

# Global Research Trends in Apremilast for Psoriasis: A Bibliometric Analysis (2008–2024)

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**Purpose:** Psoriasis is a chronic, immune-mediated skin disease that significantly affects patients' quality of life. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, has emerged as a promising treatment for moderate to severe psoriasis, offering an alternative to biologics with a favorable safety profile. This study analyzes global research trends, key contributors, and emerging focus areas concerning apremilast in the treatment of psoriasis.

**Patients and Methods:** Publications related to apremilast and psoriasis from 2008 to 2024 were retrieved from the Web of Science Core Collection (WoSCC). Bibliometric and visual analyses were performed using tools such as VOSviewer, CiteSpace, and R 4.3.3.

**Results:** A total of 437 publications on apremilast and psoriasis were identified. The United States led with 158 publications, followed by Japan with 39 and Italy with 33. Celgene Corporation was the most productive institution, contributing 96 articles. The top journals include *Journal of Dermatology*, *Journal of the European Academy of Dermatology and Venereology*, and *Journal of the American Academy of Dermatology*. Key researchers, such as Shinichi Imafuku and Bruce Strober, were identified as leading contributors. Burst analysis revealed that since 2020, keywords like “monotherapy”, “nail psoriasis”, and “pathogenesis” have gained prominence, indicating emerging research areas.

**Conclusion:** This bibliometric analysis demonstrates that research on Apremilast for psoriasis has evolved from clinical trials focused on efficacy and safety to broader applications in real-world settings, including nail psoriasis and pathogenesis. Future research is likely to concentrate on long-term outcomes, optimizing treatment regimens, and addressing unmet needs in psoriasis management, particularly among specific patient subgroups.

**Keywords:** bibliometric analysis, psoriasis, apremilast, VOSviewer, CiteSpace

## Introduction

Psoriasis is a chronic inflammatory skin disorder that presents with red, scaly plaques, significantly impacting patients' quality of life.<sup>1</sup> Globally, the prevalence of psoriasis is estimated at 2–3%, though rates vary across different regions due to genetic and environmental factors.<sup>2,3</sup> The disease pathogenesis involves a complex interaction between genetic susceptibility, immune system dysfunction, and environmental triggers.<sup>4</sup> Conventional therapies—including topical agents, phototherapy, and systemic treatments—have long been used but often face efficacy and safety limitations, particularly in moderate-to-severe cases.<sup>5,6</sup>

Administration challenges have driven the exploration of alternative treatment modalities. The advent of targeted biologic therapies (eg, tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-17, IL-12/23, and IL-23 inhibitors) has revolutionized psoriasis treatment. However, limitations including high cost, potential immunogenicity, and administration challenges have spurred the search for alternative treatments.<sup>7</sup> This has led to the emergence of oral small molecules, valued for their convenience and efficacy. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, represents one such option by targeting key inflammatory pathways.<sup>8</sup> By inhibiting PDE4, apremilast reduces pro-inflammatory cytokine levels, making it a valuable option for patients requiring systemic treatment but seeking an alternative to biologics.<sup>9,10</sup> In addition to its therapeutic efficacy, apremilast has demonstrated a favorable safety profile, supporting its use in long-term



disease management.<sup>11</sup> Since its FDA approval in 2014, clinical interest in apremilast has grown, leading to an expanding body of research evaluating its effectiveness, safety, and real-world applications.<sup>12</sup> Despite apremilast's safety and efficacy in the treatment of psoriasis and psoriatic arthritis have been well established in both clinical trials and real-world studies, practical aspects of its use—such as dosage adjustment, titration protocols, and optimal positioning either as monotherapy or in combination regimens—remain inadequately addressed.<sup>13</sup> Bibliometrics is an interdisciplinary field that applies mathematical and statistical methods to quantitatively analyze various forms of knowledge carriers. It constitutes an integrated framework drawing on mathematics, statistics, and philology, with an emphasis on quantitative evaluation. In the era of big data, bibliometrics serves as a valuable tool that allows researchers and clinicians to identify research trends and hotspots in a given field, anticipate future directions, and enhance scientific productivity.<sup>14,15</sup> While previous studies have conducted bibliometric analyses on the use of biologic agents in psoriasis over the past two decades,<sup>16</sup> no such study has specifically focused on apremilast. This gap highlights the need for a detailed assessment of research activities in this area. Through this first bibliometric analysis focused on apremilast, we aim to outline global research trends, identify leading contributors and collaborative networks, and illuminate established and emerging topics in the management of psoriasis with apremilast.

## Materials and Methods

### Literature Search and Selection

A comprehensive literature search on apremilast and psoriasis was performed in the Web of Science Core Collection (WoSCC) database for publications from January 1, 2008, to September 2, 2024. The selection of WoSCC was based on several considerations. First, the database is recognized for its coverage of high-quality, peer-reviewed academic literature worldwide, with a primary focus on journal articles, conference proceedings, and books.<sup>17</sup> Second, WoSCC provides a multidisciplinary and comprehensive repository, complete with a full citation network and essential bibliometric indicators.<sup>18</sup> In line with established methodological practices, we therefore utilized WoSCC to retrieve globally representative academic data for conducting a robust bibliometric analysis. The search was performed using the search formula: “(TS = (psoriasis)) AND (TS = (Apremilast))”. The search was limited to English-language publications, and only articles were included.

### Statistical Analysis and Visualization

Microsoft Excel was employed to organize and compute key bibliometric indicators, including the annual number of publications, citation frequencies, average citation rates, journal names, impact factor (IF), publication countries/regions, institutions, and authors. For visualization and analysis, three key tools in bibliometric analysis were used: VOSviewer (version 1.6.20), CiteSpace (version 6.3.R1), and R 4.3.3.

