

Excessive daytime sleepiness in older adults: A bibliometric and visualization analysis

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Abstract

Background: To analyse the bibliometric results of a study on the research trends in excessive daytime sleepiness (EDS) among older adults to provide clinicians and researchers with a better understanding of the current status and to identify potential new research directions. **Methods:** We searched the Web of Science Core Collection for articles on immunotherapy for EDS in older adults. We used three software packages (VOSviewer, CiteSpace, and Tableau) to analyze the articles in terms of journals, keywords, citations, co-citations, and research areas and identify research hotspots as well as promising future trends in this field. **Results:** Our findings showed an annual increase in the number of articles on EDS that were published. Among them, authors from the USA had the highest number of publications globally in this field, while in terms of institutions, the highest number of articles came from Stanford University (n = 26, 2.73%). The articles covered diverse research areas and included clinical neurology, neuroscience, and the respiratory system. As expected, journal-wise, the majority of articles were published in “*Sleep*” and “*Sleep Medicine*”. Keywords indicating research areas in recent years were ‘important difference,’ ‘obstructive sleep apnea,’ and ‘shift work.’ These were also reflected in the results of the co-citation analysis.

Conclusions: Overall, EDS is an area of increasing interest and offers excellent research opportunities for the future.

Keywords: Bibliometric, excessive daytime sleepiness, older adults, research hotspots and frontiers, visualization

INTRODUCTION

The International Classification of Sleep Disorders, Third Edition (ICSD-3) defines excessive daytime sleepiness (EDS) as the inability to remain awake and alert during the main waking hours of the day and the presence of an unsuppressed need for sleep, which may be accompanied by cognitive impairment.^{1,2} The causes of EDS are multifactorial and include drug or substance abuse and medical, psychiatric, or sleep disorders.³⁻⁵ Considering its heterogeneous etiology, its clinical manifestations vary, and EDS may be associated with monotonous activities, frequent naps, excessive sleepiness, excessive sleep demand, and a persistent state of somnolence. Nonetheless, EDS is not as acute and severe as episodic sleep.^{1-3,6} However, it has a significant impact on the quality of life and socioeconomic status of affected individuals,

and hence, there is a critical need for a timely diagnosis.^{3,7} Assessment of EDS entails a rigorous clinical approach involving the use of self-reported questionnaires and neurophysiological measures, depending on the individual’s clinical situation.¹

EDS is a highly prevalent condition³, affecting over 20% of the population^{8,9}, and is an emerging global public health issue.¹⁰ Compared to individuals without EDS, patients with EDS exhibit significant vigilance and cognitive impairments, resulting in a high disability rate, substantial medical costs and financial burden¹¹⁻¹³, as well as lower daily functioning, productivity, quality of life, and well-being.^{4,14} Thus, it is essential to develop a comprehensive treatment protocol for EDS.¹

Bibliometrics is the study of academic publications that uses statistical data to describe publishing output and trends as well as highlight

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connections among published works.¹⁵ It provides researchers with qualitative and quantitative characteristics of a body of literature by analyzing measures such as countries, journals, institutions, authors, and keywords to describe current trends and identify hotspots in the field.¹⁶ In this study, our aim was to utilize bibliometrics and visualization approaches to explore the frontiers and hotspots of literature pertaining to EDS and to identify future research directions in this field.

METHODS

Data source and search strategy

We conducted an extensive literature search in the Web of Science Core Collection (WOSCC) using Science Citation Index-Expanded (SCIE) on December 1, 2022. We limited the data source with regard to publication types to “article”. In order to acquire more accurate results, we searched the following Medical Subject Headings (MeSH) terms (<https://www.ncbi.nlm.nih.gov/mesh>): “excessive daytime sleepiness” and “elderly”.

Our data retrieval strategy was as follows: ((TS = (Aged OR Aged, 80 and over OR Centenarians OR Nonagenarians OR Octogenarians OR Frail Elderly)) AND TS = (Excessive Somnolence Disorder* OR DOES OR Hypersomn* Disorder*

OR Daytime Somnolence OR Daytime Sleepiness* OR Hypersomnia*, Recurrent OR Excessive Daytime Sleepiness* OR Disorders of Excessive Somnolence)) NOT TS= (child OR preschool OR adolescent OR young adult OR student* OR pediatric OR pregnancy OR youth). The time span was set from January 1, 2014 to December 1, 2022.

Study design

While institutional purchases of the Web of Science (WOS) date back as far as 1900, we could trace the EDS-related literature only to 2014. These papers predominantly focused on the symptoms of EDS in the elderly. We developed a detailed search strategy for this review, and two researchers (ZF and ZL) working in this area screened the articles. Meanwhile, two authors independently searched the WOSCC database for relevant literature and downloaded the relevant information (full record and cited references) in the Text, Tab, and Excel formats. Next, the researchers excluded literature that did not meet the eligibility criteria for inclusion in this study. When necessary, a third reviewer (XQ) was brought in to discuss and settle any differences of opinion that arose. A flowchart of the review process is shown in Figure 1.

