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Current Trends and Future Insights on Rosacea Treatment: A Bibliometric Analysis

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Background: Rosacea involves immune, neurovascular, and microbial factors, but its complex mechanisms are poorly understood, hindering effective treatment development. This study aims to examine research trends and significant contributions in the treatment of rosacea.

Methods: Publications related to rosacea treatment were retrieved from the Web of Science Core Collection (WoSCC). Bibliometric analysis and visualization were performed using VOSviewer, CiteSpace, and the R package "bibliometrix".

Results: By June 7, 2024, 1389 English-language publications published between 1970 and 2024 were identified for analysis. The leading research countries were the United States (446 articles) and China (149 articles), with the Central South University (95 articles) being the most productive institution. Key journals included *Journal of the American Academy of Dermatology* (impact factor = 12.8) and the *British Journal of Dermatology* (impact factor = 11). James Q. Del Rosso was identified as a major contributor (h-index = 20). Keywords cluster analysis revealed five prominent themes: 1) pharmacological treatment and clinical trials, 2) epidemiology and associated risk factors, 3) pathophysiology and pathogenesis, 4) skin barrier function and related dermatoses, and 5) laser and physical therapies. Representative terms of emerging trends include "pathogenesis", "pathophysiology", and "standard classification", suggesting increasing focus on immune dysregulation, neurovascular mechanisms, and microbiome-related pathways. These insights indicate that future rosacea treatment research may shift toward targeted, mechanism-based therapeutic strategies.

Conclusion: This study underscores the dynamic landscape of research in rosacea treatment, synthesizes current areas of emphasis, and forecasts future trends. Future developments in rosacea research may concentrate on integrating precision medicine approaches by linking molecularly defined pathogenic mechanisms with standardized classification systems, thereby facilitating targeted and multi-disciplinary treatment strategies.

Keywords: rosacea, treatment, bibliometric analysis, immune dysregulation, quality of life

Introduction

Rosacea is a prevalent chronic dermatological condition that predominantly impacts the facial region, particularly the nose, cheeks, forehead, and chin. Epidemiological studies indicate that the prevalence of rosacea varies across different populations, with an estimated 10% of adults affected, particularly among women aged 30 to 50.[1] Although the precise etiology of rosacea remains unclear, several factors are believed to play a role in its pathogenesis. These factors include genetic predisposition, abnormal immune responses (such as the involvement of Toll-like receptor 2, or TLR2), microbial infections, neurovascular dysfunction, and environmental influences. This multifactorial nature of rosacea highlights the complexity of its development and the need for a comprehensive approach in both research and treatment.[2,3]

Research has demonstrated that individuals with rosacea exhibit a compromised skin barrier, rendering their skin more susceptible to external stimuli such as temperature fluctuations, ultraviolet radiation, and chemical exposure.[4] Furthermore, an imbalance in the skin microbiome is believed to be closely associated with inflammatory responses.[5] Rosacea not only affects the physical appearance of patients but also significantly diminishes their quality of life. Affected individuals frequently experience symptoms such as facial flushing, pustules, rough skin, and tissue

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hypertrophy, which can lead to psychological distress and social difficulties. If left untreated, rosacea can result in permanent structural alterations in the skin, such as nasal thickening, thereby exacerbating the condition.[6]

In recent years, the management of rosacea has advanced significantly, incorporating a variety of treatment modalities, including pharmacological interventions, physical therapies, and lifestyle modifications. Pharmacotherapy remains central to treatment, with topical agents such as minocycline and ivermectin playing pivotal roles in reducing inflammation and controlling bacterial growth.[7] Additionally, agents like adapalene have been proven effective in improving skin aesthetics and reducing erythema. For more severe cases, oral antibiotics such as doxycycline and minocycline are frequently used due to their strong anti-inflammatory properties. In recent years, more targeted therapies like DFD-29, a modified-release formulation of minocycline, have shown significant efficacy in reducing inflammatory lesions while maintaining a favorable safety profile.[8] Concurrently, laser and light therapies have emerged as important alternatives, with pulsed dye laser (PDL) and intense pulsed light (IPL) demonstrating efficacy in alleviating facial redness and vascular dilation.[9] These interventions not only enhance dermatological health but also contribute to improvements in patient self-esteem. Lifestyle modifications are also integral to the management of rosacea, as the avoidance of specific triggers—such as spicy foods and emotional stress—can substantially reduce flare-ups.[10]

Furthermore, recent studies in fundamental research and clinical trials have introduced a wave of innovative treatments. Emerging biologics and therapies targeting specific inflammatory pathways are anticipated to enhance treatment efficacy.[11] The field of rosacea treatment is evolving rapidly, and future advancements are likely to provide more targeted therapeutic options, ultimately improving patients' quality of life. Bibliometric analysis is a method that quantitatively evaluates academic literature, utilizing statistical and visualization techniques to uncover trends, hotspots, and collaboration networks within research fields. This analysis not only helps researchers pinpoint key literature and comprehend the dynamics of research but also plays a critical role in identifying research gaps and emerging trends, providing a roadmap for future studies.[12] By offering a comprehensive and data-driven perspective, bibliometric analysis strengthens the value of this study, enabling a deeper understanding of the current research landscape and its potential directions.[13] Although there have been bibliometric analyses regarding rosacea, there was a lack of bibliometric analysis focus on rosacea treatment.[14] Although several studies have explored the pathogenesis and epidemiology of rosacea, there remains limited bibliometric evidence specifically examining research trends in rosacea treatment. Existing bibliometric analyses primarily focus on disease mechanisms or classification, leaving a gap in understanding how treatment-related research has evolved and where future therapeutic innovation may occur. To address this gap, the present study conducts a comprehensive bibliometric analysis focused exclusively on rosacea treatment.

