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Original Article

Global characteristics and trends of presbycusis research from 2002 to 2021: a bibliometric study

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Abstract: Background and objective: Age-related hearing loss, also termed presbycusis, is the most prevalent sensory impairment in older adults. Presbycusis research has considerably advanced over the past few decades, however, comprehensive and objective reports on the current state of presbycusis research are lacking. We used bibliometric methods to objectively analyzed the progress of presbycusis research over the past 20 years and to identify the research hotspots and emerging trends in this field. Methods: Eligible literature metadata published between 2002 and 2021 were obtained from the Web of Science Core Collection on September 1, 2022. Bibliometric tools including CiteSpace, VOSviewer, Bibliometrix R Package, Microsoft Excel 2019, and an online bibliometric platform were used to conduct bibliometric and visualized analyses. Results: A total of 1,693 publications related to presbycusis were retrieved. The number of publications increased continuously from 2002 to 2021, and the USA occupied the lead position in the field, with the highest research output. The most productive and influential institution, author, and journal were the University of California, Frisina DR of the University of South Florida, and Hearing Research, respectively. Co-citation cluster and trend topics analyses revealed that "cochlear synaptopathy", "oxidative stress", and "dementia" were the predominant foci of presbycusis research. Burst detection of keywords indicated that "auditory cortex" and "Alzheimer's disease" were the newly-emerged aspects. Conclusion: During the past two decades, presbycusis research has been flourishing. The current research foci are "cochlear synaptopathy", "oxidative stress", and "dementia". "Auditory cortex" and "Alzheimer's disease" may be potential future directions in this field. This bibliometric analysis represents the first quantitative overview of presbycusis research, thus providing valuable references and insights for scholars, medical practitioners, and policymakers concerned with this field.

Keywords: Presbycusis, age-related hearing loss, trend, bibliometric analysis, visual analysis

Introduction

Presbycusis, or age-related hearing loss (ARHL), is a multifactorial disorder that manifests as progressive, bilateral, and symmetrical hearing impairment occurring with age [1]. In a currently aging society, the prevalence of presbycusis increases continuously, and approximately one-third of the global population aged older than 65 years suffer from hearing loss, according to the World Health Organization [2]. Approximately 900 million older adults are predicted to suffer significant hearing impairment due to presbycusis by 2050 [3]. In addition, growing evidence suggests that presbycusis is strongly associated with frailty [4], depression [5], social isolation [6], cognitive decline [7], and even dementia [8]. Furthermore, presbycusis entails a considerable economic burden, with medical expenditures estimated to reach 30 billion USD in the USA by 2030 [9]. Globally, ARHL is becoming a major public health burden, and further insights into its pathogenesis and novel avenues of effective therapeutic intervention are urgently required.

The pathophysiology of presbycusis is associated with complex interactions between genetic and environmental factors [10]. In addition to biological age, underlying risk factors for presbycusis include gender, genetic predisposition, environmental exposure (e.g., ototoxic drugs, cigarette consumption, noise), lifestyle (e.g., diet, smoking, drinking), and comorbidities

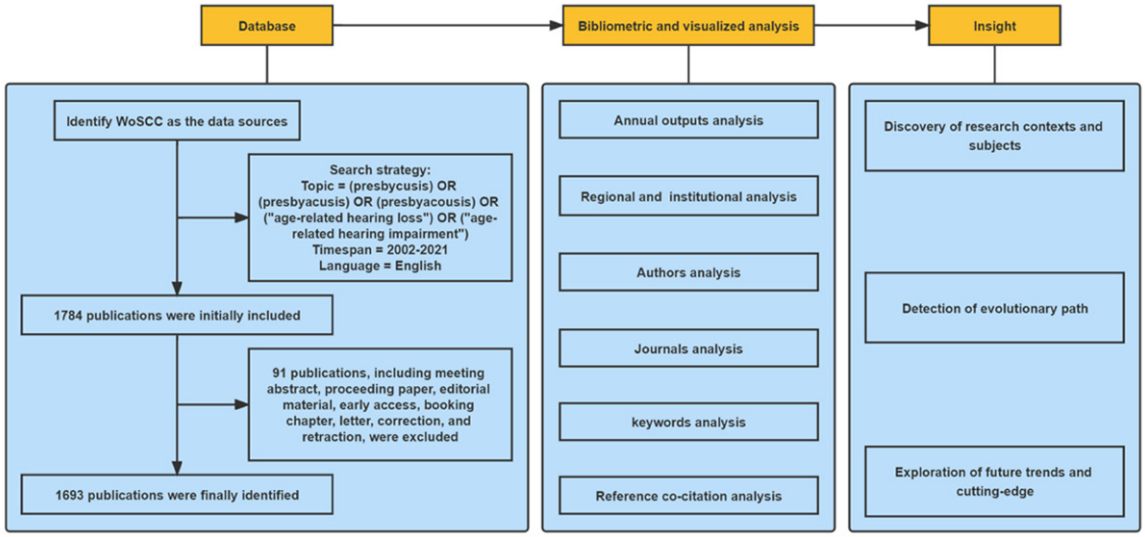


Figure 1. Flow chart for inclusion in literature screening.

(e.g., diabetes, hypertension) [11-13]. Hearing aids are an effective treatment modality at present, however, presbycusis frequently remains undertreated [14]. Despite this, the field of presbycusis research has considerably advanced in the past two decades [15]. Therefore, a comprehensive overview of the current state of presbycusis research is warranted, considering that a deeper understanding of potential directions may help develop new therapeutic strategies for this disease.

Bibliometrics is a commonly recognized method to quantitatively analyze scientific publications and assess research activities in a specific field over time [16]. As a critical analytic model, bibliometric analysis can rapidly provide an in-depth evaluation of the knowledge domain, research hotspot evolvement, and future directions in a given area [17]. These advantages are not available through other methods such as traditional reviews, meta-analyses, and evidence mapping. Previous bibliometric studies examined hereditary hearing impairment [18], noise-induced hearing loss [19], and deafness genes [20]. So far, however, no bibliometric studies on presbycusis are available. Owing to this knowledge gap, we attempted to elucidate the scientific development, past and current research hotspots, and emerging thematic areas of presbycusis research in order to provide guidance for future work.

