

A Bibliometric Analysis and Visualization of Research Trends and Hotspots in Actinic Keratosis Based on Web of Science

Zilin Cheng^{1,*}, Zeyun Qiao^{1,*}, Shaojie An¹, Jinghua Liu¹, Wenyi Ma¹ , Pingsheng Hao^{1,2} 

¹Clinical Medical College, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan Province, People's Republic of China; ²Department of Dermatology, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan Province, People's Republic of China

*These authors contributed equally to this work

Correspondence: Pingsheng Hao, Hospital of Chengdu University of Traditional Chinese Medicine, No. 37, Twelve Bridges Road, Chengdu City, Sichuan Province, 610000, People's Republic of China, Email hpswl@126.com

Background: Actinic keratosis (AK) is a precancerous intraepidermal lesion characterized by atypical keratinocyte proliferation. In recent years, research on AK has made continuous progress, but there has been no bibliometric study on it. This study aims to use bibliometric methods to analyze the research and treatment hotspots of AK in recent years, in order to further understand the development direction and frontiers of this field.

Methods: Core literature related to AK was retrieved from the Web of Science Core Collection (WoSCC) database. CiteSpace and VOSviewer software were employed to conduct a detailed analysis based on publication output, countries/regions, research institutions, journals, authors, and keywords.

Results: A total of 2,796 documents were included in this study. The United States, Germany, and Italy emerged as the leading contributors to AK research, with the University of Copenhagen identified as the most prolific research institution. Among authors, Pellacani G has published the highest number of articles, while the Journal of the European Academy of Dermatology and Venereology ranks as the most influential journal in this field. The main research hotspots and frontiers in the field of AK are as follows: (1) Molecular mechanisms of malignant transformation to cutaneous squamous cell carcinoma (cSCC), particularly involving genomic instability (eg, TP53 mutations); (2) Personalized therapies optimized through immune profiling, genetic biomarkers, and lesion morphology; (3) Emerging frontiers include non-invasive diagnostic technologies and treatment monitoring, which are receiving significant attention.

Conclusion: This study summarizes the current research status and key areas of focus in AK, providing a foundation for clinical decision-making and guiding future research directions.

Keywords: actinic keratosis, cutaneous squamous cell carcinoma, bibliometrics, visualization

Introduction

Actinic keratosis (AK) is a skin lesion characterized by the proliferation of atypical keratinocytes (epidermal and adnexal epithelia) and is widely recognized as a potential precursor to cutaneous squamous cell carcinoma. Given its malignant potential, timely and appropriate treatment is essential.¹ AK commonly develops in sun-exposed areas of the skin, such as the head and face. Clinically, it manifests as rough, scaly patches that may be flat or slightly elevated.^{2,3} AK predominantly affects middle-aged and elderly individuals, with its incidence increasing with age. Epidemiological data indicate that the incidence rate nearly doubles in individuals over 80 years old.⁴ Individuals with compromised immune systems and those with occupational sun exposure are at a significantly higher risk of developing AK.⁵ Solitary AK carries a higher risk of malignant transformation compared to multiple AK lesions.^{6,7} Mutations in the *p53* gene,⁸ immune dysregulation, oxidative stress, and cell cycle abnormalities are key risk factors for the development of AK.³ The presence of AK on the head and other exposed areas can impose a significant psychological burden on patients.