Material and Methods

Search Strategies and Data Collection

Publications related to rosacea treatment were retrieved from the Web of Science Core Collection (WoSCC). The search covered all available years in WoSCC from 1970 to 2024, the date on which the search was conducted. WoSCC is a trusted citation index for locating research across a curated, multidisciplinary set of journals, books and conferences. The search formula was (TS=(rosacea) OR TS=(Rhinophyma)) AND (TS = (therapy) OR TS= (treatment)).[14,15] The literature retrieval was performed on a single day (June 7, 2024). Reviews (n=413), editorial material (n=66), letters (n=100), meeting abstracts (n=186), and non-English articles (n=122) were excluded from the retrieval results. The collected data included the number of publications and citations, along with titles, author information, institutions, countries/regions, keywords, and journals.

Statistical Analysis

VOSviewer (version 1.6.20), CiteSpace (version 6.1.R3), and the "bibliometrix" package in R (version 4.3.3) were used for analysis and visualization. VOSviewer was selected for its ability to efficiently map bibliometric indicators and visualize complex collaboration and relationship networks within the academic field. Its strength lies in the capability to handle large datasets and provide clear visualizations of keyword co-occurrence networks, making it particularly useful for identifying emerging research trends and influential publications.[16] CiteSpace, on the other hand, was employed for

its robust functionality in detecting keyword bursts and visualizing temporal trends. Its pathfinder network pruning method is ideal for creating concise visualizations, which highlights critical shifts in research focus over time. This combination of tools enhances the rigor of the analysis by leveraging each platform's strengths for a comprehensive exploration of trends in rosacea treatment.[17]

Several parameters from WoSCC, including the h-index, g-index, and m-index, were employed to quantify the academic impact of individuals and journals.[18–20] The h-index is a vital indicator for evaluating researchers' academic contributions and predicting their future scientific achievements. The g-index enhances this evaluation by giving more weight to highly cited articles, providing a better assessment of a researcher's impact. The m-index, which is calculated by dividing the h-index by the number of years since the researcher's first publication, allows for a comparison of researchers at different career stages. We also assessed journals using Impact Factor (IF) and Journal Citation Reports (JCR).[21,22]

Results

An Overview of Publications

During 1970 to 2024, 1389 articles from 5221 authors were published in 343 journals. The flowchart of data screening is shown in Figure 1. Based on the growth in the number of publications, the research period since 2000 can be divided into three distinct phases (Figure 2): the first phase (2000–2007), the second phase (2008–2015), and the third phase (2016-present). During the first phase, the average annual number of publications was about 26, with an unstable trend, reflecting the nascent stage of research in this field. The second phase experienced rapid growth, with an average of 53 publications per year, indicating a significant increase in attention to rosacea treatment research. In the third phase, although publication numbers fluctuated, the overall trend has been a gradual increase, with an annual average of 67 publications. In 2022, the number of publications peaked at 105.

We also identified the top three most-cited publications, which focus on: (1) the use of antibiotics, particularly tetracyclines, in treating rosacea; (2) the biological factors of rosacea, such as *Demodex* mites; and (3) immune pathway alterations, including increased TLR2 expression, which stimulates keratinocytes to produce more serine proteases.[23–25]

Analysis of Countries and Institutions

Based on the number of publications, the research output from the top 20 countries is detailed in Supplementary Figure S1A and Table 1. The United States leads with 446 papers (accounting for 32.1%), followed by China (149 papers, 10.7%), Germany (85 papers, 6.1%), and Turkey (80 papers, 5.8%). The United States dominates rosacea treatment research, with its publication volume far surpassing other countries. Germany excels in multidisciplinary collaboration (MCP), while the United States stands out in single-discipline collaboration (SCP). Among the 45 countries involved in international collaborations with a minimum of three articles, the United States has the highest number of collaborations (182), followed by Germany (132) and France (114), underscoring the focus on rosacea treatment research in the Western regions. In Asia, countries such as China (34), Singapore (32), and India (41) stand out, forming a distinct research network that contributes significantly to the global landscape of rosacea studies. (Supplementary Figure S1B).

Regarding institutional contributions to rosacea treatment research, the top ten research institutions are shown in Supplementary Figure S2A, mainly located in China, North America and Europe. The top three institutions were: Central South University leads with 95 papers (6.84% of the total), followed by the University of California System with 85 papers (6.12%), and Wake Forest University with 55 papers (3.96%). Furthermore, the collaboration network (Supplementary Figure S2B) highlights that, among the 113 institutions involved in international collaborations with a minimum of five articles, Pennsylvania State University (97) has the most collaborations with other countries, followed by the University of California (89), and Thomas Jefferson University (80).

Analysis of Journals and Authors

In rosacea treatment related publications, the top three journals with the highest h-index were the *Journal of the American Academy of Dermatology* (IF = 12.8), the *British Journal of Dermatology* (IF = 11), and the *CUTIS*

