ORIGINAL RESEARCH

Prevalence of Obstructive Sleep Apnea in Glaucoma Patients: A Systematic Review and Meta-analysis

Brian E Yu[1], Ronald Cheung[2], Cindy Hutnik[3], Monali S Malvankar-Mehta[4]

Abstract

Aim and objective: Obstructive sleep apnea (OSA) is a known systemic risk factor associated with glaucoma. The purpose of the study was to determine the overall prevalence of sleep apnea among patients with glaucoma.

Design: A systematic review and meta-analysis.

Participants: Not applicable.

Materials and methods: A systematic literature search was performed through MEDLINE, EMBASE, and CINAHL and gray literature using Clinical Trials.gov, and ProQuest Dissertations and Theses and conferences held through the Association for Research in Vision and Ophthalmology, American Academy of Ophthalmology, and Canadian Society of Ophthalmology was done until June 10, 2020. Eligible articles were identified by reviewing the retrieved results. Data extracted included the total number of patients with glaucoma and the proportion of glaucoma patients with a co-occurring diagnosis of OSA. STATA 15.0 was used to perform the meta-analysis.

Results: 544 articles were gathered from the databases and 40 records were collected via the gray literature search. Ten studies with 956 subjects were included for analysis. The results of the meta-analysis demonstrated a significant rate of OSA among glaucoma patients (ES = 0.17; CI: [0.08, 0.25]).

Conclusion: We examine the prevalence of OSA in glaucoma patients and conclude that the prevalence of OSA in glaucoma patients is higher.

Clinical significance: The findings in the ongoing investigation on the link between glaucoma and OSA continue to be unclear. The results from this study contribute to evidence of an association between the two diseases.

Keywords: Glaucoma, Obstructive sleep apnea, Prevalence.

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Introduction

Glaucoma is a group of eye diseases that involves the progressive degeneration of the optic nerve and is often associated with high intraocular pressure.[1] However, left untreated, glaucoma can lead to irreversible vision loss and potential blindness. Many types of glaucoma typically do not produce noticeable symptoms until significant vision loss is experienced. Glaucoma is the leading cause of irreversible blindness in the world currently estimated that it affects 400,000 people in Canada and 67 million people worldwide.[2]

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder and is commonly measured using the apnea-hypopnea index (AHI). Individuals intermittently stop breathing for a minimum of 10 seconds during their sleep. Typically, this is due to muscle relaxation during sleep which causes the soft tissue in the back of the throat to collapse and block the upper airway. Sleep apnea can cause people to wake up gasping for breath, snore loudly, and feel tired even after a full night's sleep.[3] Approximately 29 million Americans are affected by sleep apnea with only around 6 million formally diagnosed.[4] Risk factors for sleep apnea include obesity as well as excess weight.[5]

Many studies have investigated the association between the two disorders[6] and have even claimed sleep apnea to be a potential risk factor for developing glaucoma or *vice versa*.[7–10] Evidence for a higher prevalence of OSA in glaucoma patients has also been previously found.[11] The purpose of this study is to identify the current prevalence of sleep apnea among patients concurrently diagnosed with glaucoma. A systematic literature search followed by meta-analysis was executed by investigating the total number of patients with glaucoma and the proportion of glaucoma patients with a co-occurring diagnosis of OSA.

[1,2]Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada

[3]Department of Ophthalmology, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada

[4]Department of Ophthalmology, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada; Department of Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada

Corresponding Author: Monali S Malvankar-Mehta, Department of Ophthalmology, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada; Department of Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, The University of Western Ontario, London, Ontario, Canada, Phone: +1 519-685-8500 ext. 61288, e-mail: Monali.Malvankar@schulich.uwo.ca

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Conflict of interest: None

Materials and Methods

Data Sources and Searches

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements were used to conduct the systematic review.[12] Database searches were executed on MEDLINE, EMBASE, CINAHL, Clinical Trials.gov, and ProQuest Dissertations and Theses to find studies investigating both sleep apnea and glaucoma. In each database, a search strategy was designed (Appendix A) to retrieve pertinent articles up to June 10, 2020. OVID® AutoAlerts were set up for both MEDLINE and EMBASE to send monthly updates on any new pieces of literature that may have been of relevance. The searches contained no limits.

