

Bibliometric Analysis of Cough Variant Asthma from 1993 to 2022

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Purpose: Cough variant asthma (CVA) is a chronic inflammatory disease characterized by recurrent coughing, a prevalent cause of chronic cough in children and adults. As a unique form of asthma, researchers have recently become increasingly interested in developing effective diagnostic and treatment methods. Currently, there has been no bibliometric analysis in CVA. Therefore, this study aims to enrich this knowledge network by examining the current development status, research focal points, and emerging trends in this field.

Methods: Articles and reviews on CVA published between 1993 and 2022 were collected from the Web of Science Core Collection (WoSCC) database. Relevant data from the reports were extracted, and collaborative network analysis was performed using CiteSpace and VOSviewer software.

Results: 772 articles were included in this study, indicating a significant increase since 2019. The countries with the highest output are China, Japan. The Journal of Asthma and Pulmonary Pharmacology Therapeutics emerged as the most prolific journals in this field. Keyword analysis revealed 22 clusters, highlighting airway inflammation, airway hyperresponsiveness, and eosinophil as the main focus and frontier of research on CVA.

Conclusion: From the visual analysis results, the research of CVA is still in the development stage, and there is no unified definition of pathogenesis, diagnostic criteria and treatment strategies. Therefore, researchers and teams should actively carry out cross-institutional and cross-regional cooperation, expand cooperation areas, and carry out high-quality clinical research in the future.

Keywords: Citespace, VOSviewer, keywords, hotspots

Introduction

Cough variant asthma (CVA) is a chronic inflammatory disease characterized by recurrent coughing, a prevalent cause of chronic cough in children and adults. It has been identified as the second most significant trigger for chronic cough in Europe and the USA.¹ In China, a prospective multicenter clinical trial study² found that CVA accounted for 32.6% of cases, making it the most common cause of chronic cough. CVA is typically triggered and exacerbated by climatic changes, irritating odors, fumes, dust, and pollen.³ However, due to the absence of wheezing, chest tightness, and dyspnea symptoms commonly associated with asthma, patients may be easily misdiagnosed, or their condition may go undiagnosed altogether.³ Over time, some patients will develop into classic asthma.^{4,5} A three-year follow-up on CVA children showed that 54% of them would develop asthma.⁶ Currently, the pathogenesis of CVA remains unclear, and its treatment is generally consistent with typical asthma management. The main treatment options are inhaled glucocorticoids, bronchodilators, antihistamines, and leukotriene receptor antagonists.⁷ However, long-term medication may lead to abnormal reactions such as oral ulcers, dizziness, nausea, and arrhythmia and carry risks, including drug dependence and recurrence after discontinuation. Therefore, it becomes essential to explore research hotspots and development trends within the field of CVA to find more effective and safer treatment options.

Bibliometric analysis utilizes mathematical and statistical methods to analyze and evaluate literature records in specific research fields from multiple perspectives. Constructing citation network maps allows it to sort out the knowledge structure and predict development trends.^{8,9} This method has been widely used in various disciplines, including oncology,¹⁰ immunology,¹¹ etc. However, in the case of CVA, we noticed a growing number of literature records in this field over the years. Nonetheless, the literature was relatively scattered, and no bibliometric analysis report on CVA has been conducted. We used bibliometric analysis software to review the literature in this field thoroughly. The main objectives of our research are: (i) to identify the key contributors in the field of CVA, including authors, institutions, and countries; (ii) to uncover the intrinsic interconnections of keywords and citations, and explore the current research hotspots and future trends; (iii) to provide inspiration and formulate future research plans for researchers and newcomers in the clinical diagnosis and treatment of CVA, as well as scientific research.

Materials and Methods

Data Collection

The literature data came from the Web of Science Core Collection (WOSCC) database, analyzing all CVA-related literature between 1993 and December 31, 2022. WOSCC is generally widely regarded as the most influential scientific research database compared to other databases, and its extensive collection of literature and user-friendly interface make bibliometric analysis more convenient.^{12,13} The search formula was set as “cough* variant* asthma”, “cough-variant asthma” (article topic), reviews, and other relevant literature (including), excluded document types such as “procedural file”, “seal”, “information file”, “pre-access”, and non-English language publications. Data extracted from selected literature include authors, countries, publication years, document types, research institutions, keywords, citation situations, and publication status. According to the inclusion and exclusion criteria, 772 pieces of literature were retrieved. These raw data were downloaded from WOSCC and saved in plain text format, including complete records and cited literature.

Visualized Analysis

In this study, Microsoft Excel 2019 was utilized to conduct various analyses, including counting the number of publications, calculating the total growth rate, drawing line charts, obtaining the growth curve formula, and predicting the future research trend of CVA-published articles. The prediction model equation derived is represented as $y = x - A(R^2)$, where x denotes the year of publication and y indicates the cumulative number of publications. CiteSpace, a scientific bibliometric analysis software developed by Professor Chen Chaomei, was employed due to its stability, readability, and richness. This software plays a crucial role in evaluating the research status of literature within a specific research field, analyzing collaboration networks, research topics, and research trends.^{14,15} This study used CiteSpace to analyze the distribution or co-authorship relationships of countries, institutions, authors, and journals. The LLR algorithm was utilized to cluster the results of keyword co-occurrence analysis. The CiteSpace software settings were configured with a time-slicing range from 1993 to 2022, one year per slice, and a selection criterion of g-index with $k=25$. The source of terms was set to “all selected”, node type was “one at a time”, and visualization was set to “Cluster view - static”, showing the merged network. Other parameters were adjusted by the CiteSpace manual. VOSviewer, another bibliometric analysis software, employed a similarity mapping visualization technique to display the most critical terms in the clustered publications and the co-occurrence relationships between these terms.¹⁶ In this study, two bibliometric analysis software tools were used to complement each other.

Results

Annual Publication Trends in CVA

According to the literature search and selection strategy, a total of 553 “articles” and 119 “reviews” related to CVA were identified as being published annually. Before 2000, it was in the infancy of research, and CVA research was in its initial stages. In addition, From 1993 to 2022, We can see the number of articles in [Figure 1](#) had been in a growth pattern, reaching a peak in the past two years. Furthermore, in order to further evaluate the changing trend of CVA studies, the linear function $Y=1.6885X-0.4391(R^2=0.7405)$ was established ([Figure 2](#)). Obviously, the research heat of the CVA field will increase year by year in the future.

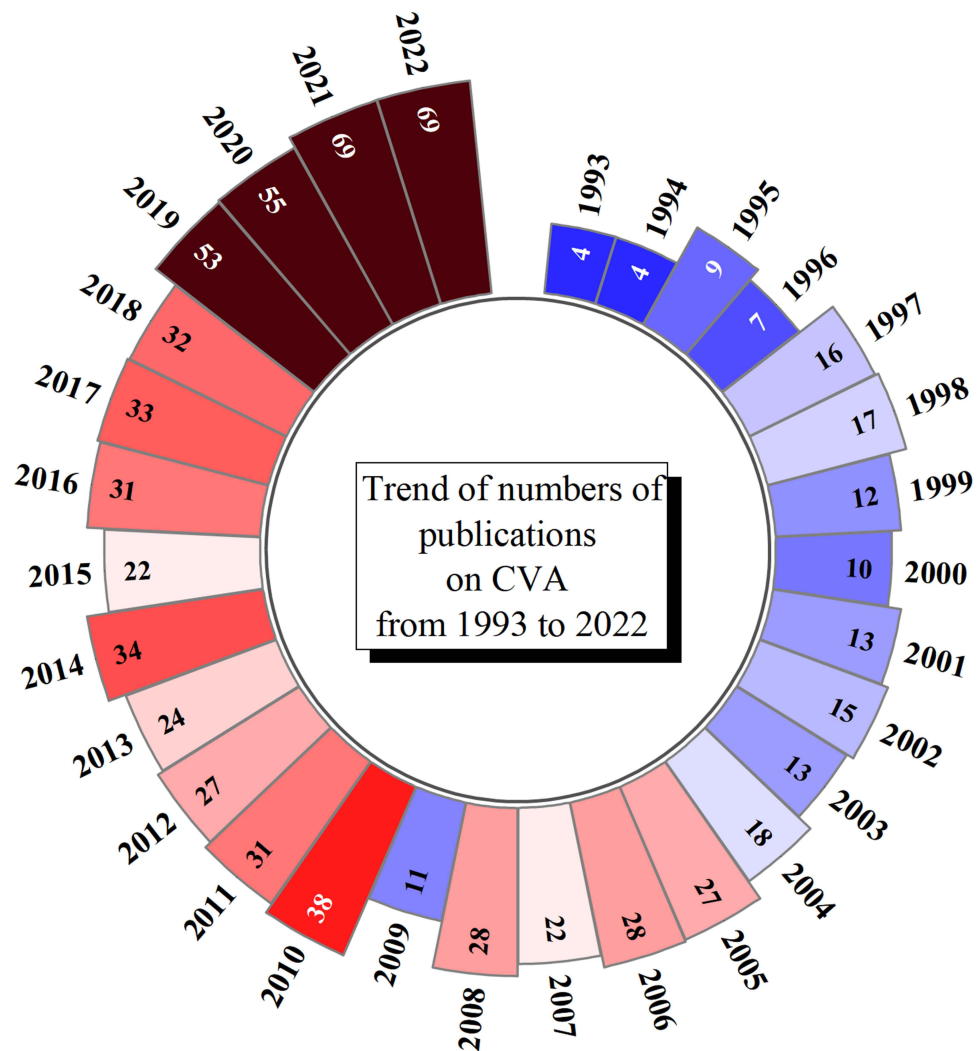


Figure 1 Number of publications on CVA from 1993 to 2022.

