

Global trends and knowledge-relationship of symptom clusters in cancer research: a bibliometric analysis over the past 20 years



Review

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Received: 9 September 2022; Accepted: 15 December 2022; Published: 20 September 2023

Abstract: **Objective:** To use CiteSpace and VOSviewer to investigate the scientific production in the field of symptom clusters in cancer research. **Methods:** The search was performed using the terms “symptom clusters,” “cancer,” and “oncology” on the Web of Science Core Collection database. The retrieval time was from 2001 to 2021, which covers the last 2 decades. Based on the production theory of scientific knowledge and the data mining of citations, data pertaining to the annual publications, journals, countries, organizations, authors, and keywords that produce symptom clusters in cancer research, as well as their cooperation (collaboration network), were extracted, and then both were clarified by the software tools VOSviewer (version 1.6.16) and CiteSpace (version 6.1.R2). **Results:** A total of 1796 publications were retrieved between 2001 and 2021, and 473 relevant publications were included after screening. The results showed an increasing trend in published articles. The United States had the largest number of publications (261/473, 55.18%), followed by China and Canada. The University of California, San Francisco, was the most productive institution. Current research hotspots included the analysis of symptom clusters and symptom management in patients with breast cancer and lung cancer, as well as any advanced cancer and cancer cachexia; fatigue-related symptom clusters and depression-anxiety symptom cluster; and the impacts of symptom clusters on quality of life. The research frontiers included analysis between health-related quality of life and symptom clusters, data mining in symptom clusters, research on the mental health status of cancer patients, and study of the mechanism and biological pathways of symptom clusters. **Conclusions:** The study provides insight into the global research perspective for the scientific progress on cancer symptom clusters, which suggests a growing scientific interest in this field, and more studies are warranted to guide symptom management.

Keywords: *bibliometrics • cancer • Citespace • symptom clusters • systematic review • VOSviewer*

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1. Introduction

Cancer ranks as a leading cause of death in most countries of the world, and the burden of cancer incidence and mortality are rapidly growing worldwide.¹ Cancer patients frequently suffer from various symptoms often impairing functional status and quality of life. Controlling disease-related and treatment-related symptoms is an important part of cancer care, and

symptom reduction is crucial for cancer patients.² Compared with non-cancer groups, patients with cancer experienced more symptoms such as tiredness, lack of energy, fatigue, disturbed sleep, distress, headache, etc.^{2,3} Therefore, an understanding of cancer symptoms and symptom management is becoming increasingly necessary.

How to cite this article: An R, Luo Y, Chen WF, Sohaib M, Liu MZ. Global trends and knowledge-relationship of symptom clusters in cancer research: a bibliometric analysis over the past 20 years. *Front Nurs*. 2023;3:273–288.

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Historically, clinicians and researchers acknowledged the presence of multiple symptoms in cancer patients; however, the focus of most research had still been on a single symptom. Patients often experience an array of multiple co-occurring distressing symptoms,⁴ and many of these symptoms tend to cluster together, which collectively impose a symptom burden that is highly disruptive to their physical and emotional functioning.^{5,6} A reduction in symptom burden in these patients has the potential to improve their quality of life.

In 2001, a study suggested that symptom clusters maybe have common underlying mechanisms, and proposed that study of clusters could advance cancer symptom management.⁷ In 2005, another study refined related concepts and published the concept analysis.⁸ The science of symptom management had thus evolved from a focus on single symptoms to the exploration of symptom clusters. While the definition of a symptom cluster was evolving, from a conceptual perspective, the definition of symptom cluster means that 2 or more related symptoms co-occur and form a stable group, and are relatively independent of other clusters, which may have shared underlying mechanisms and outcomes.⁴

In the last 2 decades, a large number of studies on symptom clusters had emerged, which provided a new perspective for symptom management. Many studies have been conducted to determine which symptom clusters exist in cancer patients at various treatment periods, how the symptom clusters affected individual outcomes, and which factors influenced them.^{5,9–11} Examining the current literature indicated the existence of many review studies on symptom clusters in cancer but a lack of bibliometric studies in this field. However, literature review or content analysis may be better suited for a micro-understanding of the details within a particular academic field. To gain a comprehensive review and describe the trends and contributions of countries/regions, journals, scholars, and keywords, bibliometric methods may play a key role.

Bibliometrics is a quantitative analysis of published academic literature, which can identify and visualize established and emerging research areas through co-authorship, co-citation, and co-occurrence analyses.¹²

The purpose of our study is to examine the latest trends in symptom clusters in cancer research using bibliometric analysis. This study was the first quantitative study to evaluate research trends and knowledge linkages in cancer symptom cluster research. It will provide valuable information on future research directions in this rapidly evolving field.

2. Research methodology

2.1. Inclusion criteria

The inclusion criteria used to determine the studies in this research were: (1) literature reviews and articles; (2) published in the Web of Science Core Collection (WOSCC); (3) published in English; (4) focused on symptom clusters in cancer; and (5) published between 2001 and 2021.

2.2. Retrieval strategy

The retrieval strategy was TS = (("cancer" OR "oncology" OR "neoplasm" OR "tumor") AND ("symptom cluster" OR "symptom clusters")). Two authors (An R and Luo Y) searched and screened the articles independently. Any discrepancy was resolved by discussion or seeking assistance from a third author (Chen WF). All data were collected from the WOSCC on 2 April 2022.

2.3. Data collection

The following information was extracted from eligible articles: author names, nationalities, affiliations, article title, year of publication, name of publishing journal, keywords, and abstract. All records were downloaded as a ".txt" file from the WOSCC. Two authors (An R and Luo Y) extracted data from the selected publications independently. If the disagreements remained unsolved, the result was mediated by the third author (Chen WF).

2.4. Bibliometric analysis

A systematic methodological review of symptom clusters in cancer research was followed along with bibliographical techniques, including reference co-citation analysis and document bibliometric coupling analysis. For these techniques, the mapping of the reference co-citation analysis and the document bibliometric coupling analysis was performed using two bibliometric software tools called the Visualization of Science (VOSviewer) mapping software¹³ (version 1.6.16) and Citespace,¹⁴ and the article feature was highlighted manually. Through network mapping, various maps were created simultaneously for countries/regions, institutions, authors, and keywords. Nodes on the map are represented by circles with labels. Larger nodes mean higher frequency, and smaller nodes mean lower frequency. Every circle has a color corresponding to the cluster in which it resides. The thickness and length of lines between nodes show the strength of the connectivity between the words. The results obtained from each of these techniques are presented in the following section.

2.5. Ethical consideration

Data on bibliometric information were retrieved and downloaded from WOSCC. This information is available to the public. Such data extraction does not involve direct contact or interaction with humans. Thus, an ethical review was not required.

3. Results

A total of 1796 articles have been identified; of these articles, literature that was not articles or reviews ($n = 254$) and was not related to the research topic ($n = 1069$) was excluded, and only 473 have been considered for the analysis. These include articles (428), reviews (45), and online submissions (19). The conference, book chapters, letters, editorials, notes, and books have been excluded, as the quality of the content may not be suppressed by peer-reviewed journal articles presented in Figure 1.