A gray literature search was performed through conferences held by the Canadian Society of Ophthalmology (COS) from the year 2010 to 2019. Meanwhile, conferences held through the Association for Research in Vision and Ophthalmology (ARVO) and the American Academy of Ophthalmology (AAO) were searched in all years available. A couple of keywords used to search through the conference archives included "sleep apnea" and "glaucoma". All gray literature searches through conference archives were all performed up until June 10, 2020.

Inclusion/Exclusion Criteria

Studies pertaining to sleep apnea diagnoses in patients with any form of glaucoma were included, as the prevalence of sleep apnea among patients concurrently diagnosed with glaucoma was of primary concern. A sample size of at least 20 eyes was a requirement for an article to be included for analysis. Clinical trials, comparative studies, and case series were included. Single case reports and secondary studies, such as editorials, were excluded. Other systematic reviews and meta-analyzes were also excluded from the analysis. Only studies on humans with a full-text article in English were included.

Screening

The results of each database search were imported into Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Upon import, the screening was performed by two independent reviewers (BY and RC) after removing duplicates. Level 1 title and level 2 abstract screening were then carried out. Cohen's Kappa coefficient was calculated after each level of screening before resolving any conflicts. Conflicts were resolved through consensus between the two independent reviewers. If consensus could not be achieved, then a third reviewer was required to arbitrate. During level 3 full-text screening, the full texts of any studies that had made it past level 2 screening were uploaded. Following level 3 screening, Cohen's Kappa was calculated before conflict resolution. The remaining articles were then checked for their quality.

Quality Check

The quality check was completed to confirm the comprehensiveness of the methodology used in our study. A modified Downs and Black checklist was used for the quality assessment of the included studies.[13] Various items were examined in the studies including reporting, external validity, internal validity (bias), internal validity (confounding), and power. All studies were then given a total score out of 28. As a result of the limited articles and studies available, all evidence was included for analysis.

Data Extraction

One investigator (BY) performed the data extraction. Baseline information extracted from the 10 studies included the first author's last name, year of publication, country of origin, study design, study groups, total sample size, the mean age of participants, and percentage of female participants. Other data extracted included the total number of patients with glaucoma and the proportion of glaucoma patients with co-occurring diagnoses of sleep apnea.

Meta-analysis

A meta-analysis was performed to combine the results from the included studies that investigated the current prevalence of sleep apnea among patients concurrently diagnosed with glaucoma. By statistically combining the findings such as the proportion of glaucoma patients with sleep apnea from the included studies, the analytic power significantly increased, resulting in a single effect estimate of proportion known as the *summary effect*.

The program STATA v. 15.0 (STATA Corporation, College Station, TX, USA) was utilized to perform the meta-analysis. Prevalence of sleep apnea among glaucoma patients was computed as the effect size. To explore the proportion of glaucoma patients with co-occurring diagnosis of sleep apnea, the included articles were pooled together through the use of the fixed-effect or the random-effects model based on the presence of heterogeneity. To test the null hypothesis, a *Z*-value was computed. To evaluate heterogeneity, I^2 statistics and χ^2 test was computed. A low *p* value, large χ^2 statistics, and I^2 statistic, indicated significant presence of heterogeneity in-between studies and therefore, a random-effects model using the DerSimonian and Laird technique was computed. Forest plot was also created to display effect sizes and a funnel plot was generated to assess the risk of publication bias.

Results

Flowchart 1 summarizes the results of the literature search. Upon searching, 584 potentially relevant studies were produced. All studies were imported into Covidence where 158 duplicates were removed from screening. The remaining 426 studies underwent level 1 screening for their titles. Three hundred and twenty-four were excluded because they did not look at sleep apnea in patients with glaucoma. 102 studies then underwent level 2 screening for their abstracts. 84 studies did not investigate the prevalence of sleep apnea in glaucoma patients and were excluded. The remaining 18 studies underwent level 3 screening for their full texts. Eight studies were excluded because they did not report a rate or proportion of patients diagnosed with sleep apnea among those presenting with glaucoma. The final 10 studies were included in the data analysis. These studies had their quality checked through the use of a modified Downs and Black checklist. One study was poor quality (≤14), one study was fair quality (15–19), eight studies were good quality (20–25), and no studies were excellent quality (26–28).

