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The top 100 papers in dry eye – A bibliometric analysis

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ABSTRACT

Purpose: Citation analysis represents one of the best currently available methods for quantifying the impact of articles. Bibliometric studies list the "best sellers" in a single field of interest. The purpose of the present study was to identify and analyze the most frequently cited papers in dry eye research that may be of high interest for researchers and clinicians.
Methods: We reviewed the database of the Institute for Scientific Information to identify articles published from 1900 to September 2016. All dry eye articles published in 59 ophthalmology journals were identified. The top 100 articles were selected for further analysis of authorship, source journal, number of citations, citation rate, geographic origin, article type, and level of evidence.
Results: The 100 most-cited articles were published between 1983 and 2011, with most of them in the 2000s. The number of citations per article ranged from 96 to 610, and was greatest for articles published in the 2000s. Each of these articles was published in one of 15 journals. Most articles represented Level-III evidence, followed by Levels II and I.
Conclusions: The present study focusing on dry eye research revealed that 55% of the most-cited articles came from the U.S. and 18% from Japan. Diagnostics and therapy were the areas of focus of most of the clinical articles; 13% of the most cited papers were review articles. This analysis provides researchers and clinicians with a detailed overview on the most cited dry eye papers over the past decades.
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1. Introduction

The field of professional scientific publication has undergone seismic evolution in the last decade [1,2]. Almost daily changes make electronic journal submission, publication, and access to periodicals increasingly straightforward [1,2]. Bibliometric sciences offer both a statistical and quantitative analysis of published articles and provide a measure of their impact in a particular field of research [3]. Bibliometric methods allow exploration of various factors, including citation counts and detailed scientific output statistics of single authors, special topics, institutions, or countries [3]. The "impact" of a journal on research can be assessed using the scientific citation index, which is the only available quantitative estimate of a journal's scientific contributions [4–9]. Citation of a work indicates its relevance for its field of interest [10,11]. The impact factor for a journal is a comparative measure of its ranking among journals in a given speciality area. The impact factor is calculated as the number of citations in a given year for articles published in the journal in the preceding 2 years, divided by the overall number of cited articles published in the same 2 years [12,13]. Since the publication of the first article regarding bibliometric methods by Eugene Garfield in the *Journal of the American Medical Association* (*JAMA*) in 1987 [14], this field of information science has continuously evolved [15].

In the field of ophthalmology, visual sciences and optometry, more than 110 periodicals are listed [4]; Thomson Reuters Journal Citation Reports lists 59 periodicals for the category "ophthalmology," of which 52 have a journal impact factor of at least 1.00 or higher [16]. Several bibliometric studies have been published that provide general analysis in the field of ophthalmology [17,18].

Dry eye research has expanded greatly over the past few decades, largely related to new clinically available devices for diagnostics and the introduction of new treatment options [19–21]. Although bibliometric information on special topics in the ophthalmology has been reported, to the best of our knowledge no

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analysis of the dry eye literature has been published [22,23]. In the present study, we identified the most frequently cited 100 articles in dry eye research, using professional scientific databases to access these publications and analyze major journals, origin of publications, and main authors. This enables specialists and new researchers in the field of dry eye to focus on these important articles.

2. Material and methods

Research platforms that provide bibliographic database services are necessary for systematic analysis of publication data. For this study, we used the Institute for Scientific Information (ISI) Web of Knowledge database from the Thomson Reuters Web of Science (WoS) Core Collection. The overall search was conducted in October 2016.

The keywords used for the search were “dry eye” as the “topic” (title, abstract, author's keywords, and KeyWords Plus), a year-of-publication range from 1900 until September 2016, the category “ophthalmology” predefined by the Web of Science, and the document type “articles.” The results were organized from the most cited to the least cited publications. Each search result was reviewed by two independent readers (AF and RK) to ensure its relation to dry eye disease; no paper had to be excluded.

If we found identical numbers of total citations, the more recent articles were ranked higher. The 100 articles with the highest number of citations that matched the search criteria were then analyzed further, again by two independent investigators (MS and AF). Data retrieved included journal name, publication date, first and last authors, year of publication, country of origin, total number of citations for the article, overall citation rate (total citations/article age), current citation rate (measured as the number of citations in the year 2015), research nature (basic science, clinical research or review), and level of evidence according to the 2009 revised Oxford (UK) Centre for Evidence-Based Medicine levels of Evidence (Level 1 to 5; Table 1). Review articles were defined as articles summarizing previously published data and literature. Articles without an identified first author but with shared authorship from different countries were classified as “multinational” origin. (These include chapters from the 2007 Report of the International Dry Eye WorkShop, whose PubMed entries note “No authors listed”).

A limitation of the citation-based searching method is that recent articles with high citation potential may not be captured because they have not had time to accumulate citations. In order to correct for this, a search was performed using the same terms of the main analysis of the highest ranked 100 articles, but using a shorter time period (2015 and 2016).

If there were any discrepancies in the evaluation of the articles between the three main investigators of our study, these were re-evaluated and discussed with a fourth investigator (VD). This method has been utilized in a range of previous publications on bibliometric data [4,13,15].

The Shapiro-Wilk test was applied to test the normality of the distribution of individual variables. We present data that were normally distributed as the mean and standard deviation, and skewed data as the median and the range. The Tukey method was also employed for plotting the whiskers and outliers. The p-values from pairwise t-tests were adjusted according to either the Bonferroni post-hoc test or Mann-Whitney test to correct for the performance of multiple statistical analyses. All p-values were two-tailed, and a p-value of ≤ 0.05 was considered to indicate statistical significance. We used one-way analysis of variance (ANOVA) to test for differences in normally distributed data, and the Kruskal-Wallis test for skewed data. The Spearman rank correlation was employed to test for correlations among non-parametric variables.

3. Results

A total of 3823 eligible publications related to “dry eye” (category “ophthalmology,” document type “articles”) were listed in peer-reviewed journals on the ISI Web of Knowledge WoS Core Collection database (October 2016). Of these, 2.4% (n = 92) had been cited at least 100 times and 0.6% (n = 24) more than 200 times. The publication dates for the 100 most-cited articles (Table 2) were between 1983 and 2011, and the total number of citations per article ranged from 96 to 610. Of the 100 articles, 16 were basic research, 71 were clinical research, and 13 were review articles. Considering the number of citations per type of article, a statistically significant difference was only found between the groups of basic research and clinical research (Mann-Whitney test p = 0.032; basic research: median = 118 [range = 96–266]; clinical research: median = 150 [range = 97–610] [Table 3, Fig. 1]). We subdivided clinical research articles according to topics: diagnostic research (n = 47, 66%), epidemiology (n = 10, 14%), and medical and surgical treatment (n = 14, 20%). Thirteen articles were review articles (mean 189 [range = 105–576]; Table 3). The review articles did not vary significantly with respect to total citations per article compared to the clinical or basic research articles (Fig. 1).

An evidence level of III was assigned to 29 articles in the field of clinical research and systematic reviews (median citations per article 146 [range = 98–438]), followed by IIa (n = 18; median citations per article 162 [range = 109–334]), IIb (n = 11; median citations per article 142 [range = 97–214]), Ib (n = 9; median citations per article 152 [range = 105–610]), Ia (n = 7; median citations per article [range = 126–576]) and IV (n = 4; median citations per article 221 [range = 117–256] (See Table 4 and Fig. 2.). The Kruskal-Wallis Test exhibited no significant differences between number of citations per article and the various levels of evidence (p = 0.216).

Most articles on the list were published from 2000 to 2009 (n = 62), followed by articles published from 2010 to 2016 (n = 6; Fig. 3 A). The total number of citations was greatest for articles published from 2000 to 2009 (mean total number of citations = 179), followed by articles published during the 1990's (mean total number of citations = 166) and those published from

Table 1
Shortened depiction of Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. Level may be graded down on the basis of study quality, imprecision, inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size (based on “Level of Evidence” published online from German Network for Evidence-based Medicine (http://www.ebm-netzwerk.de/was-ist-ebm/images/evidenzklassen.jpg/view. Accessed October 30, 2016)).

Level		Rating Criteria
I	Ia	Evidence obtained from a systematic review of relevant randomized controlled trials (including meta-analysis)
	Ib	Evidence obtained from at least one properly designed randomized, controlled trial
II	IIa	Evidence obtained from at least one well-designed controlled trial without randomization
	IIb	Evidence obtained from one well-designed, pseudo-experimental trial
III		Evidence obtained from a well-designed, non-experimental descriptive trial
IV		Evidence obtained from case reports, expert opinion, consensus conference

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Table 2
The 100 most-cited articles in dry eye.

