Dermatology Practical & Conceptual

Publication Trends and Hot Topics in Dysplastic Nevus Research: A 30-Year Bibliometric Analysis

Hazal Izol Özmen[1]

1 Department of Pathology, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey

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Corresponding Author: Hazal İzol Özmen, Basaksehir Cam and Sakura City Hospital, Pathology Department, 34480, İstanbul/Turkey. Phone: 00905436922677 E-mail: hazalizol91@gmail.com

ABSTRACT

Introduction: Dysplastic nevi are pigmented lesions that exhibit clinical and histological features of both common nevi and melanoma. In recent years, there has been an increase in publications on dysplastic nevi. Bibliometric analysis is a method of evaluating trends in large number of publications and identifying popular topics.

Objectives: The objective of this study is to provide an overview of the landscape of publications related to dysplastic nevi, visualize trends and identify popular topics in the literature.

Methods: Thomson Reuters' Web of Science database was searched with the following query in title, abstract or keywords: TS = ("dysplastic nevus" OR "clark nevus" OR "atypical nevus" OR "dysplastic nevi" OR "clark nevi" OR "atypical nevi"). Time span was set to 1992-2022. Document type was set to Article. Titles, authors, abstracts, institutions, countries, journals, references, and the citation information were recorded.

Results: Although the number of publications has declined over time, the USA remains the leading contributor to published articles. Key clusters of frequently used keywords were identified. The Journal of the American Academy of Dermatology had the highest number of published titles. Country and journal analysis were supplemented by co-citation and co-cited reference cluster analysis. Burst analyses revealed authors like Kittler, Argenziano, and Gandini as significant contributors, with their works receiving strong citation bursts extending until the end of the study period.

Conclusions: This bibliometric analysis revealed trends and interest pockets in the literature pertaining to dysplastic nevi and melanoma. This study aids in understanding the current research landscape and highlights potential future directions in this field.

Introduction

Dysplastic nevi are characterized by their large size (6 mm or more in diameter) and irregular, asymmetric, pigmented macules with varying colors. Clinically, these features may be similar to those of melanoma and a biopsy might be warranted to confirm the diagnosis [1,2].

Dysplastic nevus syndrome is characterized by a propensity for the affected person to have a large number of nevi, which appear abnormal clinically and have histologically dysplastic features. It was originally considered to be a hereditary condition; however, currently most cases are thought to occur sporadically or as a single isolated lesion [3]. The diagnosis of dysplastic nevus syndrome is significant because it suggests an increased risk for developing melanoma, especially in those with the familial form of the syndrome [4].

In the recent two decades, there has been increasing interest on the relationship and correlation between dysplastic nevi and melanoma. With a growing literature, while major trends are usually discernible, the smaller trends and pockets of interest or "hot topics" can be overlooked. Bibliometric analysis is a method of evaluating trends in large number of publications and making sense of the underlying data. This might be in the form of identifying popular topics or keywords and visualizing the network of citations, journals and other pertinent data.

Objectives

This paper aims to provide a robust overview of the field, identifying pivotal papers, influential authors, countries, journals and significant research themes.

Methods

Informed consent was not obtained for this study as only publicly available information was used. The search was conducted in Thomson Reuters' Web of Science (WoS) database using the following criteria: TS = ("dysplastic nev*" OR "clark nev*" OR "atypical nev*") in title, abstract or keywords. The document type was set to "Articles," and the indexes were set to "SCI-EXPANDED." The search was limited to articles published in English between 1992 and 2022. Duplicate results were removed. A total of 1,404 unique articles were found. Titles, authors, abstracts, institutions, countries, journals, references, and citation information were recorded.

The obtained data was imported to CiteSpace 6.1.R6, 64-Bit (Drexel University) [5] and VOSviewer 1.6.15 [6]. Keyword, authorship and citation burst analysis was performed. Network of keywords and organizations were analyzed and visualized with VOSviewer. Co-citation analysis and clustering was performed with CiteSpace. Clusters were analyzed with silhouette, centrality and sigma values, and labeled using different labeling methods (Latent Semantic Indexing (LSI), Log-Likelihood Ratio (LLR), Mutual Information (MI)). A p value of less than 0.05 was considered significant.

Results

Figure 1 shows the number of publications and citations per year from 1992 to 2022. Interestingly, the number of publications appears to have decreased in recent years, with the lowest count of 22 in 2022 The linear regression analysis of the number of publications versus year yielded a negative slope of -0.4117, suggesting a decrease in the number of publications over time ($P < 0.01$). Author keyword visualization was created using VOSviewer (Figure 2). Nine clusters of frequently used together keywords were identified.