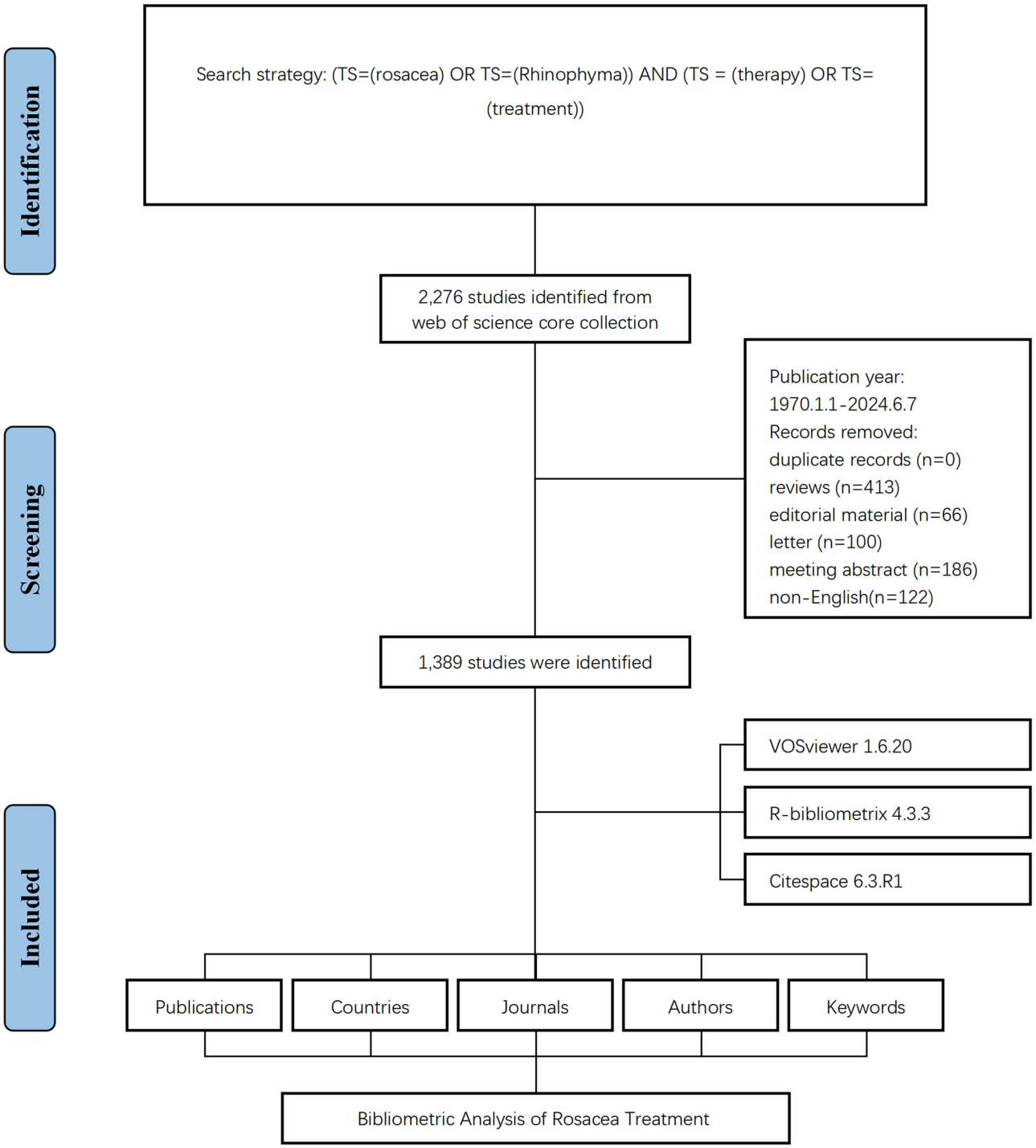

Figure 1 Flowchart of the literature screening process.

(IF = 2.1) (Table 2). The *Journal of the American Academy of Dermatology* leads in both publication count and citation number, reflecting its prominent position in the field. Although the *British Journal of Dermatology* ranks second in terms of publication count, its high impact factor ensures its strong academic reputation. Co-occurrence networks (Supplementary Figure S3A) and collaboration networks (Supplementary Figure S3B) also show strong thematic associations driven by these two journals, further highlighting their importance in rosacea treatment research. Additionally, due to the high number of published articles (93), *Journal of Drugs in*

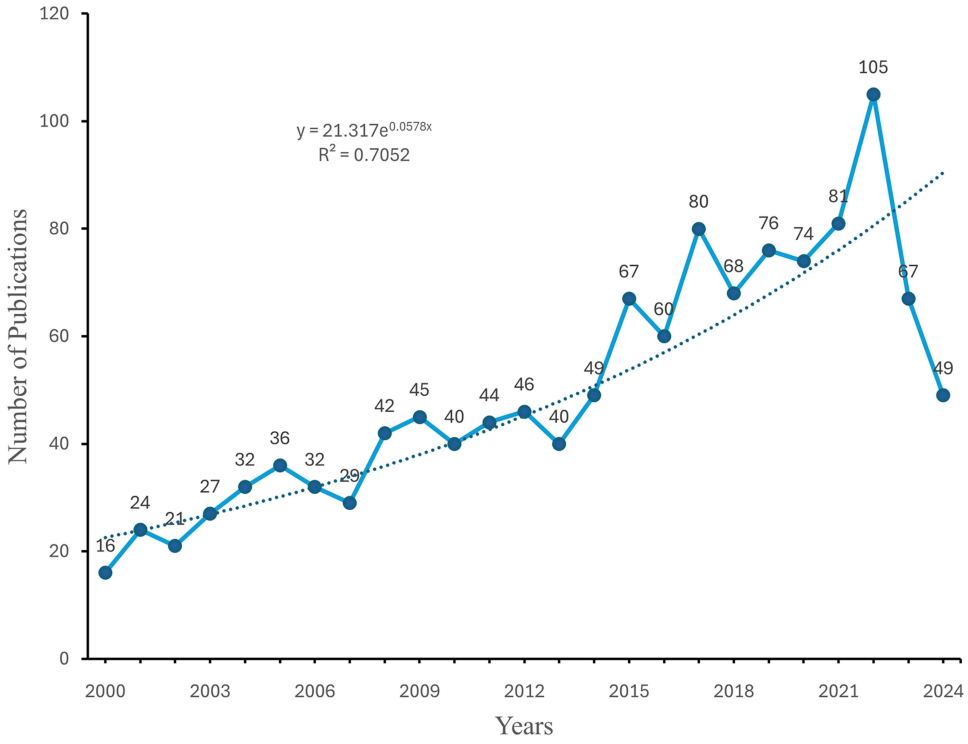

Figure 2 Annual number of publications.

Dermatology also holds a significant position within the co-occurrence and collaboration networks, further emphasizing its influence in the field of rosacea research.

