



## Research hotspots and frontiers in acral melanoma: A bibliometric analysis from 1999 to 2023

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### ABSTRACT

**Background:** Acral melanoma (AM), an aggressive subtype of melanoma with poor prognosis, has been increasingly studied. The present study aims to discuss the current status, hotspots and future directions of AM studies through visualized analysis with bibliometrics and knowledge graph.

**Method:** Publications related to acral melanoma from January 1999 to May 2023 were searched and retrieved from the Web of Science. Data extraction and visualization of the top 10 publications by year of publication, journal, country and core author were performed using R Studio (Version 4.3.0) and Scimago Graphica (Version 1.0.34). Co-reference graphs regarding country/region, organization, author, and keywords, as well as reference collaborative network, co-occurrence network, and references were plotted using VOSviewer (Version 1.6.19) and CiteSpace (Version 6.2.R3).

**Results:** A total of 1387 articles related to AM published in English from 1999 to 2023 were included in the present study. A total of 7499 authors were from 2092 organizations in 50 countries. The articles were published in 356 journals, involving 4131 keywords and 28,200 references. The 1387 articles related to AM had been cited a total of 10,014 times by the time of this study. The result showed that *Journal of the American Academy of Dermatology* had the largest number of citations and citation rate, with a total of 60 publications having been cited 2191 times. Having the top three productivity institutions in the world, the US is the most productive country in this field, with a total of 361 publications. The authors with the highest number of publications were Guo Jun (n = 43) and Si Lu (n = 38) from Peking University. The keyword burstiness test found that “ipilimumab”, “open label”, “efficacy” and “nivolumab” appeared most frequently in recent years. The co-cited reference timeline graph showed that the clustering of “advanced melanoma” and “melanocytic lesion” has been a hotspot since 2016.

**Conclusions:** The number of AM-related studies has been increasing. The clinical characteristics and immunotherapy of AM are still key research directions, with the US playing a leading role in

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this field. This bibliometric analysis found up to 1387 publications, which not only comprehensively and quantitatively reflected the research trends and hotspots, but also provided a theoretical basis for future studies of AM. Researchers can benefit from choosing the right journals and finding potential collaborators or partner institutions.

### 1. Introduction

Acral melanoma (AM) is a subtype of aggressive melanoma that mainly occurs on soles, palms and nail beds. According to several population-based epidemiological studies, the incidence of AM is higher in darker-skinned Latin American, African, Asian, and Hispanic populations, whereas cutaneous melanoma is found more common in fair-skinned Europeans, which may be related to an increase in the statistical denominator due to the high prevalence of cutaneous melanoma in fair-skinned Europeans [1–4]. Due to the special lesion sites, it is barely affected by ultraviolet rays, but trauma and mechanical stress can promote its progression [5,6]. According to the estimation of The World Health Organization, the incidence and mortality of melanoma are expected to increase by over 60 % by the year 2040 [7], especially in low- and middle-income countries, while AM is also the most common subtype in these countries. Compared to other subtypes of melanoma, AM is associated with diagnostic delays, high local recurrence rate and poor prognosis, which has significantly increased the social burden and financial pressure of patients. In recent years, the development of immune checkpoint inhibitors and targeted therapies has greatly altered the clinical outcomes of melanoma and the prognosis of patients. However, patients with AM often have relatively low immunogenicity, making them benefit less from immunotherapy and targeted therapies compared to patients with other forms of melanoma. At present, the genomic landscape, risk factors and diagnostic criteria of AM are yet to be elucidated, and there is still a lack of effective treatment options; thus, further research on AM is warranted.

In contrast to the conventional systematic review, bibliometrics can provide a quantitative and visualized analysis of thousands of scientific publications in terms of country/region, organization, author, and keyword, in order to understand the development, hotspots and trends of a certain field [8,9]. Bibliometrics has become an important research tool in medical science [10] to determine the influence or value of publications using information visualization tools such as CiteSpace and VOSviewer [8]. In the last two years, several bibliometric studies on melanoma have been published, with focuses on the immunotherapy of melanoma [11–13] [11–13]; there were also two studies examining uveal melanoma [14,15] and a study on conjunctival melanoma [16]. Despite the increased attention to AM from researchers, there are few bibliometric studies in this field. Therefore, the present study aimed to explore the development of this field using visualized analysis of publications related to AM, as well as present the latest research trends and provide a reference and more ideas for further studies.

### 2. Methods

Keywords “TS=(acral melanoma) OR TS=(acral lentiginous melanoma) OR TS=(nail melanoma)” were searched in the Web of Science Core Collection (WoSCC) for publications in English from January 1, 1999 to May 15, 2023 (Fig. 1). After excluding 13 publications for incomplete information or duplications, we finally retrieved 1387 publications and recorded their titles, authors,

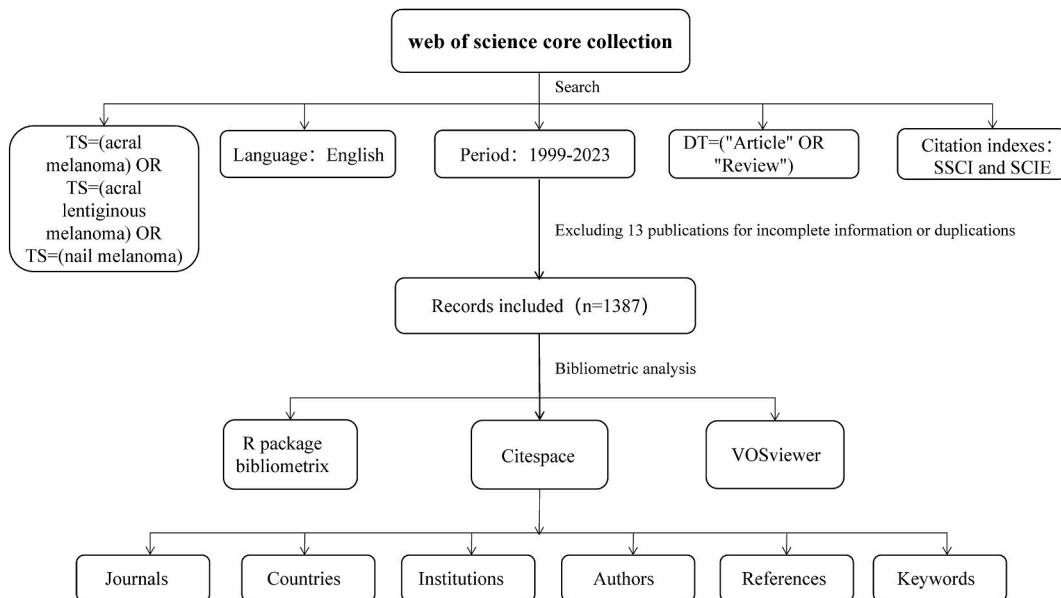


Fig. 1. Search strategy and process.