Cohen's Kappa values for the agreement between the two reviewers were 0.72, 0.61, and 0.64 for levels 1, 2, and 3 screening, respectively.

Study Characteristics

Table 1 displays the summarized characteristics of the 10 included studies. Countries in which the included studies were conducted include the USA, UK, Switzerland, Egypt, and India. One study was an observational cross-sectional case-control, one study was

Flowchart 1: PRISMA flow diagram summarizing the results of the literature search

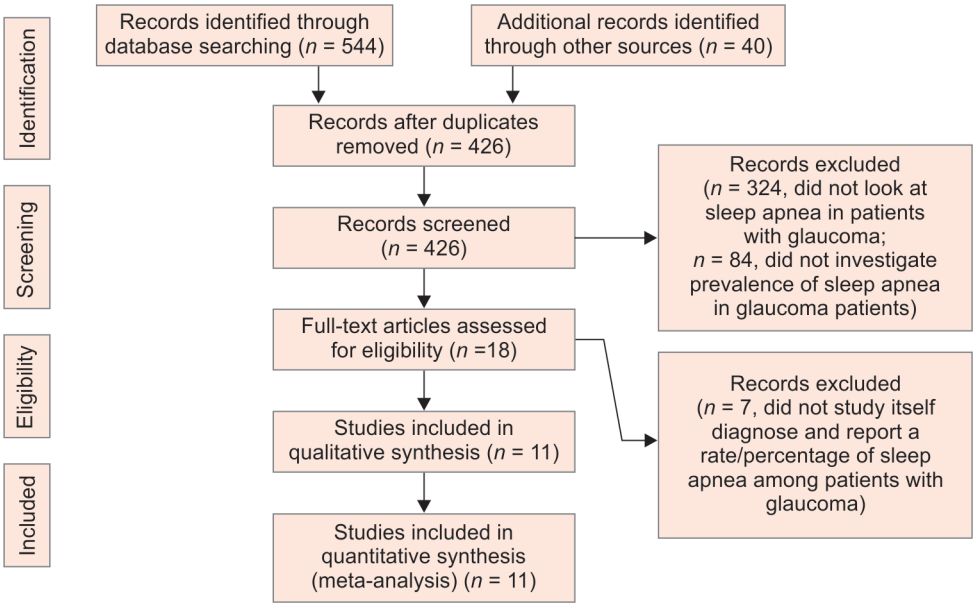

Table 1: Characteristics of included studies

Author	*Year*	*Total number of participants*	*Study design*	*Study location*	*Group*	*Mean age (SD)*	*% Female*
Balbay et al.	2014	21	Case series	Turkey		56.0 (10.1)	57.1
Khandgave et al.	2013	80	Non-randomized, cross-sectional study	India		50.8 (5.0)	72.5
Ledina et al.	2017	150	Case series	–		–	–
Marcus et al.	2001	67	Comparative case series	United States		62.9 (11.0)	46.3
Mojon et al.	2000	30	Comparative case series	Switzerland	Case	76.0 (7.9)	57.0
					Control	76.6 (5.5)	56.0
Mojon et al.	2002	16	Comparative case series	Switzerland		65.8 (13.2)	87.5
Roberts et al.	2009	166	Prospective, nonrandomized, observational trial	Australia	Case	71 (9)	45.6
					Control	70 (9)	47.4
Shalabay et al.	2016	31	Comparative case series	Egypt	OSA	53.6 (10.0)	81.3
					POAG	51.3 (11.0)	53.3
Wozniak et al.	2018	403	Prospective observational case-control	United Kingdom	Case	70.4 (9.1)	42.5
					Control	68.4 (9.4)	55.8
Wozniak et al.	2019	395	Observational cross-sectional case-control	United Kingdom	Case	70 (13)	43
					Control	68.5 (11.8)	57

nonrandomized cross-sectional, four studies were comparative case series, two studies were case series, one study was a prospective nonrandomized observational trial, and one study was a prospective observational case-control study. The mean ages of participants were 50.8–76.6 years in all studies.

