eye Study: Prevalence of open angle glaucoma. Arch Ophthalmol 1994;112:821-829.

28. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma: The Baltimore Eye Survey. JAMA 1991;266:369-374.
29. De Moraes CG, Hood DC, Thenappan A, Girkin CA, Medeiros FA, Weinreb RN, Zangwill LM, Liebmann JM. 24-2 visual fields miss central defects shown on 10-2 tests in glaucoma suspects, ocular hypertensives, and early glaucoma. Ophthalmology 2017;124(1):1449-1456.
30. Liang YB, Lin Z, Vasudevan B, Jhanji V, Young A, Gao TY, Rong SS, Wang NL, Ciuffreda KJ. Generational difference of refractive error in the baseline study of the Beijing myopia progression study. Br J Ophthalmol 2013;97(6):765-769.
31. Lin Z, Gao TY, Vasudevan B, Jhanji V, Ciuffreda KJ, Zhang P, Li L, Mao GY, Wang NL, Liang YB. Generational difference of refractive error and risk factors in the Handan offspring myopia study. Invest Ophthal Vis Sci 2014;55(9):5711-5717.
32. Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M, Rose KA. The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res 2018;62:134-149.
33. Williams KM, Bertelsen G, Cumberland P, Wolfram C, Verhoeven VJ, Anastasopoulos E, et al. Increasing Prevalence of Myopia in Europe and the Impact of Education. Ophthalmology. 2015 Jul;122(7):1489-97.
34. Wang Y, Cun Q, Li J, Shen W, Yang W-Y, Tao Y-J, Niu Z-Q, Zhang Y, Zhong H, Pan C-W. Prevalence, ethnic differences and risk factors of primary angle-

closure glaucoma in a multiethnic Chinese adult population: the Yunnan Minority Eye Study. Br J Ophthalmol 2021. Online ahead of print.

35. Gui Y, Wang YX, Zheng ZY, Yang H, Xu L, Jonas JB, Beijing Eye Study Group. Ocular axial length and its associations in Chinese: the Beijing Eye Study. PLoS One 2012;7(8):e43172.
36. Sng CC, Foo L-L, Cheng, C-Y, Allen JC, He M, Krishnaswamy G, Nongpiur ME, Friedman DS, Wong TY, Aung T. Determinants of anterior chamber depth: The Singapore Chinese Eye Study. Ophthalmology 2012;119:1143-1150.
37. Boote C, Sigal IA, Grytz R, Hua Y, Nguyen TD, Girard MJA. Scleral structure and biomechanics. Progress in Retinal and Eye Research 2020;74: 10073.
38. Juliano J, Burkemper B, Lee J, Nelson A, LeTran V, Chu Z, Zhou G, Jiang X, Wang RK, Varma R, Richter GM. Longer axial length potentiates relationship of intraocular pressure and peripapillary vessel density in glaucoma patients. Invest Ophthalmol Vis Sci. 2021;62(9):37.
39. Grant A, Leung G, Freeman EE. Ambient air pollution and age-related eye disease: a systematic review and meta-analysis. Invest Ophthalmol Vis Sci. 2022;63(9):17
40. Grzybowski A, Och M, Kanclerz P, Leffler C, Gustavo De Moraes C. Primary open angle glaucoma and vascular risk factors: A review of population based studies from 1990 to 2019. J Clin Med 2020;9:761.
41. Leung DYL, Tham CC. Normal-tension glaucoma: current concepts and approaches- a review. Clinical & Experimental Ophthalmology. 2022;50:247-259.

42. Shen SY, Wong TY, Foster PJ, et al. The prevalence and types of glaucoma in Malay people: the Singapore Malay eye study. Invest Ophthalmol Vis Sci. 2008;48(9):3846-3851.
43. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: the Liwan eye study. Am J Ophthalmol 2011;152(3):454-62 e1.
44. Rotchford AP, Johnson GJ. Glaucoma in Zulus: a population based cross-sectional survey in a rural district in South Africa. Arch Ophthalmol. 2002;120(4):471-478.
45. Pakravan M, Yazdani S, Javadi MA, et al. A population-based survey of the prevalence and types of glaucoma in Central Iran: the Yazd eye study. Ophthalmology. 2013;120(10):1977-1984.
46. Dielemans I, Vingerling JR, Wolfs RC, Hofman A, Grobbee DE, de Jong PT. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study Ophthalmology. 1994;101(11):1851-1855.
47. Jonasson F, Damji KF, Arnarsson A, et al. Prevalence of open-angle glaucoma in Iceland: Reykjavik eye study. Eye (Lond). 2003;17(6):747-753.
48. Bonomi L, Marchini G, Marraffa M, et al. Prevalence of glaucoma and intraocular pressure distribution in a defined population. The Egna-Neumarkt Study Ophthalmology. 1998;105(2): 209-215).
49. Morrison JC, Johnson EC, Cepurna W, Jia L. Understanding mechanisms of pressure-induced optic nerve damage. Prog Retin Eye Res 2005;24:217– 40.

50. Burgoyne CF, Crawford Downs J, Bellezza AJ, Francis Suh JK, Hart RT. The optic nerve head as a biomechanical structure: A new paradigm for understanding the role of IOP related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. Prog Retin Eye Res. 2005;24(1):39–73.
51. Collaborative Normal Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normaltension glaucoma. Am J Ophthalmol. 1998;126:498–505.
52. Sng CCA, Ang M, Barton K. Central corneal thickness in glaucoma. Curr Opin Ophthalmol 2017;28:120-126.
53. Toh T, Liew SH, MacKinnon JR, et al. Central corneal thickness is highly heritable: the twin eye studies. Invest Ophthalmol Vis Sci 2005; 46:3718– 3722.
54. Wang SY, Melles R, Lin SC. The impact of central corneal thickness on the risk for glaucoma in a large multiethnic population. J Glaucoma 2014;23(9):606-612.
55. Wiggs JL, Pasquale LR. Genetics of glaucoma. Hum Mol Genet 2017;26(R1):R21-R27.
56. Mars N, Lindbohm JV, Parolo PB, Widen E, Kaprio J, Palotie A, FinnGen, Ripatti S. Systematic comparison of family history and polygenic risk across 24 common diseases. Am J Hum Genetics 2022;109(12):2152-2162.
57. Mitchell P, Rochtchina E, Lee AJ, Wang JJ. Bias in self-reported family history and relationship to glaucoma: The Blue Mountains Eye Study. Ophthalmic Epidemiol 2002;9(5):333-345.
58. Paudyal I, Yadav R, Parajuli A, Singh K, Josh P, Thapa S. Screening of Accompanying First Degree Relatives of Patients with Primary Open Angle Glaucoma. Nepal J Ophthalmol 2022;14(27):4-9.

59. Zhou M, Wang W, Huang W, Zhang X. Diabetes mellitus as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. PLoS One. 2014;9(8):e102972.
60. Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis: Ophthalmology 2015;122(1):72-78.
61. Kim S-W, Kang G-W. Diabetes mellitus as a risk factor for glaucoma outcome in Korea. Acta Ophthalmol 2017;95(7):e662-e664.
62. Hayreh SS. Pathogenesis of optic nerve damage and visual field deficits in glaucoma. Doc Ophthalmol Proc Ser 1980;22: 89–110.
63. Nakamura M, Kanamori A, Negi A. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. Ophthalmologica 2005;219:1–10.
64. Chang R, Nelson AJ, LeTran V, Vu B, Burkemper B, Chu Z et al. Systemic determinants of peripapillary vessel density in healthy African Americans: the African American Eye Disease Study. Am J Ophthalmol 2019;207:240-247.
65. van Dijk HW, Verbraak FD, Kok PH, et al. Decreased retinal ganglion cell layer thickness in patients with type 1 diabetes. Invest Ophthalmol Vis Sci 2010;51(7):3660–5.
66. Shi R, Guo Z, Wang F, Li R, Zhao L, Lin R. Alterations in retinal nerve fiber layer thickness in early stages of diabetic retinopathy and potential risk factors. Curr Eye Res 2018;43(2):244–53.
67. Quigley HA. 21st century glaucoma care. Eye (Lond) 2019;33(2):254-260.

Figure Caption

Figure 1. Age-Specific Prevalence of Primary Open Angle Glaucoma (POAG) in the Chinese American Eye Study (CHES), Los Angeles Latino Eye Study (LALES), and the Baltimore Eye Study (BES).

Prevalence and Risk Factors of Open Angle Glaucoma in an Adult Chinese American Population: The Chinese American Eye Study

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Key Words: open angle glaucoma, prevalence Chinese Americans, ocular epidemiology

Introduction

Open angle glaucoma (OAG) is a progressive optic neuropathy leading to irreversible vision loss and represents ~~. It is~~ a leading cause of blindness worldwide.[1] The mainstay of glaucoma treatment is intraocular pressure (IOP) reduction, which ~~is~~ effectively~~e in~~ slow~~sing~~ progressive glaucomatous optic nerve damage and prevent~~sing~~ blindness.[2] Early in its course, OAG remains asymptomatic and can progress without patients detecting vision changes. Therefore, identifying effective approaches for early OAG detection is critical to prevent avoidable vision loss and blindness.~~the course of OAG, it is asymptomatic and can progress without patients noticing any change in their vision; thus, identifying approaches to detect early OAG are important to prevent avoidable vision loss and blindness.~~ Understanding the ~~In particular, understanding~~disease ~~the burden of OAG~~ in specific populations and associated risk factors can guide targeted detection and management strategies. ~~for disease can guide efforts in its detection and management.~~

Chinese Americans represent part of the fastest growing minority population in the United States over the past decade~~are part of the fastest growing minority population in the United States (US) in the last decade~~.[3] Due to the high prevalence of myopia in Chinese Americans[4,5], this population may experience ~~ey may be expected to experience~~ a disproportionately higher burden of myopia-related diseases, including ~~such as~~ myopic macular degeneration, retinal detachment, cataract, and open angle glaucoma.[6,7] A recent meta-analysis of 14 population-based studies demonstrated a significant association between even mild ~~low levels of~~ myopia (> -3 D) and OAG, with~~and~~ this association strengthening~~was even stronger~~ for moderate to high myopia (≤

-3 D).[6] Some studies have also demonstrated an association between progressive glaucomatous visual field loss and myopia.[8-10] However, additional~~more~~ research is needed to understand the burden and characteristics~~nature~~ of glaucoma in ~~myopic~~ populations with high ~~prevalence of~~ myopia prevalence such as Chinese Americans.

While ~~there are~~ several epidemiological studies have examined~~on~~ OAG in~~from~~ urban and rural Asia-based populations of Chinese descent[11-14], no comparable ~~such~~ data exist for~~on~~ persons of Chinese descent residing in the US ~~exist~~. The Chinese American Eye Study (CHES) represents the~~is the~~ first such investigation ~~study~~ conducted in the US. We recently reported on the prevalence of primary angle closure suspects, primary angle closure, and primary angle closure glaucoma (8.1%, 3.1%, 1.1%, respectively), in this population.[15] The current~~is~~ study ~~addresses the paucity of data and~~ provides ~~us~~ the opportunity to determine ~~the prevalence of~~ OAG prevalence and identify associated ~~its~~ risk factors in this specific US population.