Country Analysis

Table 1 displays the top 10 countries with the most published articles from the year 1992 to 2022. The USA stands out as the leading country in this regard, with a total of 676 published articles. This number is significantly larger than the number of articles published by any other country on the list, with Italy, the second-highest country, publishing 161 articles, or approximately a quarter of the number published by the USA.

Figure 3 shows the top 10 countries with the strongest citation burst. The country with the highest strength of citation burst was Canada, with a strength of 8.64 from 2007 to 2015. The most recent citation bursts were observed for Spain, Romania, France, and Poland, all persisting until the concluding date of this study.

Journal Analysis

The Journal of the American Academy of Dermatology leads with the highest number of published titles at 120. The Journal of Cutaneous Pathology follows with 68 titles, and the Archives of Dermatology with 63 titles.

Table 2 presents the top 10 most co-cited journals in terms of frequency. The Journal of the American Academy of Dermatology leads the list with 894, followed by Archives of Dermatology (JAMA Dermatology) with 825 and the Journal of Investigative Dermatology with 754. Notably, the British Journal of Cancer, despite having the lowest citation

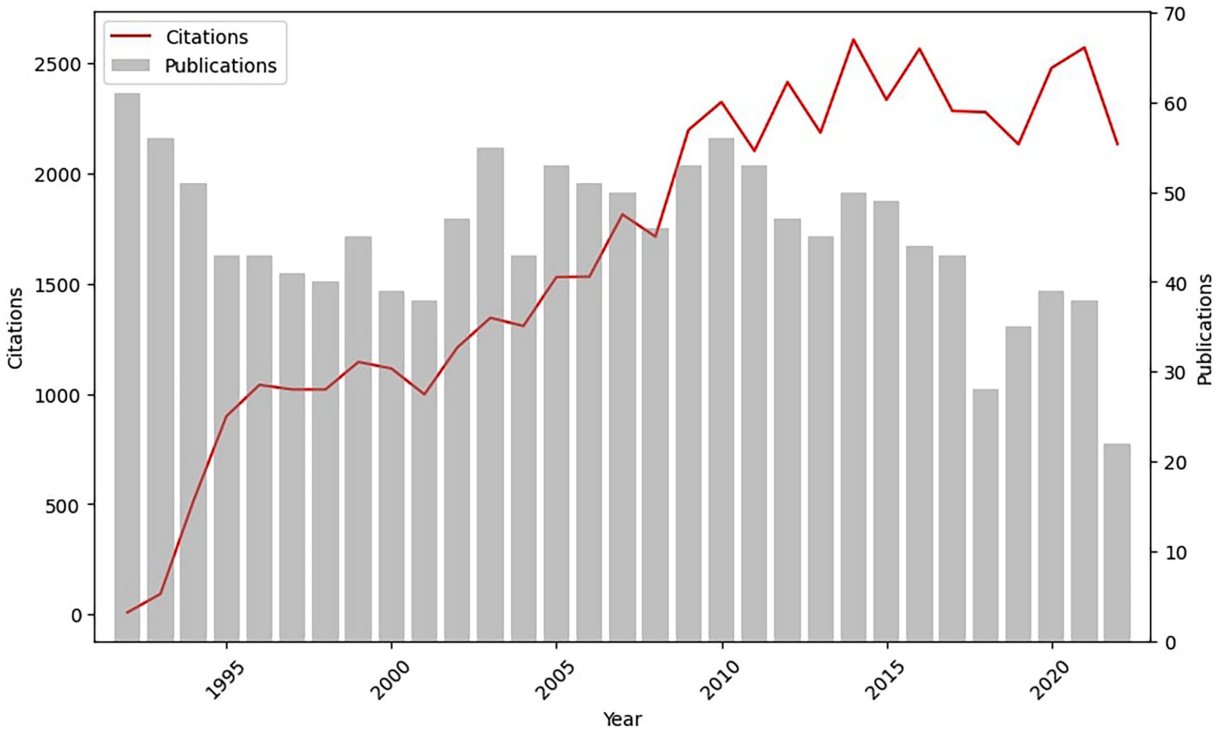

Figure 1. Number of publications and citations by year.

