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Global Trends in Alzheimer's Disease Treatment: A Bibliometric Analysis

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ABSTRACT

Alzheimer's disease is a neurodegenerative disease characterized by cognitive and functional deficiencies, such as behavioral changes. As the disease progresses, neurons in the brain are damaged or disappeared. Nowadays, Alzheimer's disease and other common dementia do not have a treatment. None of the pharmacological treatments are currently effective in slowing down Alzheimer's dementia or stopping neuron damage.

This paper offers a bibliometric analysis of the literature on treatments for Alzheimer's Disease indexed in the Web of Science database spanning 44 years. The study employed the VOSviewer visualization methodology to conduct the bibliometric analysis. The dataset consisted of articles retrieved from the Web of Science database, covering data on countries, institutions, journals, co-authorship, and international collaborations.

In total, 56,530 publications were collected from the Web of Science database. The United States of America (USA) emerged as the leading country in terms of published articles, accounting for 20,389 (36.068%) of the total, followed by China with 5,434 (9.613%) publications, and England with 4,594 (8.127%). Excluding the top three countries mentioned above, publications originated from 168 countries worldwide. Since the 2000s, there has been a notable increase in publication numbers. Leading affiliations include the University of California System (USA) (2.959%), Harvard University (USA) (2.117%), and the University of London (England) (1.951%). The majority of these prominent affiliations are situated in the USA.

In summary, this study represents the current bibliometric assessment of treatments for Alzheimer's Disease. The results of this research will provide foresight to advanced Alzheimer's Disease Treatment research and provide different perspectives on its development.

Keywords: Alzheimer's disease treatments, publications, bibliometric analysis

Introduction

The application of quantitative methods, such as bibliometric analysis (e.g., citation analysis), to bibliometric data is known as bibliometric methodology, which includes units like publications and citations. Bibliometric analysis; based on analyzing the obtained documents or articles according to their specific characteristics and revealing the findings. Studies within a specific field or research published in a particular journal are analyzed based on various parameters, with findings presented accordingly. These findings may encompass data such as keywords, number of authors, citations, and research topics. By systematically interpreting large volumes of unstructured data, bibliometric analysis effectively maps and elucidates the cumulative scientific knowledge and evolutionary nuances of well-established topics. As a result, well-executed bibliometric studies can serve as a foundation for expanding a topic in unique and significant ways by enabling researchers to 1. gain a comprehensive understanding and 2. enhance their own capabilities (1).

Dementia has a large degree of social and also economic effects. The annual cost for dementia in 2019 is $1 trillion, and this is estimated to rise to $2 trillion by 2030. Most importantly, Alzheimer's Disease (AD) stands out as the predominant form of dementia, accounting for approximately 60-80% of dementia cases (2). AD manifests as a progressive neurodegenerative condition, marked by neuronal death in brain regions crucial for cognitive functions (3). Currently, AD is the sixth leading cause of death in the United States. It is also the biggest cause of disease rate and economic burden worldwide (4). AD is associated with progressive neuronal loss and synaptic dysfunction, accompanied by senile plaques of amyloid-β (Aβ) and intracellular neurofibrillary tangles of tau in aged brains. Time is everything in age-related AD that affects the nervous system. Currently, there are only two types of FDA-

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approved drugs. These drugs that improve AD symptoms; include cholinesterase inhibitors (galantamine, rivastigmine, donepezil) and N-methyl-D-aspartate antagonist (memantine) but they do not prevent or treat AD (5). Regrettably, there have been only a scant number of clinical trials launched in the past decade, and they have predominantly ended in significant failure. Numerous mechanisms have been devised to unravel the pathology of AD, aiming to modulate its pathways and advance successful treatments. These mechanisms include abnormal tau protein metabolism, (Aβ), inflammatory response, cholinergic damage and free radical damage. Aducanumab is a monoclonal antibody, targeting soluble and insoluble (Aβ), which received FDA approval in June 2021 for the treatment of mild cognitive impairment in AD and mild AD dementia (6, 7). Aducanumab has been the only drug approved for AD since 2003 but its usage for Alzheimer's disease was withdrawn.