Methods:

Study Population and Data Collection

The study design of CHES has been detailed elsewhere~~Details of the study design of CHES have been reported elsewhere~~.[16~~5~~] Briefly, self-identified Chinese Americans, aged~~s~~ 50 years and older and residing ~~living~~ in 10 census tracts in Monterey Park, California, were invited to participate. Of the ~~79.2% (4582/~~5782~~)~~ ~~of~~ eligible Chinese American adults, 4582 (79.2%) underwent interview and comprehensive eye examination from 2010-2013. The institutional review boards from the University of Southern California, Los Angeles, and the University of Illinois at Chicago approved the

study protocol. All patients provided informed consent, and the study adhered to the tenets of the Declaration of Helsinki.

A detailed in-home interview obtained demographic characteristics and ocular and medical histories. A complete eEye examination was performed at a local eye examination center with examination by a comprehensive ophthalmologist. Visual acuity was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts and the Lea symbol charts for illiterate participants. Lensometry verifiedwas used to verify the participant's eyeglass prescriptions. Automated refraction with a Humphrey Automatic Refractor (Carl Zeiss Meditec, Dublin, CA) was performed if the presenting visual acuity was not 20/20 in either eye. Subjective refraction was performed if the participants achievedread less than 20/20 vision on the automated refractionor. IOP was measured twice using Goldman applanation tonometry (Haag-Streit, Mason, OH) and averaged for analyses. Visual field evaluation utilized theused Swedish Interactive Threshold Algorithm (SITA) Standard C24-2 test (Carl Zeiss Humphrey Field Analyzer II 750). Slitlamp examination was performed and included mManual gonioscopy, was performed by a trained ophthalmologist (D.W.), masked to other exam findings, under standardized dark conditions (<1 lux illumination) at a slit lamp (Model BM900, Haag-Streit, Bern, Switzerland) using a four-mirror gonioprism (Ocular Instruments, Bellevue, WA, USA). A 1x1mm slit beam was used to avoid having light fall on the pupil. Each quadrant of the angle was evaluated, and the presence of the pigmented trabecular meshwork and the presence and circumferential extent of peripheral anterior synechiae were recorded. In addition to documenting a dilated fundus exam, sStereoscopic disc photography was performed using an optic nerve camera (Nidek 3DX, Nidek Inc.,

Fremont, CA). Three measurements were obtained using an A-scan ultrasonographyic device (4000B A-Scan/Pachymeter; DGH Technology, Exton, PA) for axial length (AL), anterior chamber depth (ACD), central corneal thickness (CCT), and lens thickness (LT). Vitreous chamber depth was calculated by subtracting CCT, ACD, and LT from AL.

Glaucoma Diagnosis

Glaucoma was defined based on the presence of characteristic optic nerve head and/or visual field changes, which was established previously for the Los Angeles Latino Eye Study (LALES)[16], and consistent with other major epidemiologicaly studies such as the Beaver Dam Eye Study and Melbourne Vision Impairment Study[18,19,17,18]. The definitionand largely overlaps with criteriadefinitions established by the International Society of Geographical and Epidemiological Ophthalmology (ISGEO)[20,19]. Briefly, Gglaucoma was defined as: 1) characteristic or compatible glaucomatous visual field abnormality and/or evidence of characteristic or compatible glaucomatous optic disc damage in at least one eye after ophthalmologic exclusion of other possible causes; or 2) end-stage disease with visual acuity of ≤20/200 and a cup-to-disc ratio of 1.0. Glaucoma cases were further categorized as “definite” or “probable” based on the degree of correlation between optic disc and visual field changes **(Supplemental Table)**. Intraocular pressure was not considered in the definition of open-angle glaucoma.

Glaucoma diagnosis was initiallyfirst determined for each eye by 2 fellowship-trained graders (G.R., Y.P., S.B., A.R.) who reviewed each participants''s clinical

history, ~~clinical~~ examination findings, stereoscopic optic disc photographs and visual fields. C~~The c~~ases in which at least one grader diagnosed glaucoma were adjudicated by a third glaucoma fellowship-trained grader ~~(B.X.)~~. When~~In the cases where~~ both initial graders diagnosed glaucoma, but the adjudicating grader did not, the case was then adjudicated by a senior glaucoma fellowship-trained grader ~~(R.V.)~~ who provided the final diagnosis for a given eye.

Open-angle glaucoma required ~~the presence of~~ an open angle on manual gonioscopy, defined as visible pigmented trabecular meshwork in at least 2 quadrants (≥180°). Primary angle closure disease, including primary angle closure, primary angle closure suspect, primary angle closure glaucoma, and suspected primary angle closure glaucoma in the Chinese American Eye Study is discussed in detail elsewhere.[15~~20~~]

OAG diagnosis was assigned at the~~on a~~ participant level for prevalence assessments, ~~-~~where OAG was present in 1 or both eyes. In ~~the~~ 7 cases where angle closure glaucoma ~~(ACG)~~ was diagnosed in one~~1~~ eye and OAG ~~was diagnosed~~ in the contralateral~~other~~ eye, the participant-level diagnosis was assigned as angle closure glaucoma rather than OAG due to six of seven eyes being pseudophakic in the OAG eye. ~~nment was ACG rather than OAG due to 6 of the 7 eyes being pseudophakic in the OAG eye.~~ For eye-level variables, data were obtained from~~as taken from~~ the glaucomatous eye or the worse eye (based on mean deviation on VF testing) when both were glaucomatous, or from the worse eye when both were non-glaucomatous.

Statistical Analysis

Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC). Overall and sex-and age-stratified OAG prevalence estimates were calculated as the ratio of subjects with OAG ~~ in the category of interest~~ to ~~the~~ total ~~number of~~ study subjects in each~~that~~ category. 95% Wald confidence intervals (CIs) were constructed for ~~each of~~ each ~~these population~~ prevalence ~~point~~ estimate~~s~~. Variables significantly associated with OAG ~~univariately~~ were identified using ~~with~~ chi-square tests (for binary variables) and t-tests (for continuous variables), with~~using~~ two-sided tests at~~with~~ an alpha of 0.05. Multivariable logistic regression identified independent risk factors associated with OAG. For comparison with other studies, we obtained age- and sex-specific prevalence data from published reports and performed direct age standardization using the age and sex distribution of the Asian population in the 2010 US Census.~~To compare prevalence to other studies, we obtained age- and sex- specific prevalence reported by those studies. We also performed direct age standardization of the overall and sex-specific crude sample OAG prevalence using the age and sex distribution of the Asian population in the 2010 US Census.~~[2~~11~~] This ~~direct age~~ standardization allows ~~for comparison of~~ prevalence comparison between ~~different~~ studies with different~~where the~~ age and sex distributions. ~~of the population are quite different.~~

Candidate risk factors for open angle glaucoma comprised demographic, clinical, and ocular characteristics. These included age, sex, diabetes mellitus type 2 (defined as self-reported history or hemoglobin A1c $\geq$ 6.5%), history or presence of hypertension (defined as self-reported history or systolic blood pressure > 140 mmHg, or diastolic blood pressure >90 mmHg), systolic blood pressure, diastolic blood pressure, history of

ever smoking, history of hypercholesterolemia, height, weight, body mass index category (underweight/normal = less than 25 kg/m^2, overweight=25.0-29.9 kg/m^2, obese= 30 or higher kg/m^2), family history of glaucoma (in any blood relative), cortical lens opacities, nuclear lens opacities, posterior subcapsular lens opacities, pseudophakia, IOP, spherical equivalent, axial length~~AL~~, central corneal thickness, anterior chamber depth, lens thickness, vertical cup/disc ratio, and visual field mean deviation. Variables univariately associated with OAG at the 0.15 significance level were entered into separate multivariable models designed to identify demographic, clinical or ocular risk factors, respectively, controlling for other variables in the same category. Variables retained in each of these models were then entered into a final multivariable logistic regression model in which variables having beta estimates significant at the α = .05 level were retained to yield a final model. 95% CIs were built around each beta using the Wald method. Due to prior literature on the interaction of AL and IOP in OAG,[22~~22~~] this interaction was investigated in our dataset but was not found to be significant.

Results

Among the 5782 eligible adults, 4582 (79.2%) participated ~~in the study~~ and completed an in-clinic eye examination. Compared to nonparticipants, participants were similar in age (mean age, 61.3±8.9 versus 69.1±13.3~~3~~ years), less likely to be current smokers (0.6% versus 12.1%, P<0.001), and more likely to have 12 or more years of education (67.4% versus 57.9%; P<0.001). There were no differences in health insurance or vision

coverage, income, percentage born outside the United States, or self-reported history of diabetes, high blood pressure, macular degeneration, or cataracts.

Among ~~the~~ 4582 participants ~~who~~ receiv ing ~~ed~~ complete in-clinic eye exams, 272 (5.9%) participants had missing or inconclusive glaucoma grades related to: 1) missing gonioscopy grades (*N* = 57; 1.2%); 2) missing visual fields and/or fundus photos (*N* = 129; 2.8%); or 3) inability by both clinician graders to establish or exclude ~~make or rule out the diagnosis of~~ glaucoma ~~in both eyes based on available clinical data~~ (*N* = 86; 1.9%). E~~Those e~~xcluded participants were significantly older, had a higher pattern standard deviation~~PSD~~, and a more negative mean deviation. N~~There were n~~o significant differences existed~~between-group differences~~ in sex distribution, mean IOP, or CCT.

