

Bibliometric and Visual Analysis of Undifferentiated Diseases Based on the Web of Science Database: A Postprint

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Abstract

Background In recent years, Medically Unexplained Physical Symptoms (MUPS) have garnered widespread attention from scholars worldwide. However, research in this field started relatively late in China, lagging behind international progress. Studying international MUPS research is crucial for advancing the field in China. **Objective** To employ bibliometric methods to investigate the current status, research hotspots, and development trends of MUPS internationally. **Methods** In July-August 2022, MUPS-related literature was searched in the Web of Science Core Collection database, with the search period set from database inception to August 15, 2022. After screening and data processing, bibliometric analysis was conducted on the included literature from the perspectives of publication trends, authors, institutions, and research direction distribution. CiteSpace 6.1R3 software was used for visual analysis of country/region cooperation, document co-citation, keyword co-occurrence, keyword clustering, and keyword bursts. **Results** A total of 1,615 articles were finally included. From 1985-2022, the annual number of publications in the MUPS field showed an overall upward trend, with the most rapid growth occurring during 2014-2016. The top three authors by publication volume were ROSMALEN J G M (43 articles), WITTHOFT M (41 articles), and RIEF W (31 articles), and the total citation frequencies of these three scholars' papers also ranked top three, with 954, 1,275, and 1,339 citations respectively. The top three institutions were all from the United Kingdom: University of London (143 articles), King's College London (95 articles), and University of Manchester (84 articles). The top three countries/regions were England (422 articles), United States (341 articles), and Netherlands (266 articles), all of which had close cooperation with other countries. All literature involved 75 research directions, with psychiatry being the most studied. The document co-citation network map included 1,393 nodes and 6,153 links. The most frequently co-cited document

was Somatoform Disorders and Medically Unexplained Symptoms in Primary Care. The top five keywords by frequency were “primary care” (422 times), “somatoform disorder” (405 times), “somatization” (354 times), “prevalence” (217 times), and “depression” (211 times). Keyword clustering analysis yielded 12 clusters, specifically reflecting three aspects: the disciplinary scope and epidemiological characteristics of MUPS, key disease subtypes involved, and main treatment methods and management. The keyword with the strongest burst strength was “somatic symptom disorder,” and those that have emerged in recent years and continue to the present include “children,” “bodily distress syndrome,” “somatic symptom disorder,” and “model.” Conclusion International MUPS research is currently on an upward trajectory, with research hotspots and trends focusing on four main aspects: disease subtypes extensively studied in MUPS, attention to pediatric populations and creation of effective communication models, proper assessment and long-term management of medically unexplained symptoms, and the therapeutic efficacy of cognitive behavioral therapy for MUPS.

Full Text

Bibliometrics and Visualization Analysis of Medically Unexplained Physical Symptoms Based on Web of Science Database

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Abstract

Background In recent years, medically unexplained physical symptoms (MUPS) have attracted widespread attention from scholars both domestically and internationally. However, research in this field started relatively late in China, and its development lags behind international progress. Studying international research on MUPS is of significant importance for promoting the development of this field in China.

Objective To explore the current status, research hotspots, and development trends of MUPS internationally using bibliometric methods.

Methods MUPS-related literature was retrieved from the Web of Science Core Collection database between July and August 2022, with the search period set

from database inception to August 15, 2022. After screening and data processing, bibliometric analysis was performed on the included literature from the perspectives of publication trends, authors, institutions, and research direction distribution. CiteSpace 6.1R3 software was used to conduct visualization analysis of country/region collaboration, document co-citation, keyword co-occurrence, keyword clustering, and keyword bursts.