A total of 5221 authors have contributed to research on rosacea treatment. The most influential researcher in the field is James Q. Del Rosso, with an h-index of 20 and the highest citation count, reaching 1078 (Table 3). Del Rosso and his co-authors have made significant contributions, with a total of 33 publications and 1078 citations, showcasing his extensive collaboration and research capabilities. Ji Li and Martin Steinhoff have fewer publications, with 28 and 10 papers, respectively, but their citation counts, at 320 and 914, indicate that their work is highly regarded. Additionally, authors like Steven R. Feldman and Diane Thiboutot, though having fewer publications than Del Rosso, also exhibit

Table 1 Publication and Citation Profiles of Leading Countries

Country	Articles	Freq	SCP	MCP	MCP_Ratio	TP	TP_rank	TC	TC_rank	Average Citations
USA	446	0.321	398	48	0.108	1338	1	12,744	1	28.6
China	149	0.107	138	11	0.074	431	2	1365	4	9.2
Germany	85	0.061	67	18	0.212	274	3	2116	2	24.9
Turkey	80	0.058	79	1	0.013	198	4	1409	3	17.6
Korea	67	0.048	64	3	0.045	185	5	1045	7	15.6
Italy	54	0.039	46	8	0.148	147	6	1363	5	25.2
United Kingdom	51	0.037	37	14	0.275	135	7	965	9	18.9
France	41	0.030	31	10	0.244	129	8	1083	6	26.4
Japan	31	0.022	30	1	0.032	70	11	1000	8	32.3
Canada	29	0.021	20	9	0.310	95	10	719	10	24.8
Spain	27	0.019	21	6	0.222	102	9	536	12	19.9
Brazil	19	0.014	17	2	0.105	54	13	264	20	13.9

(*Continued*)

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Table 1 (Continued).

Country	Articles	Freq	SCP	MCP	MCP_Ratio	TP	TP_rank	TC	TC_rank	Average Citations
Denmark	18	0.013	13	5	0.278	64	12	402	13	22.3
Poland	18	0.013	16	2	0.111	45	15	279	19	15.5
India	15	0.011	13	2	0.133	31	21	245	21	16.3
Netherlands	15	0.011	7	8	0.533	40	17	392	14	26.1
Australia	14	0.010	13	1	0.071	31	19	317	16	22.6
Israel	13	0.009	10	3	0.231	47	14	299	18	23
Ireland	12	0.009	9	3	0.250	43	16	715	11	59.6
Switzerland	12	0.009	9	3	0.250	36	18	336	15	28

Table 2 Bibliometric Indicators of High-Impact Journals

Journal	h_index	IF	JCR	g-index	m-index	TP	TP_rank	TC	TC_rank	PY_start
Journal of the American Academy of Dermatology	33	12.8	Q1	48	0.750	48	3	3652	1	1981
British Journal of Dermatology	25	11	Q1	39	0.481	39	6	2217	2	1973
Cutis	25	2.1	Q4	32	0.595	76	2	1090	5	1983
Journal of the European Academy of Dermatology and Venereology	22	8.4	Q1	35	0.917	44	4	1104	4	2001
International Journal of Dermatology	21	3.5	Q1	30	0.538	34	7	712	9	1986
Journal of Drugs in Dermatology	20	1.5	Q4	33	1.176	93	1	1006	6	2008
Dermatology	18	3.0	Q2	31	0.600	31	9	601	11	1995
Archives of Dermatology	16	#N/A	#N/A	18	0.364	18	18	#N/A	#N/A	1981
Clinics in Dermatology	15	2.3	Q2	21	0.600	21	14	224	28	2000
Ophthalmology	15	13.1	Q1	15	0.319	15	22	325	18	1978
Cornea	13	1.9	Q2	20	0.419	20	15	456	12	1994
Dermatologic Surgery	12	2.5	Q3	20	0.414	20	16	763	8	1996
American Journal of Ophthalmology	11	4.1	Q1	15	0.275	15	21	415	15	1985
Journal of Dermatology	11	2.9	Q2	17	0.524	24	11	277	22	2004
Lasers in Surgery and Medicine	11	2.2	Q3	16	0.297	20	17	400	16	1988
American Journal of Clinical Dermatology	10	8.6	Q1	11	0.455	11	26	307	19	2003
Clinical and Experimental Dermatology	10	3.7	Q1	16	0.233	16	19	452	13	1982
Dermatologic Therapy	10	3.7	Q1	17	0.526	32	8	192	35	2006
Journal Der Deutschen Dermatologischen Gesellschaft	10	5.5	Q1	10	0.625	10	30	195	33	2009
Journal of Cosmetic and Laser Therapy	10	1.2	Q4	15	0.625	26	10	205	31	2009

Notes: H_index: The h-index of the journal, which measures both the productivity and citation impact of the publications. IF: Impact Factor, indicating the average number of citations to recent articles published in the journal. JCR_Quartile: The quartile ranking of the journal in the Journal Citation Reports, indicating the journal's ranking relative to others in the same field (Q1: top 25%, Q2: 25%-50%, Q3: 50%-75%, Q4: bottom 25%). TP: Total Publications. TP_rank: Rank of Total Publications. TC: Total Citations. TC_rank: Rank of Total Citations. Average Citations: The average number of citations per publication. PY_start: Publication Year Start, indicating the year the journal started publication.

strong citation performance. Among the 240 authors involved in international collaborations with a minimum of three articles, Ji Li has the highest number of collaborations with other countries (Supplementary Figure S4).

Keywords Co-Occurrence and Bursts

The results of keywords co-occurrence were shown in Figure 3A The keyword clustering analysis revealed that related studies primarily focus on five thematic areas. Cluster 1 (Pharmacological treatment and clinical trials) centers on