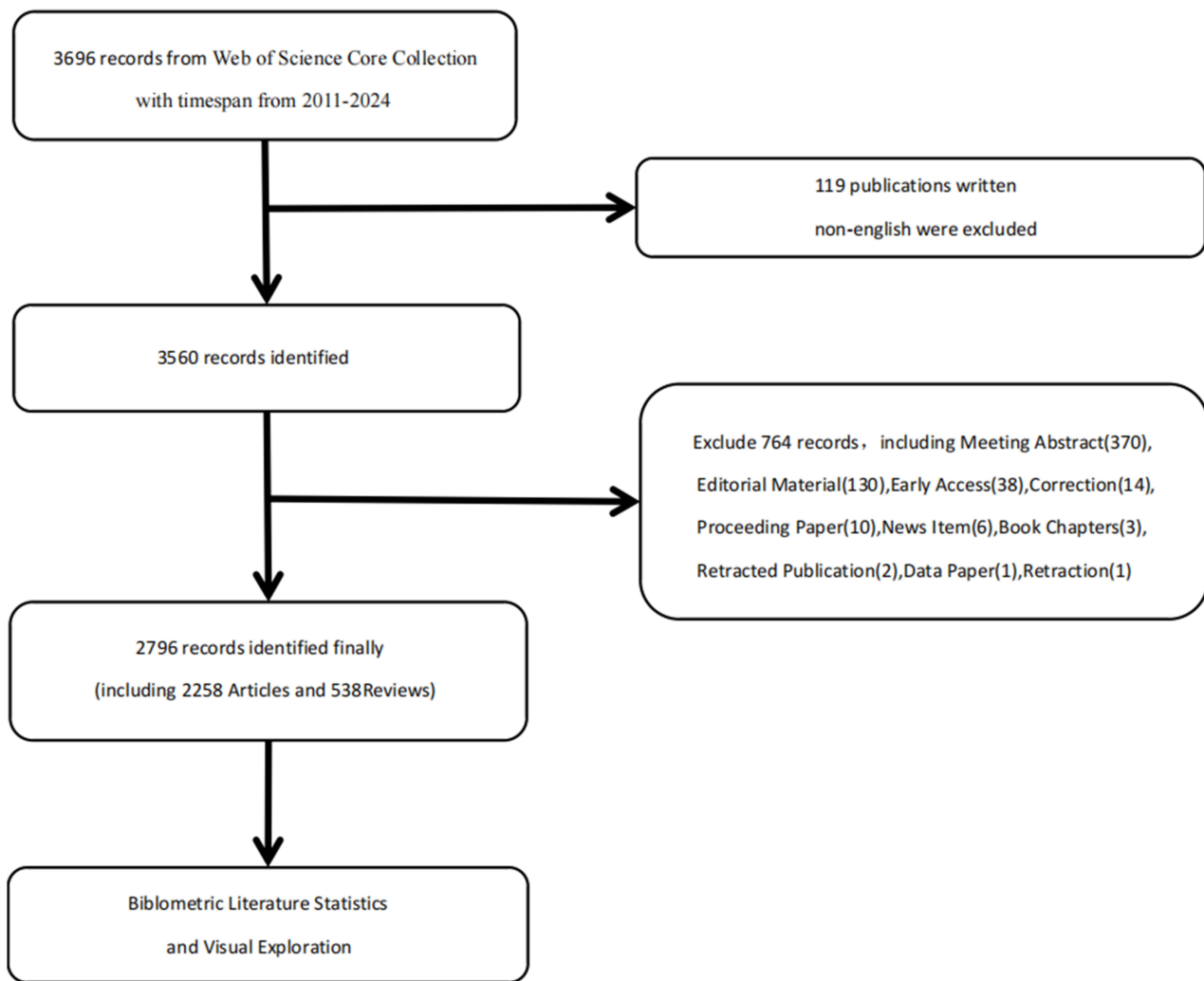


Figure 1 Flowchart of the screening process.

Moreover, public awareness of AK remains low, with limited understanding of its potential serious consequences.⁹ Currently, the best treatment for AK is the interdisciplinary guidelines on the diagnosis, treatment and prevention of actinic keratosis based on the European consensus.¹⁰ But given its potential for malignant transformation and high recurrence rate, further research is needed to develop widely accepted and standardized treatment strategies.

Methods

The Web of Science Core Collection (WOSCC) is a highly regarded academic database that indexes high-quality journals and publications across diverse disciplines.¹¹ A literature search was conducted in the WOSCC database, retrieving documents published between January 1, 2012, and December 31, 2024. The specific search strategy used was: TS = (“actinic keratosis”) AND TS = (“solar keratosis”). The search was restricted to articles and reviews published in English. Initially, 3,696 documents were identified, with the detailed filtering process illustrated in [Figure 1](#). Based on the fact that all the original data used in this study were obtained from public databases, it was deemed unnecessary to conduct an ethical review.

Results

Publication Analysis

Using the predefined retrieval strategy, annual publication data were extracted from the WOSCC and processed in Excel ([Figure 2](#)). A total of 2,796 AK-related documents were included in this study, comprising 2,258 research articles and

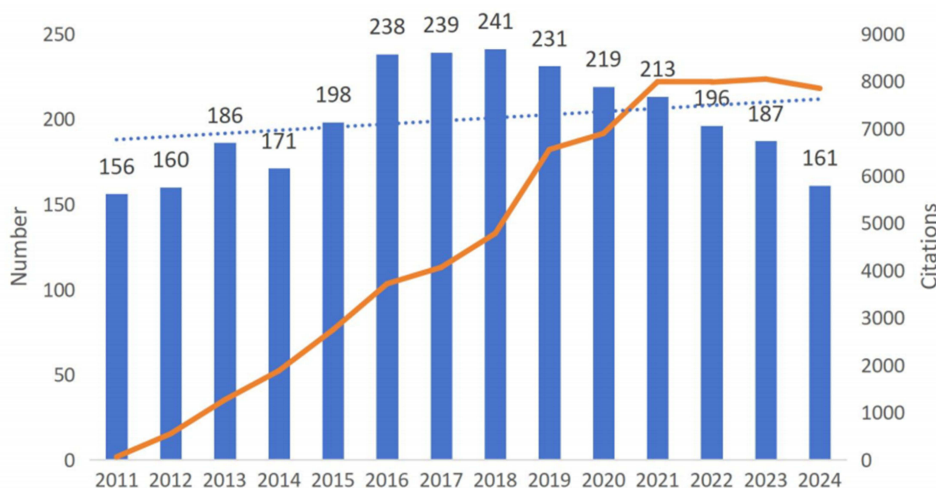


Figure 2 Temporal distribution map of publications.

538 review articles. As illustrated in Figure 2, the number of annual publications on AK from 2012 to 2024 exhibits an overall increasing trend. The first phase (2012–2015) exhibited a steady year-on-year increase in annual publications, ranging from 156 to 198 papers. The second phase (2016–2021) experienced a surge in publication volume, with over 210 papers published annually. In contrast, the third phase (2022–2024) remained relatively stable, with 161–196 papers per year. According to WOSCC statistics, the number of citations for publications within this period increased rapidly each year, reflecting the growing research interest in AK. Regarding publication volume, 2012 had the fewest publications (156 papers), while 2018 recorded the highest number (241 papers).

Country and Institutional Analysis

According to the Web of Science Core Collection (WOSCC) analysis, a total of 85 countries and regions have contributed to AK research, with the top 10 countries by publication volume illustrated in Figure 3A. The United States ranks first, publishing the highest number of articles ($n = 743$, 26.57%), followed by Germany ($n = 269$, 14.91%) and Italy ($n = 187$, 13.98%). Notably, the United States is not only the leading country in terms of publication volume but also the most frequently cited. Setting a threshold of ≥ 10 publications, a total of 41 countries/regions have established a collaborative research network (Figure 3B). The thickness of the connecting lines represents the strength of collaboration, with the United States—being the largest contributor—exhibiting the most extensive and influential international partnerships, particularly with Germany, Denmark, Spain, and Italy. Additionally, Germany, Italy, France, and China also demonstrate strong research collaborations among themselves (Figure 3C).

Using CiteSpace to analyze publishing institutions involved in AK research, we identified a total of 3,295 institutions. For visualization, we selected institutions with ≥ 10 publications (Figure 4A and B), resulting in 239 institutions. The overall collaboration among these institutions was relatively strong, with universities being the primary contributors ($n = 164$, 68.6%). The University of Copenhagen had the highest number of publications ($n = 128$, 4.57%), followed by Università di Modena e Reggio Emilia ($n = 95$, 3.39%) and Harvard University ($n = 91$, 3.25%). Betweenness centrality (BC), a concept introduced by sociologist Linton Freeman, quantifies the extent to which a node serves as an intermediary within a network.¹² A higher BC value indicates a greater role in connecting different institutions, positioning it at the center of the research network. Università di Modena e Reggio Emilia (BC = 0.16), the University of California system (BC = 0.16), and Ruhr University Bochum (BC = 0.13) exhibited high betweenness centrality, highlighting their significance as key nodes in the AK research collaboration network.



