

Prevalence of Normal-Tension Glaucoma in the Chinese Population: A Systematic Review and Meta-Analysis



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- **PURPOSE:** To investigate the prevalence of normal-tension glaucoma (NTG) in the Chinese population through systematic review and meta-analysis.
- **DESIGN:** Systematic review and meta-analysis.
- **METHODS:** All Chinese population-based studies that reported the prevalence of NTG were identified. We searched PubMed and Chinese databases including Wanfang, China National Knowledge Infrastructure, and VIP for studies published before December 31, 2017. Random effects meta-analysis was conducted to estimate the pooled prevalence of NTG.
- **RESULTS:** Twelve studies were included in this review and meta-analysis, including 9 population-based studies and 3 studies from glaucoma clinics and managed care networks. The 9 population-based studies included a total of 30,892 subjects with 498 patients with primary open-angle glaucoma (POAG) and 354 patients with NTG. The prevalence of estimated NTG ranged from 0.36% to 1.98% and the percentage of NTG among POAG ranged from 51.43% to 83.58%. In the glaucoma clinic and managed care network studies, NTG prevalence was much lower. The overall pooled proportion of NTG among POAG in the Chinese population was 70.0% (95% confidence interval [CI] 62.0–77.0%). The overall pooled prevalence of POAG and NTG was 2.0% (95% CI 1.0–2.0%) and 1.0% (95% CI 1.0–1.0%), respectively. For the meta-regression of the NTG/POAG proportion, we found that age, gender, intraocular pressure, and China versus not China were not significantly associated with NTG/POAG prevalence, although the proportional prevalence decreased with increasing age category.

- **CONCLUSIONS:** In this systematic review, we found that NTG is common among patients with POAG in the Chinese population. Our findings can help guide future glaucoma studies and public health guidelines in the Chinese population. (*Am J Ophthalmol* 2019;199:101–110. © 2018 Elsevier Inc. All rights reserved.)

GLAUCOMA IS THE SECOND-LEADING CAUSE OF irreversible blindness worldwide,¹ comprised mostly of primary open-angle glaucoma (POAG). It affects >66 million people and it is estimated that there will be 79.6 million people globally with glaucoma in 2020.² POAG is common among Africans³ and whites.^{4,5} However, in recent years, the age-adjusted incidence of Chinese POAG has increased to a level similar to that of Western countries.⁶ As a common form of POAG, normal-tension glaucoma (NTG) accounts for a significant percentage.⁷

In 1857, Von Graefe described a kind of glaucoma that had typical glaucomatous cupping of the optic nerve, but the intraocular pressure (IOP) was within the statistically normal range. The next century provided additional clues, and glaucoma specialists increasingly came to regard this form as either NTG or low-tension glaucoma. In the early 1980s, NTG was considered a condition consisting of typical glaucomatous disc and corresponding visual field changes, an open angle on gonioscopy, and an IOP within the “normal” range.⁸ Meanwhile, the controversy surrounding NTG pertains not only to the definition and characteristics of the entity itself but to the fundamental questions it raises regarding the causal relationship between IOP and disc and field changes. Recently, NTG was defined as chronic OAG with progressive optic neuropathy and visual field defect(s), despite an untreated maximum IOP <21 mm Hg.⁹

NTG is common in Asia and comprises the majority (52–92%) of cases of POAG in Asian population-based studies. The calculated average proportion of NTG in Asia was 76.3% ± 12.4% in the studies that reported the proportion of NTG.¹⁰ The proportions are higher than in white populations (30–38.9%)^{4,11,12} and black populations (57.1%).¹³ In Asia, NTG is more frequent among the Japanese population, in which it accounts for 92% of POAG.⁷ Because of the uncertainty surrounding

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the prevalence of NTG in POAG in Chinese populations, we sought to address the prevalence of NTG reported in Chinese populations and estimate the percentage of NTG among patients with POAG through a systematic review and meta-analysis.

METHODS

• **SEARCH STRATEGY FOR ENGLISH AND CHINESE PAPERS:** This systematic review and meta-analysis was performed according to a prespecified protocol, and the methods used conformed to the Meta-analysis of Observational Studies in Epidemiology and was conducted under the guidance of Preferred Reporting Items for Systematic Reviews and Meta-Analyses.¹⁴ A systematic search was carried out in PubMed and Chinese databases including Wanfang, China National Knowledge Infrastructure, and VIP before December 31, 2017. The following search terms were used: ([low tension glaucoma [Medical Subject Headings {MeSH}] OR glaucoma, low tension OR low tension glaucomas OR normal tension glaucoma OR glaucoma, normal tension OR normal tension glaucomas OR normal-tension glaucoma OR NTG] OR intraocular pressure AND [China [MeSH] OR Chinese population]). The search was run according to MeSH and no language restrictions were applied during the literature search. We contacted some authors of previously published papers to determine if they had any unpublished NTG data. We also consulted the reference lists of included articles to find additional studies.