On the other hand, AD can be modified and cardiovascular or lifestyle habits such as risk factors of AD can be prevented without medical interventions. Studies show that physical activity can ameliorate brain health and attenuate the risk of AD by reducing brain vascularization, plasticity, neurogenesis and Aβ production and activating the reduction of inflammation, all of which improve cognitive function in older people (8). Although the clinical efficacy of the drugs in the current studies has not been fully established, clinical trials of these agents are ongoing. These newly developed molecules target amyloid and tau proteins (9). Research for future treatments of AD aims at etiologic pathologies. However, debate continues about which abnormality is the best target for slowing or stopping neurological damage and how early treatment should be initiated (10). The difficulties in developing treatments for AD and the numerous failures in clinical trials suggest that new creative study designs may be needed (11). The goal of this study is to search the existing bibliometric reviews about the treatment of AD. This study is the current bibliometric study on this subject. This article uses bibliometric analysis to show the status of work in this area in the last 43 years. This study's results will guide researchers in this field in developing international cooperation to illustrate potential research directions and points of analysis in this area.

Material and Methods

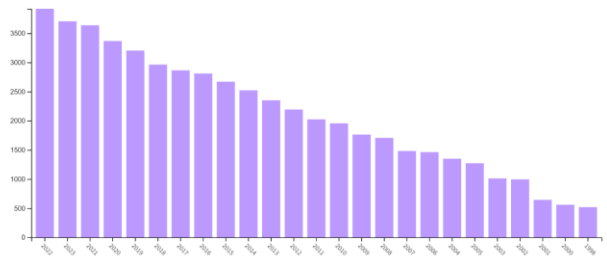
Data Collection Method: To discover *Alzheimer's Disease Treatments* research records, the Web of Science (WoS) bibliometric database (Clarivate Analytics, Philadelphia, PA, USA) was investigated. The study's data was obtained from the WoS database on January 22nd, 2024. WOS categories, publication titles, publication years, countries/regions, affiliations, the names of published journals, document types, funding agencies, languages, research areas, and citations were saved as TXT files and imported into Microsoft Office Excel 2019. (Los Angeles, CA, USA) (1).

The material was reached utilizing the online library and digital resources of Van Yüzüncü Yıl University.

Comprehensive Overview of The Wos Database Output: The WOS database was exercised to define the publication year, position of country, work method and authorship. The study's interval was between 1980 and 2023. Since the year 2024 has not been finished yet, the study did not contain the articles for the year 2024. The language was English in the search.

Search Strategy: Keywords relevant to *Alzheimer's Disease Treatments, Alzheimer Disease Treatments, Alzheimer's Treatments, Alzheimer Treatments, rivastigmine, memantine, donepezil, galantamine, treatment aims, treatment targets, treatment goals, drug developments, drug development* were chosen as the main topic in a search interrogation in the WOS search engine. The time period was arranged from 1980 to 2023. This study assayed inputs on publication growth, the most active regions and institutions, and keyword mapping. The articles were studied in detail.

Network Analysis: The text data from the included publications was obtained using the Web of Science (WoS) database. Subsequently, VOSviewer (version 1.6.10, Leiden University, Netherlands) was employed to visualize the collaboration network, highlight emphases, and forecast future trends within the pertinent topic of this bibliometric study. The data were received using the VOSviewer software. Authorship, affiliation, citation, languages, and theme words were all acquired and analyzed. Ultimately, bubble maps were created to illustrate the findings of the bibliometric analysis. The colors within these maps delineated clusters of items, while the distance and thickness of lines connecting two bubbles conveyed the frequency of co-occurrence. VOSviewer was employed to scrutinize keywords,



Graphic 1. İllustration of the yearly distribution of publication frequency

co-authorship patterns, and instances of co-occurrence.

Results

A cumulative total of 56,530 journal publications were sourced from the WoS database. Particularly notable is the upward trend in article counts, especially evident post-2000s. Graphic 1 illustrates the distribution of publication years across this dataset.

The publication years are listed in Table 1.

The majority of articles pertained to Pharmacology Pharmacy (26.673%), Oncology (12.301%), and Neurosciences (8.785%). Table 2 displays the distribution of publications across various research areas.

The United States of America (USA) led in terms of the highest number of articles published (n = 20389; 36.068%), followed by China (n = 5434; 9.613%) and England (n = 4594; 8.127%). Table 3 presents a detailed listing of the publications by country.

The primary affiliations included the University of California System (USA) (2.959%), Harvard University (USA) (2.117%), and the University of London (England) (1.951%). The majority of these affiliations were based in the USA, as detailed in Table 4.