Figure 3 (A) Top 10 countries in terms of publication volume. (B) Geographical distribution of AK's global publications. (C) Visual map of countries by VOSviewer network.

Authors and Co-Cited Authors

According to the retrieval results, a total of 10,870 authors have contributed to AK research. The top 10 authors, each with more than 40 publications, are listed in [Table 1](#). For visual analysis, we selected the top 131 authors with ≥ 10 publications, and their co-authorship network is illustrated in [Figure 5](#). Among them, Pellacani G has the highest number of publications, with 74 articles since 2011. Stockfleth E ranks second with 66 publications and has established the most extensive collaborations, forming his own academic research team. Szeimies RM ranks third with 55 publications, showing a marked increase in output after 2020. [Figure 5A](#) presents the author collaboration network visualized using CiteSpace, where lines indicate co-authorship relationships. [Figure 5B](#), generated using VOSviewer, highlights author collaborations with different colors representing distinct clusters. The analysis reveals that Stockfleth E has strong collaborative ties with Zalaudek I, Ulrich M, and Szeimies RM. The AK research network is highly clustered, with many authors having only single connection lines, indicating limited broader collaboration and exchange. Notably, Belgian scholars Piérard G.E. and Piérard-Franchimont C. exhibit strong connections, while Dawson Thomas L., despite ranking fourth in publication count, has relatively few connections within the field. Co-citation analysis refers to authors who are simultaneously cited by one or more papers. [Figure 5C](#) displays the co-cited author visualization map generated using

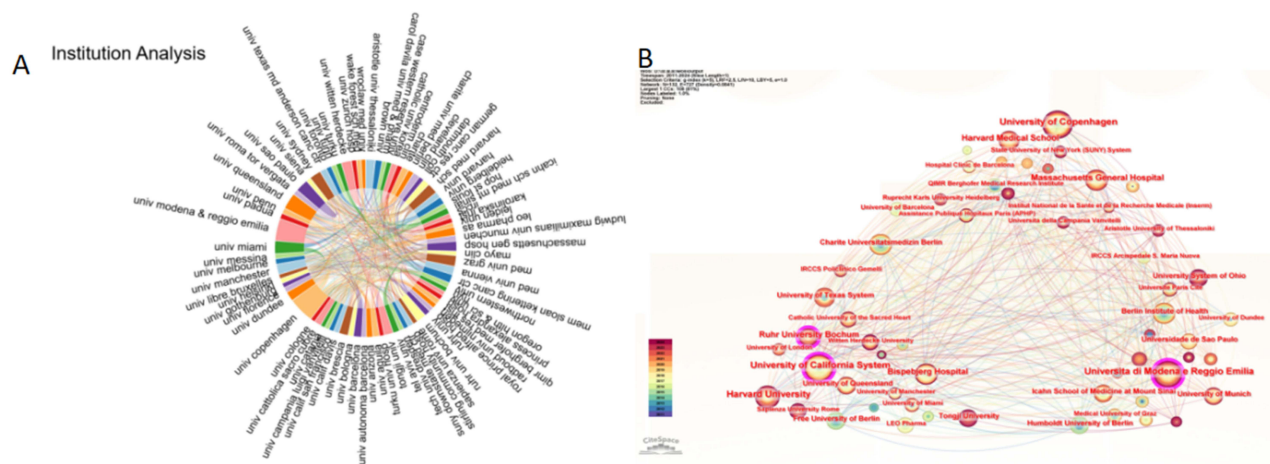


Figure 4 (A) Institutional chord diagram. Visual map of institutions by (B) CiteSpace network.

CiteSpace, while Figure 5D presents the corresponding visualization through VOSviewer. Notably, Stockfleth E exhibited significant co-citation relationships with Morton CA, Werner RN, Szeimies RM, and Marks R.

Journals and Co-Cited Journals

Journals serve as essential platforms for scholarly communication and knowledge dissemination across various fields. In this study, a total of 2,796 documents related to AK were analyzed, spanning publications in 200 journals. Table 2 presents the top 10 journals with the highest publication output. Among them, the Journal of the European Academy of Dermatology and Venereology published the most articles (n = 156, 5.6%), followed by the British Journal of Dermatology (n = 121, 4.3%), Photodiagnosis and Photodynamic Therapy (n = 118, 4.2%), Journal of Drugs in Dermatology (n = 75, 2.7%), and the Journal of the American Academy of Dermatology (n = 72, 2.6%), collectively accounting for 19.4% of all publications. The Journal Impact Factor (JIF)—calculated and published by Clarivate Analytics—is widely recognized in academia as a key metric for assessing the scholarly influence and significance of journals. Among the top 10 journals, the Journal of the American Academy of Dermatology has the highest JIF (12.8), followed by Photodiagnosis and Photodynamic Therapy (11.0) and the British Journal of Dermatology (11.0). According to the Journal Citation Reports (JCR) ranking of WoS journals, 50% of these journals are classified as Q1, with all of them specializing in the field of dermatology.