• **STUDY SELECTION:** In the present systematic review, studies were included if they met the following inclusion criteria: (1) were Chinese population-based studies and (2) evaluated the prevalence of POAG and NTG (or IOP <22 mm Hg). Studies were excluded if they met any of the following criteria: (1) studies were not conducted in human adults ≥18 years of age; (2) were not performed in a Chinese population; (3) had a population size <10; (4) covered POAG but did not clearly designate NTG; (5) covered POAG patients with normal IOP but under glaucoma treatment; (6) had an inability to obtain relevant data even after contacting the authors of the study; or (7) duplicated data.

• **DATA EXTRACTION:** Data were extracted and summarized from all eligible studies and any discrepancies were resolved by a comprehensive reassessment until consensus was reached. The following information was extracted for each study: (1) first author; (2) year of publication; (3) study scope (country, province, city, and district level); (4) study design; (5) age group; (6) number of subjects and response rate (if available); (7) number of patients with POAG; and (8) number of patients with NTG. We

calculated the NTG estimated prevalence and percentage of NTG among POAG in the Chinese population.

• **STATISTICAL METHODS FOR THE META-ANALYSIS:** Because of high anticipated levels of heterogeneity, we used a DerSimonian–Laird random effects model to estimate the pooled prevalence with a Freeman–Tukey double arcsine transformation¹⁵ to stabilize the variance to estimate the 95% confidence interval of NTG out of all patients with POAG in the studies. We used random effects meta-regression to estimate potential sources of heterogeneity, including the following variables: (1) eligible age range of the study; (2) proportion of female patients in the study^{16,17}; (3) mean IOP levels in the study; and (4) whether the study was conducted in China or outside of China. The I^2 statistic was used to determine heterogeneity across studies, which quantifies heterogeneity irrespective of the number of studies. It has been recommended to tentatively assign adjectives of low, moderate, and high to I^2 values of 25%, 50%, and 75%.¹⁸ We considered an association as statistically significant if the summary P value was < .05. Analyses were conducted using Stata software (version 14.1; StataCorp, College Station, TX, USA).

RESULTS

• **INCLUSION OF STUDIES:** Initially, 1393 studies were identified, comprising 563 from PubMed, 412 from China National Knowledge Infrastructure, 114 from Wanfang, and 304 from VIP. Among these studies, there were 679 duplicates that were excluded. Among 714 unduplicated studies, irrelevant studies were excluded through a title and abstract review, after which 40 potentially relevant studies were investigated with a full-text review. Among the 40 studies, 29 were excluded because 3 of them were reviews,^{10,19,20} 1 had patients with POAG who were under glaucoma treatment,²¹ 1 did not involve a Chinese population,²² and 24 did not meet our inclusion criteria. The main reasons for exclusion among the 24 studies were unclear designation of NTG and inclusion of patients with POAG with normal IOP (possibly NTG) but who were under glaucoma treatment. Since some of the coauthors of this systematic review are investigators with the Beijing Eye Study (BES) and have access to these data, we have added unpublished data from the BES, which was a population-based prospective cohort study performed in northern China.²³ The BES was carried out in 4 communities in the urban district of Haidian in the northern section of Central Beijing and in 3 communities in the village area of Yufa of the Daxing District south of Beijing. It has been described in detail recently.^{23–26} BES was approved by the Medical Ethics Committee of Beijing Tongren Hospital. Dr. Yaxing Wang from the Beijing Institute of