Studies conducted by Balbay et al. and Ledina et al. were both case series investigating the prevalence of OSA in glaucomatous patients.[14,15] All other studies included were comparative and included multiple groups.[11,16–22] For these studies, data on OSA from the glaucoma group were extracted for quantitative analysis. For studies with more than one glaucoma group, both groups were combined before data extraction. Both studies by Wozniak et al. were grouped as one so that only data from Wozniak et al. was extracted being that it provided an updated data set to the study by Wozniak et al.[16,21]

Diagnoses of OSA in the included studies were primarily based on sleep questionnaires, polysomnography (PSG), or a combination of the two. Four studies used a combination of sleep questionnaires and PSG.[1,17,18,20] Studies by Wozniak et al. and Mojon et al. used the only PSG for diagnoses.[11,16,21] Mojon et al. used only overnight oximetry recordings for diagnoses of OSA.[19] Roberts et al. used ambulatory pulse oximetry monitoring to determine

the oxygen desaturation index (ODI) in combination with a sleep questionnaire.[22] The study by Ledina et al. did not report how the diagnosis of OSA was made.[15]

Publication Bias

Figure 1 shows the funnel plot for studies investigating the prevalence of sleep apnea among glaucoma patients. The included studies were scattered from the central area to the bottom right and top left and right corner of the plot. As such, publication bias could not be concluded. Partial reasons for this were difficulty in interpretation of the funnel plot for a small group of studies, high heterogeneity, and small effect sizes. Furthermore, publication bias is only one of the many reasons that may account for funnel plot asymmetry.

Prevalence of Sleep Apnea

Data extracted on the total number of patients with glaucoma and the proportion of glaucoma patients with co-occurring diagnoses of sleep apnea used in the meta-analysis can be found in Table 2. Our results indicate a significant proportion of glaucoma patients with a co-occurring diagnosis of sleep apnea (Fig. 2). This finding is consistent with other results in previously published literature. The included studies in this meta-analysis had high heterogeneity ($I^2 = 97.6\%$). Thus, a random-effects meta-analysis was performed to produce a summary effect of 0.17 (95% CI: 0.08, 0.25). This result suggests 17% of glaucoma patients with a co-occurring diagnosis of sleep apnea.

Discussion

Through meta-analysis, the present study investigated the prevalence of OSA among patients with any form of glaucoma. Numerous bibliographic databases search as well as gray literature search were conducted. The principal outcome measures were the rate and proportion of patients with glaucoma identified with a diagnosis of OSA. Ten studies were included for analysis. The characteristics of the included studies such as the proportion of glaucoma patients with co-occurring diagnoses of OSA, the study population, the study design, study location, and sample size, were described. The results from this study revealed a 17% prevalence of OSA among patients with glaucoma.

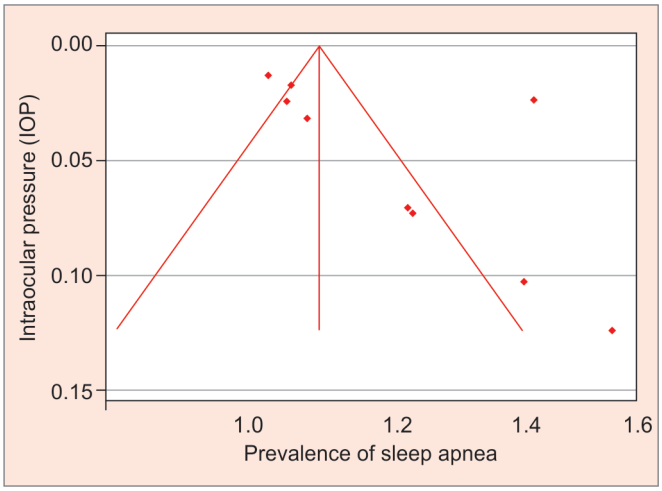

Fig. 1: Funnel plot for included studies investigating prevalence of obstructive sleep apnea in glaucoma patients showing asymmetry