Materials and methods

Data sources and search strategies

The Web of Science Core Collection (WoSCC) database is the world's leading citation-based database covering a broad range of research types, and it is commonly used for bibliometric analyses [21]. Literature metadata for this study were retrieved from the Science Citation Index-Expanded (SCI-E) and the Social Sciences Citation Index (SSCI) of the WoSCC. The following search strategy was used: topic = (presbycusis) OR (presbyacusis) OR (presbyacousis) OR ("age-related hearing loss") OR ("age-related hearing impairment") and timespan = 2002-2021. The search was restricted to articles and reviews using the respective filters, and only publications in English language were considered. To reduce bias resulting from frequent database updates, all literature retrieval and data downloads were completed on September 1, 2022. The literature search and screening process is illustrated in **Figure 1**.

Bibliometric analysis and visualization

Bibliometric and visual analyses were conducted using CiteSpace (version 5.8.R3), VOSviewer (version 1.6.16), the R package Bibliometrix (version 3.2.1), Microsoft Excel 2019, and an online bibliometric platform (https://bibliometric.com). The main advantage of VOSviewer is the feasibility to develop visual network maps

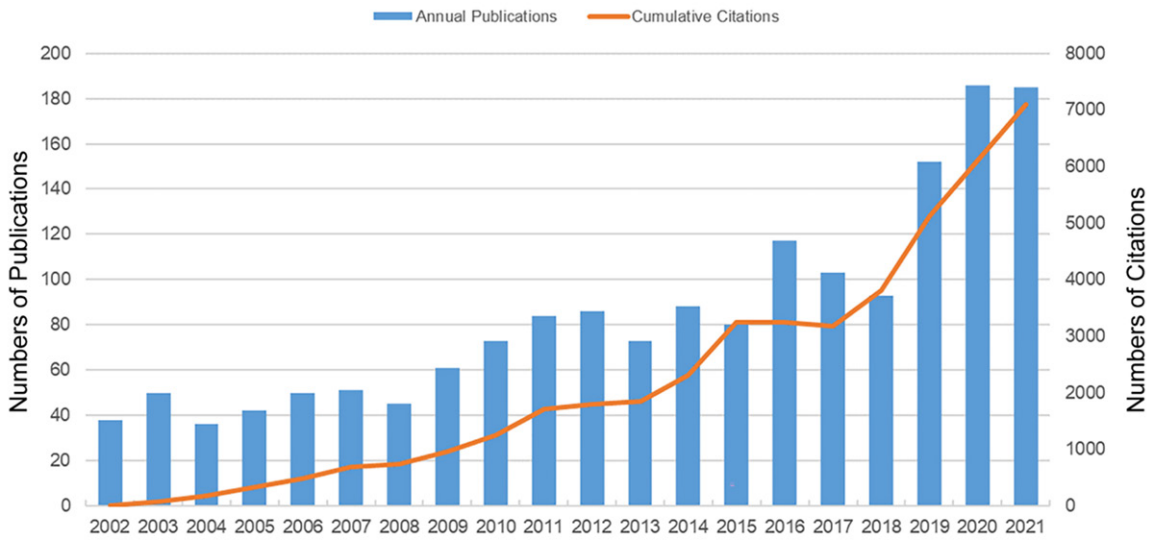


Figure 2. The distribution of annual publications and citations on presbycusis research.

based on bibliometric networks to achieve an in-depth and comprehensive understanding of the structural evolution of research domains. Here, we used VOSviewer (version 1.6.16) to build the keyword co-occurrence and cluster map based on text data.

CiteSpace [22] is a java-based software for visualizing and constructing bibliometric networks. This interactive analysis tool combines data-mining algorithms and bibliometrics, facilitating the visualization of results through scientific mapping. In this study, we visualized co-occurrences of institutions, journal dual-maps, keyword bursts, citation bursts, co-citation relationship of authors and references, and co-citation reference timeline using CiteSpace. In the respective plots, the size of the circles indicates the number of publications within a collaborative network, and the distance between circles indicates the degree of collaboration between institutions. In the co-citation analysis, node size indicates citation frequency. The lines connecting the nodes indicate co-citation associations. Line thickness indicates the strength of linkages. The warmer the color of the nodes, the more recent the publication date of the documents is.

VOSviewer, a further software tool for bibliometric mapping analysis, facilitates the creation and visualization of knowledge structures, which is particularly useful for intuitively visualizing large-scale data [23]. This tool was used to construct visualization networks of author co-authorship and keyword co-occurrence. Generally, the size of nodes in these visual maps corresponds to the number of item occurrences. The links between nodes indicate the co-occurrence or co-authorship relationships between nodes. Different colored nodes and lines represent average appearance years or different clusters.

Bibliometrix is an R language package for comprehensive bibliometric analysis and visual presentation of bibliographic data [24]. We used Bibliometrix to analyze the annual production of authors, trend topics and thematic map. In addition, a publication and collaboration analysis of countries was conducted using the online bibliometric platform (https://bibliometric.com). Microsoft Excel 2019 was used to present efferocytosis publication trends.

Results

Publication activity and citation analysis

In the time period from 2002 to 2021, 1,693 papers on presbycusis research were published. The number of publications related to presbycusis has been increasing (**Figure 2**), regardless of some fluctuations. Additionally, over the past 20 years, the annual frequency of citations in this field has generally increased (**Figure 2**). The annual number of publications and cumulative citation frequency per year

Table 1. Ranking of top-10 countries that have published the most articles from 2002 to 2021

Rank	Article counts	Centrality score	Country
1	712	0.20	USA
2	211	0.10	China
3	121	0.00	Japan
4	113	0.36	Germany
5	99	0.00	UK
6	75	0.10	Australia
7	74	0.31	Italy
8	74	0.20	Netherlands
9	70	0.00	South Korea
10	61	0.10	France

peaked at 186 publications and 7,106 cumulative citations in 2020 and 2021, respectively.

Contributions by country/region and institution

A total of 65 countries/regions and 1,608 institutions worldwide contributed to the 1,693 papers. The USA was the most productive country (n = 712), followed by China (n = 211), Japan (n = 121), Germany (n = 113), and the UK (n = 99) (**Table 1**). The annual contributions of papers related to presbycusis in the top-10 most productive countries are shown in **Figure 3A**. **Figure 3B** shows the global distribution of presbycusis research. Over 40% of presbycusis research published worldwide originated from the USA, rendering the country a global leader in this area. The centrality score is a key indicator to quantitatively evaluate the significance of nodes in a network [16], and cooperation frequency is positively correlated with centrality in a collaborative network. Germany (n = 0.36) ranked highest with regard to the centrality score. **Figure 3C** shows cooperation networks across countries/regions.