research organizations, abstracts, journals, time of publication and other relevant information. Visualized analyses were performed using Studio (Version 4.3.0), Scimago Graphica (Version 1.0.34), VOSviewer (Version 1.6.19) and CiteSpace (Version 6.2.R3), and co-reference graphs regarding country/region, organization, author, and keywords, as well as reference collaborative network, co-occurrence network, and references were plotted. This study focused on publications from January 01, 1999 to May 15, 2023 and did not involve human or animal studies or experiments. Thus, ethical approval was not required for this study.

### 3. Results

Through Web of Science Core Collection (WoSCC) search, we finally obtained 1387 articles related to AM that were published after 1999. Overall, the number of publications increased steadily. These publications were cited a total of 10,014 times, with an average citation frequency of 28.05 per article. According to the annual statistics, we found a significant association between the year of publication and the number of publications ( $R^2 = 0.8783$ , Fig. 2). To date, there have been 35 articles published in 2023, and it was expected that there would be a total of over 150 articles published by the end of this year. Interestingly, we found that only 16 articles were published in 2005, but their average number of citations was as high as 154.56. With the increase in publications, AM has become a new topic of growing interest among researchers.

#### 3.1. Distribution of publications by journal

The 1387 articles were published in a total of 356 journals, and the top 10 journals containing the largest number of publications included in the present study are listed in Table 1. Containing 60 publications included in the present study, Journal of the American Academy of Dermatology (JAAD) ranked the first, followed by Journal of Dermatology (43 publications) and British Journal of Dermatology (42 publications). Impact factor (IF) and H-index are key indicators for evaluating the impact of a journal. Among the top 10 journals, JAAD and BJD had an IF of over 10; they also had the largest number of citations, i.e., 2191 and 1526, respectively. In terms of circulation and total citations, JAAD appeared to be the most popular journal for the study of AM. We also presented the interdisciplinary citation biplot overlay regarding journals related to AM (Fig. 3). This graph determined three colors for main citations ways, indicating that publications in molecular/biological/immunological fields were significantly affected by those in molecular/biological/genetic fields, and that publications in dentistry/dermatology/surgery were mainly cited by those in molecular/biology/genetic and health/nursing/medical fields. In addition, publications in medical/clinical fields were found to be affected by those in molecular/biological/genetic and health/nursing/medical fields.

#### 3.2. Distribution of publications by country/region

The 1387 publications were sourced from 50 countries. The top 10 most productive countries are listed in Table 2. The US had the largest number of publications (361), accounting for 26 % of all the publications; it also had the largest number of citations (16,461). The US was followed by three Asian countries, namely China (173 publications), Japan (135 publications) and Korea (117

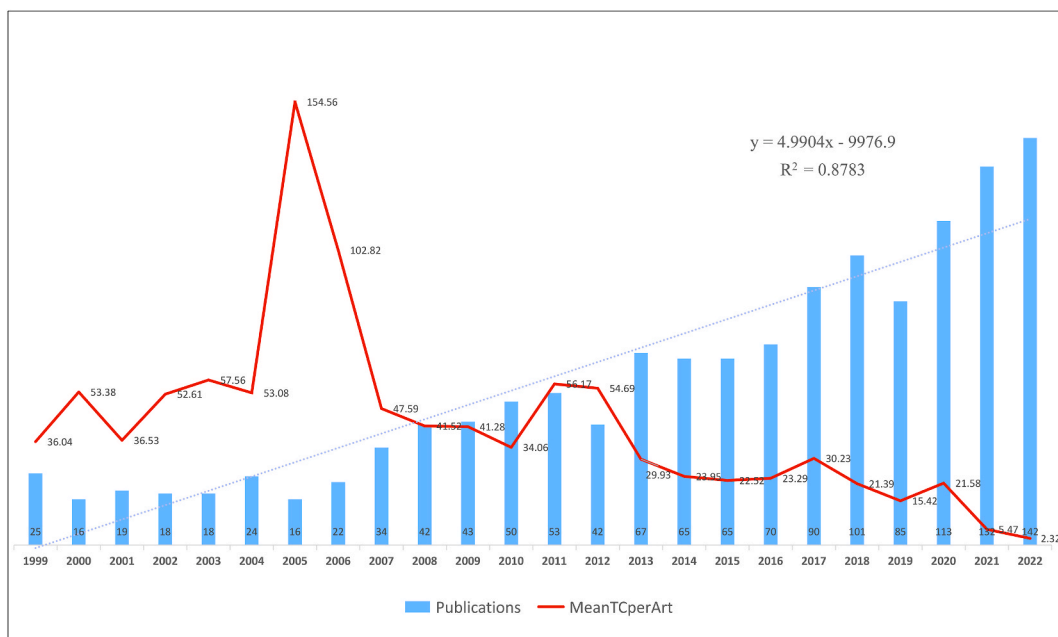
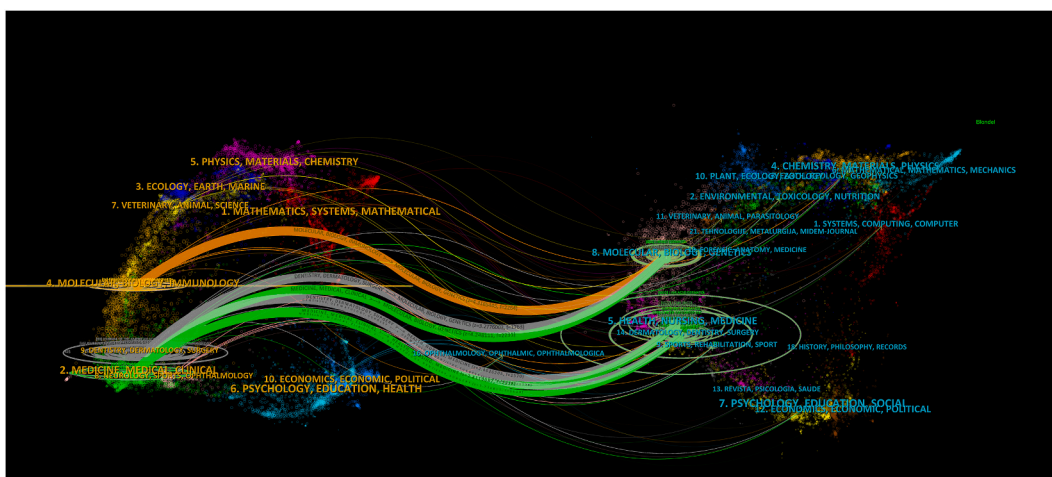


