Article Title: Complementary and Alternative Medicine Mentions and Recommendations in Glaucoma Guidelines: Systematic Review and Quality Assessment

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Abstract

Introduction: Glaucoma is one of the leading causes of irreversible vision loss and blindness. The global prevalence of glaucoma is 3.54% of the population aged 40–80 years old. Glaucoma and its associated symptoms are often self-medicated using CAM therapies. This study aims to determine the quantity and quality of CAM recommendations within clinical practice guidelines (CPGs) for the treatment and/or management of glaucoma.

Methods: MEDLINE, EMBASE and CINAHL were systematically searched from 2009 to April 2020, alongside the Guidelines International Network and the National Center for Complementary and Integrative Health websites. Eligible CPGs containing CAM therapy recommendations were assessed using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument.

Results: From 148 unique search results, 7 eligible CPGs were identified, however, only 1 CPG contained CAM recommendations. This eligible CPG scored high in the scope and purpose, editorial independence, and clarity of presentation domains for both the overall CPG and CAM sections. CAM therapies recommended for use included Dan Zhi Xiaoyaosan; Taohong Siwu decoction and Wuling powder; Wendan Tang; Lycii and Chrysanthemi and Rehmanniae bolus; gingko leaf tablets; Erigeron breviscapus tablets; Wuling capsule; fuming tablets; Mingmu Dihuang Wan; and acupuncture.

Conclusion: This review highlights the general lack of CAM recommendations across glaucoma CPGs; this hinders the ability of clinicians to have meaningful discussions surrounding shared-decision making with their patients. Despite the high prevalence of CAM use in glaucoma patients, extremely limited evidence-based CPGs with CAM therapy recommendations are available to guide their safe and effective use.

Abbreviations

AGREE II: Appraisal of Guidelines for Research & Evaluation II

CAM: complementary and alternative medicine

CHM: Chinese herbal medicine

CPG: clinical practice guideline

NCCIH: National Center for Complementary and Integrative Health

PICO: Patients, Intervention, Comparison and Outcomes

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

1. Background

Glaucoma is one of the most frequent causes of irreversible vision loss and blindness around the world [1]. It can fall into one of two categories, primary or secondary glaucoma. Glaucoma is often characterized by the cupping of the optic nerve head with visual field loss, along with high intraocular pressure [1,2]. It is often diagnosed via ophthalmoscopy, tonometry and perimetry, and elevated intraocular pressure is treated conventionally through laser therapy, surgery and topical drugs [1]. The global prevalence of glaucoma is also high; approximately 3.54% of the population aged 40–80 years have some form of glaucoma according to a study conducted in 2014 [3]. The same study also suggests that glaucoma disproportionately affects highly urban areas as well as African and Asian countries, some of the same countries where complementary and alternative medicine (CAM) use is generally more prevalent and widely accepted [3,4]. The NCCIH divides the definition of CAM in their two separate terms, whereby "complementary medicine" reflects non-conventional practices used in conjunction with conventional therapies, whereas "alternative medicine" reflects non-conventional practices used in place of conventional ones [5]. An American cross-sectional

study of CAM use for glaucoma found that the prevalence of CAM use in patients with glaucoma was 5.4% [6].

Typical CAM therapies used by patients with glaucoma including herbal therapies (including, but not limited to: bilberry, fish oils, Chinese herbal medicines, ginkgo biloba), dietary modifications (calorie restrictions, increased vegetable consumption), mineral/vitamin supplements, and acupuncture/homoeopathy [7]. The majority of these therapies have been purported to minimize symptoms in conjunction with pharmaceutical therapies, particularly focusing on the reduction of symptoms that negatively affect quality-of-life. Some therapies are also proposed to be used alongside one another, with a focus on a holistic approach in preventing a lower quality of life and improving health outcomes in patients [7]. While certain CAMs may be more widely accepted in countries with deeply-rooted traditional systems of medicine, clinicians trained in the Western world generally have a poor understanding of CAM therapies, including within the context of the treatment and/or management of glaucoma. [4].