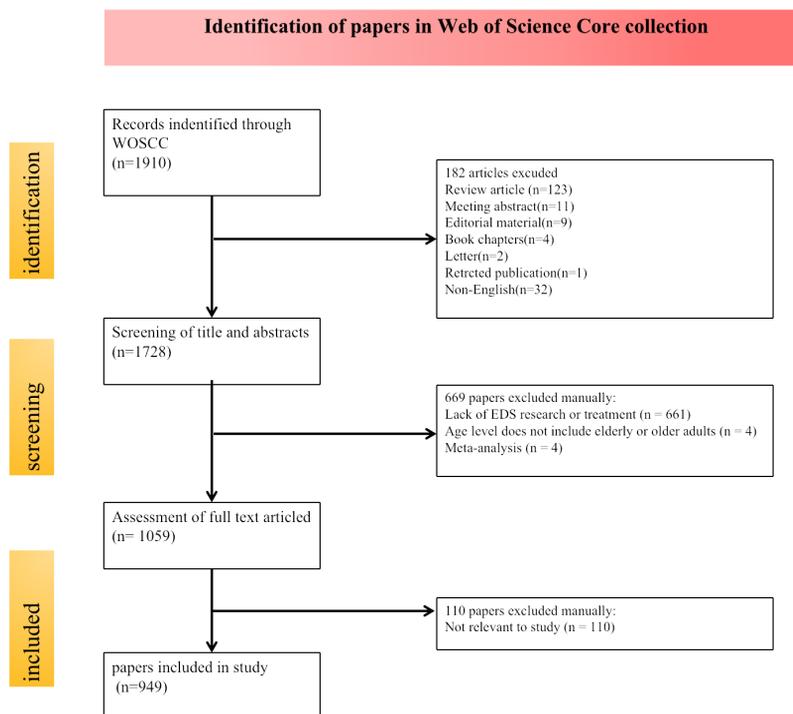


Figure 1. Flow chart of the process of article screening for analysis.

Qualification criteria

Inclusion criteria: We included articles that were written in English, and the study designs included randomized controlled trials, cohort studies, forward-looking research, longitudinal studies, or animal experiments. The primary study population was the elderly and middle-aged adults (several studies included both adult and elderly subjects) with symptoms of EDS.

Exclusion criteria: We excluded review articles, meeting abstracts, editorial materials, book chapters, meta-analyses, letters, and retracted publications from this study. Articles that did not focus on the elderly population or non-EDS studies were excluded after screening the abstracts and full texts.

Statistical analysis

VOSviewer (1.6.18) is a software tool for constructing visual bibliometric networks. For this review, we extracted the citation keywords of each article and created inter-country and inter-institutional clustering views. The size of the circles depends on the number of elements. The color of the circles represents the clusters they belong to, with different colors representing different clusters.^{17,18}

CiteSpace 6.1.R6 (created by C. Chen, Ph.D., Department of Information Science, Drexel University) is a visual analytic tool for identifying emerging trends in research based on relevant scholarly publications. In this review, we studied the strongest citation bursts of keywords and their visual representation in the form of a dual map overlay in the scholarly literature based on citations. In other words, we analyzed the timeline views of the cited literature and the strongest citation bursts of keywords to clarify the annual concerns and hotspots in the field and to predict future research trends. The dual-map overlay analyzes citation trajectories and provides information on the center of gravity drifts. The time slice of the timeline view was set to two years, with the literature time at the top; the further the literature was to the right, the more recent the literature, and the longer the time span, the longer the duration of the clusters. Altogether, this assisted in yielding a better understanding of the various temporal analyses in the EDS field. At the same time, the size of the circle indicated the frequency of the cited words. However, a large circle did not signify that the document was cited most frequently in that year but rather

that it was first cited in that year; following this, the number of citations accumulated with time. The parameters of the timeline views were as follows: Timespan: 2014-2022 (Slice length = 2); Selection criteria: g-index (k = 25), LRF = 3.0, L/N = 10, LBY = 5, e = 1.0; Network: N = 383, E = 1343 (Density = 0.0184); Largest CC: 363 (94%); Nodes labeled: 1.0%.^{18,19}

The Tableau software was developed at Stanford University as part of a computer science program that presents a procedure for interactive visualization and analysis of medical data.^{20,21} In this review, we used Tableau Desktop (2022.3) to analyze journal publications, annual trends, research areas in EDS, national publications, and the total number of documents vs. citations.²¹

RESULTS

Visual analysis of journals

A total of 949 articles were published. EDS-related publications peaked in 2019 (n = 119, 12.60%), with the least number of articles published in 2014 (n = 86, 9.11%) and an annual average of 105.44 published articles. The top ten journals and yearly trends in the number of EDS-related articles published that had a focus on the middle-aged and older adult populations, with a progressive increase in annual output, are depicted in Figure 2. The top three journals with the highest number of EDS-related publications were “*Sleep Medicine*” (n = 67, 7.06%), “*Sleep and Breathing*” (n = 62, 6.53%), and “*Sleep*” (n = 50, 5.26%). In terms of publications, the USA (40%) was ranked first in the world, followed by England (20%) (Table 1).

Visual analysis of keywords

The WOS research areas in geriatric EDS were classified into four clusters (Figure 3A), with each cluster representing a research area. The top ten keywords identified by VOSviewer in terms of frequency were EDS (564), risk (235), hypoxia (242), obstructive sleep apnea (OSA) (244), prevalence (215), quality of life (218), disorders (208), scale (205), depression (183), and insomnia (168).

