Glaucoma Publication Trends in Leading General Ophthalmology Journals During the Past Quarter Century: Where Are the Clinical Trials?

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Précis: During the past quarter century, the rate of glaucoma-related publication in general ophthalmology journals increased due to higher representation in “experimentally oriented” journals. The rate of glaucoma randomized controlled clinical trial (RCT) articles decreased during the same time period.

Purpose: To evaluate trends in rate of glaucoma publications in leading general ophthalmology journals over the past quarter century.

Materials and Methods: Q1 ophthalmology journals Web sites were reviewed. Only journals not limited to certain subspecialty were considered “general” and included in the analysis. In addition we categorized journals orientation as either “clinical” or “experimental.” The PubMed search engine was used to collect publications from the selected journals between January 1, 1995 to December 31, 2019. Publications captured by “glaucoma” or “ocular hypertension” filters were considered glaucoma related. The fraction of glaucoma articles out of total number of articles within each year for each journal was calculated. A linear mixed effects model was applied to detect trends in glaucoma publication rates during the study period.

Results: Eight journals were included: 4 “clinically oriented” and 4 “experimentally oriented.” The PubMed search yielded 72,750 publications, of which 9329 (12.8%) considered glaucoma related. The percentage of glaucoma publications remained stable within “clinically oriented” journals, and significantly increased within “experimentally oriented” journals (annual change of 0.3%, P < 0.001). The number of glaucoma-related RCTs decreased significantly in each (annual change of −0.21% and −0.13%, respectively, P < 0.05).

Conclusions: There has been a significant rise in the rates of glaucoma publications in “experimentally oriented” journals, while their representation in “clinically oriented” journals remained stable over the past quarter century. This change might be due to the increasing efforts to develop more advanced methods for evaluation and treatment in glaucoma, although still unable to address clinical demands. The decrease in glaucoma-related RCT articles might indicate reduced funding for such research.

Key Words: glaucoma, publication trends, general ophthalmology, randomized controlled trials

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The practice of medicine is ever changing as a result of ongoing new scientific breakthroughs in both diagnosis and treatment options, requiring physicians to constantly pursue updates in published literature. Moreover, even while focusing on a certain subspecialization, clinicians still attempt to keep up with developments outside their chosen subspecialty. This particularly holds true for glaucoma, as many ophthalmic pathologies and treatments lead to increased intraocular pressure and risk for glaucoma. Peer-reviewed journals are a major vehicle in the dissemination of research findings to clinicians. Schein et al found that the traditional peer-reviewed journals were considered by American surgeons as being the most important source of information. However, while information has become readily available, the huge amount of publications and journals presents a challenge for the practicing clinician. Although some journals aim to focus on a certain subspecialty, several journals are designated for comprehensive ophthalmologists, such as “Ophthalmology,” the Journal of the American Academy of Ophthalmology, which publishes “manuscripts that relate to the sense of sight,” and JAMA Ophthalmology, whose mission statement includes “to be the indispensable source of ophthalmic knowledge for the generalist, subspecialist, and trainee; to publish innovative, clinically relevant research for the vision scientist.” Thanks to the widespread distribution across disciplines and high reader volume, top-ranking journals dealing with general clinical ophthalmology serve as leading resources for medical education, publishing the latest and most important advancements. In a way, these journals dictate current best clinical practice and help establish diagnostic and treatment protocols used across the globe. As it is impossible for any single journal to encompass and deal with all aspects of research, some journals concentrate on the more experimental aspects while others concentrate on the more clinical aspects.

In this study, we used the rate of glaucoma-related articles that appeared in high-ranking general ophthalmology journals in order to investigate publication trends of ophthalmology articles that focused on glaucoma over the last quarter century.
MATERIALS AND METHODS

The category “ophthalmology” in the Web of Science contains 60 journals. A list of all Q1 Ophthalmology journals (ie, the top 25% of ranked journals based on impact factor) was obtained from the InCites Journal Citation Reports web page. The description of each journal was reviewed separately by 2 of the authors (A.L. and A.S.) in order to categorize the journal as “specialized” if the journal focuses on a specific subspecialty in ophthalmology or “general” if it encompasses all fields of ophthalmology. Review journals were excluded. In case of disagreement between the first 2 reviewers, the journal category was determined by a third reviewer (M.B.). A second categorization was done among the selected “general” journals with the highest impact factor in 2019. Each “general” journal was separately reviewed again by all 3 reviewers (A.L., M.B., A.S.) and categorized as “clinically oriented” if it focuses more on clinical studies or “experimentally oriented” if it focuses more on basic science studies.