VOSviewer was applied to map collaborations among institutions, authors, co-authorship networks, as well as citation and co-citation relationships, providing insights into the academic network structure and relationships within the field.<sup>19</sup> Additionally, VOSviewer was utilized for keyword co-occurrence analysis to uncover research hotspots in the study of apremilast for psoriasis.

CiteSpace (version 6.3.R1) was used to detect keyword bursts with time slicing set from January 2008 to August 2024, using 1-year intervals. The node type was set to keywords, with a threshold of  $N=5$  per slice. Pruning methods included pathfinder and merged network approaches, allowing for the generation of a timeline graph of keywords related to “apremilast in psoriasis”. In these visualizations, the node size reflected the number of publications, the thickness of lines indicated the strength of collaboration, and node colors represented different clusters or time periods. This tool provides critical insights into the evolution of research priorities and emerging trends.

“Bibliometrix” R package was used for additional citation analysis and to visualize global research trends in the field.<sup>20</sup> To quantify academic impact, metrics such as the h-index, g-index, and m-index were employed, as referenced in existing literature.<sup>21,22</sup> These metrics are critical for assessing the contributions of researchers and predicting future scientific output. Additionally, journal quality and impact were assessed using Journal Citation Reports (JCR) quartile

rankings and Impact Factor (IF). The JCR quartiles (Q1–Q4) categorize journals by their relative IF within specific disciplines, serving as benchmarks for academic influence.<sup>23</sup>

## Results

### An Overview of Publications

After removing duplicates, reviews, editorial materials, letters, meeting abstracts, non-English publications, and non-relevant records, 437 studies were included for bibliometric analysis (Figure 1). These publications, contributed by 2602 authors from 1958 institutions across 205 countries/regions, focused on apremilast in psoriasis treatment (Figure 2A). The highest annual publication count occurred in 2020 (n=59). From 2008 to 2024, publication activity followed three

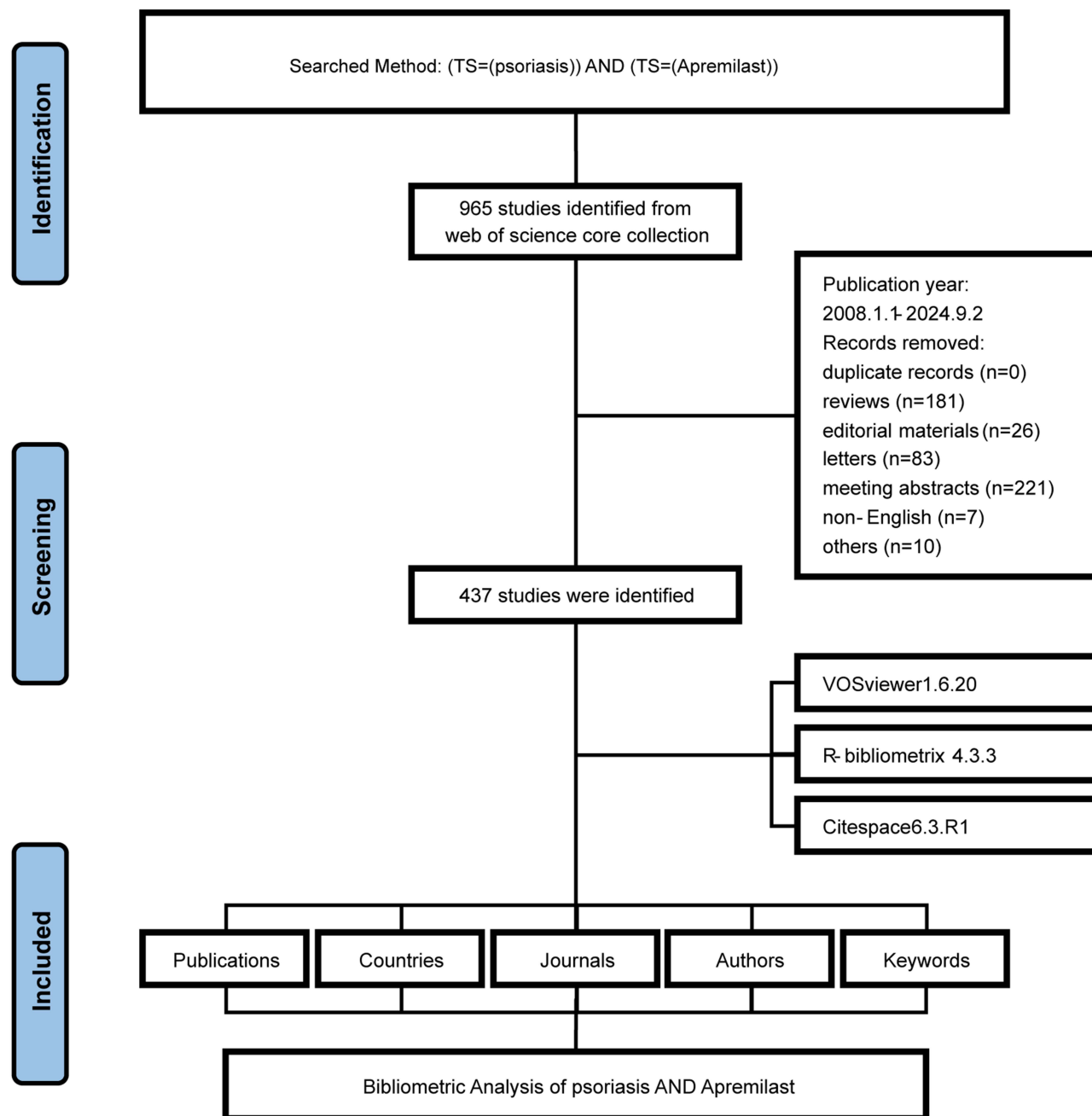
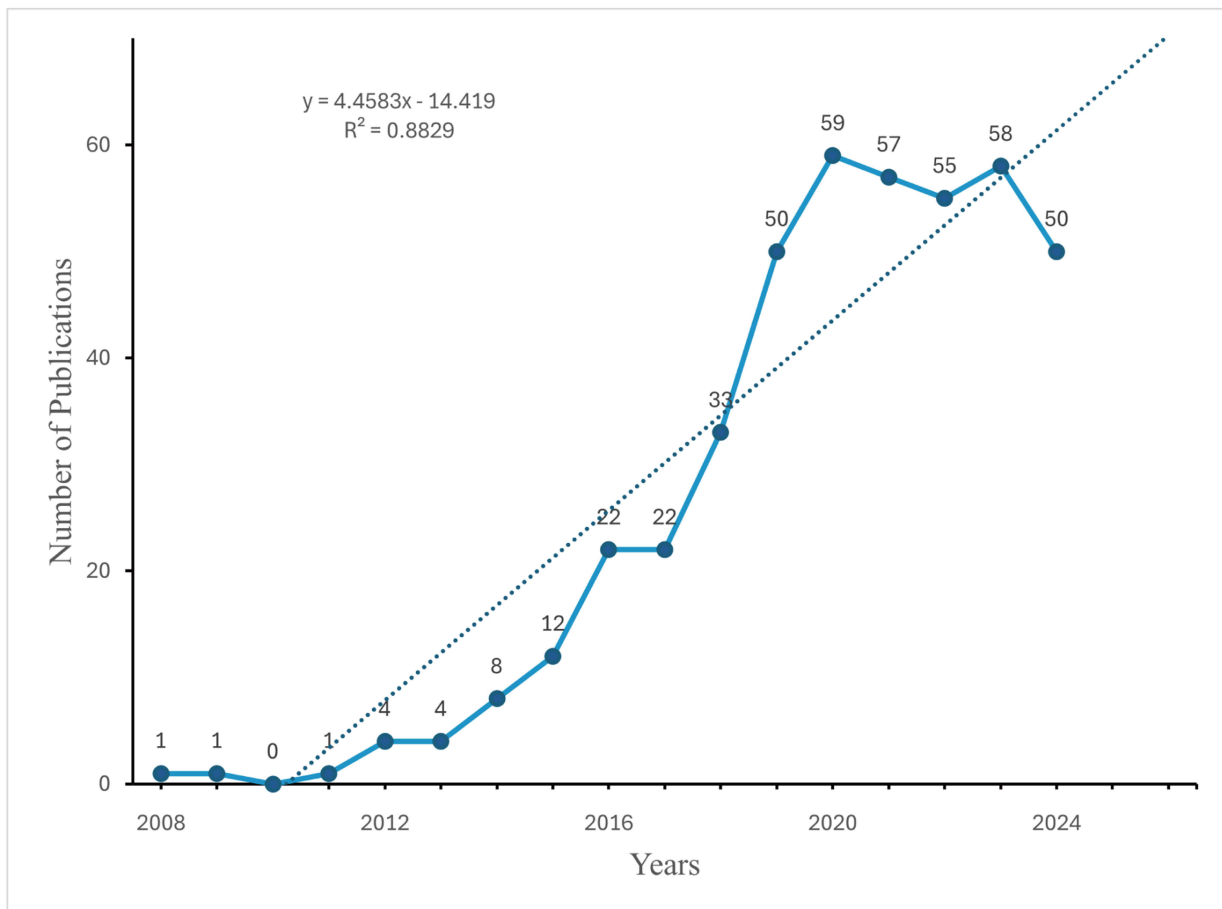


