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Research Trends and Hotspots in JAK Inhibitors for Ulcerative Colitis: A Bibliometric Analysis From 2015 to 2024

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Objective: To systematically investigate international trends and dynamics in research on Janus kinase (JAK) inhibitor applications for ulcerative colitis (UC) management over the past decade (2015–2024) and delineate current research frontiers.

Methods: Publications was retrieved from the Web of Science core collection database and subjected to bibliometric analysis. VOSviewers, CiteSpace, Scimago Graphica, and Excel were used to conduct this bibliometric analysis and visualization.

Results: A total of 696 articles were included. Publication output exhibited an overall upward trajectory. The United States ranked first in global publication volume and served as the central hub for multiple extensive collaborative networks. *Inflammatory Bowel Diseases* published the highest number of relevant studies. William J. Sandborn emerged as the most academically influential scholar. Both reference and keyword analyses revealed that early research (pre-2018) focused on clinical efficacy validation and drug development of JAK inhibitors, while post-2018 studies shifted toward systematic evaluations of efficacy and safety, integration of clinical practice guidelines, and development of novel subtype selective JAK inhibitors.

Conclusion: This study delineates the evolution of JAK inhibitor research in UC over the past decade. Future efforts should prioritize strengthening global collaboration, advancing novel subtype selective JAK inhibitors, generating long-term safety data from clinical trials, and optimizing patient-stratified treatment strategies to address unmet therapeutic needs.

Keywords: Janus kinase inhibitor, ulcerative colitis, bibliometric analysis, research trends

Introduction

Ulcerative Colitis (UC) is a chronic inflammatory bowel disease characterized by non-specific inflammation and ulcer formation in the colonic mucosa, with clinical manifestations primarily including recurrent diarrhea, mucopurulent bloody stools, and abdominal pain.[1] Epidemiological studies indicate that the global prevalence of UC reached approximately 5 million cases in 2023, showing a continued upward trajectory in recent years.[2,3] The complex disease course management, high recurrence rate, and risk of multiple complications in UC not only lead to significant deterioration in patients' quality of life, but also impose a dual burden on the socioeconomic system through prolonged healthcare expenditures and impaired work productivity.[4–6] Although traditional treatment regimens such as 5-aminosalicylic acid drugs, corticosteroids, and immunosuppressants can alleviate symptoms to some extent, some patients still exhibit poor response to existing therapies or experience severe side effects.[7–9] TNF-α inhibitors can significantly induce mucosal healing in UC and reduce steroid dependence, but they have limitations including secondary failure, increased infection risks, and high medical costs.[10,11] Therefore, developing more effective and risk-benefit treatment methods is crucial for improving the condition of UC patients.

The discovery of Janus Kinase (JAK) originated from research on interferon signaling pathways. After interferon activates cell surface receptors, the receptors first undergo phosphorylation, STAT is recruited to the vicinity of interferon

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receptors, and then undergoes phosphorylation modification catalyzed by receptor-associated kinases, triggering intracellular signal transduction.[12–14] Currently, drugs developed based on JAK inhibitors (JAKinibs) are widely used for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, atopic dermatitis, alopecia areata, and myelofibrosis.[15–21] JAKinibs have increasingly attracted researchers' attention and have been attempted in UC treatment with significant clinical benefit.[22–24] Currently, JAKinibs such as tofacitinib and upadacitinib have been approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of moderate-to-severe UC. Although the long-term safety of JAKinibs (such as infection risk and thrombosis risk) still requires further evaluation, their mechanisms of action and optimization of personalized treatment remain hot topics in current research.[25,26]

With the application of JAKinibs in the field of UC, the number of related research publications has grown rapidly, but the distribution of research topics, international collaboration networks, and evolutionary trends of focus areas have not been systematically reviewed. Bibliometrics can reveal research dynamics, core directions, and future trends in the field by quantitatively analyzing the spatiotemporal distribution of literature, author collaboration patterns, and keyword co-occurrence networks.[27,28] This study aims to conduct a multidimensional analysis of UC and JAKinib-related literature through the Web of Science (WoS) database to clarify the knowledge structure, research hotspots, and cutting-edge trends in this field, thereby providing data support for clinical decision-making, basic research, and policy formulation.

Materials and Methods

Data Acquisition and Search Strategies

The WoS Core Collection was selected as the database for this bibliometric analysis due to its high-quality, curated content, its established utility for citation network analysis, and its focus on core scholarly literature. This study conducted an advanced search in the WoS Core Collection database using the query TS = (JAK inhibitor OR Ruxolitinib OR Tofacitinib OR Baricitinib OR Upadacitinib OR Filgotinib OR Fedratinib OR Abrocitinib OR Peficitinib OR Delgocitinib OR Pacritinib OR Deucravacitinib) AND TS = (Ulcerative colitis OR Ulcer colonitis OR Colitis gravis), with a publication date range from 1 January 2015 to 31 December 2024. The databases selected Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI). After preliminary screening, non-research document types such as conference abstracts, conference papers, editorial materials, book chapters, preprints, and retracted articles were excluded, and only English-language publications were retained. Two formatted versions of the final dataset were generated: a plain text file for CiteSpace integration and a tab-delimited file meeting the VOSviewer's input standards, facilitating immediate bibliometric processing.

Analysis Tools

This research employed multiple software packages for data processing and visualization: CiteSpace, VOSviewer, Scimago Graphica, Excel and the Wei Sheng Xin bioinformatics platform (http://www.bioinformatics.com.cn).CiteSpace facilitated the removal of duplicate records and enabled the generation of co-occurrence networks, cluster analyses, timeline distributions, and burst detection of citations and keywords, with subsequent visualization. Parameter settings included: temporal segmentation (2015–2024, yearly intervals), node selection via g-index (K=10), and a dual-phase network optimization approach—initial pruning of segmented networks using the Pathfinder algorithm, followed by consolidated network refinement. Visual outputs displayed node sizes proportional to occurrence frequencies and link thickness denoting co-occurrence magnitudes. VOSviewer was applied to map collaborative interactions across journals (including cited journals), institutions, nations, authors, and cited authors. Node dimensions reflected publication or citation metrics, while connection widths quantified collaboration magnitude. For geospatial representation of international collaborations, GML-formatted collaboration data exported from VOSviewer were processed in Scimago Graphica with parameter configurations (label=country, cluster=String). Resultant maps illustrated country-specific contributions through node diameters (correlated to publication counts) and inter-country linkages scaled by collaboration frequency. Descriptive statistics and graphical outputs (eg, circular diagrams, column charts, and histograms) were developed through Excel and Wei Sheng Xin bioinformatics platform, translating quantitative findings into accessible visual formats.

Results

Annual Trends in Publications and Citations

Between 2015 and 2024, a total of 696 research articles on JAKinibs for UC were published (Figure 1). The yearly output demonstrated a consistent upward trajectory, increasing from 6 articles in 2015 to 142 articles in 2024, reflecting a 23-fold growth over the decade. Notable surges occurred in 2018 (35 articles), 2020 (68 articles), 2021 (100 articles), and 2023 (156 articles), while 2024 saw a modest decline to 142 articles compared to the previous year. Citation counts exhibited an even more pronounced growth pattern. Starting at 6 citations in 2015, the annual citations surpassed 400 in 2018, rose to 886 in 2019, and reached 1,595 in 2020. This upward trend continued, peaking at 3,949 citations in 2023 and further escalating to 5,233 citations in 2024—the highest annual count to date—underscoring the sustained and growing scholarly interest in this field.