Limitations of the present study include the deficits in the studies that were included. Although the majority of studies were of good quality, studies of less quality were also included. However, all studies were included regardless of their quality because of the limited studies that were available for analysis. Between the studies, a substantial amount of heterogeneity was revealed. However, this could reflect different study populations or demographics, participant criteria, study location, physician's experience, available facilities to conduct the research study, as well as the year the study was conducted.

Other limitations include the tools used for the diagnosis of OSA in the studies. Although many studies used a combination of sleep questionnaires and PSG,[14,17,18,20] other studies simply used only PSG[11,16,21] or only used oximetry.[11,22] It should also be noted that both the study by Marcus et al. and Shalaby et al. have important methodological limitations related to preselecting patients based on symptoms, including historical control groups.[18,20] Ultimately, the results of this meta-analysis suggest that more high-quality studies need to be reported to make strong conclusions.

Conclusion

This systematic review and meta-analysis has shown that the overall prevalence of OSA among patients with glaucoma is 35%. Future research could involve case-control studies with larger amounts of participants to further confirm the prevalence rate of OSA in glaucoma patients. Furthermore, systematic reviews on the prevalence of glaucoma among patients with OSA have not been thoroughly investigated. It will be worthwhile to continue to further investigate and summarize the relationship from the other end to further establish a possible link between the two diseases.

Clinical Significance

The findings in the ongoing investigation on the link between glaucoma and OSA continue to be unclear. The results from this study contribute to evidence of an association between the two diseases pointing to a potential concurrent glaucoma-sleep apnea screening.

Table 2: Proportion of glaucoma patients with OSA in the included studies

Author	*Year*	*Total number of participants*	*Number of glaucoma patients*	*Number of glaucoma patients with OSA*
Balbay et al.	2014	21	21	7
Khandgave et al.	2013	80	40	16
Ledina et al.	2017	150	100	4
Marcus et al.	2001	67	23	5
Mojon et al.	2000	30	30	6
			16	7
Mojon et al.	2002	16	15	6
Roberts et al.	2009	166	52	9
Shalabay et al.	2016	31	240	142
			235	136
Wozniak et al.	2019	395	100	4