Fig. 2. Publications related to acral melanoma from 1999 to 2023 and the average number of citations.

**Table 1**  
Top 10 journals containing the largest number of publications in the present study.

Rank	Journal	Publications	Total citations	Citations per publication	H-index	G-index	Impact factor (2022)	JCR
1	<i>Journal of the American Academy of Dermatology</i>	60	2191	36.52	24	46	13.8	Q1
2	<i>Journal of Dermatology</i>	43	472	10.98	13	20	3.1	Q2
3	<i>British Journal of Dermatology</i>	42	1526	36.33	24	39	10.3	Q1
4	<i>American Journal of Dermatopathology</i>	39	513	13.15	14	21	1.1	Q4
5	<i>Journal of the European Academy of Dermatology and Venereology</i>	36	481	13.36	14	20	9.2	Q1
6	<i>Melanoma Research</i>	36	730	20.28	17	26	2.2	Q3
7	<i>Dermatologic Surgery</i>	33	731	22.15	14	16	2.4	Q2
8	<i>Journal of Cutaneous Pathology</i>	32	390	12.19	10	18	1.7	Q3
9	<i>International Journal of Dermatology</i>	29	303	10.45	12	16	3.6	Q1
10	<i>Pigment Cell &amp; Melanoma Research</i>	24	623	25.96	13	24	4.3	Q1



**Fig. 3.** Biplot overlay of journal categories. Citing articles are on the left side, and cited articles are on the right side; the curves are connections of citations.

publications). Most of the studies were completed by researchers from a single country, but international collaboration was common (Fig. 4A and B). Italy and Germany had the highest MCP Ratio and collaborated the most with other countries. The VOSviewer software was used to perform visualized analysis on countries with at least 5 a.m.-related publications, with countries marked by the same color showing closer collaborations (Fig. 4C and D).

**3.3. Publication distribution by organizations**

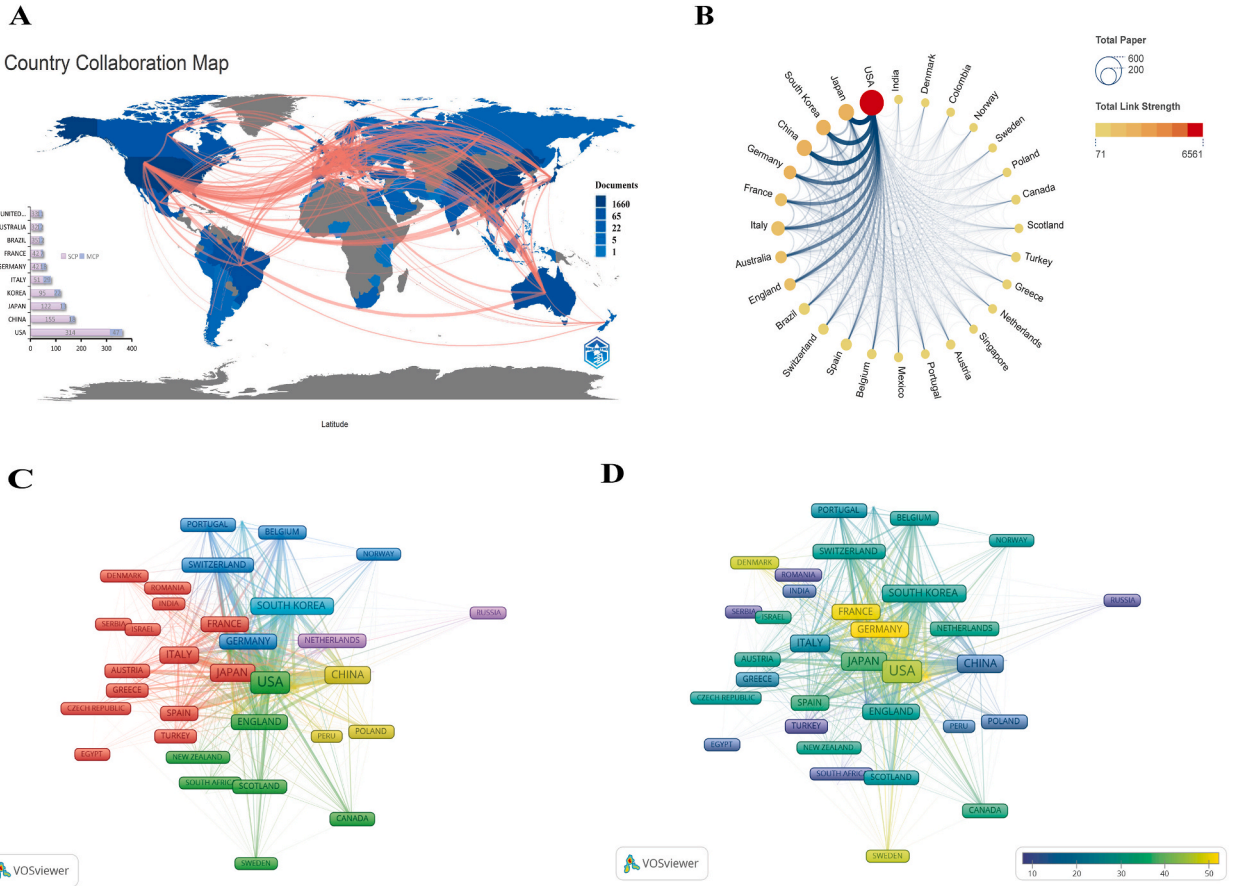
A total of 2092 organizations had AM-related articles published, and the top 10 most productive organizations are presented in (Table 3). The top three most productive organizations were the Memorial Sloan Kettering Cancer Center (104 publications), the