Figure 1 Flowchart of the literature screening process.

A



B



**Figure 2** Analysis of general information. (A) Summary Information of the included studies. (B) Annual number of publications on apremilast in the Treatment of Psoriasis.

phases: slow growth (2008–2014), moderate growth (2015–2017), and sustained high output (2018–2024). The trend equation is  $y = 4.4583x - 14.419$ , with  $R^2 = 0.8829$ . Regression analysis indicated a significant yearly growth in publications ( $\beta = 4.4583$ ), reflecting a consistent increase in research output. The high  $R^2$  value (close to 1) confirms that the linear model accounts for a high proportion of the variance, attesting to the robustness of the observed trend (Figure 2B).

### Analysis of Countries and Institutions

The United States led in publication volume ( $n=158$ ) and total citations (4288), followed by Japan ( $n=39$ ) and Italy ( $n=33$ ) in publication count, while Canada (970 citations) and Germany (857 citations) ranked second and third in total citations. Australia had the highest citations per document (62.5), with Canada (53.9) and Turkey (42.7) following (Supplementary Table 1 and Figure 3A). Among the 26 countries involved in international collaborations with

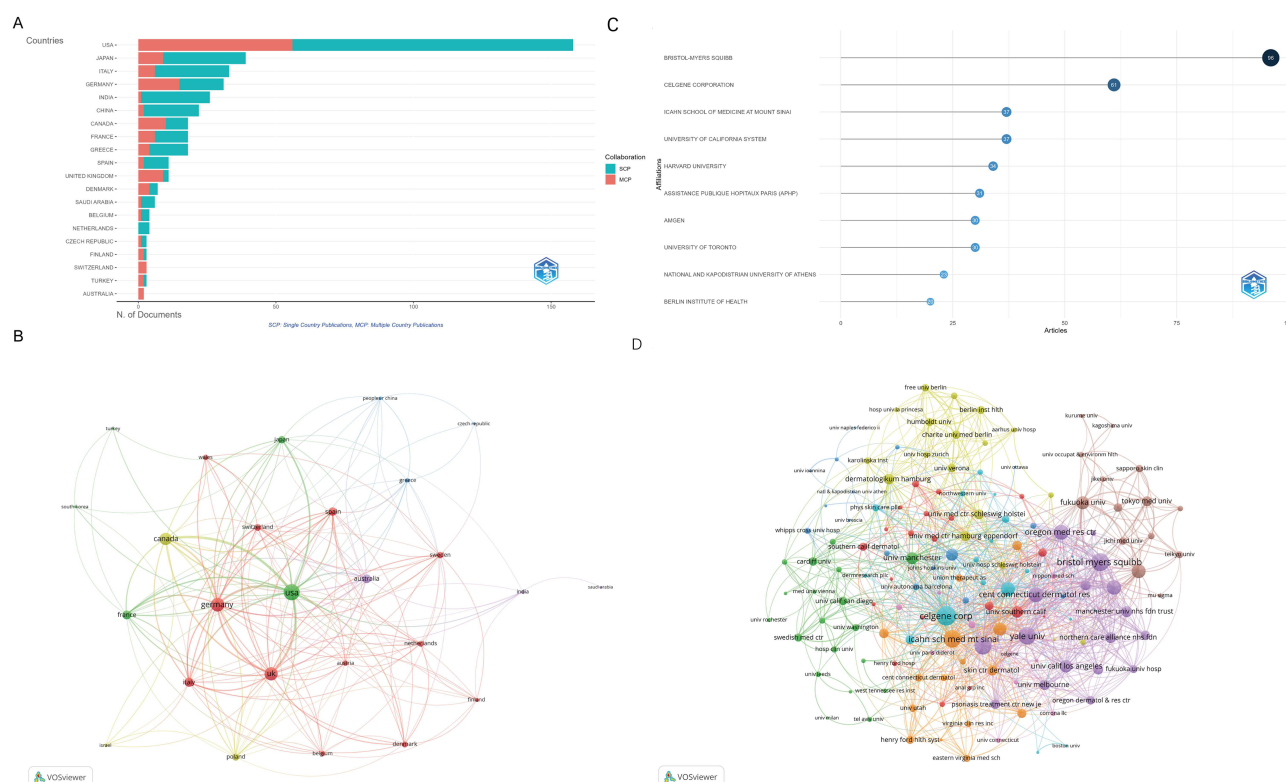
a minimum of 3 articles, the USA led global collaborations (253), with Germany and the UK ranking second and third (178 and 169 collaborations, respectively) (Figure 3B).

In terms of institutions, Celgene Corporation led with 96 publications, followed by Bristol-Myers Squibb (61) and Icahn School of Medicine at Mount Sinai & University of California System (37 each) (Figure 3C). The institutional collaboration network reveals a strong international presence, with 159 institutions having engaged in international collaborations (minimum of 3 articles each). Among these, Celgene Corporation led in global collaborative links (163), followed closely by Bristol Myers Squibb (138) and Yale University (132) (Figure 3D).

## Analysis of Journals

Supplementary Table 2 lists several bibliometric indicators for the top 10 most productive journals. These journals published 228 papers, accounting for 52.17% of all retrieved publications. Among the listed journals, the *Journal of Dermatology* ranks first with 27 total publications (TP) and is tied with the *Journal of the European Academy of Dermatology and Venereology*, which also has 27 publications. The *Journal of the American Academy of Dermatology* holds the highest total citations (TC) of 1235. In terms of IF, the *Annals of the Rheumatic Diseases* leads with the highest IF of 20.3, followed by *Journal of the American Academy of Dermatology* (IF 12.8) and *JAMA Dermatology* (IF 11.5) and the *British Journal of Dermatology* (IF 11). Regarding the H-index, both the *Journal of the American Academy of Dermatology* and the *Journal of the European Academy of Dermatology and Venereology* share the top position with an H-index of 14, followed closely by the *Journal of Drugs in Dermatology* with an H-index of 12.

The co-occurrence networks of journals include 35 publications with at least three occurrences. The three key journals with the highest total link strength in the co-occurrence networks were the *Journal of the American Academy of*



**Figure 3** Analysis of Countries and Institutions. **(A)** Distribution of corresponding author's publications by country. The number of publications attributed to corresponding authors from different countries, distinguishing between Single Country Publications (SCP) and Multiple Country Publications (MCP). **(B)** Visualization map depicting the collaboration among different countries. The collaborative relationships between countries, with nodes representing countries, the size of nodes indicating publication count, and the thickness of links showing the strength of co-authorship collaborations. Colors indicate different research clusters. **(C)** Top ten institutions by article count and rank. The circle size shows the article count, with darker shades indicating higher ranks. **(D)** Visualization map depicting the collaboration among different institutions. Nodes represent institutions, with size indicating publication count. Links represent co-authorships, with thickness showing collaboration strength of co-authorship collaborations. Colors indicate different research clusters.

*Dermatology* (243), *Journal of the European Academy of Dermatology and Venereology* (193), and *British Journal of Dermatology* (128) (Figure 4A). The coupling networks of journals include 35 publications with at least three couplings. The three key journals with the highest total link strength in the coupling networks were the *Journal of the European Academy of Dermatology and Venereology* (5923), *Journal of Drugs in Dermatology* (4935), and *Journal of Dermatology* (4921) (Figure 4B).

## Analysis of Authors

The top 10 authors collectively published 207 articles with 10,502 citations (Supplementary Table 3). Shinichi Imafuku leads with 20 publications, followed by Maria Paris and April W. Armstrong, each with 17 publications. In terms of total citations, Randall M. Stevens ranks first with 1379 citations, followed by Chiachi Hu with 1263, and Robert M. Day with 1139. For the H-index, Robert M. Day and Bruce Strober hold the top position with an H-index of 9, while Shinichi Imafuku and Maria Paris follow closely behind with an H-index of 8.

