· Bibliometric Research ·

Global research status in the treatment of glaucoma: a systematic bibliometric analysis

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Abstract

● **AIM:** To present an overview of the research on global glaucoma treatment in the last decade in terms of publication year, journals, countries/regions, organizations, references, and keywords, to investigate the current research international trends and hot topics in this area.

● **METHODS:** Bibliometric analysis was conducted on 9128 articles in the Web of Science Core Collection (WoSCC; Clarivate) database. Quantitative and qualitative analysis was employed using VOSviewer (v1.6.18), Pajek (v1.0.0.0), and CiteSpace (v6.1.R2) software.

● **RESULTS:** The 9128 papers relating to glaucoma treatment were published from April 2013 to April 2023, of which 7482 articles (82%) were original research articles and 1464 (18%) were review articles. The United States (2867) and Johns Hopkins University (166) were the most productive country and institution, respectively, but the University College London had the highest h-index (54). The *Journal of Glaucoma* was the most productive and *Ophthalmology* had the highest h-index compared with other journals. The Keywords of interest included treatment surgery, cyclophotocoagulation, minimally invasive glaucoma surgery (MIGS), trabeculectomy, baerveldt, epidemiology, medication adherence, nanoparticle, optical coherence tomography (OCT), gene therapy, and artificial intelligence (AI). Glaucoma surgery appeared as a current research hotspot through the analysis of keywords.

● **CONCLUSION:** This study provides insights into the research trends and potential research hotspots in the treatment of glaucoma. This will help researchers to evaluate research policies and to promote international cooperation.

● **KEYWORDS:** glaucoma treatment; bibliometric analysis; surgery; minimally invasive glaucoma surgery; nanoparticle

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INTRODUCTION

Glaucoma is the main reason for permanent vision loss globally, distinguished by optic disc excavation (cupping) and chronic progressive optic neuropathy[1]. It can damage the retina by destroying retinal ganglion cells (RGCs) and thinning the nerve fiber layer of the retina, leading to peripheral and, ultimately, central blindness[2]. The worldwide incidence of glaucoma in those aged 40 to 80 is estimated to be 3.5%[3]. Due to the growing number and percentage of older people, it is anticipated that there will be 111.8 million individuals affected by glaucoma by the year 2040[3]. Glaucoma can be classified into two types based on the anatomical state of the anterior chamber angle: open angle glaucoma (OAG) and angle-closure glaucoma (ACG)[2]. Each category is further classified into primary or secondary, indicating the lack or presence of additional clinically identifiable ocular or systemic disorders that might illustrate the occurrence of glaucoma[4]. Adult OAG often does not show any symptoms in its first stages, with around 50% of patients being unaware of their condition[5-7]. As OAG progresses, the patient's peripheral visual field is impaired, and the central vision decreases at advanced staging, leading to limited driving, activity, and reading[8].

In ACG, the presence of anatomical crowding between the iris and natural lens results in an unusual obstruction of the passage of aqueous humor through the pupil. The pupil block obstructs the passage of aqueous humor through the pupil. The elevated pressure exerted behind the iris causes it to flex towards the iris cornea angle, obstructing the trabecular meshwork[4]. In OAG, most glaucoma patients have open-angle but increased trabecular outflow resistance, which is usually associated with elevated intraocular pressure (IOP).

The biomechanical hypothesis indicates that IOP causes mechanical alterations in the optic nerve head (ONH) of glaucoma[9]. In addition, in vascular theory, vascular insufficiency plays a vital function in the pathogenetic mechanism of ganglion cell loss in the retina[10]. Nowadays, the therapeutic method cannot reverse the visual damage of glaucoma; however, disease progression can be prevented by early diagnosis and management. Decreasing IOP is a unique, effective method to stop or slow down glaucoma development[11]. For glaucoma patients, IOP could be decreased by the corresponding application of eye drops, laser therapy, and/or surgery[12-13]. Over the past decade, we have witnessed the development of glaucoma treatment. Here, to present an overview of the research on global glaucoma treatment in the last decade and to explore the present international trends and hot topics in this field, we conducted a bibliometric analysis of publications associated with glaucoma treatment in the previous decade.

Bibliometric analysis is a statistical technique introduced by Alan Pritchard in 1969. It aims to quantitatively assess and comprehend the influence and worth of research by assessing the scientific achievements of countries/regions, organizations, and journals. This analysis provides a comprehensive overview of a specific field[14]. In recent years, a wealth of research has been conducted in the field of glaucoma treatment, but there are few bibliometric studies. A complete and visible examination of the evolution and trends of glaucoma treatment investigations is still absent. This investigation aims to analyze the global research patterns, cooperative relationships, and new knowledge of glaucoma treatment to determine the research hotspots in the past decade. To evaluate the quality of scientific output, the current research included many bibliometric indexes, such as the number of publications, citations, and h-index, which is a recognized reflection of productivity and influence[15-18]. We also discussed some important sub-topics identified by bibliometric characteristics. Our study will assist researchers and professionals in determining the scope of investigation topics, identifying novel topics, or planning research directions in the area of glaucoma treatment.

MATERIALS AND METHODS

Data Extraction and Cleaning Process

Data retrieval Like previous bibliometric analyses[19-20], the study utilized the Web of Science Core Collection (WoSCC), which indexes approximately 21 858 journals along with books and conference proceedings (updated daily). The WoSCC database has approximately 85 million records that undergo daily updates (https://clarivate. libguides.com/librarianr esources/coverage). Our search employed the query string TS= [("glaucoma"* OR "glaucoma eyes") AND ("treatment"* OR "therapy")] to examine titles, abstracts, and keywords. The search was restricted to English-language publications dated between April 16, 2013 and April 16, 2023. We systematically excluded several document types to focus on primary research literature, including conference abstracts (*n*=412), conference papers (*n*=205), online publications (*n*=176), editorial materials (*n*=138), letters (*n*=70), book chapters (*n*=36), corrections (*n*=19), data papers (*n*=5), news items (*n*=5), retracted publications (*n*=3), hardware reviews (*n*=1), and republications (*n*=1; Figure 1).