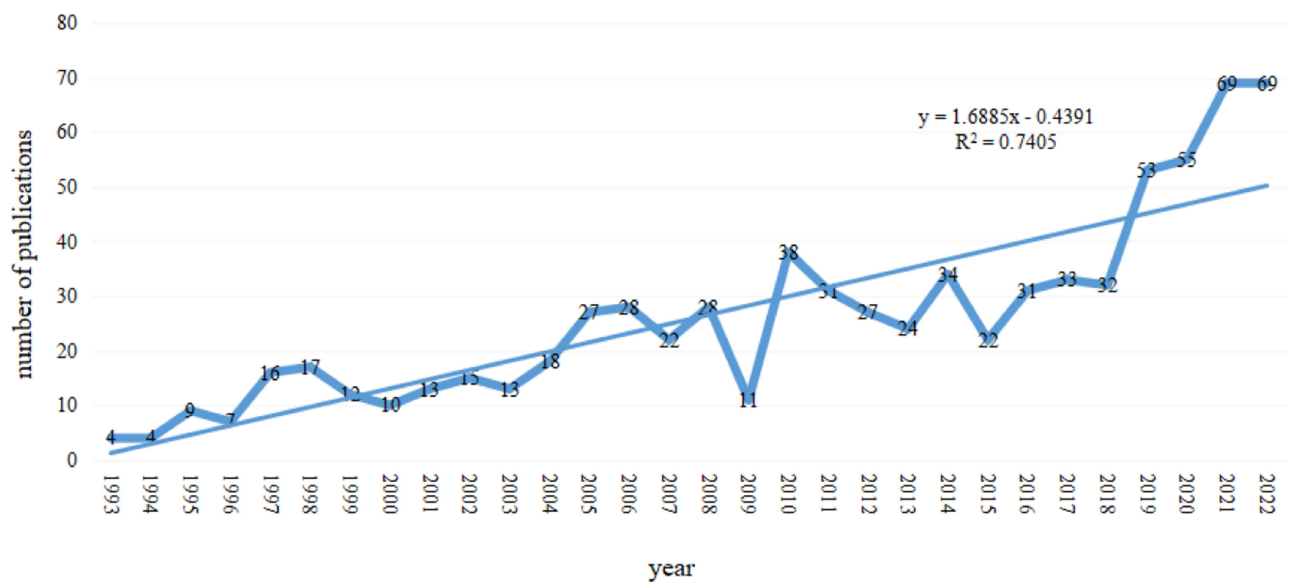


Figure 2 Trend of numbers of publications on CVA by years.

Table 1 The Count and Centrality Among Countries Involved in CVA

Number	Country	Year	Count	Centrality
1	CHINA	1998	169	0.05
2	USA	1993	137	0.39
3	JAPAN	1998	125	0.06
4	UK	1995	99	0.2
5	SOUTH KOREA	1993	46	0.05
6	ITALY	1994	35	0.14
7	CANADA	1997	32	0.16
8	AUSTRALIA	1995	27	0.03
9	FRANCE	1998	18	0.11
10	GERMANY	1997	17	0.03

Contribution of Countries and Institutions

A total of 772 articles were published from 73 different countries and 569 institutions. The top ten publishing countries are shown in Table 1. Notably, China (169, 21.8%), the USA (137, 17.6%), Japan (125, 16.1%), the UK (99, 12.7%), and South Korea (46, 5.9%) are more prominent than others. The contacts and cooperation between countries were depicted in Figures 3 and 4 using CiteSpace and VOSviewer. The thickness of the purple ring in Figure 3 describes the magnitude of the

CiteSpace, v. 6.1.R6 (64-bit) Basic
November 21, 2023 at 4:38:05 PM GMT+08:00
WOS: C:\Users\86178\Desktop\92-2\data
Timespan: 1993-2022 (Slice Length=1)
Selection Criteria: q-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0
Network: N=69, E=125 (Density=0.0533)
Largest CC: 55 (79%)
Nodes Labeled: 1.0%
Pruning: MST

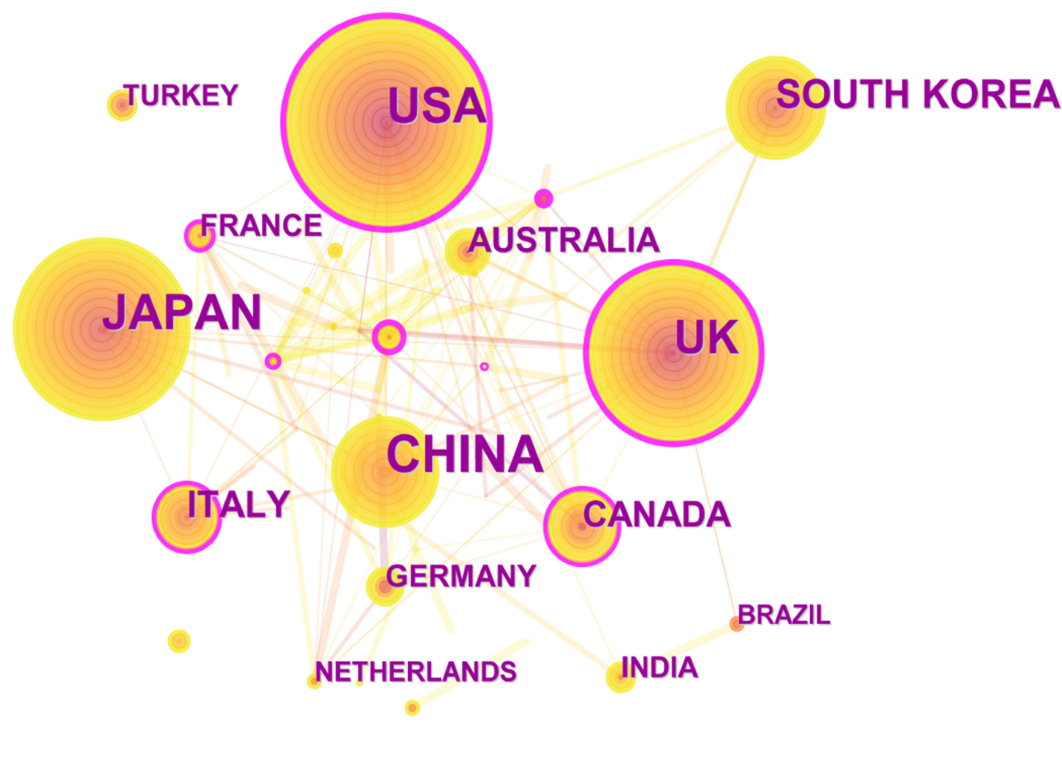
**Figure 3** Links and cooperation between countries by CiteSpace.



Figure 4 Geographical distribution and cooperation of global output by VOSviewer.

centrality value. Centrality measures the importance of nodes in the overall network structure. If the centrality exceeds 0.1, it indicates the node's significant position in the network structure. It was evident that the United States and Britain, as shown in Figure 3, have more pronounced purple, suggesting that they play a crucial role in promoting research progress in the field of CVA. Table 2 lists the top 10 institutions with the most publications, with half being from China and Japan. Notably, there is active cooperation between different institutions, as shown in Figures 5 and 6. For example, Guangzhou Medical University collaborated closely with Tongji University and Zhejiang University.