3.1. Bibliometric analysis of publication annual output

From 1 article in 2001 to 57 articles in 2021, the number of publications related to symptom clusters on cancer has steadily increased over the past 20 years, with some fluctuations over the years (Figure 2). A high and positive Pearson correlation ($r = 0.959$; $P < 0.001$) was found between the number of publications and year. The positive coefficient of correlation indicates that both variables tend to increase together. Inspecting the graphic histogram, the trend line shows a monotonic relationship between the number of publications and year; as the value of year increases, so does the value of the number of publications. The upward line represents the correlation slope. Linear regression was estimated to forecast the number of future publications. The predictive equation for this linear model calculated that: $y = 2.483x - 4.79$; where y = number of publications, x = year, slope = 2.483, and constant = -4.79 . The

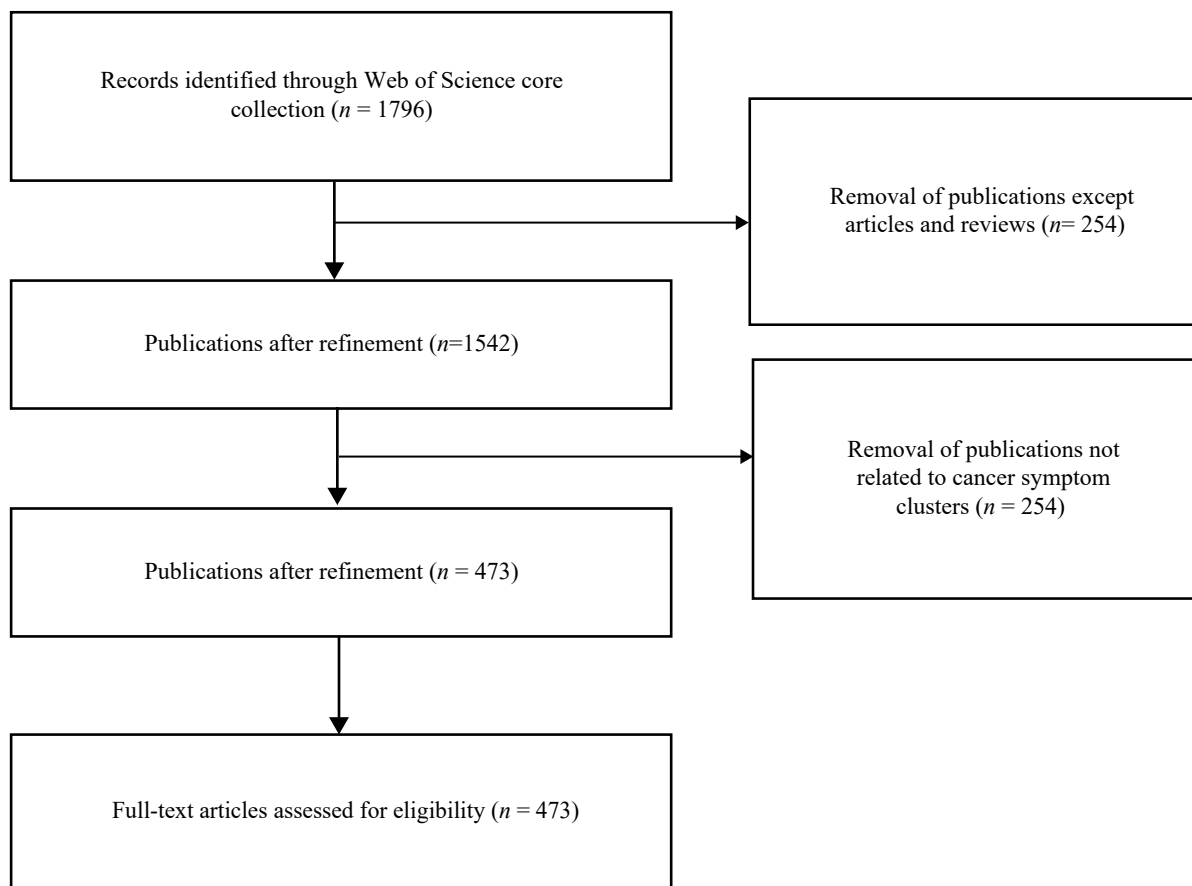


Figure 1. PRISMA flow diagram for selecting a research paper.



Figure 2. Global trends in publications about symptom clusters on cancer.

coefficient of determination was $R^2 = 0.916$, indicating that 91.6% of the data variation of publications can be explained by the variable year.

3.2. Distribution and co-authorship of countries/regions

According to the search results, 473 publications came from 49 countries/regions. As shown in Table 1, the United States has the largest number of publications (261/473, 55.18%), and China ranks second (58/473, 12.26%), followed by Canada (46/473, 9.73%). Figure 3 shows the distribution of the 49 countries/regions that were publishing symptom clusters in cancer research. The greater the weight of a country in the network, the larger the country's label and circle.

The quantity and the width of the lines indicate the intensity of the interaction between countries and the strength of the links. Besides, to measure the influence of the countries/regions, betweenness centrality (BC) is applied based on Freeman's algorithms, and purple circles are used to mark these nodes; and high BC nodes usually serve as a connecting hub between 2 nodes, also called turning points.¹⁵ Thus, by combining Table 1 and Figure 3, we can conclude that the United States has the highest number of publications and shows the closest cooperation with other countries as the core node has been formed. The highest-ranked country by centrality was the United States (centrality, 0.89), followed by England (centrality, 0.27), and Canada (centrality, 0.12).

Rank	Country/region	Centrality	Output (n)	Percent (%)	Citations
1	USA	0.89	261	55.18	9274
2	China	0.08	76	16.07	1574
3	Canada	0.12	46	9.73	1199
4	South Korea	0	37	7.82	764
5	Australia	0.15	31	6.55	822
6	England	0.27	26	5.50	773
7	Germany	0.07	12	2.54	293
8	Brazil	0.01	11	2.33	242
9	Netherlands	0.02	11	2.33	132
10	Sweden	0.01	11	2.33	329