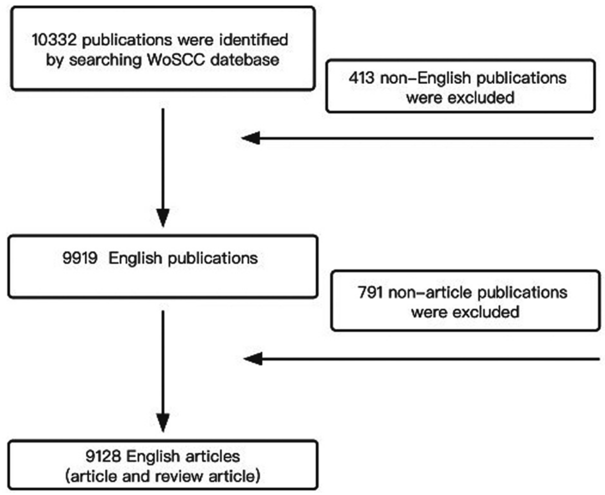

Figure 1 Flowchart demonstrating the literature screening.

Data cleaning and standardization To ensure data consistency, we performed comprehensive cleaning procedures including 1) synonym standardization [*e.g.*, merging "intraocular-pressure" and "intraocular pressure (IOP)" into "IOP"; combining "hypertension" with "ocular hypertension"]; 2) abbreviation unification (*e.g.*, "POAG" for "primary open-angle glaucoma"); 3) institutional name normalization (*e.g.*, converting "Univ." to "University"); 4) geopolitical harmonization (*e.g.*, incorporating Taiwan under China, and consolidating UK nations as United Kingdom); 5) duplicate removal using DOI and WoS accession numbers. These steps enhanced the reliability of subsequent bibliometric analyses.

Inclusion and Exclusion Criteria Studies were included if they: 1) focused on glaucoma treatment/therapy; 2) were peer-reviewed articles or reviews; 3) were published in English; 4) fell within the 10-year publication window (April 16, 2013-April 16, 2023). We excluded non-research publications (*e.g.*, editorials, news items), incomplete records (*e.g.*, conference abstracts without full text), and studies unrelated to therapeutic interventions (*e.g.*, purely diagnostic or epidemiological research).

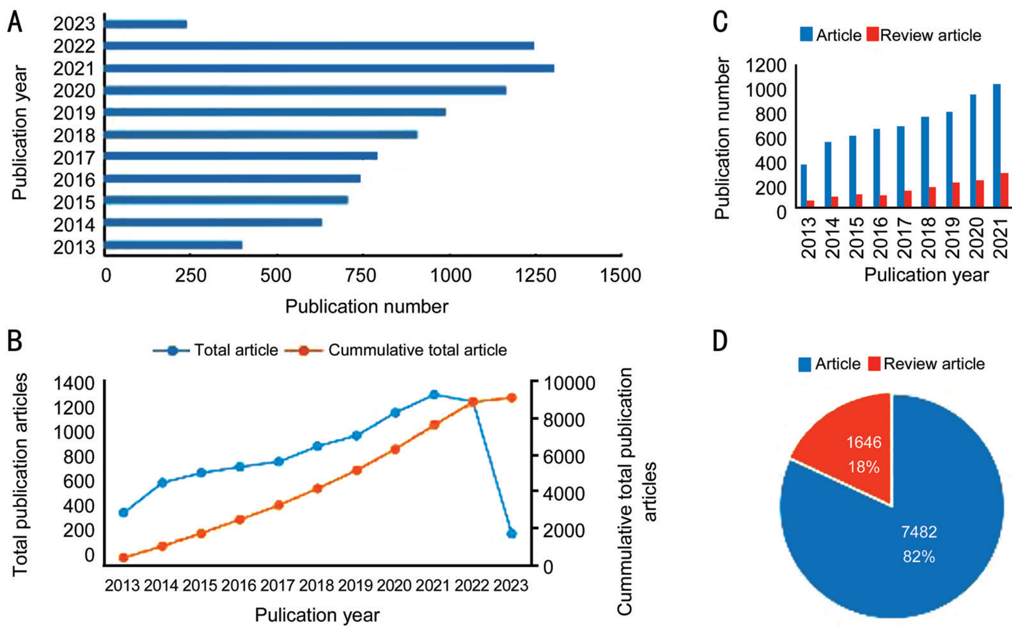

Figure 2 Annual output and the cumulative annual output of glaucoma treatment A: Annual number of publications; B: Growth trends of annual publications and cumulative publications; C: The illustration of the publication characteristic; D: The publication access type and the document type distribution.

Assessment of Database Coverage Bias Potential biases in our study include: 1) journal coverage limitations, as WoSCC prioritizes high-impact English-language journals and may underrepresent regional or non-English publications; 2) document-type bias, with less comprehensive indexing of conference materials and books compared to journal articles; 3) citation bias favoring earlier publications due to cumulative citation counts. To mitigate these limitations, we implemented several measures: cross-validation with PubMed data to identify coverage gaps, a carefully selected 10-year timeframe to balance recency and citation maturity, and full transparency in reporting excluded publication types and quantities (*e.g.*, 412 conference abstracts).

Data Analysis and Visualization We used Microsoft Office Excel 2013 (Microsoft Corporation, Redmond, Washington, USA) to describe the distribution and growth of publications. Bibliometric analysis was performed using VOSviewer 1.6.18 (Centre for Science and Technology Studies, Leiden University, Leiden, The Netherlands) to recognize and extract the information of published journals, co-cited journals, countries, institutions and co-cited references. We performed a visual analysis of the cooperation networks of countries and institutions[21]. We also used VOSviewer to create the cluster analysis of keywords.

RESULTS

Annual Growth Trend of Published Papers We searched 9128 publications relating to glaucoma treatment from April 16, 2013, to April 16, 2023 (Figure 2A), of which 7482 articles (82%) and 1464 reviews (18 %; Figure 2C-2D). In the past ten years, the annual number of publications has shown an upward trend except for the previous year, and the cumulative number of publications has shown an increasing trend (Figure 2B). In 2013, the annual publication output of glaucoma treatment research was less than 500, and from 2014 to 2017, it increased steadily from 630 to 791. Interestingly, between 2020 and 2022, production exceeded 1000 and peaked at 1301 in 2021 (Figure 2A), which increased by 212.25% compared with 2013. This result shows that the treatment of glaucoma has attracted more and more attention.