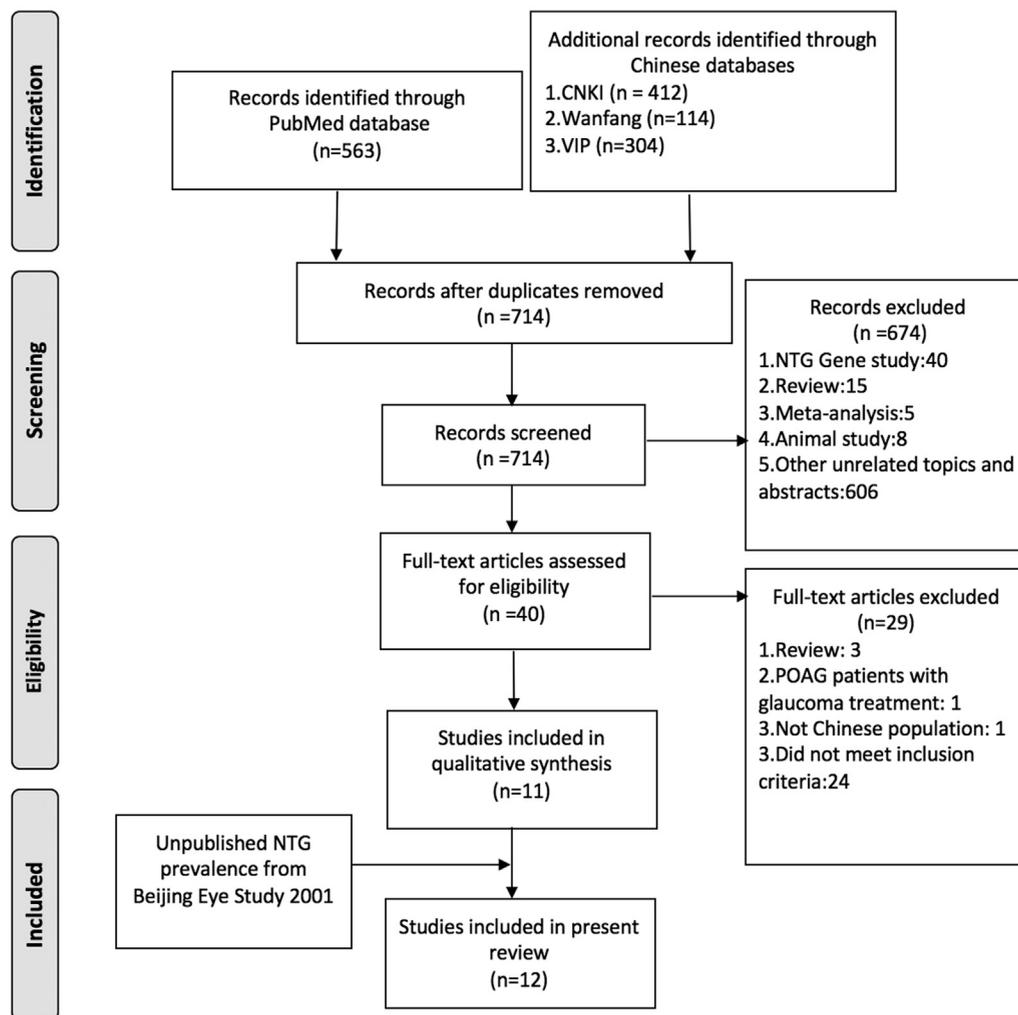


FIGURE 1. Flow chart of the systematic search and review. CNKI = China National Knowledge Infrastructure; NTG = normal tension glaucoma; POAG = primary open-angle glaucoma.

Ophthalmology, Beijing Tongren Hospital, Beijing, China, joined BES and has shared with us unpublished data on patients with NTG from the BES database. After exclusion of the unqualified studies and inclusion of data from the BES, 12 studies were included in our review, including 9 population-based studies and 3 studies from large glaucoma clinics and managed care networks. The 9 population-based studies involved a total of 30,892 subjects with 498 patients with POAG (including NTG) and 354 NTG patients. A flowchart for the literature search and the results is shown in Figure 1.

Eleven studies were published between 2006 and 2017, and all of the included studies reported NTG estimated prevalence and percentage of NTG among POAG, with a geographic distribution covering all 8 regions in China and 2 other countries (Singapore and the United States). Nine of the included studies were prospective studies and 3 were retrospective studies.

• **ESTIMATED PREVALENCE OF NTG IN THE CHINESE POPULATION:** In the Chinese population, the estimated prevalence of NTG ranged from 0.36% to 1.98% and the percentage of NTG among patients with POAG ranged from 51.43% to 83.58%. In Pudong,²⁷ the estimated prevalence of NTG was 1.98%, the highest of all included studies. In Liwan,²⁸ Beijing, and Singapore,²⁹ the estimated prevalence of NTG was between 1.28% and 1.53%. In other included studies,^{30–33} that prevalence was below 1.00%. In the Handan Eye Study,^{30,34} the percentage of NTG among patients with POAG was 83.58%, the highest of all included studies. In the Liwan Eye Study,²⁸ the percentage of NTG among patients with POAG was about 80%. In Beijing, Pudong,²⁷ Kailu,³¹ a Yunnan minority,³² and Bin County (Harbin),³³ those percentages ranged from 51.43% to 69.44%. The percentage of NTG among patients with POAG in the Chinese population outside of China was also high. In the Singapore Chinese Eye