Table 1. Top 10 countries/regions publishing symptom clusters in cancer

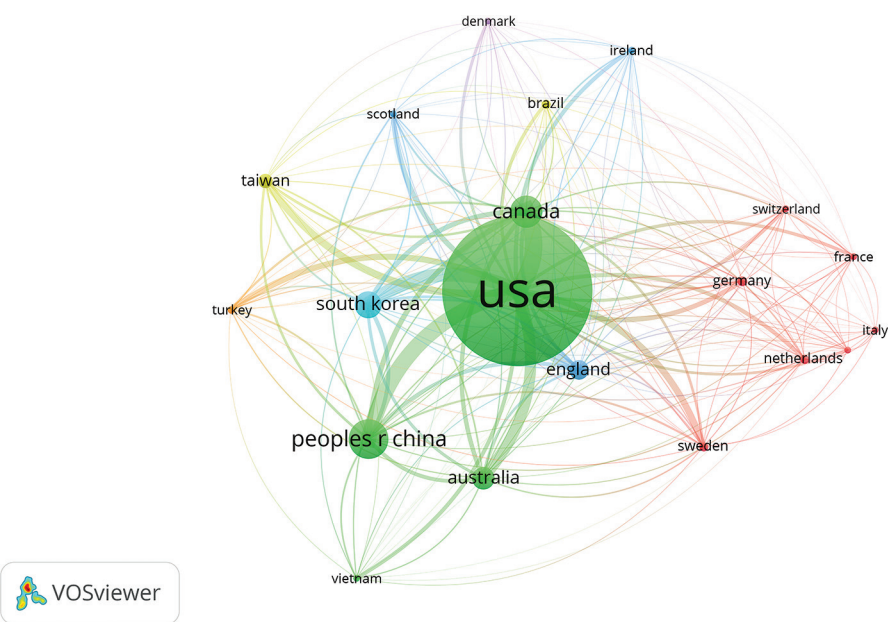


Figure 3. Distribution and co-authorship of countries/regions.

3.3. Distribution and co-authorship of institutions

According to the search results, 825 institutions contributed to cancer symptom clusters research. Table 2 presents the top 10 most productive institutions. The link between institutions is determined by the number of publications co-authored between them, each of which published at least 8 papers and formed 5 clusters (Figure 4). The institutions with the greatest total link strength were selected. The University of California, San Francisco produced 36 articles and a total link strength of 1294, followed by the University of Toronto

(26 articles and 626 collaboration links), and the University of Pittsburgh ranks third, with 24 articles and 429 collaboration links. It is worth mentioning that the average citation frequencies of the University of Pennsylvania, the University of Texas MD Anderson Cancer Center, the University of California, San Francisco, the University of Toronto, and the University of Pittsburgh, are as high as 49.5, 48.1, 35.94, 24.08, and 17.88, respectively; accordingly, it can be concluded that the 5 institutions have made highly relevant and useful contributions, which can be widely referenced by scholars.

Rank	Organization	Centrality	Country	Articles (n)	Citations
1	University of California, San Francisco	0.23	USA	36	1294
2	University of Toronto	0.04	Canada	26	626
3	University of Pittsburgh	0.10	USA	24	429
4	University of Pennsylvania	0.03	USA	18	891
5	The University of Texas MD Anderson Cancer Center	0.13	USA	18	866
6	Duke University	0.06	USA	13	103
7	Cleveland Clinic Foundation	0.02	France	12	583
8	Queensland University of Technology	0.01	Australia	12	390
9	University of Washington	0.01	USA	11	386
10	Chinese University of Hong Kong	0.03	China	11	276

Table 2. Top 10 institutions publishing symptom clusters in cancer

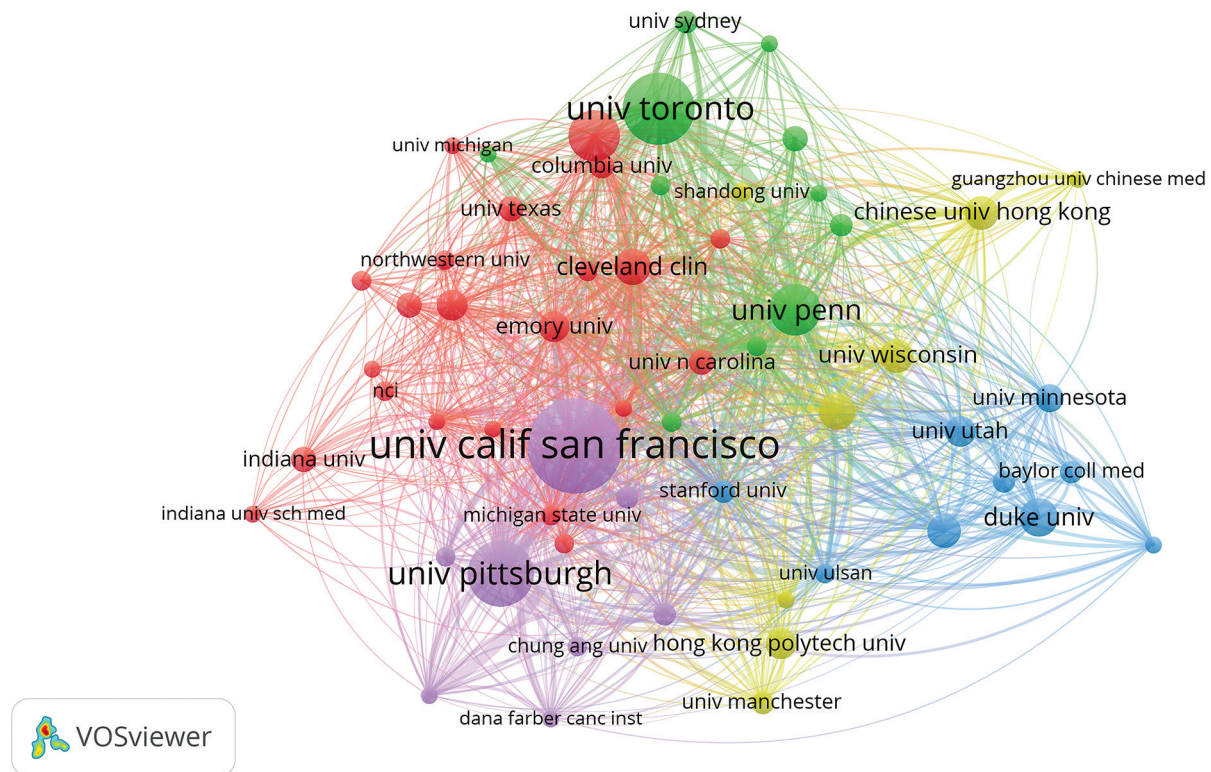


Figure 4. Institution collaboration network of symptom clusters in cancer research.

3.4. Distribution and co-authorship of journal

A total of 473 articles were published in 151 journals. Table 3 indicates the top 10 most productive journals for publishing articles on symptom clusters in cancer. The Journal of Pain and Symptom Management had the largest number of published articles (72 records,

15.22% of all articles), followed by Supportive Care in Cancer (45, 9.51%), Cancer Nursing (31, 6.55%), Oncology Nursing Forum (22, 4.65%), and European Journal of Oncology Nursing (17, 3.59%). A total of 58 journals of the references for all publications that were co-cited in more than 50 publications were analyzed by VOSviewer.