Elsevier (21.304%), Wiley (12.068%), and Springer Nature (10.713%) were the leading publishers. Publishers are **listed in** Table 5.

The majority of articles were disseminated through Cancer Research (1.564%), Abstracts of Papers of the American Chemical Society (1.127%), and Clinical Pharmacology Therapeutics (0.814%). Additional journals featuring prominently in publishing articles on the subject are detailed in Table 6.

Most of the articles were written in the English (97.371%), other languages were German (0.922%), and French (0.435%). The other languages are **listed in** Table 7.

Most of the publications' Web of Science Indexes were Science Citation Index Expanded (90.692%), Conference Proceedings Citation Index Science (15.894%) and Social Sciences Citation Index (8.100%). The other Web of Science Indexes on the topic are **listed in** Table 8.

Discussion

Bibliometric studies are carried out to evaluate scientific improvements in certain fields. Using this method, the countries where studies are conducted and the indexed journals or languages can be evaluated. Recently, there has been a large increase in the number of bibliometric analyzes (1, 12-15). Bibliometric analyzes can be performed not only using the databases of previous publications, but also based on the data chosen by the researchers themselves. Despite there are many bibliometric studies on AD in the literature, bibliometric analysis of publications on Alzheimer's Disease Treatments has not been published so far (16). The bibliometric research on Alzheimer's Disease Treatments was conducted for the first time in this study. Bibliometric software such as Gephi, Leximancer and VOSviewer analyze data practically, therefore, there has been a great deal of interest in bibliometric analyzes recently. For the same reasons, we planned to use the Wos database in our current study, and we used VOSviewer for visualization. The search language that we used was English.

The current study will provide a comprehensive view of AD research and will be a promising area of research for its treatment. According to our bibliometric analysis results, the frequency of publications by years, it has been found that the number of articles published in recent years, especially after 2000, has been increasing, which indicates that more researchers are starting to research on Treatments of Alzheimer's Disease in comparison to the previous years. When analyzed by field of study, we can find that most of the articles are in Pharmacology Pharmacy, followed by Oncology and Neurosciences. Those are the departments that deal with the treatment of neurodegenerative diseases and have therapeutic approaches (16-19).

When analyzed by country and university, the data reveals that the United States of America (USA) leads in the number of articles published, with China and England following in succession. In

Table 1: List of publication years of articles on Alzheimer's Disease Treatments

Publication Years	Record Count	% of 56.530
2022	3919	6.933
2023	3705	6.554
2021	3636	6.432
2020	3366	5.954
2019	3203	5.666
2018	2962	5.240
2017	2863	5.065
2016	2809	4.969
2015	2668	4.720
2014	2522	4.461
2013	2350	4.157
2012	2192	3.878
2011	2024	3.580
2010	1954	3.457
2009	1762	3.117
2008	1705	3.016
2007	1481	2.620
2006	1462	2.586
2004	1349	2.386
2005	1271	2.248
2003	1010	1.787
2002	993	1.757
2001	643	1.137
2000	560	0.991
1998	518	0.916

* Showing 25 out of 44 entries

terms of University, University of California and Harvard University from USA take place at the top of the list followed by University of London, England. The counts of articles on Alzheimer's Disease Treatments which listed above show that the journals of Cancer Research and Abstracts of Papers of The American Chemical Society have contributed greatly to research in this area. The journals of Cancer Research have the most publications in this field because of the cancer-related pathology of Alzheimer's disease (20-22). The Abstracts of Papers of The American Chemical Society is the second one, most likely, because of research on the chemical properties of substances used for therapeutic purposes on AD and examining the structures and activities of these substances are important (23, 24). When analyzed by languages, publications were mostly in English (97.268%). In addition, German, French, Japanese, Spanish, Russian, Chinese, Portuguese, Polish, Czech and Turkish were the 10 most preferred languages, respectively. The most Web of Science Indexes was Science Citation Index Expanded (SCI-EXPANDED) (90.692%) followed by Conference Proceedings Citation Index Science (CPCI-S) and Social Sciences Citation Index (SSCI). In conclusion, bibliometric evaluation of Alzheimer's Disease Treatments was performed for the first time in this study. Countries such as the United States (USA), England and China, which have the highest number of studies and published articles, have made great contribution to this field. Institutes located in these countries such as University of California and University of London, which is also are on top of affiliations list should develop scientific research networks with each other to increase research with interdisciplinary teams.