Table 2 The Count and Centrality Among Institutions Involved in CVA

Number	Institutions	Count	Centrality
1	Guangzhou Medicine University	26	0.01
2	Kyoto University	23	0.06
3	Kanazawa University	19	0.04
4	Shanghai Jiao Tong University	16	0.01
5	Nagoya City University	11	0
6	Tongji University	10	0
7	Seoul Natl University	9	0.02
8	Korea University	7	0
9	Guangzhou University Chinese Medicine	7	0
10	Fudan University	7	0.02

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 November 22, 2023 at 12:53:17 PM GMT+08:00
 VOS: C:\Users\86178\Desktop\92-22\data
 Timespan: 1993-2022 (Slice Length=1)
 Selection Criteria: g-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0
 Network: N=569, E=618 (Density=0.0038)
 Largest CC: 131 (23%)
 Nodes Labeled: 1.0%
 Pruning: Pathfinder

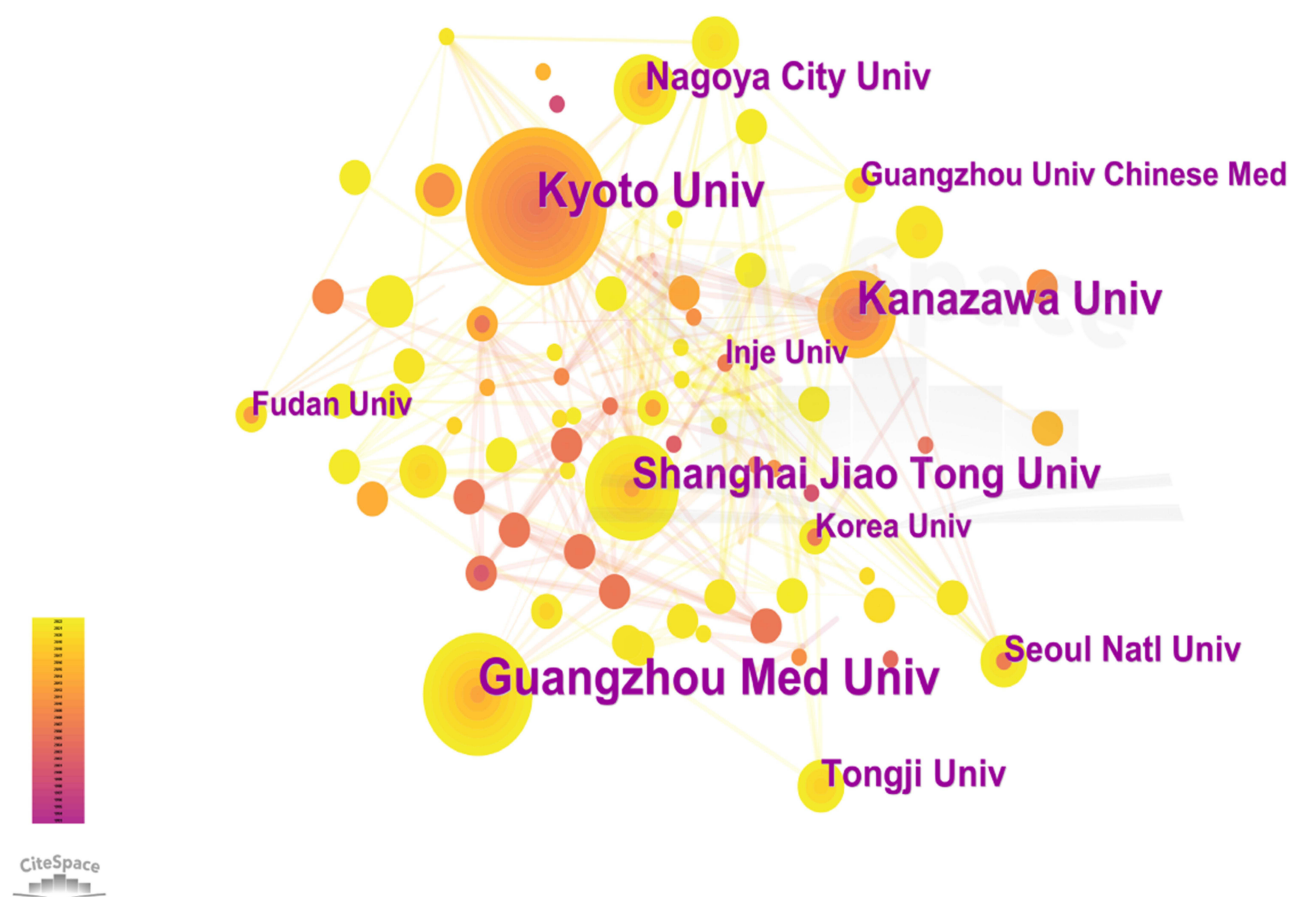


Figure 5 Number of articles and cooperation between different institutions by CiteSpace.

Analysis of Authors and Co-Cited Authors

A total of 755 authors were involved in publishing literature on CVA. As shown in Table 3 and Figure 7, the most significant number of papers were published by Niimi Akio (25, 3.21%). Professor Niimi and his team primarily focus on clinical fields such as respiratory medicine, asthma, allergy, and chronic cough.¹⁷ His research interests are centered around the inflammatory mechanisms of chronic cough, diagnosis, and treatment of chronic cough, pathogenesis and therapeutic strategies of refractory asthma based on phenotypic classification, small airways in asthma, radiologic assessment of airway remodeling, and noninvasive assessment of airway inflammation.¹⁸ The second most prolific author was Fujimura Masaki (24, 3.09%), also from Japan, and they collaborated with each other. Among the top 5 authors, Chinese authors made significant contributions.

Regarding co-cited authors from 1993 to 2022, the top five most cited authors were from the United States, Japan, and the United Kingdom (Table 4). They were Richard S Irwin (497), Fujimura Masaki (446), Niimi Akio (366), Alyn H Morice (272), and Christopher E Brightling (246). Richard S Irwin has been focusing on the etiology and treatment of chronic cough.¹⁹ In the early stage, he published evidence-based guidelines in this field in cooperation with Christopher E Brightling.²⁰ Fujimura Masaki had studied in the field of CVA in the early days.²¹ Niimi Akio and Alyn H Morice have focused on conducting randomized controlled clinical trials in the direction of cough in recent years.²² They had some

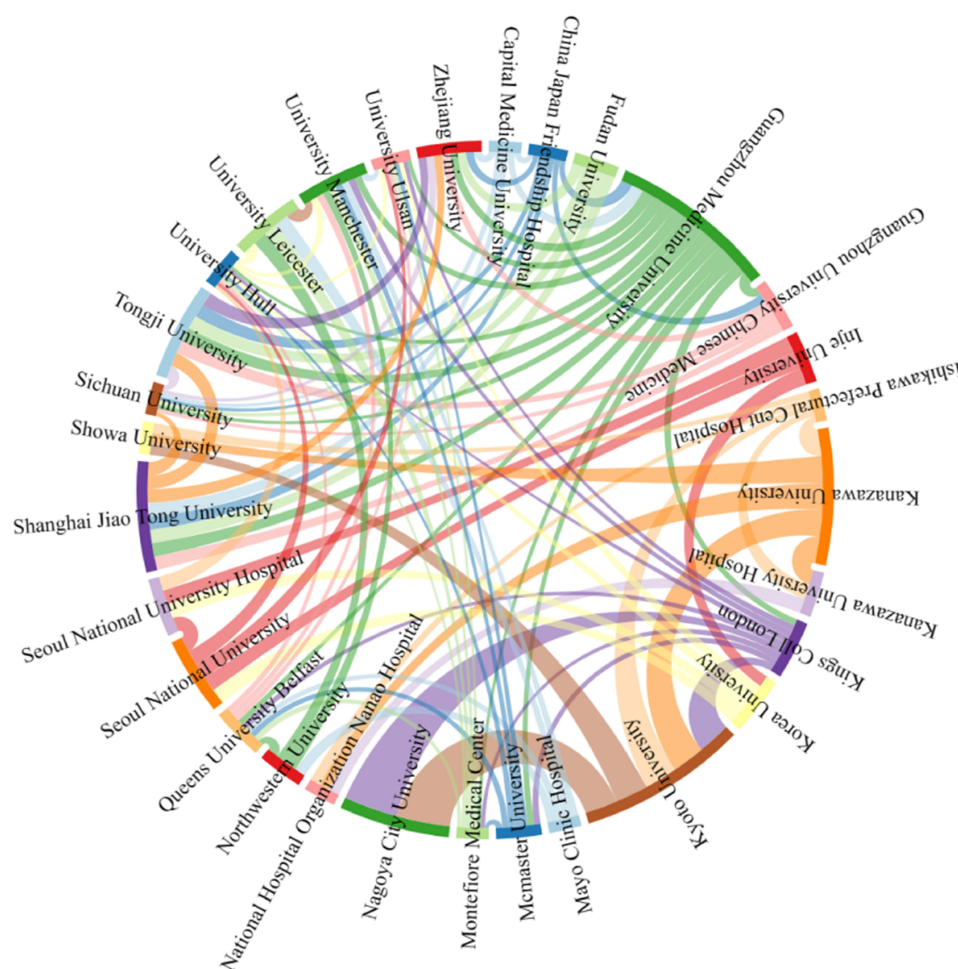


Figure 6 Contribution and cooperation of different institutions by chord chart.

cooperation with each other but belonged to different cooperative groups, each occupying a prominent research position (Figure 8).