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2015
1	Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000 May; 118(5):615-21. PubMed PMID: 10815152	610	35,88	115
2	The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr; 5(2):75–92. Review. PubMed PMID: 17508116	576	57,6	135
3	Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003 Aug; 136(2):318-26. PubMed PMID: 12888056.	438	31,29	49
4	Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol. 2000 Sep; 118(9):1264-8. PubMed PMID: 10980773	398	23,41	40
5	Schein OD, Muñoz B, Tielsch JM, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. Am J Ophthalmol. 1997 Dec; 124(6):723-8. PubMed PMID: 9402817	356	17,8	16
6	Sall K, Stevenson OD, Mundorf TK, Reis BL. Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. CsA Phase 3 Study Group. Ophthalmology. 2000 Apr; 107(4):631-9	354	20,82	27
7	Solomon A, Dursun D, Liu Z, Xie Y, Macri A, Pflugfelder SC. Pro- and anti-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease. Invest Ophthalmol Vis Sci. 2001 Sep; 42(10):2283-92. PubMed PMID: 11527941	334	20,88	30
8	Pflugfelder SC, Jones D, Ji Z, Afonso A, Monroy D. Altered cytokine balance in the tear fluid and conjunctiva of patients with Sjögren's syndrome keratoconjunctivitis sicca. Curr Eye Res. 1999 Sep; 19(3):201-11. PubMed PMID: 10487957	330	18,33	24
9	Tsubota K, Satake Y, Ohyama M, Toda I, Takano Y, Ono M, Shinozaki N, Shimazaki J. Surgical reconstruction of the ocular surface in advanced ocular cicatricial pemphigoid and Stevens-Johnson syndrome. Am J Ophthalmol. 1996 Jul; 122(1):38–52. PubMed PMID: 8659597	321	15,29	7
10	McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology. 1998 Jun; 105(6):1114-9. PubMed PMID: 9627665	305	16,05	30
11	Luo L, Li DQ, Doshi A, Farley W, Corrales RM, Pflugfelder SC. Experimental dry eye stimulates production of inflammatory cytokines and MMP-9 and activates MAPK signaling pathways on the ocular surface. Invest Ophthalmol Vis Sci. 2004 Dec; 45(12):4293-301. PubMed PMID: 15557435	266	20,46	33
12	Shimazaki J, Yang HY, Tsubota K. Amniotic membrane transplantation for ocular surface reconstruction in patients with chemical and thermal burns. Ophthalmology. 1997 Dec; 104(12):2068-76. PubMed PMID: 9400767	256	12,8	10
13	Nichols KK, Nichols JJ, Mitchell GL. The lack of association between signs and symptoms in patients with dry eye disease. Cornea. 2004 Nov; 23(8):762-70. PubMed PMID: 15502475	255	19,62	35
14	Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003 Oct; 22(7):640-50. Review. PubMed PMID: 14508260	252	18	56
15	Tsubota K, Goto E, Fujita H, Ono M, Inoue H, Saito I, Shimmura S. Treatment of dry eye by autologous serum application in Sjögren's syndrome. Br J Ophthalmol. 1999 Apr; 83(4):390-5. PubMed PMID: 10434857; PubMed Central PMCID: PMC1723012	239	13,28	22
16	The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr; 5(2):93–107. Review. PubMed PMID: 17508117	233	23,3	66
17	Miljanović B, Dana R, Sullivan DA, Schaumberg DA. Impact of dry eye syndrome on vision-related quality of life. Am J Ophthalmol. 2007 Mar; 143(3):409-15. Epub 2007 Jan 2. PubMed PMID: 17317388; PubMed Central PMCID: PMC1847608	224	22,4	39
18	Nelson JD, Havener VR, Cameron JD. Cellulose acetate impressions of the ocular surface. Dry eye states. Arch Ophthalmol. 1983 Dec; 101(12):1869-72. PubMed PMID: 6651590	214	6,29	9
19	Baudouin C, Labbé A, Liang H, Pauly A, Brignole-Baudouin F. Preservatives in eyedrops: the good, the bad and the ugly. Prog Retin Eye Res. 2010 Jul; 29(4):312-34. doi: 10.1016/j.preteyeres.2010.03.001. Epub 2010 Mar 17. PubMed PMID: 20302969	212	30,29	34
20	Tomlinson A, Khanal S, Ramaesh K, Diaper C, McFadyen A. Tear film osmolarity: determination of a referent for dry eye diagnosis. Invest Ophthalmol Vis Sci. 2006 Oct; 47(10):4309-15. PubMed PMID: 17003420	210	19,09	31
21	Pisella PJ, Pouliquen P, Baudouin C. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication. Br J Ophthalmol. 2002 Apr; 86(4):418-23. PubMed PMID: 11914211; PubMed Central PMCID: PMC1771067	206	13,73	23
22	Lin PY, Tsai SY, Cheng CY, Liu JH, Chou P, Hsu WM. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology. 2003 Jun; 110(6):1096-101. PubMed PMID: 12799232	206	14,71	24
23	Craig JP, Tomlinson A. Importance of the lipid layer in human tear film stability and evaporation. Optom Vis Sci. 1997 Jan; 74(1):8–13. PubMed PMID:9148269	204	10,2	13
24	Behrens A, Doyle JJ, Stern L, Chuck RS, McDonnell PJ, Azar DT, Dua HS, Hom M, Karpecki PM, Laibson PR, Lemp MA, Meisler DM, Del Castillo JM, O'Brien TP, Pflugfelder SC, Rolando M, Schein OD, Seitz B, Tseng SC, van Setten G, Wilson SE, Yiu SC; Dysfunctional tear syndrome study group. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006 Sep; 25(8):900-7. PubMed PMID: 17102664	202	18,36	26
25	Schein OD, Tielsch JM, Munõz B, Bandeen-Roche K, West S. Relation between signs and symptoms of dry eye in the elderly. A population-based perspective. Ophthalmology. 1997 Sep; 104(9):1395-401. PubMed PMID: 9307632	199	9,95	13
26	Shimazaki J, Sakata M, Tsubota K. Ocular surface changes and discomfort in patients with meibomian gland dysfunction. Arch Ophthalmol. 1995 Oct; 113(10):1266-70. PubMed PMID: 7575257	195	8,86	21
27	Pflugfelder SC. Antiinflammatory therapy for dry eye. Am J Ophthalmol. 2004 Feb; 137(2):337-42. Review. PubMed PMID: 14962426	189	14,54	18
28	Brignole F, Pisella PJ, Goldschild M, De Saint Jean M, Goguel A, Baudouin C. Flow cytometric analysis of inflammatory markers in conjunctival epithelial cells of patients with dry eyes. Invest Ophthalmol Vis Sci. 2000 May; 41(6):1356-63. PubMed PMID: 10798650	188	11,06	9
29	Argüeso P, Balaram M, Spurr-Michaud S, Keutmann HT, Dana MR, Gipson IK. Decreased levels of the goblet cell mucin MUC5AC in tears of patients with Sjögren syndrome. Invest Ophthalmol Vis Sci. 2002 Apr; 43(4):1004-11. PubMed PMID: 11923240	187	12,47	15
30		186	10,94	11

(*continued on next page*)

Table 2 (*continued*)