In order to explore the collaboration between different authors, we mapped the author collaboration network using VOSviewer (Figure 5). Among the 145 authors involved in international collaborations with at least 3 articles, Bruce Strober has the highest number of collaborations with other authors (123), followed by Subhashis Banerjee (118) and Diamant Thaci (110).

## Analysis of Keywords

The VOSviewer analysis identified a total of 161 keywords with a minimum of 3 occurrences. The most prominent core keywords in the diagram include “phase iii”, “efficacy”, and “safety”, as indicated by their larger nodes. Terms related to clinical trials and treatment management, such as “severe plaque psoriasis”, “moderate”, and “PDE4 inhibitor”, form a significant network. Based on the color gradient, newer keywords like “cytokines” and “monotherapy” (closer to yellow) have gained increased attention in recent years, while older terms like “controlled-trial” and “arthritis” (closer to blue) were more prevalent in earlier studies (Figure 6A).

The burst keyword analysis (2008–2024) further highlights research shifts. “Double blind” (8.41) and “placebo-controlled trial” (6.07) exhibited the strongest bursts. Earlier bursts were seen in “in vitro” (2012–2013) and “double blind” (2013–2017), while recently sustained bursts (through 2024) include “epidemiology” and “pathogenesis”, signaling ongoing research focus. Since 2018, keywords like “adalimumab”, “European league”, “drug survival”, and “nail psoriasis” have gained prominence, reflecting evolving trends in psoriasis research and treatment innovations (Figure 6B).

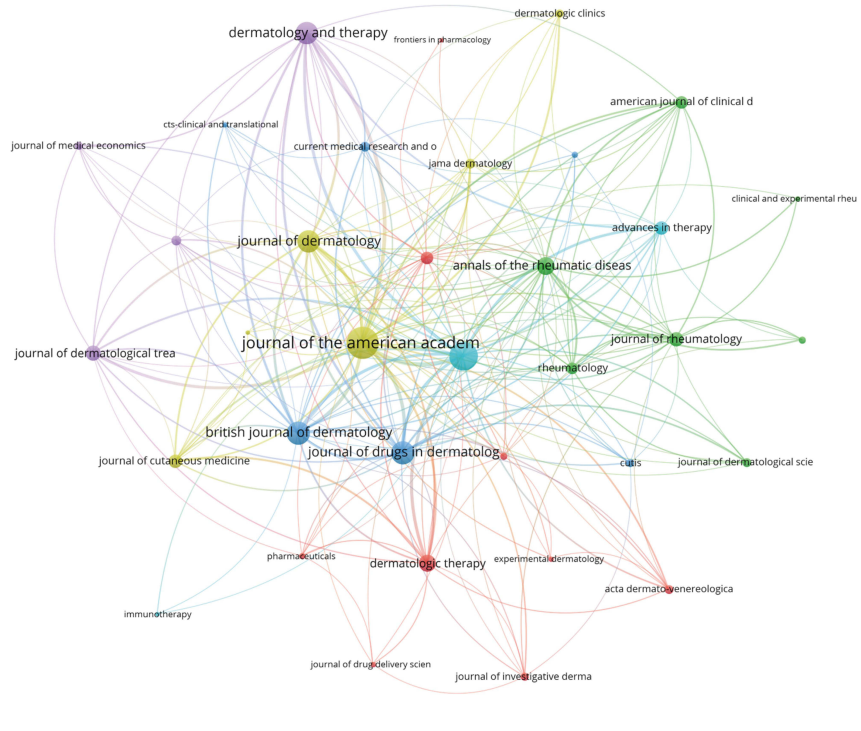
## Discussion

The bibliometric analysis provides a thorough overview of research trends and developments in the study of apremilast in psoriasis treatment from 2008 to 2024. *Journal of the American Academy of Dermatology* leads in total citations, focusing its research on the early efficacy evaluation of apremilast in the treatment of psoriasis, its application in pediatric patients, and safety management.<sup>24–26</sup> The most cited article was indeed published in this journal.<sup>27</sup> The overall upward trend in publication volume reflects the growing interest in apremilast for psoriasis. Notably, the number of publications related to apremilast has stabilized or even declined since 2020. This trend may be driven by increasing investigation into alternative treatments like deucravacitinib, which are being explored as potential successors to apremilast.<sup>28</sup>

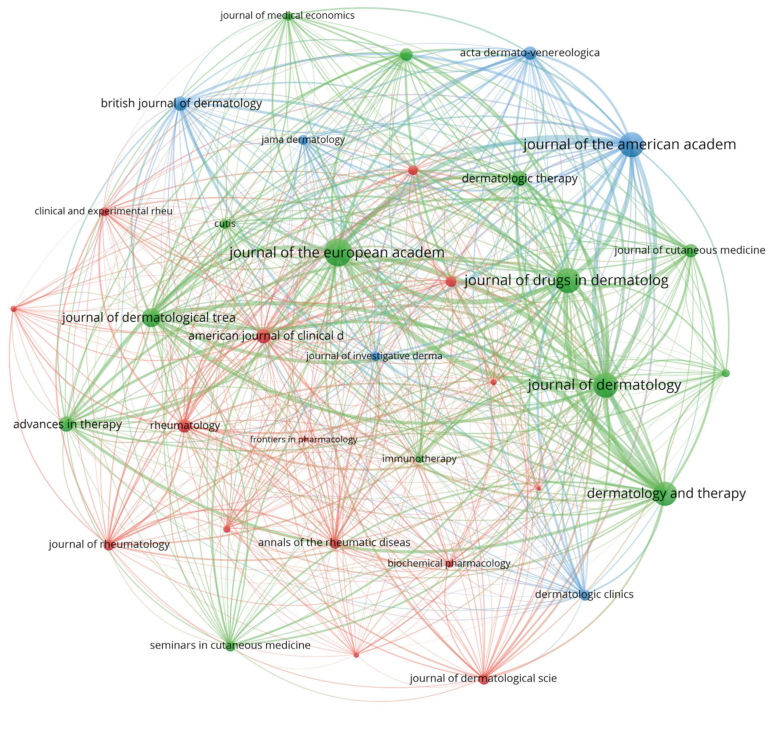
The United States dominates in publication volume and leads in total citations. The United States also demonstrates the highest number of international collaborations (253), indicating its central role in global research networks. Countries like Germany, the United Kingdom, and Italy also show strong collaboration patterns, fostering cross-border research in apremilast for psoriasis. In contrast, countries like India and China show a greater focus on single-country research output, as reflected by their lower multiple-country publication (MCP) ratios.