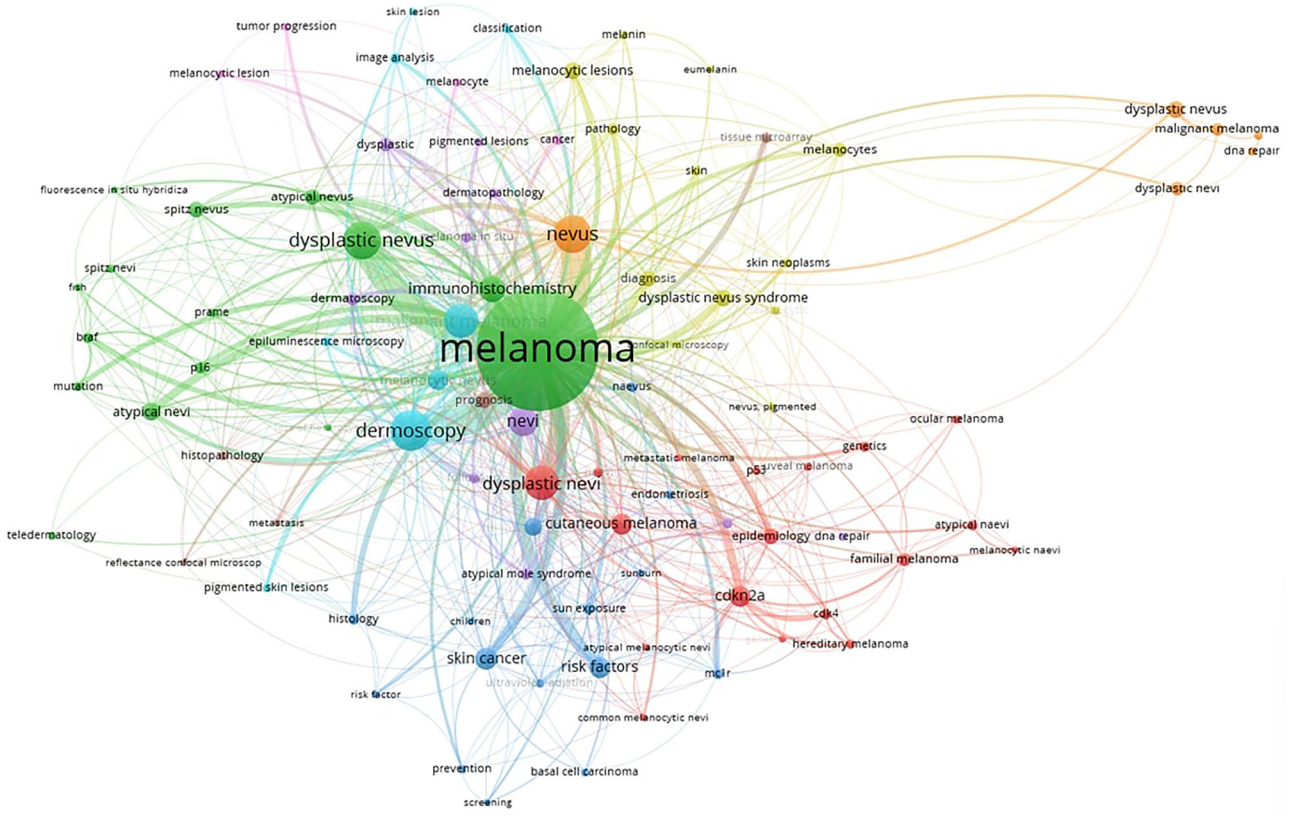

Figure 2. Network map of author keywords.

frequency among the top 10 journals, has the highest centrality score (0.02), which indicates a relatively higher influence or connectivity within the network.

Table 1. Top 10 most publishing countries between 1992-2022.

Ranks	Country	No. of articles	Centrality
1	USA	676	0.43
2	ITALY	161	0.24
3	GERMANY	86	0.28
4	CANADA	55	0.01
5	AUSTRALIA	54	0.07
6	NETHERLANDS	36	0.01
7	SPAIN	34	0.17
8	FRANCE	24	0.08
9	SWEDEN	20	0.00
10	AUSTRIA	18	0.01

Co-Citation and Co-Cited Reference Cluster Analysis

Co-citation analysis was performed using a scale factor (k) of 25. The validity of the references was checked to ensure accurate results. A total of 23,801 references (99.1337%) were deemed valid, while only 208 references (0.8663%) were invalid. The resulting merged network included 1,353 nodes and 5,402 links.

