Primary-Open Glaucoma and Myopia:
A Narrative Review

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ABSTRACT
Refractive errors and primary open-angle glaucoma are common eye conditions in the United States. The identification and quantification of risk factors for primary open-angle glaucoma is critical to understanding and managing the disease process from both individual and public health perspectives. This narrative review was conducted to present the epidemiology of primary open-angle glaucoma and to summarize epidemiologic findings on myopia as a risk factor. Epidemiologic evidence suggests an increasing prevalence of primary open-angle glaucoma over the last decade in the United States. It has been documented that primary open-angle glaucoma prevalence increases with age, and that African Americans tend to have the highest estimates. Epidemiologic data, however, are not as clear with respect to gender differences. Other factors that have been identified are increased intraocular pressure and the use of steroids. The evidence for increased risk of primary open-angle glaucoma among myopes is stronger for moderate and severe myopia and not as clear for mild myopia. The association between primary open-angle glaucoma and its multiple risk factors is complex.

INTRODUCTION
Refractive errors (RE) and primary open-angle glaucoma (POAG) are common eye conditions in the United States.1 Myopia or nearsightedness is the most common form of RE. It can be defined as having a RE of -1.0 Diopters (D) or more. The National Eye Institute estimates RE affects more than 30.5 million people >40 years old.

POAG is a progressive, chronic optic neuropathy in adults where intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which, in the absence of other identifiable causes, there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons.2 In POAG the susceptibility of the optic nerve to damage varies among patients. The vision lost to POAG is irreversible. Glaucoma affects approximately 2.2 million adults in the United States, about 1.9% of people >40.1 years old.3 POAG is the most common form of glaucoma, and as many as half of those with POAG are unaware that they have the disease.3,4 Glaucoma of all types is the second most common cause of legal blindness in the United States and the leading cause of legal blindness among African Americans.5 It has been estimated recently that 130,000 persons in the United States are blind as a result of POAG.4 More than 7 million office visits occur per year for the primary purpose of monitoring patients with glaucoma and patients at risk for developing it.6,7 The magnitude of the problem will most likely increase as the American population ages.

The identification and quantification of risk factors for POAG is critical to understanding and managing the disease process from both individual and public health perspectives. For an individual, knowing the risk for POAG can influence behaviors; it also affects the decision-making by the health care professional, and the compliance and follow-up by the patient. From the public health point of view, developing programs specifically targeting vulnerable populations to identify and treat those with POAG is crucial. Knowledge of the risk factors associated with POAG is necessary to provide preventive measures to reduce the public health burden of this disease.

This review was conducted to present the epidemiology of POAG and to summarize epidemiologic findings on myopia as a risk factor for POAG.

METHODS
The Pub Med Database from the National Library of Medicine was used to conduct a literature search on
Epidemiologic data, however, are not as clear with respect to gender differences, both within and outside the United States (Figures 3 and 4). Some studies show higher prevalence in men, while others report higher prevalence in women. One example is a study conducted in Thailand that reported after aged-standardization POAG was more prevalent in women than in men ($P=0.006$).

There are also differences by race; African populations or populations with African ancestry tend to have the highest POAG prevalence compared to other races (Table 1). Furthermore, some researchers have postulated that even within African populations differences in POAG prevalence can be observed, with some groups demonstrating a prevalence similar to that observed in white, Asian, or Hispanic populations (Table 1). The prevalence in Nigeria was reported as 1%-2%, similar to the prevalence observed in white populations in Italy (2.5%), Spain (2.2%), Australia (1.8%), and in Hispanics in Arizona (1%). In the United States, African Americans have the highest prevalence (Figure 4). The American Academy of Ophthalmology reported that the prevalence of POAG in African Americans is 4.7 (95% CI 3.8 to 5.8) compared to 1.3 (95% CI 0.8, 1.8) in whites. Some researchers looked at office visits in the United States for glaucoma and found that about 9 out of 10 (88.3%) of the visits were made by white people. Further evaluation of the visit rate by race did not show a significant difference (3.7 per 100 for whites versus 3.0 per 100 for African Americans).

Other Risk Factors
Family history of glaucoma is a known risk factor for POAG. A study conducted in Barbados with probands and relatives showed a high prevalence of the disease among relatives (9.5%). In an attempt to identify other risk factors that may be associated with the disease, this study also compared siblings with and without POAG. The siblings with POAG had higher intraocular pressure (IOP) levels, lower differences for diastolic blood pressure minus IOP levels, and more myopia.