Distribution and Visual Analysis of Journals To assess the level of quality of journals in the area of glaucoma treatment, we evaluated the top 10 journals based on their cumulative publication count (Table 1). The papers were published in a total of 1704 distinct journals. A total of 2267 articles, accounting for 24.84% of the total, were published in the best ten journals. The *Journal of Glaucoma* had the highest number of published articles on glaucoma treatment (570, 6.24%), but the citations per manuscript were very low (9.98). The *Investigative Ophthalmology & Visual Science* and the *British Journal of Ophthalmology* published 250 and 204 articles, respectively, placing them in the second and third positions in terms of publication volume. *Ophthalmology* had the highest h-index score of 52, with *Investigative Ophthalmology & Visual Science* and *American Journal of Ophthalmology* following closely with scores of 39 and 35, respectively. A co-citation connection is established when two journals are cited together in the same journal. The co-citation rate of the two journals is directly proportional to the proximity of their academic study topics.

Out of the total 21 811 co-cited journals, 10 journals have

Table 1 The top-10 journals on glaucoma treatment

Position	Top 10 journal	Country/region	IF (2021)	Publication, *n* (%)	Citations	Citation per publication	Total link strength[a]	H-index[b]
1	*Journal of Glaucoma*	USA	2.29	570 (6.24)	5686	9.98	1182	33
2	*Investigative Ophthalmology & Visual Science*	USA	4.925	250 (2.74)	5983	23.93	420	39
3	*British Journal of Ophthalmology*	England	5.907	204 (2.23)	2670	13.09	514	29
4	*American Journal of Ophthalmology*	USA	5.488	189 (2.07)	3767	19.93	624	35
5	*PLoS One*	USA	3.752	189 (2.07)	3351	17.73	325	33
6	*International Ophthalmology*	the Netherlands	2.029	188 (2.06)	942	5.01	384	13
7	*BMC Ophthalmology*	England	2.086	180 (1.97)	1390	7.72	336	18
8	*Graefes Archive for Clinical and Experimental Ophthalmology*	USA	3.535	168 (1.84)	2137	12.72	470	24
9	*European Journal of Ophthalmology*	England	1.922	165 (1.81)	972	5.89	306	16
10	*Ophthalmology*	USA	14.277	164 (1.80)	9970	60.79	1083	52

IF: Impact factor. *n*: the number of publications. [a]The total link strength (for the journal) was analyzed from the top 10 journals using VOSviewer software; [b]The calculation of the H-index was based on the literature data collected in this study, and not on all scientific publications of a journal.

Table 2 The top-10 co-cited journals on glaucoma treatment

Position	Top 10 co-cited journal	Country/region	IF (2021)	Citations	Total link strength[a]
1	*Investigative Ophthalmology & Visual Science*	USA	4.925	29096	682240
2	*Ophthalmology*	USA	14.277	28592	733134
3	*American Journal of Ophthalmology*	USA	5.488	18330	531991
4	*Archives of Ophthalmology*	USA	4.399 (2014)	14286	454230
5	*British Journal of Ophthalmology*	England	5.907	13424	368565
6	*Journal of Glaucoma*	USA	2.29	13128	360761
7	*Experimental Eye Research*	USA	3.77	8478	247346
8	*Eye*	England	4.456	6231	168244
9	*PLoS One*	USA	3.752	6057	160373
10	*Graefes Archive for Clinical and Experimental Ophthalmology*	USA	3.535	5102	155812

IF: Impact factor. [a]The total link strength (for the journal) was analyzed from the top 10 journals using VOSviewer software.

surpassed the limit of being cited together more than 5000 times. Table 2 demonstrates that *Investigative Ophthalmology & Visual Science* had the largest number of co-citations (n=29 096), with the Journal of *Ophthalmology* following closely after (n=28 592). Out of the top 10 co-cited journals, six have an impact factor of more than 4, and eight are affiliated with institutions in the United States.

Analysis of Countries/Regions and Institutions Over the last ten years, a total of 9128 papers were collaboratively authored by researchers originating from 7361 institutions across 124 nations or regions. We have chosen all the countries/regions to perform the analysis of the cooperation network visualization. Figure 3 illustrates countries/regions as circles, with the size of every circle corresponding to the number of publications in that country/region. The thickness of the loop line corresponds to the level of collaboration between countries/regions, whereas the identical color signifies strong cooperation. The co-author networks of 124 countries/regions have been separated into ten clusters and shown utilizing distinct colors. The biggest cluster, which comprises 23 nations, is mostly located in Spain, Poland, and the Netherlands. Active international collaboration was observed particularly in the United States, China, England, Japan, and Republic of Korea (Figure 3). The United States had the largest number of partners (33), followed by England (21) and Germany (14). The United States leads the list, contributing 31.41% of the world's total publications (2867 out of 9128 papers) and 29.64% of the world's total citations (59 054 out of 199 256 papers). China (Mainland) ranks second with 1361 papers published (14.91% of the world's total papers published) and 14 027 papers cited (7.04% of the world's total cited), and cooperates mainly with the USA. England and Japan have 740 and 570 publications, respectively, making them the following two countries/regions. Except for the USA, England exceeds all other European countries/regions in terms of overall citations. China (Mainland; 14 027) was the most often cited country in Asia, followed by Japan (7483) and India (5809). By employing the h-index as a measure of production and the impact of academics, we discover that American authors possess the greatest h-index across the best ten nations. Furthermore, the aggregate connection strength serves as an indication that accurately represents the level of research collaboration's strength. Table 3 displays the level of research cooperation in the best ten countries/regions. Unsurprisingly, the USA is the nation that is most dedicated to international

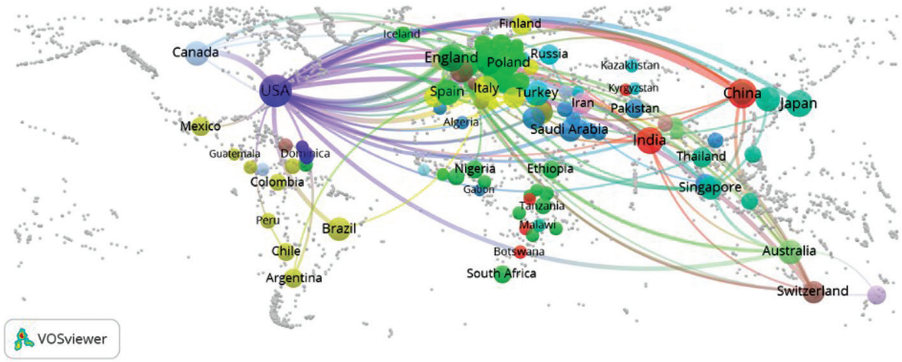

Figure 3 Geographical visualization of the publication and collaboration status of the contributing countries/regions in glaucoma treatment research Each dot symbolizes a country/region, with its size determined by the number of articles originating from that particular country/region. The thickness of the lines linking the circles represents the degree of collaboration between countries/regions, whereas the identical color denotes a substantially stronger level of cooperation.

collaboration, as seen by its overall connection strength of 850.