The majority of participants were older adults, both men and women. The studies included in this bibliometric analysis were mainly randomized controlled trials, longitudinal studies, cohort studies, follow-up studies, and epidemiological studies. EDS is a symptom related to conditions such as OSA, Parkinson’s disease, restless legs syndrome, and cardiovascular disease. Moreover,

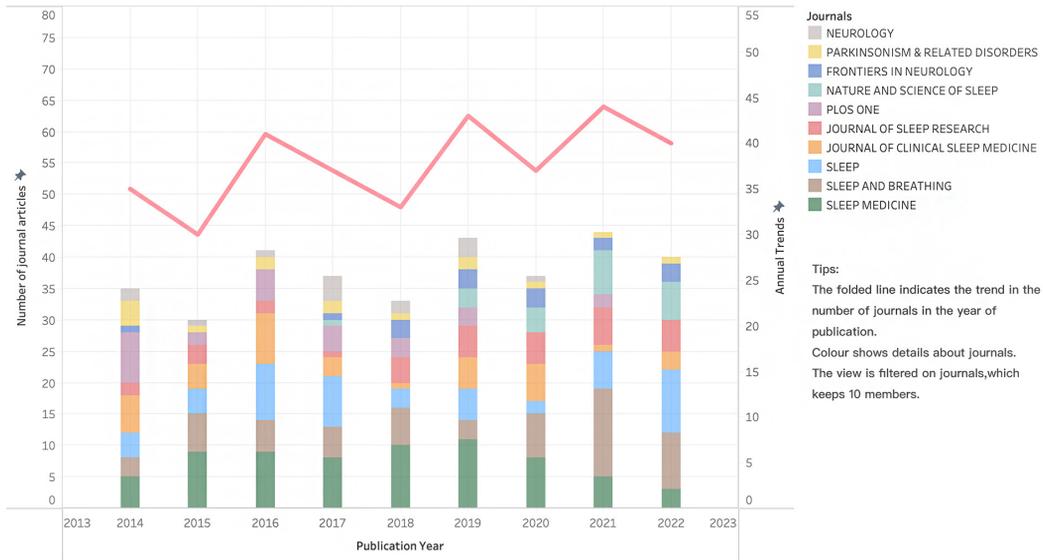


Figure 2. Publications and yearly trends from 2014–2022 in the top 10 journals.

EDS is frequently manifested in patients suffering from depression, insomnia, obesity, dementia, and diabetes, which affect the individual’s quality of life and cause life-threatening conditions resulting from driving accidents.

Common diagnostic tools are the Epworth Sleepiness Scale and polysomnography, while treatment modalities include continuous positive airway pressure (CPAP), ventilation devices, and sleeping pills. Given its prevalence in the community, there has been a growing movement to advocate for the timely diagnosis of EDS in recent years in order to enhance the quality of life of patients and prevent further progression of the disease.

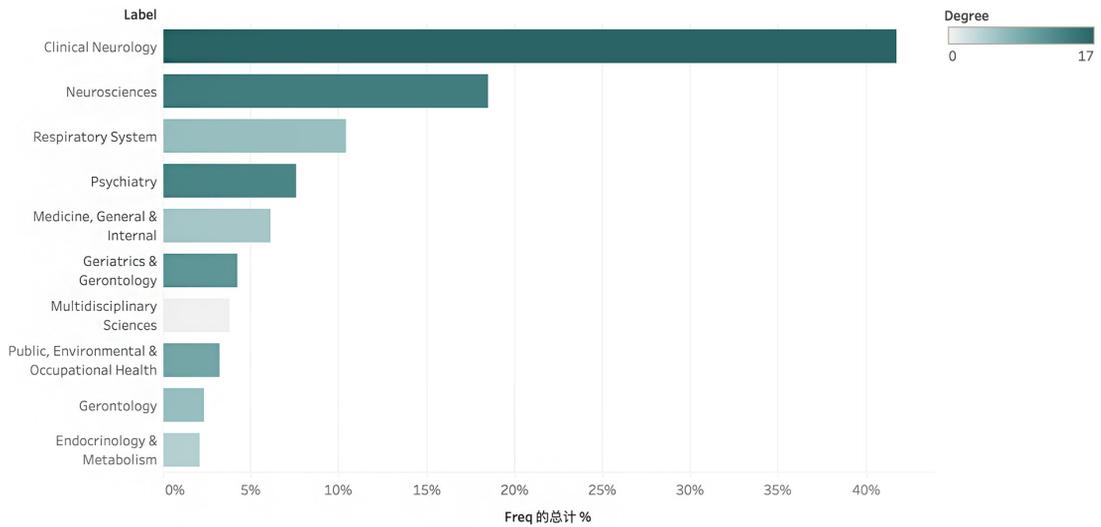
We used CiteSpace to identify emerging keywords, and we selected the top 15 keywords

with the strongest citation bursts (Figure 3B). The emerging keywords in the EDS field every two years are shown in Figure 3B. These range from “sleep,” which is closely associated with EDS, to the discovery that EDS is a symptom accompanying disease progression that can be used as an indicator of disease exacerbation.

The Epworth Sleepiness Scale (ESS) is a reliable test for quantifying daytime sleepiness and disease progression.¹¹ However, in several cases, there is no statistically significant indicator of disease progression.²² Nevertheless, symptoms significantly fluctuated in many cases, so a minimum important difference (MID) is required to identify disease progression or regression.¹¹ The MID determines alterations in sleepiness, representing whether the slightest change is

Table 1: Top 10 journals publishing papers on EDS

Rank	Journal	Documents (%)	IF	Co-cited	Country
1	Sleep Medicine	67(7.06%)	4.482	1537	Netherlands
2	Sleep And breathing	62(6.53%)	2.655	634	Germany
3	Sleep	50(5.26%)	6.313	3763	USA
4	Journal Of Clinical Sleep Medicine	37(3.89%)	4.324	1036	USA
5	Journal Of Sleep Research	36(3.79%)	5.296	819	England
6	Plos One	28(2.95%)	3.752	484	USA
7	Nature And Science Of Sleep	20(2.10%)	3.384	75	New Zealand
8	Frontiers In Neurology	16(1.68%)	4.086	87	Switzerland
9	Parkinsonism & Related Disorders	15(1.58%)	4.402	188	England
10	Neurology	15(1.58%)	12.258	670	USA



% of Total Freq for each Label. Colour shows sum of Degree. The view is filtered on Label, which keeps 10 of 61 members.