OSA, obstructive sleep apnea

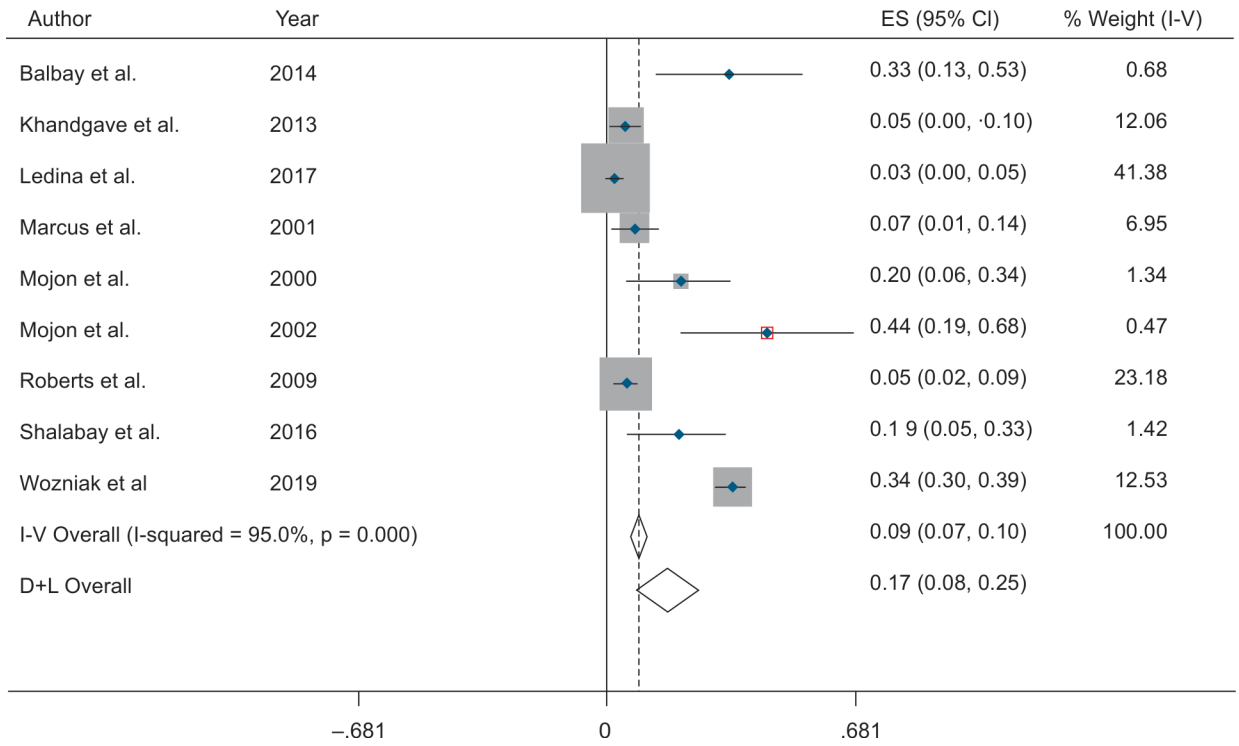

Fig. 2: Forrest plot showing a significant prevalence of obstructive sleep apnea at 17% among patients with glaucoma