The final analysis included~~re were~~ 4310 participants with complete data ~~who were included in the analysis~~. The mean age of participants was 61.4 years (±8.9 years), and 36.7% (1583) were males. Seventeen percent of participants had diabetes mellitus, and 41.9% had hypertension. The mean AL was 23.9 mm (±1.4 mm). Seven percent of all eyes included in the study were pseudophakic. In phakic eyes, the mean spherical equivalent (SE) was -0.54 D (±2.98 D), with a SE of -0.53 D (± 3.01 D) for females and -0.58 D (± 2.92 D) for males. The mean central corneal thickness was 559 ± 4 microns. The mean IOP was 15.3± 3.29 mm Hg. 12.3% of the population completed grade school or less, 48.4% completed some or all of high school, 33.1% completed some or all college, and 6.2% completed some or all post-graduate studies. Education level had no association with POAG status (p=0.146) but had a strong positive association with AL (p<0.001). Among those diagnosed with open angle

glaucoma (n=207), 91.3% had at least 1 visual field and 99.5% had a gradable disc photography (**Table 1**). Ninety five persons (2.2%) ~~(95)~~ had ocular hypertension (OHTN), ~~which was~~ defined as IOP greater than 21 mmHg, open angles ≥ 180°, and absence of glaucoma (as defined in the Los Angeles Latino Eye Study[17]) . The prevalence of OHTN was 2.1% (43/2092) for ages 50-59; 3.1% (38/1484) for ages 60-69; 2.0% (10/504) for ages 70-79; and 1.7% (4/230) for ages 80 and over. Females and males had similar OHTN (2.20% vs. 2.21%). If the definition of OHTN includes those with any type of angle (IOP greater than 21 mmHg and absence of glaucoma, with any gonioscopy grading), the overall prevalence was 3.2%, ranging from 2.7% among those in their 50s, 3.8% among those in their 60s, 4.1% among those in their 70s, to 2.2% among those 80 and over, with no significant overall difference between females and males. If ~~the definition of OHTN of~~ OHTN is defined as an ~~nstead matches the Ocular Hypertension Treatment Study (~~IOP ≥ 24mmHg, ~~open angles ≥ 180°, and absence of glaucoma~~ (per the Ocular Hypertension Treatment Study[23]), the prevalence was 0.5% in females, 1.1% in males, and 0.7% overall. ~~**Table 2** shows the age- and sex- specific distribution of OAG prevalence in Chinese Americans.~~ The overall prevalence of OAG was 4.8% (207/4310) in Chinese Americans ages 50 years and older. Age-specific prevalence ranged from ~~Prevalence of OAG~~ ranged from 2.8% (58/2092) among those aged 50-59 years to 14.8% (34/230) among those aged 80 years and older (**Table 2**). The overall prevalence of OAG was lower among women [3.85% (105/2727)~~,~~], than among men [6.4% (102/1583), P=.0002]. The lower prevalence among females was seen mostly in

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younger participants. Among those aged 80 years and older, the prevalence among women and men was 16.7% (20/120) and 12.7% (14/110) respectively (P=0.4593).

Participants ~~**Table 3** shows the clinical characteristics of the CHES participants with OAG. Overall, participants~~ with OAG (mean age, 66 years) were significantly older than those~~participants~~ without OAG (61 years). Participants with OAG had a mean IOP of 17.0 mmHg with 13.5% having an IOP >21 mmHg. Compared to those without OAG, participants with OAG had significantly longer AL (24.58mm vs 23.83mm), more negative mean deviation (-8.16 vs. -2.35 dB), greater pattern standard deviation (6.44 vs. 2.81 dB) and larger cup-disc ratios (0.7~~1~~ vs. 0.4~~0~~) (**Table 3**).

A notable finding was~~**Table 4** shows~~ that 68.5% of CHES participants with OAG had previously undiagnosed disease~~OAG~~. Of the 31.5%~~ of CHES participants~~ with OAG and~~ who had~~ prior glaucoma history and available~~with~~ treatment information available, 94% were treated with eye drops, 15% had prior laser trabeculoplasty, 13% had glaucoma surgery, 20% had laser peripheral iridotomy, and 43% had prior cataract surgery. Among ~~Furthermore, of~~ the 122 participants who were previously undiagnosed and untreated, 88.5% (108) had an untreated IOP of 21 mmHg or less. ~~Among these 122, the~~ M~~m~~ean IOP in this group was 16.8 ± 3.24 mm Hg ~~(, with a~~ range ~~of~~ 10~~ - to~~ 24.7 mm Hg) (**Table 4**).

~~**Table 5** shows the age-adjusted univariable odds ratios for candidate variables associated with OAG, as well as independent risk factors for OAG based on the final multivariable logistic regression model. I~~The ~~i~~ndependent risk factors for OAG in the final multivariable model, controlling for sex, included: ~~were~~ older age (odds ratio [95% confidence interval] = 1.06 [1.05,1.08], per year); higher IOP (1.12 [1.08,1.17], per mm

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Hg); longer axial length (1.36 [1.25,1.47], per mm); family history of glaucoma (1.88 [1.19,2.97]); and diabetes mellitus (1.49 [1.05,2.11]) (**Table 5**).

~~**Table 6** compares the age-specific and overall, OAG prevalence, age standardized based on the 2010 US Census data for the Asian population.[21]~~ Age standardized comparisons using 2010 US Census data for the Asian population demonstrated that the~~ization allows different study populations to be compared despite differences in the age profiles between studies. However, differing definitions of glaucomatous optic nerve damage may not allow for a valid comparison. **Figure 1** demonstrates that the~~ prevalence of OAG in Chinese Americans was higher than previously studied Asia-based Chinese populations[11-14], ~~and~~ non-Hispanic White populations, and Latinos in Proyecto VER (who had higher Native American genetic admixture than Los Angeles Latinos)).[~~1~~17,18,19, 24] The prevalence was comparable to Japanese population in the Kumejima Eye Study [2~~5~~4] and Indians in the Chennai Glaucoma Study,[2~~6~~5] lower than Los Angeles Latinos in LALES [1~~7~~6] and African populations in Barbados Eye Study[2~~7~~6] but similar to African Americans in the Baltimore Eye Survey.[2~~8~~7](**Table 6**)~~is comparable to that in African Americans in Baltimore, lower than the prevalence of OAG in Latinos in Los Angeles, and higher than white Americans in Baltimore.~~

Discussion

The overall prevalence of OAG among Chinese Americans was 4.8%. Independent risk factors for OAG in Chinese Americans included longer AL, older age, higher IOP, family history of glaucoma, and ~~the presence of~~ diabetes mellitus.

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When compared to other populations, the prevalence of OAG among Chinese Americans demonstrated higher OAG prevalence than previously studied was higher than among previously studied Asia-based Chinese[11-14] and, Caucasian populations,[18,19], and Latinos in Proyecto VER[23] (who had higher Native American genetic admixture than Los Angeles Latinos[17]). While Chinese Americans had similar overall prevalence to Japanese in the Kumejima Eye Study[24] and Indians in the Chennai Glaucoma Study[25], the prevalence of OAG among Chinese Americans was not quite as high as that in the Los Angeles Latino Eye Study (LALES)[17] or African descent participants in the Barbados Eye Study[26] which had identical study methodology and glaucoma definitions to CHES, but similar to African Americans in the Baltimore Eye Study[27] (**Table 6**).

Several factors may explain this finding. Potential explanations for Chinese Americans having a higher OAG prevalence than Asia-based Chinese could be related to differences in study design and methodology specifically disease definitions, differences in the risk factor burden, or unknown environmental exposures.

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First, it is important to note that disease definitions vary across studies. of glaucoma have had some differences across studies. Several studies used the International Society of Geographical and Epidemiological Ophthalmology (ISGEO)[20,25] glaucoma criteria definition, as noted in **Table 6**, which required specificvertical cup/disc ratio thresholds (vertical cup/disc ratio in the ≥97.5 percentile) with a corresponding visual field defects; or in their main category 1 diagnosis, a vertical cup/disc ratio of ≥ 99.5 percentile if visual field was not available orin their category 2 diagnosis, and an

intraocular pressure ≥ 99.5% and vision of less than 3/60 if both vertical cup/disc ratio and visual field were not available. ~~. The ISGEO definition also required both an abnormal visual field combined with glaucomatous optic nerve damage in all glaucoma cases.~~ [12][09] Our ~~The~~ definition based on conventions from ~~of glaucoma in CHES, which was based on conventions established by~~ the Beaver Dam Eye Study[18][7] and the Melbourne Visual Impairment Project[19][8], allowed ~~for a~~ glaucoma diagnosis based on expert consensus of characteristic optic nerve changes with or without visual field abnormality. ~~if there was a consensus among the glaucoma expert panel based on characteristic glaucomatous optic nerve changes or glaucomatous retinal nerve fiber layer defects with or without evidence of VF abnormality~~. A similar consensus approach has been used in the Ocular Hypertension Treatment Study and other clinical trials. This approach addresses inherent limitations of 24-2 visual field testing, which may fail to detect early glaucomatous optic nerve damage ~~Our definition addresses the inherent limitations in using 24-2 visual field data as the gold standard, which may fail to detect early glaucomatous optic nerve damage~~,[2][98] as given that structural optic nerve damage can precede ~~n occur before~~ detectable visual field loss. In addition, a specific cup disc ratio (a criteria used in the ISGEO definition) may not define whether glaucomatous optic nerve damage has occurred or not. Even excluding ~~In our study, if we exclude the cases of~~ "pre-perimetric" glaucoma cases, our prevalence remained ~~where VF abnormality was not detected on 24-2 visual field testing, the prevalence of OAG is~~ 3.76% ~~prevalence~~ - still ~~, which is still~~ higher than any other previously studied Chinese population from Asia.

Secondly, risk factor burden may differ across Chinese populations. We investigated whether these differences could be related to axial length differences. The risk of having OAG was 36% higher for every 1mm longer axial length. ~~it is also possible that the burden of risk factors may differ across different Chinese populations. We explored whether this may be true with regards to axial length. Axial length was an important independent risk factor for OAG in Chinese Americans. The risk of having OAG in CHES was 36% higher with each 1 mm longer AL.~~ Prior studies from China have reported longer AL among those living in urban areas and also among the younger populations.[30,31~~29,30~~] In fact, there is now a well-established epidemic of myopia and high myopia, due to increases in near work and less outdoor time among children especially in East and Southeast Asia but also across several other populations worldwide.[3~~21~~,3~~32~~] ~~Since our study population was skewed towards younger age (compared to non-participants in the studied geographical area), we first investigated whether we saw longer AL in our younger study participants, which would also help explain increased risk factor burden in our population. While we found no trend among males (P=0.26), we did see the association of longer AL with younger age among females (P=0.002). This suggests there may have been a higher education level and greater near work among the younger generation compared to the older generation of female Chinese Americans that may have contributed to a longer AL and thus increased risk of having OAG. We also explored whether our Chinese American population had a generally longer AL compared to other studied Chinese populations from Asia, as this could help explain the higher OAG prevalence.~~ The mean AL among CHES participants was 23.9 ~~(~~±1.4~~)~~ mm, which was ~~in fact~~ among the longest compared to most other ~~Asian~~ studies of Chinese

descent individuals ~~from Asia~~. In comparison, ~~the~~ mean AL was ~~22.6±0.9 mm in the Chennai Eye Study,[33]~~ 22.8± 0.9 mm in the Handan Eeye Sstudy,[14] 22.82 ~~(median; IQR 1.08)~~ mm in the Yunnan Eye Study,[34] 23.25±1.14 mm in the Beijing Eye Study,[35] and 24.0 (±1.32) mm in the Singapore Chinese Eye Study.[36] ~~(and among non-Chinese: 23.41 ± 0.89 mm in Kumejima,[36] and 22.6±0.9 mm in the Chennai Eye Study[33]) and 24.0 (±1.32) mm in the Singapore Chinese Eye Study[37].~~ Axial elongation and ~~the~~ associated thinning of the lamina cribrosa may ~~is thought to~~ compromise biomechanical support for the retinal ganglion cell ~~(RGC)~~ axons[37~~8~~] and ~~to~~ reduce structural support for the retinal ganglion cell~~RGC~~ microvasculature.[38~~9~~] ~~Prevention efforts, such as more time outdoors in school and low dose atropine to slow myopia progression in childhood could potentially reduce glaucoma burden in the future[40,41], however, longitudinal studies are needed to validate this.~~

Third~~ly~~, ~~there may be other~~ environmental differences may~~that could~~ alter risk for OAG across ~~various~~ Chinese populations. One ~~such~~ example is air pollution, which is poorly studied but suspected to increase ~~risk for~~ glaucoma risk.[39~~42~~] Additional~~More~~ research is needed to investigate this and other potential environmental influences.