An overview of the top 10 most productive institutions is provided in **Table 2**. The five most prolific institutions were the University of California (n = 72), Johns Hopkins University (n = 49), the Medical University of South Carolina (n = 45), the Huazhong University of Science Technology (n = 44), and the State University System of Florida (n = 44). Johns Hopkins University (n = 0.23) ranked highest with regard to centrality. In general, many institutions cooperated actively in this field, including the University of California, the University of Wisconsin, and the Huazhong University of Science Technology (**Figure 3D**). Nine of the top ten institutions were in the USA.

Authors and co-cited authors

A total of 5,916 authors contributed to the identified studies. **Table 3** shows the top 10 most prolific authors. Frisina DR of the University of South Florida was the most productive author, with 33 publications, followed by Van Camp G of the University of Antwerp (n = 31), and Dubno JR of the Medical University of South Carolina (n = 26). Regarding total citations, Van Camp G ranked first with 1,692, followed by Mitchell P (n = 1,504), and Frisina DR (n = 1,453). Assessment of the influence of authors based on the numbers of publications, citations, and H-index demonstrated that these authors were the most influential scholars in presbycusis research. The annual output of the top 20 authors between 2002 and 2021 is shown in **Figure 4A**. We identified eleven different clusters of authors (**Figure 4B**). The typical active collaborations occurred within the same clusters, such as that between Dubno JR and Gates GA, Frisina DR and Johnson KR, and Someya S and Ding DL. Furthermore, we observed active cooperation among the clusters, such as between Logroscino G and Lin FR, between Dubno JR and Cruickshanks KJ, and between Xiong H and Chen J.

Core journals and research areas

The 1,693 included papers were published in 741 academic journals. In **Table 4**, we present the characteristics of the top 10 most active journals in this field, which published 527 articles, accounting for 31.1% of all publications. *Hearing Research* published the most articles (n = 152), followed by *Neurobiology of Aging* (n = 53), *International Journal of Audiology* (n = 51), *Otology Neurotology* (n = 45), and *Acta Oto Laryngologica* (n = 41). The number of articles published per year in the top five journals increased markedly between 2002 and 2021 (**Figure 5A**). The most citations were achieved by papers published in *Hearing Research* (n = 5,526), *Jaro Journal of the Association for Research in Otolaryngology* (n = 1,593), and *Ear and Hearing* (n = 1,522). According to the number of publications, citations and the H-index, the most influential journal in this field

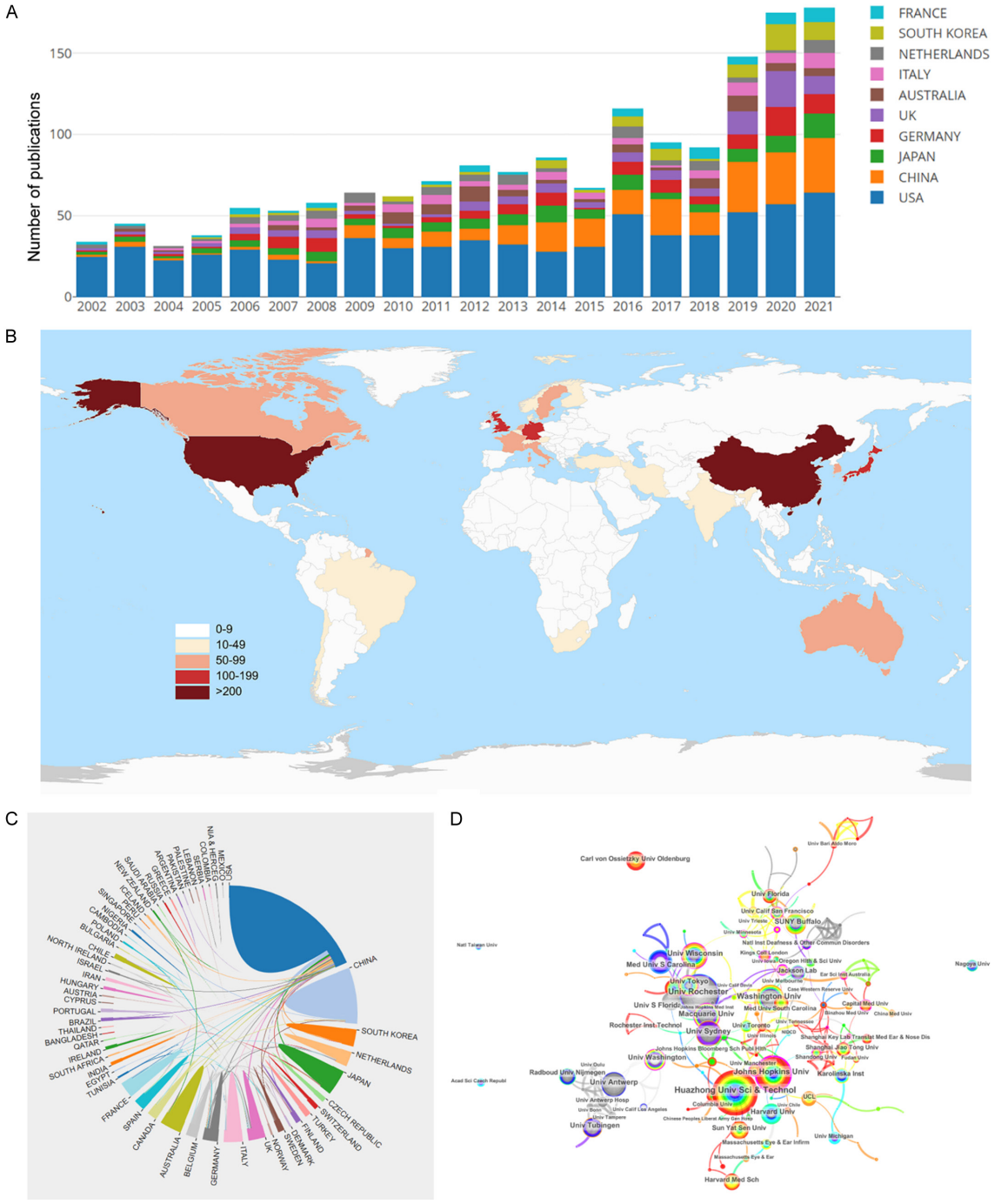


Figure 3. A. The annual distribution of publications on presbycusis among the top 10 countries from 2002 to 2021. B. World map displaying the global distribution of presbycusis research. C. The cross-country/region collaborations visualization map. D. The cross-institution collaborations visualization map.

was *Hearing Research*. These studies were further divided into different research fields, based on Web of Science subject categories. The top 10 research fields according to the number of publications are shown in **Figure 5B**.