The journals British Journal of Dermatology, Journal of the American Academy of Dermatology, and Journal of the European Academy of Dermatology and Venereology have demonstrated exceptional performance in terms of citation frequency (Table 3), establishing themselves as the most influential journals within the field. Their high citation frequency

Table 1 Top 10 Authors on Research in Actinic Keratosis

Rank	Authors	Publications	Affiliation
1	Pellacani G	74	Universit di Modena e Reggio Emilia
2	Stockfleth E	66	Ruhr University Bochum
3	Szeimies RM	55	Klinikum Vest GmbH Acad Teaching Hosp
4	Argenziano G	50	Universita della Campania Vanvitelli
5	Dirschka T	50	Centroderm GmbH
6	Longo C	49	IRCCS Arcispedale S. Maria Nuova
7	Haedersdal M	47	University of Copenhagen
8	Peris K	45	Catholic University of the Sacred Heart
9	Wulf HC	41	University of Copenhagen
10	Zalaudek I	40	University of Trieste

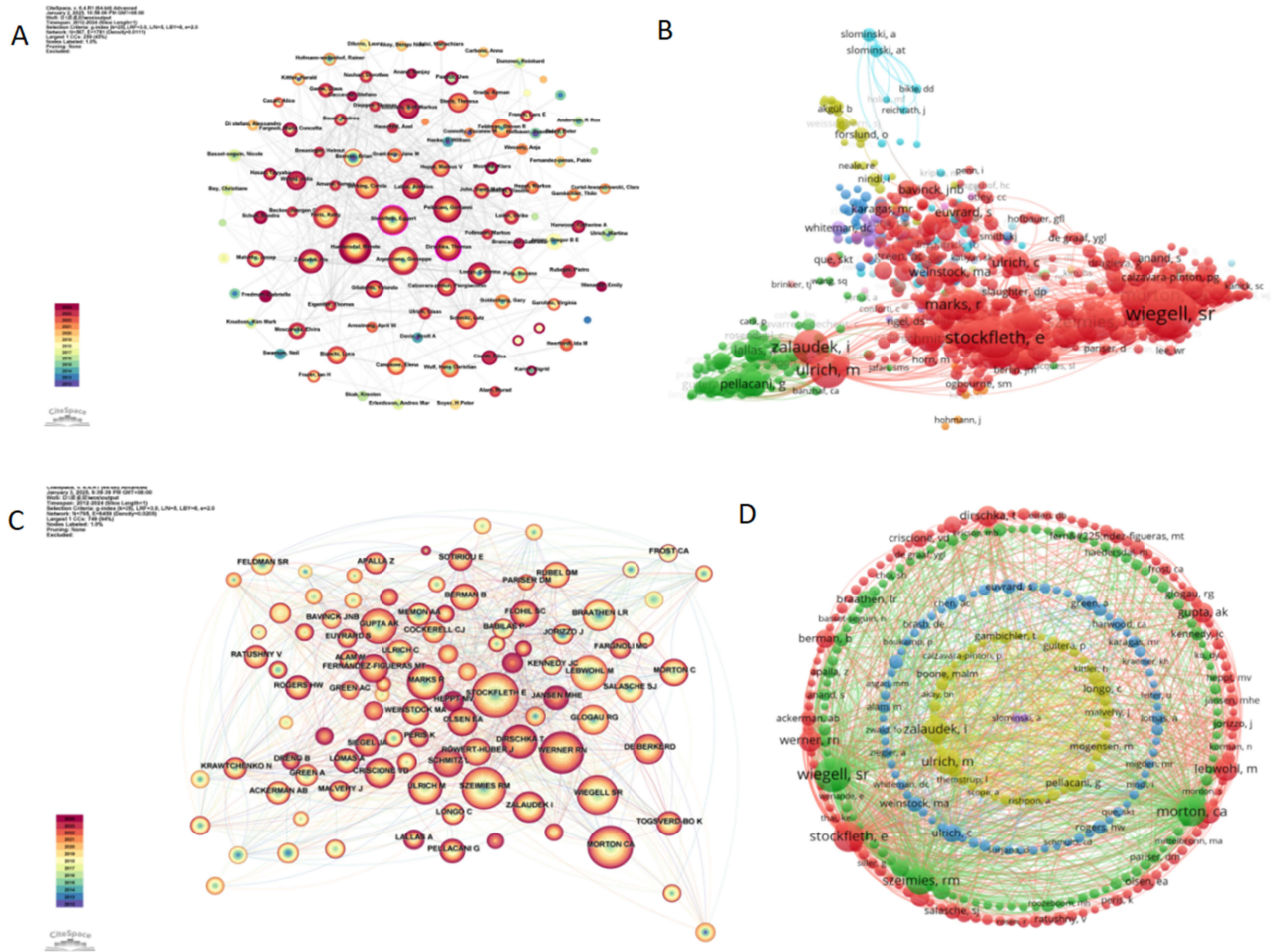


Figure 5 Visual map of authors by (A) CiteSpace network and (B) VOSviewer network. Visual map of co-cited authors by (C) CiteSpace network and (D) VOSviewer network.

reflects their substantial academic impact and the relevance of the research they disseminate. Specifically, among the top 10 journals in the field, six are ranked in the Q1, indicating a high level of academic excellence and research impact. This distribution underscores the significant academic value and research potential of dermatology studies published about AK.

It is noteworthy that most leading publishers are based in North America and Europe. Although the number of publications from Asia, particularly China, has been increasing annually, none of the top-ranked publishers currently

Table 2 Top 10 Journals in Actinic Keratosis

Rank	Journal	Publications	JIF	JCR
1	Journal of the european academy of dermatology and venereology	156	8.5	Q1
2	British journal of dermatology	121	11	Q1
3	Photodiagnosis and photodynamic therapy	118	11	Q1
4	Journal of drugs in dermatology	75	1.5	Q3
5	Journal of the american academy of dermatology	72	12.8	Q1
6	Dermatologic surgery	65	2.5	Q2
7	Giornale italiano di dermatologia e venereologia	50	2	Q3
8	Acta dermato venereologica	47	3.5	Q1
9	Photodermatology rhotimmunology photomedicine	47	2.5	Q2
10	Jouenal of dermatological treatment	45	2.9	Q2

Table 3 Top 10 Co-Cited Journals in Actinic Keratosis

Rank	Journal	Cited frequency	JIF	JCR
1	British journal of dermatology	10110	11	Q1
2	Journal of the american academy of dermatology	7842	12.8	Q1
3	Journal of the european academy of dermatology and venereology	4545	8.5	Q1
4	Journal of Investigative Dermatology	3468	5.9	Q1
5	arch dermatol	3295	4.789	Q1
6	Dermatologic surgery	2780	2.5	Q2
7	Journal of Drugs in Dermatology	1506	1.5	Q3
8	Cancer Research	1356	12.5	Q1
9	New england journal of medicine	1310	96.3	Q2
10	Photodiagnosis and Photodynamic Therapy	1242	3.1	Q2

originate from the region. Part of the reason might be that the prevalence of actinic keratosis in Asian countries is significantly lower than that in North American and European countries. This highlights the need for Asian countries, especially China, to enhance the development of internationally recognized journals to facilitate academic exchange both regionally and globally. Bibliographic coupling occurs when two papers cite the same references, suggesting a potential thematic or content-based connection between them. The journal coupling network (Figure 6A) reveals that the Journal of the European Academy of Dermatology and Venereology exhibits strong coupling relationships with the British Journal of Dermatology, Photodiagnosis and Photodynamic Therapy, Journal of Drugs in Dermatology, and the Journal of the American Academy of Dermatology, among others.