Healthcare professionals and clinicians typically rely in part on evidence-based clinical practice guidelines (CPGs) to formulate treatment plans and determine the associated risks and benefits of a particular therapy outlined by the CPG [8]. There is little research that critically appraises CPGs for glaucoma, including CAM-specific recommendations. Thus, the purpose of this study was to systematically identify the quantity and assess the quality of CAM recommendations in CPGs for the treatment and/or management of glaucoma. This is of particular importance due to the prevalent nature of glaucoma itself in the general population and will better inform ophthalmologists amongst other eye care professionals

about the safe and effective use of evidence-based CAM therapies in the context of glaucoma [3].

2. Methods

2.1. Approach

A systematic review was conducted using standard methods and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [9,10]. A protocol was registered with PROSPERO, registration number CRD42020182230. Following the screening process, any eligible CPGs containing CAM recommendations were assessed using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument, a validated instrument used for appraising of CPGs [11]. Eligible CPGs containing CAM recommendations were assessed twice; once for the overall CPG, and once for the CAM-specific sections of the same CPG. The following domains comprise 6 separate sections of the AGREE II instrument: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability, and editorial independence.

2.2. Eligibility criteria

The Population, Intervention, Comparison and Outcomes (PICO) framework was used to generate the eligibility criteria to screen CPGs. The eligibility criteria were as follows: the population comprised of adults over the age of 19 years diagnosed with glaucoma; interventions included CPGs that provided recommendations for the treatment and/or management of glaucoma to determine if CAM therapies were mentioned/recommended; comparisons were made across the assessed quality of eligible CPGs; and outcomes included AGREE II domain scores for overall and CAM-specific sections of eligible glaucoma CPGs. We used the operational definition of complementary medicine published by Cochrane

Complementary Medicine [https://cam.cochrane.org/operational-definition-complementary-medicine] to determine what therapies listed in the eligible CPGs constituted CAM.

Additionally, CPGs had to be developed by non-profit organizations (i.e., academic institutions, government agencies), publicly accessible or orderable through our university library system, and published in the English language between 2009 and 2020 to be eligible for inclusion. Eligible CPGs focused on the treatment and/or management of glaucoma; CPGs that only focused on topics such as glaucoma diagnosis, screening, education or training for healthcare professionals were not eligible. Consensus statements, protocols, abstracts, conference proceedings, letters or editorials, primary studies evaluating glaucoma management or treatment (i.e. trials, cohort studies), and those focused on glaucoma curriculum, education, training, research, professional certification or performance, were also all deemed ineligible. Eligible CPGs containing CAM-specific therapy recommendations were assessed twice using the AGREE II instrument; for any eligible CPGs that did not contain CAM therapy recommendations, only general guideline characteristics are provided.

2.3. Searching and screening

MEDLINE, EMBASE and CINAHL databases were systematically searched on April 17, 2020 from 2009 to April 16, 2020. The search strategy consisted of indexed terms and keywords commonly associated with glaucoma. A sample search strategy can be found in Supplementary File 1. In addition, the Guidelines International Network (GIN) website [https://www.g-i-n.net/] was searched using the keyword "glaucoma", and the CAM CPGs listed on the NCCIH website [https://www.nccih.nih.gov/health/providers/clinicalpractice] were also hand-searched for relevant glaucoma CPGs. Furthermore, we also hand-searched the reference lists of any relevant reviews (i.e. systematic, scoping) captured by our searches,

and if any potentially eligible CPGs were found, their full-texts were further reviewed. MN and ED screened abstracts and full-texts of all search results to determine eligibility. JYN met with both screeners to review screened articles, and resolve conflicts through discussion to standardize the screening process.

2.4. Data extraction and analysis

The date of publication, country of first author, type of guideline developer (i.e. academic institution, government agency, disease-specific foundation, or professional association or society), and whether CAM was mentioned/recommended, was extracted from each eligible CPG. For any CPGs that did mention CAM, the specific type of CAM therapy, the CAM recommendations (if any), and CAM funding sources/development panel members mentioned in the CPG were data extracted. While we anticipated that most of the data would be included in the CPG document, we also visited and reviewed the websites of each of the guideline developers to identify any relevant supplementary files, and resources in support of CPG application and implementation.