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2015
	Stevenson D, Tauber J, Reis BL. Efficacy and safety of cyclosporin A ophthalmic emulsion in the treatment of moderate-to-severe dry eye disease: a dose-ranging, randomized trial. The Cyclosporin A Phase 2 Study Group. Ophthalmology. 2000 May; 107(5):967-74. PubMed PMID: 10811092			
31	Leung EW, Medeiros FA, Weinreb RN. Prevalence of ocular surface disease in glaucoma patients. J Glaucoma. 2008 Aug; 17(5):350-5. doi: 10.1097/IJG.0b013e31815c5f4f. PubMed PMID: 18703943	183	20,33	25
32	Gipson IK, Spurr-Michaud S, Argüeso P, Tisdale A, Ng TF, Russo CL. Mucin gene expression in immortalized human corneal-limbal and conjunctival epithelial cell lines. Invest Ophthalmol Vis Sci. 2003 Jun; 44(6):2496-506. PubMed PMID: 12766048	181	12,93	12
33	Goto E, Yagi Y, Matsumoto Y, Tsubota K. Impaired functional visual acuity of dry eye patients. Am J Ophthalmol. 2002 Feb; 133(2):181-6. PubMed PMID: 11812420	174	11,6	13
34	Sullivan BD, Whitmer D, Nichols KK, Tomlinson A, Foulks GN, Geerling G, Pepose JS, Kosheleff V, Porreco A, Lemp MA. An objective approach to dry eye disease severity. Invest Ophthalmol Vis Sci. 2010 Dec; 51(12):6125-30. doi: 10.1167/iovs.10–5390. Epub 2010 Jul 14. PubMed PMID: 20631232	168	24	36
35	Begley CG, Chalmers RL, Abetz L, Venkataraman K, Mertzanis P, Caffery BA, Snyder C, Edrington T, Nelson D, Simpson T. The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. Invest Ophthalmol Vis Sci. 2003 Nov; 44(11):4753-61. PubMed PMID: 14578396	165	11,79	20
36	Nichols KK, Mitchell GL, Zadnik K. The repeatability of clinical measurements of dry eye. Cornea. 2004 Apr; 23(3):272-85. PubMed PMID: 15084861	163	12,54	20
37	Afonso AA, Sobrin L, Monroy DC, Selzer M, Lokeshwar B, Pflugfelder SC. Tear fluid gelatinase B activity correlates with IL-1alpha concentration and fluorescein clearance in ocular rosacea. Invest Ophthalmol Vis Sci. 1999 Oct; 40(11):2506-12. PubMed PMID: 10509643	163	9,06	11
38	Marsh P, Pflugfelder SC. Topical nonpreserved methylprednisolone therapy for keratoconjunctivitis sicca in Sjögren syndrome. Ophthalmology. 1999 Apr; 106(4):811-6. PubMed PMID: 10201607	162	9	7
39	Stern ME, Gao J, Schwalb TA, Ngo M, Tieu DD, Chan CC, Reis BL, Whitcup SM, Thompson D, Smith JA. Conjunctival T-cell subpopulations in Sjögren's and non-Sjögren's patients with dry eye. Invest Ophthalmol Vis Sci. 2002 Aug; 43(8):2609-14. PubMed PMID: 12147592	161	10,73	10
40	Mathers WD. Ocular evaporation in meibomian gland dysfunction and dry eye. Ophthalmology. 1993 Mar; 100(3):347-51. PubMed PMID: 8460004	159	6,62	6
41	Methodologies to diagnose and monitor dry eye disease: report of the Diagnostic Methodology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr; 5(2):108-52. Review. PubMed PMID: 17508118	158	15,8	35
42	Schaumberg DA, Dana R, Buring JE, Sullivan DA. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. Arch Ophthalmol. 2009 Jun; 127(6):763-8. doi: 10.1001/archophthalmol.2009.103. PubMed PMID: 19506195; PubMed Central PMCID: PMC2836718	157	19,62	26
43	Doughty MJ, Fonn D, Richter D, Simpson T, Caffery B, Gordon K. A patient questionnaire approach to estimating the prevalence of dry eye symptoms in patients presenting to optometric practices across Canada. Optom Vis Sci. 1997 Aug; 74(8):624-31. PubMed PMID: 9323733	156	7,8	10
44	Kunert KS, Tisdale AS, Gipson IK. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporine. Arch Ophthalmol. 2002 Mar; 120(3):330-7. Erratum in: Arch Ophthalmol 2002 Aug; 120(8):1099. PubMed PMID: 11879137	152	10,13	10
45	Kunert KS, Tisdale AS, Stern ME, Smith JA, Gipson IK. Analysis of topical cyclosporine treatment of patients with dry eye syndrome: effect on conjunctival lymphocytes. Arch Ophthalmol. 2000 Nov; 118(11):1489-96. PubMed PMID: 11074805	150	8,82	10
46	Li DQ, Chen Z, Song XJ, Luo L, Pflugfelder SC. Stimulation of matrix metalloproteinases by hyperosmolarity via a JNK pathway in human corneal epithelial cells. Invest Ophthalmol Vis Sci. 2004 Dec; 45(12):4302-11. PubMed PMID: 15557436	149	11,46	17
47	Lemp MA, Bron AJ, Baudouin C, Benítez Del Castillo JM, Geffen D, Tauber J, Foulks GN, Pepose JS, Sullivan BD. Tear osmolarity in the diagnosis and management of dry eye disease. Am J Ophthalmol. 2011 May; 151(5):792–798.e1. doi: 10.1016/j.ajo.2010.10.032. Epub 2011 Feb 18. PubMed PMID: 21310379	148	24,67	39
48	Jones DT, Monroy D, Ji Z, Atherton SS, Pflugfelder SC. Sjögren's syndrome: cytokine and Epstein-Barr viral gene expression within the conjunctival epithelium. Invest Ophthalmol Vis Sci. 1994 Aug; 35(9):3493-504. PubMed PMID: 8056525	147	6,39	8
49	Poon AC, Geerling G, Dart JK, Fraenkel GE, Daniels JT. Autologous serum eyedrops for dry eyes and epithelial defects: clinical and in vitro toxicity studies. Br J Ophthalmol. 2001 Oct; 85(10):1188-97. PubMed PMID: 11567963; PubMed Central PMCID: PMC1723716	146	9,12	12
50	Tutt R, Bradley A, Begley C, Thibos LN. Optical and visual impact of tear break-up in human eyes. Invest Ophthalmol Vis Sci. 2000 Dec; 41(13):4117-23. PubMed PMID: 11095604	146	8,59	14
51	De Paiva CS, Corrales RM, Villarreal AL, Farley WJ, Li DQ, Stern ME, Pflugfelder SC. Corticosteroid and doxycycline suppress MMP-9 and inflammatory cytokine expression, MAPK activation in the corneal epithelium in experimental dry eye. Exp Eye Res. 2006 Sep; 83(3):526-35. Epub 2006 Apr 27. PubMed PMID: 16643899	145	13,18	19
52	Yeh S, Song XJ, Farley W, Li DQ, Stern ME, Pflugfelder SC. Apoptosis of ocular surface cells in experimentally induced dry eye. Invest Ophthalmol Vis Sci. 2003 Jan; 44(1):124-9. PubMed PMID: 12506064	145	10,36	14
53	Tsubota K. Tear dynamics and dry eye. Prog Retin Eye Res. 1998 Oct; 17(4):565-96. Review. PubMed PMID: 9777650	144	7,58	7
54	Lam H, Bleiden L, de Paiva CS, Farley W, Stern ME, Pflugfelder SC. Tear cytokine profiles in dysfunctional tear syndrome. Am J Ophthalmol. 2009 Feb; 147(2):198–205. e1. doi: 10.1016/j.ajo.2008.08.032. Epub 2008 Nov 7. PubMed PMID: 18992869; PubMed Central PMCID: PMC3582020	142	17,75	18
55	Geerling G, Maclennan S, Hartwig D. Autologous serum eye drops for ocular surface disorders. Br J Ophthalmol. 2004 Nov; 88(11):1467-74. Review. PubMed PMID: 15489495; PubMed Central PMCID: PMC1772389	139	10,69	25
56	Mainstone JC, Bruce AS, Golding TR. Tear meniscus measurement in the diagnosis of dry eye. Curr Eye Res. 1996 Jun; 15(6):653-61. PubMed PMID: 8670769	139	6,62	13
57	Toda I, Asano-Kato N, Komai-Hori Y, Tsubota K. Dry eye after laser in situ keratomileusis. Am J Ophthalmol. 2001 Jul; 132(1):1–7. PubMed PMID: 11438046	137	8,56	10
58	Battat L, Macri A, Dursun D, Pflugfelder SC. Effects of laser in situ keratomileusis on tear production, clearance, and the ocular surface. Ophthalmology. 2001 Jul; 108(7):1230-5. PubMed PMID: 11425680	135	8,44	10
59		131	21,83	30

Table 2 (*continued*)

