

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.

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

Financial Support: This work was supported by grants U10 EY017337 (RV), K23 EY027855 (GMR), and K23 EY029763 (BYX) from the National Eye Institute, National Institute of Health, Bethesda, Maryland.

Conflict of Interest: No conflicting relationship exists for any author

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

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) \leq 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.

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 descent¹¹⁻¹⁴, 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 $\leq 20/200$ 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 ($\geq 180^\circ$). 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= $25.0\text{-}29.9 \text{ kg/m}^2$, 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 $\alpha = .05$ 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 ± 8.9 versus 69.1 ± 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 $\geq 180^\circ$, and absence of glaucoma (as defined in the Los Angeles Latino Eye Study¹⁷). 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 ≥ 24 mmHg, open angles $\geq 180^\circ$, and absence of glaucoma (per the Ocular Hypertension Treatment Study²³), 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 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), $P=0.0002$]. 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 ± 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 populations¹¹⁻¹⁴, 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 Study²⁵ and Indians in the Chennai Glaucoma Study,²⁶ lower than Los Angeles Latinos in LALES¹⁷ and African populations

in Barbados Eye Study²⁷ but similar to African Americans in the Baltimore Eye Survey²⁸(**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 Chinese¹¹⁻¹⁴ 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 $\geq 99.5\%$ 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 Study¹⁸ and the Melbourne Visual Impairment Project¹⁹, 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 $24.0 (\pm 1.32)$ 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 axons³⁷ 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 glaucoma⁵⁶, 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.

Acknowledgements

- A. **Funding/Support.** This work was supported by grants, U10 EY017337 (RV), K23 EY027855 (GMR), and K23 EY029763 (BYX) from the National Eye Institute, National Institutes of Health, Bethesda, Maryland.
- B. **Financial Disclosures.** No conflicting relationship or disclosures exists for any author.
- C. **Other Acknowledgments.** The authors wish to acknowledge the Chinese American Eye Study Group and the Chinese American Eye Study Data Monitoring and Oversight Committee as specified below.

The Chinese American Eye Study Group: Rohit Varma, MD, MPH (principal investigator); Roberta McKean-Cowdin, PhD (coinvestigator); Xuejuan Jiang, PhD; Stanley P. Azen, PhD (coinvestigator); Mina Torres, MS (project director); Chunyi Hsu, MPH (project manager); David Dinh, BA (research assistant); Ruzhang Jiang, MD (examiner); Jie Sun, MD, PhD, MPH (examiner); Dandan Wang, MD (examiner); YuPing Wang, Certified Ophthalmic Technician (examiner); Justine Wong, BA (clinical interviewer); Shuang Wu, MS (statistician); Bruce S. Burkemper, PhD, MPH (statistician), and Rucha Desai, MS (programmer). Battelle Survey Research Center, St Louis, Missouri: Lisa V. John, PhD (recruitment director); Michelle Cheng, MS (field supervisor).

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.