A dual-map overlay of journals was produced to visualize the thematic distribution of academic journals. The left and right sides of the map show the citing and cited journals, respectively. There was only one primary citation path

Table 2. Ranking of top-10 institutions from 2002 to 2021

Rank	Article count	Institution	Country	Centrality score
1	72	University of California	USA	0.14
2	49	Johns Hopkins University	USA	0.23
3	45	Medical University of South Carolina	USA	0.01
4	44	Huazhong University of Science Technology	China	0.04
5	44	State University System of Florida	USA	0.01
6	43	Harvard University	USA	0.04
7	41	University of Rochester	USA	0.02
8	38	State University of New York	USA	0.00
9	37	National Institutes of Health	USA	0.00
10	37	University of Wisconsin	USA	0.14

Table 3. Ranking of top-10 productive authors from 2002 to 2021

Rank	Author	Article count	Centrality score	Total number of citations	Average number of citations	H-index
1	Frisina DR	33	0.00	1453	44.03	24
2	Van Camp G	31	0.00	1692	54.58	22
3	Dubno JR	26	0.00	960	36.92	14
4	Zhu XX	25	0.00	814	32.56	18
5	Fransen E	24	0.00	1191	49.63	18
6	Huygen PLM	24	0.00	712	29.67	13
7	Kong WJ	24	0.00	649	27.04	16
9	Van Laer L	22	0.00	1373	62.41	17
10	Mitchell P	22	0.00	1504	68.36	21

(**Figure 5C**), and studies published in molecular/biology/genetic journals were generally cited by molecular/biology/immunology journals.

Analysis of keywords

Keyword cluster analysis can provide insights into the knowledge domain of a research field. A total of 6,118 keywords were retrieved from the included publications, of which 144 occurred > 20 times. **Figure 6A** shows a visualization map of keyword co-occurrences, where node size indicates the frequency of occurrence. "Presbycusis" was the most frequent term (562 co-occurrences), followed by "age-related hearing loss" (352 co-occurrences) and "hearing loss" (297 co-occurrences). Here, three clusters were identified based on the link strength of keyword co-occurrence (**Figure 6A**). Cluster 1 (red) was primarily associated with pathogenic mechanisms of presbycusis and included "oxidative stress", "inner ear", and "cochlea". Cluster 2 (green) included "epidemiology", "hearing aids", and "people". Cluster 3 (blue) comprised "aging", "noise", "responses", "recognition", and "age-related changes". Different colors were assigned to keywords based on their average publication year in an overlay visualization (**Figure 6B**). The terms "gene", "susceptibility", "mouse", "inferior colliculus", and "product otoacoustic emissions" occurred during the early stages of the field. The most recently identified keywords included "hearing aids", "cochlear implantation", "auditory cortex", "memory", and "quality of life", which indicated that these fields were novel topics. We also visualized keyword frequencies in a density map (**Figure 6C**).

Burst detection of keywords can be used to determine a sudden increase in the frequency of keywords that occur within a certain time frame [17]. From 2002 to 2021, "presbyacusis" exhibited the most pronounced burst strength (22.08), followed by "deafness" (burst strength 16.30) and "cochlea" (burst strength 14.13) (**Figure 6D**). Moreover, "auditory cortex", "Al-

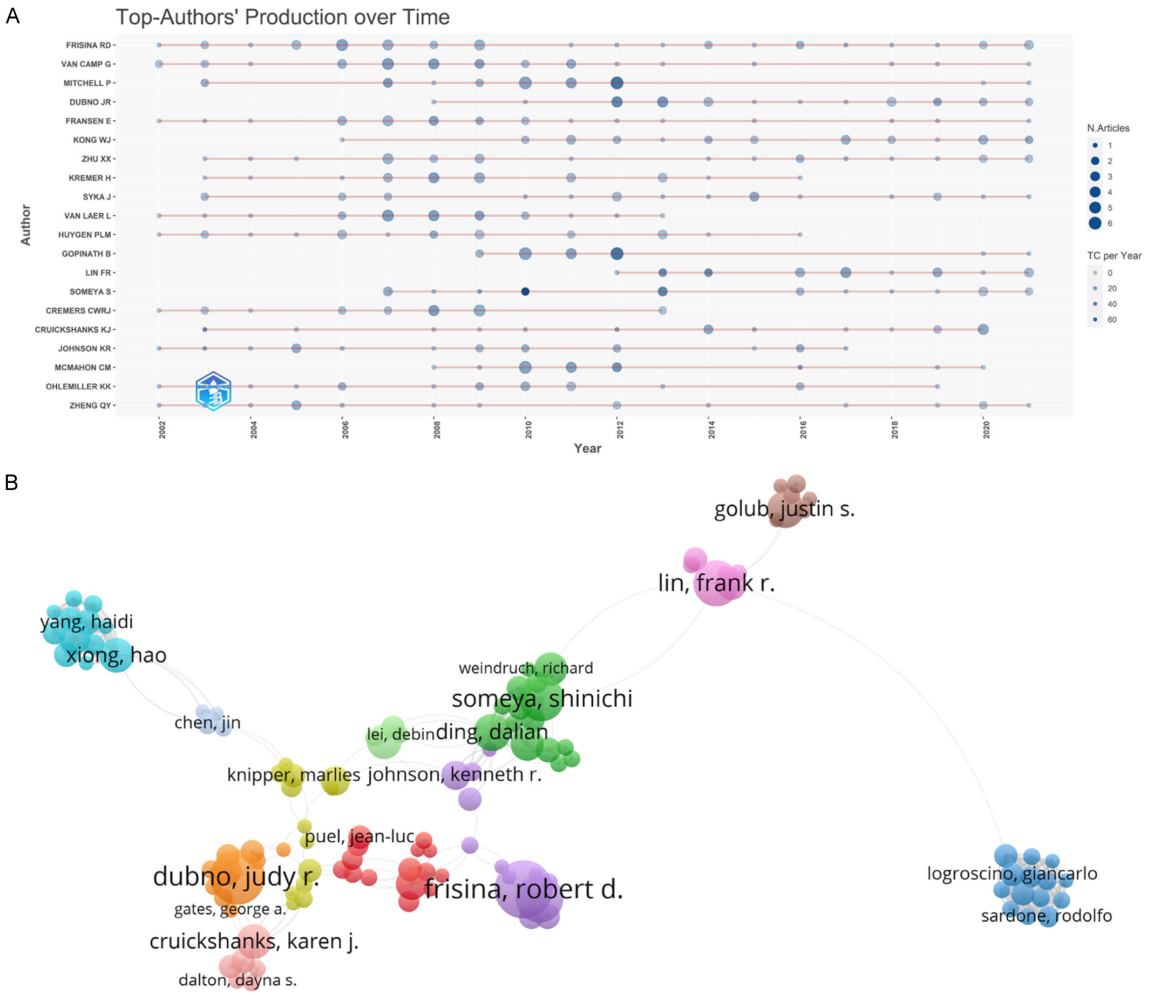


Figure 4. A. Timeline distribution of publications from the top 10 profile authors. B. The network visualization map of author collaborations analysis.