Table 3 Publication and Citation Profiles of High-Impact Authors

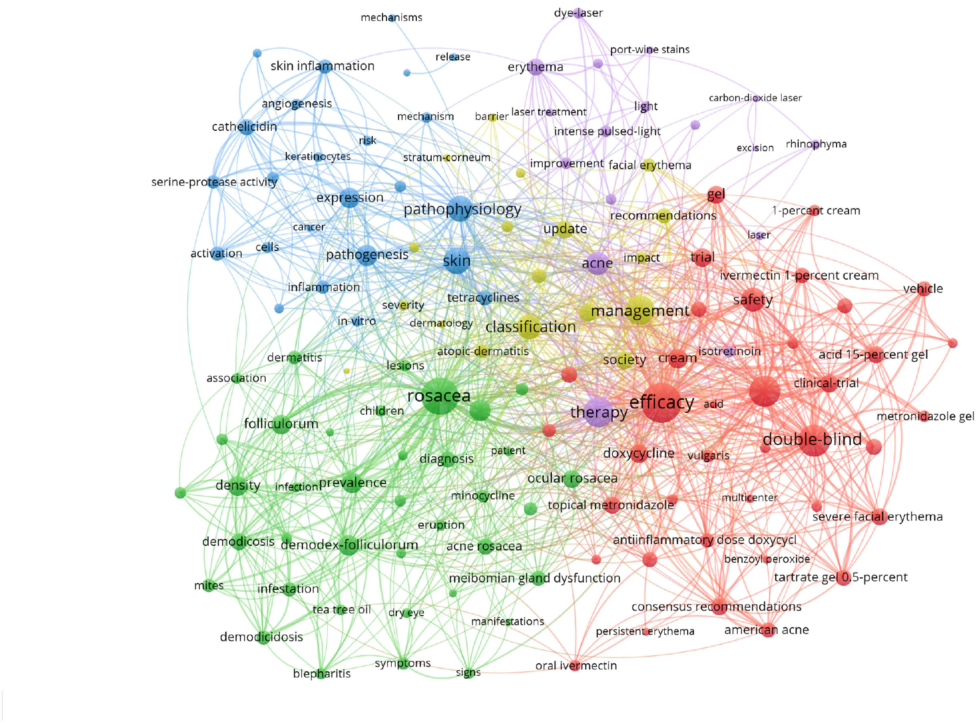
Journal	h_index	g-index	m-index	PY_start	TP	TP_Frac	TP_rank	TC	TC_rank
Del Rosso James Q.	20	32	1.05	2006	33	12.91	1	1078	1
Li Ji	11	17	1.10	2015	28	3.44	2	320	12
Steinhoff Martin	10	10	0.71	2011	10	0.91	13	914	2
Feldman Steven R.	9	12	0.53	2008	13	3.26	5	165	29
Thiboutot Diane	9	12	0.47	2006	12	2.79	7	329	10
Augustin M.	8	8	0.47	2008	8	1.39	16	409	6
Deng Zhili	8	14	1.33	2019	14	1.47	4	221	21
Draelos Zoe Diana	8	11	0.42	2006	11	3.89	9	178	27
Jackson J. Mark	8	11	0.57	2011	11	2.38	10	307	13
Schaller M.	8	8	0.80	2015	8	0.87	20	374	7
Schaller Martin	8	12	0.50	2009	12	2.57	6	206	22
Webster Guy	8	8	0.47	2008	8	1.21	22	351	9
Xie Hongfu	8	14	0.80	2015	18	1.91	3	223	20
Ahluwalia Gurpreet	7	7	1.00	2018	7	0.93	25	107	38
Gold Linda Stein	7	9	0.64	2014	9	1.46	14	283	14
Ruzicka T.	7	7	0.54	2012	7	1.00	31	256	17
Steinhoff M.	7	7	0.54	2012	7	0.63	32	372	8
Tan Jerry	7	8	0.64	2014	8	1.93	21	327	11
Zhang Yiya	7	11	1.17	2019	11	1.11	11	198	24
Berk David R.	6	6	0.86	2018	6	0.68	35	100	39

Notes: H_index: The h-index of the author, which measures both the productivity and citation impact of the publications. g_index: The g-index of the author, which gives more weight to highly-cited articles. m_index: The m-index of the author, which is the h-index divided by the number of years since the first published paper. TP: Total Publications. TP_rank: Rank of Total Publications. TC: Total Citations. TC_rank: Rank of Total Citations. Average Citations: The average number of citations per publication. PY_start: Publication Year Start, indicating the year the author started publication.

commonly used agents such as "ivermectin", "metronidazole", "doxycycline", "azelaic acid", along with "topical treatment" and "clinical trial", reflecting research hotspots in drug interventions and efficacy evaluation. Cluster 2 (Epidemiology and associated risk factors) encompasses keywords such as "children", "epidemiology", "Helicobacter pylori", "Demodex folliculorum", "prevalence", and "patient", indicating an emphasis on the distribution patterns of the disease and potential risk factors. Cluster 3 (Pathophysiology and pathogenesis) includes "inflammation", "cathelicidin", "angiogenesis", "mast cells", "pathophysiology", and "keratinocytes". Cluster 4 (Skin barrier function and related dermatoses) covers "atopic dermatitis", "skin barrier", "classification", "Demodex", "dermatology", and "inflammation", suggesting a focus on barrier impairment and its association with other dermatological conditions. Cluster 5 (Laser and physical therapies) is characterized by "laser", "intense pulsed-light", "dye-laser", "carbon-dioxide laser", "erythema", and "therapy", reflecting research trends in the clinical application of physical treatment modalities. Analysis showed that 20 important keywords in the field of rosacea treatment research exhibited varying degrees of burst intensity (Figure 3B). The burst intensity ranges from 5.04 to 18.13. The trends in keyword bursts and keyword co-occurrence show a consistent pattern, with earlier terms (circa 1997) focusing on efficacy, clinical cases, and specific medications. From 2010 onward, there has been a marked shift towards keywords related to patient health and quality of life, with these terms maintaining a burst strength of over five years. More recent bursts, such as "pathogenesis" (2021–2024), "pathophysiology" (2021–2024), and "standard classification" (2022–2024), highlight the growing emphasis on basic research and clinical categorization, reflecting an increasing drive towards standardizing research in rosacea treatment.

Based on the results of the keyword co-occurrence and clustering analysis, we summarized treatment-related high-frequency and high-strength keywords from Cluster 1 (Pharmacological treatment and clinical trials) and Cluster 5 (Laser and physical therapies). These keywords were used to construct a table of representative rosacea treatments and their corresponding mechanisms (Supplementary Table S1). As shown in Table S1, these keywords correspond to commonly studied pharmacologic agents (such as ivermectin, metronidazole, doxycycline, and azelaic acid) and widely applied