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2015
	Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011 Mar 30; 52(4):1938-78. doi: 10.1167/iovs.10-6997c. Print 2011 Mar. Review. PubMed PMID: 21450915; PubMed Central PMCID: PMC3072159			
60	Chia EM, Mitchell P, Rochtchina E, Lee AJ, Maroun R, Wang JJ. Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. Clin Exp Ophthalmol. 2003 Jun; 31(3):229-32. PubMed PMID: 12786773	131	9,36	13
61	Begley CG, Chalmers RL, Mitchell GL, Nichols KK, Caffery B, Simpson T, DuToit R, Portello J, Davis L. Characterization of ocular surface symptoms from optometric practices in North America. Cornea. 2001 Aug; 20(6):610-8. PubMed PMID	130	8,12	12
62	Danjo Y, Watanabe H, Tisdale AS, George M, Tsumura T, Abelson MB, Gipson IK. Alteration of mucin in human conjunctival epithelia in dry eye. Invest Ophthalmol Vis Sci. 1998 Dec; 39(13):2602-9. PubMed PMID: 9856770	130	6,84	8
63	Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007 Apr; 5(2):163-78. Review. PubMed PMID: 17508120	126	12,6	33
64	Jaenen N, Baudouin C, Pouliquen P, Manni G, Figueiredo A, Zeyen T. Ocular symptoms and signs with preserved and preservative-free glaucoma medications. Eur J Ophthalmol. 2007 May–Jun; 17(3):341-9. PubMed PMID: 17534814	123	12,3	15
65	Nichols JJ, Sinnott LT. Tear film, contact lens, and patient-related factors associated with contact lens-related dry eye. Invest Ophthalmol Vis Sci. 2006 Apr; 47(4):1319-28. PubMed PMID: 16565363	122	11,09	12
66	Dursun D, Wang M, Monroy D, Li DQ, Lokeshwar BL, Stern ME, Pflugfelder SC. A mouse model of keratoconjunctivitis sicca. Invest Ophthalmol Vis Sci. 2002 Mar; 43(3):632-8. PubMed PMID: 11867577	122	8,13	18
67	Herreras JM, Pastor JC, Calonge M, Asensio VM. Ocular surface alteration after long-term treatment with an antiglaucomatous drug. Ophthalmology. 1992 Jul; 99(7):1082-8. PubMed PMID: 1495787	122	4,88	6
68	Bacman S, Perez Leiros C, Sterin-Borda L, Hubscher O, Arana R, Borda E. Autoantibodies against lacrimal gland M3 muscarinic acetylcholine receptors in patients with primary Sjögren's syndrome. Invest Ophthalmol Vis Sci. 1998 Jan; 39(1):151-6. PubMed PMID: 9430556	121	6,37	4
69	Tseng SC, Tsubota K. Important concepts for treating ocular surface and tear disorders. Am J Ophthalmol. 1997 Dec; 124(6):825-35. Review. PubMed PMID: 9402829	121	6,05	7
70	Yokoi N, Takehisa Y, Kinoshita S. Correlation of tear lipid layer interference patterns with the diagnosis and severity of dry eye. Am J Ophthalmol. 1996 Dec; 122(6):818-24. PubMed PMID: 8956636	119	5,67	6
71	Lee AJ, Lee J, Saw SM, Gazzard G, Koh D, Widjaja D, Tan DT. Prevalence and risk factors associated with dry eye symptoms: a population based study in Indonesia. Br J Ophthalmol. 2002 Dec; 86(12):1347-51. Review. PubMed PMID: 12446361; PubMed Central PMCID: PMC1771386	118	7,87	16
72	Schiffman RM, Walt JG, Jacobsen G, Doyle JJ, Lebovics G, Sumner W. Utility assessment among patients with dry eye disease. Ophthalmology. 2003 Jul; 110(7):1412-9. PubMed PMID: 12867401	117	8,36	13
73	Mathers WD, Lane JA, Zimmerman MB. Tear film changes associated with normal aging. Cornea. 1996 May; 15(3):229-34. PubMed PMID: 8713923	117	5,57	4
74	Massingale ML, Li X, Vallabhajosyula M, Chen D, Wei Y, Asbell PA. Analysis of inflammatory cytokines in the tears of dry eye patients. Cornea. 2009 Oct; 28(9):1023-7. doi: 10.1097/ICO.0b013e3181a16578. PubMed PMID: 19724208	115	14,38	23
75	Nakamori K, Odawara M, Nakajima T, Mizutani T, Tsubota K. Blinking is controlled primarily by ocular surface conditions. Am J Ophthalmol. 1997 Jul; 124(1):24–30. PubMed PMID: 9222228	115	5,75	8
76	Argüeso P, Spurr-Michaud S, Russo CL, Tisdale A, Gipson IK. MUC16 mucin is expressed by the human ocular surface epithelia and carries the H185 carbohydrate epitope. Invest Ophthalmol Vis Sci. 2003 Jun; 44(6):2487-95. PubMed PMID:12766047	114	8,14	8
77	Nelson JD, Shimazaki J, Benitez-del-Castillo JM, Craig JP, McCulley JP, Den S, Foulks GN. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar 30; 52(4):1930-7. doi: 10.1167/iovs.10-6997b. Print 2011 Mar. Review. PubMed PMID: 21450914; PubMed Central PMCID: PMC3072158	110	18,33	19
78	Toda I, Fujishima H, Tsubota K. Ocular fatigue is the major symptom of dry eye. Acta Ophthalmol (Copenh). 1993 Jun; 71(3):347-52. PubMed PMID: 8362634	110	4,58	11
79	Shimazaki J, Goto E, Ono M, Shimmura S, Tsubota K. Meibomian gland dysfunction in patients with Sjögren syndrome. Ophthalmology. 1998 Aug; 105(8):1485-8. PubMed PMID: 9709762	109	5,74	11
80	Tsubota K, Yamada M. Tear evaporation from the ocular surface. Invest Ophthalmol Vis Sci. 1992 Sep; 33(10):2942-50. PubMed PMID: 1526744	109	4,36	5
81	Mathers WD, Shields WJ, Sachdev MS, Petroll WM, Jester JV. Meibomian gland dysfunction in chronic blepharitis. Cornea. 1991 Jul; 10(4):277-85. PubMed PMID: 1889213	109	4,19	10
82	Noble BA, Loh RS, MacLennan S, Pesudovs K, Reynolds A, Bridges LR, Burr J, Stewart O, Quereshi S. Comparison of autologous serum eye drops with conventional therapy in a randomized controlled crossover trial for ocular surface disease. Br J Ophthalmol. 2004 May; 88(5):647-52. PubMed PMID: 15090417; PubMed Central PMCID:PMC1772131	108	8,31	11
83	Begley CG, Caffery B, Nichols KK, Chalmers R. Responses of contact lens wearers to a dry eye survey. Optom Vis Sci. 2000 Jan; 77(1):40-6. PubMed PMID: 10654857	108	6,35	8
84	Moss SE, Klein R, Klein BE. Incidence of dry eye in an older population. Arch Ophthalmol. 2004 Mar; 122(3):369-73. PubMed PMID: 15006852	106	8,15	12
85	Brignole F, Pisella PJ, De Saint Jean M, Goldschild M, Goguel A, Baudouin C. Flow cytometric analysis of inflammatory markers in KCS: 6-month treatment with topical cyclosporin A. Invest Ophthalmol Vis Sci. 2001 Jan; 42(1):90-5. PubMed PMID: 11133852	106	6,62	3
86	Tomlinson A, Bron AJ, Korb DR, Amano S, Paugh JR, Pearce EI, Yee R, Yokoi N, Arita R, Dogru M. The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar 30; 52(4):2006-49. doi: 10.1167/iovs.10-6997f. Print 2011 Mar. Review. PubMed PMID: 21450918; PubMed Central PMCID: PMC3072162	105	17,5	22
87	Kojima T, Ishida R, Dogru M, Goto E, Matsumoto Y, Kaido M, Tsubota K. The effect of autologous serum eyedrops in the treatment of severe dry eye disease: a prospective randomized case-control study. Am J Ophthalmol. 2005 Feb; 139(2):242-6. PubMed PMID: 15733983	105	8,75	15
88		104	10,4	13

(*continued on next page*)

Table 2 (*continued*)