TABLE 1. Characteristics of Studies Included in the Meta-analysis

| Reference, y | Province/City of Chinese Population | Study Type | Age Group, y | Subjects, n (Response Rate, %) | Patients With POAG, n (%) | Patients With NTG, n | Estimated NTG Prevalence, % | Percentage of NTG Among POAG |
|---|-------------------------------------|------------|--------------|--------------------------------|---------------------------|----------------------|-----------------------------|------------------------------|
| Liang and associates, ³⁰ 2011 | Handan | P | ≥30 | 6716 | 67 (1.00) | 56 | 0.83 | 83.58 |
| Wang and associates, ³⁴ 2011 | Handan | P | ≥30 | 66 | 47 | 39 | — | 82.98 |
| He and associates, ²⁸ 2006 | Liwan District, Guangzhou | P | ≥50 | 1504 (75.38) | 29 (1.93) | 23 | 1.53 | 79.31 |
| Baskaran and associates, ²⁹ 2015 | Singapore | P | ≥40 | 3353 (72.81) | 57 (1.70) | 43 | 1.28 | 75.44 |
| He and associates, ²⁷ 2015 | Pudong New District, Shanghai | P | ≥50 | 2528 (80.36) | 72 (2.85) | 50 | 1.98 | 69.44 |
| Unpublished, 2001 | Beijing | P | ≥50 | 4439 | 96 | 59 | 1.33 | 61.46 |
| Song and associates, ³¹ 2011 | Kailu County, Inner Mongolia | P | ≥40 | 5197 (87.36) | 73 (1.40) | 44 | 0.85 | 60.27 |
| Zhong and associates, ³² 2012 | Yunnan Minority | P | ≥50 | 2133 (77.79) | 22 (1.03) | 12 | 0.56 | 54.55 |
| Sun and associates, ³³ 2012 | Bin Country, Harbin | P | ≥40 | 4956 (86.00) | 35 (0.71) | 18 | 0.36 | 51.43 |

NTG = normal tension glaucoma; POAG = primary open-angle glaucoma; P = prospective.

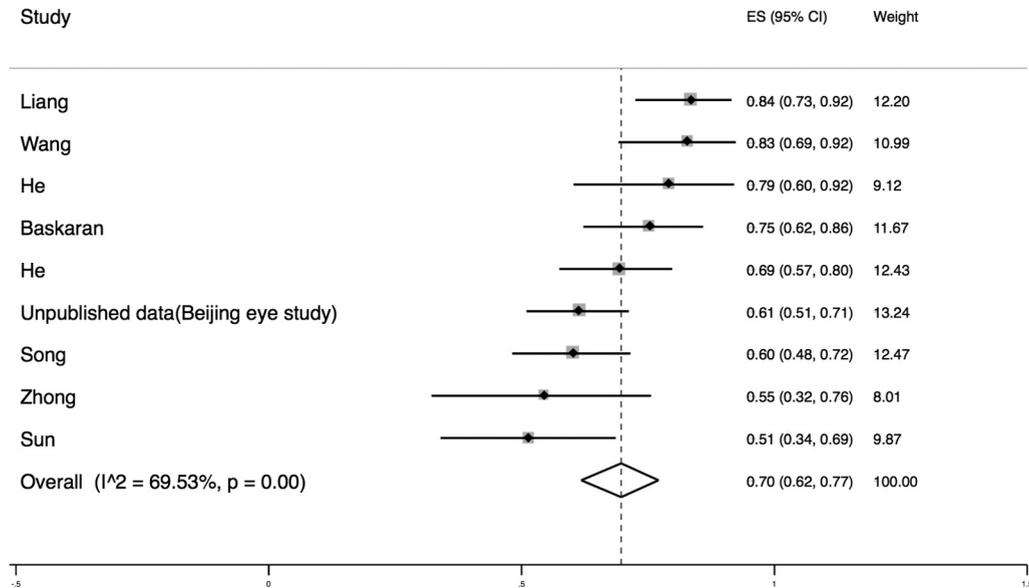


FIGURE 2. Forest plot of overall pooled prevalence of normal tension glaucoma among patients with primary open-angle glaucoma. CI = confidence interval; ES = effect size.

Study,²⁹ the estimated prevalence of NTG was 1.28%, while the percentage of NTG among patients with POAG was 75.44%. Table 1 shows the characteristics of all included studies.