Some studies suggest that genetic characteristics may be responsible for an increased risk among relatives. Recently, researchers mapped a new adult-onset POAG locus on 5q22.1 (GLC1G), and identified its disease-causing gene (WDR36). New genetic discoveries provide a better understanding of the mechanisms involved. Additionally, genetic research provides the opportunity for the development of diagnostic techniques that possibly can be helpful in the identification of high-risk individuals at an early stage of the disease.
Another factor that may be associated with increased risk for POAG is the use of steroids. Some studies reported that steroid use in elevated IOP patients can increase the risk for glaucoma.46-48 One study reported that, after controlling for RE, the use of ocular corticosteroids presented an approximate 6-fold increase in the risk for POAG (OR=7.79, 95% CI=2.73, 22.21).39

Additionally, increased IOP has been implicated in the loss of optic nerve fibers, and therefore can increase the risk for glaucoma.50-52,42 However, approximately 15%-40% of patients with otherwise characteristic POAG will have an IOP consistently below 21 mmHg.43 These patients constitute a subgroup of POAG commonly referred to as normal-tension glaucoma. Therefore, the effectiveness of IOP measurements as a diagnostic tool is limited. Furthermore, only between 25%-50% of patients with elevated IOP develop glaucoma.44-47 Because the mechanisms for normal-IOP glaucoma are not clear, further research is warranted.

**Myopia as a Risk Factor**

The evidence for increased risk of POAG among myopes is stronger for moderate and severe myopia and not as clear for mild myopia.48-51 As early as 1948, Posner and Scholssman presented data that suggested a myopic eye was as susceptible to glaucoma as a hyperopic eye.52 Today it is still unclear if the increased risk is associated with increased IOP levels or with the increased susceptibility to nerve damage of the myopic eye. Most of the studies were not designed to answer this question. Researchers in Japan conducted a 5-year follow-up of 122 patients with POAG and IOP levels <25 mmHg in order to estimate the risk for visual field loss.48 Severe myopia was identified as the only risk factor associated with visual field loss after adjustment for other factors such as mean IOP, age, gender, baseline cup-to-disk ratio, and use of topical β-adrenergic antagonists. Researchers only reported the Chi-Square (χ²) and the P-value as the measure of correlation; for refractive error, χ²=5.17 (P-value=0.02). This finding points toward an independent effect of myopia when increased IOP levels are not present. In 1994, Quigley and colleagues reported a risk ratio (calculated by Cox proportional hazard model) for visual field loss of 2.09 (95%CI 0.85 to 5.14) for severe myopia (-4.5 to -12.0D) and 1.53 (95%CI 0.70 to 3.34) for mild myopia (-0.125 to -4D), however these estimates were not statistically significant.49

The observed associations between myopia and POAG may be explained by a surveillance bias for POAG in cases of myopia, resulting in an increased false positive rate for the diagnosis of POAG, compared with emmetropes. In myopes the disks may appear glaucomatous with larger diameters, greater cup-to-disk ratios, and larger and shallower optic cups.53,54 The vast majority of ophthalmologists believe that myopes have an increased sensitivity to elevated IOP and will interpret the abnormal optic nerve head findings as glaucomatous cupping resulting in an over-diagnosis of POAG. The clinical diagnosis of POAG in myopia is difficult and fraught with uncertainty.55 Multiple factors lead to the high false positive POAG cases with myopia including a greater frequency of office visits to the eye doctor, increased visual field perimetry testing, increased abnormal visual field perimetry secondary to the corrective lens, falsely elevated IOP, over-interpretation of optic nerve findings, and practitioners' belief of an increased susceptibility to POAG and of a strong association with POAG.54,55

Recent studies have provided additional evidence on increased risk associated with myopia.50,51 A population-based study conducted in Wisconsin showed that myopes were 60% more likely to have glaucoma than emmetropic patients (OR=1.60, 95% CI=1.1, 2.3).51 Other researchers have looked at the risk factors associ-
ated with the progression from elevated IOP to POAG.
In a study that estimated the odds ratio for POAG compared to increased levels of IOP, multivariate analysis showed old age, myopia, and increased IOP at diagnosis were significantly associated with POAG.\textsuperscript{50}

Interactions between the risk factors may be important. The interaction between RE and elevated IOP levels is of particular interest. Researchers have postulated that the presence of RE and elevated IOP levels can have a synergistic effect.\textsuperscript{56} This means that the risk for the combined effect is higher than the sum of 2 independent effects. These researchers also showed that the observed excess risk for those with both factors was 11.16, compared to the expected excess risk of 5.04, based on adding the 2 individual risks. This indicates patients with both factors are at a much higher risk for developing POAG compared to those without any of the factors, or to patients with just 1 or the other.

**CONCLUSIONS**

The epidemiologic evidence suggests that severe myopia and elevated IOP are risk factors for the development of POAG. Particular attention should be given to patients who present with both elevated IOP levels and myopia, and patients with family history (close relatives with POAG), as the combined presence of these factors will place the patient at a much higher risk. Other important risk factors are age, race, and use of corticosteroids. The association between glaucoma and its multiple risk factors is very complex. There is need for the development of a risk calculator that could take into account independent effects as well as effect modification (interactions) when multiple factors are present.

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**REFERENCES**


### Table 1. Prevalence of POAG by Race

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<tr>
<th>Source</th>
<th>Location</th>
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<td>-</td>
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<tr>
<td>Iwase, A et al, 2004\textsuperscript{25}</td>
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NA=not available

* 99% Confidence Interval


44. Fleming C, Whitlock EP, Beil T, Smit B, Harris RP. Screening for primary open-angle glaucoma in the primary care setting: continued on page 95
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