References

1. Bendel RE, Kaplan J, Heckman M, et al. Prevalence of glaucoma in patients with obstructive sleep apnoea - a cross-sectional case-series. Eye 2008;22(9):1105–1109. DOI: 10.1038/sj.eye.6702846.
2. Hong C, Trope G. Glaucoma. CMAJ 2015;187(12):E398–E399. DOI: 10.1503/cmaj.140401.
3. Young T, Skatrud J, Peppard PE. CLINICIAN'S CORNER risk factors for obstructive sleep apnea. JAMA 2004;291(16):2013–2016. DOI: 10.1001/jama.291.16.2013.
4. Nisha M, Saranyah K, Shankar M, et al. Enhanced saccharification of lignocellulosic agricultural biomass and increased bioethanol titre using acclimated *Clostridium thermocellum* DSM1313. 3 Biotech 2017;7(1):35. DOI: 10.1007/s13205-017-0606-z.
5. Keenan TDL, Goldacre R, Goldacre MJ. Associations between obstructive sleep apnoea, primary open angle glaucoma and age-related macular degeneration: record linkage study. Br J Ophthalmol 2017;101(2):155–159. DOI: 10.1136/bjophthalmol-2015-308278.
6. Cabrera M, Benavides AM, Hallaji NAE, et al. Risk of obstructive sleep apnea in open-angle glaucoma versus controls using the STOP-Bang questionnaire. Can J Ophthalmol 2018;53(1):76–80. DOI: 10.1016/j.jcjo.2017.07.008.
7. Yuan-Yao F. Glaucoma progression in patients with obstructive sleep apnea-hypopnea syndrome: study of the CGMH polysomnography database. Investig Ophthalmol Vis Sci 2018;59(9):5110.
8. Huon LK, Liu SYC, Camacho M, et al. The association between ophthalmologic diseases and obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath 2016;20(4):1145–1154. DOI: 10.1007/s11325-016-1358-4.
9. Liu S, Lin Y, Liu X. Meta-analysis of association of obstructive sleep apnea with glaucoma. J Glaucoma 2016;25(1):1–7. DOI: 10.1097/IJG.0000000000000357.
10. Chuang LH, Koh YY, Chen HSL, et al. Normal tension glaucoma in obstructive sleep apnea syndrome: a structural and functional study. Medicine (Baltimore) 2020;99(13):e19468. DOI: 10.1097/MD.0000000000019468.
11. Mojon DS, Hess CW, Goldblum D, et al. Normal-tension glaucoma is associated with sleep apnea syndrome. Ophthalmologica 2002;216(3):180–184. DOI: 10.1159/000059625.
12. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62(10):1006–1012. DOI: 10.1016/j.jclinepi.2009.06.005.
13. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52(6):377–384. DOI: 10.1136/jech.52.6.377.
14. Balbay EG, Balbay O, Annakkaya AN, et al. Obstructive sleep apnoea syndrome in patients with primary open-angle glaucoma. Hong Kong Med J 2014;20(5):379–385. DOI: 10.12809/hkmj134021.
15. Ledina MJ, Ledina TM, Milanović VB, et al. Do glaucoma, nonarteritic ischemic anterior optic neuropathy and sleep apnea march hand in hand? Eur Respir J 2017;50:PA2324.
16. Wozniak D, Bourne R, Peretz G, et al. Obstructive sleep apno ea in patients with primar y-open angle glaucoma: no role for a screening program. J Glaucoma 2019;28(8):668–675. DOI: 10.1097/IJG.0000000000001296.
17. Khandgave TP, Puthran N, Ingole AB, et al. The assessment of sleep apnoea as a risk factor in glaucoma. J Clin Diagnostic Res 2013;7(7):1391–1393. DOI: 10.7860/JCDR/2013/5383.3147.
18. Marcus DM, Costarides AP, Gokhale P, et al. Sleep disorders: a risk factor for normal-tension glaucoma? J Glaucoma 2001;10(3):177–183. DOI: 10.1097/00061198-200106000-00006.
19. Mojon DS, Hess CW, Goldblum D, et al. Primary open-angle glaucoma is associated with sleep apnea syndrome. Ophthalmologica 2000;214(2):115–118. DOI: 10.1159/000027478.
20. Shalaby AEO, Elshazly MI, El Sayed YM, et al. Co-existence of obstructive sleep apnea and primary open angle glaucoma. Egypt J Chest Dis Tuberc 2016;65(2):511–516. DOI: 10.1016/j.ejcdt.2015.12.003.
21. Wozniak D, Kean J, Peretz G, et al. Prevalence of obstructive sleep apnoea in glaucoma: the posag study. Investig Ophthalmol Vis Sci 2018;59(9):28–30.
22. Roberts TV, Hodge C, Graham SL, et al. Prevalence of nocturnal oxygen desaturation and self-reported sleep-disordered breathing in glaucoma. J Glaucoma 2009;18(2):114–118. DOI: 10.1097/IJG.0b013e318179f80c.

Appendix A: Search Strategies for All Databases

Medline

#	Searches	Results
1	sleep apnea.mp. or Sleep Apnea Syndromes/	43,851
2	glaucoma.mp. or Glaucoma, Angle-Closure/ or Glaucoma, Open-Angle/ or Glaucoma/ or Glaucoma, Neovascular/ or Low Tension Glaucoma/	69,842
3	1 and 2	141
		2020/06/10

Embase

#	Searches	Results
1	sleep apnea.mp. or sleep disordered breathing/	82,898
2	closed angle glaucoma/or low tension glaucoma/or open angle glaucoma/or congenital glaucoma/or neovascular glaucoma/or primary glaucoma/or glaucoma.mp. or secondary glaucoma/or glaucoma/	102,373
3	1 and 2	356
		2020/06/10

Cinahl

Search ID#	Search terms	Results
S1	(MH "Sleep Apnea, Central") OR (MH "Sleep Apnea, Obstructive") OR (MH "Sleep Apnea Syndromes") OR "sleep apnea"	17,638
S2	(MH "Glaucoma") OR "glaucoma" OR (MH "Glaucoma, Angle-Closure")	10,500
S3	S1 AND S2	47
		2020/06/10

Gray Literature

1. Clinical trials—https://clinicaltrials.gov/ (Searched June 10, 2020)
    a. Sleep apnea and glaucoma
    b. 8 results https://clinicaltrials.gov/ct2/results?cond=sleep+apnea+and+glaucoma&term=&type=&rslt=&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&lupd_s=&lupd_e=&sort=
2. ProQuest—Dissertations and theses (Searched June 10, 2020)
    a. Noft(sleep apnea) AND noft(glaucoma)
    b. 2 results
3. Conference proceeding searches