Quantity (reflecting productivity) and quality (indicating impact) are considered to be the criteria for measuring scientific performance. Therefore, this study also used h-index, an indicator that combines productivity and impact. The results show that at the h-index level, the United States leads, followed by England (60), China (Mainland) (45), Italy (44), Germany (44), Canada (43) and Japan (40).

Regarding research institutions, WoSCC identified 7361 institutions that contribute to glaucoma treatment publications. Next, we selected 193 institutions with over 20 publications for visual network analysis (Figure 4). Every node in the network diagram indicates an individual organization. A higher degree of connectivity between nodes indicates a greater level of collaboration, whereas a smaller distance suggests a tighter link among nodes of identical coloration. The co-author network, consisting of 193 institutions, is separated into 9 clusters, each denoted by a unique coloration. The red cluster comprises 42 universities, with its focus on the University of Miami, the University of California, San Diego, and Columbia University. It is the biggest cluster among them. We found close cooperation between institutions, especially between Johns Hopkins University and Duke University. The University of Miami also actively cooperated with these two institutions (Figure 4), in the top 193 organizations, most institutions have close cooperation with each other.

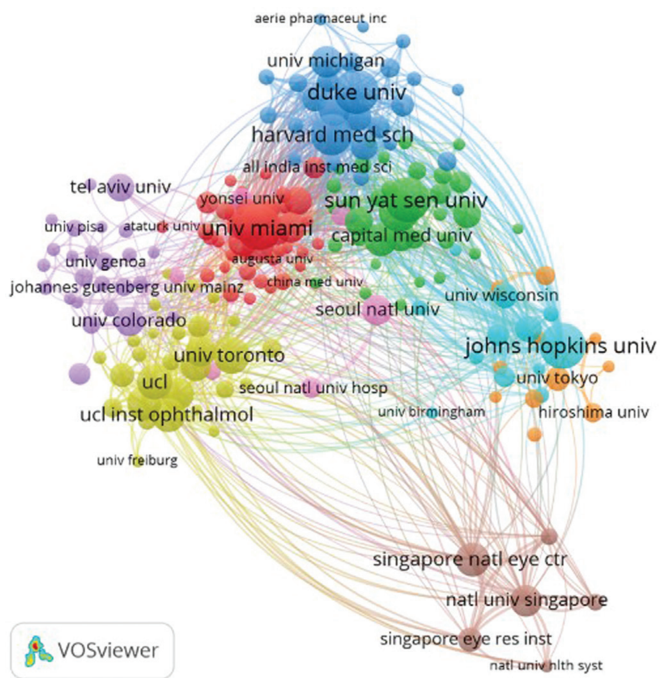

Figure 4 Collaboration networks among institutions The weight of institutions is represented by the size of each node, the cooperative link among organizations is shown by the lines connecting nodes, and nodes of identical color suggest the same cluster, with this size corresponding to the number of publications of institutions.

Visual Analysis of Keywords Keywords are an important part of publications, reflecting the theme of publications. Typically, 23 789 keywords were extracted from the data, which have been retrieved for additional analysis of the keyword emergence network. The first 202 keywords that appear at least 55 times are visualized (Figure 5A). The larger the node size, the more keywords appear, the shorter the distance indicates the stronger the correlation and the nodes of the same color indicate the similarity between topics. It can be seen that the keywords are divided into four main clusters (Figure 5A). The red cluster contained the most entries (68 keywords) associated with glaucoma surgery therapy including trabeculectomy, trabeculotomy, phacoemulsification (cataract-surgery), minimally invasive glaucoma surgery (MIGS), cyclophotocoagulation and postoperative complications. Given that the choice of the three major treatment options for glaucoma has a certain relationship with the type of glaucoma, refractory glaucoma, and neovascular glaucoma are also included. The second cluster, often known as the green cluster, focuses on investigating the causes and development

Table 3 Top 10 countries/regions according to the total publication number

Position	Top 10 country/region	Publication	Citation	Citation per publication	Total link strength[a]	H-index[b]
1	USA	2867	59054	20.6	850	92
2	China (mainland)	1361	14027	10.31	307	45
3	England	740	16039	21.67	371	60
4	Japan	570	7483	13.13	109	40
5	India	568	5809	10.23	155	38
6	Italy	499	10021	20.08	206	44
7	Germany	481	9813	20.4	193	44
8	Republic of Korea	348	3702	10.64	63	31
9	Türkiye	328	2836	8.65	30	25
10	Canada	317	6569	20.72	194	43

[a]The VOSviewer program was used to examine the overall link strength of the top 10 countries/organizations/scholars (for the country/organization/scholar); [b]The calculation of the H-index was based on the literature data collected in this study and not on all scientific publications of a particular country/region, organization, or scholar.

Table 4 The top-10 co-cited references on glaucoma treatment

Position	Author	Title	Journal	Citations	Total link strength[a]
1	Quigley HA	The number of people with glaucoma worldwide in 2010 and 2020	*British Journal of Ophthalmology*	1138	1166
2	Tham YC	Global prevalence of glaucoma and projections of glaucoma burden through 2040	*Ophthalmology*	885	960
3	Kass MA	The ocular hypertension treatment study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma	*Archives of Ophthalmology*	671	1319
4	Heijl A	Reduction of intraocular pressure and glaucoma progression: results from the early manifest glaucoma trial	*Archives of Ophthalmology*	645	1216
5	Weinreb RN	The pathophysiology and treatment of glaucoma a review	*JAMA-Journal of The American Medical Association*	581	676
6	Van veldhuisen PC	The advanced glaucoma intervention study (AGIS): 5. encapsulated bleb after initial trabeculectomy	*American Journal of Ophthalmology*	467	956
7	Gordon MO	The ocular hypertension treatment study: baseline factors that predict the onset of primary open-angle glaucoma	*Archives of Ophthalmology*	352	662
8	Leske MC	Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial	*Archives of Ophthalmology*	347	757
9	Weinreb RN	Primary open-angle glaucoma	*Lancet*	293	448
10	Gedde SJ	Treatment outcomes in the tube versus trabeculectomy (TVT) study after five years of follow-up	*American Journal of Ophthalmology*	262	214

