CASE WESTERN RESERVE UNIVERSITY
School of Medicine

Master of Public Health Program

MPH practicum: Familiarizing with TriNetX and Open-Angle Glaucoma

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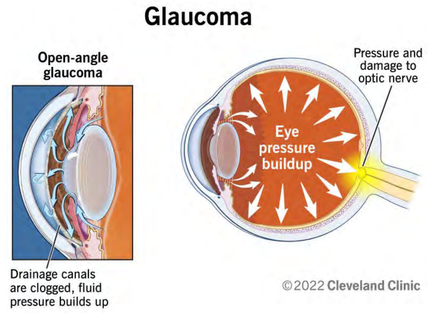
Background

- Glaucoma is the leading cause of blindness worldwide, estimated to affect over 70 million people in 2020
- **Primary open-angle glaucoma (POAG)** is a chronic type of glaucoma, the mechanism for which is poorly understood
  - Main known risk factor is intraocular pressure (IOP)
- **Normal tension-glaucoma (NTG)** is similar to POAG, but patients have normal IOP
- TriNetX is a large national database platform with data from >70 million patients



Goals

1. To perform a thorough literature search on POAG and NTG to discover which public health-relevant comorbidities would be best to explore for my capstone.
2. Learn about statistical techniques that can be applied using the TriNetX platform (e.g. calculating odds ratios using propensity scores, creating forest plots on R)

Activities and deliverable

Literature search on glaucoma:

- Reading reviews on POAG and NTG to learn about disease pathophysiology and epidemiology
- Using key references from reviews to read further into key primary sources
- Learning which systemic conditions or demographic characteristics have been associated with POAG and NTG in the past

Statistics and TriNetX:

- Familiarizing with concept of propensity score matching
- Learning how to generate forest plots of odds ratios using R and RStudio
  - Learned some foundational statistical skills in MPHP 431 & 432
- Playing with TriNetX platform to understand how to use it for calculating odds ratios

Deliverable:

Summary of findings culminating in a final list of potential comorbidities and demographic characteristics I pursued correlating with POAG and NTG in TriNetX.

Findings

I thoroughly read 34 articles about open angle glaucoma and associations with various systemic conditions, psychiatric conditions, and demographic characteristics based on review articles and recommendations from my PI.

Final list of associations that can easily be explored with TriNetX:

- Demographics
  - Race, ethnicity
- Cardiovascular diseases:
  - Sleep apnea, obesity, hypertension, hypotension, hyperlipidemia, diabetes mellitus, stroke
- Vascular dysfunction
  - Migraine, Raynaud syndrome
- Neurodegenerative
  - Multiple sclerosis, optic neuritis, Alzheimer's, Parkinson's
- Psychiatric
  - Major depressive disorder, generalized anxiety disorder
  - Use disorders: alcohol, cannabis, opioid, tobacco

All systemic conditions will be associated with POAG and NTG using propensity score 1:1 Greedy matched cohorts.

Lessons learned

1. Open angle glaucoma, especially POAG, has particularly affected Black individuals for reasons that are unclear. GWAS studies and sociodemographic analyses have been performed to understand how much genetics vs. socioeconomic status contributes to this effect. So far, potentially both seem true[1,2].
2. POAG is a complex disease with an unclear underlying pathophysiology. Whereas NTG has stronger associations with certain conditions, such as vascular dysfunction[3], giving a sense of its mechanism, POAG is not regularly associated with any given condition. I sought to validate this with a much larger database to ensure the lack of association has not been due to lack of power.

Public health implications

POAG is a disease that has few known risk factors other than family history, older age, and Black race. Understanding its epidemiological patterns and associations would help to establish screening guidelines and better understand the mechanisms of the disease.

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References
1. Hauser MA, Allingham RR, Aung T, et al. Association of Genetic Variants With Primary Open-Angle Glaucoma Among Individuals With African Ancestry. JAMA. 2019;322(17):1682-1691.
2. King AJ, Hudson J, Azuara-Blanco A, et al. Effects of socioeconomic status on baseline values and outcomes at 24 months in the Treatment of Advanced Glaucoma Study randomised controlled Trial. Br J Ophthalmol. 2024;108(2):203-210.
3. Killer H, Pircher A. Normal tension glaucoma: review of current understanding and mechanisms of the pathogenesis. Eye. 2018;32(5):924-930.

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