2.5. Guideline quality assessment

Prior to assessing eligible CPGs containing CAM recommendations, JYN, MN and ED participated in a pilot test of the AGREE II instrument, which involved the appraisal of three separate CPGs. Following the appraisal of these CPGs, all three authors met and any discrepancies between the scores were compared and discussed to ensure that consensus was reached with respect to the application of the AGREE II instrument in consultation with the user manual. MN and ED then independently assessed eligible glaucoma CPGs containing CAM recommendations using the AGREE II instrument twice; once for the overall CPG, and once for the CAM-specific sections of the CPG. They assessed CPGs independently and in

duplicate for the 23 items across the 6 domains using a seven-point Likert scale, from strongly disagree (1) to strongly agree (7). A score was also provided for the overall quality of the CPG, along with a recommendation for or against the use of the CPG. The modified AGREE II questions used to score the CAM-specific subsections of the CPGs can be found in Supplementary File 2. Both assessors then met with JYN, and any score discrepancies were resolved by discussion without unduly modifying scores. Average appraisal scores were calculated by taking the average of all 23 scores for each appraiser and averaging those scores between both appraisers. The average overall assessment was calculated as the average score of both appraisers' overall CPG scores for each CPG. Scaled domain percentages were formulated for inter-domain comparison. These were generated by adding both appraisers' scores for items within each domain, and scaling based the total off the possible maximum and minimum scores for each domain, which was there converted into a percentage value.

3. Results

3.1. Search results (Fig. 1)

Searches retrieved 150 items, of which 140 were unique. Elimination of 129 titles/abstracts left 11 CPGs that were considered for full-text screening. Out of the 11 CPGs, 4 were eliminated because they either lacked treatment/management recommendations with respect to glaucoma (n = 2), or they could not be retrieved (n = 2). A list of these 4 excluded full-text articles by citation are provided in Supplementary File 3. The remaining 7 CPGs were deemed eligible and included in this review [12], [13], [14], [15], [16], [17], [18]. Of these 7 CPGs, only 1 made mention of and contained recommendations pertaining to CAM [12].

3.2. Guideline characteristics (Table 1)

Eligible CPGs were published from 2009 to 2020, originating from the following countries: Australia (n = 1), Brazil (n = 1), Canada (n = 1), China (n = 1), Sweden (n = 1), the United Kingdom (n = 1), and the United States (n = 1) [12], [13], [14], [15], [16], [17], [18]. The CPGs were funded and/or developed by either a professional association or society (n = 6) or an academic committee (n = 1). Only one CPG made mention of CAM therapies [12]. These CAM therapies included different Chinese herbal medicine (CHM) therapies for the treatment of glaucoma and its associated symptoms. Recommendations relating to CAM were made in the same CPG, and also related to CHMs. We provide a summary of CAM recommendations made within this glaucoma CPG for the benefit of clinicians and researchers in Fig. 2.

3.3. Average appraisal scores, average overall assessments and recommendations regarding use of guidelines: overall guideline

Average appraisal scores, average overall assessments, and recommendation regarding use for each CPG are shown in Supplementary File 4. The average appraisal score for the CPG was 5.0 (where 1 equals strongly disagree that the item is met and 7 equals strongly agree that the item is met). The average overall assessment for the CPG was 5.5.

3.4. Average appraisal scores, average overall assessments and recommendations regarding use of guidelines: CAM sections

Average appraisal scores, average overall assessments, and recommendation regarding use for the CAM section of the CPG are shown in Supplementary File 4. The average appraisal score for the CAM section of the CPG was 4.9 on the seven-point Likert scale. The average overall assessment for the CAM section of the CPG was 5.5.

3.5. Overall recommendations: overall guideline

With respect to the overall CPG, both appraisers agreed upon the recommendation of the use of this CPG as "No" [12]. This is shown in Supplementary File 4.