[a]The VOSviewer program was used to examine the overall link strength of the top 10 references for the given reference.

of glaucoma. This includes studying the impact of oxidative stress on the trabecular meshwork, aberrant gene expression, abnormalities in the dynamics of aqueous humor or outflow facility, and the death of ganglion cells in the retina. The third significant subject comprises many subcategories of glaucoma, including clinical manifestations of elevated IOP and visual field impairment, alterations in the nerve fiber layer, techniques for conducting optical coherence tomography (OCT) examinations, and the utilization of selective laser trabeculoplasty (SLT) as a therapy strategy. Especially, primary open angle glaucoma (POAG, also identified as the main topic) and normal-tension glaucoma (NTG) have gained more attention over the past decade. Keywords of intraocular hypertension and efficacy medication treatment such as latanoprost and latanoprost analogs were included in the fourth cluster (yellow cluster).

To analyze the evolution in trends as time passes, the keywords obtained from the publications were assigned colors employing VOSviewer, depending on their average appearing year (AAY), and coded utilizing a heat map (Figure 5B). The keywords in cooler colors represent those that appeared early and keywords labeled warmer colors indicate that their average year of occurrence is recent, so they are now more likely to become hot topics, which include (treatment) surgery, cyclophotocoagulation, MIGS, trabeculectomy, implantation, tube, baerveldt, epidemiology, medication adherence, ocular surface disease, nanoparticle, gene therapy, OCT, drainage device, gene therapy, and so on. It is indicated that the outcomes of several glaucoma surgeries have been identified as an emerging topic. Especially, advances in MIGS surgery and other implantation surgeries like tube and drainage device applications have been greatly studied by scholars. Because glaucoma has family heredity, gene therapy research has become a hot spot.

Analysis of Co-Cited References Subsequently, we employ VOSviewer to analyze the co-cited references. The co-citation analysis identified seminal studies that have fundamentally shaped glaucoma research and treatment paradigms. As

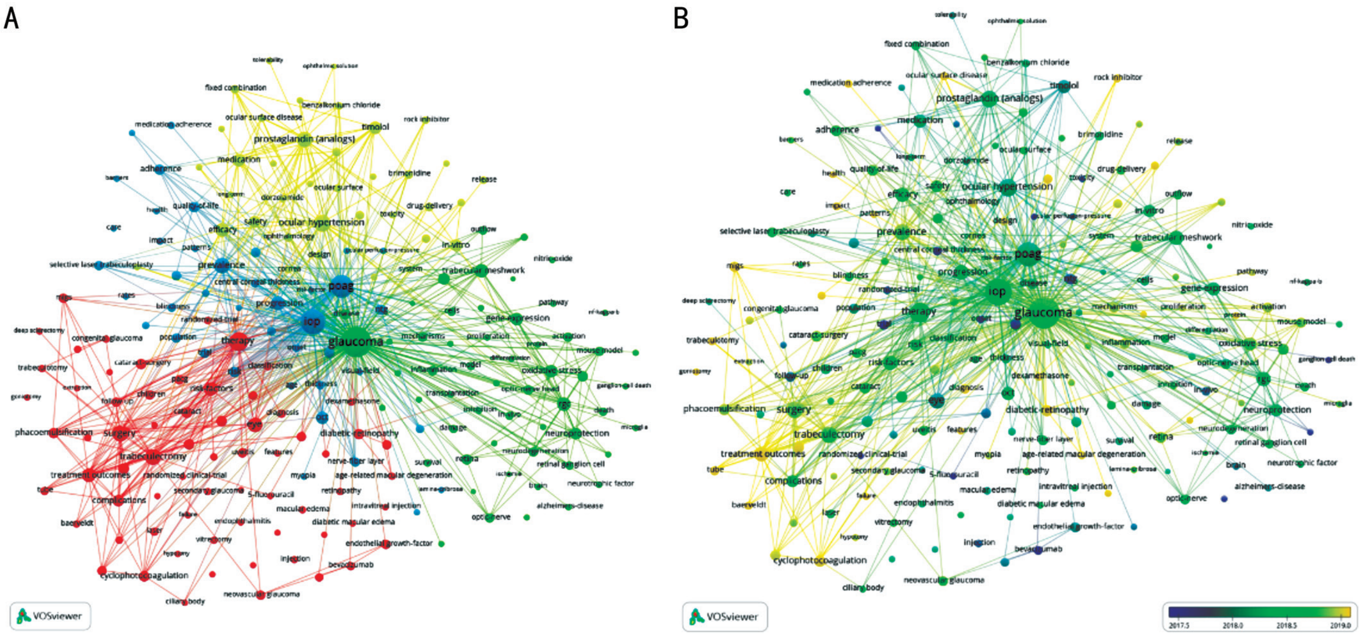

Figure 5 The occurrences network clustering of the top 200 keywords based on different domains (A) and the chronological overview of keywords is based on average occurrences per year (B) A: Bigger node sizes correspond to a greater frequency of keywords, shorter distances indicate a closer relevance, and nodes of similar color indicate similarity across topics. B: Keywords that are closer to the color green indicate that their average year of occurrence is more recent, suggesting that they are more likely to be trending topics now.

presented in Table 4, the co-citation frequency of the first 10 co-cited articles is more than 258 times, and the co-citation frequency of the first article is more than 1000 times and was published in the *British Journal of Ophthalmology* by Quigley and Broman[22] in 2006 titled "The number of people with glaucoma worldwide in 2010 and 2020". The most cited work by Quigley and Broman (2006)[22] established critical global prevalence estimates using UN population projections, revealing glaucoma as the world's second-leading cause of blindness with disproportionate impacts on Asian populations and women - findings that have guided resource allocation and public health strategies for two decades. The second highest co-cited article was published in *Ophthalmology* in 2014 by Tham *et al*[3]. Through innovative Bayesian Meta-regression analysis, this study proposes an evidence-based approach to achieve accurate risk stratification and provides a basis for modern screening programs and targeted interventions.

We note that four of the other top ten common references are published in the *Archives of Ophthalmology* and two of them are published in the *American Journal of Ophthalmology.* Weinreb RN has two articles in the top 10 co-cited articles.