The reference co-citation analysis revealed the central papers in the field of melanoma research (Table 3). The paper of Gandini et al was the most cited and held the highest centrality, indicating its pivotal role in this research field. Paper of Landi et al and of Goldstein et al on high-risk melanoma susceptibility genes both had a centrality of 0.20, also emphasizing their influential positions [7-9].

Clustering of the co-cited references revealed 21 clusters. The largest cluster (Cluster 0) centered on 'melanocytic nevi' included 130 articles from around 1990. Table 4 summarizes the characteristics of the clusters along with different

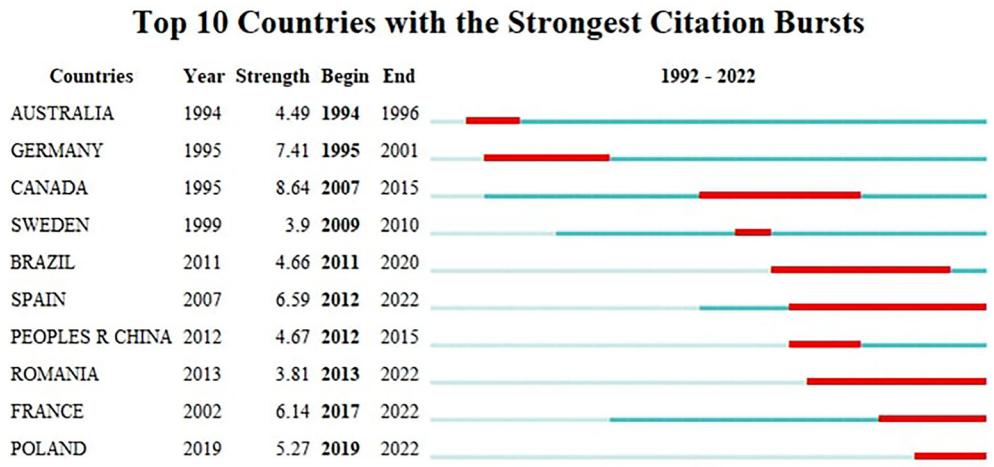

Figure 3. Top 10 countries with the strongest citation bursts.

Table 2. Top 10 most co-cited journals ranked according to co-citation counts.

Ranks	Co-citation count	Journal	Impact Factor (IF) 2021	Centrality
1	894	Journal of the American Academy of Dermatology	12.077	<0.01
2	825	Archives of Dermatology (JAMA Dermatology)	3.033	<0.01
3	754	Journal of Investigative Dermatology	7.590	<0.01
4	578	British Journal of Dermatology	11.113	<0.01
5	563	Cancer Research	13.312	0.01
6	516	Cancer	6.921	<0.01
7	506	Melanoma Research	3.199	<0.01
8	481	International Journal of Cancer	7.316	0.01
9	455	New England Journal of Medicine	176.079	0.01
10	381	British Journal of Cancer	9.082	0.02

Table 3. Reference co-citation analysis ranked by centrality.

Ranks	Co-citation count	Centrality	Year	Lead author, title
1	26	0.24	2005	Gandini S, "Meta-analysis of risk factors for cutaneous melanoma"
2	10	0.20	2002	Landi MT, "DNA repair, dysplastic nevi, and sunlight sensitivity in the development of cutaneous malignant melanoma"
3	6	0.20	2006	Goldstein AM, "High-risk melanoma susceptibility genes and pancreatic cancer, neural system tumors, and uveal melanoma across GenoMEL"
4	4	0.20	2009	Chang YM, "A pooled analysis of melanocytic nevus phenotype and the risk of cutaneous melanoma at different latitudes"
5	8	0.19	1998	Bataille V, "The association between naevi and melanoma in populations with different levels of sun exposure: a joint case-control study of melanoma in the UK and Australia"
6	20	0.17	1996	Zuo L, "Germline mutations in the p16INK4a binding domain of CDK4 in familial melanoma"
7	14	0.17	2002	Bishop DT, "Geographical variation in the penetrance of CDKN2A mutations for melanoma"
8	6	0.16	2009	Bishop DT, "Genome-wide association study identifies three loci associated with melanoma risk"
9	13	0.15	2013	Goldstein AM, "Dysplastic nevi and melanoma"
10	8	0.15	1999	Aitken J, "CDKN2A variants in a population-based sample of Queensland families with melanoma"

Table 4. Top 10 Cluster groups with relevant characteristics according to keywords.