National Contributions and Cross-Border Research Networks

In the geographic collaboration network, major research hubs are centered in the United States, Canada, the United Kingdom, China, and Japan (Figure 2A). Clustering analysis of the collaboration network yielded 3 clusters. Cluster 1 (blue)—encompassing the United States, Canada, the United Kingdom, China, Japan, India, and Poland—emerges as the dominant cluster with the most extensive connections and densely interconnected structure in the collaboration network. Cluster 2 (green) includes Australia, Israel, Spain, and Brazil, while Cluster 3 (pink) consists Denmark and Netherlands, forming an independent cluster. Node sizes reflect national publication volumes, and line thickness indicates collaboration intensity. The United States and the United Kingdom exhibit the broadest international connections, actively participating in multiple transcontinental collaborative pathways.

The collaboration network further reveals intercountry partnerships, with the United States positioned as the network core, demonstrating the densest connections and forming stable collaborative frameworks with Canada, the United Kingdom, Italy, and Germany (Figure 2B). Italy also displays strong connectivity within its cluster, while European nations collectively exhibit high-frequency collaborative interactions. In the analysis of publication volume and citation frequency, the United States leads with over 300 publications—significantly surpassing other nations—and has accrued more than 10,000 citations (Figure 2C). Italy ranks second with nearly 150 publications, followed by Canada (98), France (79), and China (76). The United Kingdom, Spain, Germany, Belgium, and Japan complete the top ten countries, with citation frequencies generally trending upward in tandem with publication volumes. Notably, Belgium achieves the highest average citation count (68 citations per paper), followed by Spain (63) and Germany (51) (Table 1).

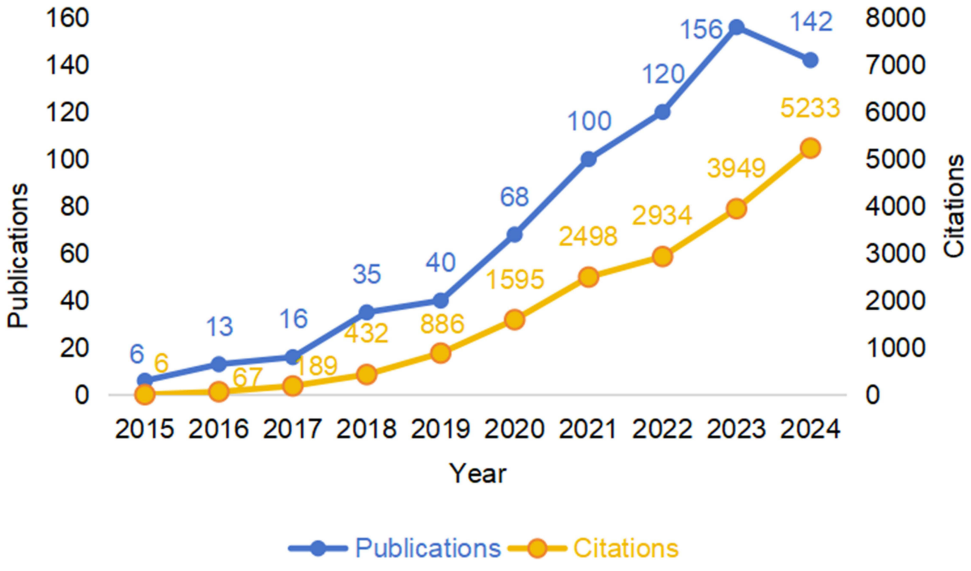

Figure 1 Annual publications and citations related to JAK inhibitors in ulcerative colitis (2015–2024).

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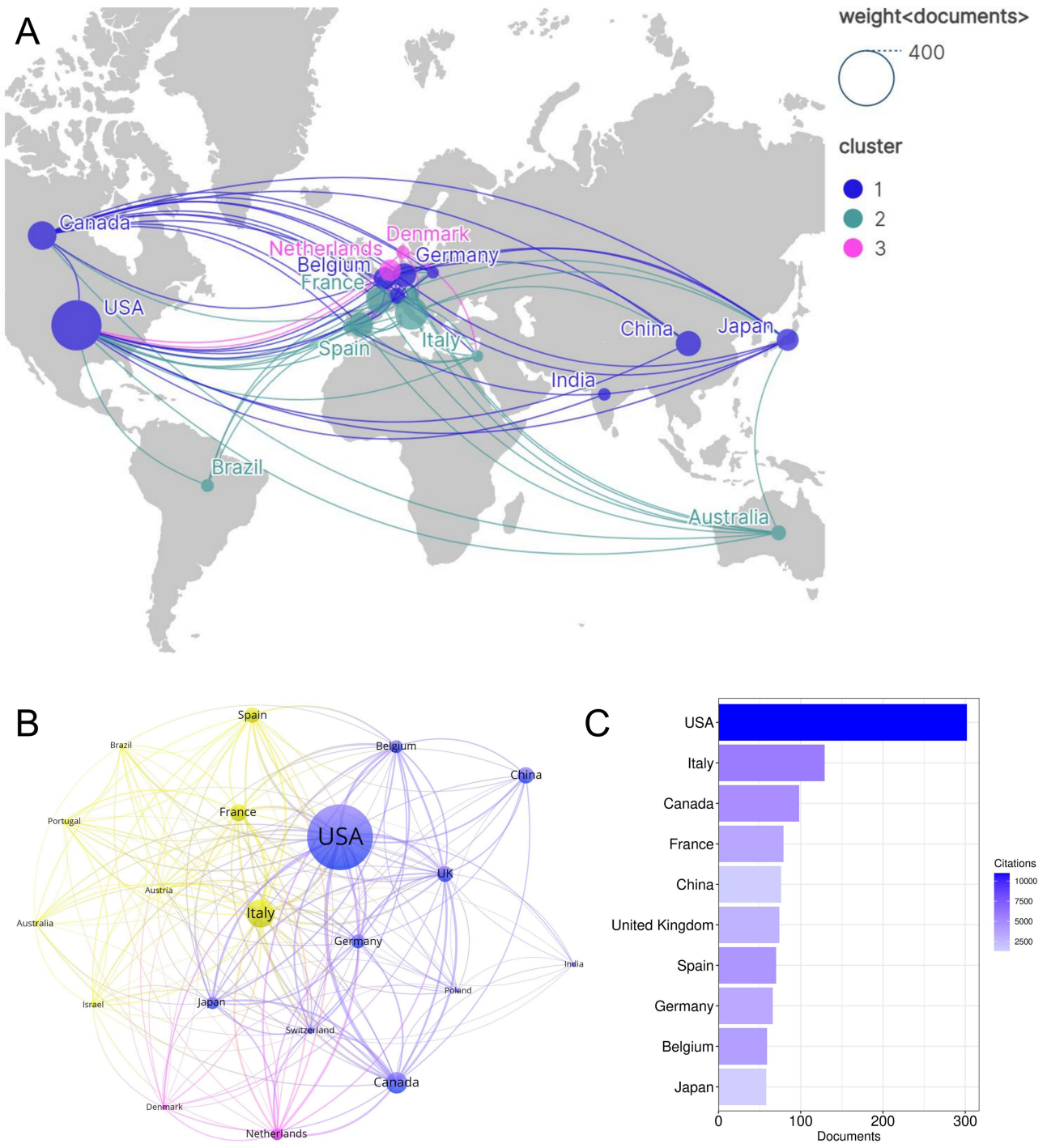

Figure 2 (**A**) Geographical distribution and collaboration network of countries in JAK inhibitor research for ulcerative colitis. (**B**) International co-authorship network. (**C**) Top 10 most productive countries based on number of publications and citations.

Core Journals and Citation Profile

Based on the journal co-citation network constructed using VOSviewer, *Inflammatory Bowel Diseases* occupied the central position in the network, characterized by a prominent node with dense connections (Figure 3A). This was followed by *Journal of Crohn's & Colitis* and *Alimentary Pharmacology & Therapeutics*, which served as pivotal hubs in the backbone network, reflecting their scholarly influence in this field.