Figure 4. Bar charts illustrating the top 10 research areas in EDS, with each research area listed on the Y-axis and its proportion as the corresponding percentage on the X-axis. The color shows the sum of degrees; the darker the color, the stronger the connection to other areas of study.

beneficial or harmful.²³ It assists in interpreting the minimal variation in outcomes. In clinical practice, the MID is beneficial for identifying disease progression or assessing the effectiveness of treatment.²³ However, a definitive MID has not been established for EDS.^{11,22,23}

Visual analysis of research areas

We found 61 research areas that are associated with EDS, and the main ones were clinical

neurology, neuroscience, and the respiratory system (Figure 4). In addition, the most extensive collaborations with other study disciplines were clinical neurology, neuroscience, psychology, and psychiatry.

The Dual-May Overlays visualization with five different citation paths is shown in Figure 5. The primary subject areas of the citing document were medicine, medical, clinical, neurology, sports, ophthalmology, physiology, education, and health; the first main subject of the cited

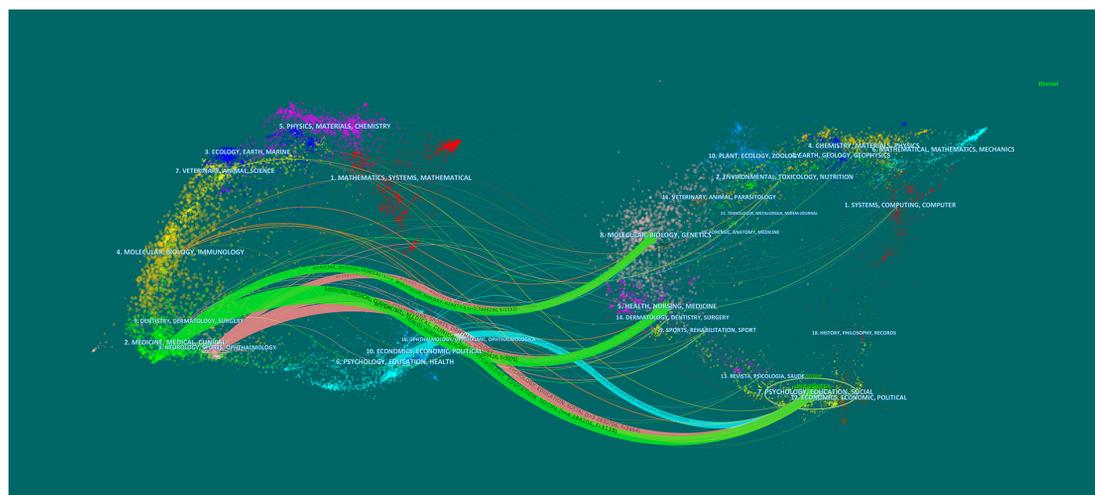


Figure 5. The Dual-Map Overlay visualization, with citation topics on the left and cited topics on the right; the longer the horizontal axis of the ellipse, the higher the number of papers published in the corresponding journal.

document was physiology, education, and social; and the subject direction of the citing document was: medicine, medical, and clinical, neurology, sports, ophthalmology, physiology, education, and health.

The secondary subject area of the cited article was molecular, biology, and genetics; the subject direction of the cited article was medicine, medical, clinical, neurology, sports, and ophthalmology. The third central theme of the cited literature was health, nursing, and medicine; the subject direction of its citing literature was medicine, medical, and clinical. Medicine, medical, and clinical source themes generated the most diversity in the cited literature.

Visual analysis of countries, institutions, and authors

The top three countries in terms of publications are shown in Figure 6A. Based on the number of published articles, the USA ($n = 276$, 19.74%) ranked first, followed by China ($n = 97$, 6.94%), and Australia ($n = 81$, 5.79%). The distribution of countries and the interactions between the country with the highest number of published articles, the USA, and other countries are shown in Figure 6A. The color of an element represents the cluster it belongs to, with different clusters represented by different colors. In terms of the research area of the publications, the top three countries, namely, the USA, China, and Australia, were in close proximity to one another and belonged to the same cluster.

There were 118 institutions that contributed these articles; there were 199 institutions in the top 10, with four institutions each from the United States and Australia. The top three institutions in terms of the number of publications were Stanford University ($n = 26$, 2.73%), the University of Sydney ($n = 24$, 2.52%), and Harvard Medical School ($n = 23$, 2.42%). The top three institutions with the highest number of citations were Harvard University, Northwestern University, and the University of Sydney (Figure 7).

In total, there were 4,902 authors who contributed to the field of EDS; the top 10 authors with the highest number of publications are listed in Table 2. Susan Redline was the most influential author (h -index = 122), followed by Janson and Christer (h -index = 79).

Visual analysis of co-cited references

We developed the timeline views of the cited literature using CiteSpace, and cluster analysis

revealed a total of 10 clusters (Figure 8A). We also created a timeline display of the co-cited references (Figure 8A). The timeline view is a method of visualizing data by combining clustering and time-slicing techniques, thereby showing trends and interrelationships of research topics over time. The time slice was set to 2.

In the timeline view, the darker the color, the closer the research heat for that cluster is to 2022. The closer the node is to the right, the newer the reference. The straight line at the same horizontal position denotes the attributed set of all clustered references, with the cluster labels located at the far-right end of the line. The cluster close to 2022 on the timeline was “#8 narcolepsy”, followed by “#3 shift work” and “#0 continuous positive”.

CiteSpace evaluates references with high citation bursts (Figure 8B), representing a reference that has been widely cited over time and whose findings are well known in the field. The highest citation burst in the recent past was “Benjafeld, AV, 2019, LANCET RESP MED, V7, P687, DOI 10.1016/S2213-2600(19) 30198-5” (Strength 6.14, Begin-End 2020-2022).