Using a syntax search code on PubMed (Supplementary 1, Supplemental Digital Content 1, http://links.lww.com/IGJ/A528), a list was obtained of all articles published in the selected journals between January 1, 1995 and December 31, 2019. The list was cross-referenced with similar lists that were obtained by using the same syntax, in addition to activating the filter “glaucoma” and “ocular hypertension” and/or article type filter “clinical trial” and/or “randomized controlled clinical trial” (RCT) on PubMed, in order to classify articles as “glaucoma,” and/or “clinical trial,” and/or “RCT,” respectively. The overall and the annual numbers of publications in each journal were summarized, and the percentage of glaucoma publications was calculated from the total amount of publications each year in each journal. The percentage of glaucoma-related RCTs was also calculated from the total number of RCTs as well as from the total number of glaucoma-related publications during the study period.

Ethics

Ethical approval was not required for the study, and the research was performed in compliance with the Declaration of Helsinki guidelines.

Statistical Analysis

All analyses and calculations were carried out with SAS and MATLAB software. Graphs were generated with Excel or MATLAB. A linear mixed effects model was employed in order to estimate the relationships between the dependent variables, such as the rate of glaucoma publications and clinical studies publications over the years. In the mixed effects models, the jth journal at the jth measurement occasion (year) was by:

\[ Y_{ij} = \beta_0 + \beta_1 j + \beta_2 X_{ij} + \epsilon_{ij}, \]

where the fixed effects are represented by the first 2 components of the equation and the random effects are represented by the third and fourth components of the equation. The last term corresponds to the error term related to the jth journal in the jth year. This form of analysis help to reduce the skewed effect of any single journal, as well as the effect of epidodic fluctuations, thereby providing less biased and more reliable results.

RESULTS

Eight of 15 Q1 journals were considered as being “general” by both reviewers. Four of those 8 were categorized as being “clinically oriented” (ie, having more emphasis on clinical research) and they included Ophthalmology, American Journal of Ophthalmology, JAMA Ophthalmology, and British Journal of Ophthalmology. The other 4 were categorized as being “experimentally oriented” (ie, having more emphasis on basic science publications) and they included Investigative Ophthalmology & Visual Science, Clinical and Experimental Ophthalmology, Acta Ophthalmologica, and Experimental Eye Research. There was complete consensus regarding journal selection. Overall, these 8 journals had 72,750 publications between January 1, 1995 and December 31, 2019, of which 3545 (4.9%) were RCTs. Of all publications, 9329 (12.8%) were classified as “glaucoma related,” and 798 (22.5%) of them were classified as glaucoma RCTs. Table 1 compares the number of publications between the “clinically oriented” and the “experimentally oriented” groups.

The prevalence of glaucoma publications was similar in both journal groups. Although the prevalence of RCTs was significantly higher in the “clinically oriented” journals, the prevalence of glaucoma RCTs (ie, glaucoma RCTs from the total of RCTs in each category) was similar in both journal subgroups.

Overall, while the total number of publications increased during the study period, the increase occurred mainly in the “experimentally oriented” journals (Fig. 1A). A similar trend was observed regarding the number of glaucoma publications (Fig. 1B).

The annual rate of glaucoma publications per journal in each group is depicted in Figure 2. Although the rate of glaucoma publications was higher in the clinical journals group at the beginning of the study period, there was a gradual reversal, resulting in a higher rate of glaucoma publications in