Age represented a major risk factor, with~~The risk of having OAG was~~ 79% higher risk per ~~each~~ decade of aging.~~greater with every 10 years of older age.~~ The OAG prevalence~~e of OAG~~ in CHES in those aged 80 years and older was five~~5~~ times higher than ~~the~~ prevalence in those aged 50-59 years ~~of age~~. Age-related changes including ~~to scleral biomechanics, with~~ increased scleral thinning and stiffness~~,~~ and ~~as well as~~ reduced vascular health contribute to ~~are some factors thought to contribute to~~ age-related glaucoma risk.[37~~8~~,40~~3~~] With rapid global population aging, glaucoma cases are

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projected to reach 111.8 million by 2040, disproportionately affecting ~~Because of the rapid increase in the aging population worldwide, the number of people with glaucoma is estimated to increase to 111.8 million by 2040, and it is expected to disproportionately affect those in~~ Asia and Africa.[1] ~~Efforts to identify glaucoma in a timely fashion in our aging populations are critical to prevent avoidable blindness.~~

A prominent feature of our study~~the OAG cases in CHES~~ was that 68.5% were ~~had~~ previously undiagnosed ~~glaucoma~~ with 88.5% having a screening~~n~~ IOP of 21 mmHg or less. This ~~e~~ high proportion of undiagnosed glaucoma highlights the importance of improving screening strategies ~~for glaucoma~~. The predominance of~~In addition, the high proportion of~~ "normotensive" glaucoma emphasizes ~~highlights a~~ major limitations of IOP based screening. This finding is consistent with other Asia-based studies reporting high proportions of normal tension OAG: ~~glaucoma screening based primarily on IOP measurements. The high proportion of normotensive OAG is consistent with other Asian based epidemiology studies, which also reported high proportions of normotensive OAG (~~92.3% in Japan, 84.6% in Singapore, 83.6% in northern China, 82% in south India, and 79.3% in southern China~~)~~.[14,26,41-43~~5~~,42~~4~~-44~~6~~ ~~This is in c~~ This contrasts with non-Asian populations showing lower ~~to~~ proportions: ~~of normotensive OAG in non-Asian populations (57.1% in South Africa, 46.9% in Iran, 38.9% in the Netherlands, and~~ 31.7% in U.S. Caucasians, 31.5% in Iceland, and 30% in Italy~~)~~.[18~~7~~,44~~7~~-48~~51~~ Mounting evidence suggests that vascular health, oxidative stress, and endothelial dysfunction interact with IOP and contribute to glaucoma pathogenesis.[4,14] ~~Increased awareness among clinicians and the public alike of the high proportion of OAG that has~~

~~"normal" untreated IOPs could help prevent early glaucoma cases from being overlooked based on "normal" IOP.~~

Despite ~~Even though~~ most~~t new glaucoma~~ new cases having screening~~ad~~ IOP ≤ 21 mmHg, higher IOP remained an~~was another~~ independent risk factor ~~for having OAG~~. Each ~~A~~ 1mm Hg higher IOP conferred~~was associated with~~ 12% higher risk ~~of having OAG~~. This matches findings from the Ocular Hypertension Treatment Study showing 10% higher risk per mm Hg of IOP~~Though our study comprised mostly normotensive subjects and the Ocular Hypertension Treatment Study obviously comprised those with ocular hypertension, the OAG risk with higher IOP is interestingly consistent with OHTS, where there was a 10% higher risk of developing OAG for a 1 mmHg higher IOP~~.[5~~2~~3~~2~~] Elevated IOP causes ~~is thought to cause~~ progressive ~~structural damage to~~ retinal ganglion cell axons damage at the lamina cribrosa, reduces retinal blood flow and increase cytokine expression.[5~~49-51~~3,54] ~~Reducing IOP from baseline IOP, whether the baseline IOP is "high" or "normal", is the mainstay of glaucoma treatment and is well established in both hypertensive and normotensive glaucoma.~~[2,55]

Interesting~~ly, CCT~~ly, CCT, which has been reported a risk factor in other populations,[56] was not an independent risk factor in our study, contrasting with other populations.[54]. Similarly, the Beijing Eye Study found no CCT-glaucoma association ~~did not find an association between CCT, a highly heritable trait, with glaucoma~~ in a mainland Chinese population.[13,5~~37~~] Wang et al previously demonstrated ~~assessed CCT in a large multiethnic population in northern California and found~~ that CCT explained a significant glaucoma risk ~~portion of the higher risk of having glaucoma~~ among Black and Hispanic individuals, but not among Asians in a large multiethnic population.[54] They also

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reported that average CCT was 6 to 13 microns thicker among Chinese, Japanese, and Koreans compared to Southeast Asians, Filipinos, and Pacific Islanders. This highlights differences within ~~different~~ Asian populations; therefore, our ~~findings on~~ Chinese American findings~~s~~ may not generalize to other Asian groups.[5,6,8]

Family history of glaucoma (in any blood relative) conferred ~~d relative) was another independent risk factor for having OAG, with a positive family history being associated with an~~ 88% higher OAG risk ~~of having OAG~~. ~~Prior studies have reported that the risk for OAG is higher when the affected relative is a sibling rather than a parent or child.[59]~~ Complex inheritance predominates in adult-onset OAG with~~is most common with onset over the age of 40, which is the case for the majority of OAG; thus, there are still~~ many unknowns regarding ~~about~~ glaucoma inheritance patterns. ~~Novel loci for POAG have recently been identified using genome-wide association studies, and additional efforts will continue to hone the specific genetic influences on glaucoma risk.[6550]~~ Recent genome-wide association studies have identified POAG loci, and other efforts continue refining specific genetic influences.[6550] ~~Since family history is an indirect measure of inherited susceptibility for disease,~~ Mars et al recently demonstrated that high polygenic risk scores and family history have equal but largely independent effects for glaucoma[6561], suggesting substantial gaps remain in understanding genetic risk or environmental exposures common within families. ~~performed a systematic comparison of family history and polygenic risk score (PRS), which has the potential to directly capture genetic risk, for several human diseases. For glaucoma, they reported that a high PRS and family history had equal but largely independent effects, suggesting that there is still a lot about genetic risk, or perhaps environmental exposures common~~

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within families, that we still do not understand.[6581] It is important to note, however, that Sself-reported family history is subject to recall, selection, and survival bias and subject to community under-diagnosis limitationsof glaucoma.[6572] Thus, there may be an underestimation of genetic influence on glaucoma risk.[6592] A recentstudy from Nepalese study demonstrated recently demonstrated that screening of accompanying first degree relatives of POAG patients identified d a remarkable numbers of individuals with previously undiagnosed glaucoma cases.[6583] Future screening efforts targetingfocusing on family members of OAG patientssubjects would likely represent be a high yield approach for detecting undiagnosed to identify previously undetected glaucoma.

Diabetes mellitus conferredwas an independent risk factor for OAG, conferring 49% higher OAG risk of having OAG in CHES participants. Prior studies and meta-analyses have supported this association.[6559-614-66] Diabetes is thought to causes microvascular damage and vascular dysregulation of the retina and optic disc, thus increasing the optic nerve's susceptibility to glaucomatous damage.[62,6337,68] The African American Eye Disease Study, which utilized optical coherence tomography angiography, recently demonstrated the associations between of diabetes duration and with reduced peripapillary retinal vessel density among non-glaucomatous subjects.[649] Optical coherence tomography (OCT) studies showed that reduced retinal nerve fiber layer (RNFL) and ganglion cell layer thickness are associated with diabetes duration inamong non-glaucoma subjects.[765,6600,71] This supports the conceptidea that diabetes compromises the peripapillary neurovascular bundle before the onset of clinically detectable glaucoma onset. While healthy diet and exercise are well known to prevent diabetes, there is also increasing evidence that healthy diet and exercise may help to

prevent glaucoma and its progression.[7,69-72,75] Future work in this area could identify modifiable factors beyond IOP for at-risk individuals to help prevent the development of glaucoma or its progression.

Our findings suggest several important clinical considerations. The high prevalence of undiagnosed normal tension glaucoma emphasizes the need for improved screening strategies beyond IOP measurement alone. Targeting high-risk populations including family members of glaucoma patients and individuals with high myopia may enhance screening efficiency. The strong association between longer axial length and glaucoma risk suggests that myopia prevention strategies in childhood warrant investigation as potential glaucoma prevention approaches. In summary, Chinese Americans had a high prevalence of OAG, approaching that of other racial minority populations in the US. Independent risk factors among Chinese Americans included longer AL, older age, higher IOP, family history of glaucoma, and diabetes. Future research investigating alternative treatment strategies, such as myopia prevention in childhood or optimizing lifestyle choices for diabetes prevention, could be beneficial. Additionally, future screening strategies for glaucoma could be enriched by targeting those at highest risk, including family members of OAG patients and individuals with high myopia. Finally, our findings that over half of OAG was undiagnosed and about 88% of those had "normal" IOP highlight the room for improvement in earlier disease detection and the need for greater education among patients and eye care providers.

Several limitations of our study merit consideration. First One limitation is that our study population may not fully represent the broader Chinese American community,

as participants were more frequently female, more educated and less likely to smoke than non-participants. Second the~~Glaucoma~~ definition of glaucoma lacks a universal "gold standard" and varies between experts, representing a common source of debate. ~~population of Chinese Americans. For example, study responders were 36.7% males, less likely to smoke and more likely to have at least 12 years of education compared to non-participants in the community they represent.~~ A second limitation in our analysis is ~~in our definition of glaucoma. As has recently been highlighted by glaucoma experts,~~[~~76~~76] However, our consensus approach using a glaucoma expert panel may represent the most robust definition currently available. Third longitudinal data are needed to validate identified risk factors and their relative contributions to OAG development in Chinese Americans. ~~the definition of glaucoma has no "gold standard", can vary between experts, and is a common source of debate. Nonetheless, with the goal of obtaining the most accurate assessment of OAG burden, our use of the consensus of a glaucoma expert panel may be the most robust definition currently available. Finally, longitudinal data are needed to validate the risk factors and their relative contribution to the development of OAG in Chinese Americans.~~

Chinese Americans demonstrate a high prevalence of OAG (4.8%) approaching that of other racial minority populations in the United States. Independent risk factors including longer axial length, older age, higher IOP, family history of glaucoma and diabetes mellitus. The finding that over two thirds of OAG cases were previously undiagnosed, with approximately 88% having "normal" IOP, highlights substantial opportunities for improved early disease detection and underscores the need for

enhanced education among patients and eye care providers. Future research investigating alternative prevention strategies and targeted screening approaches for high-risk individuals may help reduce the burden of preventable vision loss from OAG in this population.