3.6. Overall recommendations: CAM sections

With respect to the CAM-specific subsection of the CPG, both appraisers agreed upon the recommendation of the use of this CPG as "Yes, with modifications" [12]. This is shown in Supplementary File 4.

3.7. Scaled domain percentage quality assessment

Scaled domain percentages of the overall CPG were as follows: scope and purpose (88.9%), stakeholder involvement (66.7%), rigour of development (74.0%), clarity of presentation (77.8%), applicability (16.7%), and editorial independence (79.2%). Scaled domain percentages of the CAM section were as follows: scope and purpose (88.9%), stakeholder involvement (66.7%), rigour of development (70.8%), clarity of presentation (83.3%), applicability (14.6%), and editorial independence (79.2%). This is shown in Supplementary File 4.

3.7.1. Scope and purpose

The CPG outlined and suggested CAM recommendations clearly; the overall objectives, health questions, and target population (both patient population and the clinician population) were also adequately addressed. The overall CPG itself was entirely focused on assessing the impact of CAM and CHMs in Chinese glaucoma patient populations; the authors had made this very clear throughout the CPG. Both the overall scores and the CAM specific scores for this domain were similar, due to the fact that the CPG itself was focused on CAM therapies for the treatment of glaucoma [12].

3.7.2. Stakeholder involvement

The guideline development panel included a variety of different clinicians and healthcare professionals. There was variation within panel member characteristics regarding degrees held, institutional affiliations, and roles of members within the panel [12]. The CPG clearly identified the target users of the CPG as clinicians and ophthalmologists treating primary open-angle glaucoma looking for non-conventional CAM therapies for glaucoma patients. The CPG also provided clear descriptions of who should be implementing specific CAM recommendations and when they should be implemented. However, the CPG failed to collect and detail the views and preferences of the target population to be receiving the CAM treatment itself [12].

3.7.3. Rigour of development

Systematic methods were used to conduct searches for the evidence which informed the development of the CPG; the search process, along with inclusion and exclusion criteria used to screen searches, were both outlined. The criteria used to screen the searches were clearly defined. The strengths and limitations of the body of evidence used to generate the recommendations were also detailed, with the CPG citing the utilization of the GRADE evidence rating system [12]. The methods for formulating recommendations were well-defined; risks and benefits of the individual CAM recommendations were also detailed. All recommendations made within the CPG were also linked to a body of evidence. While the CPG was externally reviewed, no plan was outlined to update the recommendations in the future [12].

3.7.4. Clarity of presentation

Generally, items within this domain were well-represented within the CPG. All recommendations were very specific and lacked ambiguity. Different treatment options were presented for different glaucoma symptoms and severities, and all key recommendations were easily identifiable through the use of headings [12].

3.7.5. Applicability

The CPG scored very poorly across items in the applicability domain. With respect to recommendations, the CPG failed to address facilitators and barriers to their application within the healthcare setting. The CPG also failed to provide resources to assist in the application of recommendations for patients and clinicians, particularly failing to link the CPG to any external tools or resources. Resource implications were discussed, but did not provide the sufficient detail needed to achieve higher scores within this item. The CPG also did not provide any monitoring and/or auditing criteria [12].

3.7.6. Editorial independence

The CPG reported the views of the funding body. While not clear within the CPG itself, it was reported that views of the funding body did not influence the development of the CPG. Similarly, competing interests were stated, but were not quickly nor clearly identifiable within the CPG.

4. Discussion

The purpose of this study was to identify the quantity and assess the quality of CAM recommendations found in CPGs for the treatment and/or management of glaucoma. Of the 7 eligible CPGs published from 2009 to 2020 that were relevant to glaucoma