Analysis of Journals and Co-Cited Journals

We utilized the VOSviewer software to visualize and analyze the published journals. Our analysis revealed that 772 CVA-related articles were published in 315 academic journals. The Journal of Asthma published the most significant number of papers, with 35 articles carrying substantial weight in the density map (Figure 9), followed closely by Chest (30, 3.86%). Among the top 10 scientific journals, the European Respiratory Journal boasts the highest impact factor (IF) of 12.339. Furthermore, our analysis indicated that 60% of the journals were categorized in the Q1 or Q2 JCR region

Table 3 Top 5 Most Active Authors in CVA from 1993 to 2022

Number	Author	Count	Country
1	Niimi Akio	25	JAPAN
2	Fujimura Masaki	24	JAPAN
3	Lai Kefang	16	CHINA
4	Luo Wei	8	CHINA
5	Abo Miki	8	JAPAN

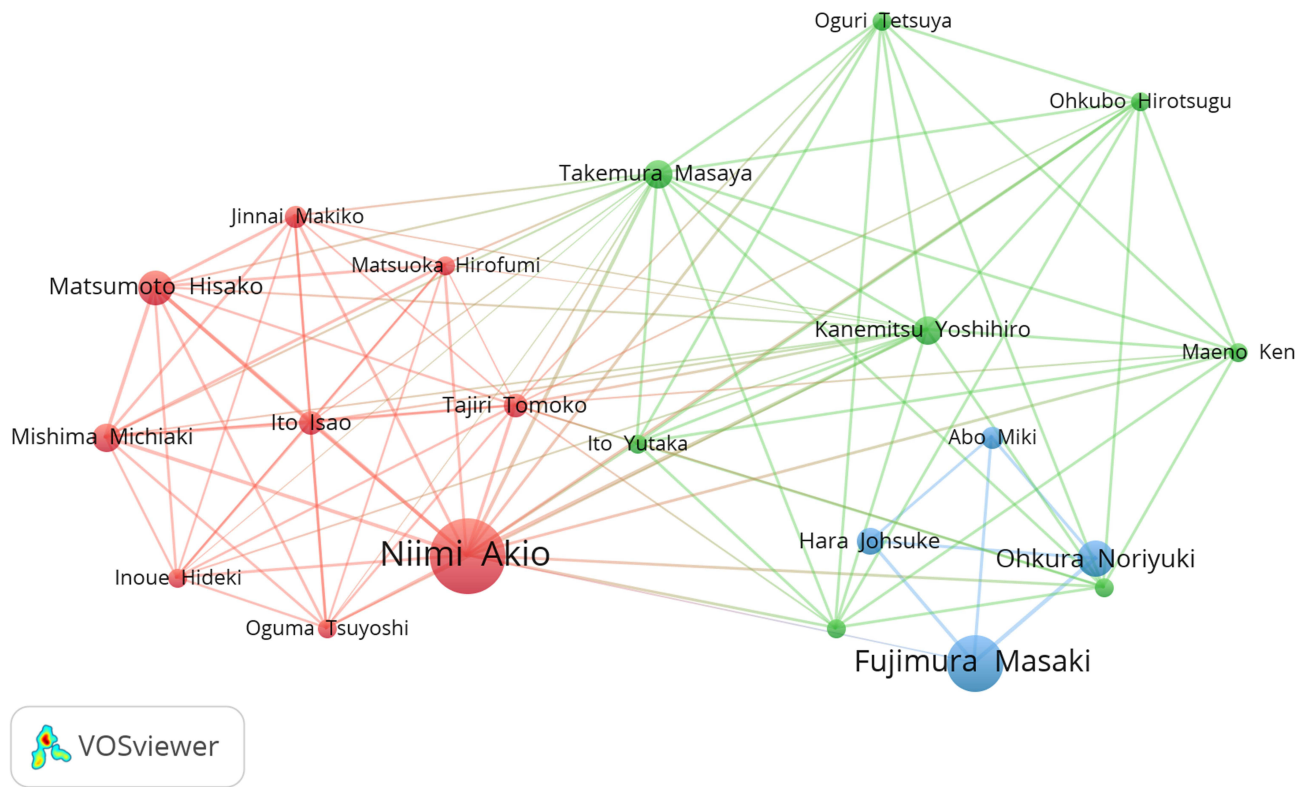


Figure 7 The network on authors of CVA by VOSviewer.

(Table 5). In Table 6, we found five journals cited more than 1000 times among the top 10 co-cited academic journals. The American Journal of Respiratory and Critical Care Medicine had the largest citations (1839), followed by Chest (1769). According to the 2023 Journal Citation Reports (JCR), 90% of the co-cited journals in the top 10 were located in the Q1 region. In Figure 10, the VOSviewer software drew a network visualization map of journal co-citation analysis. The dual-map overlaid journals can intuitively display citation combinations of various documents, clarify the cooperative relationship between citing journals and cited journals in different research fields, and reflect the mobility of disciplines at the journal level.²³ The green path revealed that MEDICINE/MEDICAL/CLINICAL, often referred to as MOLECULAR/BIOLOGY/GENETICS and DERMATOLOGY/DENTISTRY/SURGERY, as well as HEALTH/NURSING/MEDICINE. MOLECULAR/BIOLOGY/GENETICS were often referenced by MOLECULAR/BIOLOGY/IMMUNOLOGY and MEDICINE/MEDICAL/CLINICAL.

Analysis of Keywords

Keywords are crucial elements of a paper, providing a concise summary of the topic and content of literature research. High-frequency keywords can reveal a particular discipline’s development process, research focus, and direction, offering

Table 4 Top 5 Most Active Co-Cited Authors in CVA from 1993 to 2022

Number	Institutions	Count	Country
1	Richard S Irwin	497	USA
2	Fujimura Masaki	446	JAPAN
3	Niimi Akio	366	JAPAN
4	Alyn H Morice	272	UK
5	Christopher E Brightling	246	UK

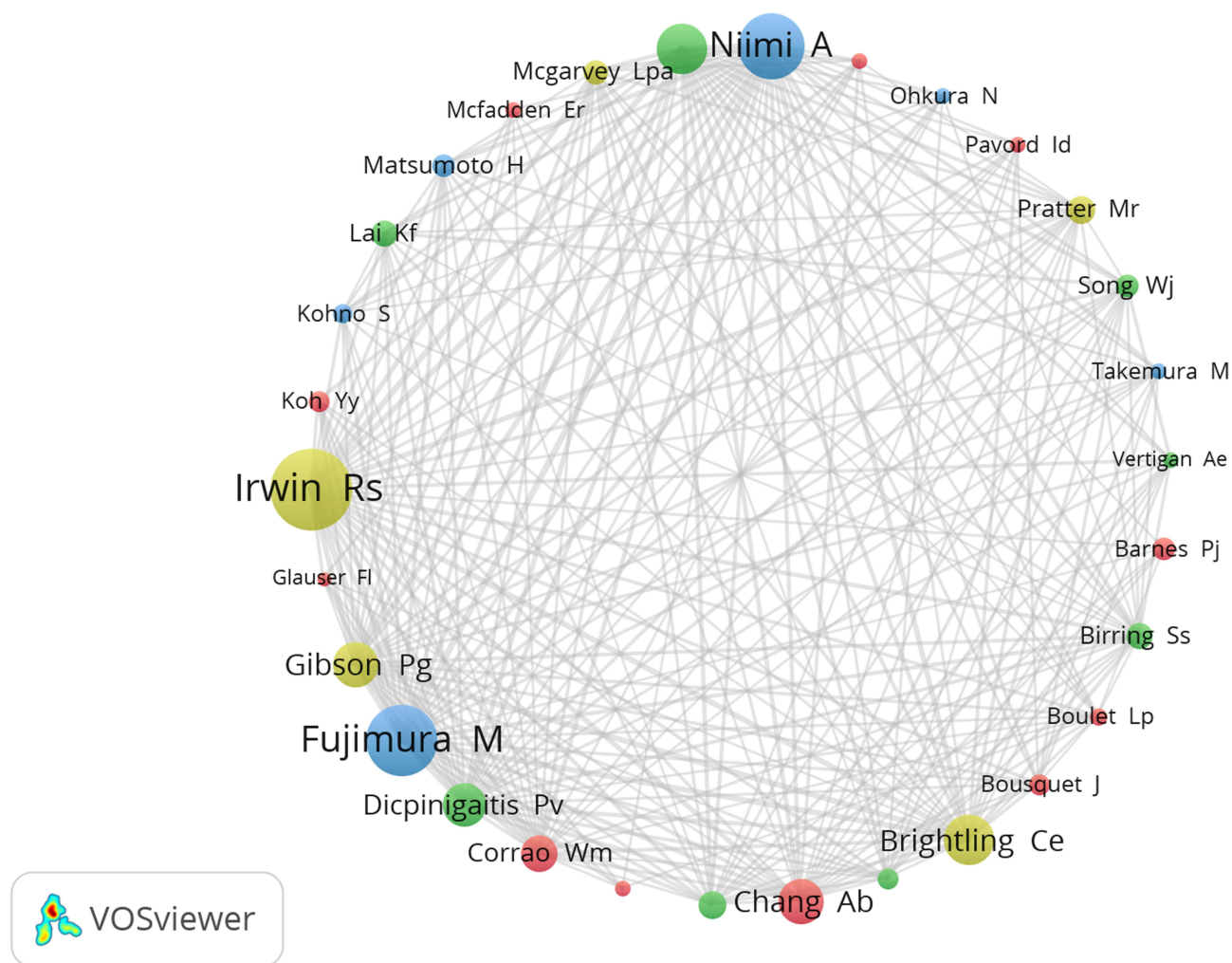


Figure 8 Contribution and cooperation of different authors by VOSviewer.

insights into future trends.²⁴ In this study, 669 keywords appeared, with 2652 connections between them, as depicted in Figure 11. High-frequency keywords included airway inflammation, asthma, chronic cough, airway hyperresponsiveness, children, respiratory symptoms, diagnosis, management, eosinophils, and more. Among these, airway inflammation and airway hyperresponsiveness were identified as crucial research mechanisms of the disease. Additionally, asthma, allergic rhinitis, and chronic cough were found to be closely related to this condition (Table 7).