**Table 2**  
Top 10 countries with the largest number of publications related to acral melanoma.

Rank	Country	Paper	Percentage (N/1387)	SCP	MCP	MCP ratio	Total number of citations	Average number of citations
1	USA	361	26.0 %	314	47	0.13	16461	45.60
2	CHINA	173	12.5 %	155	18	0.104	2715	15.69
3	JAPAN	135	9.7 %	122	13	0.096	3208	23.76
4	KOREA	117	8.4 %	95	22	0.188	1485	12.69
5	ITALY	80	5.8 %	51	29	0.362	1474	18.43
6	GERMANY	60	4.3 %	42	18	0.3	2143	35.72
7	FRANCE	49	3.5 %	42	7	0.143	2226	45.43
8	BRAZIL	47	3.4 %	35	12	0.255	557	11.85
9	AUSTRALIA	44	3.2 %	32	12	0.273	2136	48.55
10	UNITED KINGDOM	44	3.2 %	33	11	0.13	1043	23.70

Abbreviations: SCP, single country publication; MCP: multiple country publication.





**Fig. 4.** Analysis of the publications by countries. (A) The number of single country publication (SCP) and multiple country publication (MCP) of the 10 most productive countries. Network mapping of the collaboration between different countries (C) Visualization of the publications and inter-national collaboration (D) Clusters network visualization map of journals. The size of the square indicates the number of publications, and the thickness of the line indicates the strength of connection.

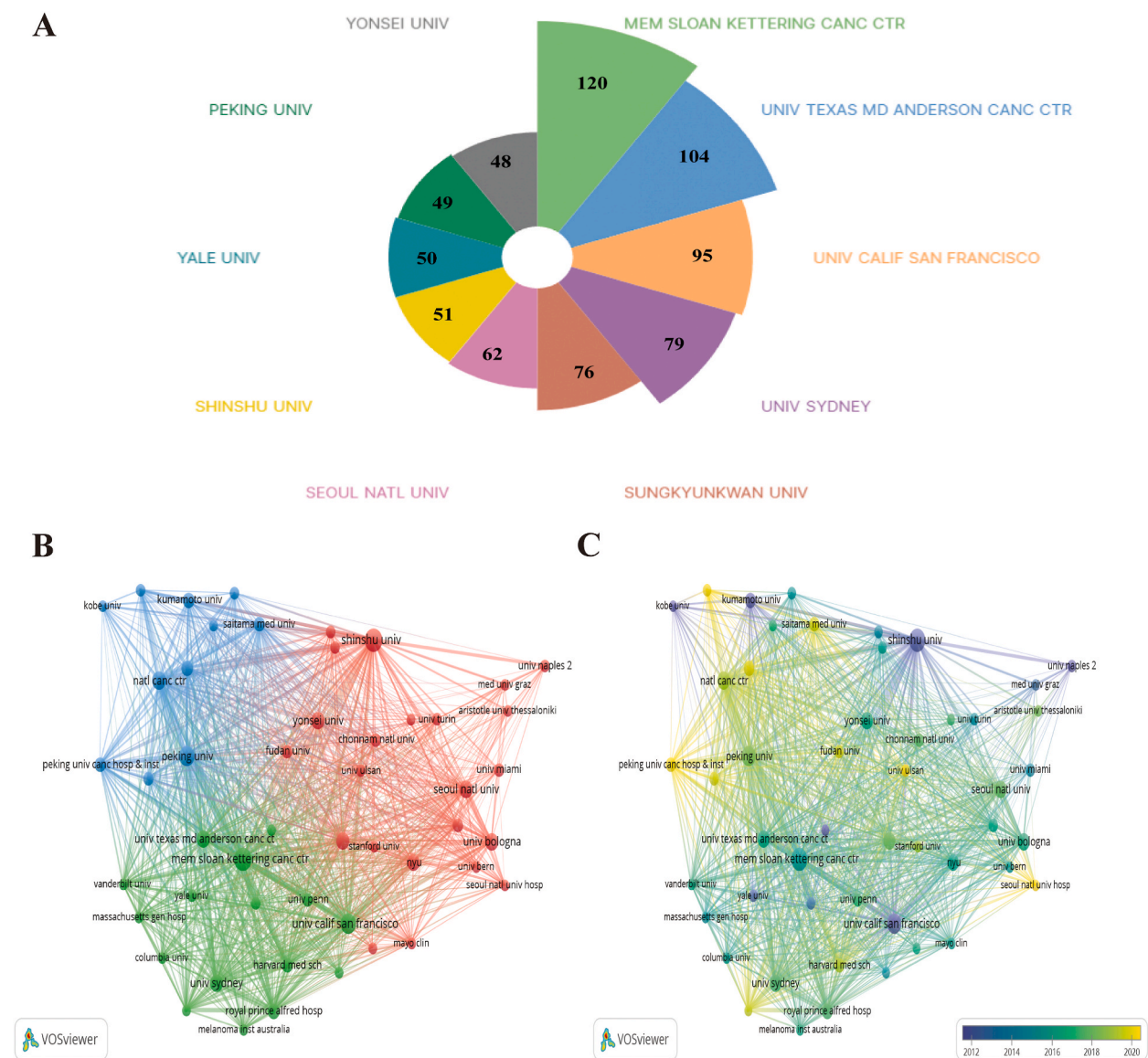
University of Texas MD Anderson Cancer Center (95 publications) and the University of California, San Francisco (79 publications), all of which are in the US (Fig. 5A) and are relatively independent. The VOSviewer software was used to perform visualized analysis on organizations with at least 10 a.m.-related publications, with organizations marked by the same color showing closer collaborations (Fig. 5B and C).