DISCUSSION

In the present study, we analyzed the characteristics of countries/regions, organizations, scholars, keywords, journals, and co-cited references of 9128 papers relating to glaucoma treatment in the past decade from a bibliometric analysis perspective. The results generated a visualized display of global research on glaucoma treatment including publication trends, productivity, and impact, global collaboration patterns hotspots, and new frontiers.

Global Trends in Glaucoma Treatment Research The first glaucoma surgery of iridencleisis was back in 1902; however, the earliest documented publication on iridectomy was published in 1857 and can be found in PubMed[23-25]. In addition to glaucoma surgery, the history of glaucoma treatment is earlier. Nowadays, drug therapy (medication) and surgical treatment (surgery) of glaucoma have been widely applied in clinical management[26-32] (Figure 5). Our bibliometric analysis of 9128 articles from 7361 organizations in 124 nations reveals a consistent increase in the number of publications on this issue throughout the years. Figure 2 demonstrates a consistent increase in the number of papers related to glaucoma therapy investigations during the previous ten years. Even though the number of articles fluctuated slightly in some years, the number of cumulative manuscripts is growing smoothly. The total of publications in the last year (2022) was more than three times that of 2013. Glaucoma treatment research has grown exponentially, reflecting the global attention to the problem of glaucoma blindness. The surge in publications from 2020 to 2022 may reflect the clinical adoption of novel technologies, including MIGS and nanomedicine, indicating accelerated translation of research into practice. It is necessary to pay attention to whether the high volume of publications is accompanied by the simultaneous growth of high-quality evidence (such as randomized controlled trial studies).

An examination of published journals and co-cited publications shows that the *Journal of Glaucoma* is the main source of published papers, greatly promoting the sharing of glaucoma treatment knowledge. While the current influence of the publication, as measured by the number of citations per publication and h-index, may not be very high, it is anticipated that more significant and high-quality articles will be released in the future. *Ophthalmology* has the highest h-index and citations per paper, indicating its influence in the field of glaucoma treatment. Therefore, highly published journals (such as the *Journal of Glaucoma*) are important sources for clinicians to acquire surgical techniques and case experience, but low citations suggest that the level of evidence needs to be carefully evaluated. *Ophthalmology*'s high impact suggests that it is more likely to publish research that changes clinical practice (such as epidemiology or surgical innovation).

The USA was an example of productivity and the center of global collaboration. Therefore, the USA led the way in scientific and scholarly studies related to the management of glaucoma. These achievements have benefited from a large amount of financial support (data not shown) and the outstanding contributions of a group of scholars. European countries/regions like England, Italy, and Germany often exhibit more academic impact, as seen by their relatively elevated citation rates and h-index scores. Over the last decade, Asian countries/regions, including China (Mainland), Japan, and India, have experienced a significant increase in production. A decade ago, China (Mainland) was not among the top 10 countries in terms of productivity. Currently, it ranks as the second top-producing country/region for publishing research on glaucoma treatment, surpassed only by the United States. In addition, international cooperation has significantly promoted the development of glaucoma research, such as the achievements of the United States, China (Mainland), and England, thus encouraging more and deeper international cooperation.

It is worth noting that the academic influence of Asian countries (regions) still has room for improvement. Although they are productive, their citation frequency and h-index are relatively low. One potential explanation is that academics prefer to prioritize research organizations that have established a dominant position over a long period and often cite their works in publications. An additional aspect to consider is that, in certain regions, the significance placed on the quantity of papers produced is exaggerated when assessing an individual's academic achievement. In the next decades, we anticipate them to provide an increased amount of cutting-edge scientific output. The primary objective of performing research on glaucoma treatment is to get a comprehensive understanding of this complicated condition that causes blindness and to develop highly effective treatment choices for every patient in clinical practice, rather than only focusing on expanding the number of published studies.

Hotspots and New Frontiers of Glaucoma Treatment Research The co-cited literature constitutes a knowledge base in the corresponding research field. Analysis of highly co-cited articles can guide researchers in monitoring the progress and path of experimental or clinical trial investigations. In general, the first ten articles cited focused on the epidemiology of glaucoma (local or distant), the treatment of high intraocular pressure, and the progressive factors and therapeutic effect of glaucoma, and these articles demonstrated the evolution of glaucoma treatment. These foundational studies continue to influence clinical guidelines through their: 1) standardized epidemiological frameworks; 2) identification of high-risk demographic patterns; 3) methodological innovations in disease modeling-collectively driving both therapeutic advances and global vision of health policies while highlighting persistent healthcare disparities in glaucoma management. Keywords often represent the primary topics of a publication; we analyze their profile and select several hot keywords in recent years to explain in this study, combining the VOSviewer network diagram (Figure 5).

Overview of Glaucoma Treatment The only established treatment for glaucoma is the reduction of IOP. A number of investigations have demonstrated that reducing IOP slows down the advancement of glaucoma in people who already have the condition and decreases the possibility of acquiring glaucoma in individuals with ocular hypertension[33-35]. All therapies, like medical treatment, laser treatments, and surgical procedures, are focused on either decreasing the formation of aqueous humour, enhancing the outflow of the conventional or uveoscleral channel, or both. As shown in Figure 5, with the development of inspection equipment including gonioscopy, OCT and field of vision investigation instruments, drug research, surgical equipment, *etc*., ocular hypertension (OHT) treatment research of IOP-lowering drugs and laser and surgery acting on different ocular structures has made great progress.

Historically, topical medications have been first-line therapy. The first topical medication for treating glaucoma, known as pilocarpine, was developed in 1875[36]. Subsequently, epinephrine was introduced 50 years later[37]. The most regularly prescribed medications to promote outflow *via* the unconventional route are prostaglandin analogues (Figure 5). Beta-blockers, which decrease the generation of aqueous, are utilized as a second-choice therapy owing to the potential negative effects from absorption into the bloodstream. Alpha-adrenergic agonists and carbonic anhydrase inhibitors are frequently utilized as third or fourth options in therapeutic protocols[38]. Rho kinase inhibitors exert their effects by directly influencing the cells of the trabecular meshwork and

Schlemm's canal, specifically by affecting the formation of the extracellular matrix and the adhesion and contractility of trabecular meshwork cells, which leads to an increase in outflow[39]. Additionally, these inhibitors also mitigate the damage caused by reactive oxidative stress to the trabecular meshwork[40]. Figure 5B illustrates that drug adherence, also known as adherence, has become a significant issue in glaucoma management in recent years. It is considered one of the primary concerns[41]. Enhancing patient education, simplifying treatment regimen, and minimizing adverse effects would be expected to enhance adherence. Additionally, this problem might be addressed via other methods, including slow-release implants that can be injected into the anterior chamber, subconjunctival space, or intravitreal space. By increasing the utilization of SLT and reducing surgical thresholds, there are now additional therapeutic alternatives that do not need strict adherence by patients.