The top 10 papers cited in this review are illustrated in Table 3. Five of these assessed EDS and sleep measurement approaches; three described subjective measurement questionnaires; two were practical recommendations for objective measures; two explored the importance of sleep for public health; two were analyses and updates of risk factors for sleep; and one was a practical recommendation from the American Academy of Sleep Medicine (Table 3).

DISCUSSION

General information

In this analysis, we performed a systematic literature search of literature on EDS-related articles published in the Web of Science database over the last nine years (January 1, 2014–December 1, 2022) (Figure 1). After a rigorous selection process, we assessed 949 papers published in 362 journals for this scientometric study. In terms of annual journal trends (Figure 2), the number of EDS-related publications has steadily increased yearly, with the topic gaining increasing interest in recent years. “*Sleep*” and “*Sleep Medicine*” lead the research trend in EDS (Table 1).

The United States has the highest number of publications (Figure 6), with 29.39% of the world’s publications, implying that the prevalence

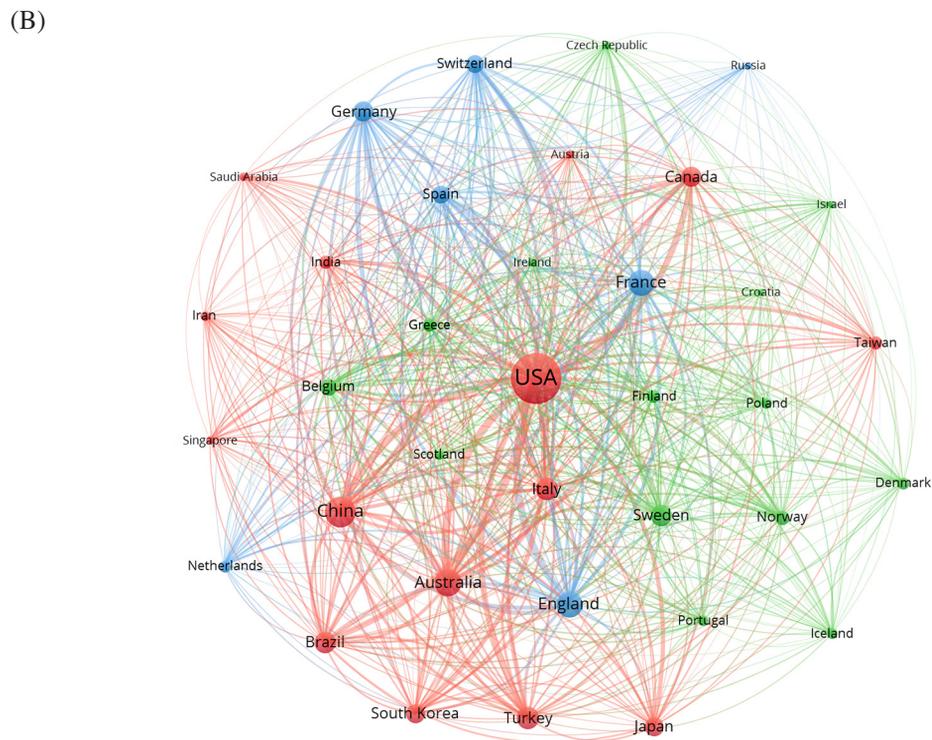
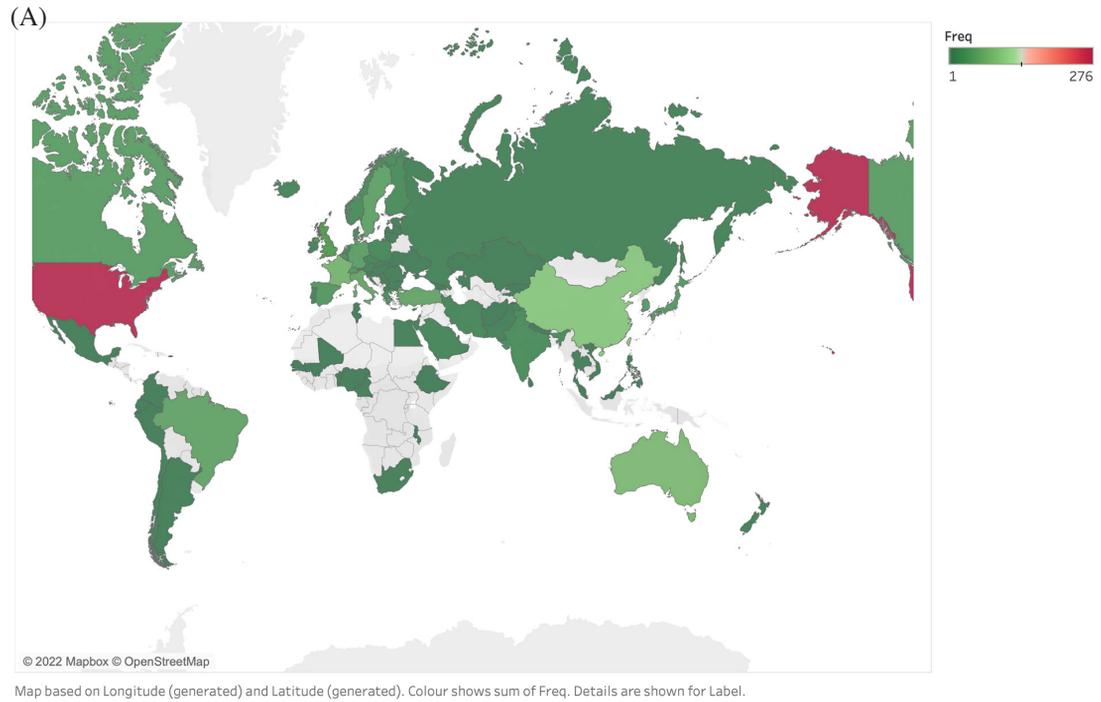
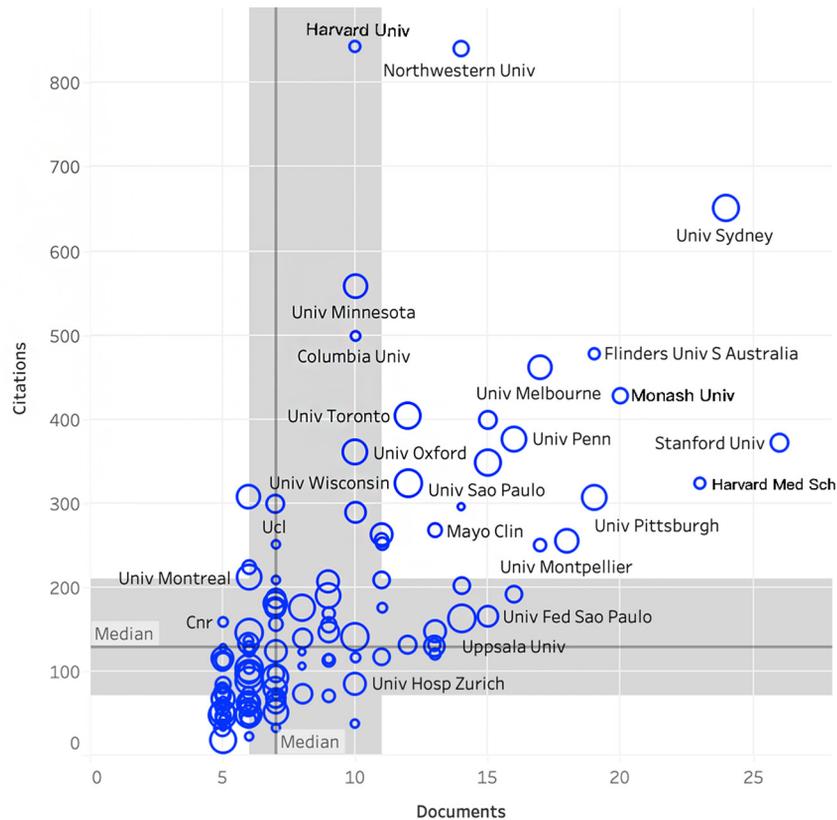