Rank	Journal	Impact factor	Best quartile	Articles (n)	Citations	Percent (%)
1	Journal of Pain and Symptom Management	3.612	Q2	72	3059	15.22
2	Supportive Care in Cancer	3.603	Q2	45	1608	9.51
3	Cancer Nursing	2.592	Q1	31	1004	6.55
4	Oncology Nursing Forum	2.172	Q2	22	920	4.65
5	European Journal of Oncology Nursing	2.398	Q1	17	437	3.59
6	Psycho Oncology	3.894	Q1	13	338	2.75
7	Cancer	6.860	Q1	10	475	2.11
8	Seminars in Oncology Nursing	2.315	Q2	9	225	1.90
9	Journal of Clinical Nursing	3.036	Q1	8	180	1.69
10	Nursing Research	2.381	Q1	7	177	1.48

Table 3. Top 10 journals publishing symptom clusters on cancer

Impact factor and best quartile were calculated based on Journal Citation Reports™ 2020.

3.5. Analysis of keywords

3.5.1. Keyword research hotspot analysis

A total of 188 keywords were identified as having occurred more than 5 times. We used VOSviewer to extract and cluster these keywords. The analysis was conducted after excluding the search terms “symptom clusters” and “cancer.” As shown in Figure 5, we used VOSviewer to build a visualization network map of the 100 keywords with co-occurrence. The node label is the keyword, and the node size represents its frequency. Links connecting 2 nodes represent a co-occurrence relationship between the keywords.

Table 4 shows the 20 keywords with high frequency and high centrality. From the high-frequency keywords and high-centrality keywords, we can analyze the research hotspots in this field. In addition to the search term “symptom cluster,” high-frequency keywords include: symptom cluster, quality of life, breast cancer, fatigue, depression, prevalence, lung cancer, distress, women, pain, etc. The highest-ranked keywords by centrality were “diagnosis” (centrality, 0.21), “adjuvant chemotherapy” (centrality, 0.19), “depression” (centrality, 0.14), and so on.

Combining high-frequency keywords and high-high-centrality keywords and keyword clustering

co-occurrence mapping (Figure 5), the international research hotspots of cancer symptom clusters were ascertained. (1) Focus groups of cancer symptom clusters. In this study, the results showed that the symptom cluster research population was mainly breast cancer, lung cancer, patients with advanced cancer, and patients undergoing palliative care. (2) Common symptoms of the cancer symptom cluster. The common symptoms of cancer symptom clusters include fatigue, cancer-related fatigue (CRF), depression, distress, pain, sleep disturbance, insomnia, sickness behavior, anxiety, etc. (3) Correlation analysis between cancer symptom clusters and quality of life, mainly the investigation of the current status of the quality of life of patients with cancer symptom clusters and the analysis of the impact of cancer symptom clusters on patients' quality of life. (4) Assessment modalities and management of cancer symptom clusters; the main keywords are: assessment scale, models, patient self-reported outcomes, confirmatory factor analysis, functional assessment, symptom management, behavior, acupuncture, etc.

3.5.2. Keyword clustering and evolutionary timeline mapping analysis

CiteSpace analyses helped to closely group associated keywords and identify keyword group clusters,

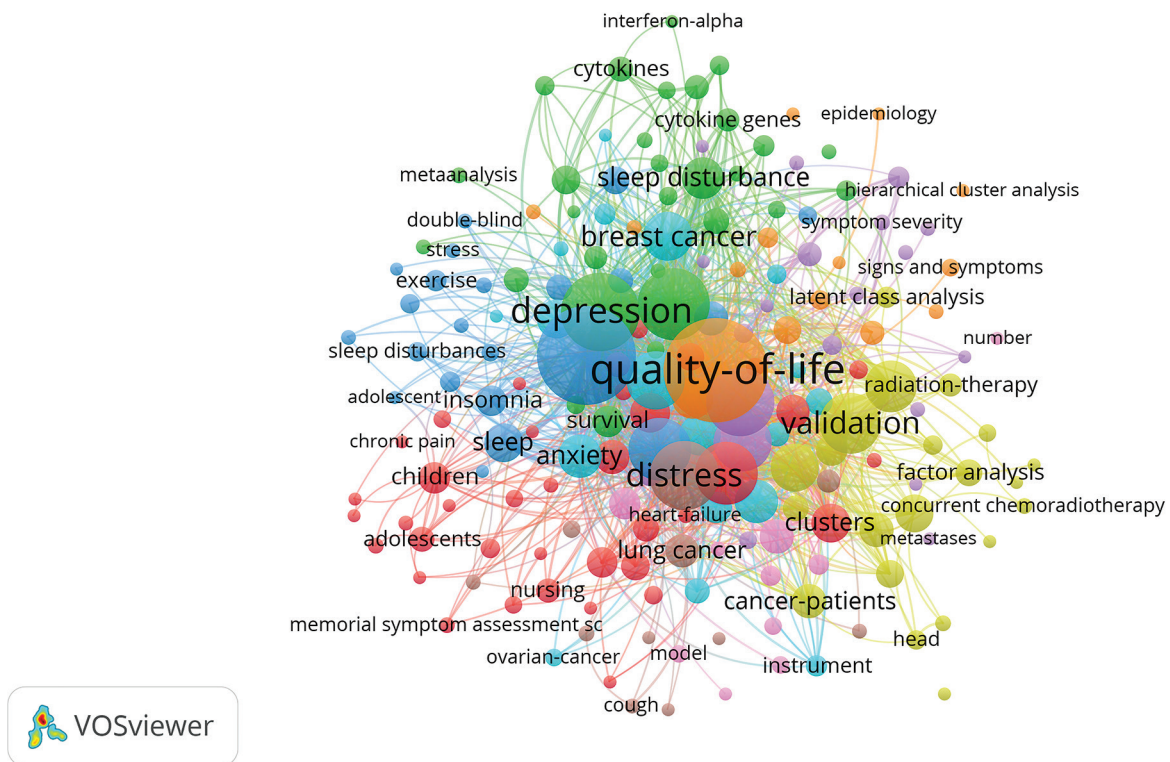


Figure 5. Co-occurrence analysis of top keywords.

Rank	Keywords	Frequency	Rank	Keywords	Centrality
1	symptom cluster	387	1	diagnosis	0.21
2	quality of life	329	2	adjuvant chemotherapy	0.19
3	breast cancer	192	3	depression	0.14
4	fatigue	160	4	lung cancer	0.14
5	depression	110	5	assessment scale	0.14
6	prevalence	100	6	model	0.14
7	lung cancer	99	7	cancer-related fatigue	0.14
8	distress	98	8	symptom management	0.13
9	women	94	9	actigraphy	0.13
10	pain	83	10	advanced cancer	0.12
11	validation	79	11	insomnia	0.12
12	management	65	12	disease	0.12
13	survivor	60	13	sickness behavior	0.12
14	chemotherapy	54	14	cluster	0.10
15	sleep disturbance	51	15	confirmatory factor analysis	0.10
16	palliative care	49	16	acupuncture	0.10
17	cancer	48	17	patient-reported outcome	0.10
18	impact	47	18	family caregiver	0.10
19	anxiety	42	19	Korean version	0.10
20	cancer patient	38	20	functional assessment	0.09

Table 4. The top 20 keywords related to cancer symptom cluster.

and the labels derived from the log-likelihood ratio (LLR) are preferred because they are used to provide a more comprehensive view of the intellectual network structure. After adopting the LLR to cluster the keywords, 10 clusters were obtained (2 clusters about symptom clusters and symptom-related clusters and 8 clusters about symptom cluster focus groups). These clusters were arranged along with horizontal timelines in Figure 6. The smaller the keyword clustering label, the larger the keyword clustering, and so the largest clustering is #0 experiencing fatigue. The keyword timeline mapping revealed that similarly to keyword co-occurrence analysis, the focus population and common symptoms of the cancer symptom cluster were used as key lines throughout the overall study. The study was based on fatigue, depression, and anxiety symptoms, and the study population was based on lung cancer, transgender cancer survivor, advanced cancer, cancer cachexia, cancer population, and high-grade glioma; and the method of identifying symptom clusters was mainly the study of symptoms and exploratory factor analysis.