In 1979, Wise and Witter[42] introduced argon laser trabeculoplasty (ALT). Twenty years later, in 1998, Latina *et al*[43] proposed SLT, which is another hotspot near 2018 (Figure 5B). SLT is the prevailing and widely accepted laser therapy for POAG[44]. Recent randomized controlled trial evidence supports SLT as a first-line treatment and earlier surgical intervention before significant visual field loss, which represents a paradigm shift in glaucoma treatment and OHT[45-46]. Employing the analysis of the keyword, we discovered that the research on laser therapy focused on cyclophotocoagulation in recent years (Figure 5B). In the early 1970s, cyclophotocoagulation was first introduced as the last surgical method to reduce intraocular pressure, mainly for the management of refractory glaucoma. In the process of ciliary body photocoagulation, the semiconductor diode laser is used to destroy the ciliary body and make it lose the function of producing aqueous humor[47]. Attention should be paid to the scope of ciliary body photocoagulation; too large may lead to low IOP, eye atrophy, and other complications.

Surgery is often conducted when non-invasive treatment, such as maximum-tolerated medications and/or laser trabeculoplasty, fails to achieve the desired level of IOP[48]. In 1857, Gräfe[49] designed an iris resection to treat glaucoma. This procedure has been improved many times and has been improved to a modern modified composite of trabeculectomy (TRAB) through techniques such as removable scleral flap suture, combined use of anti-metabolic drugs, and pre-evaluation of intraoperative and postoperative excessive filtration. Using the keywords analysis, we found that studies on signaling pathways, gene therapy, drug delivery systems, and adjuvant radiation therapy for fibrosis of the filtration channel are also being carried out to improve the long-term filtration channel scarring after TRAB surgery and lead to surgical failure[50-51]. Currently, trabeculectomy is the prevailing surgical procedure for glaucoma filtration. Now, with the development of examination technology, drug research and development, surgical equipment, *etc.*, the treatment of ocular hypertension has made progress. Recently, non-invasive glaucoma surgery, such as MIGS has been welcomed with the regular launch of new devices[45].

Minimally Invasive Glaucoma Surgery As shown in Figure 5B, using the keywords analysis, we discovered that the research on glaucoma treatment concentrated on MIGS. This is in line with the recommendation of MIGS and the expansion of clinical application in a number of international guidelines (such as the European Glaucoma Association guidelines) after 2016[52]. For example, the high frequency of "Hydrus microstents" and "Xen gel stents" in bibliometrics directly corresponds to the surge in clinical research on FDA-approved MIGS devices. Still, their safety studies (such as the 5-year follow-up data of Cypass microstents[53]) further promote academic output in this field.

MIGS refers to a group of unique surgeries and equipment designed to reduce intraocular pressure, which has become the latest member of the surgical treatment model for glaucoma[54] and has developed a lot in recent years[32]. In general, MIGS can be classified into surgical procedures that enhance the flow through the trabecular [such as Trabectome, iStent (first and second generations), Hydrus microstent, Kahook Dual Blade, and gonioscopy-assisted transluminal trabeculotomy], surgical procedures that improve suprachoroidal outflow (Cypass microstent and iStent Supra), and procedures that create blebs in the conjunctiva (Xen gel stent and InnFocus microshunt). Minimally invasive ciliary body destruction surgery includes ultrasonic ciliary body plasty, micropulse ciliary body photocoagulation, endoscopic ciliary body photocoagulation, *etc.*

In comparison with conventional glaucoma surgery like trabeculectomy and glaucoma drainage device implantation (Ahmed, Baerveldt, Molteno valve), MIGS is defined as six characteristics: no incision approach, minimal trauma to the target tissue, at least moderate efficacy, good safety, shorter operation time and rapid recovery[55]. Most MIGS aims to reconstruct the physiological drainage channel of aqueous humor. These procedures can be performed in conjunction with cataract surgery to provide a more substantial decrease in intraocular pressure. However, at present, most MIGS are more appropriate for individuals with mild to moderate glaucoma and OAG due to their small IOP reduction and the operation on trabecular meshwork and Schlemm tube. Patients with severe or refractory glaucoma who need a reduction in target IOP are recommended to choose filtration or ciliary secretion weakening surgery as the main treatment method according to the guidelines or consensus[56]. The problem of IOP spikes in the early stage after MIGS has been plaguing glaucoma physicians. International cooperation and collaborative research should be strengthened to solve this problem[57]. The existing data on MIGS in children with glaucoma are from cohort studies and case series or reports. The majority of the published studies tend to apply gonioscopy-assisted transluminal trabeculotomy (GATT) and 360 trabeculotomy (Trab360), which is similar to the full-cycle external trabeculotomy in terms of safety and efficacy in the management of glaucoma in children[57-58]. Thus, MIGS is a developing area, and the effectiveness and potential problems of each surgical procedure should be evaluated separately, with more focus on high-quality and extensive research conducted over a long period. Using the keywords analysis, we believe that in the future, ophthalmic surgery will also develop towards the mainstream trend of MIGS. With the advancement of science and technology, MIGS is still constantly improving. It is believed that shortly, there will be a variety of surgical options for different types of patients and truly personalized treatment under the premise of safety and effectiveness. At the same time, more high-quality investigations are required to discover the clinical application of MIGS. The surge of MIGS research results from the joint action of policy support, capital investment, market demand, and technological progress[52]. Among them, policy and capital are the core driving forces, which directly promote the transformation of technology from laboratory to clinical by reducing R&D barriers, stimulating innovation, and expanding market access. In the future, with the application of precision medicine and artificial intelligence in ophthalmology, MIGS research may be further deepened, but its development still needs continuous policy guidance and financial guarantee.