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Figure Caption

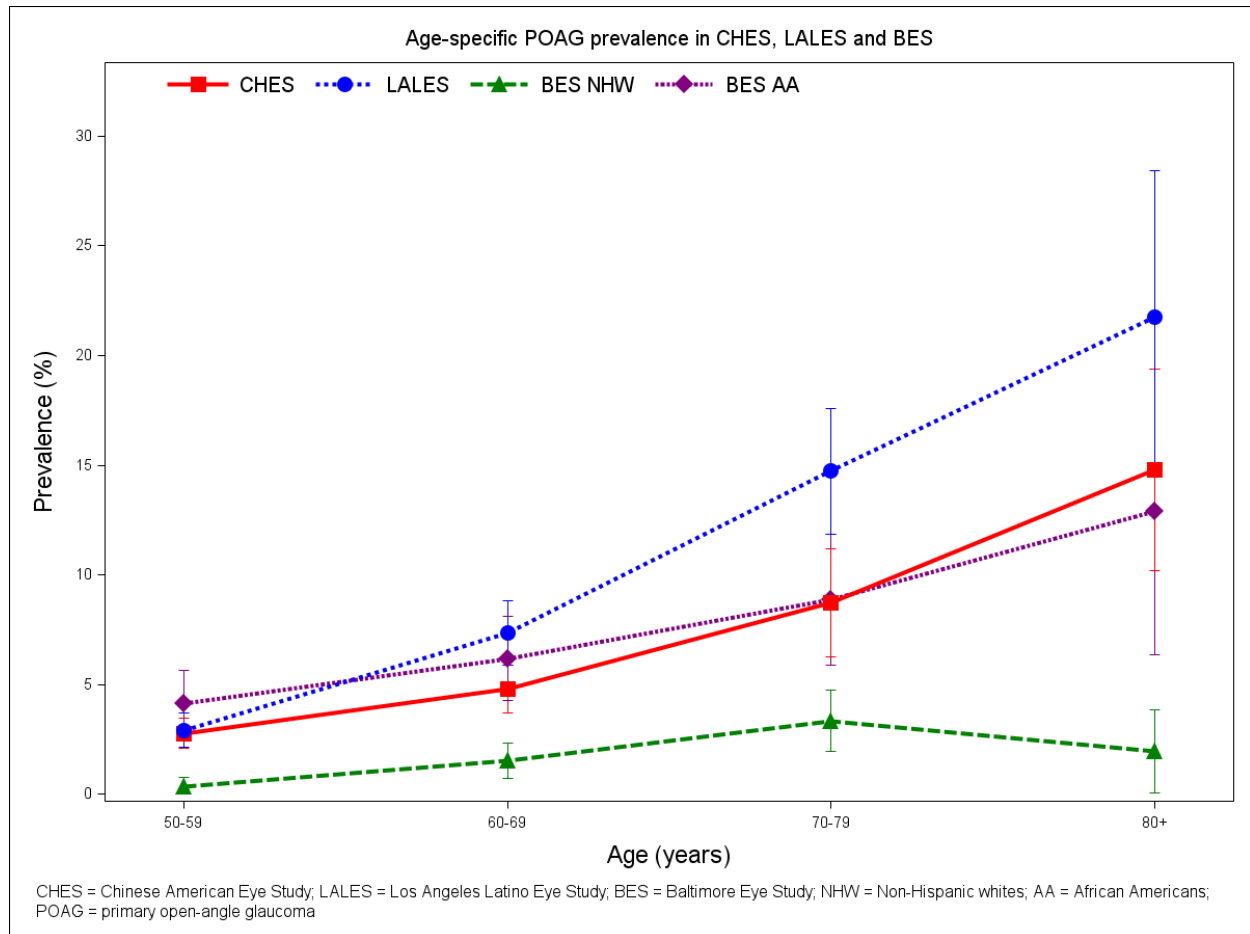


Figure 1. Age-Specific Prevalence of Primary Open Angle Glaucoma (POAG) in the Chinese American Eye Study (CHES), Los Angeles Latino Eye Study (LALES), and the Baltimore Eye Study (BES).

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	
<i>Age Group (yrs)</i>	<i>Total N</i>	<i>n (%)</i>	<i>95% CI</i>	<i>n (%)</i>	<i>95% CI</i>	<i>n (%)</i>	<i>95% CI</i>
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)			
<i>Mean +- SD</i>	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				
<i>Variable</i>	<i>Univariable Odds Ratio (95% CI) controlling for age</i>	<i>P-value (Chi-square)</i>	<i>Multivariable Odds Ratio (95% CI) *</i>	<i>P-value</i>
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	1.21 (0.90-1.63)	0.20		
Obese	1.17 (0.66-2.08)	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+						

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.

Declaration of Interest Statement

- No conflicting relationship exists for any author

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 $\leq 20/200$ 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