Results A total of 1,615 documents were included. Annual publications in the MUPS field showed an overall upward trend from 1985 to 2022, with the most rapid growth occurring between 2014 and 2021. The top three authors in terms of publication volume were ROSMALEN J G M (43 papers), WITTHOFT M (41 papers), and RIEF W (31 papers), whose total citation counts also ranked in the top three at 954, 1,275, and 1,339 times, respectively. The top three institutions were all from the UK: University of London (143 papers), King' s College London (95 papers), and University of Manchester (84 papers). The top three countries/regions were England (422 papers), the United States (341 papers), and the Netherlands (266 papers), all of which maintained close collaborations with other countries. The literature encompassed 75 research directions, with psychiatry being the most common. The co-citation network included 1,393 nodes and 6,108 connections, with the most frequently co-cited paper being "Somatoform Disorders and Medically Unexplained Symptoms in Primary Care." The top five keywords by frequency were "primary care" (422 times), "somatoform disorder" (405 times), "somatization" (354 times), "prevalence" (217 times), and "depression" (211 times). Keyword clustering analysis yielded 12 clusters, reflecting three main themes: the disciplinary scope and epidemiological characteristics of MUPS, key disease subtypes, and primary treatment methods and management. The keyword with the strongest burst was "somatic symptom disorder," while "children," "bodily distress syndrome," "somatic symptom disorder," and "model" have emerged recently and continue to persist.

Conclusion International research on MUPS is currently in an upward phase. Research hotspots and trends focus on four main aspects: disease subtypes with substantial MUPS research, attention to juvenile populations and creation of effective communication models, proper assessment and long-term management of MUPS, and the therapeutic effectiveness of cognitive behavioral therapy for MUPS.

Keywords Medically unexplained physical symptoms; bibliometrics; visual analysis; CiteSpace

Introduction

In 1985, American physicians Slavney and Teitelbaum first proposed the concept of "Medically Unexplained Symptoms (MUS)" [1]. Because patients typically present with physical discomfort, it was later termed "Medically Unexplained Physical Symptoms (MUPS)" [2], which refers to physical symptoms that cannot

be medically explained. In China, this is commonly known as “undifferentiated disease” [3]. MUPS is characterized by symptoms for which no abnormalities are found after detailed physical examination and auxiliary tests, or only mild abnormalities exist. These symptoms represent an undifferentiated stage of disease that cannot be attributed to any organic condition, and the severity cannot be reasonably explained. MUPS can occur at any age, with complex and diverse clinical manifestations potentially involving one or multiple systems, often accompanied by mental health issues. Its etiology and pathogenesis remain unclear, and there is currently no unified and detailed diagnostic standard domestically or internationally.

Bibliometrics is a science that applies mathematical and statistical methods to conduct quantitative and qualitative research on literature, enabling analysis of development patterns, identification of research hotspots, and prediction of future research directions and trends [4]. CiteSpace [5-6] is an information visualization software developed by Professor Chen Chaomei’s team from Drexel University based on the Java environment. It is a commonly used tool for mapping scientific knowledge graphs [7] and has been widely applied in bibliometric research across numerous fields including information science [8], climate change [9], ecological environment [10], and medicine [11].

Currently, research on MUPS in China is in its infancy with limited findings. General practitioners (GPs), as the primary first-contact physicians, face considerable challenges in managing these patients, making systematic research on MUPS essential. This study employs bibliometric methods and utilizes CiteSpace 6.1R3 and Excel 2019 software to analyze literature in the MUPS research field from multiple dimensions, exploring international research hotspots and potential development trends. The aim is to enhance Chinese GPs’ capacity for early recognition, diagnosis, and treatment of MUPS, and to lay a foundation and broaden perspectives for Chinese scholars’ research in this field.

Methods

1.1 Data Sources

Between July and August 2022, we searched the Web of Science Core Collection, including citation indexes such as SCI-EXPANDED, SSCI, AHCI, CPCI-S, CPCI-SSH, BKSI-S, BKSI-SSH, ESCI, and CCR-EXPANDED. The search field was limited to “Topic” using precise retrieval. The search strategy was: TS=(“Medically unexplained symptoms” OR “Medically Unexplained Symptom” OR “Symptom, Medically Unexplained” OR “undifferentiated illness”). The search period was set from database inception to August 15, 2022. A total of 2,007 relevant documents were retrieved. After setting the language to English and document type to Article and Review Article, and excluding conference papers, newspaper articles, dissertations, etc., we obtained 1,615 documents.