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**TABLE 1. Comparison of the Prevalence of Article Types Published Between 1995 and 2019**

|                      | Clinically Oriented [n (%)] | Experimentally Oriented [n (%)] | Total [n (%)] | P*          |
|----------------------|-----------------------------|---------------------------------|--------------|-------------|
| All publications     | 40,296                      | 32,454                          | 72,750       |             |
| Glaucoma publications| 5223 (13.0)                 | 4106 (12.7)                     | 9329 (12.8)  | 0.214       |
| All clinical trials  | 3621 (9.0)                  | 1128 (3.5)                      | 4749 (6.5)   | <0.001      |
| Glaucoma clinical trials | 748 (20.7)†                 | 242 (21.5)†                     | 990 (20.8)†  | 0.565       |
| All RCTs             | 2731 (6.8)                  | 814 (2.5)                       | 3545 (4.9)   | <0.001      |
| Glaucoma RCTs        | 617 (22.6)‡                  | 181 (22.2)‡                     | 798 (22.5)‡  | 0.831       |

*χ² test—comparison between clinical and experimental journals.
†% of all clinical trial publications.
‡% of all RCT publications.
RCT indicates randomized controlled trial.
the experimentally oriented journals by the end of the study period. The linear mixed model analysis showed that while the rate of glaucoma publications remained relatively unchanged in the clinical journal group, there was a statistically significant increase over time among the experimentally oriented journal group, with an average annual increase of 0.30% [95% confidence interval (CI), 0.20%-0.41%; \( P < 0.001 \)].

Both journal groups had an increase in the rate of RCT publications (Fig. 3). Although the increase was statistically significant in the clinical journals group (an annual increase of 0.05%; 95% CI, 0.0%-0.09%; \( P = 0.048 \)), it did not reach a level of significance in the experimentally oriented group (annual change of 0.01%; 95% CI, −0.03% to 0.04%; \( P = 0.717 \)). Figure 4 depicts the annual rate of glaucoma-related RCT publications from the total of RCTs (Fig. 4A) and from all glaucoma-related publications (Fig. 4B) published during the study period. In contrast to the other investigated rates, both groups showed a decline over time in the rate of glaucoma-related RCT publications (Table 2).

In addition, there was an inverse trend between the 2 groups in the rate of RCT publications among all glaucoma-related clinical trial publications (Fig. 5). Although the rate of glaucoma-related RCT publications increased significantly over time in the clinical journal group (annual change of 0.52%; 95% CI, 0.02%-1.01%; \( P = 0.040 \)), there was a trend toward decrease in the experimentally oriented journal group (annual change −0.28%; 95% CI, −1.35% to 0.79%; \( P = 0.601 \)).

### DISCUSSION

The present study analyzed trends in publications of glaucoma-related articles in leading general ophthalmology journals over the past quarter century. There have been studies that investigated and characterized various trends in ophthalmology journals, but, to the best of our knowledge, this is the first and largest study to address this important issue with regard to glaucoma. As Jones et al demonstrated that most physicians are exposed to only a few key journals, we believe that our analysis reflects the changes in exposure of ophthalmologists across subspecialties to the field of glaucoma.

As expected, the overall number of publications increased during the studied period, with a similar trend for glaucoma-related publications. These findings may be the result of aging of the population and the raising of public awareness that have resulted in a considerable increase in the detection of glaucoma patients. The majority of these patients are treated by nonglaucoma specialists or general eye care providers worldwide, and these changes might have increased the level of interest and the need for updated clinical and experimental glaucoma data among general ophthalmologists. In addition, the emergence of new topical drops, such as prostaglandin analogs that were approved by the FDA in 1996, new imaging modalities, such as the optical coherence tomography, which was first introduced into the market in 1996, as well as new surgical devices, such as minimally invasive glaucoma surgeries, may have also raised the level of interest in the field of glaucoma.
throughout the entire ophthalmological and optometric communities, subsequently yielding an increase in publications in the peer-reviewed literature. Recent advancements in neuroregeneration and stem-cell research associated with glaucoma might have also been a contributing factor.

Our results are in line with a study by Yu et al,\textsuperscript{11} which investigated the trend of published papers in ophthalmology. Those authors also retrieved their data from Science Citation Index Expanded and included all publications from 2007 to 2016. Their results showed an average annual increase in ophthalmology publications of 2.2%, a finding that was probably due to more ophthalmic research being performed at more sites worldwide. Another interesting finding was that the top 3 keywords in highly cited papers were “endothelial growth factor,” “optical coherence tomography,” and “open-angle glaucoma.” This result might also indicate that progressively more attention has been given to innovations in imaging modalities, treatment, and the subject of glaucoma. Resnikoff et al\textsuperscript{12} have recently reported that the global ophthalmologist population has increased 14% since 2010, and that it appears to be growing at a rate of \(\sim 2.6\%\) each year. Such an increase in the number of ophthalmologists has most probably had an effect on both the amount of ophthalmic research work being carried out globally and its related publications, as well as the greater number of journal readers who increased the level of interest.