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References

1. Tham YC, Li X, Wong TY, Quigley H, Aung T, Cheng C-Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology 2014;121(11):2081-90.
2. Heijl, A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, Early Manifest Glaucoma Trial. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120(1):1268-79.
3. Hoeffel, E., Rastogi, S., Kim, MO., Shahid, H. 2010 Census Briefs. Washington, DC: U.S. Census Bureau; 2012. The Asian population: 2010. 20. Pew Research Center. The Rise of Asian Americans. 2012. http://www.pewsocialtrends.org/files/2012/06/SDT-The-Rise-of-Asian-Americans-Full-Report.pdf.
4. Varma R, Torres M, Mckean-Cowdin R, Rong F, Hsu C, Jiang X. Prevalence and risk factors for refractive error in adult Chinese Americans: The Chinese American Eye Study. Am J Ophthalmol 2017:175:201-212.
5. Pan C-W, Klein BEK, Cotch MF, Shrager S, Klein R, Folsom A, Kronmal R, Shea SJ, Burke GL, Saw S-M, Wong TY. Racial variations in the prevalence of refractive errors in the United States: The Multi-Ethnic Study of Atherosclerosis. Am J Ophthalmol 2013;155(6):1129-1138.
6. Haarman AEG, Enthoven CA, Tiderman MWL, Tedja MS, Verhoeven VJM, Klaver CW. Complications of myopia: A review and meta-analysis. Invest Ophthalmol Vis Sci 2020;61(4):49.

7. Choudhury F, Meuer SM, Klein R, Wang D, Torres M, Jiang X, McKean-Cowdin R, Varma R. Prevalence and characteristics of myopic degeneration in an adult Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2018;187:34-42.
8. Ohno-Matsui K, Shimada N, Yasuzumi K, et al. Long-term development of significant visual field defects in highly myopic eyes. Am J Ophthalmol. 2011;152:256–265.e1.
9. Perdicchi A, Iester M, Scuderi G, Amodeo S, Medori EM, Recupero SM. Visual field damage and progression in glaucomatous myopic eyes. Eur J Ophthalmol. 2007;17:534– 537.
10. Lee YA, Shih YF, Lin LL, Huang JY, Wang TH. Association between high myopia and progression of visual field loss in primary open-angle glaucoma. J Formos Med Assoc. 2008;107:952–957.
11. Baskaran M, Foo RC, Cheng C-Y, Narayanaswamy AK, Zheng Y-F, Wu R, Saw S-M, Foster PJ, Wong T-Y, Aung T. The prevalence and types of glaucoma in an urban Chinese population: The Singapore Chinese Eye Study. JAMA Ophthalmol 2015;133(8):874-880.
12. Pan C-W. Zhao C-H. Yu M-B. Cun Q, Chen Q, Shen W, Li J, Xu J-G. Yuan Y. Zhong H. Prevalence, types and awareness of glaucoma in a multi-ethnic population in rural China: the Yunnan Minority Eye Study. Ophthalmic Physiol Opt 2016, 36: 664-670.
13. Wang YX, Xu L, Yang H, Jonas JB. Prevalence of glaucoma in north China: The Beijing Eye Study. Am J Ophthalmol 2010;150:917-924.

14. Liang YB, Friedman DS, Zhou Q, Yang X, Sun LP, Guo LX, Tao QS, Chang DS, Wang NL. Prevalence of primary open angle glaucoma in a rural adult Chinese population: The Handan Eye Study. Invest Ophthalmol Vis Sci 2011;52:8250-8257.
15. Xu BY, Richter GM, Burkemper BS, Wang D, Jiang X, Torres M, McKean-Cowdin R, Dhablania N, Varma R. Prevalence and risk factors of primary angle closure disease in an adult Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2025;274:32-41.
16. Varma R, Hsu C, Wang D, Torres M, Azen SP; Chinese American Eye Study Group. The Chinese American Eye Study: Design and methods. Ophthalmic Epidemiol 2013;20(6):335-47.
17. Varma R, Ying-Lai M, Francis BA, Nguyen BB-T, Deneen J, Wilson MR, Azen SP. Prevalence of open-angle glaucoma and ocular hypertension in Latinos. Ophthalmology 2004;111:1439-1448.
18. Klein BEK, Klein R, Sonsel WE, Franke T, Cantor LB, Martone J, Menage MJ. Prevalence of glaucoma: The Beaver Dam Eye Study. Ophthalmology 1992;99:1499-1504.
19. Wensor MD, McCarty CA, Stanislavsky YL, Livingston PM, Taylor HR. The prevalence of glaucoma in the Melbourne Visual Impairment Project. Ophthalmology 1998;105(4):733-9.
20. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002;86(2):238-242.

21. 2019 Population Estimates by Age, Sex, Race and Hispanic Origin. June 25, 2020. United States Census Bureau. https://www.census.gov/newsroom/press-kits/2020/population-estimates-detailed.html
22. Tham Y-C, Aung T, Fan Q, et al. Joint effects of intraocular pressure and myopia on risk of primary open-angle glaucoma: The Singapore epidemiology of eye diseases study. Sci Rep. 2016;6(1):1–7.
23. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Philip Miller J, Parrish RK, Roy Wilson M, Kass MA. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120(6):714-720.
24. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. Arch Ophthalmol 2001;119:1819-1826.
25. Yamamoto S, Sawaguchi S, Iwase A, Yamamoto T, Abe H, Tomita G, Tomidokoro A, Araie M. Primary open-angle glaucoma in a population associated with high prevalence of primary angle-closure glaucoma: The Kumejima Study. Ophthalmology 2014;121:1558-1565.
26. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai glaucoma study. Ophthalmology 2008;115(4):848-54.e1.
27. Leske MC, Connel AMS, Schachat AP, Hyman L. The Barbados Eye Study: Prevalence of open angle glaucoma. Arch Ophthalmol 1994;112:821-829.

28. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma: The Baltimore Eye Survey. JAMA 1991;266:369-374.
29. De Moraes CG, Hood DC, Thenappan A, Girkin CA, Medeiros FA, Weinreb RN, Zangwill LM, Liebmann JM. 24-2 visual fields miss central defects shown on 10-2 tests in glaucoma suspects, ocular hypertensives, and early glaucoma. Ophthalmology 2017;124(1):1449-1456.
30. Liang YB, Lin Z, Vasudevan B, Jhanji V, Young A, Gao TY, Rong SS, Wang NL, Ciuffreda KJ. Generational difference of refractive error in the baseline study of the Beijing myopia progression study. Br J Ophthalmol 2013;97(6):765-769.
31. Lin Z, Gao TY, Vasudevan B, Jhanji V, Ciuffreda KJ, Zhang P, Li L, Mao GY, Wang NL, Liang YB. Generational difference of refractive error and risk factors in the Handan offspring myopia study. Invest Ophthal Vis Sci 2014;55(9):5711-5717.
32. Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M, Rose KA. The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res 2018;62:134-149.
33. Williams KM, Bertelsen G, Cumberland P, Wolfram C, Verhoeven VJ, Anastasopoulos E, et al. Increasing Prevalence of Myopia in Europe and the Impact of Education. Ophthalmology. 2015 Jul;122(7):1489-97.
34. Wang Y, Cun Q, Li J, Shen W, Yang W-Y, Tao Y-J, Niu Z-Q, Zhang Y, Zhong H, Pan C-W. Prevalence, ethnic differences and risk factors of primary angle-

closure glaucoma in a multiethnic Chinese adult population: the Yunnan Minority Eye Study. Br J Ophthalmol 2021. Online ahead of print.

35. Gui Y, Wang YX, Zheng ZY, Yang H, Xu L, Jonas JB, Beijing Eye Study Group. Ocular axial length and its associations in Chinese: the Beijing Eye Study. PLoS One 2012;7(8):e43172.

36. Sng CC, Foo L-L, Cheng, C-Y, Allen JC, He M, Krishnaswamy G, Nongpiur ME, Friedman DS, Wong TY, Aung T. Determinants of anterior chamber depth: The Singapore Chinese Eye Study. Ophthalmology 2012;119:1143-1150.

37. Boote C, Sigal IA, Grytz R, Hua Y, Nguyen TD, Girard MJA. Scleral structure and biomechanics. Progress in Retinal and Eye Research 2020;74: 10073.

38. Juliano J, Burkemper B, Lee J, Nelson A, LeTran V, Chu Z, Zhou G, Jiang X, Wang RK, Varma R, Richter GM. Longer axial length potentiates relationship of intraocular pressure and peripapillary vessel density in glaucoma patients. Invest Ophthalmol Vis Sci. 2021;62(9):37.

39. Grant A, Leung G, Freeman EE. Ambient air pollution and age-related eye disease: a systematic review and meta-analysis. Invest Ophthalmol Vis Sci. 2022;63(9):17

40. Grzybowski A, Och M, Kanclerz P, Leffler C, Gustavo De Moraes C. Primary open angle glaucoma and vascular risk factors: A review of population based studies from 1990 to 2019. J Clin Med 2020;9:761.

41. Leung DYL, Tham CC. Normal-tension glaucoma: current concepts and approaches- a review. Clinical & Experimental Ophthalmology. 2022;50:247-259.

42. Shen SY, Wong TY, Foster PJ, et al. The prevalence and types of glaucoma in Malay people: the Singapore Malay eye study. Invest Ophthalmol Vis Sci. 2008;48(9):3846-3851.
43. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: the Liwan eye study. Am J Ophthalmol 2011;152(3):454-62 e1.
44. Rotchford AP, Johnson GJ. Glaucoma in Zulus: a population based cross-sectional survey in a rural district in South Africa. Arch Ophthalmol. 2002;120(4):471-478.
45. Pakravan M, Yazdani S, Javadi MA, et al. A population-based survey of the prevalence and types of glaucoma in Central Iran: the Yazd eye study. Ophthalmology. 2013;120(10):1977-1984.
46. Dielemans I, Vingerling JR, Wolfs RC, Hofman A, Grobbee DE, de Jong PT. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study Ophthalmology. 1994;101(11):1851-1855.
47. Jonasson F, Damji KF, Arnarsson A, et al. Prevalence of open-angle glaucoma in Iceland: Reykjavik eye study. Eye (Lond). 2003;17(6):747-753.
48. Bonomi L, Marchini G, Marraffa M, et al. Prevalence of glaucoma and intraocular pressure distribution in a defined population. The Egna-Neumarkt Study Ophthalmology. 1998;105(2): 209-215).
49. Morrison JC, Johnson EC, Cepurna W, Jia L. Understanding mechanisms of pressure-induced optic nerve damage. Prog Retin Eye Res 2005;24:217– 40.