Figure 6. (A) Colors representing the total country-wise publications pertaining to EDS in older adults; the redder the color, the higher the number of articles published, and the greener the color, the fewer the publications. (B) Collaborations between countries. The size of the node indicates the number of published articles from different countries; the larger the node, the higher the number of published articles by the country. The distance between the nodes indicates the degree of collaboration; the closer the nodes, the higher the degree of collaboration; the same color indicates the same research topic.

(A)



Sum of Documents vs. sum of Citations. Size shows details about Organization. The marks are labelled by Organization. Details are shown for Organization. The view is filtered on Organization, which keeps 118 of 118 members.

(B)

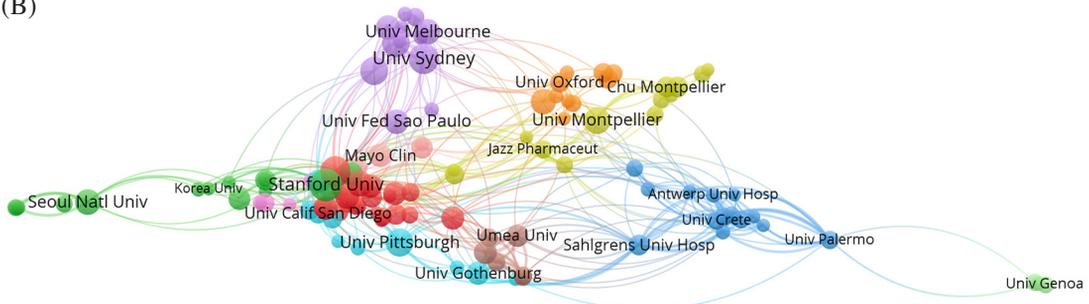


Figure 7. (A) Total of publications vs. total of citations. Size shows details about the organizations, which consist of 118 institutions. (B) Collaborations between institutions.

of EDS in the United States is high and that it places considerable emphasis on its diagnosis and treatment. Among the top ten countries with the most publications, three were developing countries (China, Turkey, and Brazil), while the remaining seven were developed countries. This observation indicates that there is an urgent need to strengthen the diagnosis and treatment of EDS in developing countries.

Likewise, this trend was also reflected in

the institutions, whereby the top ten institutions with the highest number of published articles were located in developed countries (Figure 6). Close cooperation can be seen internationally and between institutions (Figures 6 and 7).

EDS covers a wide range of pathologies and thus encompasses many research areas; journals related to clinical neurology, neurosciences, and the respiratory system have published the majority of articles (Figure 4), and its source themes are

Table 2: Top 10 authors with the most posts in the EDS field

Rank	Author	Count	Citations	H-index	Country
1	Dauvilliers, Yves	26	471	68	France
2	Redline, Susan	14	650	122	USA
3	Jaussent, Isabelle	12	227	41	France
4	Lindberg, Eva	11	145	33	Sweden
5	Tufik, Sergio	10	80	27	Brazil
6	Foldvary-Schaefer, Nancy	9	76	23	USA
7	Janson, Christer	9	134	79	Sweden
8	Lopez, Regis	9	155	11	France
9	Partinen, Markku	9	224	68	Finland
10	Yun, Chang-Ho	9	113	28	South Korea

more diverse in the cited literature (Figure 5).