Table 1 The Top 10 Countries by Total Publication Volume

Rank	Country	Documents	Citations	Total Link Strength	Average Citations
1	Usa	302	10958	453	36
2	Italy	129	5770	299	45
3	Canada	98	4848	309	49
4	France	79	3435	250	43
5	China	76	1476	71	19
6	United Kingdom	74	2873	211	39
7	Spain	70	4416	154	63
8	Germany	66	3368	174	51
9	Belgium	59	4021	221	68
10	Japan	54	2075	133	38

Regarding publication output, the top ten journals were ranked as follows: *Inflammatory Bowel Diseases* (67 articles), *Journal of Crohn's & Colitis* (54 articles), *Alimentary Pharmacology & Therapeutics* (39 articles), *Clinical Gastroenterology and Hepatology* (19 articles), *Therapeutic Advances in Gastroenterology* (18 articles), *Digestive Diseases and Sciences* (18 articles), *American Journal of Gastroenterology* (16 articles), *Digestive and Liver Disease* (14 articles), *Journal of Clinical Medicine* (14 articles), and *Expert Review of Gastroenterology & Hepatology* (12 articles) (Table 2).

In terms of journal rankings, 4 of the top 10 journals fell within the JournaI Citation Reports (JCR) Q1 category, 5 in Q2, and only 1 in Q3, indicating that high-quality research on this topic is predominantly disseminated through high-impact journals. The bubble chart further visualizes the relationships among publication volume, citation frequency, and impact factor (IF) (Figure 3B). A color gradient from lighter to darker shades represents decreasing citation rates, while bubble size corresponds to IF. Notably, *Clinical Gastroenterology and Hepatology*, despite its relatively lower publication volume, achieved the highest citation rate (75 citations per article).

Institutional Productivity and Collaboration Patterns

The institutional collaboration network reveals the formation of several regional collaborative clusters (Figure 4A). Node size corresponds to publication output, while thicker connecting lines indicate more frequent collaborations. The network

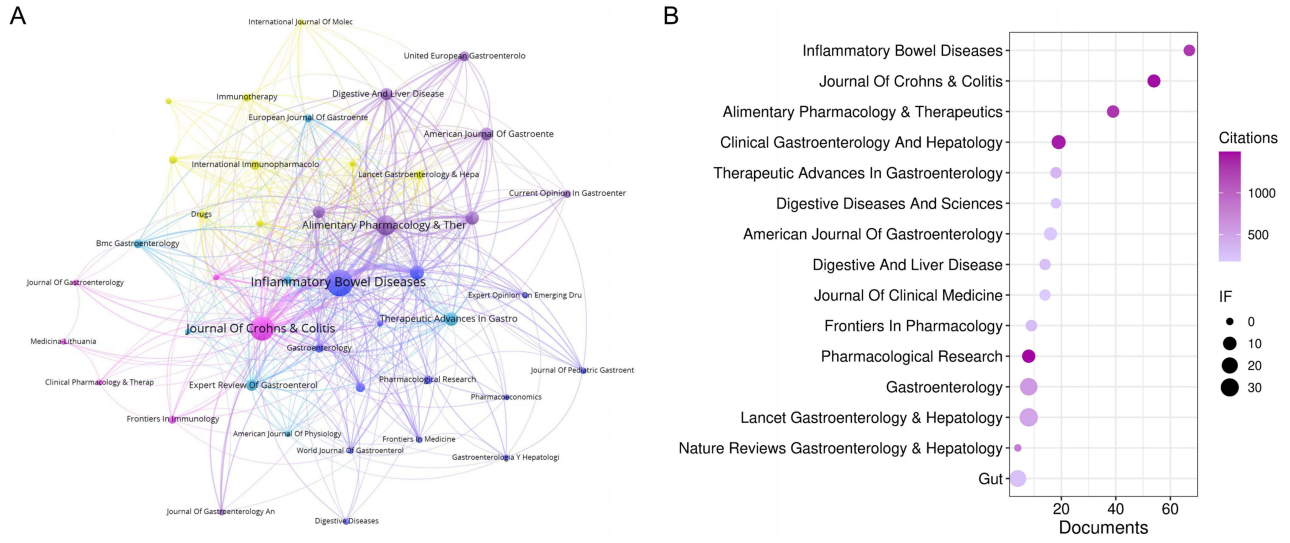

Figure 3 (**A**) Journal co-citation network of JAK inhibitor research in ulcerative colitis. (**B**) Distribution of the top 15 journals by publication volume, citation count, and impact factor.

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Table 2 Top 10 Journals by Total Number of Publications

Rank	Journal Name	Publications	Citations	Average Citations	IF (2024)	JCR
1	*Inflammatory Bowel Diseases*	67	1294	19	4.5	Q2
2	*Journal of Crohn's & Colitis*	54	1472	27	8.3	Q1
3	*Alimentary Pharmacology & Therapeutics*	39	1309	34	6.6	Q1
4	*Clinical Gastroenterology and Hepatology*	19	1428	75	11.6	Q1
5	*Therapeutic Advances in Gastroenterology*	18	354	20	3.9	Q2
6	*Digestive Diseases and Sciences*	18	240	13	2.3	Q3
7	*American Journal of Gastroenterology*	16	200	12	8.5	Q1
8	*Digestive and Liver Disease*	14	258	18	4.0	Q2
9	*Journal of Clinical Medicine*	14	180	13	3.8	Q2
10	*Expert Review of Gastroenterology & Hepatology*	12	205	17	3.8	Q2

highlights U.S.-based institutions occupying central positions, characterized by dense domestic collaborations and extensive international partnerships.

The top ten institutions by publication output were ranked as follows: Pfizer Inc (82 articles), Icahn School of Medicine at Mt Sinai (53 articles), University of California San Diego (51 articles), Mayo Clinic (41 articles), Humanitas University (37 articles), Western University (34 articles), University of Calgary (32 articles), University of Lorraine (32 articles), Università Vita-Salute San Raffaele (31 articles), and Hospital Clínic Barcelona (26 articles) (Table 3). US institutions dominated the top four positions, underscoring their absolute leadership in this research domain. Canada and Italy each contributed two institutions to the list, reflecting high activity levels in both North America and Europe.

The bubble chart further illustrates the relationship between institutional publication output and citation frequency (Figure 4B). The University of California San Diego, ranked third in publications, received the highest total citations (4,838), demonstrating the greatest average influence. Icahn School of Medicine at Mt Sinai and Pfizer also achieved notable citation counts, both exceeding 3,000 citations, highlighting their significant academic impact.

Author Influence and Collaboration Structure

In the author collaboration network diagram, each node represents an individual author (Figure 5A). The node size corresponds to the author's publication count, while the node color indicates their membership in distinct collaborative