**3.4. Publication distribution by core authors**

A total of 7499 authors were involved in all the publications, and the top 10 authors are presented in Table 4. Interestingly, 9 of the top 10 authors were from Peking University in China; among them, Guo Jun had the largest number of publications (43), followed by Si Lu (38 publications), Chi Zhihong (31 publications) and Kong Yan (31 publications). This indicated the leading role of Chinese

**Table 3**  
Top 10 organizations with the largest number of publications related to acral melanoma.

Rank	Organizations	Country	Publications	Percentage (N/1387, %)
1	Memorial Sloan-Kettering Cancer Center	USA	104	7.50
2	University of Texas MD Anderson Cancer Center	USA	95	6.85
3	University of California San Francisco	USA	79	5.70
4	University of Sydney	AUSTRALIA	76	5.48
5	SungKyunKwan University	KOREA	62	4.47
6	Seoul National University	KOREA	51	3.68
7	Shinshu University	JAPAN	50	3.60
8	Yale University	USA	50	3.60
9	Peking University	CHINA	49	3.53
10	Yonsei University	KOREA	48	3.46



**Fig. 5.** Analysis of publications by organizations. (A) The number of publications of the 10 most productive organizations. (B) Clusters network visualization map of organizations. The size of the circle indicates the number of publications, and the thickness of the line indicates the strength of connection. (C) Overlay visualization map of organizations.

researchers. Fig. 6A showed that Saida Toshiaki, a Japanese author, had the largest total number of citations (1274). Fig. 6B is the network visualization map of authors having at least 10 publications, with authors marked by the same color showing closer collaborations.

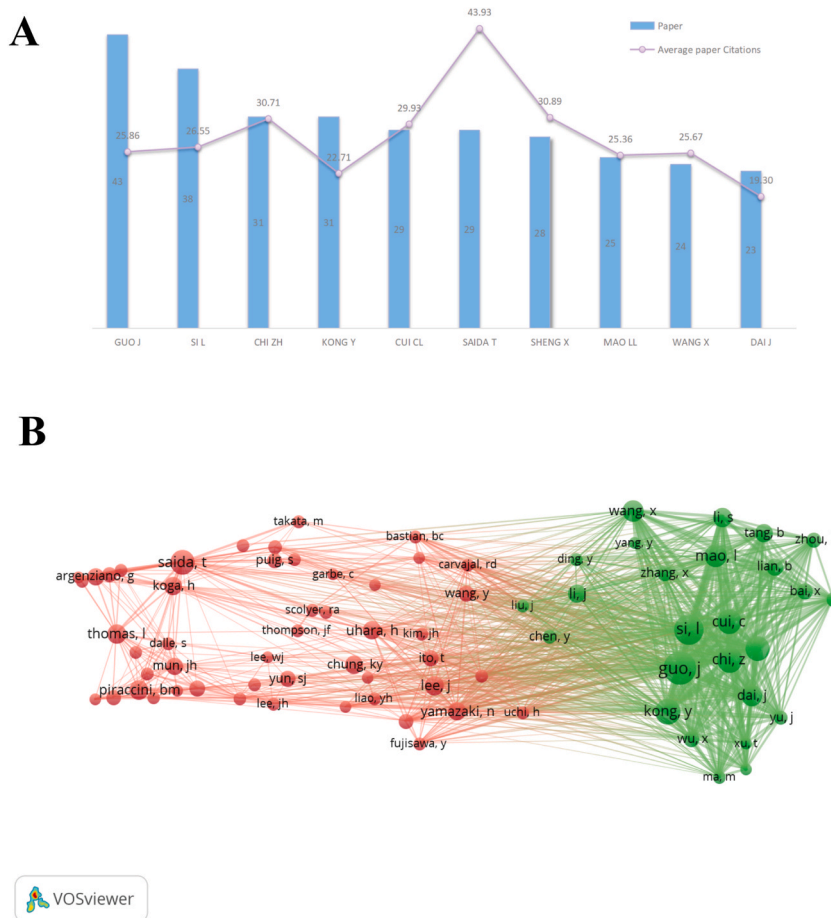
### 3.5. Keywords and research trends

Keywords are the center of an article. Statistics generated by VOSviewer showed a total of 4131 keywords in the 1387 publications, and the 25 most cited keywords are presented in Fig. 7A. The highly ranked keywords included “malignant melanoma”, “ipilimumab”, “imatinib mesylate” and “phase II trial”. The keyword burstiness test showed that “ipilimumab”, “open label”, “efficacy” and “nivolumab” appeared most often in recent years. Co-occurrence network analysis of keywords showed that 138 keywords appeared over 15 times. The co-occurrence and density distribution of the keywords are presented in Fig. 7B and C. Keywords that differed from prior analyses included “malignant melanoma”, “cutaneous melanoma”, “diagnosis” and “survival”. Through the calculation of Log-Likelihood Ratio (LLR) of keywords, we obtained six natural clusters of keywords (Fig. 7D), with “early acral melanoma”, “advanced melanoma” and “sentinel lymph node biopsy” being the focus of attention of researchers.

**Table 4**  
Top 10 authors with the highest number of papers related to acral melanoma.

Rank	Name	Organization	Country	Paper	Total number of citations	Average number of citations per paper <sup>a</sup>	Total link strength
1	Guo Jun	Peking University	CHINA	43	1112	25.86	61679
2	Si Lu	Peking University	CHINA	38	1009	26.55	54105
3	Chi Zhihong	Peking University	CHINA	31	952	30.71	45818
4	Kong Yan	Peking University	CHINA	31	704	22.71	47214
5	Cui Chuanliang	Peking University	CHINA	29	868	29.93	43009
6	Saida Toshiaki	Shinshu University	JAPAN	29	1274	43.93	15804
7	Sheng Xinan	Peking University	CHINA	28	865	30.89	42047
8	Mao Lili	Peking University	CHINA	25	634	25.36	33933
9	Wang Xuan	Peking University	CHINA	24	616	25.67	30029
10	Dai Jie	Peking University	CHINA	23	444	19.30	38501

<sup>a</sup> Average number of citations per paper = Total number of citations/Paper number.