A



B

Keywords	Year	Strength	Begin	End	1994 - 2024
therapy	1997	18.13	1997	2008	
acne rosacea	1998	5.99	1998	2013	
topical metronidazole	2000	6.31	2000	2005	
clinical trial	2001	10.35	2001	2007	
tetracycline	2001	6.27	2001	2008	
cream	2003	8.95	2003	2011	
ocular rosacea	2001	5.32	2005	2016	
azelaic acid	2012	6.52	2012	2014	
management	2011	6.76	2013	2018	
moderate	2014	5.04	2014	2018	
safety	2011	7.83	2015	2019	
quality of life	2013	9.52	2017	2019	
pulsed dye laser	2009	7.26	2017	2020	
folliculorum	2012	5.76	2019	2022	
recommendations	2019	5.52	2019	2022	
update	2020	12.24	2020	2024	
activation	2020	5.65	2020	2021	
pathogenesis	2005	7.32	2021	2024	
pathophysiology	2012	7.24	2021	2024	
standard classification	2022	5.54	2022	2024	

Figure 3 (**A**) Visual analysis of keywords co-occurrence network analysis. This network visualization displays the co-occurrence of keywords in selected literature. Each node represents a keywords, with size indicating its frequency of occurrence. Links between nodes represent co-occurrence in the same documents, with thicker lines showing stronger associations. Colors reflect the average publication year of the articles, as indicated by the color gradient at the bottom right. (**B**) Top 20 Keywords with the Strongest Citation Bursts.

physical modalities (including laser therapy and intense pulsed light). The table provides an overview of representative treatments and their mechanisms, consistent with the thematic focus of the keyword clusters.

Discussion

General Information

This study encapsulates several critical dimensions of rosacea treatment research. The United States stands out, leading in publication volume and citation counts, which underscores its pivotal role in this field. The *Journal of the American Academy of Dermatology* and the *British Journal of Dermatology* serve as essential academic platforms, offering high impact factors and frequent citations. James Q. Del Rosso is recognized as the most influential scholar.

Keywords Cluster Analysis

Cluster 1: Pharmacological Treatment and Clinical Trials

This cluster gathers research on core pharmacologic interventions such as "ivermectin", "metronidazole", "doxycycline", and "azelaic acid", often used in "topical treatment" or in combination with oral regimens. "Ivermectin" is a relatively recent topical agent with dual anti-inflammatory and acaricidal properties against *Demodex* mites, targeting one of the hypothesized etiologic factors.[26] Topical ivermectin 1% cream has been shown in Phase III randomized trials and a 40-week extension study to provide superior efficacy and long-term safety compared to azelaic acid 15% and metronidazole 0.75%.[27,28] A network meta-analysis reported that ivermectin was more effective in reducing inflammatory lesion counts and had a lower risk of treatment-related adverse events than comparators. Azelaic acid 15–20% formulations also demonstrate strong efficacy and are well-supported by direct comparison trials and meta-analyses. In particular, 20% azelaic acid cream ranked highest in a network meta-analysis in terms of Investigator Global Assessment (IGA) improvement scores.[29] Topical metronidazole remains a widely used option with moderate-quality evidence from Cochrane reviews and long-standing clinical use, although some newer agents like azelaic acid and ivermectin have shown better performance in head-to-head trials.[30] Oral doxycycline 40 mg (sub-antimicrobial dose) has been validated in community-based clinical trials as effective add-on therapy, achieving significant improvement in inflammatory lesion counts and erythema with a favorable safety profile.[31] Importantly, this formulation minimizes the risk of antibiotic resistance. Combination therapies, such as azelaic acid+doxycycline or metronidazole+doxycycline, have demonstrated faster onset of efficacy and higher patient satisfaction in randomized trials.[31] These findings support a multi-modal approach, especially in moderate to severe cases.

Despite robust short-term data, limitations include the lack of standardized outcome measures and limited studies on long-term maintenance. High relapse rates post-treatment underscore the need for trials addressing remission sustainability and phenotype-based treatment selection.[28]

Cluster 2: Epidemiology and Associated Risk Factors

Epidemiological studies consistently show that the disease affects diverse populations, with prevalence estimates ranging from under 1% to over 20%, largely due to variations in diagnostic criteria and study design.[32] Large-scale meta-analysis indicates a significantly higher prevalence of *Helicobacter pylori* infection among affected individuals compared to controls, supporting a potential link between chronic gastric infection and cutaneous inflammation.[33] Although causality remains debated, some interventional studies report that eradication therapy can alleviate clinical symptoms, suggesting a contributory role for *H. pylori* in certain patient subgroups.[34] Microbial skin colonization also emerges as a relevant factor. *Demodex folliculorum* infestation shows significantly higher density in affected skin compared to controls and correlates with disease severity. In a prospective three-year follow-up, targeted acaricidal therapy not only reduced mite density but also maintained long-term remission in a subset of patients.[35]

Dietary factors have also been shown to modulate rosacea symptoms through effects on neurovascular activity and immune signaling. Trigger foods such as spicy foods, alcohol, hot beverages, and histamine-rich items can activate sensory neurons or promote vasodilation, exacerbating flushing and inflammatory responses.[36,37] As a result, dietary modification remains an important non-pharmacological therapeutic measure. Individualized trigger avoidance,

combined with structured dietary counseling, can significantly reduce flare frequency and improve responsiveness to pharmacologic therapy, thereby serving as a practical adjunct to standard rosacea management.

Cluster 3: Pathophysiology and Pathogenesis

The pathophysiology of the condition involves dysregulated innate immunity, abnormal vascular responses, and neuroimmune crosstalk. These mechanisms contribute directly to the hallmark symptoms of rosacea, including persistent erythema, papules, and telangiectasia. Central to this is the overproduction and aberrant activation of the antimicrobial peptide cathelicidin LL-37, which drives inflammation, angiogenesis, and skin barrier disruption. Mast cells amplify this cascade by releasing proteases and cytokines, and their inhibition has shown promise in reducing inflammation and vascular dilation.[38] Environmental triggers, especially ultraviolet (UV) radiation, exacerbate the inflammatory process. UVB exposure works synergistically with LL-37 to enhance inflammasome activation, interleukin-1β release, and angiogenesis, which explains the common observation that rosacea symptoms worsen with sun exposure and highlights the importance of photoprotection.[39] Recent evidence links microbial dysbiosis—particularly overgrowth of *Bacillus oleronius*—to kallikrein 5–mediated LL-37 activation, inducing a pathogenic type I interferon signature and IL-22–driven angiogenesis, further supporting the microbial component in rosacea pathogenesis.[40] This integrated understanding suggests that therapies targeting upstream regulators like toll-like receptor 2 or kallikrein 5 could address multiple pathogenic pathways simultaneously.