In addition to the number of publications, the influence of journals also depends on the number of times they are co-cited in specific research fields. In this work, the co-citation analysis of journals was performed using the VOSviewer software. As shown in Figure 6B, the visualization analysis includes journals that have been cited at least 100 times. The network mapping includes 150 nodes, 5 clusters, and 10,862 links. The top five journals with the most co-citations are British Journal of Dermatology (co-citation = 10,110), Journal of the American Academy of Dermatology (co-citation = 7,842), Journal of the European Academy of Dermatology and Venereology (co-citation = 4,545), Journal of Investigative Dermatology (co-citation = 3,468), and arch dermatol (co-citation = 3,295). The results indicate that many research articles published in highly cited journals are highly regarded in the field, representing the cutting edge of the discipline. As seen above, all the journals are representative journals in the field of dermatology.

In the citation double overlay analysis, the base map consists of 10,000 journals indexed in the Web of Science, represented as foundational points. After importing the literature data, CiteSpace generates an overlay visualization, producing a streamline diagram that illustrates citation relationships among journals. As shown in Figure 6C, citing journals are displayed on the left, while cited journals appear on the right. The colorful streamlines represent citation linkages between different journal categories. The visualization reveals five core citation paths: The orange path indicates that journals categorized under Molecular/Biology/Genetics primarily cite journals within Molecular/Biology/Immunology. The green and brown paths demonstrate that papers published in journals under Dentistry/Dermatology/Surgery and Medicine/Medical/Clinical are frequently cited by journals classified under Dermatology/Surgery/Dentistry and Health/Nursing/Medicine, respectively.

Hotspots and Frontiers

Keyword emergence analysis identifies terms that exhibit a significant increase in frequency within a specific time frame, revealing research trends and evolving focus areas. This method effectively highlights cutting-edge topics in the field and assists researchers in analyzing research directions, hotspots, and dynamic developmental trends. Using CiteSpace for emergent keyword analysis, a total of 2,761 high-frequency keywords were identified within the study's scope, with the top 25 keywords by frequency presented in Figure 7A. The intensity of keyword emergence—indicating the frequency of a term's occurrence within its research period—can be broadly divided into three developmental stages: 2012–2017: Prominent keywords included “imiquimod 5% cream”, “sun exposure”, and “organ transplant recipients”, suggesting that

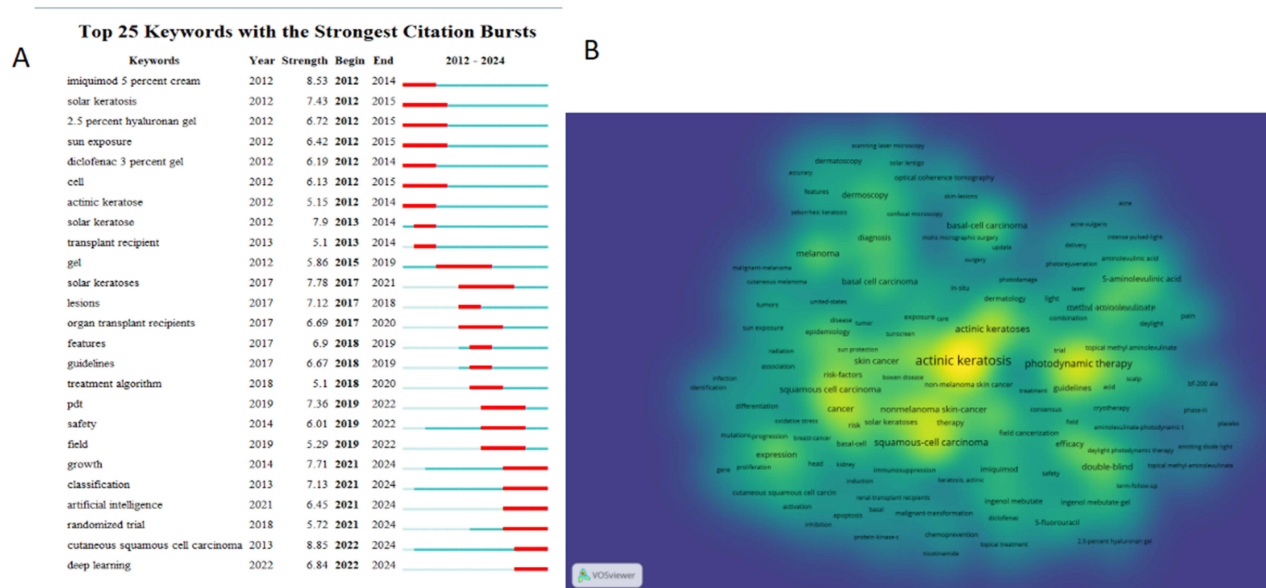


Figure 7 (A) Top 20 keywords with the strongest bursts. **(B)** Visual map of keywords.

treatment strategies. Notably, after 2012, the widespread adoption of new diagnostic techniques and an improved understanding of disease mechanisms have contributed to a significant surge in AK research.