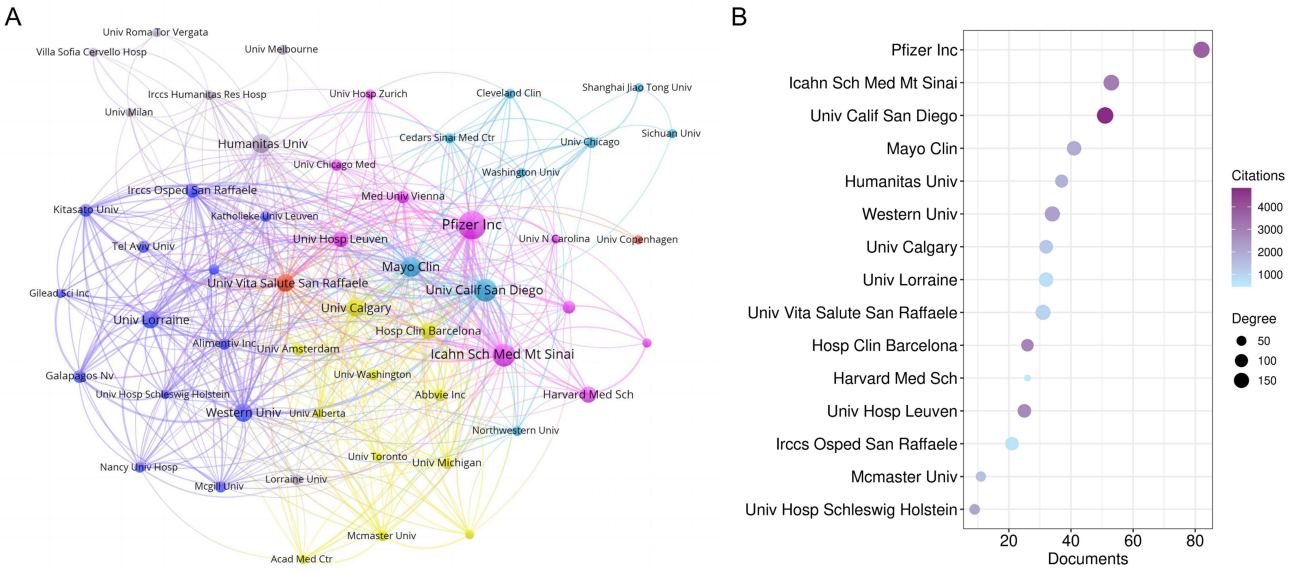

Figure 4 (**A**) Institutional co-authorship network in JAK inhibitor research on ulcerative colitis. (**B**) Bubble chart displaying the top institutions by publication volume, citation count, and degree.

Table 3 Top 10 Most Productive Institutions in JAK Inhibitor Research for Ulcerative Colitis

Rank	Institution	Publications	Citations	Total Link Strength	Country
1	Pfizer Inc	82	3733	184	USA
2	Icahn School of Medicine at Mt Sinai	53	3065	165	USA
3	University of California San Diego	51	4838	187	USA
4	Mayo Clinic	41	1976	131	USA
5	Humanitas University	37	1799	98	Italy
6	Western University	34	2232	149	Canada
7	University of Calgary	32	1273	111	Canada
8	University of Lorraine	32	746	130	France
9	Univ Vita-Salute San Raffaele	31	1043	146	Italy
10	Hospital Clínic Barcelona	26	2890	88	Spain

clusters. Within this network, Danese, Silvio; Sandborn, William J.; and Su, Chinyu occupy central positions, characterized by dense connections and extensive collaborations.

According to publication volume statistics, the top ten authors were ranked as follows: Danese, Silvio (61 articles), Peyrin-Biroulet, Laurent (47 articles), Su, Chinyu (42 articles), Sandborn, William J. (35 articles), Vermeire, Severine (31 articles), Panes, Julian (28 articles), Lawendy, Nervin (27 articles), Jairath, Vipul (26 articles), Sands, Bruce E. (21 articles), and Rubin, David T. (20 articles) (Figure 5B). These authors demonstrated high research productivity. Geographically, U.S.-based researchers dominated both in quantity and influence, while scholars from Italy, France, Belgium, Spain, and Canada also exhibited strong representation in this field.

In terms of total citation frequency, the top ten authors by publication count were: Danese, Silvio (3,818 citations), Sandborn, William J. (3,648 citations), Vermeire, Severine (3,240 citations), Panes, Julian (2,998 citations), Su, Chinyu (2,962 citations), Lawendy, Nervin (2,569 citations), Peyrin-Biroulet, Laurent (1,509 citations), Sands, Bruce E. (2,213 citations), Jairath, Vipul (647 citations), and Rubin, David T. (592 citations) (Figure 5C). Notably, Danese, Silvio led by a significant margin in total citations, underscoring his pivotal role in advancing this research domain.

Research Hotspots and Thematic Evolution Based on Keywords

Keyword co-occurrence analysis demonstrated distinct thematic clusters and evolving research trends in studies on JAKinibs for UC. A cluster network diagram and timeline map identified 14 keyword clusters, reflecting interdisciplinary subfields and their temporal dynamics (Figure 6A and B). Cluster #0 (herpes zoster) integrated themes such as *combination therapy, rheumatoid arthritis*, and *clinical remission*, highlighting safety concerns related to herpes zoster infections in the treatment of ulcerative colitis. Cluster #1 (maintenance therapy) emphasized long-term efficacy evaluation of tofacitinib, with keywords like multicenter trials and activation. Studies of biologics, particularly adalimumab and infliximab, dominated Cluster #2, while Cluster #3 (clinical response) focused on therapeutic outcomes in active ulcerative colitis. Cluster #4 (inadequate response) addressed the inadequate response to JAKinibs, employing trial designs such as placebo-controlled and double-blind methodologies. Cluster #5 (small molecule) explored agents like *upadacitinib* and *vedolizumab*, alongside randomized trials and evidence based consensus. Patient-centered metrics, including quality of life and safety assessments, formed Cluster #6 (questionnaire), whereas Cluster #7 (venous thromboembolism) specifically linked Janus kinase inhibitors to thrombotic risks. Related disease spectrum analyses emerged in Cluster #8 (Crohn's disease), encompassing inflammatory bowel disease subtypes. Cluster #9 (biologic treatment) emphasized management strategies, while Cluster #10 (risk) prioritized clinical trial design and risk assessment. Pharmacokinetic studies of Janus kinase inhibitors defined Cluster #11, whereas Cluster #12 (JAK inhibitors) refined classifications of small-molecule inhibitors. Finally, Cluster #13 (acute severe ulcerative colitis) singularly addressed outcome research in critically ill patients. These clusters collectively illustrate the field's progression from mechanistic exploration to clinical application, with sustained emphasis on safety, comparative efficacy, and patient-centric outcomes.

Keyword burst analysis revealed distinct phase-specific evolutionary patterns in research priorities within this field. Figure 6C displays the top 14 keywords with the highest burst strength and their corresponding surge periods. Keywords