Increasing evidence indicates that dysregulated innate immune signaling substantially influences treatment responsiveness in rosacea. Aberrant activation of pattern-recognition pathways—particularly TLR2-mediated signaling—amplifies downstream inflammatory cascades and promotes an exaggerated cutaneous response to microbes and environmental stimuli.[41,42] These mechanisms help explain the efficacy of several current therapies: ivermectin attenuates inflammatory activation while reducing Demodex-associated triggers; azelaic acid modulates oxidative and inflammatory pathways influenced by TLR2 activity; and sub-antimicrobial-dose doxycycline suppresses key mediators such as matrix metalloproteinases and neutrophil-derived cytokines.[43–45] Understanding these upstream immune disruptions underscores why anti-inflammatory agents remain central in rosacea management and supports ongoing efforts to develop treatments that more precisely target early immune pathways.

In addition to immune pathways, neurovascular dysregulation represents a key mechanism underlying persistent erythema and flushing. Environmental stimuli such as heat, UV light, and emotional stress activate TRPV1 and related transient receptor potential channels, leading to vasodilation and neurogenic inflammation.[46,47] These mechanistic insights directly support the therapeutic use of vasomodulatory agents such as brimonidine and oxymetazoline, which target abnormal vasoreactivity and rapidly reduce persistent erythema.[48,49] Recognition of neurovascular hyperreactivity also highlights the importance of photoprotection and avoidance of thermal triggers as complementary therapeutic strategies.[50]

Cluster 4: Skin Barrier Dysfunction and Demodex-Associated Inflammation

Skin barrier impairment plays a pivotal role in the pathogenesis of this condition, with evidence showing marked alterations in the stratum corneum structure, lipid composition, and tight junction integrity. Molecular profiling of papulopustular lesions has revealed disruption in cornified envelope proteins, intercellular lipid lamellae, and desmosome organization, resembling patterns observed in atopic dermatitis and underscoring the importance of barrier repair as part of management.[51] The barrier disruption not only increases transepidermal water loss but also facilitates the colonization and proliferation of *Demodex* mites, which can trigger and sustain inflammation. *Demodex folliculorum*–associated bacteria, such as *Bacillus oleronius*, have been shown to activate innate immune responses through toll-like receptor pathways, leading to cytokine release and recruitment of inflammatory cells.[52] This inflammatory cascade may explain the tendency for papulopustular flares in patients with high *Demodex* density, as well as the frequent co-occurrence of ocular involvement due to mite colonization in eyelash follicles. Recent non-invasive imaging studies using reflectance confocal microscopy have provided in vivo visualization of barrier weakness in rosacea, revealing greater superficial stratum corneum permeability compared to both healthy controls and atopic dermatitis patients. These findings suggest that in rosacea, upper epidermal vulnerability predominates, making it especially susceptible to environmental insults and

microbial invasion.[53] Such insights are reinforcing the rationale for integrated therapeutic approaches that combine anti-inflammatory agents, barrier repair strategies, and targeted anti-*Demodex* treatments.

Beyond local skin alterations, increasing evidence supports the involvement of the gut-skin axis in rosacea pathophysiology. Conditions such as small intestinal bacterial overgrowth and Helicobacter pylori infection can amplify systemic inflammatory signals that influence cutaneous immune responses.[54] Inversely, eradication therapy for gastrointestinal dysbiosis has been shown to not improve rosacea symptoms in selected patients.[55] Probiotics represent another emerging adjunctive therapy, as they can help restore microbial balance, reduce systemic inflammation, and enhance the effectiveness of standard pharmacologic treatments.[56] These findings suggest that microbiome-directed interventions may complement topical and systemic therapies, particularly in patients with gastrointestinal comorbidities.

The psychosocial burden of rosacea extends well beyond visible skin changes, with clear evidence of reduced health-related quality of life (HRQoL) and increased anxiety and depression. A Jordanian case-control study of 198 patients showed significantly higher DLQI scores and markedly elevated rates of moderate-to-severe anxiety (57%) and depression (31%), especially among newly diagnosed patients with severe disease.[57] These results align with global data: a Danish cohort of 4.6 million individuals found that both mild and moderate-to-severe rosacea increased the risk of depression (IRR 1.89–2.04) and anxiety disorders (IRR 1.80–1.98).[58] Improvement in skin symptoms often leads to better emotional well-being, as reductions in inflammatory lesions and erythema correlate with gains in HRQoL and self-esteem.[59] Collectively, the evidence supports integrating dermatologic and psychological care, including routine screening for mood disorders and use of patient-reported outcomes in rosacea management.

Cluster 5: Laser and Physical Therapies

As indicated by the keyword clustering results, Cluster 5 highlights the prominence of laser and physical therapies—such as PDL, long-pulsed Nd:YAG laser, IPL, and carbon dioxide laser—in rosacea treatment.[60,61] These modalities primarily target the vascular abnormalities underlying persistent erythema and telangiectasia. PDL and IPL act through selective photothermolysis, inducing controlled photocoagulation of superficial dilated vessels and thereby improving baseline erythema and flushing.[62] The long-pulsed Nd:YAG laser penetrates more deeply and is particularly useful for refractory or thicker telangiectatic vessels.[63] Ablative carbon dioxide laser remains a key option for phymatous rosacea by facilitating tissue debulking, contouring, and dermal remodeling.[64]

Current recommendations support the use of vascular-selective lasers or IPL as first-line physical therapies for persistent erythema unresponsive to topical vasoconstrictors, and as adjunctive treatments in multimodal regimens combining anti-inflammatory or anti-Demodex agents.[65] The prominence of laser-related keywords in this cluster reflects growing acceptance of integrating pharmacologic and light-based approaches to achieve simultaneous control of vascular and inflammatory manifestations. Cross-country differences are also evident. North American and European centers more frequently report the use of PDL and Nd:YAG lasers due to wider device availability and reimbursement structures,[63] whereas Asian studies more commonly emphasize IPL-based protocols and individualized regimens tailored to Fitzpatrick skin types.[66,67] These geographic variations underscore the need for harmonized global recommendations and further comparative studies assessing optimized laser sequences and combination strategies across diverse patient populations.