Shinichi Imafuku, Bruce Strober, and April W. Armstrong are leading contributors in this field. Shinichi Imafuku’s research has centered on the clinical efficacy and safety of long-term apremilast use in Japanese psoriasis patients,<sup>29,30</sup> underscoring in particular the importance of managing adverse effects such as diarrhea and nausea. These three authors

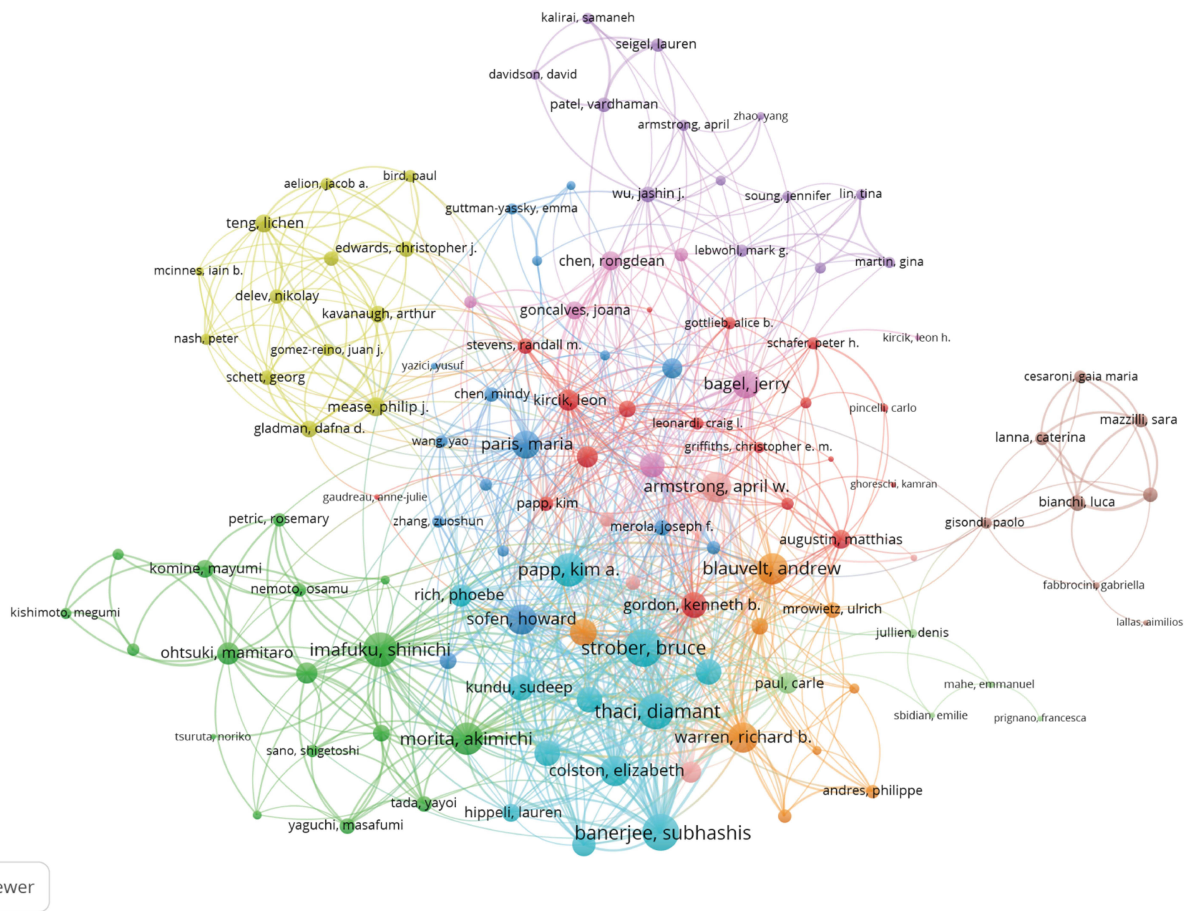
A



B



**Figure 4** Analysis of journals. **(A)** Co-occurrence Network of Journals. The frequency with which journals are cited together within the same articles reflects thematic or topical connections between the research they publish. **(B)** Coupling Network of Journals. The extent to which journals are linked is based on common references cited in their articles, indicating a shared intellectual foundation or research focus.