50. Burgoyne CF, Crawford Downs J, Bellezza AJ, Francis Suh JK, Hart RT. The optic nerve head as a biomechanical structure: A new paradigm for understanding the role of IOP related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. Prog Retin Eye Res. 2005;24(1):39–73.
51. Collaborative Normal Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normaltension glaucoma. Am J Ophthalmol. 1998;126:498–505.
52. Sng CCA, Ang M, Barton K. Central corneal thickness in glaucoma. Curr Opin Ophthalmol 2017;28:120-126.
53. Toh T, Liew SH, MacKinnon JR, et al. Central corneal thickness is highly heritable: the twin eye studies. Invest Ophthalmol Vis Sci 2005; 46:3718– 3722.
54. Wang SY, Melles R, Lin SC. The impact of central corneal thickness on the risk for glaucoma in a large multiethnic population. J Glaucoma 2014;23(9):606-612.
55. Wiggs JL, Pasquale LR. Genetics of glaucoma. Hum Mol Genet 2017;26(R1):R21-R27.
56. Mars N, Lindbohm JV, Parolo PB, Widen E, Kaprio J, Palotie A, FinnGen, Ripatti S. Systematic comparison of family history and polygenic risk across 24 common diseases. Am J Hum Genetics 2022;109(12):2152-2162.
57. Mitchell P, Rochtchina E, Lee AJ, Wang JJ. Bias in self-reported family history and relationship to glaucoma: The Blue Mountains Eye Study. Ophthalmic Epidemiol 2002;9(5):333-345.
58. Paudyal I, Yadav R, Parajuli A, Singh K, Josh P, Thapa S. Screening of Accompanying First Degree Relatives of Patients with Primary Open Angle Glaucoma. Nepal J Ophthalmol 2022;14(27):4-9.

59. Zhou M, Wang W, Huang W, Zhang X. Diabetes mellitus as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. PLoS One. 2014;9(8):e102972.
60. Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis: Ophthalmology 2015;122(1):72-78.
61. Kim S-W, Kang G-W. Diabetes mellitus as a risk factor for glaucoma outcome in Korea. Acta Ophthalmol 2017;95(7):e662-e664.
62. Hayreh SS. Pathogenesis of optic nerve damage and visual field deficits in glaucoma. Doc Ophthalmol Proc Ser 1980;22: 89–110.
63. Nakamura M, Kanamori A, Negi A. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. Ophthalmologica 2005;219:1–10.
64. Chang R, Nelson AJ, LeTran V, Vu B, Burkemper B, Chu Z et al. Systemic determinants of peripapillary vessel density in healthy African Americans: the African American Eye Disease Study. Am J Ophthalmol 2019;207:240-247.
65. van Dijk HW, Verbraak FD, Kok PH, et al. Decreased retinal ganglion cell layer thickness in patients with type 1 diabetes. Invest Ophthalmol Vis Sci 2010;51(7):3660–5.
66. Shi R, Guo Z, Wang F, Li R, Zhao L, Lin R. Alterations in retinal nerve fiber layer thickness in early stages of diabetic retinopathy and potential risk factors. Curr Eye Res 2018;43(2):244–53.
67. Quigley HA. 21st century glaucoma care. Eye (Lond) 2019;33(2):254-260.

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1. Tham YC, Li X, Wong TY, Quigley H, Aung T, Cheng C-Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology 2014;121(11):2081-90.
2. Heijl, A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, Early Manifest Glaucoma Trial. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120(1):1268-79.
3. Hoeffel, E., Rastogi, S., Kim, MO., Shahid, H. 2010 Census Briefs. Washington, DC: U.S. Census Bureau; 2012. The Asian population: 2010. 20. Pew Research Center. The Rise of Asian Americans. 2012. http://www.pewsocialtrends.org/files/2012/06/SDT-The-Rise-of-Asian-Americans-Full-Report.pdf.
4. Varma R, Torres M, Mckean-Cowdin R, Rong F, Hsu C, Jiang X. Prevalence and risk factors for refractive error in adult Chinese Americans: The Chinese American Eye Study. Am J Ophthalmol 2017:175:201-212.
5. Pan C-W, Klein BEK, Cotch MF, Shrager S, Klein R, Folsom A, Kronmal R, Shea SJ, Burke GL, Saw S-M, Wong TY. Racial variations in the prevalence of refractive errors in the United States: The Multi-Ethnic Study of Atherosclerosis. Am J Ophthalmol 2013;155(6):1129-1138.
6. Haarman AEG, Enthoven CA, Tiderman MWL, Tedja MS, Verhoeven VJM, Klaver CW. Complications of myopia: A review and meta-analysis. Invest Ophthalmol Vis Sci 2020;61(4):49.
7. Choudhury F, Meuer SM, Klein R, Wang D, Torres M, Jiang X, McKean-Cowdin R, Varma R. Prevalence and characteristics of myopic degeneration in an adult

Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2018;187:34-42.

8. Ohno-Matsui K, Shimada N, Yasuzumi K, et al. Long-term development of significant visual field defects in highly myopic eyes. Am J Ophthalmol. 2011;152:256–265.e1.

9. Perdicchi A, Iester M, Scuderi G, Amodeo S, Medori EM, Recupero SM. Visual field damage and progression in glaucomatous myopic eyes. Eur J Ophthalmol. 2007;17:534–537.

10. Lee YA, Shih YF, Lin LL, Huang JY, Wang TH. Association between high myopia and progression of visual field loss in primary open-angle glaucoma. J Formos Med Assoc. 2008;107:952–957.

11. Baskaran M, Foo RC, Cheng C-Y, Narayanaswamy AK, Zheng Y-F, Wu R, Saw S-M, Foster PJ, Wong T-Y, Aung T. The prevalence and types of glaucoma in an urban Chinese population: The Singapore Chinese Eye Study. JAMA Ophthalmol 2015;133(8):874-880.

12. Pan C-W, Zhao C-H, Yu M-B, Cun Q, Chen Q, Shen W, Li J, Xu J-G, Yuan Y, Zhong H. Prevalence, types and awareness of glaucoma in a multi-ethnic population in rural China: the Yunnan Minority Eye Study. Ophthalmic Physiol Opt 2016, 36: 664-670.

13. Wang YX, Xu L, Yang H, Jonas JB. Prevalence of glaucoma in north China: The Beijing Eye Study. Am J Ophthalmol 2010;150:917-924.

14. Liang YB, Friedman DS, Zhou Q, Yang X, Sun LP, Guo LX, Tao QS, Chang DS, Wang NL. Prevalence of primary open angle glaucoma in a rural adult Chinese

population: The Handan Eye Study. Invest Ophthalmol Vis Sci 2011;52:8250-8257.

15. Varma R, Hsu C, Wang D, Torres M, Azen SP; Chinese American Eye Study Group. The Chinese American Eye Study: Design and methods. Ophthalmic Epidemiol 2013;20(6):335-47.

16. Varma R, Ying-Lai M, Francis BA, Nguyen BB-T, Deneen J, Wilson MR, Azen SP. Prevalence of open-angle glaucoma and ocular hypertension in Latinos. Ophthalmology 2004;111:1439-1448.

17. Klein BEK, Klein R, Sonsel WE, Franke T, Cantor LB, Martone J, Menage MJ. Prevalence of glaucoma: The Beaver Dam Eye Study. Ophthalmology 1992;99:1499-1504.

18. Wensor MD, McCarty CA, Stanislavsky YL, Livingston PM, Taylor HR. The prevalence of glaucoma in the Melbourne Visual Impairment Project. Ophthalmology 1998;105(4):733-9.

19. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002;86(2):238-242.

20. Xu BY, Richter GM, Burkemper BS, Wang D, Jiang X, Torres M, McKean-Cowdin R, Dhablania N, Varma R. Prevalence and risk factors of primary angle closure disease in an adult Chinese American population: The Chinese American Eye Study. Am J Ophthalmol 2025;274:32-41.

21. 2019 Population Estimates by Age, Sex, Race and Hispanic Origin. June 25, 2020. United States Census Bureau. https://www.census.gov/newsroom/press-kits/2020/population-estimates-detailed.html

22. Tham Y-C, Aung T, Fan Q, et al. Joint effects of intraocular pressure and myopia on risk of primary open-angle glaucoma: The Singapore epidemiology of eye diseases study. Sci Rep. 2016;6(1):1–7.

23. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. Arch Ophthalmol 2001;119:1819-1826.

24. Yamamoto S, Sawaguchi S, Iwase A, Yamamoto T, Abe H, Tomita G, Tomidokoro A, Araie M. Primary open-angle glaucoma in a population associated with high prevalence of primary angle-closure glaucoma: The Kumejima Study. Ophthalmology 2014;121:1558-1565.

25. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai glaucoma study. Ophthalmology 2008;115(4):848-54.e1.

26. Leske MC, Connel AMS, Schachat AP, Hyman L. The Barbados Eye Study: Prevalence of open angle glaucoma. Arch Ophthalmol 1994;112:821-829.

27. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma: The Baltimore Eye Survey. JAMA 1991;266:369-374.

28. De Moraes CG, Hood DC, Thenappan A, Girkin CA, Medeiros FA, Weinreb RN, Zangwill LM, Liebmann JM. 24-2 visual fields miss central defects shown on 10-2 tests in glaucoma suspects, ocular hypertensives, and early glaucoma. Ophthalmology 2017;124(1):1449-1456.
29. Liang YB, Lin Z, Vasudevan B, Jhanji V, Young A, Gao TY, Rong SS, Wang NL, Ciuffreda KJ. Generational difference of refractive error in the baseline study of the Beijing myopia progression study. Br J Ophthalmol 2013;97(6):765-769.
30. Lin Z, Gao TY, Vasudevan B, Jhanji V, Ciuffreda KJ, Zhang P, Li L, Mao GY, Wang NL, Liang YB. Generational difference of refractive error and risk factors in the Handan offspring myopia study. Invest Ophthal Vis Sci 2014;55(9):5711-5717.
31. Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M, Rose KA. The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res 2018;62:134-149.
32. Williams KM, Bertelsen G, Cumberland P, Wolfram C, Verhoeven VJ, Anastasopoulos E, et al. Increasing Prevalence of Myopia in Europe and the Impact of Education. Ophthalmology. 2015 Jul;122(7):1489-97.
33. Vijaya L, Rashima A, Panday M, Choudhari NS, Ramesh SV, Lokapavani V, Boddupalli SD, Sunil GT, George R. Predictors for incidence of primary open-angle glaucoma in a south Indian population: The Chennai Eye Disease Incidence Study. Ophthalmology 2014;121:1370-1376.
34. Wang Y, Cun Q, Li J, Shen W, Yang W-Y, Tao Y-J, Niu Z-Q, Zhang Y, Zhong H, Pan C-W. Prevalence, ethnic differences and risk factors of primary angle-

closure glaucoma in a multiethnic Chinese adult population: the Yunnan Minority Eye Study. Br J Ophthalmol 2021. Online ahead of print.

35. Gui Y, Wang YX, Zheng ZY, Yang H, Xu L, Jonas JB, Beijing Eye Study Group. Ocular axial length and its associations in Chinese: the Beijing Eye Study. PLoS One 2012;7(8):e43172.