1.2 Data Conversion and Processing

Data retrieved from the Web of Science Core Collection were exported in plain text format containing all information (Full Record and Cited References) and renamed in the format `download_{xxx}.txt`. The “Remove Duplicates” function in CiteSpace software was used to screen and clean the data, supplemented with manual review to exclude irrelevant literature. The final dataset comprised 1,615 documents, which were imported into CiteSpace.

1.3 Analysis Methods

1.3.1 Bibliometric Analysis We utilized the statistical analysis functions of the Web of Science database to compile: (1) annual publication counts; (2) top 10 authors by publication volume, total citations, citations per paper, and h-index; (3) top 10 institutions by publication volume; and (4) top 10 research directions by publication volume. Annual publication count, total citations, citations per paper, and h-index are common bibliometric indicators. The h-index, or Hirsch index, is a new metric for measuring academic achievement where h represents “high citations.” A researcher’s h-index means that among their n published papers, at least h papers have been cited at least h times each, while the remaining (n-h) papers have fewer than h citations each [12]. It should be noted that since a single paper may involve authors from different countries and institutions, some data overlap exists, but this does not affect the overall analysis of author and institutional productivity.

1.3.2 Visualization Analysis We used CiteSpace 6.1R3 software to visualize the 1,615 imported documents. Parameter settings were: (1) Time Slicing: 1985-2022; (2) Years Per Slice: 1; (3) Link strength algorithm: Cosine; (4) Selection Criteria: g-index; (5) Pruning algorithm: Pathfinder; and (6) Clustering algorithm: Log-Likelihood Ratio (LLR).

In co-citation network maps, nodes are displayed using the classic Tree Ring History method, while betweenness centrality measures the probability that a node lies on the shortest path between any two other nodes [13] and serves as an important indicator of node importance in the network. In CiteSpace, nodes with high betweenness centrality (≥ 0.1) are displayed with a purple ring around them, with thickness representing the centrality value.

In co-citation networks, red nodes represent papers identified through burst detection as having mutation characteristics, indicating they were published in large numbers within a short period. The LLR algorithm was used for keyword clustering analysis, which groups closely related keywords into “clusters” and selects the most representative keyword as the cluster label. Keyword burst detection refers to a sudden surge in keyword frequency within a short time period [14], directly reflecting research frontiers and development trends in the field.

Results

2.1 Publication Trends

Statistical analysis of the 1,615 included documents showed an overall upward trend in international MUPS research publications. A polynomial fit of cumulative annual publications yielded $y=1.9969x^2-36.86x+130.2$, $R^2=0.9941$, indicating good fit quality. The first paper on MUS was published by SLAVNEY et al. [1] in the United States in 1985, followed by essentially no publications for six years until research reports emerged in 1992. Publication growth was rapid during 2001-2002, 2003-2004, 2012-2013, and 2014-2016, with the most rapid increase occurring in 2014-2016. In 2021, publication volume reached its peak in recent years [Figure 1: see original paper]. Overall, since MUPS was first proposed in 1985, publications have shown a steady growth trend over the past 30+ years, reflecting increasing researcher attention, with further increases expected.

2.2 Author and Institution Analysis

Between 1985 and 2022, 4,707 authors from 1,605 institutions published MUPS-related papers internationally. Among the top 10 authors by publication volume, five scholars published ≥ 30 papers: ROSMALEN J G M (43 papers), WITTHOFT M (41 papers), RIEF W (31 papers), LOWE B (30 papers), and SHARPE M (30 papers). In terms of citation frequency, SHARPE M (2,181 citations), SALMON P (1,933 citations), and RIEF W (1,339 citations) ranked in the top three. Combined with h-index data, these three scholars' papers demonstrate substantial academic influence in MUPS research and are widely recognized by peers .