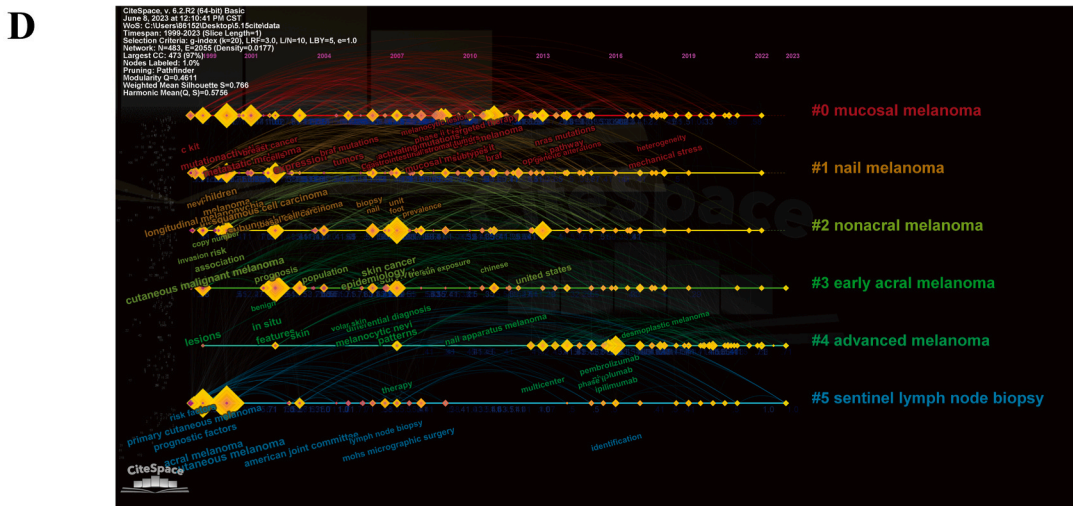
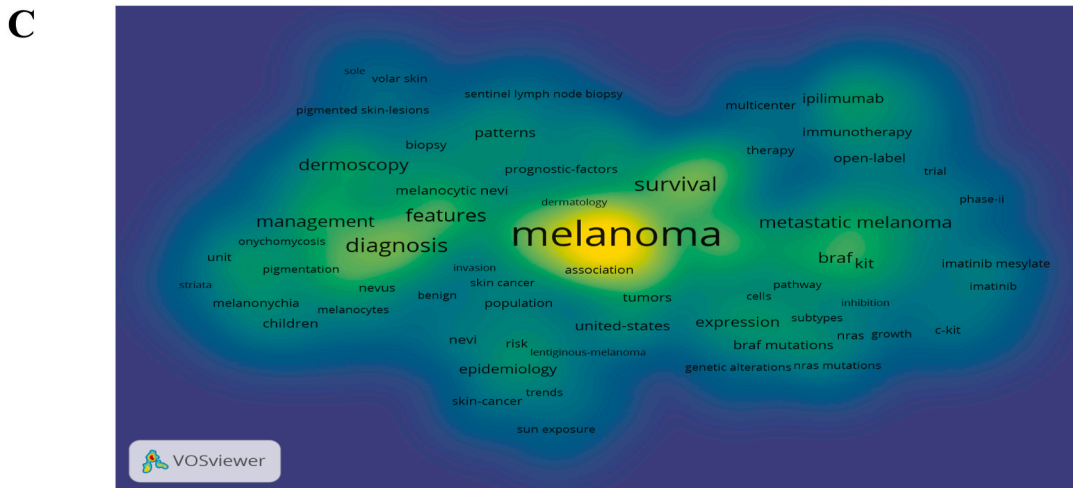
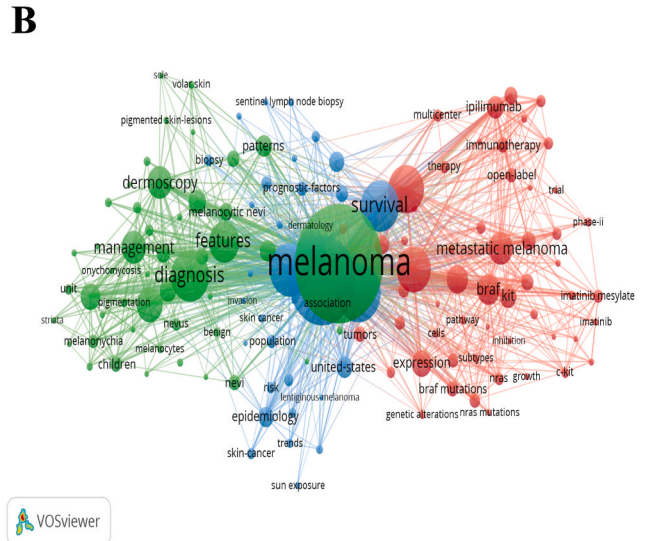
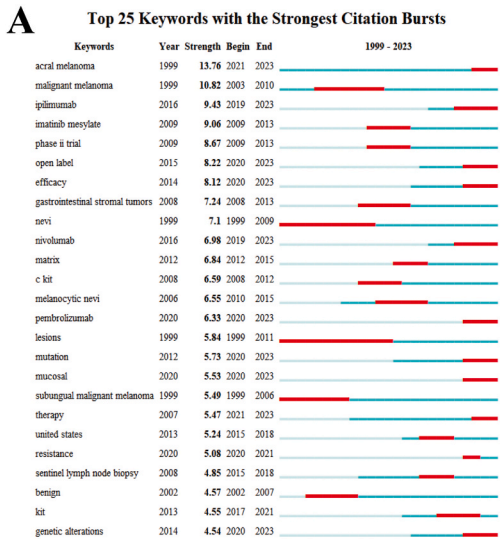


**Fig. 6.** Analysis of publications by authors. (A) The number of publications of the 10 most productive authors. (B) Clusters network visualization map of organizations. The size of the circle indicates the number of publications, and the thickness of the line indicates the strength of connection.

### 3.6. Publication distribution by co-cited reference

Of the 28,492 co-cited references, the top 10 most cited references are presented in Table 5. Among them, the article titled *Distinct Sets of Genetic Alterations in Melanoma* had the largest number of citations (n = 1955); this article elaborated on the hereditary changes of different types of melanoma, indicating that CDK4 amplification was more common in AM [17]. With the minimum number of citations set at 20, all the references were clustered into five directions (Fig. 8A), with most of the references being sourced from top





(caption on next page)

**Fig. 7.** Analysis of keywords and research trends. (A) Burstiness of keywordsThe green line indicates the timeline, and the red lines on the timeline indicate the duration of the keyword burst. (B) Clusters network visualization map of keywords. The size of the circle indicates the number of publications, and the thickness of the line indicates the strength of connection. (C) Destiny visualization map of keywords. (D) The timeline view of keywords related to acral melanoma.

medical journals. The timeline of co-cited AM-related articles (Fig. 8B) revealed 9 clusters, which directly showed the hotspots in different stages and the direction of development from the time dimension. This graph also showed that “advanced melanoma” and “melanocytic lesion” have become new hotspots since 2016.