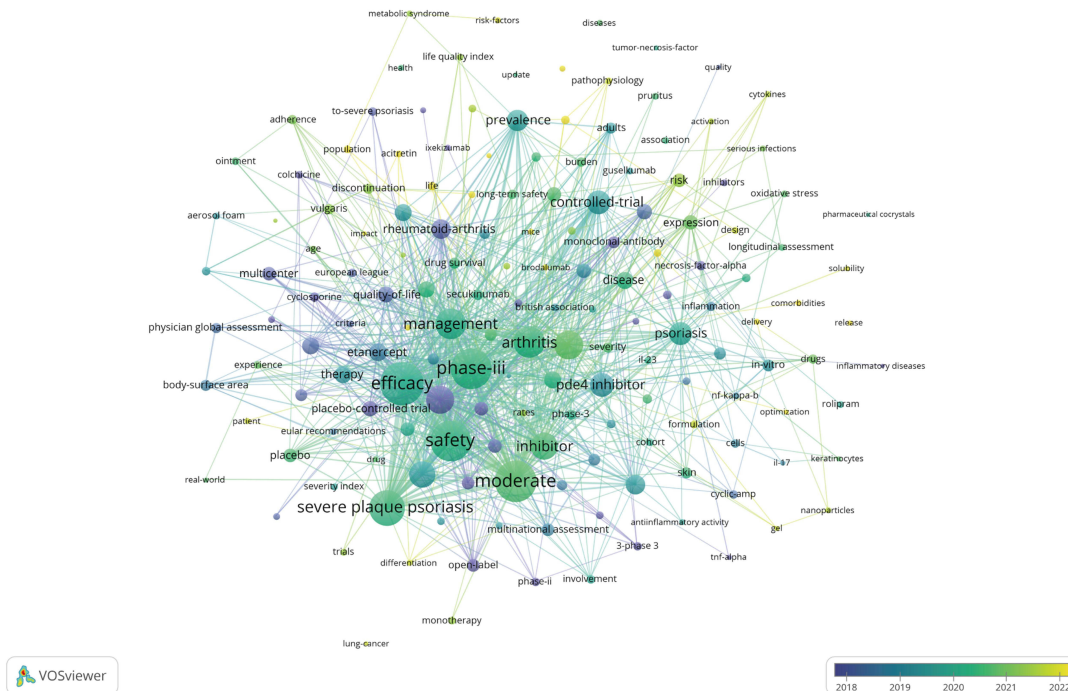
**Figure 5** Visualization map depicting the collaboration among different authors. Nodes represent authors, with size indicating publication count. Links represent co-authorships, with thickness showing collaboration strength. Colors indicate different research clusters. Link strength in collaboration networks measures the frequency of co-authorship between authors, indicating the level of collaborative research.

have also established extensive collaborative networks. In a 52-week randomized, double-blind, placebo-controlled Phase 3 trial, they demonstrated that deucravacitinib was more effective than both placebo and apremilast, with a favorable tolerability profile in patients with moderate to severe plaque psoriasis.<sup>31</sup> In another phase 3 trial, they reported that deucravacitinib exhibited significant efficacy as early as the first week of treatment, with sustained clinical responses maintained through 52 weeks.<sup>32</sup> These findings collectively reinforce deucravacitinib as an efficacious and well-tolerated long-term therapeutic option for moderate to severe plaque psoriasis.<sup>28</sup>

## Research Hotspots

Before 2020, research on apremilast in the treatment of psoriasis focused heavily on keywords such as “efficacy”, “safety”, and “severe plaque psoriasis”. These studies primarily concentrated on assessing the clinical outcomes of apremilast, particularly in managing moderate to severe psoriasis, and its effectiveness in improving patients’ quality of life. Additionally, there was significant attention on clinical trials, especially “phase III” trials, to establish apremilast as a safe and reliable alternative for patients who were unable to tolerate biologics. E Papadavid and colleagues<sup>33</sup> conducted a real-world study and concluded that apremilast is a safe and effective treatment for moderate-to-severe plaque psoriasis, with 70.4% of patients achieving significant clinical improvements ( $\Delta$ PASI75 or  $\Delta$ PASI50 with Dermatology Life Quality Index  $\leq 5$ ) at 16 weeks. Reich et al<sup>34</sup> conducted a phase 3b clinical trial and concluded that apremilast provided significant and sustained improvements in skin, scalp, nails, and patient-reported outcomes over 104 weeks in patients with moderate to severe plaque psoriasis, with a safety profile consistent with previous findings.

A



B

### Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2008 - 2024
in vitro	2012	1.98	2012	2013	[Timeline bar with red burst from 2012-2013]
double blind	2013	8.41	2013	2017	[Timeline bar with red burst from 2013-2017]
janus kinase inhibitor	2014	4.34	2014	2017	[Timeline bar with red burst from 2014-2017]
open label	2014	2.41	2014	2015	[Timeline bar with red burst from 2014-2015]
placebo controlled trial	2015	6.07	2015	2017	[Timeline bar with red burst from 2015-2017]
pde4 inhibitor	2015	4.23	2015	2017	[Timeline bar with red burst from 2015-2017]
therapy	2015	1.46	2015	2016	[Timeline bar with red burst from 2015-2016]
randomized controlled trial	2016	3.86	2016	2018	[Timeline bar with red burst from 2016-2018]
etanercept	2016	2.59	2016	2019	[Timeline bar with red burst from 2016-2019]
adalimumab	2018	2.44	2018	2019	[Timeline bar with red burst from 2018-2019]
european league	2018	2.39	2018	2019	[Timeline bar with red burst from 2018-2019]
drug survival	2018	2.09	2018	2020	[Timeline bar with red burst from 2018-2020]
body surface area	2018	1.91	2018	2019	[Timeline bar with red burst from 2018-2019]
guidelines	2018	1.73	2018	2020	[Timeline bar with red burst from 2018-2020]
disease	2019	2.8	2019	2020	[Timeline bar with red burst from 2019-2020]
care	2019	1.8	2019	2020	[Timeline bar with red burst from 2019-2020]
expression	2019	1.77	2020	2021	[Timeline bar with red burst from 2020-2021]
nail psoriasis	2021	2.28	2021	2022	[Timeline bar with red burst from 2021-2022]
epidemiology	2021	2	2021	2024	[Timeline bar with red burst from 2021-2024]
pathogenesis	2016	1.99	2022	2024	[Timeline bar with red burst from 2022-2024]

**Figure 6** Analysis of Keywords. **(A)** Keyword Co-occurrence Network. Each node represents a keyword, with size indicating its frequency of occurrence. Links between nodes represent co-occurrence in the same documents, with thicker lines showing stronger associations. Link strength measures the frequency of co-authorship between keywords. 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. The blue lines represent the period, and the red lines indicate the burst periods of the keywords.