Among the top 10 institutions by publication volume, University of London, King' s College London, and University of Manchester ranked in the top three, all from the UK, accounting for 20% of total publications [Figure 2: see original paper].

2.3 Country/Region Analysis

Using CiteSpace with node type set to "Country," we mapped the country/region collaboration network [Figure 3: see original paper]. The visualization included 75 nodes and 379 connections, with 1,615 papers from 75 countries/regions. The top five countries/regions by publication volume were England (422 papers), USA (341 papers), Netherlands (266 papers), Germany (196 papers), and Denmark (83 papers). China published 31 papers, collaborating with England, Germany, New Zealand, Brazil, Australia, and others. Chinese scholars have explored the relationship between MUPS and psychosocial aspects [15-17], and in 2022, one study examined stellate ganglion block for chronic pain in MUPS patients [18]. Taiwanese scholars have approached MUPS from a sociological perspective, discussing the relationship between autonomic imbalance

(AI) and MUPS, considering AI as a convenient clinical communication term that essentially represents MUPS [19-20].

Denmark ranked fourth in publication volume with centrality of 0.01, while Australia ranked eighth in volume but had centrality of 0.07, indicating stronger international collaboration than Denmark. Considering both publication volume and centrality, England, USA, Netherlands, and Germany are the main countries researching MUPS, maintaining close collaborations and robust academic exchange.

2.4 Research Direction Distribution

Analysis of research directions in the Web of Science Core Collection revealed that the 1,615 documents involved 75 research directions. Since each paper could be classified into one or more categories, the sum of all direction percentages could exceed 100%. The most studied fields were Psychiatry, Psychology, General Internal Medicine, and Neurosciences [Figure 4: see original paper].

2.5 Document Co-citation Analysis

Using CiteSpace with node type set to “Reference,” we conducted document co-citation analysis to rapidly identify important classic literature in MUPS research. The co-citation network included 1,393 nodes and 6,108 connections, with highly cited papers primarily from 2005 onward [Figure 5: see original paper]. Most burst documents were also highly cited. lists literature with co-citation frequency \$ 34 times, all with centrality <0.1. The most frequently co-cited paper (54 times) was by HALLER et al. [21] published in 2015 in DTSCH ARZTEBL INT, titled “Somatoform Disorders and Medically Unexplained Symptoms in Primary Care,” which analyzed the prevalence of somatoform disorders and MUPS in primary care from an evidence-based perspective to improve healthcare professionals’ understanding. VAN DESSELN et al. [22] systematically evaluated the role of psychotherapy in somatoform disorders and MUPS in adult patients.

2.6 Keyword Analysis

2.6.1 Keyword Co-occurrence Analysis Keyword co-occurrence analysis using CiteSpace (node type: “Keyword”) generated a network with 155 nodes and 797 connections [Figure 6: see original paper]. Excluding keywords related to the search strategy (“medically unexplained symptoms” and “medically unexplained physical symptoms”), the top 20 keywords by frequency are shown in . The most frequent keyword was “primary care” (422 times). Keywords with centrality >0.1 included “anxiety,” “somatization,” “prevalence,” “primary care,” “somatic symptom,” “depression,” and “somatization disorder,” indicating their critical importance.

2.6.2 Keyword Clustering Analysis Twelve clusters were identified (Modularity $Q=0.7668$ [>0.3], Mean Silhouette= 0.9261 [>0.7]), indicating significant and convincing clustering structure [23]. The 12 cluster labels summarized three main research themes: (1) Disciplinary scope and epidemiological characteristics of MUPS: #0 primary care, #3 prevalence, #6 general practice, #9 care; (2) Key disease subtypes: #1 somatic symptoms, #7 chronic fatigue syndrome, #8 somatic symptom disorder, #10 conversion disorder, #11 somatoform disorders; (3) Primary treatment methods and management: #2 management, #4 cognitive behavioral therapy, #5 communication [Figure 7: see original paper].