Experiencing fatigue

In terms of the evolutionary process of the timeline, the largest cluster is Cluster#0 experiencing fatigue; as

early as 2003, researchers began to focus on the common symptoms of cancer symptom clusters, of which the first symptom to be focused on was depression, the population was colorectal cancer patients, and the measurement method may have been through communication or inventory; from 2010 to 2013, attention began to be paid to anxiety, using measurement tools for the assessment of symptom clusters and noting the influence of sociodemographic factors on anxiety, and further noting the role of self-efficacy at the psychological level; and from 2020 to 2021, symptom clusters were identified and identified methodologically using big data mining techniques for data analysis.

The depression-anxiety symptom cluster

Cluster#1 is labeled as the depression-anxiety symptom cluster. The earliest keyword appeared in 2007 as “breast cancer,” noting the coexistence of multiple symptoms, i.e., “multiple symptoms,” and the emergence of the term “Chinese version” related to “measurement tools.” From focusing on the patients, the focus was shifted to their family caregiver, as seen in the keyword “family caregiver.” From 2013 to 2015, the measurement method was no longer limited to traditional scale assessment, but also focuses on the patient-reported outcome and the use of cognitive-behavioral therapy to

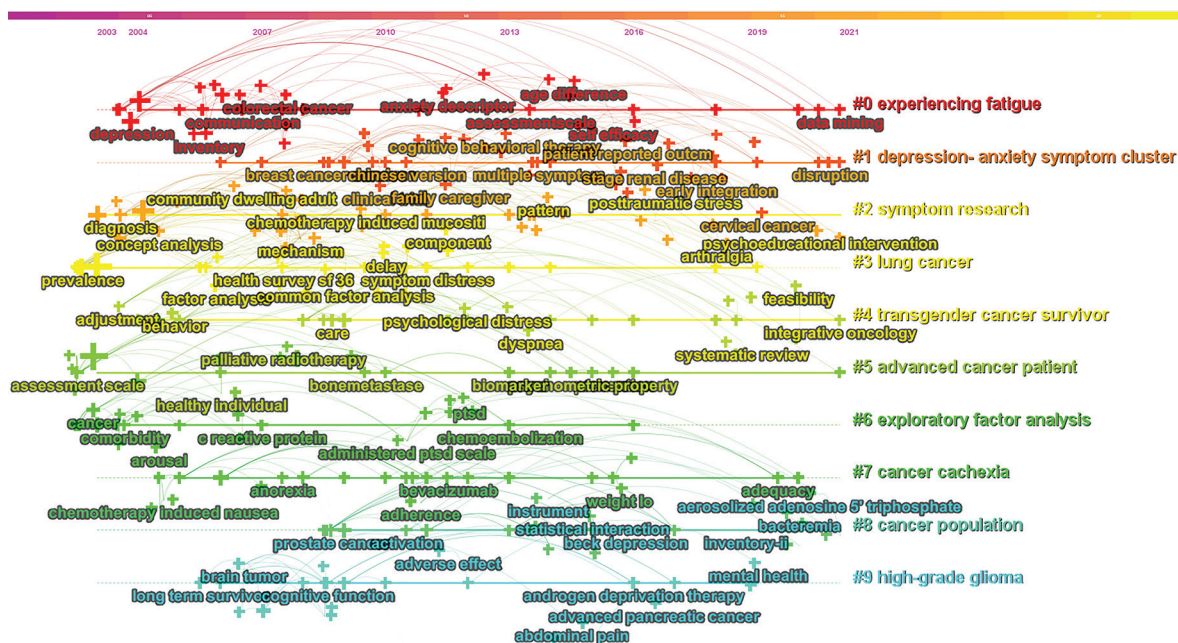


Figure 6. The evolutionary timeline mapping of keywords about cancer symptom clusters.

intervene in depression and anxiety symptom clusters. From 2016 to 2018, depression and anxiety symptom clusters in patients with renal disease and cervical cancer received extensive attention. In 2021, the keyword that emerged was “disruption,” which focuses on the impact of depression and anxiety symptom clusters on daily life and work, similar to the previous analysis of research hotspots in recent years.

Symptom research

Cluster#2 is labeled as symptom research. The cluster is mainly about the analysis of symptoms. From 2003 onward, it mainly focuses on the analysis of symptom clusters during cancer diagnosis, and the research content is conceptual analysis, which corresponds to the developmental stages of symptom clusters. According to the 4-stage theory of literature growth (budding stage, discipline development, increasingly mature discipline, and decreasing discipline), international cancer symptom cluster research was in the budding stage from 1999 to 2008, and the number of publications was relatively small and unstable; and it was still in the conceptualization and instrumentalization stage according to the 4-stage theory of scientific development. From 2007 to 2010, there was a change in the study population, as evidenced by the keyword “community-dwelling adult,” which was no longer limited to the inpatient period of cancer diagnosis and treatment, but also focused on the home recovery period, extended the geographical

scope to the community, and focused on chemotherapy-induced mucositis. From the analysis of individual symptoms of cancer to the exploration of symptom evolution patterns, after 2016, the focus of attention was mainly on posttraumatic stress and arthralgia, and the intervention was psychoeducational.

Lung cancer

Cluster#3 is labeled as lung cancer. The emergence of lung cancer as a separate cluster indicates the extent to which symptom clusters of lung cancer patients have attracted the attention of international scholars; as early as 2003, attention was paid to the incidence of symptom clusters of lung cancer patients, and between 2005 and 2013, research focused on the components of symptom clusters, the occurrence mechanism, the analysis of symptom clusters, and quality of life. The method of determining symptom clusters was mainly factor analysis, distress was the main symptom, and the hotspots of research in this field were not prominent in the years thereafter. It indicates that the research on symptom clusters of lung cancer patients has been decreasing in hotness in recent years.

Transgender cancer survivor

Cluster#4 is labeled as a transgender cancer survivor. Research hotspots in this field started in 2004 with the earliest research on adjustment and behavior. The main

symptoms around 2019 were psychological distress and dyspnea, with high-frequency keywords including systematic review, integrative oncology, and feasibility.