The current bibliometric study shows that research mostly emphasizes the importance of early diagnosis, multimodal therapeutic approaches, and multi-targeted interventions with different drug classes for AD treatment.(25, 26).

Table 2: Publication Categories

Research Areas	Record Count	% of 56.530
Pharmacology Pharmacy	15078	26.673
Oncology	6954	12.301
Neurosciences	4966	8.785
Clinical Neurology	4637	8.203
Biochemistry Molecular Biology	3755	6.642
Psychiatry	3510	6.209
Chemistry Multidisciplinary Medicinal	2986	5.282
Chemistry Medicinal	2943	5.206
Medicine Research Experimental	2451	4.336
Medicine General Internal	1962	3.471

**Showing 10 out of 234 entries*

Table 3: List of countries with more than 10 documents

Countries/Regions	Record Count	% of 56.530
The USA	20389	36.068
Peoples Republic of China	5434	9.613
England	4594	8.127
Germany	3879	6.862
Japan	2960	5.236
Italy	2753	4.870
India	2680	4.741
Canada	2241	3.964
France	2197	3.886
AustralİIa	1640	2.901
Netherlands	1639	2.899
Spain	1600	2.830
Switzerland	1528	2.703
Sweden	1190	2.105
South Korea	1068	1.889
Belgium	1039	1.838
Brazil	920	1.627
Denmark	717	1.268
Poland	658	1.164
Iran	599	1.060
Austria	572	1.012
Scotland	553	0.978

Showing 22 entries with ≥10 documents

Although several studies have been conducted for the treatment of AD, its diagnostic and therapeutic potential in relation to the gut microbiota has not been fully addressed. More studies could be conducts on the potential therapeutic effects of probiotics and diets, thus offering new perspectives on the treatment of this progressive disease.

Limitations: Several limitations were implemented in this study, such as the publications which were not examine and analyze articles in the WOS indexes were not indexed. Also, the keywords were only in English and these words were not found in articles in other languages. The study excluded databases like Scopus and solely relied on VOSviewer for conducting analyses. Content analysis was

Table 4: List of the top affiliations

Affiliations, Country	Record Count	% of 56.530
University Of California System, USA	1673	2.959
Harvard University, USA	1197	2.117
University Of London, England	1103	1.951
University Of Texas System, USA	902	1.596
Pfizer, USA	899	1.590
National Institutes Of Health, USA	890	1.574
Harvard Medical School, USA	699	1.237
Novartis, Switzerland	691	1.222
Institut National De La Sante Et De La Recherche Medicale Inserm, France	688	1.217
Food Drug Administration FDA, USA	676	1.196

10 entries from a total of 25,641 were displayed; within these records, 3,496 entries (6.184%) were found to lack data in the analyzed field

Table 5: List of Publishers

Publishers	Record Count	% of 56.530
Elsevier	12043	21.304
Wiley	6822	12.068
Springer Nature	6056	10.713
Taylor & Francis	2715	4.803
Lippincott Williams & Wilkins	2300	4.069
MDPI	1748	3.092
American Chemical Society	1668	2.951
Bentham Science	1534	2.714
Oxford Univ Press	1420	2.512
American Association Cancer Research	1334	2.360

Showing 10 out of 1.580 entries

Table 6: List of journals that published the greatest number of articles on Alzheimer's Disease Treatments

Publication Titles	Record Count	% of 56.530
Cancer Research	884	1.564
Abstracts Of Papers of The American Chemical Society	637	1.127
Clinical Pharmacology Therapeutics	460	0.814
Journal Of Clinical Oncology	436	0.771
Neurology	372	0.658
Blood	366	0.647
International Journal of Molecular Sciences	361	0.639
Drug Discovery Today	312	0.552
Value In Health	295	0.522
Annals Of Oncology	294	0.520
Current Pharmaceutical Design	289	0.511
European Neuropsychopharmacology	287	0.508
Neurobiology Of Aging	272	0.481
International Journal of Pharmaceutics	260	0.460
Journal Of Alzheimer's Disease	260	0.460
Journal Of the American Geriatrics Society	255	0.451
European Journal of Neurology	249	0.440

Showing 17 out of 7.476entries

Table 7: List of languages of articles on Alzheimer Disease Treatments

Languages	Record Count	% of 56.530
English	55044	97.371
German	521	0.922
French	246	0.435
Japanese	218	0.386
Spanish	149	0.264
Russian	114	0.202
Chinese	48	0.085
Portuguese	48	0.085
Polish	34	0.060
Czech	23	0.041
Turkish	19	0.034
Korean	17	0.030
Italian	12	0.021
Norwegian	11	0.019