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2015
	De Paiva CS, Villarreal AL, Corrales RM, Rahman HT, Chang VY, Farley WJ, Stern ME, Niederkorn JY, Li DQ, Pflugfelder SC. Dry eye-induced conjunctival epithelial squamous metaplasia is modulated by interferon-gamma. Invest Ophthalmol Vis Sci. 2007 Jun; 48(6):2553-60. PubMed PMID: 17525184			
89	Begley CG, Caffery B, Chalmers RL, Mitchell GL; Dry Eye Investigation (DREI) Study Group. Use of the dry eye questionnaire to measure symptoms of ocular irritation in patients with aqueous tear deficient dry eye. Cornea. 2002 Oct; 21(7):664-70. PubMed PMID: 12352083	101	6,73	11
90	Gao J, Schwalb TA, Addeo JV, Ghosn CR, Stern ME. The role of apoptosis in the pathogenesis of canine keratoconjunctivitis sicca: the effect of topical Cyclosporin A therapy. Cornea. 1998 Nov; 17(6):654-63. PubMed PMID: 9820947	101	5,32	5
91	Korb DR. Survey of preferred tests for diagnosis of the tear film and dry eye. Cornea. 2000 Jul; 19(4):483-6. PubMed PMID: 10928763	100	5,88	6
92	Baudouin C, Brignole F, Becquet F, Pisella PJ, Goguel A. Flow cytometry in impression cytology specimens. A new method for evaluation of conjunctival inflammation. Invest Ophthalmol Vis Sci. 1997 Jun; 38(7):1458-64. PubMed PMID: 9191610	100	5	2
93	Grus FH, Podust VN, Bruns K, Lackner K, Fu S, Dalmasso EA, Wirthlin A, Pfeiffer N. SELDI-TOF-MS ProteinChip array profiling of tears from patients with dry eye. Invest Ophthalmol Vis Sci. 2005 Mar; 46(3):863-76. PubMed PMID: 15728542	99	8,25	8
94	Arita R, Itoh K, Inoue K, Amano S. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. Ophthalmology. 2008 May; 115(5):911-5. doi: 10.1016/j.ophtha.2007.06.031. PubMed PMID: 18452765	98	10,89	20
95	Mertzanis P, Abetz L, Rajagopalan K, Espindle D, Chalmers R, Snyder C, Caffery B, Edrington T, Simpson T, Nelson JD, Begley C. The relative burden of dry eye in patients' lives: comparisons to a U.S. normative sample. Invest Ophthalmol Vis Sci. 2005 Jan; 46(1):46–50. PubMed PMID: 15623753	98	8,17	9
96	Tsubota K, Hata S, Okusawa Y, Egami F, Ohtsuki T, Nakamori K. Quantitative videographic analysis of blinking in normal subjects and patients with dry eye. Arch Ophthalmol. 1996 Jun; 114(6):715-20. PubMed PMID: 8639084	98	4,67	6
97	Yoon KC, Jeong IY, Park YG, Yang SY. Interleukin-6 and tumor necrosis factor-alpha levels in tears of patients with dry eye syndrome. Cornea. 2007 May; 26(4):431-7. PubMed PMID: 17457192	97	9,7	12
98	Nishida T, Nakamura M, Mishima H, Otori T. Hyaluronan stimulates corneal epithelial migration. Exp Eye Res. 1991 Dec; 53(6):753-8. PubMed PMID: 1783012	97	3,73	6
99	Fujihara T, Murakami T, Fujita H, Nakamura M, Nakata K. Improvement of corneal barrier function by the P2Y(2) agonist INS365 in a rat dry eye model. Invest Ophthalmol Vis Sci. 2001 Jan; 42(1):96–100. PubMed PMID: 11133853	97	6,06	14
100	Rocha EM, Wickham LA, da Silveira LA, Krenzer KL, Yu FS, Toda I, Sullivan BD, Sullivan DA. Identification of androgen receptor protein and 5alpha-reductase mRNA in human ocular tissues. Br J Ophthalmol. 2000 Jan; 84(1):76–84. PubMed PMID: 10611104; PubMed Central PMCID: PMC1723240	96	5,65	4

Table 3
Citations per type of article.

	Citations per type of article				P*		
	N	Range (Min/Max)	Mean (±SD)	Median (Q25/Q75)	*Gr1 vs Gr2*	*Gr1 vs Gr3*	*Gr2 vs Gr3*
Basic research (Gr1)	16	96/266	134 (±48)	118 (99/147)	0.032	0.827	0.652
Clinical research (Gr2)	71	97/610	179 (±93)	150 (117/204)			
Review article (Gr3)	13	105/576	189 (±124)	144 (126/210)			
Total	100	96/610	173 (±93)	146 (115/197)	* *Mann-Whitney test*		

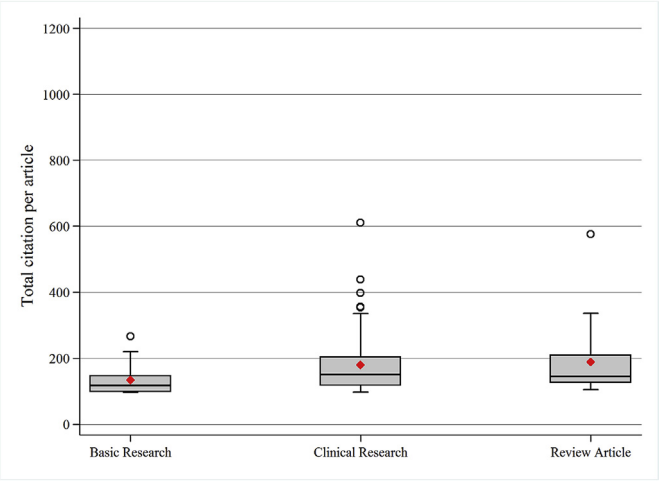

Fig. 1. Bar graph showing the number of citations (and standard deviation) for the 100 most-cited articles according to type of article (clinical or basic research, review article). Red point = Mean value. Box: lower line = 25th quartile, upper line = 75th quartile; black line in box = Median value. White points = Outliers. The Tukey method was used for plotting the whiskers and outliers.

2010 to 2016 (mean total number of citations = 146; Fig. 3 B.) The overall citation rate of an article was independent of its publication date ($r = 0.00$, $p < 0.969$, Mann-Kendall test; Fig. 4 A). However, the current citation rate (measured as the number of citations in 2015) of an article indicated that articles published after 2000 were more likely cited in recent years. This correlation was statistically significant ($r = 0.46$, $p < 0.001$, Mann-Kendall test; Fig. 4 B).

The 100 most-cited articles were published in 15 journals (Table 5). Articles originated from 13 countries, led by the United States (n = 55), followed by Japan (n = 18), France and the United Kingdom (5 each), Australia (n = 3) and Germany (n = 3); Table 6.

Table 4
Citations per level of evidence (clinical research articles (n = 78)).

	N	Range (Min/Max)	Mean (±SD)	Median (Q25/Q75)
Ia	7	126/576	243 (±151)	210 (158/233)
Ib	9	105/610	222 (±166)	152 (108/224)
IIa	18	109/334	172 (±66)	162 (122/188)
IIb	11	97/214	138 (±35)	142 (100/161)
III	29	98/438	182 (±95)	146 (117/206)
IV	4	117/256	204 (±62)	221 (160/248)
Total	78	97/610	184 (±100)	157 (118/206)

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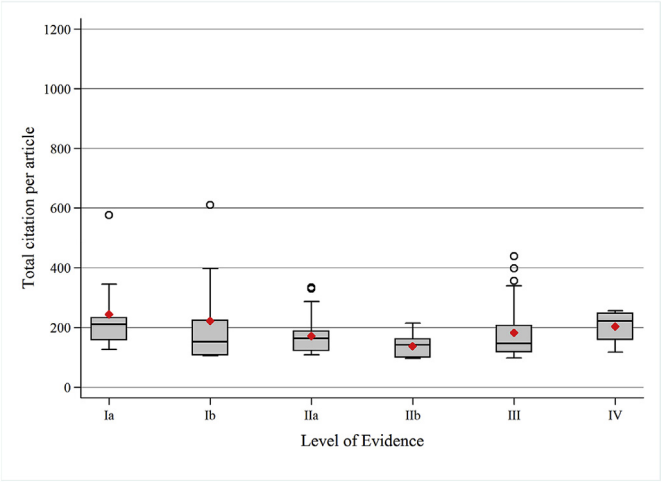

Fig. 2. Bar graph showing the number of citations (and standard deviation) for the 100 most-cited articles according to the level of evidence based on the 2009 revised Oxford (UK) CEBM Levels of Evidence. Red point = Mean value. Box: lower line = 25th quartile, upper line = 75th quartile; black line in box = Median value. White points = Outliers. The Tukey method was used for plotting the whiskers and outliers.

Four articles were of multinational origin, with no individual authors named. As shown in Table 6, several other countries were the origin of one publication each.

There were 18 authors who had multiple first authorships and 10 with multiple last authorships in the list of 100 most-cited articles (Table 7). Stephen C. Pflugfelder had 12 last authorships and was thus the most-cited author in this category. All of Pflugfelder's last 12 authorship articles were cited a total of 1826 times (October 2016). The article entitled "Reliability and validity of the ocular surface disease index" from Rhett M. Schiffman was the most-cited paper according to our analysis (total number of citations = 610) [24]. The number of citations of this paper increased every year since publication until 2015 up to 115 citations per year.

The top 25 most-cited articles from 2015 to 2016 using the same search details are listed in Table 8.