• **NTG META-ANALYSIS RESULTS:** Pooled prevalence of NTG and POAG. In the systematic review, the overall

pooled prevalence of NTG among those with POAG was 70.0% (95% CI 62.0–77.0%). There was significant heterogeneity in NTG/POAG prevalence ($I^2 = 69.5\%$, $P < .001$; Figure 2). There was 1 small study³⁴ that was not in line with the other studies because it had only 66 patients with untreated POAG identified in the Handan Eye Study³⁰ who were invited to attend a follow-up study in

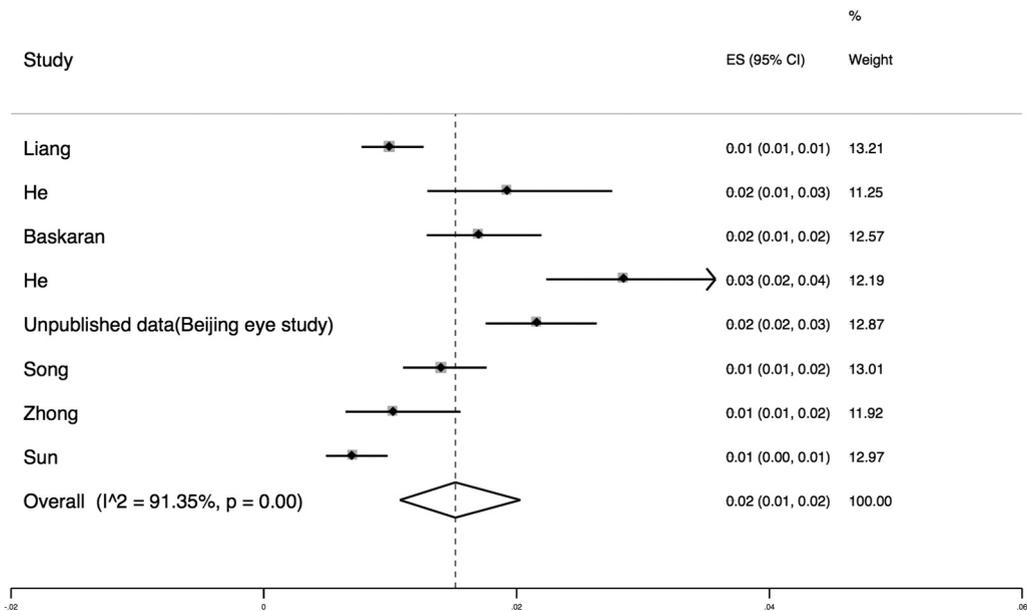


FIGURE 3. Forest plot of overall pooled prevalence of primary open-angle glaucoma. CI = confidence interval; ES = effect size.

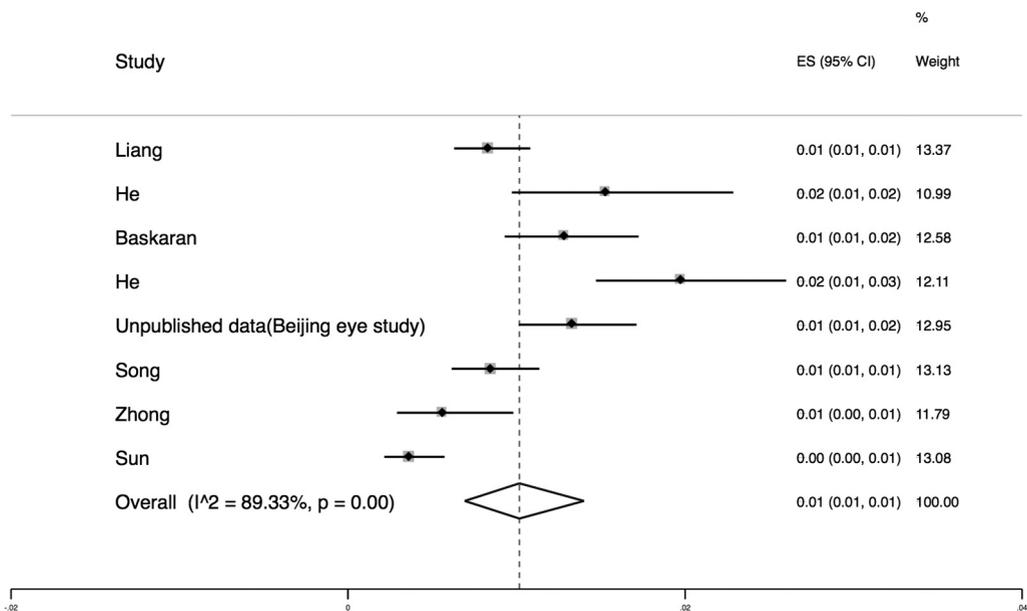


FIGURE 4. Forest plot of overall pooled prevalence of normal tension glaucoma. CI = confidence interval; ES = effect size.

which IOP was tested over 24 hours. These subjects were already in our analysis and thus we excluded this follow-up study before evaluating the overall pooled prevalence of NTG and POAG in Chinese populations. In the final analysis, the overall pooled prevalence of POAG and NTG was 2.0% (95% CI 1.0–2.0%) and 1.0% (95% CI 1.0–1.0%), respectively.