Advanced cancer patient

Cluster#5 is labeled as an advanced cancer patient. This clustering was first seen in 2003 as an assessment tool and healthy individuals, followed by palliative radiotherapy. This was followed by several high-frequency keywords from 2013 to 2016, including biomarker, bone metastases, property, biomarker, bone metastases, and property, indicating that this stage focuses on biochemical indicators and changes in cancer progression.

Exploratory factor analysis

Cluster#6 is labeled as exploratory factor analysis. Exploratory factor analysis as a statistical analysis method for symptom cluster identification stands alone as a cluster, indicating the important role of this research method for symptom cluster identification and determination. Cancer, comorbidity, arousal, and C-reactive protein were also high-frequency keywords in this period, indicating the deepening of symptom cluster research, combining cancer comorbidities and inflammatory factors such as C-reactive protein. From 2010 to 2013, PTSD was widely studied as a major symptom cluster, including PTSD measurement tools.

Cancer cachexia

Cluster#7 is labeled as cancer cachexia. The study of cancer cachexia was first seen in 2005, including chemotherapy-induced nausea, anorexia, and weight loss, as well as the common chemotherapeutic drug bevacizumab, and in 2020 the term "literacy" became a hot topic of research, considering that nutritional management of cachexia is closely related to nutritional literacy with the rise of health literacy.

Cancer population

Cluster#8 is labeled as a cancer population. The earliest keywords were seen in 2008, the study population is comprised of prostate cancer patients, the high-frequency keywords include activation and side effects, and an in-depth analysis of the intrinsic mechanism was a common characteristic of the researches published in this period; on the other hand, after 2013, Beck depression and its measuring instruments, statistical interpretation, etc. received attention; further, in recent years, research hotspots focus on aerosolized adenosine, 5' triphosphate, bacteremia, and inventory-II.

High-grade glioma

Cluster#9 is labeled as high-grade glioma. Research hotspots in this field are concentrated in 2 time periods. The first phase was from 2005 to 2010, and focused on brain tumors, especially the cognitive function of long-term survivors of brain tumors; the second was from 2016 to 2020, and involved androgen deprivation therapy, a treatment for prostate cancer; this urology term was published in 2014 and subsequently became a high-frequency keyword for a short period, indicating a high level of research interest regarding patients with prostate cancer. Also of concern to the population is advanced pancreatic cancer, with the main symptom being abdominal pain, and in recent years the focus has been mainly on mental health.

3.5.3. Keywords bursts analysis based on stage research

Frontier research refers to the grouping of concepts and underlying research issues that emerges and changes over time. By adapting Kleinberg's¹⁶ burst detection algorithm, emergent research frontier concepts were identified with the burst keyword analysis method, a method highlighting keywords that changed rapidly in a short period or increased dramatically in number, emphasizing sudden changes in keywords. After running Citespace, the top 31 keywords with the strongest strength were obtained and are shown in Figure 7. Occurrence burst, which indicates a steep increase in occurrence over some time, represents changes in frontier topics and dynamics in a research field. A burst contains 2 dimensions: burst strength and bursting time. From Figure 7, it can be observed that all the strength values were above 2, with the highest at 4.61. The longest duration of burst time is "factor analysis," with a burst duration of 8 years, and the largest burst strength is "randomized controlled trial."

According to Figure 7, the first phase is from 2003 to 2010, and the emergent keywords mainly revolve around the methods of determining cancer symptom clusters (mainly statistical analysis methods), such as confirmatory factor analysis, factor analysis, cluster analysis, and also the measurement of cancer symptom clusters. The use of tools, such as assessment scales, validation, and detailed inventory, and other emergent words focused around cancer treatment and diagnosis, indicating that at this time, the main focus was on the identification and validation of symptom clusters during inpatient cancer treatment and diagnosis, and the understanding of symptom clusters belonged to the initial stage. The second stage was from 2010 to 2015, and the focus of attention in this period centered around

Top 31 Keywords with the Strongest Citation Bursts

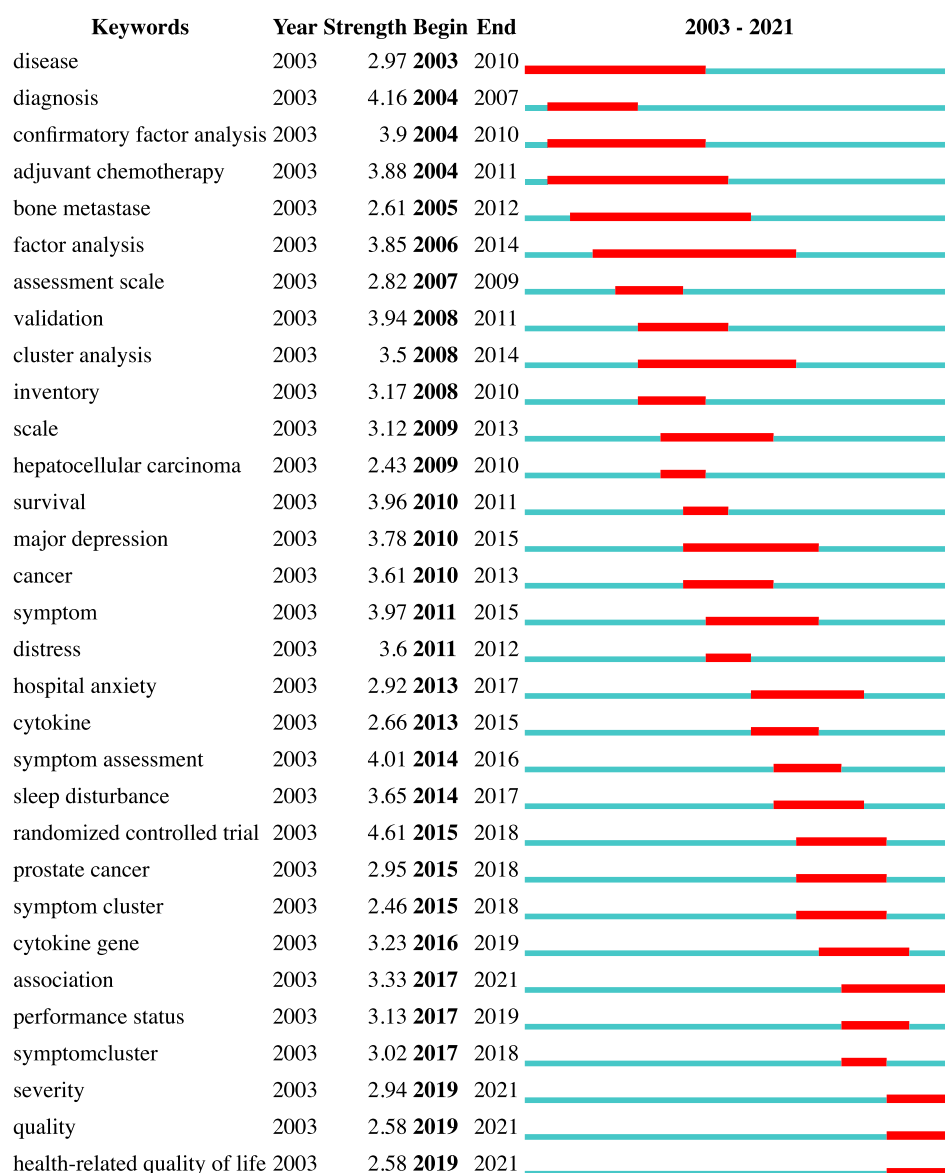


Figure 7. Keywords with the strongest citation bursts.