Table 4. Ranking of top-10 journals from 2002 to 2021

Rank	Journal	Article count	Journal citation reports (2021)	Impact factor (2021)	Total number of citations	Mean number of citations
1	*Hearing Research*	152	Q1	3.672	5526	36.36
2	*Neurobiology of Aging*	53	Q2	5.133	1448	27.32
3	*International Journal of Audiology*	51	Q2	2.437	1499	29.39
4	*Otology Neurotology*	45	Q2	2.619	1219	27.09
5	*Acta Oto Laryngologica*	41	Q4	1.698	757	18.46
6	*Jaro Journal of the Association for Research in Otolaryngology*	40	Q2	3.263	1593	39.83
7	*Ear and Hearing*	38	Q1	3.562	1522	40.05
8	*Frontiers in Aging Neuroscience*	37	Q1	5.702	598	16.16
9	*Laryngoscope*	35	Q2	2.97	952	27.2
10	*PLOS ONE*	35	Q2	3.752	596	17.03

zheimer's disease", "health", and "threshold" had bursts that lasted until 2021, reflecting the most recent research trends.

To thoroughly assess the current research trends, we used Bibliometrix to conduct trend topic and thematic map analyses. **Figure 7A**

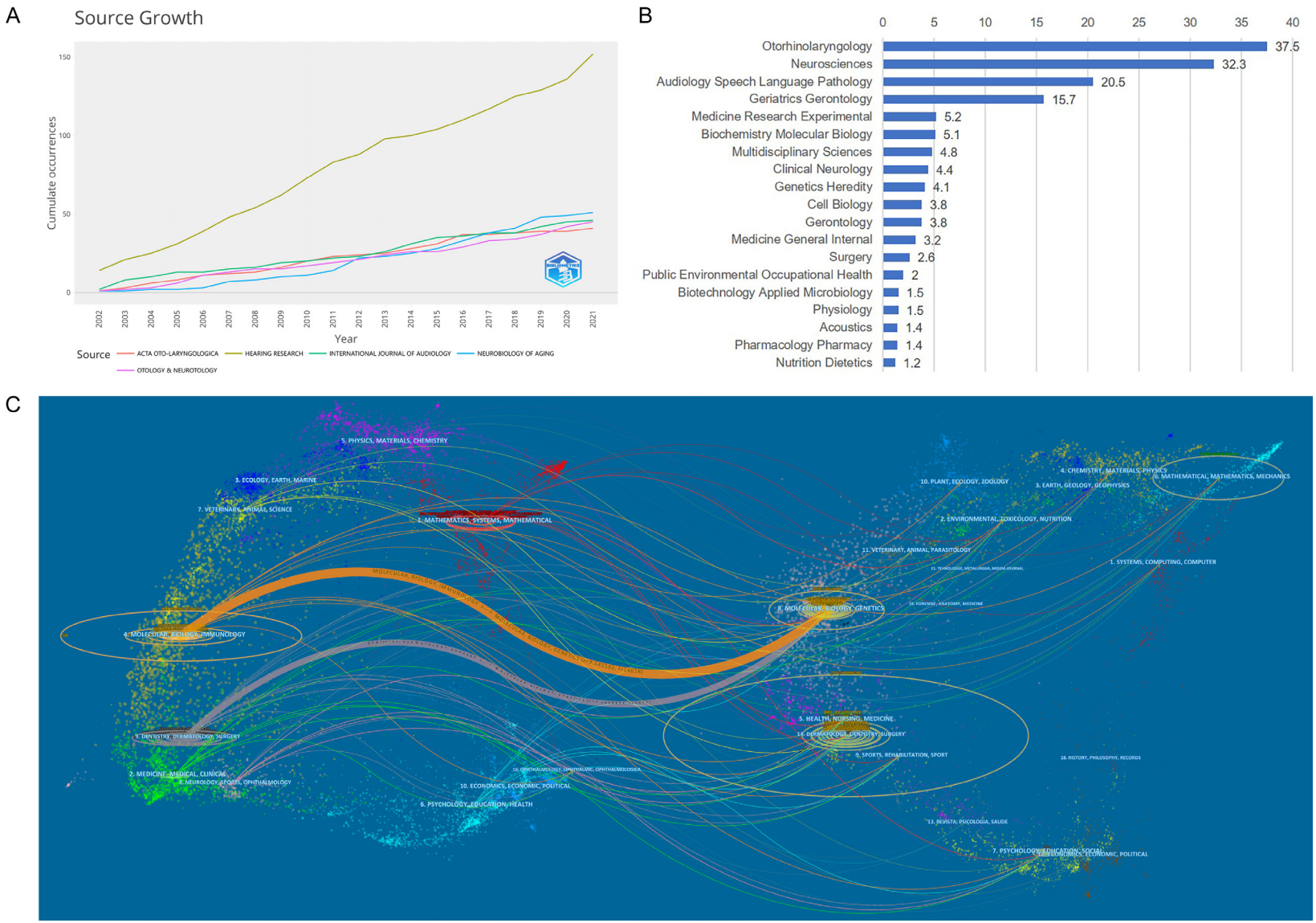


Figure 5. A. Cumulative publication trend of the top 5 prolific journals from 2002 to 2021. B. Top 20 WoS subject categories. C. The dual-map overlay of journals related to presbycusis.