Both pooled estimates of overall POAG ($I^2 = 91.4\%$, $P < .001$) and overall NTG ($I^2 = 89.3\%$, $P < .001$) had substantial heterogeneity (Figures 3 and 4).

Meta-regression results for NTG/POAG. In order to estimate potential sources of heterogeneity, we used random-effects meta-regression. The difference in prevalence of eligible age range of the study was -19.4% (>40 group vs >30 , 95% CI -39.2 – 0.3% , $P = .05$) and -16.4% (>50 group vs >30 , 95% CI -35.1 – 2.3% , $P = .08$; Table 2). The difference in prevalence per 1-unit increase in proportion female was -1.0% (95% CI -3.7 – 1.6% , $P = .38$). The difference in prevalence per 1-unit increase in IOP was 4.2% (95% CI -7.2 – 15.6% , $P =$

TABLE 2. Meta-regression Results for Normal Tension Glaucoma/Primary Open-Angle Glaucoma: Difference in Prevalence Using Demographic Characteristics

| Parameter | Difference in Prevalence | 95% CI ^a | P Value |
|---------------------------------|--------------------------|---------------------|---------|
| Age, y | | | |
| >30 | Reference | | |
| >40 | -19.4% | -39.2% to 0.3% | .05 |
| >50 | -16.4% | -35.1% to 2.3% | .08 |
| Gender (female) | -1.0% | -3.7% to 1.6% | .38 |
| IOP | 4.2% | -7.2% to 15.6% | .41 |
| Studies from China ^a | 2.4% | -21.2% to 26.0% | .82 |

CI = confidence interval; IOP = intraocular pressure.

^aDifference in prevalence for studies in China vs those not in China.

.41). The difference in prevalence for studies in China vs not in China was 2.4% (95% CI -21.2–26.0%, $P = .82$; Table 2). None of the meta-regression results were statistically significant. It is possible that some of the heterogeneity in studies in the NTG/POAG pooled prevalence is related to differences in included age ranges in the studies.

• **ESTIMATED PREVALENCE OF NTG IN THE CLINIC:** In glaucoma clinics, the prevalence of NTG among patients with POAG in the Chinese population was much lower. There were 106 patients with NTG among 400 patients with POAG in the Hong Kong Eye Hospital and the Eye Clinic of the Prince of Wales Hospital,³⁵ where the percentage of NTG among POAG was 26.50%. Yan and associates³⁶ reported that there were 4383 patients with glaucoma seen in the glaucoma clinic of Beijing Tongren Eye Center between 2014 and 2016; 1321 of them had POAG and only 10 patients were diagnosed with NTG. Therefore, the percentage of NTG among patients with POAG in the Tongren Eye Center study was 0.76%. In the United States,³⁷ among 2,259,061 beneficiaries ≥ 40 years of age who were enrolled in a large, national managed care network in 2001 to 2007, 15,918 were determined to be Chinese-Americans, and 917 of them had POAG, while 99 were patients with NTG. The overall percentage of NTG among patients with POAG was 10.80%. Table 3 shows the proportion of NTG in glaucoma clinics or managed care networks in the Chinese population.

DISCUSSION

TO THE BEST OF OUR KNOWLEDGE, THIS IS THE FIRST systematic review and meta-analysis of all reported estimated prevalence of NTG in Chinese populations. This study involved a total of 30,892 subjects with 498 patients with

POAG and 354 patients with NTG and was conducted to investigate the prevalence of NTG in the Chinese population and to understand the percentage of NTG among patients with POAG. We confirmed that NTG is common in the Chinese population.

In the present study, the percentage of patients with NTG among patients with POAG ranged from 51.43% to 83.58%, and the overall pooled prevalence of NTG among those with POAG was 69.8%, which is similar to the calculated average proportion of NTG in Asia ($76.3 \pm 12.4\%$) in a recent systematic review.¹⁰ The overall pooled prevalence of POAG and NTG in the present study was 2.0% and 1.0%, respectively.