We found that the increase in total number of ophthalmology publications and in the glaucoma-related publications was attributed mostly to the increase of publications in the experimentally oriented journals, compared...
with considerable stability in the number of publications in the “clinically oriented” journals (Figs. 1A, B). An alternative explanation may be that “clinically oriented” journals have a fixed volume which can be published and are interested in maintaining a relatively fixed share of representation for each of the different ophthalmologic disciplines to accommodate the interests of their readership. However, this could not be verified without access to data on confidential issues such as acceptance rates and editors’ considerations before acceptance for publication. Shifting of submissions and publications to either online-only papers or to more specialized subspecialty glaucoma journals may also explain the observed trend as these journals tend to publish more clinically oriented than experimentally oriented publications. Another explanation may be that while there are many attempts to develop new detection methods and treatments for glaucoma management, most of them do not successfully reach the level of clinical use (neither in trials nor incorporation to clinical practice). In addition, regulatory, financial, and development limits may cause a substantial time lag between first publications of a certain new development, most likely in an “experimental journal” and the report of its clinical efficacy, most likely in a “clinical journal.” Assuming this is the case, we expect to see an increase in glaucoma-related publication among “clinically oriented” general ophthalmology journals in future years.

Chien et al recently reported that the Journal of Glaucoma, currently the main subspecialty glaucoma journal, has shown a trend toward an increase in the number of original articles from its debut in 1992 until 2017. A rapid increase in the number of articles was most notable from 2012 to 2017 when the number of articles more than doubled from 103 to 242 (a 234% relative increase). This finding may also explain the plateau in the number of total glaucoma publications we counted during these years (Fig. 1B). Chien et al also found that during the years 1992 to 2017, an increase in the number of disclosures per Journal of Glaucoma publication was noted. Those authors suggested that research interest in glaucoma as a field is increasing as more research grants, third party funding, and/or private industry funding are being awarded to glaucoma researchers.

Another interesting finding in our study is the trend of RCT publications. RCTs along with their meta-analyses are the most reliable form of scientific evidence in the hierarchy of evidence that influences health care policy and practice. However, such experiments have significant logistical and financial barriers which limit their applicability. Although the overall prevalence of RCTs increased over time and in both types of journals, the rate of glaucoma-related RCTs (Fig. 4A) and the rate of RCTs among glaucoma-related publications decreased over time (Fig. 4B). This trend might be partially affected by the dependence on federal and industrial sources of funding, with several studies having shown an association between industrial funding and academic bibliometrics.

It is possible that many RCTs for new interventions end up being published in smaller journals or not published at all (eg, they may remain at the level of the regulatory agencies). In addition, not all RCTs test new treatment modalities (examples are The Ocular Hypertension Treatment Study, The Early Manifest Glaucoma Trial, The Collaborative Initial Glaucoma Treatment Study, and others) and their results are now mostly analyzed as ancillary studies. Finally, there has been little to no NIH-funded RCT in glaucoma in the United States since the major landmark trials decades ago; most of

## Table 2. Annual Rate Change of Glaucoma-related RCT Publications 1995 to 2019

| Publication Type Denominator | Group                  | Annual Rate Change (%) | 95% CI   |
|-----------------------------|------------------------|------------------------|---------|
|                             |                        |                         | Low     | High     | P       |
| All RCT publications        | Experimentally oriented| −0.63                  | −1.33   | 0.06     | 0.0741  |
|                             | Clinically oriented    | −0.57                  | −0.84   | −0.30    | <0.001  |
| All glaucoma publications   | Experimentally oriented| −0.13                  | −0.25   | −0.01    | 0.041   |
|                             | Clinically oriented    | −0.21                  | −0.35   | −0.08    | 0.003   |

CI indicates confidence interval; RCT, randomized controlled trial.
them are industry-sponsored and that may have been perceived as subject to conflicts of interest.