As depicted in Figure 12, the data was divided into five crucial clusters based on color. The red cluster included keywords such as asthma, eosinophils, lung function, smooth muscle, and airflow obstruction. The green cluster encompassed disease, impact, protein, cells, and activation. The blue cluster included chronic cough, management, diagnosis, and therapy. The yellow cluster included children, adults, allergic rhinitis, respiratory symptoms, and prevalence. Lastly, the purple cluster comprised the airway, atopic cough, cough variant asthma, induced sputum, and methacholine.

Keyword emergence can serve as an indicator for tracking shifts in research focal points within a specific field.²⁵ As depicted in Figure 13, the red part indicated a sudden increase in the use of the keyword during this period, while blue represented the relative unpopularity of the word. The chart on keyword emergence revealed that the majority of studies focused on children in the past. However, as research advanced, subsequent investigations also included a significant number of adult patients. In terms of research direction, since 2016, there has been a growing inclination towards clinical observation and application, encompassing randomized double-blind controlled studies and evidence-based guidelines.

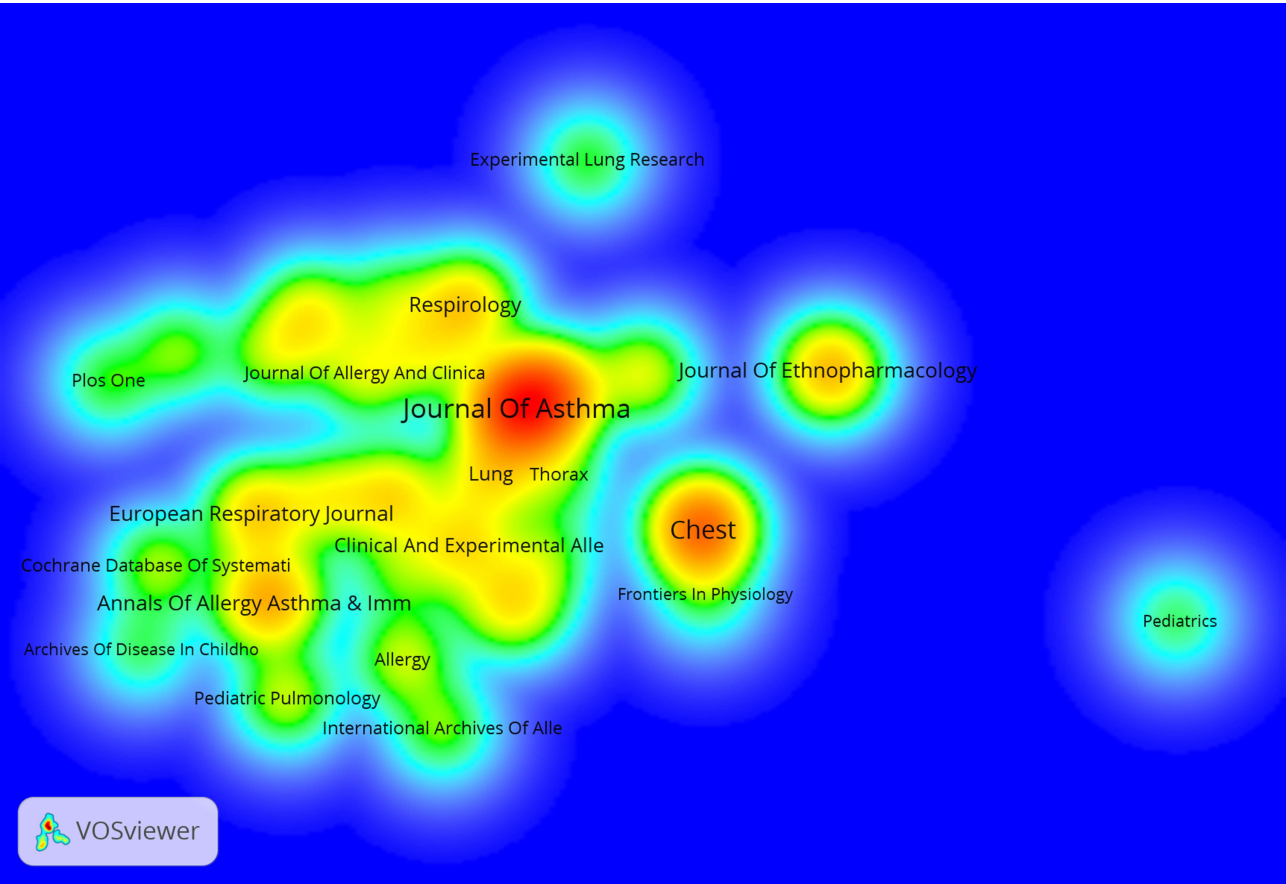


Figure 9 The weight of different publications in the density map.

CiteSpace 6.1.R6 software was utilized to conduct a cluster analysis of the LLR test algorithm on keywords, further exploring the profound relationship between research hotspots. In [Figure 14](#), $Q=0.8261>0.3$ indicated that the network clustering structure was significant, and $S=0.9157>0.5$ indicated that the clusters were reasonable. A total of 22 clusters were formed in [Table 8](#), represented by different color blocks. Among them, the related pathogenesis classified as CVA includes airway inflammation and bronchial responsiveness, while the related disease classified as CVA includes classic asthma and allergic rhinitis. This aligned with the keyword emergence results. Additionally, from the perspective of the

Table 5 Top 10 Most Active Journals in CVA from 1993 to 2022

Number	Journals	Count	IF	JCR
			(JCR2023)	
1	Journal Of Asthma	35	1.899	Q4
2	Chest	30	8.308	Q1
3	Pulmonary Pharmacology & Therapeutics	23	2.681	Q3
4	Journal Of Ethnopharmacology	18	3.69	Q2
5	European Respiratory Journal	15	12.339	Q1
6	Respirology	15	4.88	Q2
7	Annals Of Allergy Asthma & Immunology	14	4.969	Q2
8	Respiratory Medicine	13	3.095	Q3
9	Clinical And Experimental Allergy	12	4.217	Q2
10	Lung	12	1.817	Q3

Number	Institutions	Count	IF	JCR
			(JCR2023)	
1	American Journal Of Respiratory And Critical Care Medicine	1839	17.452	Q1
2	Chest	1769	8.308	Q1
3	European Respiratory Journal	1567	12.339	Q1
4	Journal of Allergy and Clinical Immunology	1470	10.228	Q1
5	Thorax	1251	8.834	Q1
6	American Review of Respiratory Disease	736	/	Q1
7	New England Journal of Medicine	700	74.699	Q1
8	Lancet	620	60.392	Q1
9	Clinical & Experimental Allergy	607	4.217	Q2
10	Allergy	550	8.706	Q1