Cluster	Size	Silhouette	Label (LSI)	Label (LLR, p-value)	Label (MI score)	Average Year
0	130	0.876	melanocytic nevi	melanocytic nevi (213.09, p<0.001)	different body site (0.88)	1990
1	122	0.85	melanocytic lesion	melanocytic lesion (235.12, p<0.001)	skin tumor (1.66)	2002
2	108	0.915	familial melanoma	familial melanoma (423.98, p<0.001)	familial melanoma mlm (0.79)	1992
3	108	0.875	familial melanoma	cdkn2a mutation (163.4, p<0.001)	cutaneous malignant melanoma risk (0.54)	2000
4	104	0.922	dysplastic nevi	dysplastic nevus (156.51, p<0.001)	clinical use (0.45)	2009
5	97	0.928	dysplastic nevi	severe atypia (155.34, p<0.001)	melanoma antigen (0.45)	2015
6	73	0.9	melanoma-prone families	melanoma risk (142.34, p<0.001)	cdkn2a-mutated melanoma families (0.3)	2005
7	72	0.92	high risk	high risk (204.41, p<0.001)	patient-initiated mobile teledermoscopy (0.34)	2011
8	59	0.908	cutaneous melanoma	hereditary melanoma (187.53, p<0.001)	chronic sun exposure (0.38)	1995
9	53	0.965	diagnosing skin	diagnosing skin (84.42, p<0.001)	telemedicine support (0.04)	2018

labeling methods. Figure 4 is a visual representation of the clusters with lighter colors indicating a more recent average year of references within the cluster. Table 5 presents the most cited member of each cluster.

The top three publications with the highest sigma scores in the dataset were established. Topping the list is the study by Gandini et al. in 2005, titled "Meta-analysis of risk factors for cutaneous melanoma," with a sigma score of 20.45