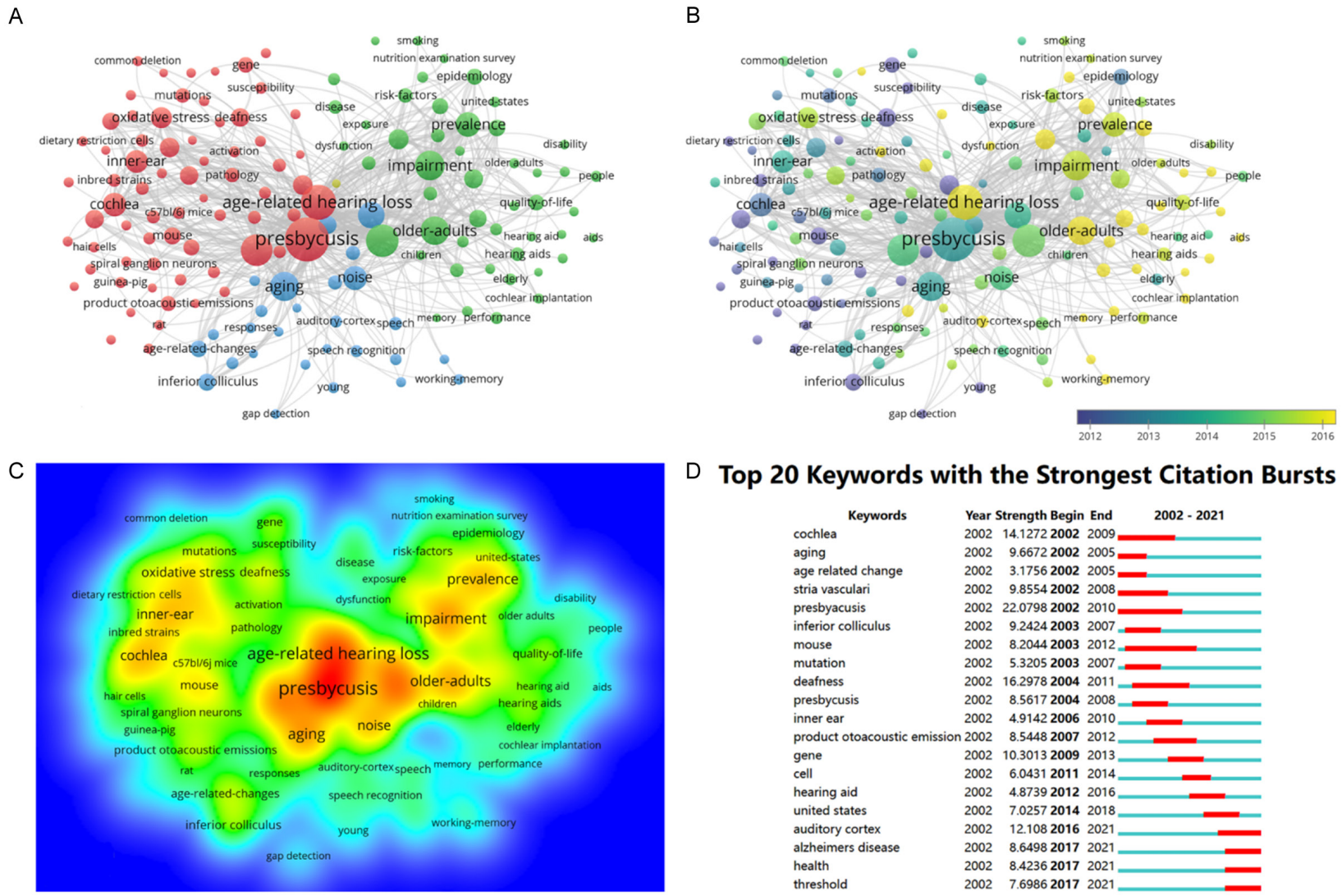


Figure 6. A. Clustering co-occurrence map of keywords. B. Distribution of keywords based on the average time of appearance. C. Keywords density visualization map. D. Top 20 keywords with the strongest citation bursts.

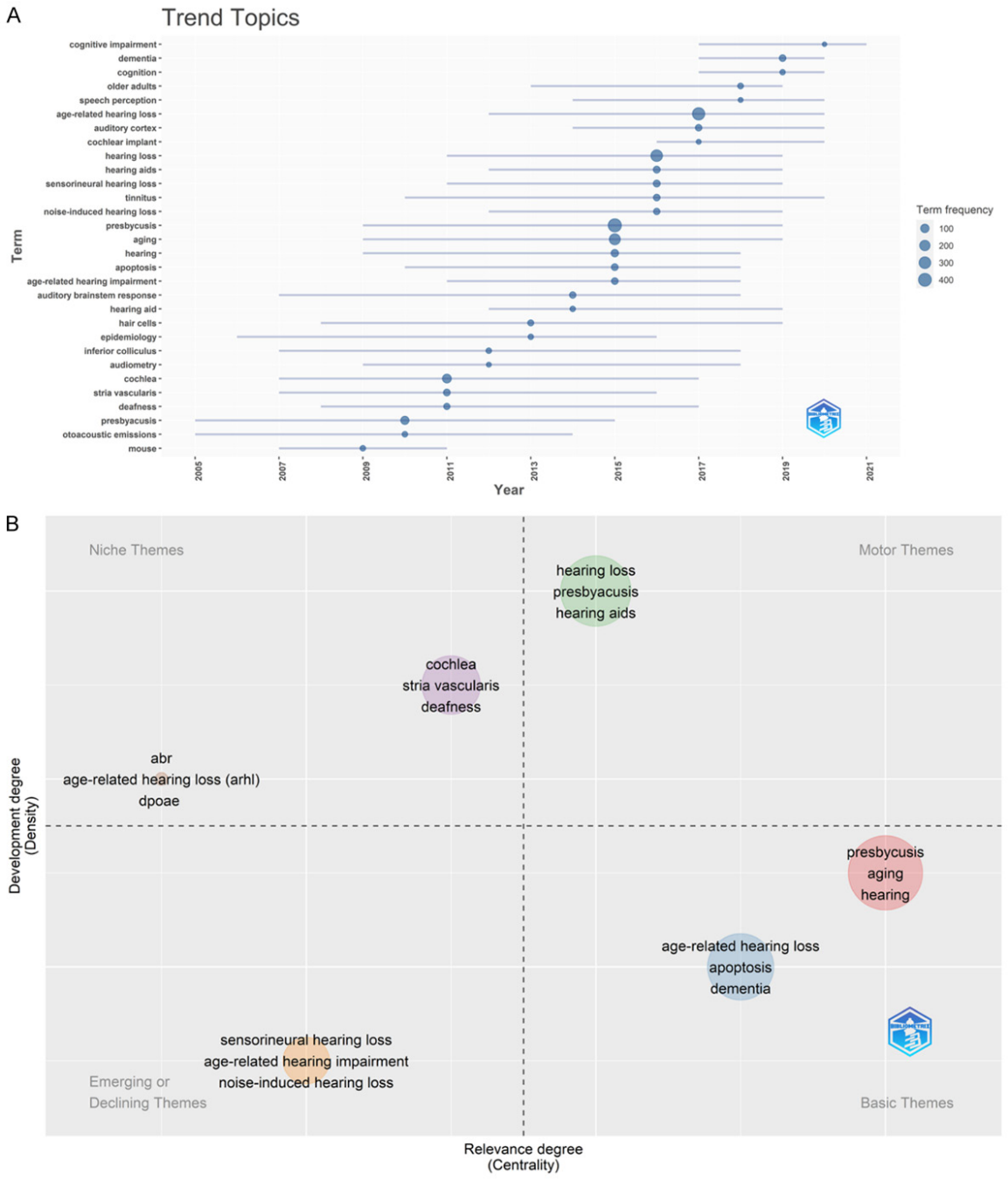


Figure 7. A. Trend topics map. B. The strategy map of identified topics clustered by keywords plus.