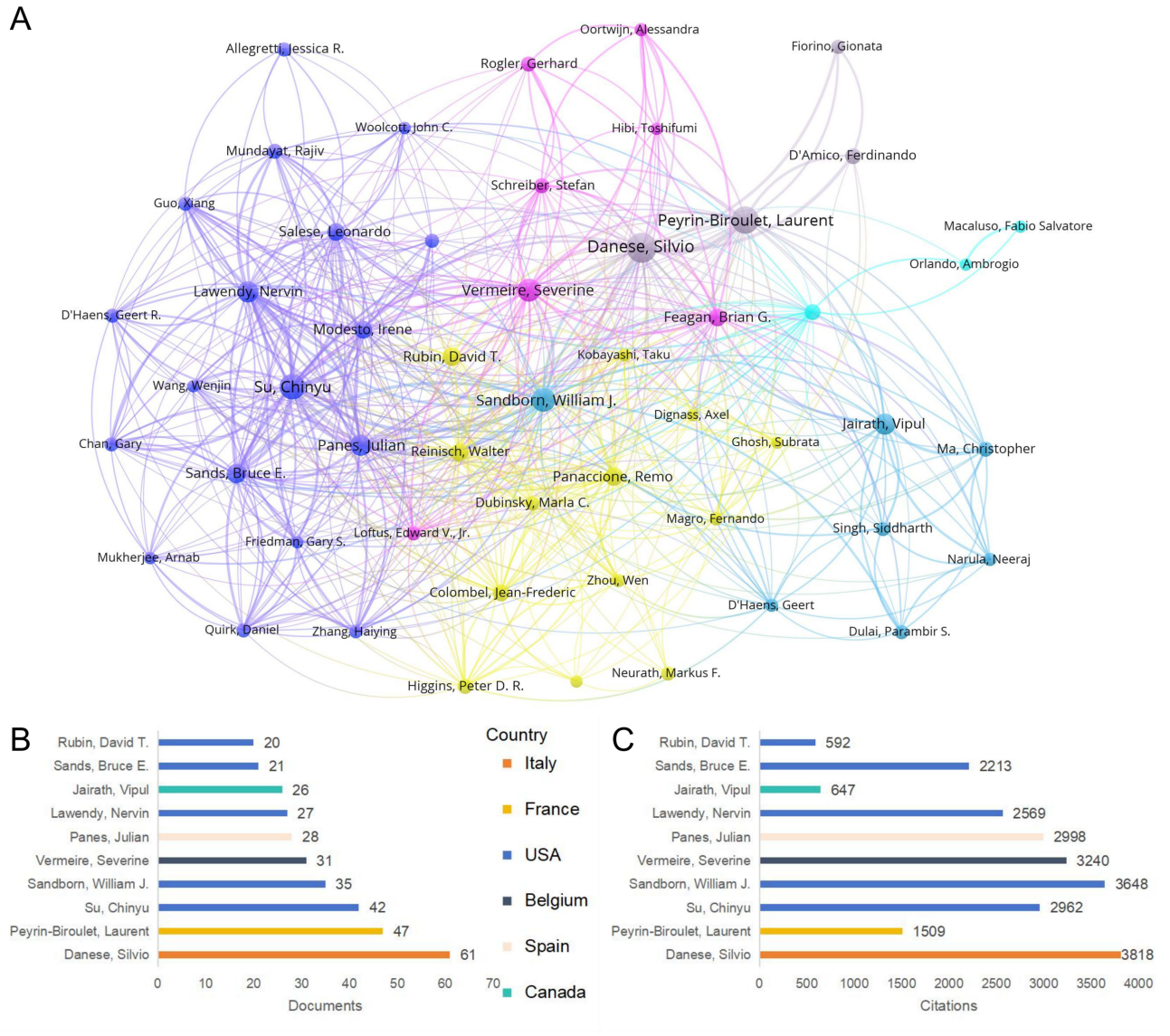

Figure 5 (**A**) Author collaboration network on JAK inhibitor research in ulcerative colitis. (**B**) Top 10 authors by publication volume. (**C**) Total citations for the top 10 authors.

emerging in 2015 included janus kinase inhibitor (burst strength: 9.73, 2015–2019), Crohn's disease (2.93, 2015–2017), and CP 690 (2.48, 2015–2020), with janus kinase inhibitor exhibiting the strongest burst intensity. In 2016, new emergent keywords encompassed active rheumatoid arthritis (3.88, 2016–2017) and active ulcerative colitis (3.25, 2016–2020). Keywords surging in 2017—placebo-controlled trial (4.26, 2017–2018), monoclonal antibody (3.76, 2017–2018), open label (3.15, 2017–2021), and pharmacokinetics (2.73, 2017–2018)—were predominantly associated with clinical trial design and pharmacokinetic studies. Theyear 2018 saw the emergence of inadequate response (3.42, 2018–2020) and Janus kinase (2.71, 2018–2021), both sustaining prolonged activities. Post-2020 keywords included inhibitor (2.86, 2020–2022) and *antibody* (2.77, 2020–2022). And *impact* (2.68, 2022–2024) emerged in 2022 and remains active, reflecting sustained scholarly interest in this theme in recent years.

Highly Cited Authors

The co-citation network of the most frequently cited core scholars in this field identified Sandborn WJ as the central node, demonstrating exceptional scholarly influence and extensive collaborative linkages (Figure 7A). Feagan BG, Sands BE, Danese S, and Vermeire S were clustered around this central node, forming a tightly interconnected academic citation cluster.

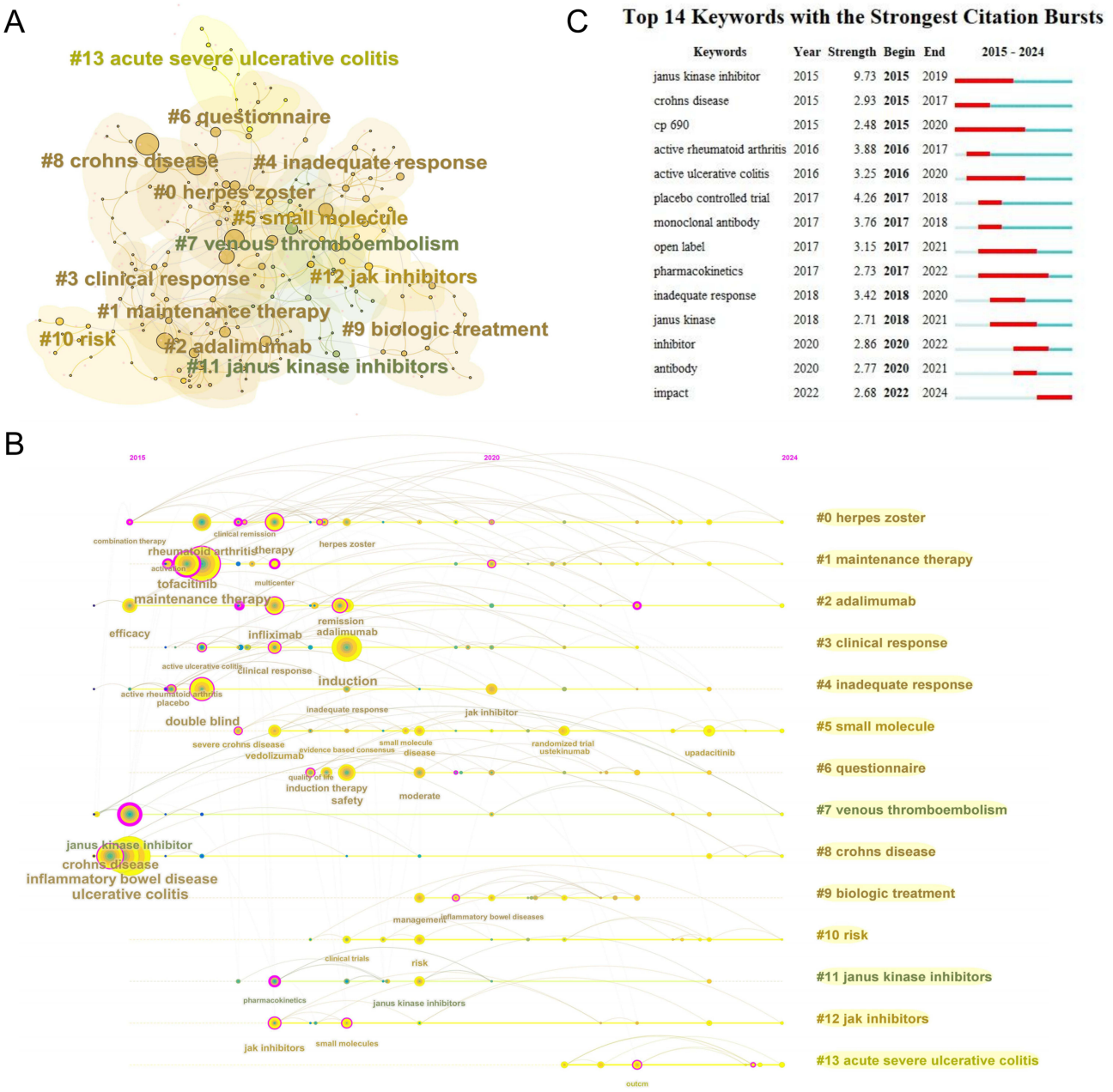

Figure 6 (**A**) Co-occurrence network of keywords in the field of JAK inhibitors and ulcerative colitis. (**B**) Timeline view of keyword evolution across clusters. (**C**) Top 14 keywords with the strongest citation bursts and their active time periods.

Statistical results indicated that Sandborn WJ ranked first with the highest total citations (1,944), followed by Feagan BG (495 citations), Sands BE (489 citations), Danese S (437 citations), and Vermeire S (320 citations). Other highly cited authors included Winthrop KL (241 citations), Colombel JF (233 citations), Panés J (229 citations), Singh S (223 citations), and Peyrin-Biroulet L (202 citations) (Figure 7B). When combined with the Total Link Strength (TLS) metric, Sandborn WJ again dominated with the highest TLS (27,634), far exceeding other authors, underscoring the pivotal role of his research in shaping this field (Table 4).