2.6.3 Keyword Burst Analysis Based on keyword clustering, burst analysis identified the top 31 burst keywords [Figure 8: see original paper]. “Strength” represents burst intensity, while “Begin” and “End” indicate start and end times, corresponding to the length of red bars in the figure. The keyword with the strongest burst was “somatic symptom disorder.” The longest burst duration was “illness,” persisting from 1993 to 2010 (18 years). Keywords that have emerged recently and continue to persist include “children,” “bodily distress syndrome,” “somatic symptom disorder,” and “model,” suggesting these directions will likely continue to develop.

Discussion

Contemporary GPs face challenges from global population aging and chronic disease prevalence [24-25], as well as discomfort caused by chronic symptoms leading to MUPS. MUPS falls within the scope of general practice, with GPs serving as primary first-contact physicians. This study employs bibliometric methods to comprehensively analyze relationships among published MUPS literature, reflecting the field’s structure, characteristics, and patterns [26] to uncover current status, hotspots, and trends.

International MUPS research is in an upward phase, with increasing researcher attention and publication volume, most rapidly during 2014-2016. A total of 4,707 authors, 1,605 institutions, and 75 countries/regions contributed to MUPS publications. The most productive author was ROSMALEN J G M (43 papers), and the most productive country/region was England (422 papers). Considering both volume and centrality, England, USA, Netherlands, and Germany are major MUPS research countries with close international collaborations and strong academic exchange. Overall, the UK holds a pivotal position in MUPS research. The literature encompassed 75 research directions, with psychiatry, psychology, general internal medicine, and neuroscience being the most common, demonstrating that GPs must understand MUPS from multiple perspectives and confirming that general practice integrates clinical, preventive, rehabilitative, and humanities-social science disciplines.

Document co-citation analysis established a network of 1,393 nodes and 6,108

connections, with “Somatoform Disorders and Medically Unexplained Symptoms in Primary Care” being the most frequently co-cited paper (54 times). Integrating keyword co-occurrence, clustering, and burst analyses, we identified international MUPS research hotspots and trends from keywords including “primary care,” “general practice,” “somatoform disorder,” “somatic symptom disorder,” “somatization disorder,” “cognitive behavioral therapy,” “anxiety,” “depression,” “communication,” “children,” “management,” and “model.”

3.1 Disease Subtypes with Substantial MUPS Research

In psychiatric diagnostic criteria, somatization, somatoform disorder, somatic symptom disorder, and somatization disorder have undergone conceptual evolution due to overlapping concepts and have consistently been linked with MUPS in international research. Unexplained pain, fatigue, edema, weight loss, dizziness, and other physical discomfort symptoms all fall within MUPS scope. There is also overlap with specialist diseases such as chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia syndrome [27]. While these subtypes have been extensively studied and may seem complex to diagnose, current MUPS diagnosis tends to be more subjective. A 2020 Dutch qualitative study explored when and what triggers MUPS diagnosis in primary care [27]. Results showed most GPs label symptoms as MUPS shortly after consultation begins (average ~4 minutes), with triggers primarily being symptom presentation and form. As research deepens, MUPS diagnosis no longer overemphasizes exhaustive testing but starts from symptoms, based on effective communication during consultation, making it more subjective.