Showing 14 out of 29 entries (least 10 publications)

Table 8: List of Web of Science Index of publications on Alzheimer's Disease Treatments

Web of Science Index	Record Count	% of 56.530
Science Citation Index Expanded (SCI-EXPANDED)	51268	90.692
Conference Proceedings Citation Index Science (CPCI-S)	8985	15.894
Social Sciences Citation Index (SSCI)	4579	8.100
Emerging Sources Citation Index (ESCI)	2579	4.562
Book Citation Index – Science (BKCI-S)	1172	2.073

Showing 5 out of 10 entries

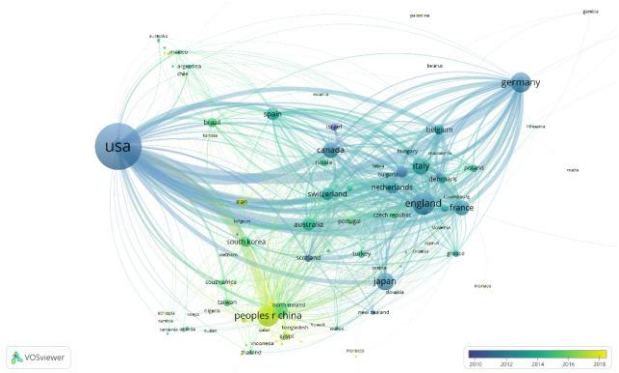


Fig. 1. The international collaboration network map

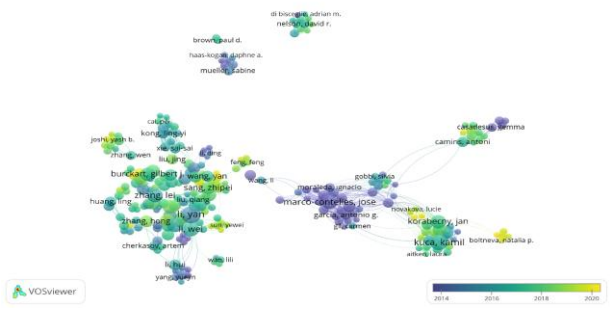


Fig. 2. On the map, authors who have amassed at least 5 publications and 100 citations are depicted. The connections between nations represent citations, with authors boasting larger circles or font sizes indicating a higher citation count

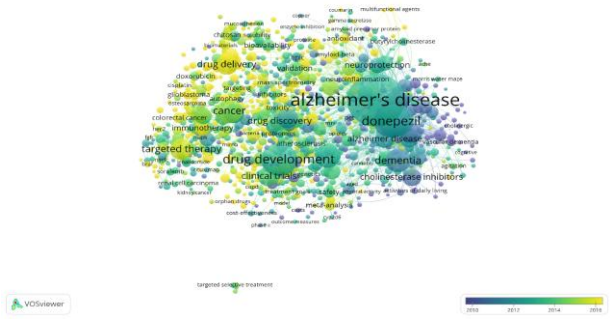


Fig. 3. The keyword visualization map displays articles with a minimum of 5 occurrences. Lines connecting keywords signify their occurrence relations within the articles, while keywords depicted with larger circle sizes or font sizes indicate a relatively higher occurrence frequency

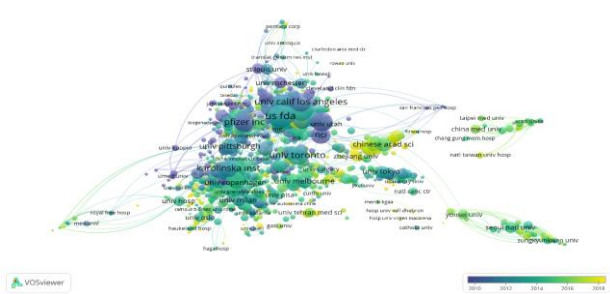


Fig. 4. The visualization map of citation networks among affiliations showcases those with a minimum of

5 publications. Lines connecting affiliations denote collaboration, with thicker lines indicating stronger cooperation. Affiliations represented by larger circles or text sizes demonstrate a higher degree of international collaboration

omitted. Future studies may incorporate more comprehensive comparative analyses.

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