Co-Citation Relationships and Burst Characteristics of High-Impact Literature

The co-citation network of references revealed a well-defined core literature group in this research field (Figure 8A). Sandborn WJ emerged as the central node in the network, with publications concentrated between 2017 and 2020,

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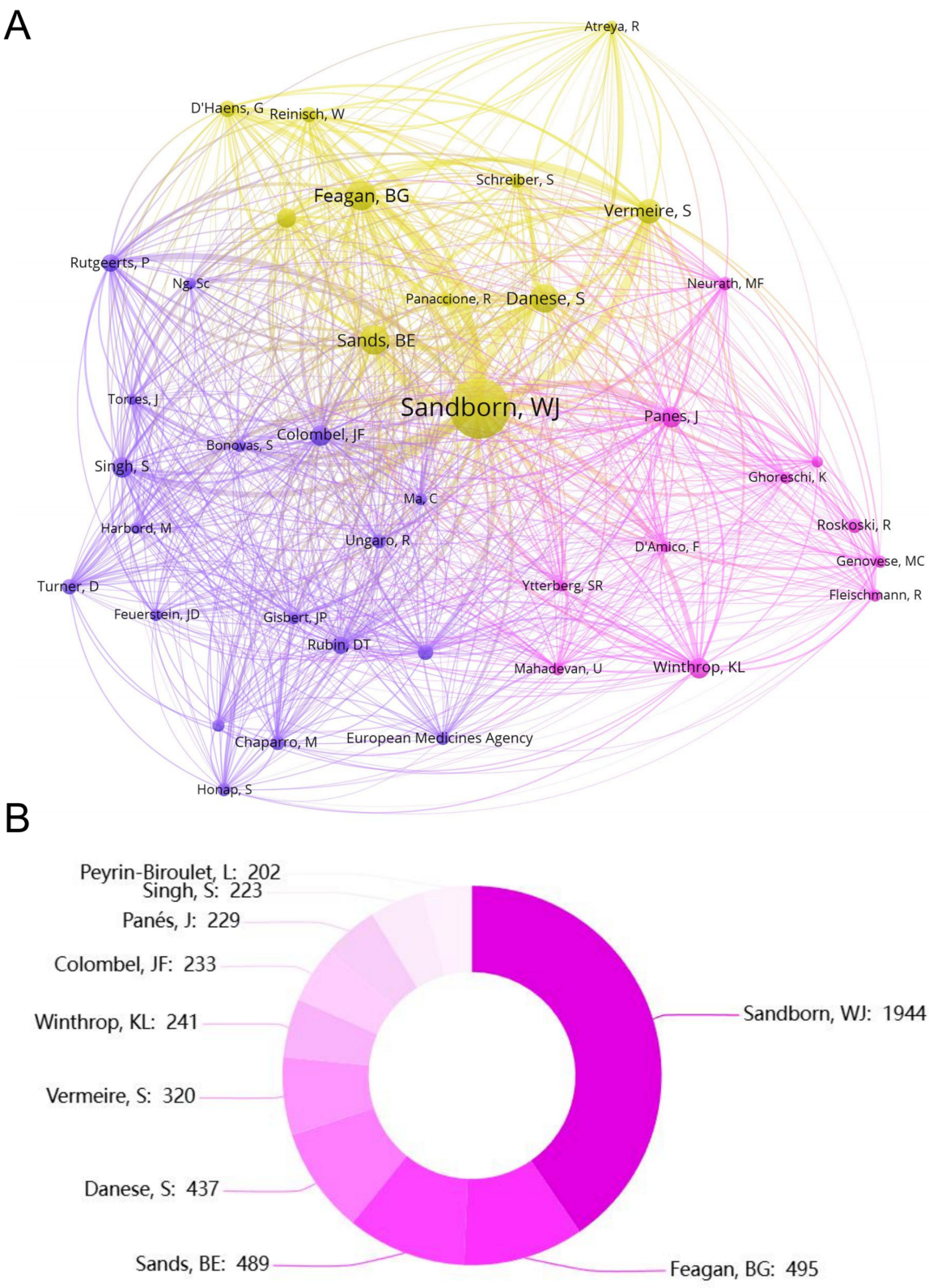


Figure 7 (**A**) Author co-citation network of highly cited researchers. (**B**) Citation volume distribution of the top 10 most-cited authors in the field.

Table 4 Top 5 Most-Cited Authors in the Field of JAK Inhibitors for Ulcerative Colitis

Rank	Author	Citations	Total Link Strength
1	Sandborn WJ	1944	27634
2	Feagan BG	495	10109
3	Sands BE	489	9694
4	Danese S	437	7875
5	Vermeire S	320	6955

demonstrating high connectivity to related works. Other frequently co-cited references included Sands BE (2019), Vermeire S (2017), Turner D (2021), and Danese S (2022). Cluster analysis further delineated the thematic structure of the references, identifying 15 clusters (Figure 8B). These clusters encompassed keywords such as #0 "tofacitinib", #1 safety, #2 cardiovascular risk, #3 mongersen, #4 cancer, #5 oral therapy, #6 shingles, #7 acute severe ulcerative colitis, #8 smad7, #9 biologics, #10 vedolizumab, #11 upadacitinib, #12 steroid-free, #13 sphingosine-1-phosphate receptor modulators, and #14 clinical guidelines.

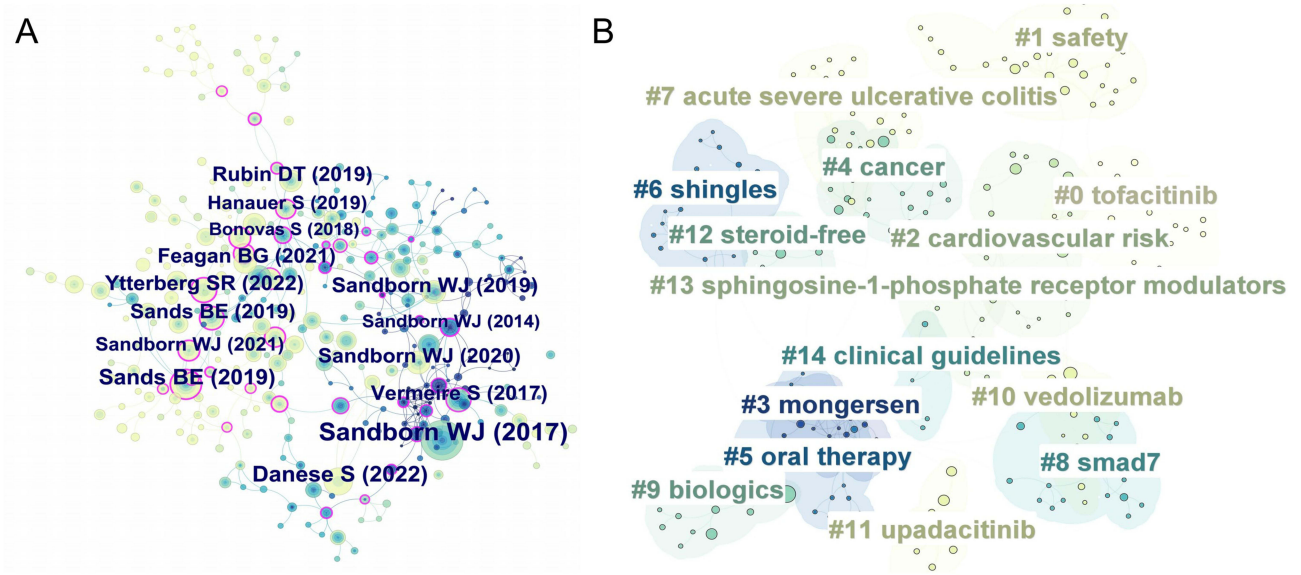
Burst detection analysis identified the top 15 core references with the highest burst strength (Figure 8C). The work by Sandborn WJ (2017, *New England Journal of Medicine*) exhibited the strongest burst intensity (43.36),[22] with an active surge period from 2018 to 2021. Other high-burst references included Sandborn WJ (2014, *Clinical Gastroenterology and Hepatology*, burst strength: 20.88),[29] Sandborn WJ (2012, *New England Journal of Medicine*, 17.73),[23] Feagan BG (2013, *New England Journal of Medicine*, 15.55),[30] and Vermeire S (2017, *Lancet*, 14.83).[37] Most frequently cited references appeared in high-impact journals such as *New England Journal of Medicine, Lancet*, and *Gastroenterology* (Table 5).