shows the buzz topics in presbycusis research. Recent research topics, particularly between 2019 and 2021, included "cognitive impairment", "dementia", and "cognition". According to the keywords thematic map (**Figure 7B**), "hearing loss", "presbyacusis", and "hearing aids" were motor theme (upper-right quadrant), which represents the important and well-developed themes of the presbycusis research field. The basic themes (lower-right quadrant) included "age-related hearing loss", "apoptosis", "dementia", "presbycusis", "aging", and "hearing". These aspects concern general topics that are transversal to different research areas of the field.

Analysis of co-cited references and reference bursts

Co-cited references refer to publications that are cited by one or more publications at the

Table 5. Top-10 most cited references from 2002 to 2021

Rank	Title	Author	Year	Journal	Citation frequency
1	Sirt3 Mediates Reduction of Oxidative Damage and Prevention of Age-Related Hearing Loss under Caloric Restriction	Someya S	2005	*Cell*	822
2	Presbycusis	Gates GA	2005	*The Lancet*	702
3	The impact of hearing loss on quality of life in older adults	Dalton DS	2003	*Gerontologist*	662
4	Acceleration of age-related hearing loss by early noise exposure: Evidence of a misspent youth	Kujawa SG	2006	*Journal of Neuroscience*	427
5	Synaptopathy in the noise-exposed and aging cochlea: Primary neural degeneration in acquired sensorineural hearing loss	Kujawa SG	2015	*Hearing Research*	384
6	Cadherin 23 is a component of the tip link in hair-cell stereocilia	Siemens J	2004	*Nature*	327
7	Association of cadherin 23 with polygenic inheritance and genetic modification of sensorineural hearing loss	Noben-Trauth K	2003	*Nature Genetics*	323
8	Hearing impairment and health-related quality of life: The Blue Mountains Hearing Study	Chia EM	2007	*Ear and Hearing*	310
9	Current concepts in age-related hearing loss: Epidemiology and mechanistic pathways	Yamasoba T	2013	*Hearing Research*	299
10	Association of Age-Related Hearing Loss With Cognitive Function, Cognitive Impairment, and Dementia A Systematic Review and Meta-analysis	Loughrey DG	2018	*JAMA Otolaryngology-Head & Neck Surgery*	293

same time, representing the knowledge bases of a particular field [18]. **Table 5** presents the top 10 cited articles. Among them, eight publications were cited > 300 times. The paper published by Someya et al. [23] in *Cell* (n = 822) was the most frequently cited, followed by the studies of Gates et al. [24] in *The Lancet* (n = 702) and of Dalton et al. [25] in *The Gerontologist* (n = 662). **Figure 8A** shows a references co-citation network map created through the CiteSpace analysis including 45,869 cited references from 1,693 articles, with 160 nodes and 253 links (**Figure 8A**). Links between nodes indicate how frequently the same article was cited. The node diameter is proportional to the frequency with which the cited reference is cited. **Figure 8B** presents the 12 largest clusters of the reference co-citation network. The largest cluster was "spiral limbus" (#0), followed by "cochlear synaptopathy" (#1), "oxidative stress" (#2), "dementia", and "age-related hearing impairment". A timeline of the 12 clusters is shown in **Figure 8C**. The recent hotspots of presbycusis research were "cochlear synaptopathy", "oxidative stress", and "dementia".

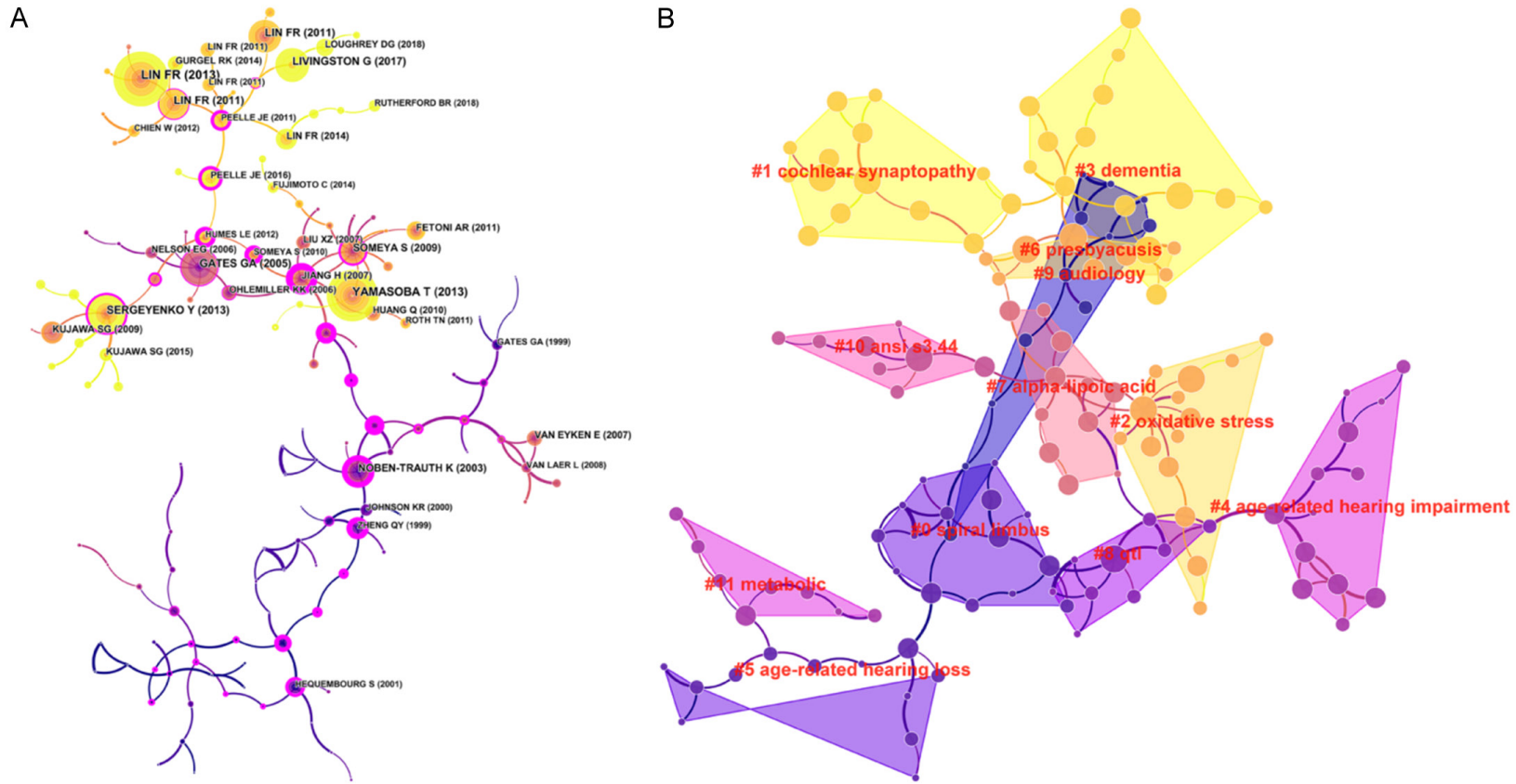
Citation bursts refers to references that frequently occur during a particular period and attract more attention from scholars in a particular area [21]. **Figure 9** displays the top 20 references with the strongest citation bursts. The earliest citation bursts of co-cited references began in 2002, and all three respective studies explored the molecular mechanisms of hearing loss on mouse models. The publications with the strongest burst (28.43), titled "Hearing loss and cognitive decline in older adults", by Lin et al. [25] was published in *JAMA Internal Medicine* in 2013. Additionally, three references produced a citation burst that lasted until 2021.