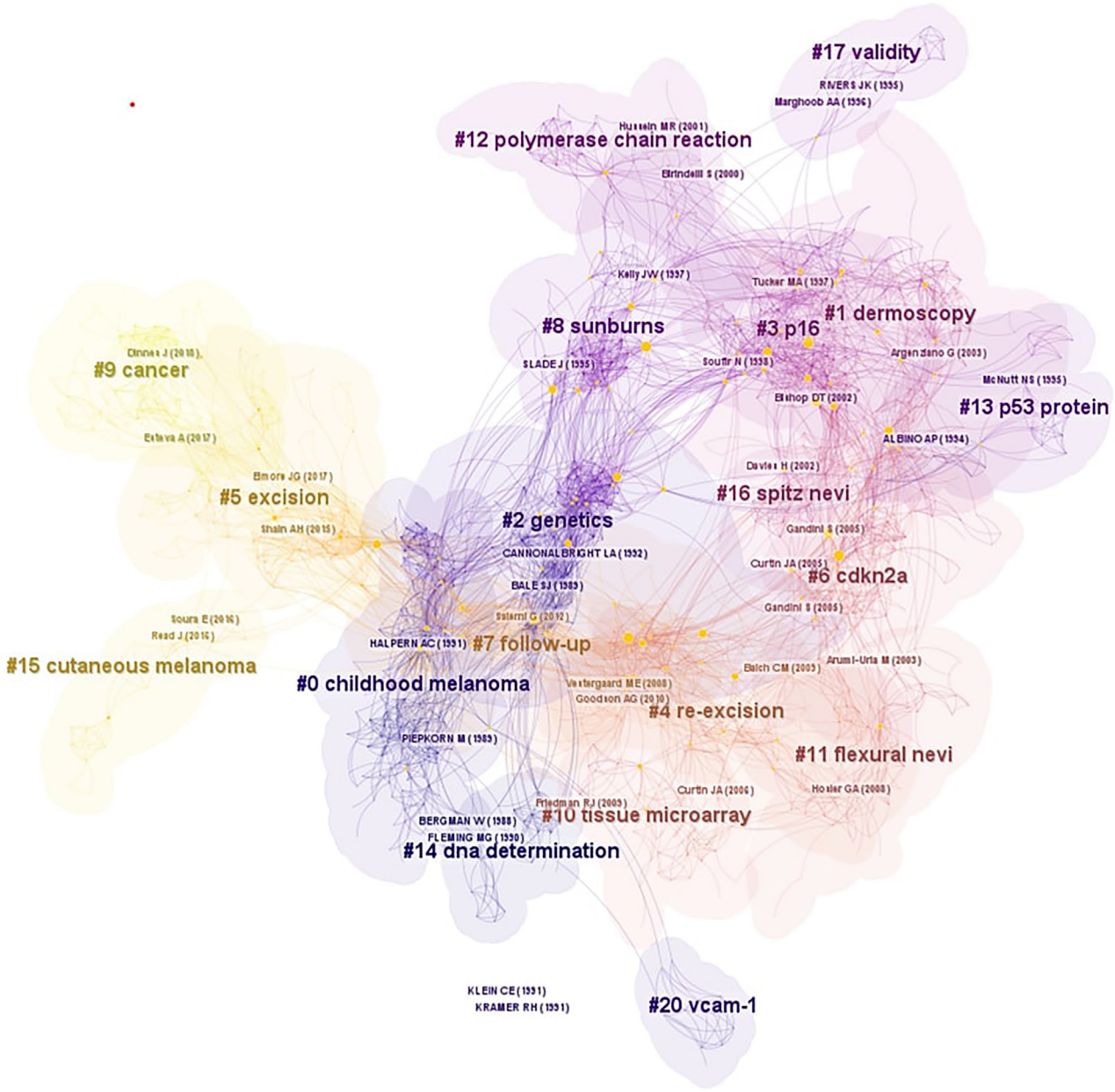

Figure 4. Clustered network map of co-cited references with log-likelihood ratio labels.

located in Cluster 6 [7]. Following closely is the publication by Zuo in 1996, titled "Germline mutations in the p16INK4a binding domain of CDK4 in familial melanoma," with a sigma score of 5.09 located in Cluster 2 [10]. Another significant publication, with a sigma score of 4.89 located in Cluster 1, is the study by Tucker in 1997, titled "Clinically recognized dysplastic nevi: a central risk factor for cutaneous melanoma [11]."

Cited Author Burst Analysis

Figure 5 shows top 10 cited authors with the strongest citation bursts. The author with the highest strength of burst is Gandini, with a strength of 28.08 from 2008 to 2022. The longest burst was by Argenziano and Kittler, lasting from 2006 to 2022, and 2004 to 2022, respectively. The most recent bursts are also by Argenziano, Kittler, and Gandini, continuing into the end date of the study.

Discussion

Dysplastic nevus, also called atypical or Clark nevus, can be precursor to melanoma, as the observation that 36% of melanomas have dysplastic nevi near the invasive tumor supports [12]. Signs that a dysplastic nevus may have transitioned into a melanoma include asymmetry in contour, a noticeable increase in pigment variations, or a grayish tint indicating regression. These malignancies typically arise at a younger age (mid-thirties), are sometimes multiple, and are often found on the trunk [1].

Table 5. Top co-cited member of each cluster.

Cluster	Cluster Label	Lead Author, Year,Title
0	melanocytic nevi	Halpern AC, 1991, "Dysplastic nevi as risk markers of sporadic (nonfamilial) melanoma: a case-control study"
1	melanocytic lesion	Tucker MA, 1997, "Clinically recognized dysplastic nevi: a central risk factor for cutaneous melanoma"
2	familial melanoma	Bal SJ, 1989, "Mapping the Gene for Hereditary Cutaneous Malignant Melanoma–Dysplastic Nevus to Chromosome Lp"
3	cdkn2a mutation	Soufir N, 1998, "Prevalence of p16 and CDK4 Germline Mutations in 48 Melanoma-Prone Families in France"
4	dysplastic nevus	Balch CM, 2009, "Final version of 2009 AJCC melanoma staging and classification"
5	severe atypia	Elmore JG, 2017, "Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study"
6	melanoma risk	Gandini S, 2005, "Meta-analysis of risk factors for cutaneous melanoma"
7	high risk	Vestergaard ME, 2008, "Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting"
8	hereditary melanoma	Kelly JW, 1997, "A high incidence of melanoma found in patients with multiple dysplastic naevi by photographic surveillance"
9	diagnosing skin	Esteva A, 2017, "Dermatologist-level classification of skin cancer with deep neural networks"