Discussion

The treatment of UC has evolved from empirical treatment to precision therapies, such as targeted therapy. Sulfasalazine (SASP), developed in the 1940s by Swedish physician Nanna Svartz, was initially used to treat rheumatoid arthritis.[49,50] It was later proven effective for UC and became the first 5-aminosalicylic acid (5-ASA) agent clinically applied for UC treatment. Pure 5-ASA formulation mesalazine remains the first-line treatment for mild to moderate UC to this day, yet demonstrate suboptimal efficacy in moderate-to-severe disease.[51] Capitalizing on the potent non-specific anti-inflammatory and immunomodulatory effects, corticosteroids have progressively been applied in moderate-to-severe UC management. However, their limitations include unsuitability for maintenance therapy while also carrying high relapse rates upon discontinuation.[52]

Consequently, immunomodulators have emerged as essential maintenance therapies for UC, particularly in steroid-dependent patients or those with frequent relapses. However, they carry risks of hepatotoxicity and other adverse effects, along with potential teratogenic concerns.[53] Building upon an advanced understanding of UC's immunopathogenesis, biologics were developed, ushering in a new era of targeted therapy. These agents have significantly improved treatment response rates, mucosal healing rates, and quality of life in UC patients; nevertheless, challenges persist regarding primary non-response or secondary loss of response.[54] Over the past decade, small-molecule drugs have gained prominence. JAKinibs, which act by blocking the JAK-STAT signaling pathway, offer advantages such as oral administration, short serum half-life, intracellular targeting, and non-antigenic properties.

They demonstrate promising efficacy in immune-mediated inflammatory diseases (IMIDs) and hold significant potential for UC patient refractory to existing therapies. A recent meta-analysis comparing biologics and small-molecule drugs for moderate-to-severe UC revealed that upadacitinib outperformed all other interventions in inducing clinical remission.[55] Currently, JAKinibs such as tofacitinib and upadacitinib have been approved for UC treatment, with numerous others in preclinical development or clinical trials. Nevertheless, the safety profile of JAKinibs remains controversial, and their cost continues to pose a barrier in many healthcare settings.[43] Therefore, elucidating the developmental trajectory of JAKinibs in UC, clarifying their therapeutic role, and identifying current research priorities are critical to optimizing their clinical application.



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Top 15 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2015 - 2024
Sandborn WJ, 2014, CLIN GASTROENTEROL H, V12, P1485, DOI 10.1016/j.cgh.2014.01.029, DOI	2014	20.88	2015	2019	
Sandborn WJ, 2012, NEW ENGL J MED, V367, P616, DOI 10.1056/NEJMoa1112168, DOI	2012	17.73	2015	2017	
Feagan BG, 2013, NEW ENGL J MED, V369, P699, DOI 10.1056/NEJMoa1215734, DOI	2013	15.55	2015	2018	
Feagan BG, 2016, NEW ENGL J MED, V375, P1946, DOI 10.1056/NEJMoa1602773, DOI	2016	11.79	2017	2021	
Sandborn WJ, 2016, NEW ENGL J MED, V374, P1754, DOI 10.1056/NEJMoa1513248, DOI	2016	10.8	2017	2021	
Sandborn WJ, 2017, NEW ENGL J MED, V376, P1723, DOI 10.1056/NEJMoa1606910, DOI	2017	43.36	2018	2022	
Panés J, 2017, GUT, V66, P1049, DOI 10.1136/gutjnl-2016-312735, DOI	2017	18.23	2018	2021	
Vermeire S, 2017, LANCET, V389, P266, DOI 10.1016/S0140-6736(16)32537-5, DOI	2017	14.83	2018	2021	
Ungaro R, 2017, LANCET, V389, P1756, DOI 10.1016/S0140-6736(16)32126-2, DOI	2017	12.6	2018	2022	
Danese S, 2016, AM J PHYSIOL-GASTR L, V310, PG155, DOI 10.1152/ajpgi.00311.2015, DOI	2016	8.6	2018	2021	
Bonovas S, 2018, ALIMENT PHARM THER, V47, P454, DOI 10.1111/apt.14449, DOI	2018	8.59	2018	2020	
Singh S, 2018, ALIMENT PHARM THER, V47, P162, DOI 10.1111/apt.14422, DOI	2018	8.35	2018	2021	
Harbord M, 2017, J CROHNS COLITIS, V11, P769, DOI 10.1093/ecco-jcc/jjx009, DOI	2017	8.53	2019	2022	
Ng SC, 2017, LANCET, V390, P2769, DOI 10.1016/S0140-6736(17)32448-0, DOI	2017	8.3	2019	2021	
Sands BE, 2018, J CROHNS COLITIS, V12, P1158, DOI 10.1093/ecco-jcc/jjy085, DOI	2018	8.14	2019	2021	

Figure 8 (**A**) Co-citation network of references on JAK inhibitors in ulcerative colitis. (**B**) Reference clustering results based on thematic similarity. (**C**) Top 15 references with the strongest citation bursts.[22,23,29–41]

Bibliometric research indicates that over the decade from 2015 to 2024, both publication output and citation count in the field of UC and JAKinibs have demonstrated an overall upward trend, suggesting sustained academic attention to this field in recent years. The publication output stood at only 6 articles in 2015, indicating that this research field was in its nascent stage at the time. The minor decline observed in 2024 may be attributed to delayed indexing. At the national level, the United States leads in publication volume, followed by Italy, Canada, and France. This distribution aligns with epidemiological findings showing the highest UC prevalence in Europe and North America, reflecting these nations' central roles in this research domain. China ranks fifth, while newly industrialized countries represented by China show increasing UC incidence rates and substantial research potential in this field.[40] Regarding international collaboration, multiple extensive collaborative networks have been established with the United States as the central hub, while the proportion of international cooperation in articles published in China is relatively low. This phenomenon may be related

Table 5 The Top 10 Most Frequently Cited References

Rank	Author	Year	Citations	Journal	DOI
1	Sandborn WJ	2017	218	*The New England Journal of Medicine*	10.1056/NEJMoa1606910[22]
2	Sands BE	2019	106	*The New England Journal of Medicine*	10.1056/NEJMoa1900750[42]
3	Danese S	2022	104	*The Lancet*	10.1016/s0140-6736(22)00581-5[24]
4	Sandborn WJ	2019	80	*Clinical Gastroenterology and Hepatology*	10.1016/j.cgh.2018.11.035[43]
5	Rubin DT	2019	75	*The American Journal of Gastroenterology*	10.14309/ajg.0000000000000152[44]
6	Ytterberg SR	2022	75	*The New England Journal of Medicine*	10.1056/NEJMoa2109927[45]
7	Sandborn WJ	2020	74	*Gastroenterology*	10.1053/j.gastro.2020.02.030[46]
8	Sands BE	2019	74	*The New England Journal of Medicine*	10.1056/NEJMoa1905725[47]
9	Vermeire S	2017	72	*The Lancet*	10.1016/S0140-6736(16)32,537-5[37]
10	Turner D	2021	69	*Gastroenterology*	10.1053/j.gastro.2020.12.031[48]

to linguistic barriers, sample-selection bias, and the characteristics of China's research landscape. Although the English proficiency of Chinese researchers has improved, barriers to international collaboration persist. Furthermore, the predominant focus of on English-language journals may underestimate collaborative efforts published in regional journals, thus underrepresenting actual collaboration rates. Finally, the vast number of research institutions in China and its self-sufficient research ecosystem may also reduce the necessity to explore international partnerships. At the institutional level, the top four productive organizations are all American institutions. Pfizer Inc. leads in publication quantity, likely due to its FDA-approved tofacitinib and ongoing development of other JAKinibs. In terms of academic influence, the University of California, San Diego ranks first, demonstrating exceptional research capabilities and academic leadership in this field.