Analysis of References

Journal of Asthma and Allergy 2024:17

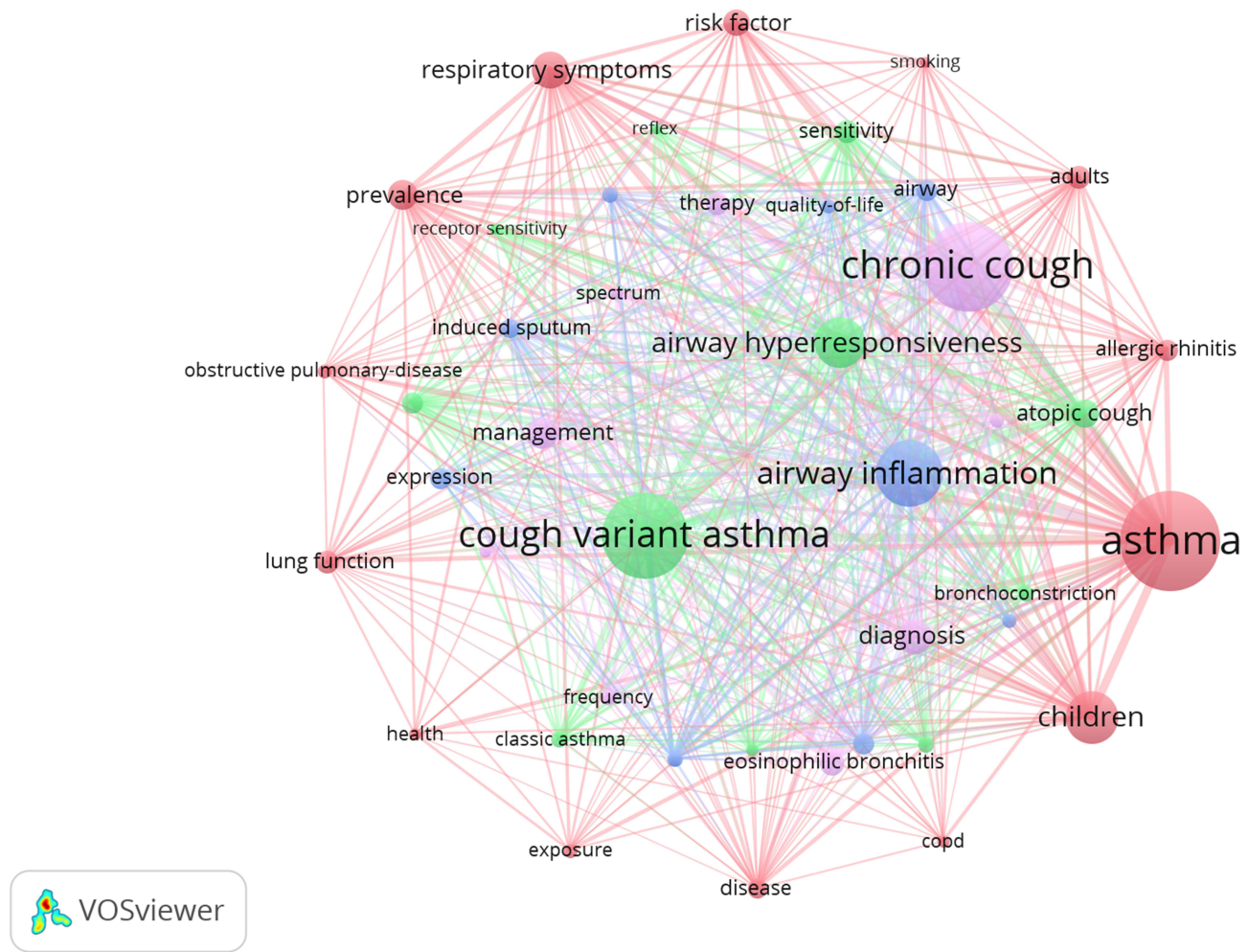


Figure 11 Network on keywords of CVA by VOSviewer.

Discussion

General Information

Bibliometric analysis is a valuable scientific method that combines mathematical and statistical techniques with data visualization. It can assist in determining the overall knowledge structure, identifying development trends, and

Table 7 Top 20 Keywords with the Highest Frequency of Occurrence

Number	Keyword	Year	Count	Centrality
1	Cough variant asthma	1995	240	0.04
2	Airway inflammation	1997	171	0.12
3	Asthma	1993	156	0.14
4	Chronic cough	1995	152	0.15
5	Airway hyperresponsiveness	1996	107	0.13
6	Children	1993	101	0.16
7	Respiratory symptom	1997	84	0.1
8	Diagnosis	1993	72	0.06
9	Management	2006	68	0.05
10	Eosinophilic	2000	55	0.09

(Continued)

Top 20 Keywords with the Strongest Citation Bursts

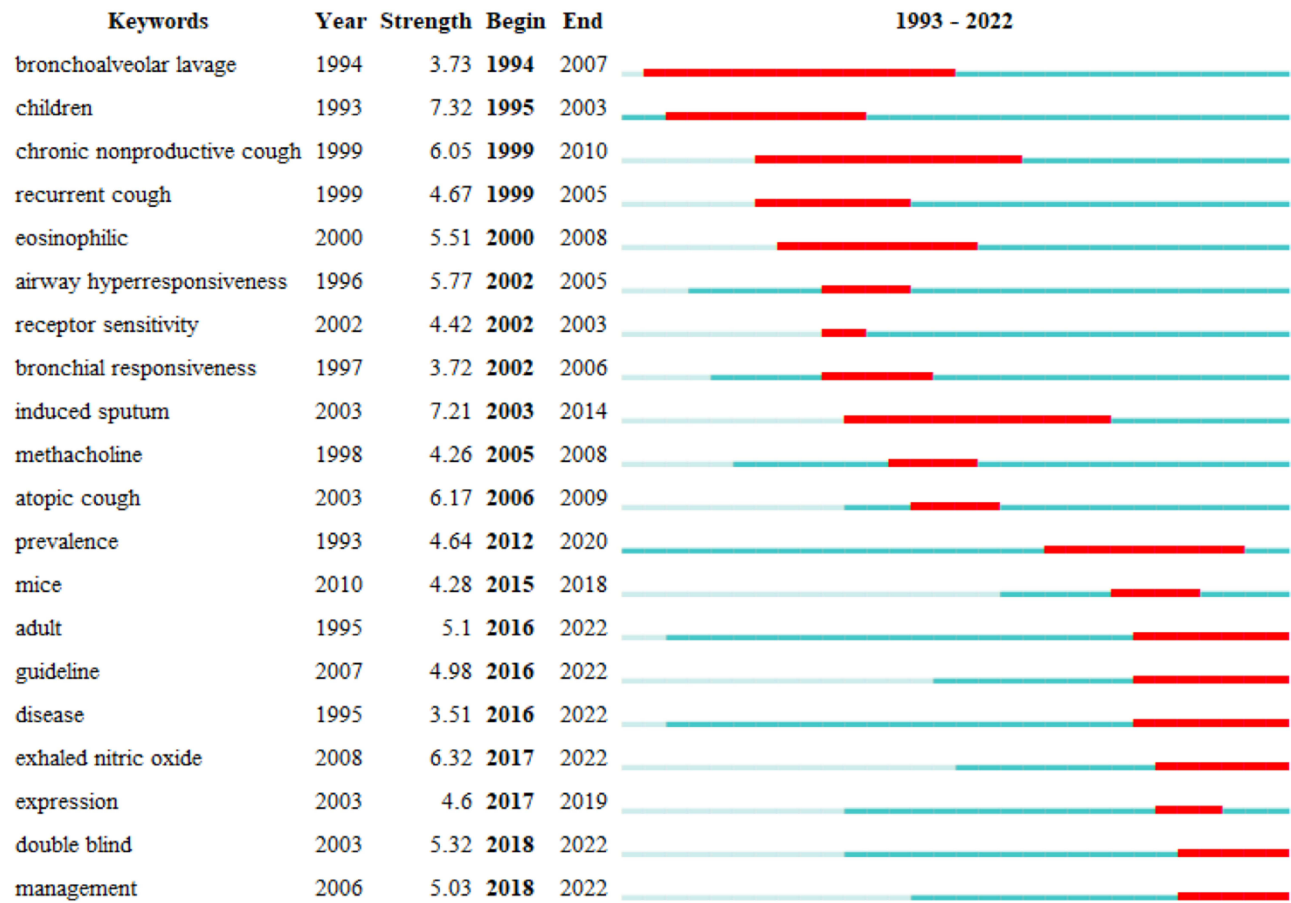


Figure 13 Top 20 representative burst keywords in CVA research by CiteSpace.

increasing global air pollution levels. In clinical practice, CVA is challenging in diagnosis and often gets misdiagnosed as other bronchial diseases. If left untreated, CVA can progress to typical asthma. Currently, glucocorticoids remain the primary choice for clinical management of CVA.^{1,37} While conventional medications can alleviate symptoms and reduce inflammation, the adverse effects associated with long-term use and the recurrence of the disease have led to a focus on the development of new effective drugs. Given CVA’s diagnostic and treatment challenges, we undertook a bibliometric analysis spanning the past three decades to gain insights into this field.

From the analysis of annual publication trends, it was evident that CVA research has shown consistent growth from 1993 to 2022, indicating increasing interest from researchers in this field. Approximately 80% of the publications analyzed were original research studies. To the best of our knowledge, this study represented the first comprehensive bibliometric analysis in the field of CVA research. Despite the continuous growth in publications over the years, the specific mechanisms underlying the development of CVA remain unclear. Current treatment options for CVA lack specificity and can only provide symptomatic relief and anti-inflammatory effects without addressing long-term outcomes. This highlights the need for further breakthroughs and innovations in the field to explore more effective therapeutic targets.