It is also possible that although glaucoma ophthalmology is an attractive field for industry, due to its relatively large commercial market, there may be a desire of some of these companies to insert their products into the market without an adequate number of clinical RCTs which take a considerable amount of time to produce results. Such a trend can be noted in some of the minimally invasive glaucoma devices, which have suffered until recently from a relative lack of RCTs, together with clinical evidence limited by the retrospective and nonmasked nature in the majority of cases.\textsuperscript{19} Alternatively, the lack of increase in glaucoma-related RCTs in clinically oriented journals might suggest that new developments that showed promising results in a lab setting were later found ineffective clinically. Unfortunately, an objective evaluation of this assumption is beyond the scope of this study. This trend in reduction in glaucoma RCTs being published in the main high-circulation journals might have major implications on the exposure of non-glaucoma ophthalmologists to studies with lower levels of evidence, especially before adopting new developments in glaucoma management. This decrease in the number of RCTs was also shown by Kumar et al\textsuperscript{20} who investigated the publishing trends of the top general clinical ophthalmology journals from 2005 through 2009. Those authors reported that case-control or cohort studies comprised most of the study designs that were used (40.1%), followed by, in order of decreasing frequency, nonanalytic studies (28.7%), basic science (24.6%), and RCTs (3.3%), review articles (2.6%), and meta-analyses (0.3%). They also observed that glaucoma had the highest proportion of case-controlled and cohort studies (56.8%).

The strength of the present study lies in the length of time period that was reviewed. Taking the top 8 general ophthalmology journals over a 25-year period allows sufficient power to capture significant trends with a robust analysis. However, this study has some limitations. First, it covered an arbitrary time span, from 1995 through 2019. An analysis of a wider or shorter time span might have led to different conclusions. An additional limitation is the division of the journals into 2 groups: while both groups publish clinical and experimental content, the proportions were different, and that feature may have affected our results. Notably, however, the clinically oriented journal group had a significantly higher percentage of total clinical trials and RCTs compared with the experimentally oriented journal group (Table 1), supporting our assumptions in regard to the journals’ orientation. Another limitation is that all forms of publications, such as review articles, letters, and perspectives were also included in this analysis: although they represent a small percentage of the total number of publications, excluding them would have resulted in a selection bias. Basing the data solely on the PubMed database could also pose a limitation. Our analysis focused on 8 selected journals based on their significant impact on the scientific community and ophthalmologist in general. Although it is logical to assume that the observed increase in publication in these journals reflects a general rise in glaucoma publication we are unable to confirm this assumption. It should so be taken into account that the journals were selected based on their current status which might have been different in the past. Finally, our results may have been affected by additional factors, such as the increase in number of open access journals, as well as the increase in publications on specific topics, and the lack of confidential data on decision-making guidelines of articles received by the journals that were not accepted for publication. The mixed model analysis employed herein, however, reduced the skewed effect of any single journal, as well as the effect of episodic fluctuations, thereby providing less biased and more reliable results.

In summary, medical publications are among the most important tools for staying updated both in general medicine and in a specialty field. Given the recent exponential increase in knowledge and data, many physicians base their reading strategies on journal ranking as a guideline. Indeed, the top-ranked journals in general ophthalmology are an important source of medical education, keeping general ophthalmologists informed of the latest advances in treatment across the discipline.\textsuperscript{20} We reviewed publication trends in the general ophthalmology literature over a 25-year period and observed a steady increase in glaucoma publications since 2005 with a substantial increase in the number of clinical trials and RCTs. This increase in knowledge and data, many physicians base their reading strategies on journal ranking as a guideline. Indeed, the top-ranked journals in general ophthalmology are an important source of medical education, keeping general ophthalmologists informed of the latest advances in treatment across the discipline.\textsuperscript{20} We reviewed publication trends...
of glaucoma articles in high-ranking and high impact factor general ophthalmology journals over the course of the last quarter century and found that the representation of glaucoma articles has been stable in the leading “clinically oriented” ophthalmology journals while it has increased in the “experimentally oriented” ophthalmology journals. In parallel, there was a significant decrease in the number of publications on RCTs on glaucoma-related subjects, which may be indicative of either reduced funding for this type of research or low priority by the main journals. Regardless of the reasons for such trends, exposure of nonglaucoma ophthalmologists to data with lower level of evidence may have implications in clinical practice.

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