the psychological symptoms and the assessment of symptoms, such as depression, distress, hospital anxiety, and sleep disturbance, focusing on not only symptom clusters during cancer diagnosis and treatment during hospitalization but also the correlation between symptom clusters and survival, and involved an exploration of the occurrence mechanism, especially the correlation between cytokines and symptom clusters, indicating that the research at this time is deepening in

content. The third stage is from 2015 to 2021, in which randomized controlled studies are the most intense, indicating that the research methodologies of randomized controlled studies are more important than those of the original questionnaires and mechanism studies, the depth of research is expanding, the research population is refined, and more attention is paid to prostate cancer. In the past 2 decades, the relationship between symptom clusters and quality of life, and especially between

symptom clusters and health-related quality of life, has attracted extensive attention from international scholars; this reflects that these elements are at the forefront of research on symptom clusters and deserve scholars' attention and exploration.

4. Discussions

In this study, to provide a significant reference for researchers in China and assist them in mastering the development of research hotspots in this field, Citespace and VOSviewer were used to make bibliometric analyses on annual publications, countries or regions, institutions, journals, and keywords. Overall, symptom clusters in cancer research have become a growing research field worldwide. This research collected and analyzed bibliometrics information about cancer symptom clusters. A change in the number of academic publications in a field is an important indicator of its evolutionary trend. Although cancer symptom cluster research emerged in 2001 and has been a topic in healthcare-related research for over 20 years, it was initially a niche topic, while the global trend of the number of publications has been growing continually with some fluctuations over the years. And the fluctuation of the number of documents each year demonstrated that the relevant research was immature and deserved to be explored and improved.

Based on the co-occurrence analysis of countries or regions, institutions, journals, and keywords, it can be concluded that publications vary greatly among countries or regions, among which the United States, as in many other fields, tends to lead research in this field. China, Canada, and South Korea are also driving forces in some cancer research,^{5,17–19} and they also have the greatest number of international research collaborations; however, it is worth noting that although China ranks second in terms of the overall number of publications, no influential research institution has yet been ranked within the top 10. And the institutions active in cancer symptom clusters research were mostly universities and university hospitals in the USA. America, Europe, and Asia dominated prominently in all the categories explored, contributing to research through authorship, institution representation, and funding agency by means of publications in the WOS. However, there is a notable absence of emerging countries, which need extensive support to improve their research output and could reap the benefits of reducing the burden of cancer symptoms. As the incidence and survival of cancers worldwide increase, cancer patients must manage their symptom burden, reduce their economic stress, and improve their quality of life by managing their symptom clusters.²⁰ Therefore, strengthening international

cooperation is recommended for supporting scientific research cooperation and medical technology in countries with a weaker economic development and scientific research base.

Through the analysis of journals, we could find that the journals publishing cancer symptom clusters are mostly well-known and high-impact journals, but there is no doubt concerning the fact that lower-impact journals also add to the increasing reach and availability of research. The top 10 journals with the largest number of publications accounted for 49.47%, which demonstrates a relative concentration of academic journals and a stable output of academic outputs. With an average of 5 authors per publication (2151/473), cancer symptom clusters have seen growth in co-authorship over time. In terms of citations, high-impact journals take the lead.

From the analysis of the keywords with high-frequency and high-centrality and keyword cluster analysis, the following 4 research hotspots were assumed: (1) Analysis of symptom clusters and symptom management in patients with breast cancer, lung cancer, ovarian cancer, prostate cancer, and any advanced cancer. This is related to the fact of the high incidence and the large population of breast cancer, lung cancer, and so on. Symptom clusters vary depending on the type of disease, stage of disease, and functional status of the cancer survivor. Identification of symptom clusters in cancer survivors may have clinical implications through improved symptom management.¹⁹ (2) Fatigue-related symptom clusters, in particular symptom clusters consisting of fatigue and depression, sleep disturbance, anxiety, and pain. This is related to the fact that CRF is the most common symptom of patients,²¹ and several studies have shown that fatigue, sleep disturbance, and depression symptom clusters are the most common and severe symptom clusters of oncology patients.^{22–24} Describing the characteristics of fatigue-related symptom clusters, exploring the associated factors, and identifying high-risk groups are hot topics of research in this field, which are important for guiding the prevention and intervention of symptom clusters and improving patients' quality of life. CRF is one of the most frequently reported symptoms in cancer survivors, and SC containing fatigue, anxiety, and depression are common sequelae of a cancer diagnosis, which are associated with reduced physical functioning. Previous studies have shown that symptom clusters consisting of fatigue, anxiety, and depression are stable and central in cancer patients during chemotherapy cycles, which seriously influence the health-related quality of life.^{25–27} Besides, some studies show the patient fatigue severity cluster was positively related to caregivers' depressive symptoms.²⁸ Recent studies have shown that chemotherapy patients, elderly cancer patients, and patients

with advanced cancer are at high risk for fatigue-related symptom clusters.^{26,29} (3) Effects of symptom clusters on quality of life, functional status, mental health, and interactions between symptoms within symptom clusters. Researchers should explore the mechanisms of interactions between symptoms within clusters and enhance the management of symptom clusters to improve patients' quality of life and emotional health. There is a multitude of studies indicating the prevalence of a negative relationship between the symptom clusters and quality of life.^{17,19} (4) Assessment methods and management of cancer symptom clusters. Correlation, factor analysis, principal component analysis, and cluster analysis are analytical methods to identify symptom clusters. More recent techniques include latent variable methods, such as latent profile analysis, to examine the phenotypes of symptom cluster experience and growth modeling to examine the longitudinal nature of symptom cluster experience.³⁰ At present, there is no standard method for identifying symptom clusters, and the results of different identification methods vary even for the same group and the same data. Further research is required on understanding patients' subjective experiences.