36. Yamashita T, Iwase A, Sakai H, Terasak H, Sakamoto T, Araie M. Differences of body height, axial length, and refractive error at different ages in Kumejima study. Graefe's Arch Clin Exp Ophthalmol 2019;257(2):371-378.

37. Sng CC, Foo L-L, Cheng, C-Y, Allen JC, He M, Krishnaswamy G, Nongpiur ME, Friedman DS, Wong TY, Aung T. Determinants of anterior chamber depth: The Singapore Chinese Eye Study. Ophthalmology 2012;119:1143-1150.

38. Boote C, Sigal IA, Grytz R, Hua Y, Nguyen TD, Girard MJA. Scleral structure and biomechanics. Progress in Retinal and Eye Research 2020;74: 10073.

39. Juliano J, Burkemper B, Lee J, Nelson A, LeTran V, Chu Z, Zhou G, Jiang X, Wang RK, Varma R, Richter GM. Longer axial length potentiates relationship of intraocular pressure and peripapillary vessel density in glaucoma patients. Invest Ophthalmol Vis Sci. 2021;62(9):37.

40. Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M, Rose KA. The epidemics of myopia: Aetiology and prevention. Progress in Retinal and Eye Research 2018;62:134-149.

41. Wu P-C, Chuang M-N, Choi J, Chen H, Wu G, Ohno-Matsui K, Jonas JB, Cheung CMG. Update in myopia and treatment strategy of atropine use in myopia control. Eye (Lond) 2019;33(1):3-13).

42. Grant A, Leung G, Freeman EE. Ambient air pollution and age-related eye disease: a systematic review and meta-analysis. Invest Ophthalmol Vis Sci. 2022;63(9):17

43. Grzybowski A, Och M, Kanclerz P, Leffler C, Gustavo De Moraes C. Primary open angle glaucoma and vascular risk factors: A review of population based studies from 1990 to 2019. J Clin Med 2020;9:761.

44. Leung DYL, Tham CC. Normal-tension glaucoma: current concepts and approaches- a review. Clinical & Experimental Ophthalmology. 2022;50:247-259.

45. Shen SY, Wong TY, Foster PJ, et al. The prevalence and types of glaucoma in Malay people: the Singapore Malay eye study. Invest Ophthalmol Vis Sci. 2008;48(9):3846-3851.

46. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: the Liwan eye study. Am J Ophthalmol 2011;152(3):454-62 e1.

47. Rotchford AP, Johnson GJ. Glaucoma in Zulus: a population based cross-sectional survey in a rural district in South Africa. Arch Ophthalmol. 2002;120(4):471-478.

48. Pakravan M, Yazdani S, Javadi MA, et al. A population-based survey of the prevalence and types of glaucoma in Central Iran: the Yazd eye study. Ophthalmology. 2013;120(10):1977-1984.

49. Dielemans I, Vingerling JR, Wolfs RC, Hofman A, Grobbee DE, de Jong PT. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study Ophthalmology. 1994;101(11):1851-1855.

50. Jonasson F, Damji KF, Arnarsson A, et al. Prevalence of open-angle glaucoma in Iceland: Reykjavik eye study. Eye (Lond). 2003;17(6):747-753.
51. Bonomi L, Marchini G, Marraffa M, et al. Prevalence of glaucoma and intraocular pressure distribution in a defined population. The Egna-Neumarkt Study Ophthalmology. 1998;105(2): 209-215).
52. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Philip Miller J, Parrish RK, Roy Wilson M, Kass MA. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120(6):714-720.
53. Morrison JC, Johnson EC, Cepurna W, Jia L. Understanding mechanisms of pressure-induced optic nerve damage. Prog Retin Eye Res 2005;24:217–40.
54. Burgoyne CF, Crawford Downs J, Bellezza AJ, Francis Suh JK, Hart RT. The optic nerve head as a biomechanical structure: A new paradigm for understanding the role of IOP-related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. Prog Retin Eye Res. 2005;24(1):39–73.
55. Collaborative Normal Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normaltension glaucoma. Am J Ophthalmol. 1998;126:498–505.
56. Sng CCA, Ang M, Barton K. Central corneal thickness in glaucoma. Curr Opin Ophthalmol 2017;28:120-126.
57. Toh T, Liew SH, MacKinnon JR, et al. Central corneal thickness is highly heritable: the twin eye studies. Invest Ophthalmol Vis Sci 2005; 46:3718–3722.

58. Wang SY, Melles R, Lin SC. The impact of central corneal thickness on the risk for glaucoma in a large multiethnic population. J Glaucoma 2014;23(9):606-612.
59. Jonas HB, Bourne RR, Bron AM, Ritch R, Panda-Jonas S. Glaucoma. Lancet 2017;390:2083-93.
60. Wiggs JL, Pasquale LR. Genetics of glaucoma. Hum Mol Genet 2017;26(R1):R21-R27.
61. Mars N, Lindbohm JV, Parolo PB, Widen E, Kaprio J, Palotie A, FinnGen, Ripatti S. Systematic comparison of family history and polygenic risk across 24 common diseases. Am J Hum Genetics 2022;109(12):2152-2162.
62. Mitchell P, Rochtchina E, Lee AJ, Wang JJ. Bias in self-reported family history and relationship to glaucoma: The Blue Mountains Eye Study. Ophthalmic Epidemiol 2002;9(5):333-345.
63. Paudyal I, Yadav R, Parajuli A, Singh K, Josh P, Thapa S. Screening of Accompanying First Degree Relatives of Patients with Primary Open Angle Glaucoma. Nepal J Ophthalmol 2022;14(27):4-9.
64. Zhou M, Wang W, Huang W, Zhang X. Diabetes mellitus as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. PLoS One. 2014;9(8):e102972.
65. Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis: Ophthalmology 2015;122(1):72-78.
66. Kim S-W, Kang G-W. Diabetes mellitus as a risk factor for glaucoma outcome in Korea. Acta Ophthalmol 2017;95(7):e662-e664.
67. Hayreh SS. Pathogenesis of optic nerve damage and visual field deficits in glaucoma. Doc Ophthalmol Proc Ser 1980;22: 89–110.

68. Nakamura M, Kanamori A, Negi A. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. Ophthalmologica 2005;219:1–10.
69. Chang R, Nelson AJ, LeTran V, Vu B, Burkemper B, Chu Z et al. Systemic determinants of peripapillary vessel density in healthy African Americans: the African American Eye Disease Study. Am J Ophthalmol 2019;207:240-247.
70. van Dijk HW, Verbraak FD, Kok PH, et al. Decreased retinal ganglion cell layer thickness in patients with type 1 diabetes. Invest Ophthalmol Vis Sci 2010;51(7):3660–5.
71. Shi R, Guo Z, Wang F, Li R, Zhao L, Lin R. Alterations in retinal nerve fiber layer thickness in early stages of diabetic retinopathy and potential risk factors. Curr Eye Res 2018;43(2):244–53.
72. Kang JH, Willett WC, Rosner BA, Buys E, Wiggs JL, Pasquale LR. Association of Dietary Nitrate Intake With Primary Open-Angle Glaucoma: A Prospective Analysis From the Nurses' Health Study and Health Professionals Follow-up Study. JAMA Ophthalmol. 2016 Mar;134(3):294-303.
73. Vergroesen JE, de Crom TOE, Blekkenhorst LC, Klaver CCW, Voortman T, Ramdas WD. Dietary Nitrate Intake Is Associated with Decreased Incidence of Open-Angle Glaucoma: The Rotterdam Study. Nutrients. 2022 Jun 15;14(12):2490.
74. Tribble HR, Hui F, Joe M, Bell K, Chrysostomou V, Crowston J, Williams PA. Targeting Diet and Exercise for Neuroprotection and Neurorecovery in Glaucoma. Cells. 2021 Feb 1;10(2):295.

75. Lee MJ, Wang J, Friedman DS, Boland MV, De Moraes CG, Ramulu PY. Greater physical activity is associated with slower visual field loss in glaucoma. Ophthalmology 2019;126(7):958-64.

76. Quigley HA. 21st century glaucoma care. Eye (Lond) 2019;33(2):254-260.

Figure Caption

Figure 1. Age-Specific Prevalence of Primary Open Angle Glaucoma (POAG) in the Chinese American Eye Study (CHES), Los Angeles Latino Eye Study (LALES), and the Baltimore Eye Study (BES).

Table 1. Completeness of Data for Glaucoma Classification in Chinese Americans in the Chinese American Eye Study (n=207)

	Gradable Disc Photos [n (%)]	Clinical Disc Exam Data only [n (%)]	No Disc Data [n (%)]	Total [n (%)]
>=2 visual fields	154 (74.4)	1 (0.5)		155 (74.9)
1 visual field	34 (16.4)			34 (16.4)
No visual field	18 (8.7)			18 (8.7)
Total	206 (99.5)	1 (0.5)		207 (100)

Table 2. Age- and Sex-Specific Distribution of the Prevalence of Open-Angle Glaucoma in Chinese Americans in CHES

		Males (N=1583)		Females (N=2727)		Total	
Age Group (yrs)	*Total N*	*n (%)*	*95% CI*	*n (%)*	*95% CI*	*n (%)*	*95% CI*
50-59	2092	32 (4.70)	3.11-6.29	26(1.84)	1.11-2.54	58 (2.77)	2.07-3.48
60-69	1484	35 (6.15)	4.18-8.13	36 (3.93)	2.67-5.19	71 (4.78)	3.70-5.87
70-79	504	21 (9.42)	5.58-13.25	23 (8.19)	4.98-11.39	44 (8.73)	6.27-11.19
≥80	230	14 (12.73)	6.50-19.0	20 (16.67)	10.0-23.3	34 (14.78)	10.20-19.37
Total	4310	102 (6.44)	5.23-7.65	105 (3.85)	3.13-4.57	207 (4.80)	4.16-5.44
Age-standardized	**4310**	**102 (6.37)**	**5.16-7.58**	**105 (4.72)**	**4.00-5.44**	**207 (5.21)**	**4.57-5.85**

Table 3. Clinical characteristics of Chinese Americans with and without open-angle glaucoma (OAG)			
Mean +- SD	OAG (n= 207)	No OAG (n= 4057)	P
Age (yrs)	66.64 (10.57)	61.02 (8.70)	<0.0001
Female [freq (%)]	102 (49.28)	2593 (63.91)	0.0001
Intraocular Pressure (mm Hg)	17.03 (4.58)	15.21 (3.06)	<0.0001
Intraocular Pressure >21 mmHg [freq (%)]	28 (13.53)	119 (2.93)	<0.0001
Mean Deviation (dB)	-8.16 (6.18)	-2.35 (3.56)	<0.0001
Pattern Standard Deviation (dB)	6.44 (3.56)	2.81 (1.88)	<0.0001
Central Corneal Thickness (mm)	558 (35.3)	559 (35.6)	0.72
Vertical Cup-Disc Ratio	0.71 (0.17)	0.40 (0.16)	<0.0001
Spherical Equivalent (diopters)	-1.91 (3.84)	-0.49 (2.84)	<0.0001
Axial Length (mm)	24.58 (1.78)	23.83 (1.41)	<0.0001