The analysis of publication and collaboration trends among authors and institutions indicated that research on CVA was concentrated in Japan, China, and the United States, with a strong presence of authors affiliated with the research teams led by Niimi Akio and Fujimura Masaki. The impact factors of journals publishing CVA-related articles were relatively low, while the cited articles often had high impact factors but were published many years ago. These findings suggested a lack of cross-regional communication and collaboration, leading to fragmented research efforts and uneven

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 October 20, 2023 at 10:55:14 AM GMT+08:00
 WoB: C:\Users\86170\Desktop\92-22\data
 Timespan: 1993-2022 (Slice Length=1)
 Selection Criteria: g-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0
 Network: N=469, E=1424 (Density=0.0954)
 Largest CC: 625 (93%)
 Nodes Labeled: 1.0%
 Pruning: Pathfinder
 Modularity Q=0.8281
 Weighted Mean Silhouette S=0.9157
 Harmonic Mean(Q, S)=0.8997

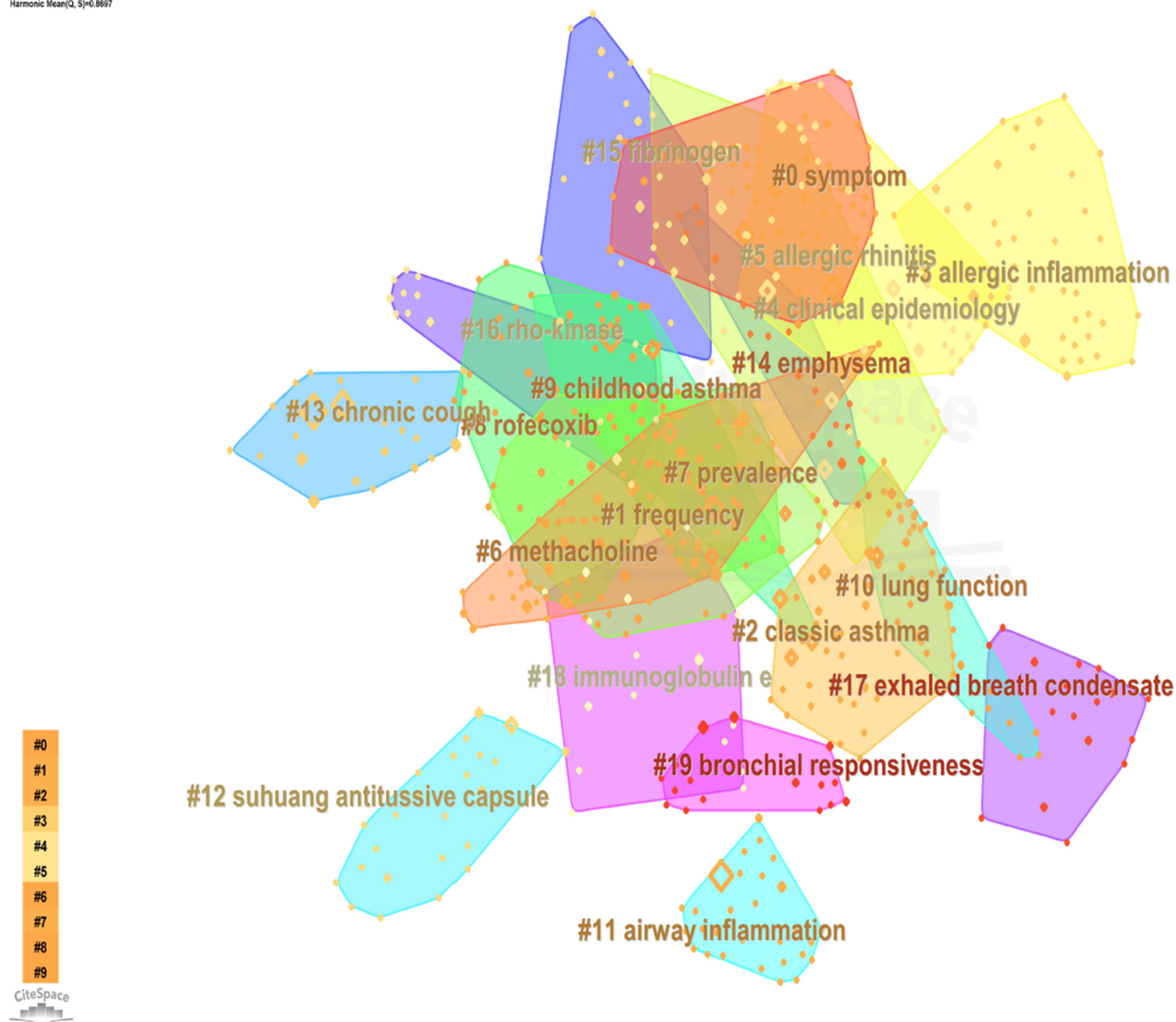


Figure 14 Cluster analysis of the LLR test algorithm on keywords by CiteSpace.

regional development. It is recommended that future research in the field of CVA break down regional barriers, expand research networks, strengthen regional collaborations, conduct multicenter and large-scale randomized controlled trials, and strive to generate higher-quality evidence. These efforts will contribute to advancing academic progress and development in the field of CVA.

The Hotspots and Frontiers

Keyword analysis can reveal current research hotspots and future research trends, including mechanisms, diagnosis, treatment, and related diseases. The research findings highlighted that the main areas of focus in understanding the pathogenesis of CVA are airway inflammation and airway hyperresponsiveness. Research conducted by Gibson et al³⁸ indicated that up to 50% of CVA patients have eosinophilic bronchitis, with eosinophilia levels similar to those observed in asthma. Numerous studies have shown that the dysfunction of Helper T Cells plays an essential role in the

Table 8 22 Clusters Formed with the LLR Test Algorithm on Keywords by Citespace

ClusterID	Size	Silhouette	Mean (Year)	Label (LLR)
#0	50	0.936	2005	Symptom; controlled trial; asthma; chronic cough; rural
#1	46	0.78	2008	Frequency; spectrum; gastroesophageal reflux disease; therapy; postnasal drip syndrome
#2	45	0.875	2005	Classic asthma; cough-variant asthma; maximal airway response; fractional exhaled nitric oxide; airway hypersensitivity
#3	42	0.925	2010	Allergic inflammation; air pollution; release; asian dust; daily cough symptom
#4	40	0.943	2008	clinical epidemiology; questionnaire; exposure; methacholine challenge test; community
#5	34	0.937	2012	Allergic rhinitis; asthma control; rhinosinusitis; sputum; small airways dysfunction
#6	33	0.849	2006	Methacholine; bronchial hyper-responsiveness; azelastine hydrochloride; dry powder; variable airflow obstruction
#7	32	0.947	2004	Prevalence; diagnosis; childhood; respiratory symptom; chronic bronchitis
#8	32	0.922	2007	Rofecoxib; analgesic intolerance; meloxicam; aspirin; exercise
#9	31	0.89	2000	Childhood asthma; chronic cough; risk factors; cough variant asthma; infection
#10	29	0.941	2007	Lung function; occupational asthma; wood dust; respiratory symptoms; paradoxical vocal fold motion
#11	29	0.975	1998	Airway inflammation; bronchoalveolar lavage; inflammation; sensitivity; suppurative lung disease
#12	24	1	2014	Suhuang antitussive capsule; phytochemistry; fungus-associated chronic cough; basidiomycetous fungi; empirical therapy
#13	23	0.848	2004	Chronic cough; gastroesophageal reflux; variant asthma; chronic persistent cough; upper airway cough syndrome
#14	22	0.957	2006	Emphysema; biopsy; allergic bronchopulmonary aspergillosis; chronic bronchitis; alternaria alternata
#15	18	0.835	2011	Fibrinogen; t; macrophage polarization; muscarinic; acute viral bronchiolitis
#16	18	0.974	2006	Rho-kinase; single nucleotide polymorphisms; muscarinic receptors; mechanism; genetic variants
#17	17	0.943	2004	Exhaled breath condensate; hydrocarbons; clinical practice; arterial hypertension; non-invasive monitoring
#18	16	0.865	2016	Immunoglobulin; pulmonary safety; acupuncture combined; 120 mg; precision medicine
#19	16	0.994	2001	Bronchial responsiveness; capsaicin; lymphocytes t; IFN-gamma/IL-4; intracellular cytokine
#20	15	1	2001	Sweeteners; dyes; inertingredients; theophylline; antidiarrheal drugs
#21	13	1	2010	Antioxidant activity; anti hsv-1 activity; cecropia glaziovii; traditional healer; Congo basin

Table 9 The 10 Most Frequently Cited References Involved in CVA

Number	Author	Journals	Years	References	Count
1	Corrao W M	New England Journal of Medicine	1979	[26]	146
2	Richard S Irwin	American Review of Respiratory Diseases	1990	[27]	82
3	Fujimura Masaki	Thorax	2003	[28]	80
4	Niimi Akio	European Respiratory Journal	1998	[29]	77
5	Niimi Akio	Lancet	2000	[30]	64
6	Gibson PG	Lancet	1989	[31]	62
7	Christopher E Brightling	American Journal of Respiratory and Critical Care Medicine	1999	[32]	57
8	Richard S Irwin	Archives of Internal Medicine	1997	[33]	56
9	Kohno S	Respirology	2006	[34]	55
10	Fujimura Masaki	Respirology	2005	[21]	51