From the keyword burst analysis and keyword clustering timeline evolution mapping presented in Figures 6 and 7, we can also observe that the topics in the cancer symptom cluster field over the past 2 decades were generally as follow: (1) Correlation between quality of life and symptom clusters. The correlation analysis of symptom clusters and quality of life is both a hot topic and a research frontier, and the research field will remain hot for some time to come. (2) Application of data mining in symptom clusters. There is a large volume of data generated by the healthcare industry. It is critical for the healthcare industry to effectively obtain, collect, and mine data. Data mining involves the use of mathematical sciences, statistics, artificial intelligence, and machine learning to determine the relationships between variables from a large amount of data. It has previously been shown that data mining can improve the prediction and precision of symptoms.³¹ Traditional Chinese medicine has achieved a lot of results in symptom data mining and has shown corresponding advantages, especially for chronic symptoms such as fatigue, anxiety, and sleep disturbance. By utilizing the data within the electronic health record (EHR), a recent study showed that for breast and colorectal cancer patients, various symptom types and severity were associated with different periods after chemotherapy. Patients with a history of smoking and severe fatigue were likely to have severe gastrointestinal symptoms 6 months after chemotherapy.³² (3) Research on the mental health status of cancer patients. Cancer diagnosis and treatment can give rise to considerable mental health issues

for individuals, such as anxiety and depression. Compared with healthy populations, cancer patients are at a higher risk of mental health problems. A survey during the COVID-19 pandemic showed that the mental health of cancer patients is a concern; among the 6213 cancer patients forming part of the survey's respondents, 23.4% had depression, 17.7% had anxiety, 9.3% had PTSD, and 13.5% had hostility.³³ Mental health conditions are associated with increased healthcare costs among cancer survivors compared with people without a history of cancer, and total medical costs and costs for most types of services were significantly higher for cancer survivors with poor mental health status.³⁴ (4) Study on the mechanism and biological pathways of symptom clusters. In psychoneurological symptoms (such as depressive symptoms, cognitive impairment, fatigue, sleep disturbance, and pain), there is evidence that common biological pathways (i.e., pro-inflammatory cytokines, hypothalamic–pituitary–adrenal axis, and monoamine neurotransmitter systems) may play a role at the molecular level.³⁵

There are multiple strengths in the present study. Unlike previous reviews or meta-analysis reviews focusing on symptom clusters from several narrow perspectives, this study reviewed cancer symptom cluster research as a whole instead of concentrating on a particular subfield, which provided a bird's eye view of the current hotspots and research frontiers. The visualized knowledge maps created by CiteSpace provide a deeper insight into the major countries, institutions, and hotspots in cancer symptom cluster research, as well as the evolution of the field over time, and the understanding resultantly made available serves as a supplement to the previous reviews, with the results carrying the potential to provide valuable information to researchers. Moreover, the study is consistent with The Whole Health Model in recent years and has a wide audience.³⁶ As the present study conducts a detailed exploration of the literature, together with adopting the use of vivid figures and appropriate tables to convey the derived inferences, we hope that it would be beneficial to all readers of related scholars, doctors, nurses, psychologists, rehabilitation therapists, etc.

5. Research gap and future scope

This section undertakes a review of research gaps and an exploration of possible directions for future research against the backdrop of the current status of research in this field. (1) The research related to cancer symptom clusters is mainly based on cross-sectional surveys, and the measurement tools are mainly self-assessed or other-rated scales or questionnaires, as well as patient-reported outcomes; however, so far as

the more subjective symptoms are concerned, especially the psychological symptoms, these tools might lack the accuracy and depth that would be needed in arriving at any definitive conclusions; and since there is limited qualitative research that could be used as a basis for guiding in-depth analyses of patients' symptom experiences, it is suggested that scholars can consider strengthening qualitative research on cancer symptom clusters, exploring patients' experiences and feelings in depth, and taking patients' needs into full consideration when formulating intervention strategies. (2) Most of the current studies are limited to the period of hospitalization of cancer patients and are based on cross-sectional surveys. It is recommended to conduct longitudinal studies with longer duration and broader study populations, and to explore the trends of the development of symptom clusters during radiotherapy, perioperative period, and home rehabilitation period, as well as the end stage of symptom clusters, to accurately predict the changes of symptom clusters of patients in different contexts during different periods. (3) In addition, although there have been many research results on the mechanisms of cancer symptom clusters, they are still far from enough. Revealing the intrinsic mechanisms of symptom clusters will provide a reference for the formulation of prevention and intervention strategies. (4) Last but not least, the identification of patients with symptom clusters should be followed by the exploration of intervention models that are based on the best evidence and are clinically appropriate to improve the quality of life of cancer patients. However, studies on the intervention of symptom clusters are currently scarce and relatively homogeneous. From an analysis of the main keywords, it can be inferred that the intervention methods mainly focus on psychological-related symptom clusters, such as cognitive-behavioral therapy and psychoeducation. In the future, more research should be conducted on intervention strategies for different symptom clusters.

6. Limitations

This bibliometric analysis has some limitations. First, our search was limited to the WOSCC, which is a widely used academic database, and we did not include other databases, such as Scopus or Google Scholar, which may have provided slightly different results. Second, our analysis only included articles published in English, and the scope of the literature considered for selection was limited to articles and reviews. The inclusion of other languages, gray literature, and books might also have led to different outcomes. Third, the fact that only a selective collection of search terms was used was highly limiting. As our goal was to focus on literature

that related to symptom clusters in cancer as the main research theme, it may be possible that we might have missed some literature that is expressed in other ways such as "symptoms" or "syndrome" or "symptom pairs"; therefore, we encourage future research to extend the range of search terms, and standardize the usage of this term. Lastly, whereas publication and citation numbers are objective, the interpretation of keyword clusters has a subjective character; other researchers may have drawn different conclusions. Nevertheless, we believe that the visualization results and bibliometric methods of CiteSpace and VOSviewer demonstrate the growing interest in cancer symptom cluster research, as seen from the results presented by the visualization. It is hoped that this research will facilitate understanding of the fundamental ideas and terms involved in cancer symptom clusters, which are key to the developmental process, and will allow experts to visualize identification modes and tendencies.

7. Conclusions

To our knowledge, this is the first study to employ a bibliometric method to analyze the literature about cancer symptom clusters over the past 2 decades systematically and comprehensively. The analysis of scientific production is an essential tool for evaluating knowledge, raising research questions, and determining the progress of a discipline. Twenty years of cancer symptom clusters research outputs were investigated and analyzed through bibliometric methods based on the Web of Science. We confirm that it is a promising field of research worldwide and has great potential to improve symptom management in cancer patients and improve their quality of life. By comprehensively analyzing and summarizing research trends, the present research has arrived at findings that we expect to have value in terms of providing additional direction in which future research can be pursued, in such a way that there is advancement in the knowledge that the field has to offer.

Author contributions

Both authors (An R and Luo Y) have equally contributed in the following phases: study conception and design, data acquisition, statistical analysis, and interpretation of data. Data analysis and interpretation: An R and Liu MZ. Revision of manuscript: Liu MZ and Muhammad Sohaib. Final approval of manuscript: An R, Muhammad Sohaib, Liu MZ, and Chen WF. All authors have read and approved the final version of the manuscript submitted for publication. All authors take responsibility for the public content of the manuscript and agree to its publication in the present form.

Ethical approval

Ethical issues are not involved in this paper.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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