In terms of geographical distribution, the United States and Europe lead in AK research, with the top three countries—the United States, Germany, and Italy—accounting for over 50% of total publications. This dominance may be attributed to the higher incidence of skin cancer in these regions and their well-established research foundations.¹³ The United States exhibits high research intensity in this field, with institutions such as Harvard University and the University of Copenhagen making notable contributions. This reflects active research efforts, strong scientific capabilities, and significant academic influence. AK is among the most prevalent skin diseases in the United States, yet underdiagnosis remains a challenge, leading to a substantial economic burden for patients requiring preventive treatment to avoid progression to cSCC.¹⁴ Additionally, research output from countries such as China and Australia has been steadily increasing, signifying the growing diversification of global research efforts. At the same time, collaborations between institutions are extensive, forming a large and interconnected research network that fosters international scientific exchange and knowledge sharing.

In terms of authorship, Pellacani G, Stockfleth E, Szeimies RM, Argenziano G, and Dirschka T are among the most prolific contributors to AK research. Regarding citation impact, Stockfleth E and Szeimies RM are the most influential authors in the field, having played a key role in the development of multiple AK treatment guidelines. Professor Stockfleth E specializes in clinical treatment research for AK,¹⁵ publishing numerous studies that investigate various therapeutic approaches, assess their clinical efficacy, and provide expert treatment recommendations to guide the optimization of personalized treatment protocols. Professor Szeimies RM is a leading expert in photodynamic therapy (PDT) research. In recent controlled trials, he has advocated for the use of 10% aminolevulinic acid (ALA) gel (BF-200 ALA) in PDT, combined with narrow-spectrum red light illumination, as the most effective treatment strategy. This approach has demonstrated a higher clearance rate compared to broad-spectrum light-based PDT.¹⁶ He has also conducted preliminary investigations into the treatment of AK patients with compromised immune systems. Notably, among the top ten most prolific authors, there is a clear team-based research dynamic. Szeimies RM, Haedersdal M, and Peris K have collaborated on a substantial number of studies and publications, demonstrating a strong collaborative network. Similarly, Argenziano G and Zalaudek I have established close research partnerships. The high degree of interconnectivity among authors and research teams suggests that AK research is characterized by strong team cohesion and a tendency toward cluster-based collaboration.

Hotspots and Frontiers

Genomic Studies of AK and cSCC

Keyword analysis reveals that current research hotspots and emerging trends in AK focus on its close association with cSCC. In recent years, genomic studies have provided critical insights into the molecular mechanisms underlying the progression of AK to cSCC. Research has identified overlapping genetic mutations between AK and cSCC, with the TP53 gene mutation occurring at a high frequency in both conditions, suggesting a pivotal role in malignant transformation.^{4,17} TP53 is a tumor suppressor gene, and its mutation disrupts cell cycle regulation, allowing DNA-damaged cells to evade apoptosis, thereby increasing the risk of carcinogenesis. Additionally, mutations in the NOTCH1 and NOTCH2 genes have been identified as potential drivers of AK progression to cSCC, further highlighting their role in malignant transformation.^{18–20} Genes involved in the TGF- β signaling pathway exhibit significant mutations in cSCC. During the progression from AK to cSCC, TGF- β pathway expression gradually declines, and its dysregulation is considered a critical step in the carcinogenic process.²¹ Compared to AK, cSCC exhibits a significantly higher percentage of basal cells, particularly within the Basal1 gene subgroup, which is characterized by high expression of stem cell-related markers. This finding suggests that impaired terminal differentiation may play a crucial role in cSCC progression. Additionally, tumor progression is closely associated with the tumor microenvironment (TME), highlighting its potential impact on cSCC development and therapeutic response.²² Zou DD²³ and others conducted a cellular communication analysis of the TME in collected cSCC samples and found that higher malignancy was associated with stronger interactions between keratinocytes and TME cells. In summary, the differences in gene expression profiles between AK and cSCC provide valuable insights into disease progression. However, research on the molecular subtypes of AK remains in its early stages. Integrating these genetic characteristics with clinical manifestations and patient prognosis remains a critical challenge that requires further investigation.

Common Pathogenesis of AK and cSCC

As a precursor lesion to cSCC, AK often exhibits indistinct histopathological boundaries with cSCC, leading to a high degree of overlap in pathological features. This similarity is so pronounced that even gene microarray analyses have failed to identify significant genetic differences between the two conditions.²⁴ The shared pathogenesis of AK and cSCC involves multiple molecular pathways, particularly those related to keratin expression, cell cycle regulation, and the differential expression of molecular markers.

The shared pathogenesis of AK and cSCC includes: (1) Differential activation of the MAPK signaling pathway, which enhances cell migratory capacity, facilitating basement membrane disruption and invasion into adjacent tissues.²⁵ Studies have shown that in cSCC tissues, overactivation of the MAPK signaling pathway significantly enhances cell motility and invasiveness. Additionally, aberrant MAPK pathway activation not only promotes uncontrolled cell proliferation but also impairs DNA damage repair mechanisms, contributing to genomic instability and tumor progression.²⁶ (2) AK and cSCC exhibit significant similarities in the expression of cell cycle-related molecular markers, particularly in the altered expression patterns of regulatory proteins and cyclins (such as Cyclin D1 and Cyclin E) during the G1/S phase transition, as well as in the dysregulation of cyclin-dependent kinase inhibitors (CDKIs).²⁷ The changes in these molecular markers reveal the imbalance in cell cycle regulation. The overexpression of Cyclin D1 is common in both, suggesting abnormal cell proliferation in these diseases.²⁸ Cyclin D1 exerts its function by binding to CDK4/6, thereby activating downstream signaling pathways and promoting cell cycle progression into the S phase. Additionally, the upregulation of Cyclin E further facilitates the G1-to-S phase transition, increasing DNA replication opportunities and creating a favorable environment for malignant transformation. In AK, dysregulation of these cyclins may have already occurred, allowing cells to proliferate unchecked, bypassing normal repair and surveillance mechanisms, ultimately leading to the development of cSCC. These findings provide a conceptual framework for a deeper understanding of the molecular mechanisms underlying AK-to-cSCC progression and lay the foundation for early diagnosis, prevention, and personalized treatment strategies.