Burst Analysis

The recent burst keywords “pathogenesis” (2021–2024), “pathophysiology” (2021–2024), and “standard classification” (2022–2024) mark a pronounced shift in rosacea research towards mechanistic elucidation and unified clinical frameworks. In pathogenesis, recent work has consolidated evidence that dysregulated innate immunity—particularly toll-like receptor 2 (TLR2) overactivation—leads to excessive production of cathelicidin peptides such as LL-37, which in turn drive leukocyte recruitment, mast cell degranulation, and vascular proliferation.[68] These findings offer direct targets for therapy, and agents modulating TLR2 or LL-37 pathways may interrupt these inflammatory cascades.[69,70]

Concurrently, oxidative stress and neurovascular hyperreactivity have been implicated as amplifiers of these inflammatory cascades, with external triggers such as UV exposure and temperature shifts acting as catalysts.[70] Such insights underpin the recommendation of daily photoprotection as a non-pharmacologic adjunct to all rosacea treatments.

From a pathophysiology perspective, the field has expanded beyond a purely cutaneous model. The gut-skin axis has become a significant research focus, with multiple studies linking gastrointestinal dysbiosis—especially small intestinal bacterial overgrowth (SIBO) and *Helicobacter pylori* infection—to exacerbated skin inflammation in rosacea. Importantly, eradication therapies for SIBO and H. pylori have demonstrated adjunctive benefits in treatment-resistant rosacea, highlighting systemic intervention potential.[54,55] Additionally, probiotic supplementation combined with doxycycline has shown promising dual benefits in improving both gut microbial balance and rosacea symptoms, pointing to novel combination approaches.[71]

In parallel, the keyword "standard classification" reflects a growing push towards harmonizing clinical categorization to facilitate both research and patient care. The recent German S2k guideline (2022) proposed phenotype-based classification, moving away from rigid subtype systems. This approach links treatment more directly to clinical features, for example, using brimonidine for persistent erythema or ivermectin for papulopustular lesions, resulting in more personalized and effective interventions.[72] As mechanistic insights deepen, they inform the creation of more clinically meaningful diagnostic categories that can better predict disease course and therapeutic response.

Future Research Predictions for Rosacea Treatment

Given that these three keywords continue to show burst activity into 2024, they likely represent sustained research priorities for the next phase of rosacea investigation. Mechanistically, future studies are expected to expand on multi-omics approaches—integrating genomics, transcriptomics, and metabolomics—to identify novel pathogenic signatures and molecular targets. Building on recent work in targeted immunomodulation, emerging therapies such as toll-like receptor 2 antagonists, Janus kinase inhibitors, and microvesicle-targeted agents are predicted to enter early-phase trials, aiming to modulate core inflammatory circuits described in current pathophysiology models.[68]

Clinically, the standard classification framework is expected to become more granular, potentially integrating digital imaging biomarkers and machine-learning–based lesion recognition to improve patient stratification and outcome tracking. Furthermore, given increasing evidence linking rosacea to systemic comorbidities—such as gastrointestinal disorders and cardiovascular risk—future treatment algorithms may adopt a multidisciplinary approach, where dermatologic, gastroenterologic, and psychological assessments are integrated into routine care.[73] These trajectories suggest that the next generation of rosacea research will focus on precision medicine—matching targeted interventions to distinct pathogenic endotypes—while leveraging standardized classification systems to enable global data harmonization and large-scale clinical trial comparability.

Our results indicate that current rosacea treatments primarily target innate immune dysregulation, neurovascular reactivity, and microbial imbalance. For example, ivermectin exerts dual anti-inflammatory and anti-*Demodex* effects, while sub-antimicrobial doxycycline modulates cytokine and matrix metalloproteinase activity. Laser and light therapies focus on vascular abnormalities, aligning with mechanisms related to neurovascular dysregulation. Across regions, treatment patterns differ, with North American studies emphasizing combination therapy and Asian countries reporting more frequent use of oral antibiotics. These findings highlight the need for harmonized treatment guidelines informed by mechanistic insights.

Limitations

The limitations of this study are primarily reflected in the following aspects. First, bibliometric analysis relies on the quantity and quality of existing literature, which may not fully capture all the progress in rosacea research. Some relevant studies may not be included in the databases, leading to an incomplete understanding of certain areas. Furthermore, while this study provides an overview of the trends in rosacea research, it does not delve into the specific methods and outcomes of individual studies, which may lead to misunderstandings or overgeneralizations of some research conclusions. Lastly, the keywords predictions for future research are based on current trends, which may be influenced by future discoveries or technological advancements, introducing a degree of uncertainty.

Conclusion

In conclusion, this study provides a comprehensive bibliometric analysis of rosacea treatment research, highlighting key trends and the contributions of leading institutions, authors, and journals. The five prominent themes in this field concentrate on pharmacological treatment and clinical trials, epidemiology and associated risk factors, pathophysiology and pathophysiology, skin barrier function and related dermatoses, and laser and physical therapies. Future rosacea research is expected to integrate precision medicine approaches by linking molecularly defined pathogenic mechanisms with standardized classification systems to enable targeted and multidisciplinary treatment strategies.

Abbreviations

WoSCC, Web of Science Core Collection; PDL, pulsed dye laser; IPL, intense pulsed light; MCP, multidisciplinary collaboration; SCP, single-discipline collaboration; IGA, Investigator Global Assessment; UV, ultraviolet; HRQoL, health-related quality of life; DLQI, Dermatology Life Quality Index.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics Approval and Informed Consent

This study does not require ethical review approval, as it is based on bibliometric analysis of publicly available data. The research involves no direct interaction with human subjects, nor does it involve the collection of personal or sensitive information. All data used in this study are aggregated and derived from published literature, ensuring that no individuals can be identified or harmed. As a non-invasive research method, bibliometric analysis focuses solely on trends and patterns in scientific publications without posing any ethical risks.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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