treatment/management, only one CPG made mention and provided recommendations about CAM, which included CHM therapies for the treatment of glaucoma and its associated symptoms [12]. The authors of this CPG stated that their aim was to develop an evidence-based CPG of CHM for primary open-angle glaucoma with a focus on Chinese medicine pattern differentiation and treatment as well as approved herbal proprietary medicine. CAM therapies that they recommended for use included the following: Dan Zhi Xiaoyaosan; Taohong Siwu decoction and Wuling Powder; Wendan Tang; Lycii and Chrysanthemi and Rehmanniae bolus; Gingko leaf tablets; Erigeron breviscapus tablets; Wuling capsules; fuming tablets; Mingmu Dihuang Wan; and acupuncture [12]. Using the 23-item AGREE II instrument, the quality of this CPG was assessed twice: once for the overall CPG, and once for the CAM-specific sections. Since this CPG was entirely focused on CAM therapies for glaucoma treatment, most of the overall CPG scores were nearly equivalent to the CAM scores. The average appraisal score was 5.0 for the overall CPG, and 4.9 for the CAM-specific section; the average overall assessment for the overall CPG and for the CAM section were both 5.5. The scaled domain percentages for the overall CPG from highest to lowest were, as follows: scope and purpose (88.9%), editorial independence (79.2%), clarity of presentation (77.8%), rigour of development (74.0%), stakeholder involvement (66.7%), and applicability (16.7%). The scaled domain percentages for the CAM sections of the CPG from highest to lowest were, as follows: scope and purpose (88.9%), clarity of presentation (83.3%), editorial independence (79.2%), rigour of development (70.8%), stakeholder involvement (66.7%), and applicability (14.6%).

To our knowledge, this is the first study which has identified the quantity and assessed the quality of CAM recommendations for the treatment and/or management of glaucoma. With respect to glaucoma guidelines in general, a 2011 study assessed the quality of three

guidelines published by the following organizations: the American Academy of Ophthalmology, the European Glaucoma Society, and the South East Asia Glaucoma Interest Group. The authors found that variability exists in the quality of the guideline development process and how it is reported, as evaluated by AGREE II instrument [19]. A 2015 study also assessed the quality of three primary open-angle glaucoma guidelines, this time published by the American Academy of Ophthalmology, Canadian Ophthalmological Society, and the National Institute for Health and Care Excellence, also using the AGREE II instrument. The authors reported that the highest scoring domains were scope and purpose and clarity of presentation, while the poorest scoring domains were stakeholder involvement and editorial independence [20]. Most recently, a 2018 study assessed the methodological quality of glaucoma CPGs and their recommendations on microinvasive glaucoma surgery, also using the AGREE II instrument. They found that while a small proportion of CPGs assessed included basic information regarding the aforementioned clinical topic of interest, no CPGs provided specific recommendations regarding indications or patient populations which would benefit most from them [21]. The findings captured by the present study is, therefore, not dissimilar from that of the aforementioned comparative literature.

As only 1 out of the 7 eligible CPGs provided CAM recommendations for the treatment/management of glaucoma, it is difficult to make comparisons between the quality of CAM recommendations and that of other conventional treatments. However, there have been several studies that have assessed CAM recommendations in CPGs for different diseases/conditions. It is known from the literature that CPGs for chronic and non-chronic medical conditions tend to lack mention and recommendations of CAM-specific therapies alongside conventional treatments. A 2009 study assessed 88 guidelines, reporting that very few even mentioned CAM, and that there were large inconsistencies among studies that did

mention them [22]. They also noted that very few CPGs recognized CAM therapies as effective treatments, and encouraged patients to determine the value of CAM by trial and error [22]. In a 2016 study, domain scores amongs CAM CPGs published in 2003 or later were found to have an order from highest to lowest, as follows: clarity of presentation, scope and purpose, rigour of development, editorial independence, stakeholder involvement, and applicability [23]. The hierarchical order of the domain scores within the present study are relatively comparable to the order presented in the 2016 study, suggesting that although variability does exist between studies including CAM recommendations, many general characteristics of CPGs that have CAM recommendations tend to be similar among each other [23]. Across CPGs for different diseases/conditions, it has been found that the prevalence of CAM recommendations vary widely; while the majority, if not all, depression [24], low back pain [25], and cancer-related pain [26] CPGs contain CAM recommendations, they are more scarce across arthritis [27], multiple sclerosis [28], lung cancer [29], and hypertension [30] CPGs, and absent altogether in colon cancer [31] and ovarian cancer [32] CPGs. In general, these studies assessing the quality of available CAM recommendations across the aforementioned disease/condition CPGs also reported similar trends with respect to the order of domains when compared to the present study, whereby the scope and purpose and clarity of presentation domains typically scored most highly, while the domain of applicability typically scored most poorly [23], [24], [25], [26], [27], [28], [29], [30], [31], [32].