4. Discussion

Our analysis has identified the articles with the greatest impact on the citation of results in the field of dry eye research over the past decades. This study highlights contributions that have led to significant developments in dry eye research and indicates current trends in this field.

The number of citations for an article is a measure of the impact that it has on that particular field, and has thus become a valuable

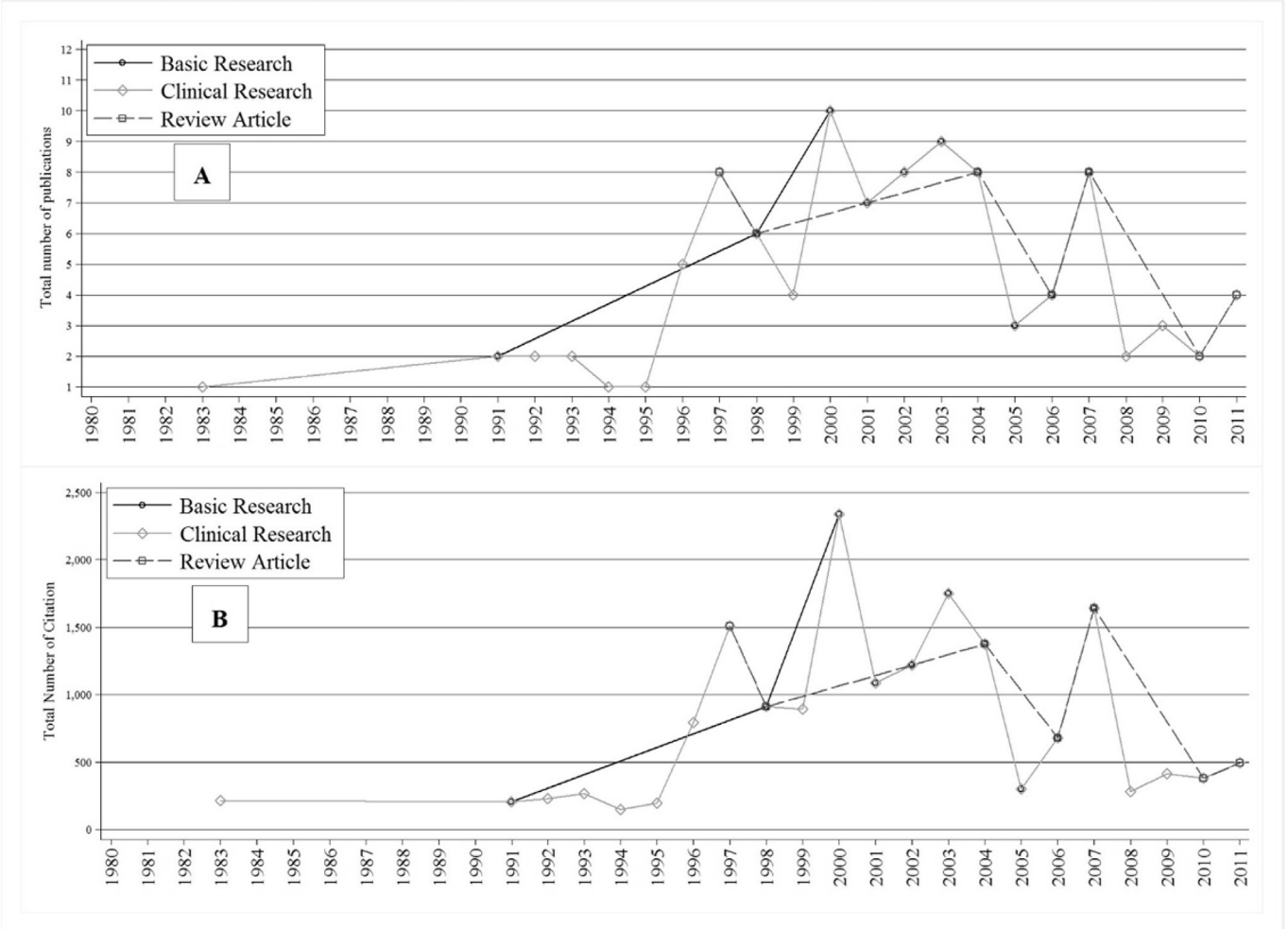

Fig. 3. For each type of article (clinical or basic research, review article), the total number of publications according to publication year (A) and the total number of citations (B) were visualized.

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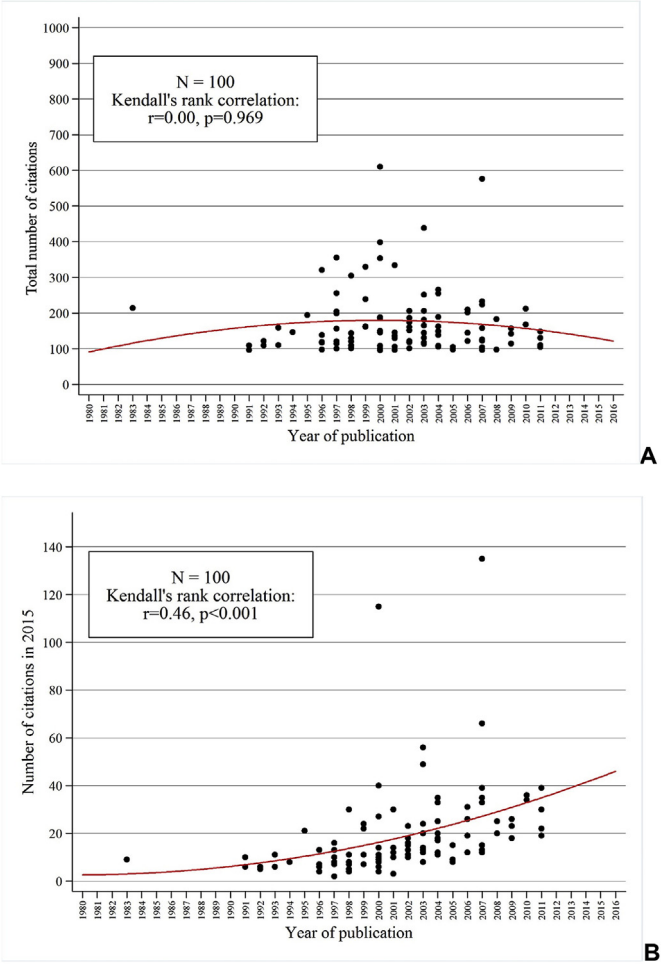

Fig. 4. (A) Overall citation rate since publication, and (B) current (2015 = last full year) citation rate for the 100 most-cited articles according to the publication date of the article.

Table 6
Countries from which the articles in the most-cited list originated.

Country	No. of articles
U.S.	55
Japan	18
France	5
U.K.	5
Multinational	4
Australia	3
Germany	3
Argentina	1
Belgium	1
Canada	1
Singapore	1
South Korea	1
Spain	1
Taiwan	1

Table 7
First and last authors with multiple articles in the most-cited list.

Frequent first authors	No. of articles	Frequent last authors	No. of articles
Tsubota, K	5	Pflugfelder, SC	12
Begley, CG	4	Tsubota, K	9
Mathers, WD	3	Gipson, IK	5
Shimazaki, J	3	Reis, BL	3
Baudouin, C	2	Sullivan, DA	3
De Paiva, CS	2	Baudouin, C	3
Nichols, KK	2	Klein, BEK	2
Schiffman, RM	2	Smith, JA	2
Schaumberg, DA	2	Mitchell, GL	2
Toda, I	2	West, S	2
Nelson, JD	2		
Schein, OD	2		
Kunert, KS	2		
Moss, SE	2		
Brignole, F	2		
Argueso, P	2		
Tomlinson, A	2		
Pflugfelder, SC	2		

tool for assessing both authors' works and journals [5,12]. However, it must be borne in mind that the number of citations for an article accrues over time, so that the impact of an article as assessed by citation numbers, besides judging the quality of the article, has a time factor; even the most-cited papers had no citations when just published [15]. Garfield suggested that older papers are more likely to be cited [12]. Therefore, the group of highest-ranking articles might be dominated by the oldest articles [25]. This may, however, be counteracted by the phenomenon of "obliteration by incorporation," which occurs when the data from the most cited works become part of current knowledge, so that the original papers are cited less frequently [26]. According to our data, the overall citation rate of an article was independent of its publication date. However,

Table 5
Journals in which the 100 most-cited articles were published.