Table 4. Self-reported history of glaucoma and glaucoma treatment in Chinese Americans with open angle glaucoma in CHES	
	n (%)
Participants with Open Angle Glaucoma (N=207*)	
Newly detected glaucoma (no prior history)	122 (68.5)
Known history of glaucoma	55 (31.5)
Prior treatment among those with known glaucoma history (n=46**)	
Ocular hypotensive medication	43 (93.5)
Previous laser trabeculoplasty	7 (15.2)
Previous laser peripheral iridotomy	11 (19.6)
Previous incisional glaucoma surgery	6 (13.0)
Previous cataract surgery	24 (42.9)
*missing data for 30 subjects; **missing data for 9 subjects	

Table 5. Candidate variables and independent risk factors associated with open angle glaucoma in Chinese Americans in CHES

Variable	*Univariable Odds Ratio (95% CI) controlling for age*	*P-value (Chi-square)*	*Multivariable Odds Ratio (95% CI) **	*P-value*
Age (yrs)**	-		1.06 (1.05,1.08)	<0.0001
Male Sex	1.53 (1.15-2.03)	0.0034	1.17 (0.87,1.58)	0.30
Any Nuclear lens opacities	1.08 (0.76-1.53)	0.67		
Any Cortical lens opacities	1.39 (0.97-1.98)	0.074		
Any Posterior subcapsular lens opacities	1.93 (0.96-3.88)	0.065		
Pseudophakia	2.92 (1.94-4.40)	<0.0001		
Body Mass Index Category Under/Normal Overweight Obese	 1.21 (0.90-1.63) 1.17 (0.66-2.08)	 0.20 0.59		
Family History of Glaucoma	1.88 (1.21-2.93)	0.0054	1.88 (1.19,2.97)	0.0067
Diabetes Mellitus	1.59 (1.13-2.22)	0.0073	1.49 (1.05,2.11)	0.027
Self-Reported Hypertension	1.26 (0.93-1.70)	0.14		
Ever smoking history	1.00 (0.67-1.49)	0.99		
Hyperlipidemia	0.58 (0.29-1.15)	0.008		
Height (cm)	1.02 (1.01-1.04)	0.16		
Weight (kg)	1.02 (1.01-1.03)	.007		
Systolic Blood Pressure (mm Hg)	1.01 (1.00-1.014)	.068		
Diastolic Blood Pressure (mm Hg)	1.01 (1.00-1.03)	.08		
Intraocular pressure (mm Hg)	1.13 (1.09,1.17)	<.0001	1.12 (1.08, 1.17)	<0.0001

Spherical equivalent (D)	0.87 (0.84-0.90)	<.0001		
Axial length (mm)	1.35(1.25-1.46)	<.0001	1.36 (1.25,1.47)	<0.0001
Anterior chamber depth (mm)	1.30 (1.09-1.55)	.0032		
Central corneal thickness (microns)	1.00 (0.996-1.004)	0.99		
Vertical cup-disc ratio	2.46 (2.23-2.71)	<.0001		
Lens thickness (microns)	0.662 (0.435,1.006)	0.054		
Visual field mean deviation (dB)	0.847 (0.827,0.868)	<.0001		
*controlling for sex **independent risk factors are boldened				

Table 6. Age-specific Open Angle Glaucoma Prevalence (%) in different population studies

Study (exam dates)	*Population*	*50-59*	*60-69*	*70-79*	*>80*	*Total Age-Standardized***
United States Populations						
Chinese American Eye Study (2010-2013)	**Chinese Americans**	**2.8**	**4.8**	**8.7**	**14.8**	**5.21 (4.57-5.85)**
Baltimore Eye Study (1985-1988)	African Americans	4.2	6.2	8.9	12.9	6.15% (5.02-7.29)
Baltimore Eye Study (1985-1988)	Non-Hispanic white Americans	0.3	1.5	3.3	1.9	1.27% (0.74-1.79)
LALES (2000-2003)	Latino	2.9	7.4	14.7	21.8	7.50 (6.69-8.30)
Proyecto VER* (1997-1999)	Latino	0.6	1.7	5.7	12.6	2.63 (2.07-3.20)
Beaver Dam Eye Study (1987-1988)	Non-Hispanic White	1.3[1]	2.7[1]	4.7[1]		2.34 (1.88-2.80)
Asia-based Chinese Populations						
Singapore Chinese Eye Study* (2009-2011)	Urban Chinese	1.5	2.0	3.0	--	2.00 (1.46-2.54)
Yunnan Minority* (2010; 2016)	Rural Chinese	1.6	2.2	2.4	2.7	1.98 (1.63-2.33)
Beijing Eye Study* (2001; 2010)	Urban and rural Chinese	1.6	3.3	5.7		3.05 (2.43-3.67)
Handan Eye Study* (2007, 2011)	Rural Chinese	1.0	1.7	2.9	1.7	2.31 (1.86-2.76)
Other Non-US populations						
Kumejima* (2005-2006)	Japanese					4.38 (3.55-5.22)
Chennai Glaucoma Study* (2002-2004)	Urban and Rural Indian	3.6	4.1	5.9	10.2	4.59 (3.79-5.39)
Barbados Eye Study (1988-1992)	African descent	4.1	6.7	14.8	23.2	7.99 (6.99-8.98)

*utilized International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definition of OAG; ** 2010 Census data for Asian Population was used for age-standardization.
[1] Beaver Dam Eye Study age groups reported were: 55-64;65-74;75+

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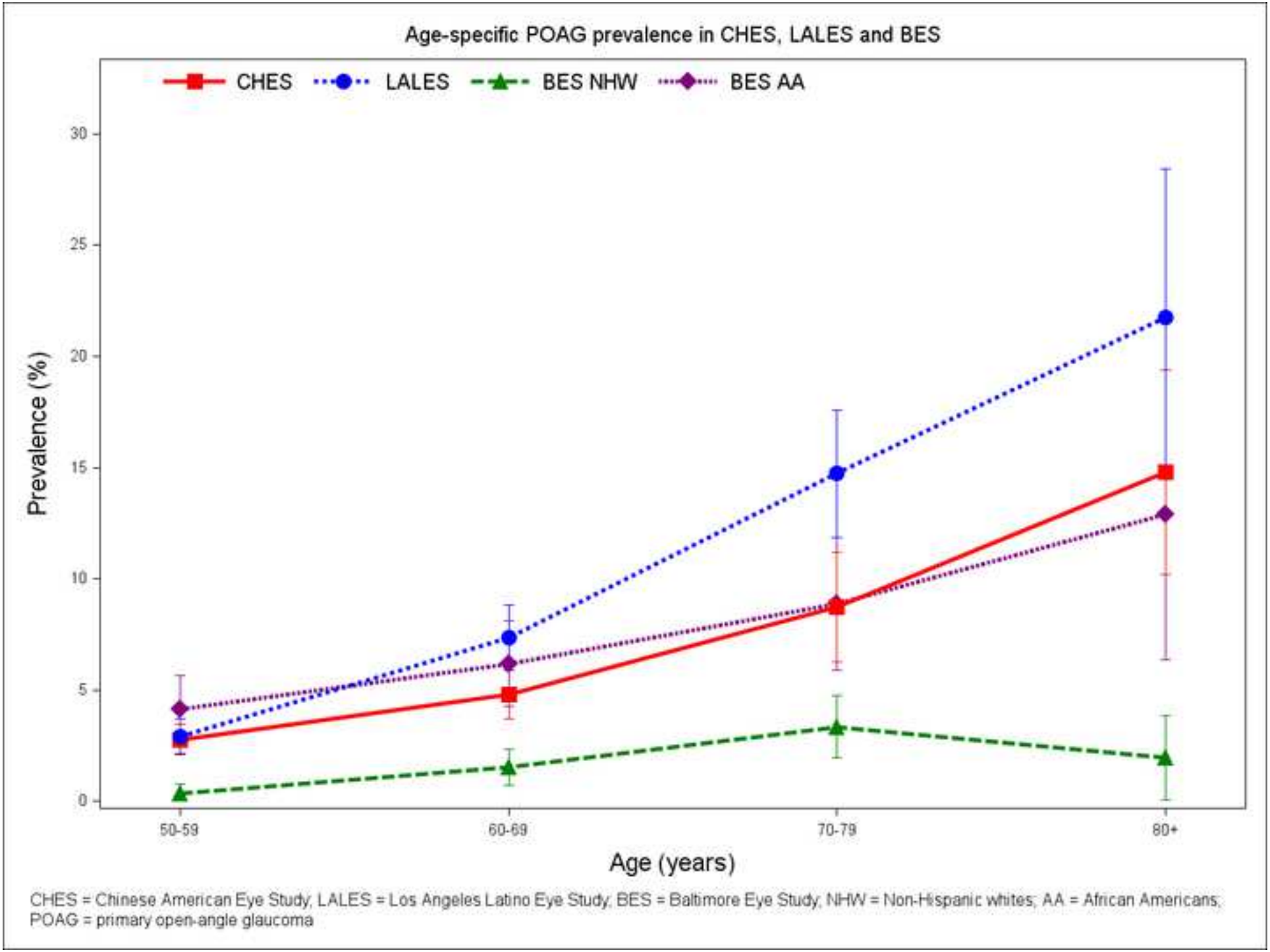

Chinese Americans had high prevalence of open angle glaucoma, with the majority having untreated intraocular pressure (IOP) under 21 mm Hg. Risk factors included older age, higher IOP, longer axial length, family history, and diabetes.

Highlights

- The prevalence of open angle glaucoma among Chinese Americans was 4.8%.
- This is higher than populations of European descent and Asia-based Chinese populations but lower than Latinos and those of African descent.
- 88.5% of Chinese Americans with OAG had baseline intraocular pressure (IOP) of 21 mmHg or less.
- Risk factors for OAG were older age, longer axial length, higher IOP, family history, and diabetes mellitus.
- Given the growing myopia epidemic, future research should investigate whether myopia prevention efforts can help mitigate the burden of glaucoma.

Supplemental Table. Frequency of specific diagnostic criteria for defining open-angle glaucoma in Chinese American Eye Disease Study Participants		
Diagnostic Criteria	N	%
Evidence of visual field and optic disc damage		
Open angle, ≥2 reliable, abnormal visual field tests with excellent congruence and optic disc damage, both characteristic of glaucoma	71	34.3
Open angle, 1 abnormal visual field test and optic disc damage, both characteristic of or compatible with glaucoma	39	18.8
End-stage disease with visual acuity ≤20/200 and a CDR of 1.0 and absence of visual field data	1	0.004
Open angle, Combinations of visual field and optic disc abnormalities with fair congruence between fields that are both compatible with glaucoma	51	24.6
Evidence of either visual field or optic disc damage		
≥1 abnormal visual field test that are characteristic of or compatible with glaucoma and no optic disc data available	0	0
Characteristic or compatible glaucomatous optic disc damage with no evidence of visual field abnormality	45	21.7

Declaration of Interest Statement

- No conflicting relationship exists for any author