This lack of CAM recommendations across CPGs in general can be due to a variety of factors, including confirmation biases from clinicians, and the role of clinical translation of certain therapies into real-world settings [33,34]. Despite the fact that there is a high prevalence of CAM use across patients with glaucoma, the lack of CAM mention and

recommendations within glaucoma CPGs highlights the disconnect between patient preference and recommended therapies prioritized by guideline developers. Future CPG developers should aim to discuss the impact of CAM therapies for the treatment and/or management of glaucoma, alongside the potential benefits and risks of using CAMs to treat associated symptoms. Notably popular CAM therapies for glaucoma include CHMs and acupuncture, which have shown promise in reducing intraocular pressure. For example, a 2016 study concluded that surgery in conjunction with traditional Chinese medicines was found to be beneficial for patients with glaucoma [35]. Physicians and other healthcare providers use recommendations from credible CPGs associated with the condition they are treating to guide their clinical decision making [8]. Therefore, it is important that future CPGs outlining CAM therapies for glaucoma are developed with a high level of quality; this includes developing CPGs using one, if not multiple, of the many validated CPG development tools, such as those developed by the National Institute of Health and Clinical Excellence (NICE), World Health Organization (WHO), Scottish Intercollegiate Guidelines Network (SIGN) and the GRADE working group [36], [37], [38], [39]. In addition, ensuring that CAM experts are present during the development process will ensure that such therapies will be considered within CPGs, encouraging discussion between patients and healthcare providers about promising and preferred CAM therapies.

4.1. Strengths and limitations

Notable strengths of the present study included the use of a systematic review methodology to search for and identify relevant CPGs for the treatment/management of glaucoma, in addition to using the AGREE II instrument, which has been found to be valid and reliable and which is regarded as the gold standard for assessing the quality of CPGs. [11]. One limitation included the use of two appraisers instead of the recommended four, as suggested by the

AGREE II instrument user manual. To mitigate this and standardize scoring across appraisers, JYN, MN and ED conducted a pilot test, where they independently appraised three separate CPGs using the instrument, and then discussed and reached consensus on how to apply the AGREE II instrument. Additionally, MN and ED met with JYN to review any discrepancies in scoring across eligible CPGs containing CAM recommendations without unduly modified scores. We did not specifically search for, nor did we include, CPGs for the treatment and/or management of general eye conditions, thus we acknowledge that such CPGs may have contained CAM recommendations that may have been specific to glaucoma. Lastly, we only included CPGs published in English, which may not have captured CAM recommendations found in CPGs such as those originating from non-English speaking countries.

5. Conclusions

This study identified a single CPG providing CAM recommendations for the treatment and/or management of glaucoma. Appraisal of this CPG was conducted twice using the AGREE II instrument, once for the overall CPG and once for the CAM section. Given the limited findings, it is not possible to make comparisons between multiple different CPGs for glaucoma treatment specific to CAM therapy recommendations. This study identifies and highlights the lack of CAM representation in CPGs published to assist clinicians in the development of treatment plans for glaucoma. Despite the high prevalence of CAM use by patients with glaucoma, CAM recommendations for the treatment and/or management of this condition are sparse across evidence-based CPGs. It is important for future guideline developers to consider the impact of CAM therapies in glaucoma treatment, to bridge the gap between conventional therapies and patient preference for CAM use, as well as encourage

relevant discourse between clinicians and patients with respect to the safe and effective use of CAM.

6. Authors' contribution

JYN: designed and conceptualized the study, collected and analysed data, co-drafted the manuscript, and gave final approval of the version to be published.