Journal	No. of articles	First issue	Impact Factor[a]
Investigative Ophthalmology & Visual Science	29	1962	3.303
Ophthalmology	13	1980	8.204
American Journal of Ophthalmology	13	1884	5.052
Cornea	12	1982	2.010
Archives of Ophthalmology (now: JAMA Ophthalmology)	9	1929	5.625
British Journal of Ophthalmology	7	1917	3.806
Ocular Surface	4	2003	4.383
Optometry and Vision Science	3	1924	1.409
Progress in Retinal and Eye Research	2	1994	11.587
Current Eye Research	2	1981	2.238
Experimental Eye Research	2	1961	3.332
Acta Ophthalmologica	1	1923	3.157
Journal of Glaucoma	1	1992	2.263
European Journal of Ophthalmology	1	1999	1.192
Clinical and Experimental Ophthalmology	1	1973	3.000

[a] Journal Citation Report Impact Factor for 2016.

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Table 8
The 25 most-cited articles in dry eye in 2015 and 2016.

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2016
1	Denoyer A, Landman E, Trinh L, Faure JF, Auclin F, Baudouin C. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology. 2015 Apr; 122(4):669-76. doi: 10.1016/j.ophtha.2014.10.004. Epub 2014 Nov 22. PubMed PMID: 25458707.	39	13	22
2	Foulks GN, Forstot SL, Donshik PC, Forstot JZ, Goldstein MH, Lemp MA, Nelson JD, Nichols KK, Pflugfelder SC, Tanzer JM, Asbell P, Hammitt K, Jacobs DS. Clinical guidelines for management of dry eye associated with Sjögren disease. Ocul Surf. 2015 Apr; 13(2):118-32. doi: 10.1016/j.jtos.2014.12.001. Epub 2015 Jan 15. Review. PubMed PMID: 25881996.	27	9	13
3	Tauber J, Karpecki P, Latkany R, Luchs J, Martel J, Sall K, Raychaudhuri A, Smith V, Semba CP; OPUS-2 Investigators. Lifitegrast Ophthalmic Solution 5.0% versus Placebo for Treatment of Dry Eye Disease: Results of the Randomized Phase III OPUS-2 Study. Ophthalmology. 2015 Dec; 122(12):2423-31. doi: 10.1016/j.ophtha.2015.08.001. Epub 2015 Sep 11. PubMed PMID: 26365210.	22	7.33	11
4	Bunya VY, Fuerst NM, Pistilli M, McCabe BE, Salvo R, Macchi I, Ying GS, Massaro-Giordano M. Variability of Tear Osmolarity in Patients With Dry Eye. JAMA Ophthalmol. 2015 Jun; 133(6):662-7. doi: 10.1001/jamaophthalmol.2015.0429. PubMed PMID: 25811641; PubMed Central PMCID: PMC4466048.	21	7	7
5	Shetty R, Ghosh A, Lim RR, Subramani M, Mihir K, Reshma AR, Ranganath A, Nagaraj S, Nuijts RM, Beuerman R, Shetty R, Das D, Chaurasia SS, Sinha-Roy A, Ghosh A. Elevated expression of matrix metalloproteinase-9 and inflammatory cytokines in keratoconus patients is inhibited by cyclosporine A. Invest Ophthalmol Vis Sci. 2015 Feb 3; 56(2):738-50. doi: 10.1167/iovs.14–14831. PubMed PMID: 25648341.	20	6.67	11
6	Aragona P, Aguennouz M, Rania L, Postorino E, Sommario MS, Roszkowska AM, De Pasquale MG, Pisani A, Puzzolo D. Matrix metalloproteinase 9 and transglutaminase 2 expression at the ocular surface in patients with different forms of dry eye disease. Ophthalmology. 2015 Jan; 122(1):62–71. doi: 10.1016/j.ophtha.2014.07.048. Epub 2014 Sep 18. PubMed PMID: 25240629.	20	6.67	11
7	Galor A, Zlotcavitch L, Walter SD, Felix ER, Feuer W, Martin ER, Margolis TP, Sarantopoulos KD, Levitt RC. Dry eye symptom severity and persistence are associated with symptoms of neuropathic pain. Br J Ophthalmol. 2015 May; 99(5):665-8. doi: 10.1136/bjophthalmol-2014-306057. Epub 2014 Oct 21. PubMed PMID: 25336572.	19	6.33	7
8	Xu Y, Yang Y. Small-incision lenticule extraction for myopia: results of a 12-month prospective study. Optom Vis Sci. 2015 Jan; 92(1):123-31. doi: 10.1097/OPX.0000000000000451. PubMed PMID: 25397926.	16	5.33	8
9	Galor A, Felix ER, Feuer W, Shalabi N, Martin ER, Margolis TP, Sarantopoulos CD, Levitt RC. Dry eye symptoms align more closely to non-ocular conditions than to tear film parameters. Br J Ophthalmol. 2015 Aug; 99(8):1126-9. doi: 10.1136/bjophthalmol-2014-306481. Epub 2015 Feb 20. PubMed PMID: 25710726.	15	5	8
10	Schmidl D, Schmetterer L, Witkowska KJ, Unterhuber A, dos Santos VA, Kaya S, Nepp J, Baar C, Rosner P, Werkmeister RM, Garhofer G. Tear film thickness after treatment with artificial tears in patients with moderate dry eye disease. Cornea. 2015 Apr; 34(4):421-6. doi: 10.1097/ICO.0000000000000358. PubMed PMID:25651494.	15	5	4
11	Braun RJ, King-Smith PE, Begley CG, Li L, Gewecke NR. Dynamics and function of the tear film in relation to the blink cycle. Prog Retin Eye Res. 2015 Mar; 45:132-64. doi: 10.1016/j.preteyeres.2014.11.001. Epub 2014 Dec 3. Review. PubMed PMID: 25479602; PubMed Central PMCID: PMC4364449.	15	5	8
12	Bron AJ, Argüeso P, Irkec M, Bright FV. Clinical staining of the ocular surface: mechanisms and interpretations. Prog Retin Eye Res. 2015 Jan; 44:36-61. doi: 10.1016/j.preteyeres.2014.10.001. Epub 2014 Oct 23. Review. PubMed PMID: 25461622.	15	5	6
13	Blum M, Täubig K, Gruhn C, Sekundo W, Kunert KS. Five-year results of Small Incision Lenticule Extraction (ReLEx SMILE). Br J Ophthalmol. 2016 Sep; 100(9):1192-5. doi: 10.1136/bjophthalmol-2015-306822. Epub 2016 Jan 8. PubMed PMID: 26746577.	14	7	3
14	Arita R, Morishige N, Koh S, Shirakawa R, Kawashima M, Sakimoto T, Suzuki T, Tsubota K. Increased Tear Fluid Production as a Compensatory Response to Meibomian Gland Loss: A Multicenter Cross-sectional Study. Ophthalmology. 2015 May; 122(5):925-33. doi: 10.1016/j.ophtha.2014.12.018. Epub 2015 Jan 24. PubMed PMID: 25626757.	14	4.67	7
15	van der Vaart R, Weaver MA, Lefebvre C, Davis RM. The association between dry eye disease and depression and anxiety in a large population-based study. Am J Ophthalmol. 2015 Mar; 159(3):470-4. doi: 10.1016/j.ajo.2014.11.028. Epub 2014 Nov 26. PubMed PMID: 25461298; PubMed Central PMCID: PMC4329250.	14	4.67	6
16	Aggarwal S, Kheirkhah A, Cavalcanti BM, Cruzat A, Colon C, Brown E, Borsook D, Prüss H, Hamrah P. Autologous Serum Tears for Treatment of Photoallodynia in Patients with Corneal Neuropathy: Efficacy and Evaluation with In Vivo Confocal Microscopy. Ocul Surf. 2015 Jul; 13(3):250-62. doi: 10.1016/j.jtos.2015.01.005. Epub 2015 Feb 20. PubMed PMID: 26045233; PubMed Central PMCID: PMC4499014.	13	4.33	6
17	Yokoi N, Uchino M, Uchino Y, Dogru M, Kawashima M, Komuro A, Sonomura Y, Kato H, Tsubota K, Kinoshita S. Importance of tear film instability in dry eye disease in office workers using visual display terminals: the Osaka study. Am J Ophthalmol. 2015 Apr; 159(4):748-54. doi: 10.1016/j.ajo.2014.12.019. Epub 2014 Dec 30. PubMed PMID: 25555800.	13	4.33	8
18	Schmidl D, Witkowska KJ, Kaya S, Baar C, Faatz H, Nepp J, Unterhuber A, Werkmeister RM, Garhofer G, Schmetterer L. The association between subjective and objective parameters for the assessment of dry-eye syndrome. Invest Ophthalmol Vis Sci. 2015 Feb 3; 56(3):1467-72. doi: 10.1167/iovs.14–15814. PubMed PMID: 25650419.	13	4.33	7
19	Pucker AD, Haworth KM. The presence and significance of polar meibum and tear lipids. Ocul Surf. 2015 Jan; 13(1):26–42. doi: 10.1016/j.jtos.2014.06.002. Epub 2014 Oct 8. Review. PubMed PMID: 25557344.	13	4.33	8
20	Perez VL, Pflugfelder SC, Zhang S, Shojaei A, Haque R. Lifitegrast, a Novel Integrin Antagonist for Treatment of Dry Eye Disease. Ocul Surf. 2016 Apr; 14(2):207-15. doi: 10.1016/j.jtos.2016.01.001. Epub 2016 Jan 22. Review. PubMed PMID: 26807723.	12	6	6
21	Villani E, Garoli E, Termine V, Pichi F, Ratiglia R, Nucci P. Corneal Confocal Microscopy in Dry Eye Treated with Corticosteroids. Optom Vis Sci. 2015 Sep; 92(9):e290-5. doi: 10.1097/OPX.0000000000000600. PubMed PMID: 25909241.	12	4	5
22	Kaya S, Schmidl D, Schmetterer L, Witkowska KJ, Unterhuber A, Aranha Dos Santos V, Baar C, Garhöfer G, Werkmeister RM. Effect of hyaluronic acid on tear film thickness as assessed with ultra-high resolution optical coherence tomography. Acta Ophthalmol. 2015 Aug; 93(5):439-43. doi: 10.1111/aos.12647. Epub 2015 Jan 20. PubMed PMID: 25601227.	12	4	5
23	Schargus M, Ivanova S, Kakkassery V, Dick HB, Joachim S. Correlation of Tear Film Osmolarity and 2 Different MMP-9 Tests With Common Dry Eye Tests in a Cohort of Non-Dry Eye Patients. Cornea. 2015 Jul; 34(7):739-44. doi: 10.1097/ICO.0000000000000449. PubMed PMID: 25909238.	12	4	9