It has been established that the percentage of NTG among patients with POAG varies significantly by region, from 30% to 92%^{10,30} worldwide. For white populations, it is 30% in the Egna-Neumarkt Study from Italy,¹¹ 31.0% in the Reykjavik Eye Study from Iceland,³⁸ 31.7% in the Beaver Dam Eye Study from the United States,¹² and 38.9% in the Rotterdam Study from the Netherlands.³⁹ According to some studies conducted in the 1960s to 1980s,^{40–42} NTG was common in white populations at that time, accounting for $\geq 50\%$ of all cases with POAG. Overall, the proportion of NTG in POAG in the white population was similar to that in the Chinese population several decades ago but is perhaps now lower than that in the Chinese population currently. For the black populations, it is 57.1% in a rural district in South Africa¹³ and about 30% in the Barbados Eye Study from North America,⁴³ suggesting that the prevalence of NTG is lower in black populations than in the Chinese population.

Within Asian populations, there is also significant variability in the proportion of POAG attributable to NTG. The highest prevalence of NTG has been reported in Japan (Tajimi study, 92%⁷) and Singapore (Singapore Malay Eye Study, 84.6%⁴⁴), followed by north China (Handan Eye Study, 83.6%³⁰), urban south India (Chennai Glaucoma Study, 82%⁴⁵), south China (Liwang Eye Study, 79.3%²⁸) and South Korea (The Namil Study, 77%⁴⁶). The percentage of NTG among patients with POAG in south India was reported to be 66.7% in the Andhra Pradesh Eye Study,⁴⁷ 67.2% in the Chennai Glaucoma Study,⁴⁸ and 52.3% in the Aravind Comprehensive Eye Survey,⁴⁹ which are similar to the prevalence of NTG in most areas of China.

There are several risk factors for the development and progression of NTG. First, patients with NTG tend to be older than patients with POAG.⁵⁰ The aging population of China could potentially explain the high prevalence of NTG in this population. The second risk factor is gender. Females, who are known to more frequently suffer optic nerve head damage and have longer life spans compared with males, also more frequently have NTG.^{16,17} The third risk factor is central corneal thickness. Several studies showed a thinner mean central corneal thickness

TABLE 3. Proportion of NTG in Glaucoma Clinics or Managed Care Networks in the Chinese Population

| Reference, y | Province/City of Chinese Glaucoma Patient | Study Type | Age Group, y | Patients with Glaucoma, n | Patients With POAG, n | Patients With NTG, n | Percentage of NTG Among POAG |
|--|---|------------|-------------------|---------------------------|-----------------------|----------------------|------------------------------|
| Lam and associates, ³⁵ 2006 | Hong Kong (Eye Hospital) | R | 8–91 ^a | | 400 | 106 | 26.50 |
| Stein and associates, ³⁷ 2011 | United States | R | ≥40 | | 917 | 99 | 10.80 |
| Yan and associates, ³⁶ 2017 | Beijing (Tongren Eye Center) | R | 0–92 ^a | 4383 | 1321 | 10 | 0.76 |

NTG = normal tension glaucoma; POAG = primary open-angle glaucoma; R = retrospective.

^aAge group of all patients with glaucoma in the clinic or network, including patients with congenital glaucoma.

in patients with NTG.^{51–54} Fourth, systemic vascular diseases are known risk factors of NTG,^{55,56} including migraine,^{17,57} systemic low blood pressure,⁵⁸ low diastolic ocular perfusion pressure,⁵⁹ Alzheimer disease,^{60–62} primary vascular dysregulation (PVD),⁶³ Flammer syndrome,⁶⁴ and others. Some systemic vascular diseases, such as hypotension, could increase the risk of NTG progression because of optic nerve hypoperfusion.⁵⁸ Vasospasm, which is perhaps related to migraine, was found to be more common in female¹⁷ and Asian populations.⁶⁵ It has also been reported that 60% of all patients diagnosed with dementia live in Asian countries^{66,67}; for example, China is among the top 7 countries with the greatest prevalence of patients with dementia. PVD syndrome, which is associated with blood flow reduction, was frequently observed in patients with NTG.⁶³ Interestingly, patients with PVD syndrome were reportedly more susceptible to migraines,⁶⁸ and PVD syndrome occurs more frequently in females than in males⁶⁹ and in Japanese patients more than in white patients.⁷⁰ Overall, systemic vascular diseases were more common in Asian populations, especially in Japanese and Chinese populations, which could explain the high prevalence of NTG in these populations.^{66,67,70} Ambulatory monitoring of systemic vascular diseases could become part of routine assessment of patients with NTG in China. Other risk factors of NTG are genetics,^{71,72} obstructive sleep apnea syndrome,^{73,74} metabolic syndrome,⁷⁵ and myopia.⁷⁶