Since 2020, the research focus has shifted toward keywords like “cytokines” and “monotherapy”. This indicates that the spotlight has turned to expanding apremilast’s use in broader populations and understanding its application as a standalone therapy (monotherapy) in various settings. Alexis Ogdie and colleagues<sup>35</sup> conducted a study using the Corrona Psoriatic Arthritis/Spondyloarthritis Registry and concluded that apremilast monotherapy is an effective treatment option for patients with oligoarticular psoriatic arthritis, showing greater disease activity improvements than methotrexate and similar improvements to biologic disease-modifying antirheumatic drug. Akimichi Morita and colleagues<sup>36</sup> conducted a randomized controlled trial and concluded that the combination of apremilast and phototherapy was more effective than phototherapy alone in reducing PASI scores in patients with psoriasis vulgaris, though adverse events were more frequent in the combination group, and longer treatment periods may be necessary for further improvements.

## Research Frontiers

Based on the analysis of keyword bursts, research trends for apremilast in psoriasis treatment since 2021 appear to be concentrating on several key areas. Keywords such as “nail psoriasis”, “epidemiology”, and “pathogenesis” have shown increased prominence in recent years. This may indicate a gradual shift in research attention toward nail psoriasis—a specific and often challenging manifestation of the disease. For instance, in a real-world observational study, C Lanna et al<sup>37</sup> reported that apremilast led to rapid and sustained improvements in nail psoriasis, significantly enhancing patients’ quality of life over a 24-week period. The emergence of “epidemiology” as a keyword may reflect growing interest in understanding the prevalence,<sup>38,39</sup> clinical patterns,<sup>40</sup> and risk factors<sup>41</sup> of psoriasis across diverse patient populations, which could help inform treatment strategies and public health initiatives.

Furthermore, the appearance of “pathogenesis” after 2022 suggests a deepening focus on the underlying biological mechanisms of psoriasis. Studies in this area seek to clarify the molecular pathways involved in disease progression. For example, Athanasios Mavropoulos et al<sup>42</sup> observed that apremilast increased IL-10-producing regulatory B cells (B10 cells) while reducing proinflammatory T helper 1 (Th1) cells, interferon-gamma (IFN- $\gamma$ )-producing natural killer T (NKT) cells, and IL-17-producing NKT cells, suggesting a potential immunomodulatory role in psoriatic disease. In a prospective study, Lyn D. Ferguson et al<sup>43</sup> found that apremilast was associated with weight loss—mainly in abdominal fat—and improved disease activity, with the latter effect appearing independent of weight change, pointing to direct immunological mechanisms. Despite these advances, challenges remain in fully elucidating the complex immune pathways involved in psoriasis and translating such insights into targeted therapies that address both cutaneous and systemic disease manifestations.

## Practical Implications

The broader potential of apremilast in psoriasis and other immune-mediated skin diseases continues to be explored. Current trials evaluating its efficacy and safety remain limited by small sample sizes, yielding promising but not yet conclusive results.<sup>44</sup> Future studies should aim to overcome these limitations through larger cohorts, improved methodological rigor, longer follow-up periods, and enhanced relevance to real-world clinical practice. It is also important to note that while apremilast acts through PDE4 inhibition, its interactions with disease-specific pathways are not fully elucidated. Further research is needed to clarify the mechanistic drivers of treatment response—such as baseline PDE4 expression levels or distinct cytokine profiles—which may vary across different diseases. By integrating larger, longer-term, and more diverse clinical trials with standardized endpoints, mechanistic investigations, and real-world evidence, the application of apremilast in immune-mediated dermatoses can be optimized toward a more personalized and effective approach. Notably, the emerging application of ethosomes, niosomes, liposomes, and nanostructured lipid carriers in psoriasis treatment reflects recent advances in nanoscale drug delivery systems.<sup>45</sup> By improving solubility and enabling targeted delivery, the advancement of these novel formulations facilitates to enhance the therapeutic efficacy of apremilast and reduce its associated adverse effects.

## Strengths and Limitations

This bibliometric study is the first to comprehensively explore the distribution trends and facilitate major research focuses on apremilast for psoriasis treatment. One of the main strengths of our research is its analysis spanning multiple years, aimed at identifying relevant literature in apremilast for psoriasis treatment. However, like previous bibliometric studies, our research also has several limitations. A potential bias in this study is the use of metrics that may not fully represent clinical value, such as citation counts that include self-citations. Additionally, like other bibliometric investigations, this study was limited to English-language publications indexed in the WoSCC, which may have introduced linguistic and database bias. As a result, relevant studies published in non-English languages or indexed in other bibliographic platforms may have been overlooked, potentially underrepresenting contributions from non-English-speaking countries. Future research could incorporate multilingual and multi-database strategies to broaden coverage and minimize regional bias.

## Conclusion

This is the first bibliometric mapping of apremilast in psoriasis, revealing a research shift from efficacy to pathogenesis and long-term outcomes. Future research should prioritize optimizing apremilast monotherapy and its application in specific subtypes like nail psoriasis, alongside elucidating its mechanistic role via systematic reviews and mechanistic studies. Beyond these priorities, research should also address personalized treatment strategies, long-term adherence, and adverse effect minimization to improve real-world outcomes.

## Data Sharing Statement

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

## Acknowledgment

The authors would like to acknowledge the data support provided by the National Key Research and Development Program of China (2023YFC2508100) and the National Clinical Research Center for Skin and Immune Disease.

## 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.

## Funding

This work was supported by National Key Research and Development Program of China (2023YFC2508100) and the National Clinical Research Center for Skin and Immune Disease and Chengdu Municipal Health Commission (Grant No. 2022278).

## Disclosure

The authors report no conflicts of interest in this work.

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