The Prospects of Personalized Treatment

Despite advancements in research, clinical diagnosis and treatment of AK remain challenging. Enhancing the diagnostic and therapeutic framework is crucial for early detection, risk stratification, and personalized treatment strategies. Currently, available treatment modalities include diclofenac (DCF), 5-fluorouracil (5-FU), imiquimod (IMI), 5-aminolevulinic acid (ALA)-photodynamic therapy (PDT), and cryotherapy.²⁹ A field-directed intervention efficacy study 5-FU as the most effective treatment in terms of complete and partial clearance rates, while having the fewest side effects.^{30,31} The latest AK treatment guidelines emphasize the importance of selecting the optimal combination therapy based on the patient's individual clinical profile.³² The integration of dermatoscopy and reflectance confocal microscopy has significantly improved the precision of treatment planning.³³ For immunosuppressed patients, personalized treatment approaches are particularly critical, as immune status significantly influences treatment response.³⁴ Moreover, ongoing research into genetics-based personalized therapy aims to optimize treatment strategies and enhance patient adherence, ultimately leading to better clinical outcomes for AK patients.³⁵ As a result, personalized treatment is not only the future direction of AK management but also a key factor in improving patient quality of life and treatment efficacy.

Limitations

All data in this study were obtained from the WOSCC, which is widely regarded as one of the most reliable and comprehensive academic databases. A bibliometric analysis was conducted to assess the current status and research hotspots in AK, providing valuable insights for researchers. However, despite WOSCC's extensive coverage of high-quality literature, it may under-represent contributions from non-English publications and research conducted in certain regions, such as the Asia-Pacific. Additionally, this study focused on literature published between 2012 and 2024, which may have led to the exclusion of earlier studies with advanced insights, including meta-analyses, case reports, and other important findings outside this timeframe.

Conclusion

This study, leveraging data from the WOSCC and integrating bibliometric analysis with visualization techniques, reveals that current research hotspots and frontiers in AK primarily focus on the mechanisms underlying AK-to-cSCC transformation and the advancement of personalized treatment approaches. Future treatment strategies will increasingly rely on individual patient characteristics, including immune function, genetic background, lesion attributes, and treatment response. The integration of digital technologies has significantly enhanced precision in diagnosis and therapeutic monitoring, particularly through the use of dermatoscopy and reflectance confocal microscopy (RCM). These advancements refine treatment planning and offer valuable insights and research directions for further in-depth research on AK pathogenesis and management.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, acquisition of data, analysis and interpretation, 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

The study was supported by the Sichuan Provincial Department of Science and Technology Seedling Cultivation Foundation (No. MZGC20240096).

Disclosure

The authors report no conflicts of interest in this work.