Conference	Link	Years searched	Search terms	Results/Comments
ARVO	https://arvojournals.org/index.aspx	All years	"Meeting abstract" AND (sleep apnea) AND (glaucoma)	Searched through meeting abstracts
	https://arvojournals.org/solr/searchresults.aspx?q=%22Meeting%20abstract%22%20AND%20(sleep%20apnea)%20AND%20(glaucoma)&restypeid=1#q=%22Meeting+abstract%22+AND+(sleep+apnea)+AND+(glaucoma)&restypeid=1&rg_ArticleDate=01/01/2010%20TO%2009/14/2019			29 results
				2020/06/10

Contd…

Contd…

Conference	*Link*	*Years searched*	*Search terms*	*Results/Comments*
AAO All Meetings	https://secure.aao.org/aao/meeting-archive	"All years available"	Topic: Glaucoma	No relevant abstracts/presentations found
			Keywords: "sleep apnea" "glaucoma"	2020/06/10
COS	http://www.cos-sco.ca/cpd/annual-meeting/	2010-2019	"sleep apnea"	Searched through abstracts and presentations
			"glaucoma"	1 result
				Prospective Study Comparing Frequency of Obstructive Sleep Apnea in Open-Angle Glaucoma vs Controls · Ana Maria Benavides-Vargas, Mariana Cabrera, Numan Hallaji, Colin Shapiro, Naheed K. Hossain, Graham E. Trope, Yvonne M. Buys (duplicate from ARVO)
				2020/06/10

Appendix B: Cohen's Kappa Statistic for Screening

Kappa Statistics (Title Screening)

		Ronald			
Review authors		*Include*	*Exclude*	*Unsure*	*Total*
Brian	Include	103	4	1	108
	Exclude	28	270	20	318
	Unsure	0	0	0	0
	Total	131	274	21	426

$$\text{Kappa} = \frac{P(O) - P(E)}{1 - P(E)}$$

$$P(O) = \frac{103 + 270 + 0}{426}$$

$$P(O) = 0.875586854$$

$$P(E) = \frac{(108 \times 131) + (318 \times 274) + (0 \times 21)}{426^2}$$

$$P(E) = 0.558090326$$

$$\text{Kappa} = \frac{P(O) - P(E)}{1 - P(E)}$$

$$\text{Kappa} = \frac{0.875586854 - 0.558090326}{1 - 0.558090326}$$

Kappa = 0.718464761

Kappa Statistics (Abstract Screening)

		Ronald			
Review authors		*Include*	*Exclude*	*Unsure*	*Total*
Brian	Include	14	9	0	23
	Exclude	2	75	0	77
	Unsure	0	2	0	2
	Total	16	86	0	102

Kappa = 0.611599297

Kappa Statistics (Full-text Screening)

Review authors		Ronald		
		Include	*Exclude*	*Total*
Brian	Include	11	2	13
	Exclude	1	4	5
	Total	12	16	18

Kappa = 0.608695652

Appendix C: Scores from Study Quality Assessment

		Reporting	*External validity*	*Bias*	*Confounding*	*Power*	
Study	*Year*	*Items 1–10*	*Items 11–13*	*Items 14–20*	*Items 21–26*	*Item 27**	*Total/28*
Balbay et al.	2014	10	2	6	4	1	23
Khandgave et al.	2013	7	1	6	2	1	17
Ledina et al.	2017	5	1	5	1	1	13
Marcus et al.	2001	11	1	5	4	1	22
Mojon et al.	2000	9	2	6	4	1	22
Mojon et al.	2002	8	3	6	4	1	22
Roberts et al.	2009	10	1	6	4	1	22
Shalabay et al.	2016	10	1	5	4	1	21
Wozniak et al.	2018	10	2	6	4	1	23
Wozniak et al.	2019	11	3	5	4	1	24