Of the top ten most active authors in terms of volume of publications (Table 2), France had the highest proportion of such authors, suggesting that French authors are making significant contributions to the field of EDS. The author Yves Dauvilliers published far more articles than any other author, and his research focused on the diagnosis, epidemiology, pathophysiology, and treatment of sleep disorders, primarily neurological disorders comprising not only episodic sleeping disorders but also central hypersomnia, allergic sleep, and restless legs syndrome (RLS).

In terms of co-cited authors, the top 10 authors made significant contributions to EDS in older adults with at least 99 co-citations. The most notable were Johns *et al.* (714 co-citations, 13.79%), ranked first, followed by Buysse *et al.* (294 co-citations, 5.68%, Doi), and Young *et al.* (246 co-citations, 4.75%). Johns *et al.* have been studying various sleep disorders for decades; Johns MW, the pioneer behind the Epworth sleepiness scale (Table 3), a subjective self-measurement scale, is currently developing different methods for assessing sleepiness. Moreover, this team has been collaborating with researchers in other countries to study EDS.

Research hotspots and frontiers

We analyzed the burst keywords in Citespace to further grasp the latest research hotspots and frontiers in EDS. As shown in Figure 3B, the latest research hotspots or frontiers were ‘important difference,’ ‘OSA,’ and ‘shift work.’ Due to the heterogeneous etiology of EDS and its complex pathophysiology, treatment measures largely depend on what causes it.^{1,24}

Shift work is a common experience for many workers worldwide in modern societies,

where economies operate based on supply and demand.²⁵ The prevalence of sleep disorders in shift workers is as high as 32%²⁶, and these sleep disorders lead to daytime sleepiness and impaired daytime functioning, eventually resulting in severe cardiovascular, pulmonary, endocrine, neurological, and psychological disorders.²⁶⁻³⁰ Considering this, earlier studies focused on the results of personality tests and found that individuals with higher levels of neuroticism reported poorer sleep quality and higher levels of insomnia; conversely, shift workers with higher levels of extroversion developed fewer insomnia symptoms and better sleep quality. Further studies on personality and EDS are warranted.²⁹

Individuals with obstructive sleep apnea (OSA) often experience EDS³¹, and this can result in fatigue, reduced performance at work, difficulty staying awake while driving, and impaired concentration and personal relationships.³²⁻³⁶ CPAP is currently the gold standard for treating symptomatic OSA.^{32,33} It improves sleep quality and minimizes EDS symptoms.^{33,37} CPAP is an evident current research hotspot, as demonstrated by the clustering of co-cited references (Figure 8A). However, CPAP is not well tolerated by many patients.³³ Despite considerable improvements in medical technology over the last two decades to help improve patient tolerance, the results remain far from ideal.^{33,38} Therefore, it is essential to develop personalized treatment options.³³

Researchers have also investigated alternative treatments such as mandibular advancement devices, maxillary osteotomies, upper airway stimulation³³, and multilevel airway surgery.³⁸ Notably, pharmacological treatment has been used as an adjunct to CPAP to address the problem of residual EDS.^{14,32,33} Adjunctive treatments for

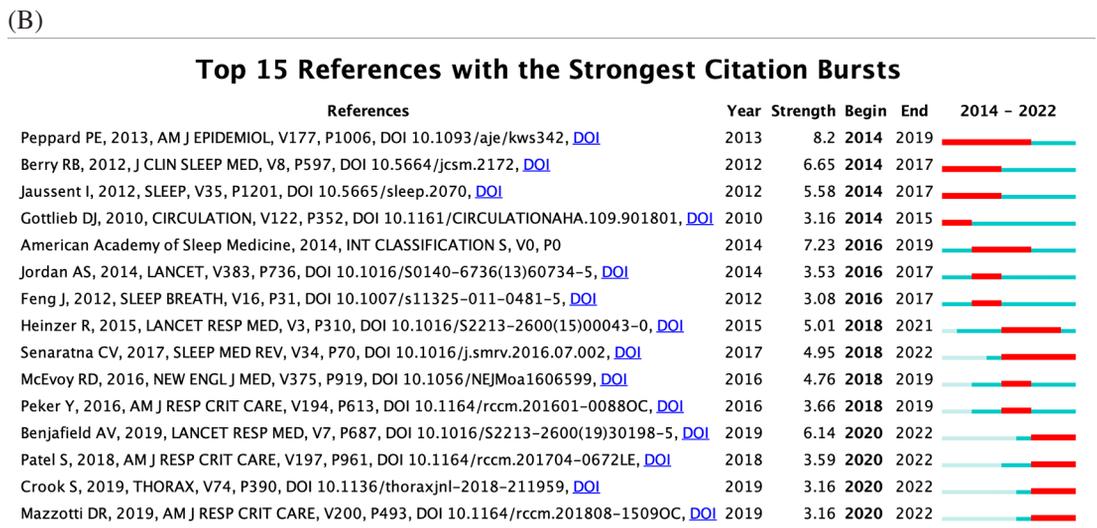
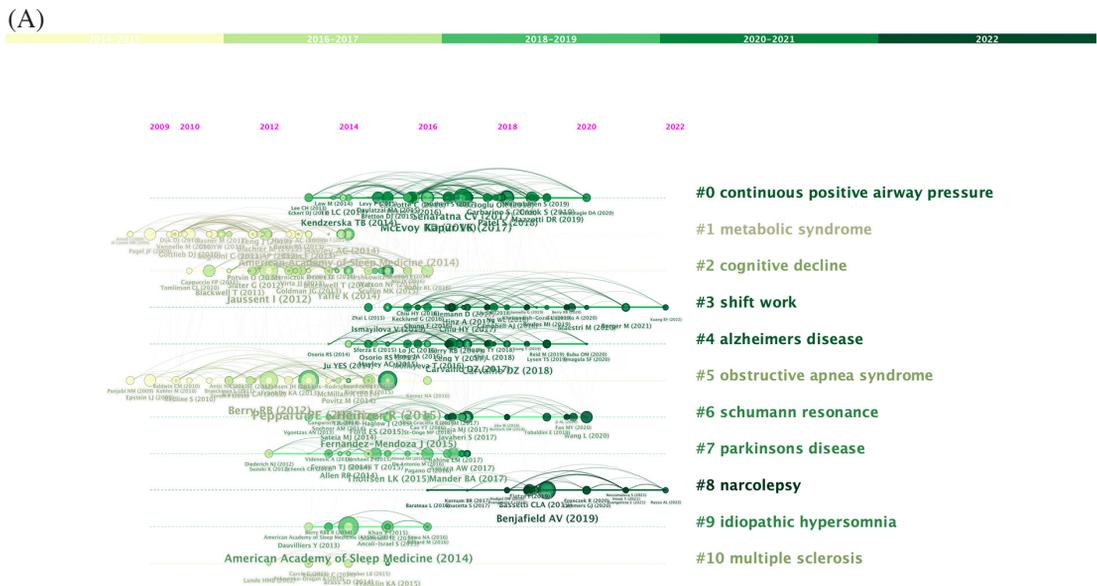