References

- Malvehy J, Stratigos AJ, Bagot M, Stockfleth E, Ezzedine K, Delarue A. Actinic keratosis: current challenges and unanswered questions. *J Eur Acad Dermatol Venereol.* 2024;38(Suppl 5):3–11. doi:10.1111/jdv.19559
- Röwert-Huber J, Patel MJ, Forschner T, et al. Actinic keratosis is an early in situ squamous cell carcinoma: a proposal for reclassification. *Br J Dermatol.* 2007;156(suppl 3):8–12. doi:10.1111/j.1365-2133.2007.07860.x
- Thamm JR, Welzel J, Schuh S. Diagnosis and therapy of actinic keratosis. *J Dtsch Dermatol Ges.* 2024;22(5):675–690. doi:10.1111/ddg.15288
- Yaldiz M. Prevalence of actinic keratosis in patients attending the dermatology outpatient clinic. *Medicine.* 2019;98(28):e16465. doi:10.1097/MD.00000000000016465
- Jiyad Z, Marquart L, O'Rourke P, et al. The natural history of actinic keratoses in organ transplant recipients. *J Am Acad Dermatol.* 2017;76(1):162–164. doi:10.1016/j.jaad.2016.09.003
- Footo JA, Harris RB, Giuliano AR, et al. Predictors for cutaneous basal- and squamous-cell carcinoma among actinically damaged adults. *Int J Cancer.* 2001;95(1):7–11. doi:10.1002/1097-0215(20010120)95:1<7::AID-IJC1001>3.0.CO;2-X
- Quaedvlieg PJ, Tirsli E, Thissen MR, Krekels GA. Actinic keratosis: how to differentiate the good from the bad ones? *Eur J Dermatol.* 2006;16(4):335–339.
- Heerfordt IM, Nissen CV, Poulsen T, et al. Thickness of actinic keratosis does not predict dysplasia severity or P53 expression. *Sci Rep.* 2016;6:33952. doi:10.1038/srep33952
- MacKie RM. Awareness, knowledge and attitudes to basal cell carcinoma and actinic keratoses among the general public within Europe. *J Eur Acad Dermatol Venereol.* 2004;18:552–555. doi:10.1111/j.1468-3083.2004.00993.x
- Kandolf L, Peris K, Malvehy J, Mosterd K, Hept MV, Fargnoli MC, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists (Union Européenne des Médecins Spécialistes). European consensus-based interdisciplinary guideline for diagnosis, treatment and prevention of actinic keratoses, epithelial UV-induced dysplasia and field cancerization on behalf of European Association of Dermato-Oncology, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists (Union Européenne des Médecins Spécialistes). *J Eur Acad Dermatol Venereol.* 2024;38(6):1024–1047. doi:10.1111/jdv.19897
- Ma L, Ma J, Teng M, Li Y. Visual analysis of colorectal cancer immunotherapy: a bibliometric analysis from 2012 to 2021. *Front Immunol.* 2022;13:843106. doi:10.3389/fimmu.2022.843106
- Brandes U. A faster algorithm for betweenness centrality. *J Math Sociol.* 2001;25:163–177. doi:10.1080/0022250X.2001.9990249
- Flohil SC, van der Leest RJ, Dowlatshahi EA, Hofman A, de Vries E, Nijsten T. Prevalence of actinic keratosis and its risk factors in the general population: the Rotterdam Study. *J Invest Dermatol.* 2013;133(8):1971–1978. doi:10.1038/jid.2013.134
- Stockfleth E. The importance of treating the field in actinic keratosis. *J Eur Acad Dermatol Venereol.* 2017;31(Suppl 2):8–11. doi:10.1111/jdv.14092
- Stockfleth E, Hept MV, Bégeault N, Delarue A. Evaluating the efficacy and safety of 4% 5-fluorouracil cream in patients with actinic keratosis: an expert opinion. *Acta Derm Venereol.* 2023;103:adv11954. doi:10.2340/actadv.v103.11954
- Bierhoff E, Szeimies R-M, Reinhold U, Dirschka T. High efficacy of red light photodynamic therapy with 10 % aminolevulinic acid gel irrespective of the extent of keratinocyte atypia in actinic keratosis – exploratory post-hoc analysis of three pivotal Phase III trials, Photodiagnosis and Photodynamic Therapy. 2024;50:104361.
- Ortonne JP. From actinic keratosis to squamous cell carcinoma. *Br J Dermatol.* 2002;146(Suppl 61):20–23. doi:10.1046/j.1365-2133.146.s61.6.x
- Kim YS, Jung SH, Park YM, et al. Targeted deep sequencing reveals genomic alterations of actinic keratosis/cutaneous squamous cell carcinoma in situ and cutaneous squamous cell carcinoma. *Exp Dermatol.* 2023;32(4):447–456. doi:10.1111/exd.14730
- Kim YS, Shin S, Jung SH, et al. Genomic progression of precancerous actinic keratosis to squamous cell carcinoma. *J Invest Dermatol.* 2022;142(3 Pt A):528–538.e8. doi:10.1016/j.jid.2021.07.172
- Hedberg M, Seykora JT. Clarifying progress on the genomic landscape of actinic keratosis. *J Invest Dermatol.* 2021;141(7):1622–1624. doi:10.1016/j.jid.2021.02.761
- Thomson J, Bewicke-Copley F, Anene CA, et al. The genomic landscape of actinic keratosis. *J Invest Dermatol.* 2021;141(7):1664–1674.e7. doi:10.1016/j.jid.2020.12.024
- Parker TM, Gupta K, Palma AM. Cell competition in intratumoral and tumor microenvironment interactions. *EMBO J.* 2021;40(17):e107271. doi:10.15252/embj.2020107271
- Zou DD, Sun YZ, Li XJ, et al. Single-cell sequencing highlights heterogeneity and malignant progression in actinic keratosis and cutaneous squamous cell carcinoma. *Elife.* 2023;12:e85270. doi:10.7554/eLife.85270
- Ra SH, Li X, Binder S. Molecular discrimination of cutaneous squamous cell carcinoma from actinic keratosis and normal skin. *Mod Pathol.* 2011;24(7):963–973. doi:10.1038/modpathol.2011.39
- Li N, Zhang K, Mu X, et al. Astragalin attenuates UVB radiation-induced actinic keratosis formation. *Anticancer Agents Med Chem.* 2018;18(7):1001–1008. doi:10.2174/1871520618666171229190835
- Lambert SR, Mladkova N, Gulati A, et al. Key differences identified between actinic keratosis and cutaneous squamous cell carcinoma by transcriptome profiling. *Br J Cancer.* 2014;110(2):520–529. doi:10.1038/bjc.2013.760
- Balcer A, Sperga M, Čema I, et al. Expression of p53, p63, p16, Ki67, Cyclin D, Bcl-2, and CD31 markers in actinic keratosis, in situ squamous cell carcinoma and normal sun-exposed skin of elderly patients. *J Clin Med.* 2023;12(23):7291. doi:10.3390/jcm12237291
- Brasnanac D, Stojkovic-Filipovic J, Bosic M, Tomanovic N, Manojlovic-Gacic E. Expression of G1/S-cyclins and cyclin-dependent kinase inhibitors in actinic keratosis and squamous cell carcinoma. *J Cutan Pathol.* 2016;43(3):200–210. doi:10.1111/cup.12623
- Gupta AK, Paquet M, Villanueva E, Brintnell W. Interventions for actinic keratoses. *Cochrane Database Syst Rev.* 2012;12(12):CD004415. doi:10.1002/14651858.CD004415.pub2
- Jansen MHE, Kessels JPHM, Nelemans PJ, et al. Randomized trial of four treatment approaches for actinic keratosis. *N Engl J Med.* 2019;380(10):935–946. doi:10.1056/NEJMoa1811850

31. Ezzedine K, Painchault C, Brignone M. Systematic literature review and network meta-analysis of the efficacy and acceptability of interventions in actinic keratoses. *Acta Derm Venereol.* 2021;101(1):adv00358. doi:10.2340/00015555-3690
32. Morton C, Baharlou S, Basset-Seguin N, et al. Expert recommendations on facilitating personalized approaches to long-term management of actinic keratosis: the Personalizing Actinic Keratosis Treatment (PAKT) project. *Acta Derm Venereol.* 2023;103:adv6229. doi:10.2340/actadv.v103.6229
33. Soare C, Cozma EC, Celarel AM, et al. Digitally enhanced methods for the diagnosis and monitoring of treatment responses in actinic keratoses: a new avenue in personalized skin care. *Cancers.* 2024;16(3):484. doi:10.3390/cancers16030484
34. Szeimies RM, Ulrich C, Ferrández-Pulido C, et al. The “Personalising actinic keratosis treatment for Immunocompromised Patients” (IM-PAKT) Project: an expert panel opinion. *Dermatol Ther.* 2024;14(7):1739–1753. doi:10.1007/s13555-024-01215-y
35. Del Regno L, Catapano S, Di Stefani A, Cappilli S, Peris K. A review of existing therapies for actinic keratosis: current status and future directions. *Am J Clin Dermatol.* 2022;23(3):339–352. doi:10.1007/s40257-022-00674-3

Clinical, Cosmetic and Investigational Dermatology

Publish your work in this journal

Clinical, Cosmetic and Investigational Dermatology is an international, peer-reviewed, open access, online journal that focuses on the latest clinical and experimental research in all aspects of skin disease and cosmetic interventions. This journal is indexed on CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinical-cosmetic-and-investigational-dermatology-journal>

Dovepress
Taylor & Francis Group