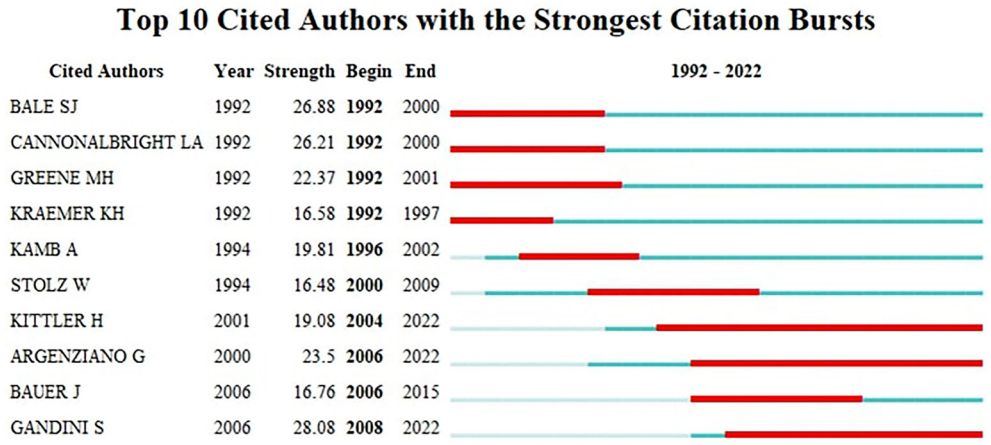

Figure 5. Top 10 authors with the strongest citation bursts.

Molecularly, dysplastic nevi have a profile intermediate between benign nevi and malignant melanoma. There are certain described gene mutations that are present in dysplastic nevi and two genes – MC1R and BRAF - are present in the cluster analysis of our dataset. The melanocortin 1 receptor (MC1R) gene encodes the receptor of melanocortin-stimulating hormone, which is found on the surface of melanocytes. MC1R phenotypic traits make an individual more susceptible to ultraviolet (UV) damage, leading to melanoma even without excessive UV exposure. People with MC1R gene variants tend to develop melanoma more frequently and at an earlier age than the general population. However, it is important to note that the risk of melanoma due to MC1R mutations is still lower than that associated with mutations in CDKN2A and CDK4 [13-14]. It is also shown that MC1R variants are strongly associated with BRAF mutations in non- chronic sun-induced damage melanomas [14,15]. The cluster timeline analysis shows that the co-cited references of both genes were popular in the same timeframe and relatively less popular since then.

There has also been specific genetic findings on patients with dysplastic nevus syndrome, which dysplastic nevus syndrome is inherited as an autosomal dominant with incomplete penetrance. About 40% of families with the dysplastic nevus syndrome have mutations in the CDKN2A gene [1,16,17]. A new gene linked to the development of atypical

nevi has also been found on the 7q21.3 chromosome, called CDK6 [18]. It has been shown that there is loss of heterozygosity in the p16INK4a and p53 genes in sporadic dysplastic nevi [19]. The patients with dysplastic nevus syndrome have increased risk of developing other malignancies such as pancreatic cancer [13,20].

While there is a recognized connection between dysplastic nevi and melanoma, it's crucial to note that only about 20% to 30% of melanomas evolve from preexisting nevi. The rate of a single nevus transforming into a malignant form is estimated to be less than 3 in 1000 annually. Given that the majority of dysplastic and typical nevi do not develop into melanoma, preventive removal of melanocytic nevi is not typically advised [21].

Presently, the understanding is that nevi with mild to moderate histological dysplasia are not direct precursors to melanoma and, hence, do not require re-excision if diagnosed through intended full (not partial) biopsies that remove the whole visible lesion. Nevertheless, nevi that exhibit severe dysplasia ought to be completely removed due to their shared histopathological characteristics with melanomas, which can potentially lead to diagnostic errors. There is ongoing debate regarding whether severe dysplastic nevi with just narrowly clear biopsy margins can be safely observed [21].

This paper aims to provide a robust overview of the field, identifying pivotal papers, influential authors, countries, journals and significant research themes using bibliometric techniques. Bibliometric analysis allows researchers to make sense of the large amount of data using scientific methods. It also provides points of view that traditional review of literature cannot reveal. This study aimed to identify hotspots and popular topics in this area using bibliographic analysis. WoS by Thomson-Rheuters, Scopus by Elsevier and Google Scholar are the three mainly used databases literature and bibliometric research. However, the accuracy of the data presented by Google Scholar has been questioned [22]. WoS and Scopus are the main databases currently used for bibliometric analysis and citation data [23], with WoS including articles before 2000 as well.

With 676 published articles, the USA has been the most prolific contributor to the scientific literature during this period. Its centrality score of 0.43, the highest among the countries examined, underscores the central role the USA plays in the global scientific collaboration network. The most recent citation bursts in Spain, Romania, France, and Poland reflect emerging trends in influential research from these countries. Observing these shifts in citation bursts could offer insights into evolving research strengths and future research trends, highlighting these countries as potential rising players in the international research landscape.