Nanoparticle and Nanotechnology As shown in Figure 5, "Nanoparticle" is another hot keyword. At present, there are a variety of eye drops that decrease intraocular pressure. Nevertheless, research conducted estimated that patient adherence to the strict usage of glaucoma ocular drops was below 50%[59]. The need to provide easy, secure, and efficient sustained-release medication delivery techniques for long-term treatment to enhance patient adherence and effectiveness has not been met. Recently, as shown in Figure 5, nanomedicines have emerged as the best alternative to traditional ophthalmic preparations because of their advantages in enhancing barrier permeability, prolonging drug release, targeting specific tissues, and minimizing systemic absorption[29]. Nanotechnology can address the restrictions of existing therapies by encapsulating and coupling drugs for reducing intraocular pressure and anti-fibrosis, utilizing biodegradable or biocompatible nanoparticles to continuously release medications to protect injured eye cells[60]. The explosive growth of "nanoparticle" keywords in bibliometrics (Figure 5B) reflects the acceleration of nanotechnology from basic research to clinical transformation. For example, the Bimatoprost implant study published in 2021 directly contributed to the first nano-implant into phase III clinical trials (NCT02250651)[61], which significantly improved patient compliance through long-term sustained release and targeted delivery, confirming the synchronization of literature trends and clinical innovation. Recently, an investigation project demonstrated that zwitterionic OPDEA-PCL micelles enhance trans-corneal delivery of brinzolamide through adsorptive-mediated transcytosis, achieving sustained IOP normalization in glaucomatous rats and presenting a noninvasive therapeutic strategy for glaucoma[62]. These results have significant implications for the development of nanodrug administration methods in clinical glaucoma treatment.

Glaucoma is defined by the gradual death of RGCs and the subsequent loss of their axons, mostly due to abnormally elevated IOP. However, there is no clinical drug to prevent or protect RGC injury caused by glaucoma. Utilizing the analysis of the keyword, we discovered that the research on glaucoma treatment concentrated on drug delivery aiming to more effectively protect RGC damage caused by glaucoma. Investigations have created a range of novel nanomaterials, including inorganic materials, organic polymer materials, and nanozymes, to eliminate reactive oxygen species (ROS) in RGCs and prevent cell injury[63-65]. These results have significant implications for the development of nanodrug methods of administration in clinical treatment of glaucoma. Nanotechnology is reshaping the pattern of glaucoma treatment: by breaking through the biological barrier, achieving multi-target intervention, and improving the accuracy of treatment, it not only solves the compliance and efficacy limitations of traditional therapies but also opens a paradigm shift from "symptom control" to "nerve repair". Although the transformation challenges remain, with the deep integration of materials science and molecular biology, the nano-diagnosis and treatment integration platform is expected to become the core tool for the clinical management of glaucoma in the next decade.

Artificial Intelligence This study found that the keyword "AI" rose rapidly in the past five years (Figure 5B), which was highly consistent with the timeline of the first AI-assisted glaucoma diagnosis study[66] and multi-center clinical validation study[67]. AI technology has been deeply infiltrated into the whole process of diagnosis and treatment of glaucoma, showing a revolutionary application prospect[68]. In terms of diagnosis, the image analysis system based on deep learning has achieved a breakthrough in early glaucoma screening by intelligently interpreting fundus photography and OCT images[69-70]. Studies have shown that the accuracy of the AI algorithm in identifying characteristic optic disc changes in glaucoma [area under the curve (AUC) >0.95] has reached or even exceeded the level of senior ophthalmologists[71-72]. More importantly, the AI system can quantitatively analyze the changes in retinal nerve fiber layer thickness and establish a precise correlation with visual field defects, providing an objective basis for predicting disease progression[73-74]. In the field of treatment, AI technology is reshaping clinical decision-making models[75]. By integrating multi-dimensional clinical data, including IOP curves, medication records, imaging features, *etc.*, AI systems can generate personalized treatment recommendations[76]. It is particularly noteworthy that machine learning algorithms perform well in predicting the prognosis of surgery, can accurately evaluate the expected effects of different surgical methods (such as traditional trabeculectomy *vs* MIGS), and provide data support for surgical selection[68,77]. In addition, the AI-assisted postoperative follow-up system achieves dynamic monitoring and timely adjustment of glaucoma treatment effects by automatically analyzing OCT and other examination results[68,78-80]. For the next ten years, additional cutting-edge technology will be utilized for the investigation of glaucoma treatment. For example, the quick advancement of omics technology and AI allows us to view the relationship between genetics[81-83], inflammatory molecules[84-86], cells[87-89] and glaucoma from a new perspective. However, the application of AI in the diagnosis and treatment of glaucoma still faces several challenges. In terms of data quality, the existing models are mainly developed based on European and American population data, and the generalization performance in the Asian population needs to be verified. At the technical integration level, how to seamlessly embed AI systems into existing clinical workflows still needs to be explored. More importantly, we need to establish a normative ethical framework for AI application, clarify the boundary of responsibility for AI-assisted diagnosis, and avoid over-reliance on technology and neglect of clinical judgment. Future research should focus on multi-center real-world verification, promote the substantive transformation of AI technology from laboratory to clinical, and finally realize the precision and intelligence of glaucoma diagnosis and treatment.

This work has several limitations. First, we only analyze the English publications of the type of articles and reviews from WoSCC. And other kinds of scientific contributions, like works, conference abstracts, collections, *etc.*, cannot be defined in this analysis. Studies with regional characteristics in Chinese, Spanish, and German literature (such as integrated traditional Chinese and Western medicine treatment, low-cost screening techniques, and innovative nanomaterials) may be omitted, resulting in coverage bias in the analysis of global glaucoma treatment trends and weakening the contribution of non-English speaking countries in clinical practice and technology transformation. Second, as with any bibliometric analysis, there is no absolute guarantee that all publications on glaucoma treatment are included in this investigation. Papers whose titles, abstracts, or keywords do not contain any words related to glaucoma treatment are not included in this study. Finally, the replacement of a large number of synonymous keywords may not be sufficient, and the impact on the average occurrence time may not be ruled out after replacement.

In conclusion, research on the treatment of glaucoma has made consistent progress over the last ten years, including both clinical and fundamental scientific studies. By bibliometric analyses, this study presented an overview of the global research on glaucoma treatment and identified the emerging frontiers that can guide future research in this area. The hot subjects in this study area were considered to be treatment surgery, ocular delivery (nanoparticle), cyclophotocoagulation, MIGS, nanoparticle, AI, *etc.* This will assist both researchers and specialists in identifying new topics, planning research directions, and promoting international cooperation. Based on our comprehensive review of our present investigation, we have a positive outlook that increased productivity will result in a greater level of scientific production of superior quality and more impactful discoveries in the next ten years.

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