3.2 Attention to Juvenile Populations and Creation of Effective Communication Models

Due to unclear etiology and predominant physical symptoms often accompanied by mental health issues like anxiety and depression, patients’ illness experiences are real, yet many do not recognize psychosocial factors, creating communication problems. Doctors aim to rapidly identify causes and make diagnoses, while patients feel doctors forcibly interpret their illness experiences as mental health issues, leading to resistance and trust crises [28]. Integrating effective psychotherapy can double treatment efficacy. Children and adolescents are the most overlooked populations in MUPS research, which has traditionally focused on adults. However, common somatic symptoms often begin in childhood and develop into chronic somatization [29-30], with early adolescence considered a critical period for developing chronic and recurrent somatic symptoms [31]. Healthcare professionals face increased communication difficulties when interacting with adolescent MUPS patients, affecting treatment outcomes. One study indicated that professionally created “explanatory models” provide conceptual frameworks for healthcare providers, and creative communication methods may help overcome communication barriers between clinicians and adolescent MUPS patients [32]. Future research should adopt a bio-psycho-social medical

model, focus on human-centered care, pay greater attention to children and adolescents as special populations, and create different communication models tailored to various age groups to address doctor-patient communication issues and apply professional medical knowledge to relieve patients' suffering.

3.3 Proper Assessment and Long-term Management of MUPS

As MUPS represents an undifferentiated disease stage that cannot be cured quickly, disease outcomes are unpredictable—potentially improving, resolving, developing into chronic symptoms, or differentiating into specific diseases under various factors. When GPs first encounter MUPS patients or receive referrals from specialists, proper assessment, management, and long-term care are required. A 2021 study proposed a practical approach for assessing and managing MUPS [33], involving thorough history-taking, vital signs, and laboratory tests, with added screening for physical and mental health impacts and assessment of how disease affects various life aspects. The approach identifies possible factors perpetuating symptoms from physiological, social, cognitive, and behavioral perspectives. Management should be stepwise: first making positive diagnoses and explanations to gain patient trust, then explaining how physiological, social, cognitive, and behavioral factors may influence disease, and finally providing comprehensive treatment plans. Future efforts should establish more complete assessment and management systems based on deeper MUPS understanding.

3.4 Therapeutic Effectiveness of Cognitive Behavioral Therapy for MUPS

MUPS treatment considers medication, psychological intervention, and social intervention. Cognitive behavioral therapy (CBT), which combines cognitive and behavioral approaches to address patients' cognitive errors [34], is considered the most effective psychological intervention for MUPS [22,35-36]. A 2021 meta-analysis indicated that pretreatment differences in patients' cognitive-emotional characteristics predict CBT outcomes, and tailored CBT may be beneficial for addressing the wide range of MUPS needs, while encouraging researchers and clinicians to recognize how these characteristics affect CBT response [37]. CBT is also the first-line treatment for somatic symptom disorder in children and adolescents [38]. Considering that medication alone for pediatric somatic symptoms often leads to chronicity, combining CBT with other psychosocial interventions may largely prevent chronic symptom development.

China is currently in the exploratory initial stage of MUPS research, primarily focusing on symptom-based assessment, treatment, and management of adult MUPS [3,39-40]. The *Handbook for Diagnosis and Treatment of Common Undifferentiated Diseases in General Practice* details multi-system MUPS management measures based on SOAP notes and RICE interviewing. A "National Multicenter Real-World Study of Undifferentiated Diseases" led by the First Affiliated Hospital of Zhejiang University with participation from multiple medical institutions across China is also underway.

This study has limitations: due to limited MUPS research in Chinese databases, only English literature from Web of Science was included. However, the discussion section incorporates relevant Chinese literature to illustrate China's current research status.

In summary, future domestic and international scholars must continue exploring MUPS. Building on existing research while considering regional and ethnic differences, we must clarify etiology and pathogenesis, establish specific diagnostic criteria, and develop comprehensive treatment strategies with improved referral processes. GPs should collaborate with psychiatrists, psychologists, neurologists, and social scientists to provide individualized, high-quality diagnosis and long-term management. China must explore a path with Chinese characteristics suited to its healthcare system, enabling GPs as “gatekeepers” of residents' health to provide lifelong medical services.

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