Risk factors influencing the effectiveness of referral to intermediate or tertiary specialist care for patients initially suspected of having glaucoma – Protocol for a systematic review and meta-analysis

Jack Phu, Henrietta Wang, Michael Kalloniatis, Gordon Doig

Centre for Eye Health, UNSW

BACKGROUND

The present study aims to understand risk factors that influence the effectiveness of the referral process by primary care optometrists to intermediate or tertiary specialist care for patients suspected to have glaucoma.

METHODS

This systematic review and meta-analysis will be conducted and reported in compliance with established methodological guidelines.[1, 2] Study selection, risk of bias and data abstraction will be undertaken by at least two investigators. Disagreements will be settled by obtaining the opinion of a third investigator. Majority decisions will prevail.

LITERATURE SEARCH

PubMed (www.pubmed.gov) and EMBASE (www.embase.com) will be searched using appropriate combinations of MeSH and Emtree terms to identify the main topics of interest.[3, 4] Complete search strategy details will be reported in the Online Supplement at the time of manuscript publication. We will not use any language restrictions in the electronic search. Reference lists of retrieved primary studies and review articles will be manually searched for additional references not captured in the electronic search. Close out date of the electronic search will be reported in the main manuscript.

STUDY SELECTION

All studies evaluating primary care optometrist referrals for suspected glaucoma to intermediate or tertiary specialist care will be reviewed for eligibility. Any study assessing pathways (health services and delivery research[5]) from a primary care optometrist to an intermediate or tertiary care clinic will be considered for inclusion. We will define a primary care optometrist as any optometrist who is working within the community and not within an intermediate- or tertiary-level practice or clinic.[6] Randomised and non-randomised studies are eligible for inclusion. Papers providing data to allow univariable analysis and papers reporting multivariable analysis to assess risk factors that influence effectiveness of referral will be included. Exclusion criteria will be case reports, review articles, non-human studies and any article type where primary data cannot be abstracted from the paper. Overall effectiveness of the referral process will be assessed using the percent of patients who are referred and found to have normal ocular health.

RISK of BIAS

Risk of bias for included observational studies[7] will be ascertained using the ROBINS-I tool[8]. Risk of bias for randomised studies will be assessed using the key RoB II criteria: 1) maintenance of allocation concealment; 2) use of blinding and; 3) completeness of follow-up.[9] High risk of bias is defined *a priori* as clear failure to maintain allocation concealment and loss of follow-up exceeding 20%.

OUTCOMES

Overall effectiveness of the referral process will be assessed using the percent of patients who were referred and found to have normal ocular health. The primary outcome of interest will be the main clinical characteristic assessed by the primary care optometrist to support the decision to refer (for example: IOP level only, IOP level plus optic disc, visual field, family history of glaucoma, etc).

Secondary outcomes of interest include type of IOP measurement obtained to support referral (for example, noncontact tonometry, applanation tonometry, rebound tonometry, dynamic contour tonometry, home monitoring self-tonometry, etc), visual field results (for example, the type of perimeter, the number of perimetry results available, etc) and imaging device used to support referral (for example, colour fundus

photography, OCT etc), whether a protocol (for example, jurisdictional or clinical guidelines) was followed to guide referral versus independent clinical judgement [10-12]. Due to the exploratory nature of this systematic review, additional meaningful outcomes may be added as studies are identified and included, especially due to the changing nature of glaucoma diagnosis over time [13].

Preference will be given to effect estimates obtained from multivariable analysis, however if multivariable analysis is not available, univariable effect estimates will be analysed.

ANALYSIS

Analysis will be undertaken when at least two studies report the same risk factor using the same metric for assessing magnitude of effect (odds ratio, relative risk, risk difference). If reported data allows, differing metrics may be transformed to allow pooling. Publication bias will be assessed using visual inspection of Funnel-plots.

A simple random effects model will be employed for outcome analysis with magnitude of effect of the risk factor as a continuous outcome. I^2 greater than 50% or P-value for the test of heterogeneity less than 0.10 will be accepted to indicate the presence of important heterogeneity.

All statistical analyses will be conducted using RevMan 5.4.1 (The Cochrane Collaboration®, Oxford, England, 2020). A two-sided p-value less than 0.05 will be accepted to indicate statistical significance.

Heterogeneity and stratified analysis

If important heterogeneity is detected, the following sources of heterogeneity will be investigated using stratified analysis: 1) risk of bias; 2) IOP measurement technique; 3) type of visual field instrument (perimeter), 4) type of imaging device; 5) measurement/definition of pertinent risk factors; 6) type of study design (randomised, non-randomised).

REFERENCES

1. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.* J Clin Epidemiol, 2009. **62**(10): p. 1006-12.
2. Stroup, D.F., et al., *Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group.* JAMA, 2000. **283**(15): p. 2008-12.
3. Kang, P., M. Kalloniatis, and G.S. Doig, *Using Updated PubMed: New Features and Functions to Enhance Literature Searches.* JAMA, 2021.
4. Li, L., et al., *Search strategies to identify observational studies in MEDLINE and Embase.* Cochrane Database Syst Rev, 2019. **3**: p. MR000041.
5. Ayorinde, A.A., et al., *Assessment of publication bias and outcome reporting bias in systematic reviews of health services and delivery research: A meta-epidemiological study.* PLoS One, 2020. **15**(1): p. e0227580.
6. Huang, J., et al., *Impact of referral refinement on management of glaucoma suspects in Australia.* Clin Exp Optom, 2020. **103**(5): p. 675-683.
7. Metelli, S. and A. Chaimani, *Challenges in meta-analyses with observational studies.* Evid Based Ment Health, 2020. **23**(2): p. 83-87.
8. Sterne, J.A., et al., *ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions.* BMJ, 2016. **355**: p. i4919.
9. The Cochrane Collaboration, *Cochrane Handbook for Systematic Reviews of Interventions*, ed. J.P. Higgins and S. Green. 2011.
10. Prum, B.E., Jr., et al., *Primary Open-Angle Glaucoma Preferred Practice Pattern((R)) Guidelines.* Ophthalmology, 2016. **123**(1): p. P41-P111.

11. National Health and Medical Research Council, *Guidelines for the screening, prognosis, diagnosis, management and prevention of glaucoma.* 2010, Commonwealth of Australia: Internet.
12. Prum, B.E., Jr., et al., *Primary Open-Angle Glaucoma Suspect Preferred Practice Pattern((R)) Guidelines.* Ophthalmology, 2016. **123**(1): p. P112-51.
13. Phu, J., et al., *Management of open-angle glaucoma by primary eye-care practitioners: toward a personalised medicine approach.* Clin Exp Optom, 2021. **104**(3): p. 367-384.

Digitally signed by Gordon S. Doig
DN: cn=Gordon S. Doig,
o=Solutions.EvidenceBased.net,
ou=EvidenceBased.net,
email=Gordon.Doig@EvidenceBased.net, c=AU
Date: 2021.08.04 10:47:53 +10'00'