MN: assisted with the collection and analysis of data, co-drafted the manuscript, and gave final approval of the version to be published.

ED: assisted with the collection and analysis of data, critically revised the manuscript, and gave final approval of the version to be published.

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Declaration of Competing Interests

The authors declare that they have no competing interests.

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Data availability

All relevant data are included in this manuscript.

Supplementary Materials

Supplementary File 1: MEDLINE Search Strategy for Glaucoma Clinical Practice Guidelines

Executed April 17, 2020

Supplementary File 2: Modified AGREE II Questions Used to Guide Scoring of CAM

Sections of Each Guideline

Supplementary File 3: List of Excluded Full-Text Articles

Supplementary File 4: AGREE II Scoring Data

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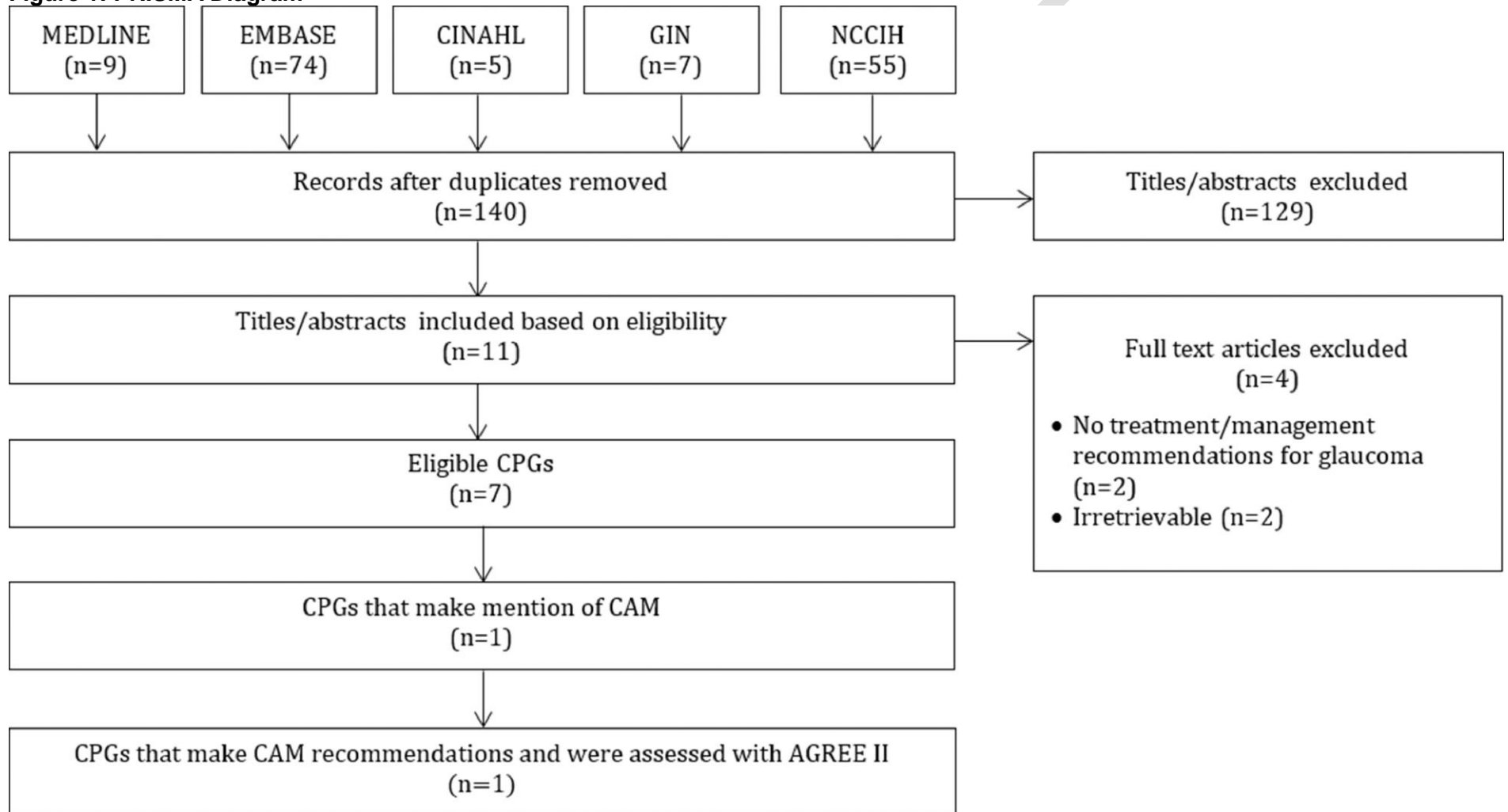
Figures
Figure 1: PRISMA Diagram