Figure 8. (A) Timeline Views of the cited literature. Timespan, 2014–2022 (Slice length = 2); the darker the color, the closer the research heat for that cluster is to 2022. (B) The 15 most cited references. The red line represents the highest-cited reference for the year.

Table 3: Top 10 co-cited references involved in research on elderly in EDS

Rank	Co-cited reference	citations	type	IF
1	Johns Mw, 1991, Sleep, V14, P540.	503	Clinical research	6.313
2	Buyssse Dj, 1989, Psychiat Res, V28, P193.	176	Clinical research	11.225
3	Johns Mw, 1992, Sleep, V15, P376.	82	Clinical research	6.313
4	Young T, 1993, New Engl J Med, V328, P1230.	79	Clinical research	176.079
5	Bixler Eo, 2005, J Clin Endocr Metab, V90, P4510.	70	Clinical research	6.134
6	Berry Rb, 2012, J Clin Sleep Med, V8, P597.	67	Review	4.324
7	Peppard Pe, 2013, Am J Epidemiol, V177, P1006.	59	Clinical research	5.363
8	Heinzer R, 2015, Lancet Resp Med, V3, P310.	52	Clinical research	102.642
9	Johns Mw, 2000, J Sleep Res, V9, P5.	51	Clinical research	5.296
10	Bastien Ch, 2001, Sleep Med, V2, P297.	49	Clinical research	4.842

EDS patients include wakefulness-promoting drugs such as modafinil, armodafinil, and sodium oxybate^{33,39,40}, which have demonstrated positive outcomes in residual drowsiness in randomized controlled trials.³⁷ Besides, the use of stimulants such as methylphenidate and amphetamines is recommended in refractory EDS cases.³⁹ Newer drugs, such as pitolisant and solriamfetol, have recently been approved for the treatment of OSA.³⁹ The former has been used not only as an adjunct to CPAP therapy³⁷ but has also significantly improved mobility and quality of life in patients not on CPAP.^{41,42} Solriamfetol has shown long-term efficacy in alleviating EDS⁴³, with no known drug interactions.⁴⁴ The combination of ventilation devices and pharmacological treatment is clearly a popular topic of current research in EDS. In clinical practice, it is necessary to identify important changes in the severity of EDS in patients following an intervention.^{11,45} Understanding the patient's perception of change is as important when inferring the clinical significance of change; analysis of significant statistical findings alone can prove insufficient.^{22,45,46} Estimating the MID (minimally important difference) allows clinicians to compare the baseline and the change perceived by the patient.⁴⁵ It represents the minimum threshold at which patients can identify the treatment effect, and this can aid clinicians in interpreting patient outcomes and guiding further treatment measures.^{45,47} Research into known MIDs should be prioritized as a critical area in the future.¹¹

Strengths and limitations

To the best of our knowledge, this is the first study involving a systematic analysis of publication trends in EDS in an intuitive, objective, and accurate manner using a variety of bibliometric software to examine research hotspots multidimensionally. It can serve as a comprehensive guide for clinicians and scholars in this field.

There are some limitations to our bibliometric analysis: 1. We searched for literature in only one database (WOSCC), and our search was restricted to articles written in English. This might have led to incompleteness and bias. 2. It is likely that, owing to their low citation rate, the most recent high-quality articles received insufficient attention. 3. We only included all articles up to December 1, 2022, in this review and excluded articles published after this cut-off date from the analysis.

In conclusion, we have provided a comprehensive overview of the characteristics and trends in EDS literature, highlighting current and future research hotspots and themes that will help clinicians and researchers identify and treat EDS, thereby improving the quality of life and preventing disease exacerbation. The etiology of EDS is very complex and requires individualized treatment. The treatment and care of patients with EDS must comprehensively consider the personality aspects of the patient as well as ventilation equipment and pharmacological drugs. More importantly, there is an urgent need to recognize minimally important differences in patients, which offers a promising and exciting direction for future research.

DISCLOSURE

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Conflicts of interest: None

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