In relation to the percentage of patients with NTG among patients with POAG, myopia was found to be a reason for the high proportion of NTG. Myopia has emerged as a major health issue in east Asia,⁷⁷ especially in Japan and China,^{78,79} and the prevalence of myopia in Japanese and Chinese populations were similar to that in other Asian surveys but higher than in white or black populations.^{80,81} At the same time, NTG prevalence was reported to be the highest in Japanese populations, which perhaps has resulted in the prevalence of NTG and POAG being higher in this group than in whites and blacks.⁸² Grørdum and associates⁸³ demonstrated that an association between

myopia and glaucoma was stronger at lower IOP levels and weakened gradually with increasing IOP, indicating that myopia is an important risk factor, particularly for NTG.^{50,84}

For meta-regression in our study, there was a nonsignificant decrease in the percentage of NTG among patients with POAG with increasing age category. It is possible that some of the heterogeneity in studies about NTG among POAG pooled prevalence is related to differences in included age ranges in the studies. Our meta-regression shows the possibility that the percentage of NTG among patients with POAG is going down as the age range gets older, but future studies are needed to prove this trend. However, no other variables were found to be associated with NTG prevalence, although a higher proportion of females in the study population was associated with a higher prevalence of NTG.

In the present study, the proportion of NTG out of POAG in glaucoma clinics or managed care networks in Chinese populations was much lower than that in the Chinese population, which shows that NTG is at risk of being seriously underdiagnosed, particularly in retrospective studies. It was 0.76% in Tongren Hospital, Beijing, 10.80% in a national managed care network in the United States (2001–2007), and 26.5% in Hong Kong Eye Hospital and the Eye Clinic of the Prince of Wales Hospital. Interestingly, a low prevalence of NTG in glaucoma clinics was also reported in other studies. In west Africa, the percentage of NTG among patients with POAG was only 6.3% in Douala General Hospital, Cameroon.⁸⁵ In the Congo, it was reported as 2.36% at a nonuniversity center between 1991 and 1995.⁸⁶ In central Sweden, it was reported as 23.5%,⁸⁷ which is more similar to the prevalence of NTG in Hong Kong. In the west coast of Iceland, the survey population in the eye clinic of Akranes ≥50 years of age was 1443, and NTG was only noted in 3 cases (5.5%).⁸⁸ Overall, the percentage of NTG among patients with POAG in glaucoma clinics is roughly <30% worldwide, although many patients with NTG may not know they have glaucoma and this may lead to poor outcomes. This issue of underdiagnosis is a worldwide problem. The

education regarding NTG and the need for regular eye examinations among the populace may be helpful in catching it early and preventing its progression toward blindness, especially for those at elevated risk and in countries where there is a high prevalence.

There are several limitations that need to be acknowledged. First, a main limitation of this systematic review is that for some of the NTG studies included, only 1 IOP measurement was conducted in the daytime, which may not reflect the range of IOP values of the tested subjects at other time points and might generate bias toward a higher rate of NTG. Many population-based studies performed in Asia only define NTG with a single IOP measurement in the day, which could inflate the prevalence of NTG in the Asian population. Therefore, follow-up IOP measurements and possible diurnal curves of IOP can be recommended for population-based studies in the future. Second, there was substantial heterogeneity between the studies, which may result from differences in study designs, targeted populations, analysis strategies, and participant characteristics. Third, few tools exist to assess the quality

of observational studies of disease prevalence.⁸⁹ Of the few tools that exist, there are significant limitations that preclude their use, including the lack of discrimination between internal and external validity, and none have been widely adopted for assessing the risk of bias. As a result, we were unable to adequately perform a risk of bias assessment without significant modification of existing tools. Fourth, some patients with POAG may have been under glaucoma treatment and have a normal IOP; therefore, these patients would not be diagnosed as having NTG. However, in our systematic review, we excluded the studies with unclear glaucoma treatment data.

In conclusion, this systematic review and meta-analysis provides evidence of a high percentage of NTG among patients with POAG in the Chinese population. The results also corroborate the predicted trend of NTG prevalence in Asia. However, the proportions of patients with NTG are much lower in the glaucoma clinic populations that have been studied, suggesting that regular eye examinations with vigilance in detecting NTG in the Chinese population are highly recommended.

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