Top 25 References with the Strongest Citation Bursts

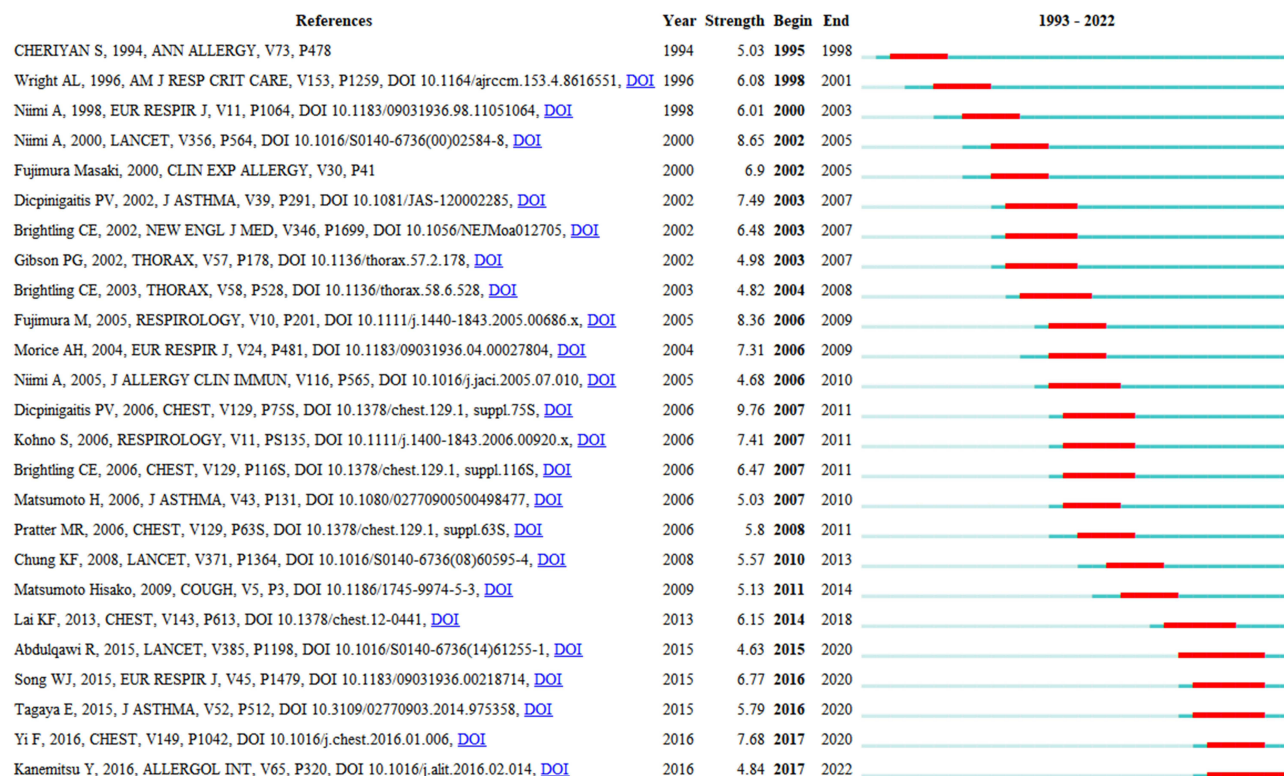


Figure 15 Top 25 most cited references based on the strength of the citation burst.

pathogenesis of CVA, and its development is mainly related to the Th2 lymphocytes.³⁹ Airway hyperresponsiveness is another notable feature of CVA, although it is not specific to this subtype. Koh et al⁴⁰ found a correlation between wheezing in CVA patients and increased bronchial hyperresponsiveness. Additionally, clinical studies⁴¹ have observed changes in airway hyperresponsiveness during the treatment of CVA, with initial diagnoses indicating that 76.5% of affected children had mild or very mild hyperresponsiveness. In comparison, 23.5% showed moderate to severe hyperresponsiveness. In the past twenty years, there have been studies mentioning the relationship between CVA and genetics,⁴² but there have been few recent reports on the genetics of CVA, which requires further in-depth research.

In the diagnosis of CVA, several methods are commonly used, including induced sputum, lung function, fractional exhaled nitric oxide (FENO) measurement, and bronchoalveolar lavage fluid analysis.⁴³ Among these methods, induced sputum cell count is a relatively non-invasive and safe approach to identifying airway inflammation. It can accurately differentiate between eosinophilic and non-eosinophilic airway inflammation, providing valuable guidance for treatment decisions.⁴⁴ Studies^{45,46} have found that CVA patients have significantly higher levels of induced sputum histamine concentration, eosinophil cationic protein (ECP), and eosinophil percentage compared to healthy individuals. FENO, a marker of airway inflammation, can be used as a diagnostic tool for eosinophilic airway diseases. It is helpful in evaluating patients with chronic cough and predicting the response to inhaled corticosteroids (ICS) in CVA patients.^{47,48} Yanqi Wang et al⁴⁷ found that the critical value of FENO to distinguish typical asthma from CVA was 48.5 ppb (sensitivity 90.4%, specificity 42.2%). Lung function testing is a primary method for diagnosing CVA, and it primarily focuses on assessing small airway obstruction. In a clinical study⁴⁹ involving 324 patients with chronic cough, it was found that a critical value of 74.6% for forced expiratory flow between 25% and 75% of forced vital capacity (FEF25-75%) had good sensitivity (80.8%) and specificity (72.7%) for identifying CVA. However, the clinical application of small airway indices is still in its early stages, and further clinical research and evidence from evidence-based medicine are needed to establish the diagnostic value of these indices in CVA.

Treatment options include Corticosteroids, Leukotriene Receptor Antagonist, beta-2 agonists, and so on. First, Aspects of Disease Treatment: (1) Corticosteroids: Inhaled corticosteroids are the primary drugs for CVA treatment as bronchiectasis is sensitive to their effects. However, the dosage and treatment duration vary across different countries, such as the United States, Japan, and China. Zafirlukast has been identified as an alternative to corticosteroids in treating refractory CVA with inhaled bronchodilators. It works by inhibiting cough receptor sensitivity.⁵⁰ Bronchodilators have a dual role in diagnosing and treating CVA, including beta-2 agonists. However, it is currently not recommended to use bronchodilators as monotherapy for the maintenance treatment of CVA. They are typically used in combination with ICS. Another study⁵¹ comparing the effectiveness of LTRAs alone and in combination with ICS/LABA found that montelukast alone effectively improved cough VAS score, reduced sputum eosinophil count, and had an antitussive effect. However, patients treated with ICS/LABA experienced more significant improvements in lung function index and peripheral eosinophils. Traditional Chinese Medicine Treatment: Treatment of CVA with traditional Chinese medicine has become a research hotspot, including monomer,⁵² compound,⁵³ acupuncture, etc. Although there are various treatment options available, there is a lack of prospective, multicenter, large sample, randomized controlled clinical studies for CVA. Therefore, future research should focus on higher-quality studies and explore safer, more effective, and environmentally friendly treatment options.

Related diseases: (1) Asthma: Cough variant asthma is considered to be a precursor to typical asthma, and many patients who initially present with cough variant asthma eventually show typical signs of asthma.^{6,28} Moreover, studies have found that cough variant asthma may have a higher wheezing threshold than asthma,⁵⁴ and although the clinical symptoms are not as severe as typical asthma, it still has an imbalance in Th1/Th2 immunity and excessive Th2 secretion in its pathogenesis.⁵⁵ In addition, Fujimura M et al⁵⁶ demonstrated similar levels of exhaled NO and cough reflex sensitivity, and bronchial responsiveness in typical asthma was higher than that in cough variant asthma. This may be related to the high percentage of sputum eosinophils that activate the cytokines of mast cells or other inflammatory cells.⁵ (2) Atopic cough: Investigators found that, although atopic cough and CVA share similar cough characteristics except for the response to bronchodilator therapy, they differ in pathophysiological features. Fujimura M et al²⁸ found that the frequency of typical asthma attacks in patients with atopic cough was significantly lower than that in patients with cough variant asthma, and the level of exhaled NO was significantly lower in patients with atopic cough compared to CVA.⁵⁶ (3) Allergic rhinitis: Tomoko Tajiri et al⁵⁷ first found that CVA was clinically related to allergic rhinitis. The mechanism may be due to persistent eosinophilic inflammation of the lower respiratory tract caused by allergic rhinitis. At the same time, allergic rhinitis often appears as a complication of CVA, indirectly proving the correlation between them.

Limitation

Although we used bibliometric methods to analyze the research content in the field of CVA for the first time. However, there are some limitations to this study. Firstly, we only analyzed the development of CVA research over the past three decades, which may not represent the entire origin and development of the CVA research field. Secondly, we only included the data retrieved from the WoSCC database, resulting in the possibility of incomplete data. In addition, we only covered English-language publications since there were many studies conducted in Asian countries such as China and Japan, which could be subject to language bias, leading to potentially biased results. Therefore, facilitating the integration of large-scale and cross-platform literature data is our next goal.

Conclusion

As far as we know, this study is the first to use bibliometric analysis to analyze trends in research on CVA from 1993 to 2022 regarding temporal evolution and spatial distribution characteristics. From the results of the visual analysis, it was evident that research on CVA is still in the development stage, with limited collaboration between countries, institutions, and individuals. At the same time, there is significant potential for further research in CVA areas, some questions still have no clear answers, such as the pathogenesis and diagnostic criteria of CVA. Therefore, we recommend that researchers and teams actively engage in inter-institutional and inter-regional collaborations, expand their areas of cooperation, and conduct high-quality clinical studies.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China [82074489]; the Major Research Plan of Natural Science Foundation of the Higher Education Institutions of Jiangsu Province [21KJA360002]; National Key Discipline of Pediatrics (Nanjing University of Chinese Medicine) of the State Administration of Traditional Chinese Medicine[NZYEK001]; and Peak talents project of Jiangsu Provincial Hospital of Traditional Chinese Medicine [Y2021rc21].

Disclosure

The authors report no conflicts of interest in this work.

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