#### 4. Discussion

Through a bibliometric analysis of AM-related literature retrieved from WoSCC, we find that the number of relevant publications has been increasing, indicating that AM has attracted great attention in recent years. Compared with systematic review and meta-analysis, the present study is based on a large data set and a rigorous analytical approach to provide a more comprehensive and objective examination of the current state of AM-related studies, trends and keywords.

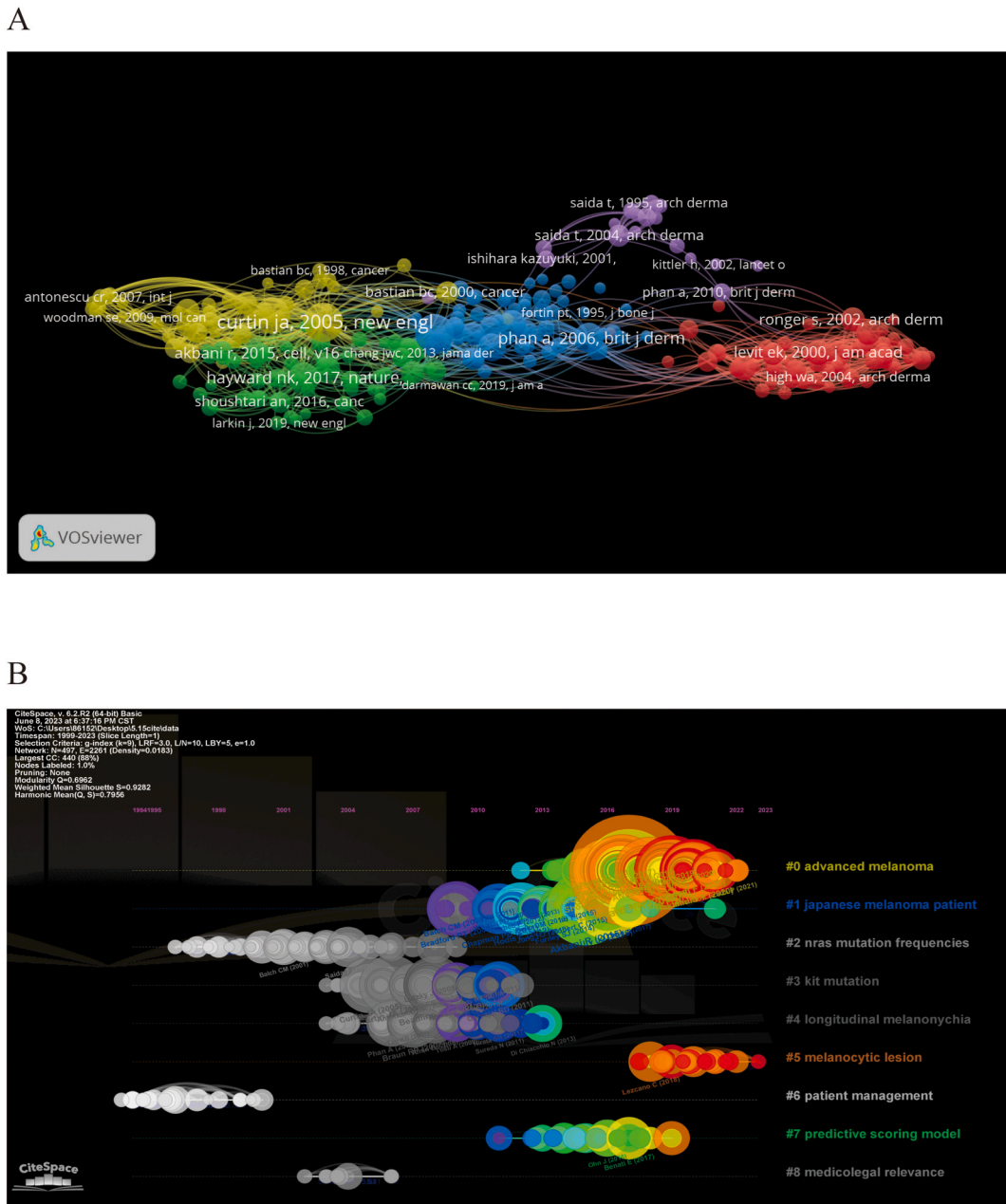
The US contributed most to the research on AM; compared to other organizations, the Memorial Sloan-Kettering Cancer Center, the University of Texas MD Anderson Cancer Center and the University of California, San Francisco had the largest number of articles published, suggesting that these three organizations are core institutions in this field and that their research hotspots and directions deserve more attention. Authors having the largest number of publications were GUO Jun and SI Lu from Peking University, who are highly accomplished in the research of AM and collaborate closely with other institutions and universities. With regard to the number of publications, China has a markedly larger number of publications than Japan and Italy but has a lower average number of citations compared to these countries; there are also fewer collaborations between China and other countries. Thus, China still needs to enhance its international collaboration, thereby improving the international recognition of Chinese organizations.

Through keyword co-occurrence and cluster analyses, we found that the AM-related studies during the last two decades could be classified into three major categories: (1) clinical findings, including the diagnosis, features, management, and dermoscopy, (2) molecular findings, including BRAF, KIT, expression, and mutations, and (3) epidemiological findings, including survival, cancerization, risk, and population. Some clinical studies [27,28] found that AM was likely to occur under thumbnails, on the back of hands and on the soles of feet. Through collection of the clinical information of 1157 Chinese patients with AM, Wei et al. [29]found that apart from NRAS, the mutation frequency of BRAF, C-Kit and PDGFRA were similar; compared to AM on the palms and nail beds, AM on the soles of feet was found associated with poorer prognosis. AM on the feet is often misdiagnosed as verruca plantaris, tinea pedis, diabetic foot ulcer, etc., leading to delayed diagnosis. Trauma, mechanical stress and acral naevi have been determined as potential risk factors [27,30], while the use of dermoscopy has increased the accuracy of the early diagnosis of AM, which indirectly improves the survival rate of the patients [31]. The major factors affecting the prognosis of AM [32,26] include Breslow depth, ulceration and vascular invasion, while data for the prognostic value of sentinel lymph node biopsy and mitotic count is slightly insufficient.