At the journal level, *Inflammatory Bowel Diseases* has published the highest number of relevant research papers, while *Pharmacological Research* emerges as the most influential journal, highlighting its stronger academic leadership in this field. In terms of citation volume, articles published in *Clinical Gastroenterology and Hepatology* rank first in total citations, indicating that this journal has exerted a more profound impact on advancing the discipline. At the author level, Silvio Danese has contributed the highest number of publications. His primary research achievements include clinical trials on Upadacitinib and comprehensive reviews of JAKinib therapeutic mechanisms, reflecting remarkable research activity and scholarly productivity. William J. Sandborn's work has received the highest citation counts, demonstrating greater academic influence. He has led multiple landmark clinical trials, which serve as the cornerstone of evidence-based medicine in this field.

Reference analysis demonstrates the construction of this field's knowledge framework. The research reveals that the most highly cited papers in this field predominantly focus on high-quality clinical trials and guidelines for JAKinib therapies in UC.[22,24,37,43,44,46,48] Other top 10 cited publications include studies on biological agents for UC treatment[42,47] and investigations into adverse effects of JAKinibs in rheumatoid arthritis.[45] The former may relate to the shared status of JAKinibs and biologics as novel UC therapies, with JAKinibs often serving as adjunctive treatments to biologics, while the latter reflects growing concerns about JAKinib safety profiles and their expanding clinical indications. Burst detection analysis of references highlights distinct thematic shifts: early studies (2015–2018) primarily concentrated on JAKinib clinical trials, indicating that the field remained in an exploratory phase of clinical validation. Post-2018, emergent literature shifted toward systematic evaluations of JAKinib efficacy and safety and international authoritative treatment guidelines, along with some clinical validation of novel JAKinibs. This evolution suggests a transition from generating clinical evidence to integrating evidence and standardizing clinical practice, mirroring the field's maturation and the growing demand for enhanced evidence hierarchies in evidence-based medicine and refined risk-benefit assessments. Meanwhile, the continued emergence of new drug trials underscores persistent opportunities for breakthrough innovations, particularly in therapeutic target development (eg, JAK1-selective inhibition), demonstrating the field's ongoing potential for transformative advancements.

Analysis of high-frequency and burst keywords reveals research hotspots and frontier trends in the field. Keywords with high frequency and centrality demonstrate that the research on this field focused on efficacy comparisons and therapeutic strategy selection between JAKinibs (particularly tofacitinib) and classical biologics for UC and characterized

by an "induction-maintenance" treatment strategy, exploring both the cross-disease mechanisms and extended indications of JAKinibs, originally developed for immune-mediated inflammatory disorders such as rheumatoid arthritis. Burst keyword analysis reveals distinct thematic evolution in research priorities. During 2015–2017, the focus centered on preliminary clinical validation of JAKinibs in UC *(placebo-controlled trial, open-label*), cross-disease exploration (*active rheumatoid arthritis*), and target validation/drug development (*Janus kinase inhibitor, CP-690*[tofacitinib]), establishing the foundational evidence base for the field. Post-2018, priorities shifted toward precision therapeutics (*inadequate response, pharmacokinetics*) and integration of clinical practice (*impact*), aligning closely with trends identified in burst reference analysis. Future research is expected to prioritize novel subtype selective JAKinibs and long-term safety data from clinical trials, alongside patient-stratified therapeutic positioning.

While JAKinibs have gained prominence in UC management, significant challenges persist. The most frequently cited concern is safety controversies. In 2021, the US FDA issued a boxed warning for the tofacitinib, indicating that studies showed an increased risk of serious infections and cardiovascular events associated with this class of drugs.[45,56] However, several recent real-world studies suggest that JAKinibs are effective and safe in treating UC, with acne being the most frequently reported adverse reaction.[24,57,58] At present, biologics (such as anti-TNF-α agents and IL-23 inhibitors) are still considered superior to JAKinibs in terms of safety and treatment priority.[59,60] JAKinibs need to further demonstrate their differentiated advantages in efficacy, cost, and convenience of use. To improve safety profiles, increasingly selective JAKinibs are being developed. These agents are categorized into three generations based on mechanism and selectivity: first-generation orthosteric inhibitors (eg, tofacitinib, baricitinib) broadly inhibit multiple JAK enzymes; second-generation inhibitors (eg, upadacitinib, filgotinib) target specific JAK isoforms with greater selectivity to reduce off-target effects; and third-generation allosteric inhibitors (eg, deucravacitinib) bind outside the ATP site, offering enhanced specificity and potential safety benefits.[61] Additionally, dosing strategies such as higher induction followed by lower maintenance dosing (eg, with tofacitinib or upadacitinib) have proven effective in balancing efficacy and safety.[62] A deeper understanding of JAK regulation post-cytokine receptor activation remains essential to identifying new therapeutic targets. Concurrently, exploring localized delivery systems offers a promising strategy to mitigate systemic exposure and enhance the therapeutic window by targeting colonic inflammation more precisely. Several pan-JAKinibs are being developed as a non-absorbable for UC.[61] Ultimately, the value of selective JAK inhibition will be further clarified by accumulating real-world evidence from both approved and investigational agents.

Limitations

This study exclusively utilized the WoS Core Collection database, as we prioritized its high-quality curated content and well-established utility for robust citation network analysis, which aligns with our objective of mapping the core scholarly landscape. The inclusion criteria restricted the scope to articles and review papers, excluding other publication formats. While this approach ensures analytical reliability and focuses on authoritative literature, it may not encompass the entire spectrum of published work. Therefore, to achieve a more comprehensive analysis, expanding the search to include additional databases (eg, Scopus, PubMed) and all format of publication would be beneficial. Furthermore, bibliometric analysis primarily focuses on quantitative metrics inherently lacking in-depth exploration of research quality or mechanistic insights. Future studies should address these limitations by incorporating multidisciplinary databases and mixed-methods approaches such as qualitative synthesis alongside bibliometrics to holistically evaluate the evolving landscape of JAKinib research in UC. Additionally, integrating non-traditional publications and leveraging advanced analytical tools could provide a more nuanced understanding of translational challenges and innovation trajectories in this field.

Conclusion

This study employs bibliometric methods to analyze research on JAKinib therapies for UC from 2015 to 2024, systematically mapping the field's current landscape, research hotspots, and frontier trends. The findings provide insights to refine UC disease management and therapeutic strategies while identifying critical research directions. Over the past decade, global interest in JAKinib-related UC research has grown substantially. Key research foci include clinical investigations and systematic evaluations of JAKinib efficacy and safety profiles, comparative studies with classical biologics to inform treatment decision-making, and development of novel JAK selective inhibitors. Future research should prioritize several

key directions to advance JAKinib therapy. First, long-term studies are essential to further validate the safety and efficacy profiles of these agents in real-world settings. Second, efforts should focus on developing novel subtype-selective drugs, particularly third-generation allosteric inhibitors, to enhance target specificity and reduce off-target effects. Third, pharmacodynamic and pharmacokinetic investigations are needed to optimize induction and maintenance dosing strategies that maximize mucosal healing while minimizing long-term risks. Additionally, further investigation into tissue-specific and non-systemic formulations may help limit systemic exposure and improve safety profiles.

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