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┌──────────┐ ┌──────────┐ ┌──────────┐ ┌──────────┐ ┌──────────┐
│ MEDLINE  │ │ EMBASE   │ │ CINAHL   │ │   GIN    │ │  NCCIH   │
│  (n=9)   │ │ (n=74)   │ │  (n=5)   │ │  (n=7)   │ │ (n=55)   │
└──────────┘ └──────────┘ └──────────┘ └──────────┘ └──────────┘
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Records after duplicates removed
(n=140)

Titles/abstracts excluded
(n=129)

Titles/abstracts included based on eligibility
(n=11)

Full text articles excluded
(n=4)

- No treatment/management recommendations for glaucoma (n=2)
- Irretrievable (n=2)

Eligible CPGs
(n=7)

CPGs that make mention of CAM
(n=1)

CPGs that make CAM recommendations and were assessed with AGREE II
(n=1)

Figure 2: Summary of CAM Recommendations in Clinical Practice Guidelines

Guideline	CAM Therapy	Recommendation	Evidence Level	Recommendation Level
Yang et al. 2018	Dan Zhi Xiaoyaosan	+	Very Low	Slightly Recommended
	Taohong Siwu decoction and Wuling Powder	N/A	Expert Consensus	N/A
	Wendan Tang	+	Expert Consensus	Weakly Recommended
	Lycii and Chrysanthemi and Rehmanniae Bolus	+	Very Low	Slightly Recommended
	Gingko Leaf Tablets	+	Very Low	Slightly Recommended
	Erigeron Breviscapus Tablets	+	Moderate	Strongly Recommended
	Wuling Capsule	+	Expert Consensus	Weakly Recommended
	Fuming Tablets	+	Low	Slightly Recommended
	Mingmu Dihuang Wan	+	Very Low	Slightly Recommended
	Acupuncture	0	Expert Consensus	N/A

Legend:
+/green = recommendation for the therapy's use
-/red = recommendation against the therapy's use
0/yellow = recommendation unclear/uncertain/conflicting
N/A/grey = no recommendation provided

Tables
Table 1: Characteristics of Eligible Guidelines

Guideline	Country (First Author)	Developer	CAM Category	Guideline Topic
Yang 2018 [12]	China	Beijing Traditional Chinese Medicine Hospital	Chinese herbal medicines	Chinese herbal medicines for treatment of primary open-angle glaucoma
NICE 2017 [13]	United Kingdom	National Institute for Health Care Excellence	N/A	Guidelines for practitioners in the treatment of glaucoma in adult patients
Prum 2014 [14]	USA	Glaucoma Preferred Practice Pattern Panel	N/A	Preferred practice patterns for the treatment of primary open-angle glaucoma suspect
Prata 2014 [15]	Brazil	Brazilian Council of Ophthalmology	N/A	Treatment of angle-closure glaucoma
Heijl 2012 [16]	Sweden	Swedish Council on Health Technology Assessment Expert Panel	N/A	General treatment of glaucoma in adult patients
NHRMC 2010 [17]	Australia	National Health and Medical Research Council Expert Working Committee	N/A	Guidelines for the screening, prognosis, diagnosis, management and prevention of glaucoma
Rafuse 2009 [18]	Canada	Canadian Ophthalmologic Society– Glaucoma Clinical Practice Guideline Expert Committee	N/A	General guidelines for the treatment of glaucoma in the adult eye