Through the exploration of AM-related research progress with the use of keywords burstiness, we found that the key term “malignant melanoma” appeared most often, suggesting that AM is a highly destructive malignancy. Keywords frequently appeared in recent years also include “ipilimumab”, “open label”, “efficacy”, “nivolumab”, “pembrolizumab” and “mutation”, indicating that the

**Table 5**  
Top 10 co-cited references related to acral melanoma.

Rank	Title	DOI	Total citations	Year	Journal	Impact factor (2022)
1	Distinct sets of genetic alterations in melanoma [14]	10.1056/NEJMoa050092	1955	2005	<i>New Engl J Med</i>	158.5
2	Somatic activation of kit in distinct subtypes of melanoma [18]	10.1200/JCO.2006.06.2984	1159	2006	<i>J Clin Oncol</i>	45.3
3	Pan-cancer analysis of whole genomes [19]	10.1038/s41586-020-1969-6	894	2020	<i>Nature</i>	64.8
4	Exome sequencing identifies recurrent somatic RAC1 mutations in melanoma [20]	10.1038/ng.2359	823	2012	<i>Nat Genet</i>	30.8
5	Whole-genome landscapes of major melanoma subtypes [21]	10.1038/nature22071	730	2017	<i>Nature</i>	64.8
6	Kit as a therapeutic target in metastatic melanoma [22]	10.1001/jama.2011.746	581	2011	<i>Jama-J Am Med ASSOC</i>	120.7
7	Kit gene mutations and copy number in melanoma subtypes [23]	10.1158/1078-0432.CCR-08-0575	470	2008	<i>Clin Cancer Res</i>	11.5
8	Imatinib for melanomas harboring mutationally activated or amplified kit arising on mucosal, acral, and chronically sun-damaged skin [24]	10.1200/JCO.2012.47.7836	361	2013	<i>J Clin Oncol</i>	45.3
9	Melanoma [25]	10.1038/nrdp.2015.3	352	2015	<i>Nat Rev Dis Primers</i>	81.5
10	Classifying melanocytic tumors based on DNA copy number changes [26]	10.1016/S0002-9440(10)63536-5	332	2003	<i>Am J Pathol</i>	6



**Fig. 8.** Co-cited reference analysis. (A) Visual cluster analysis of co-occurrence among co-cited references. (B) Distribution of the top 9 clusters on the timeline. The size of the node indicates the number of citations, and the curve between nodes indicates the co-citation relationship.

immunotherapy of AM has become a focus of studies. However, there is still a lack of cohort study evidence on the efficacy of systematic treatment for AM across the world, suggesting an urgent need for a standardized and effective systematic treatment regimen. At present, the standard treatment for primary AM is wide local excision; considering the usual sites of AM, the patients often need amputations or plastic and reconstructive surgeries, which may result in prolonged recovery. However, surgical treatment alone may result in limited improvement, and its combination with immunotherapy and targeted therapies is likely to improve the patients' prognosis. At present, the immune checkpoint inhibitors used to treat MM mainly include CTLA (e.g., ipilimumab), anti-PD-1 antibodies (e.g., nivolumab and pembrolizumab) and anti-PD-L1 antibodies. The tumor mutation burden (TMB) of AM is lower than lesions on other sites of the skin, indicating that the primary site of AM is associated with TMB differences. Studies have also found that a higher TMB is associated with longer survival after treatment with immune checkpoint inhibitors [22]. Prachi et al. [23] found that, compared to monotherapy with an anti-PD-1 antibody, the combination of an anti-PD-1 antibody and ipilimumab was associated with a significantly higher objective response rate (ORR) and prolonged progression-free survival (PFS) among patients with AM, but it did



not significantly improve the overall survival (OS). The limited genetic analyses of AM also pointed out that the use of PTEN/PI3K, c-Kit or cell cycle inhibitors might bring benefits; some of these medications have been used to treat other types of cancers, but none of them has shown significant effects in clinical trials to date. Through the visualized analyses of the AM-related research hotspots and trends, we have found that molecular mutation is a hotspot of the basic research on AM, and understanding the clinical features of AM as well as how to further improve the efficacy of treatment for AM is a direction for future studies.

We also analyzed the top 10 publications with the largest number of citations; interestingly, most of these studies were comparative studies [17,20], clinical trials [19,21] and original articles [18] on the genomic analysis of AM, suggesting that the oncogene mutation spectrum might be different between subtypes of MM. Among patients with AM, BRAFV600E and NRAS mutations are rare, while KIT mutations and increases in DNA copy number are more common in patients with AM; treatment with imatinib may bring benefits to some of the patients. In addition, an increasing number of studies have begun to focus on the genomic landscape of AM, and they found that AM might be associated with an increased frequency of genomic aberrations (e.g., chromosomes 5p, 11q, 12q and 15) and point mutations of somatic cells, which might affect multiple cancer-associated genes [24,25]. Thus, the etiology of AM is still unclear at the molecular level, and further research into its molecular genetics and the search for potential therapeutic targets remain a priority for future studies.

In summary, AM has attracted increasing attention from researchers, and more convincing epidemiological studies and exploration of its mechanisms are needed to facilitate the future development of the field related to AM. There are still some limitations to the present study. As only publications in English from WoSCC are included, there might be source bias or omission of important studies. In addition, some of the recently published high-quality studies have not received great attention due to their low citation rates, leading to possible bias in the results of the present study. Despite the limitations, the AM-related research hotspots and trends identified in the present study are still of great referential value, and we will continue relevant studies in the future.

## 5. Conclusion

To our best knowledge, this is the first comprehensive and quantitative study on AM-related literature, which has revealed the current status, hotspots and trends of relevant studies across the world with reproducible and reliable results. The present study is also useful in helping researchers select topics they are interested in, choose target journals and find potential collaborators.

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## Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

## CRedit authorship contribution statement

**Yi Wang:** Writing - original draft, Formal analysis, Data curation. **Jie Pan:** Supervision, Data curation. **Mi Wang:** Methodology, Conceptualization. **Juan Su:** Writing - review & editing, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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