(*continued on next page*)

Table 8 (*continued*)

Rank	Article	Citations	Citations/Year Since Publication	Citations in 2016
24	Bhargava R, Kumar P, Phogat H, Kaur A, Kumar M. Oral omega-3 fatty acids treatment in computer vision syndrome related dry eye. Cont Lens Anterior Eye. 2015 Jun; 38(3):206-10. doi: 10.1016/j.clae.2015.01.007. Epub 2015 Feb 16. PubMed PMID: 25697893.	12	4	8
25	Bhargava R, Kumar P. Oral omega-3 fatty acid treatment for dry eye in contact lens wearers. Cornea. 2015 Apr; 34(4):413-20. doi: 10.1097/ICO.0000000000000386. PubMed PMID: 25719253.	12	4	6

articles published after 2000 were more likely to be cited in recent years. This correlation was statistically significant ($r = 0.46$, $p < 0.001$, Mann-Kendall test, Fig. 4 A).

Electronic access to publishing houses has continued to evolve, making the whole process of article submission, review and publication, as well as accessing publications, now possible online [4]. We believe that the increasing number of publications in the field of dry eye after 1990 is due to the rise of the World Wide Web with its easy accessibility and its new and great advantages to the scientific community (Fig. 3).

Dry eye diagnostics and treatment have evolved rapidly over the past decades. The top 100 list shows that most clinical articles fall into three subject areas: diagnostic research (66%), medical and surgical treatment (20%) and epidemiology (14%). Correspondingly, the focus of individuals who were first or last authors of multiple articles in the list was also frequently on one of the first two areas.

As in other medical fields (e.g., urology and general surgery), the U.S. was the most frequent country of origin, probably as a consequence of the greater resources compared to Europe [10,27]. In some bibliometric studies, attempts have been made to get a clearer view of research activity in countries with fewer resources by correcting for population size, without affecting the impact of the authors of the most frequently cited articles [15,28]. One of the main confounding factors arises from the tendency of authors to cite articles published in 'local' journals, i.e., authors publishing in European journals citing articles published in those journals, and authors publishing in American journals citing papers from their national journals [15,29]. In our study, the most-cited dry eye articles from the U.S. were nearly always published in American journals. Since the English-language journals from the U.K. and the U.S. have the highest rank in ophthalmology, most authors of high-quality material want their work to appear there, maintaining the status of these British and American journals. The 100 most-cited articles in dry eye research were published in only 15 journals, and 76 of the articles were published in 5 American journals. The American journal "Investigative Ophthalmology and Visual Science," established in 1962, topped the list with 29 articles.

As for earlier bibliometric studies [15,30,31], our top 100 list of dry eye articles is not mainly comprised of articles with a high level of evidence. Most articles in the list (29, with a mean of 182 ± 95 citations per article) were clinical outcome studies with an evidence level of III, demonstrating that small case series or cohort studies presenting an original concept can still attract the interest of researchers and readers in the field [15].

The top 3 most-cited authors in this study period (S.C. Pflugfelder, K. Tsubota, and I.K. Gibson) contributed 34 articles as first and/or last author, accruing a total of 4700 citations. Of these 34 articles, 20 were from American institutions and 14 from Japan. All were single-centre studies. This highlights how a relatively few authors can substantially contribute to the impact of a journal or a field of research [4]. Indeed, the three key authors contributed 34% of the top 100 articles and they attracted almost 27% of citations.

Diagnostic test methods are frequently described in the framework of dry eye articles and were therefore frequently cited. The article entitled "Reliability and validity of the ocular surface disease index" (R.M. Schiffman et al.) was the most-cited paper according to our analysis (with 610 citations; Table 2).

Citation analysis does have certain limitations. First, most journals are not open access but pay-per-view and are therefore not accessible for everyone. Second, language barriers are given between authors and readers. Finally, yet importantly, papers have to be listed within the common online scientific search robots to get a high attraction for new authors.

Although bibliometrics provide a valuable snapshot of articles that have been frequently cited, methods and treatments change, especially in a rapidly developing field such as ophthalmology, and the importance of some previously frequently cited articles wanes [15].

Notwithstanding that citation count provides a valuable quantitative assessment, it does not offer a precise measure of the status of a journal or article by itself [4]. There are several reasons for this: citation reports rely on only a selected number of journals; there will be a bias towards larger journals that publish more articles [15]. Publications will also be cited for several reasons: because of the results of a well-designed study or interesting statistical analysis, but, on the other hand, citations might also been used to show studies with study design errors and studies with strong bias or interpretation problems. Therefore, the number of citations is only one of many quality indicators.

In addition, the basis for selecting articles may differ; varying selection criteria may lead to a different list. When using citation counts as a measure to quantify article impact in bibliometrics, the most-cited articles are often regarded as "citation classics" [15].

Obviously, recent papers are less cited due to limited timespan since publication. This "bias" is the key reason why papers after the year 2011 are not listed under the top 100 dry eye papers. For this reason, we added a list of the top cited papers of 2015 and 2016 to identify the new "rising stars" in their field (Table 8). This subanalysis does not reflect the overall trend, as the citation rate might change significantly over the next years on this actual selection of papers.

Analysis of authors and countries of origin were done only for first and last authorships. The main reason for this was the better visualization of the results and the fact that these authors normally have the highest impact on the work. Even if several previous bibliometric papers applied this method in the past, one could state that this selection is a bias of the current work because not all authors were taken into account [11,15].

Finally, the choice of key words for the search can be a limitation. Since we used the key word "dry eye," it is possible that other relevant articles that did not include this specific term may not have been detected in the database search [31].

In conclusion, this is, to our knowledge, the first bibliometric study to identify the top 100 most-cited papers in dry eye research. Our study focusing on dry eye research shows that the majority of the most-cited articles were published in five of the top-ranked journals. Most of the clinical articles were concerned with diagnostics. The majority of articles represented evidence level III clinical outcome studies, indicating that small case series or cohort studies can also gain attention. Bibliometric studies also need to be

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updated occasionally to include the more recent developments [1,32]. Despite its limitations, citation analysis provides an important quantitative method for comparing research in scientific fields. Bibliometric studies are invaluable for researchers who are new to the field, and highlight the contributions leading to developments, in this case in dry eye research. The results of bibliometric studies emphasize the quality of prior scientific research and could even stimulate new approaches [15].

Conflict of interest

No conflict of interest exists for any author. The authors have no commercial or proprietary interest in any concept or product described in this article. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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