Leading with the highest number of published titles, the Journal of the American Academy of Dermatology exhibits a significant influence in the field. Furthermore, it also tops the list of the most co-cited journals. Interestingly, the centrality scores, reflective of influence and connectivity within the scientific network, present an intriguing contrast. Despite high citation frequencies, the Journal of the American Academy of Dermatology, the Archives of Dermatology, and the Journal of Investigative Dermatology all show centrality scores of less than 0.01. In contrast, the British Journal of Cancer stands out with the highest centrality score (0.02) among the top 10 journals, despite having the lowest citation frequency.

One method used in bibliometric analysis is called "co-citation analysis". Co-citation means citing of two sources by the same article. Since related literature is usually cited together, the network of co-cited sources can present a new angle in analyzing the underlying research trends. This makes it an excellent tool for unveiling the hidden structure and thematic patterns in a vast corpus of literature. Furthermore, by analyzing centrality measures, it becomes possible to reveal the most influential works or 'landmark' papers in that field. In addition, co-citation analysis can help detect emerging trends and shifts in a scientific field by tracking changes in co-citation patterns over time, thus providing guidance in future research directions [24].

The co-citation and co-cited reference cluster analysis in this study provides critical insights into the key works and authors within melanoma research. In this context, centrality and sigma values provide unique perspectives, particularly when compared to traditional literature review methodologies. Centrality is a metric used in network analysis that quantifies the importance of a node within the network. A work with a high centrality score is considered influential, not necessarily because of the frequency of citations, but due to its pivotal role in connecting various other works or researchers [25]. Sigma, on the other hand, is a metric in co-citation analysis that combines both the frequency of co-citation and the centrality of a work within the co-citation network. A high sigma value implies that a publication is both highly co-cited and centrally located in the co-citation network [26]. By examining Tables 3 and 4, a researcher can gain a clear understanding of the most influential papers and authors in the field, the key ideas that these papers introduced, and how these ideas have shaped the development and trajectory of the field. This can be invaluable for identifying research gaps, determining future research directions, and understanding the context and significance of one own research within the broader field.

Burst analyses of countries and cited authors were performed in this study. In the traditional method of literature review, one of the metrics to understand the influence of a work is the total citation count, as more influential works are cited more often than others. However, since older

publications tend to have more citations over the years, a literature search based on citation counts for influential articles will be biased towards older references. The term "citation burst" refers to a situation where an author work receives a high number of citations over a specific period. This might indicate that the author work has made a significant contribution to the field, or sparked controversy, during that period and has thus attracted a lot of attention from other researchers. In this study, Bale and Cannonbright had the strongest citation bursts early on from 1992 to 2000. On the other hand, authors such as Kittler, Argenziano and Gandini continuing up until the end of the selected study date. This provides a temporal overview of the popularity of authors for researchers at a quick glance and suggests whose work is more relevant recently.

Despite the effectiveness of bibliometric analysis, it is essential to be mindful of its limitations. First, the data derived from scientific databases such as Scopus and Web of Science can contain errors. These inaccuracies can influence any subsequent analysis. Furthermore, the very methodology of bibliometrics poses inherent constraints. Specifically, drawing qualitative interpretations from bibliometric analysis can be misleading, given its fundamentally quantitative nature. As such, caution should be exercised when drawing qualitative inferences from bibliometric findings [25].

Conclusions

The present bibliometric study provides a comprehensive overview of dysplastic nevi and melanoma research field over the past three decades. Despite a noticeable decrease in the number of publications over the years, the focus on this topic remains significant due to the established correlation between dysplastic nevi and melanoma. The US holds a central role in this field, contributing the highest number of publications, yet recent citation bursts in Spain, Romania, France, and Poland indicate growing contributions from these countries.

Co-citation analysis revealed influential works and authors in the field, with Gandini et al 2005 [7] paper holding the highest centrality, reflecting its pivotal role in the research landscape. Journals including the Journal of the American Academy of Dermatology, Archives of Dermatology, and Journal of Investigative Dermatology dominate the publishing sphere in this area. Burst analyses showcased authors like Kittler, Argenziano, and Gandini as significant contributors, with their works receiving strong citation bursts extending until the end of the study period.

Overall, this bibliometric review offers critical insights into the evolving landscape of dysplastic nevi and melanoma research, shedding light on influential contributors, key themes, and potential future directions.

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