Discussion

General information

A total of 5,916 authors from 1,608 institutions in 65 countries/regions published 1,693 articles related to presbycusis in 376 academic journals between 2002 and 2021, according to the WoSCC database. During the past two decades, the production of publications on presbycusis has continuously increased. The number of publications related to presbycusis represented over 40% of the total output during 2017-2021, suggesting a rapid development in this field. Furthermore, the overall increasing trend of publications in this field suggests that this is an area of growing interest.

Visual analysis of contributions by country/region revealed that the USA dominated this field. A total of 712 papers originated from the USA, representing 42.1% of all respective publi-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#8 gti
#11 metabolic
#5 age-related hearing loss

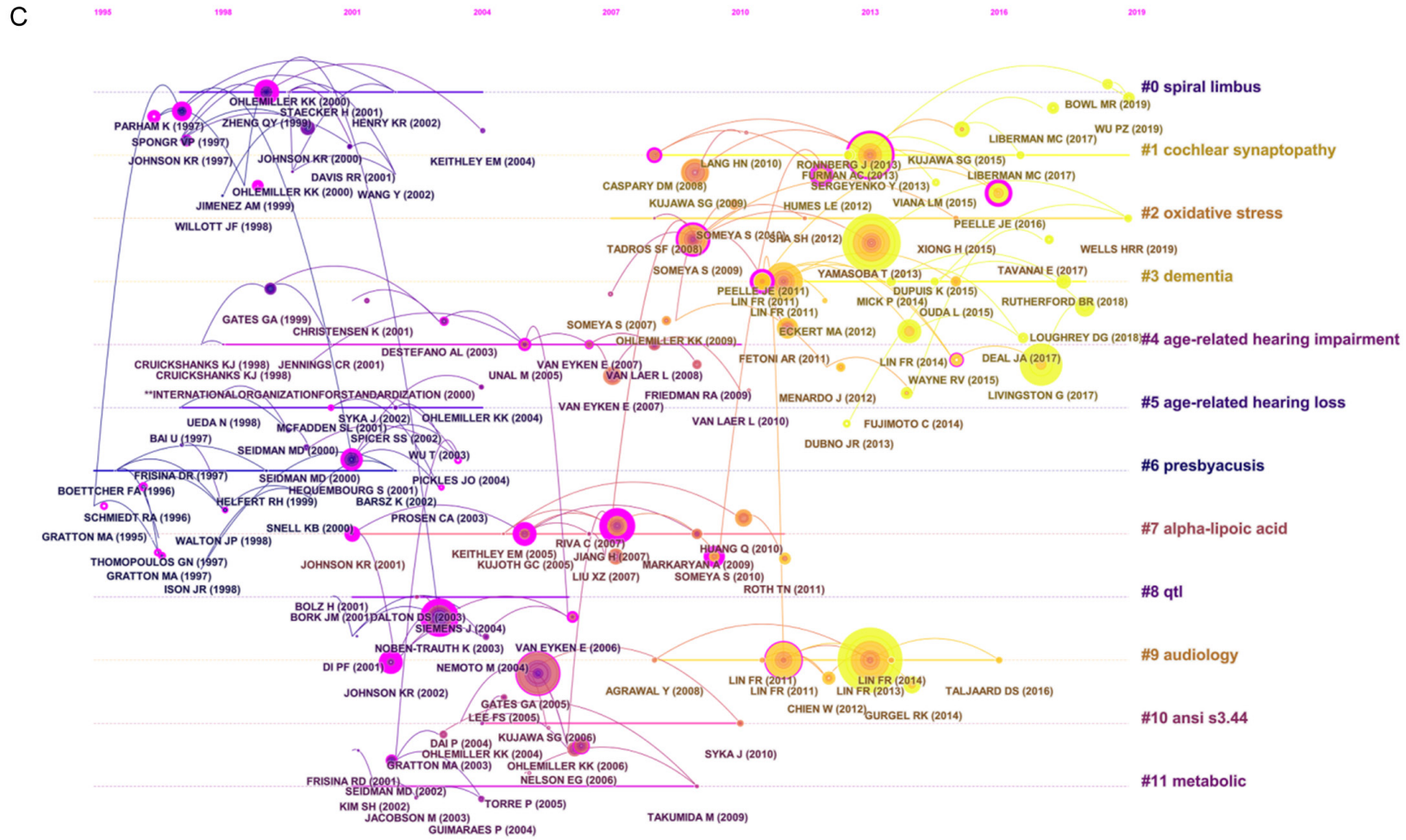

Figure 8. A. Co-citation map of references on presbycusis. B. The clustered network map of co-cited references on presbycusis. C. The timeline view of co-citation clusters.

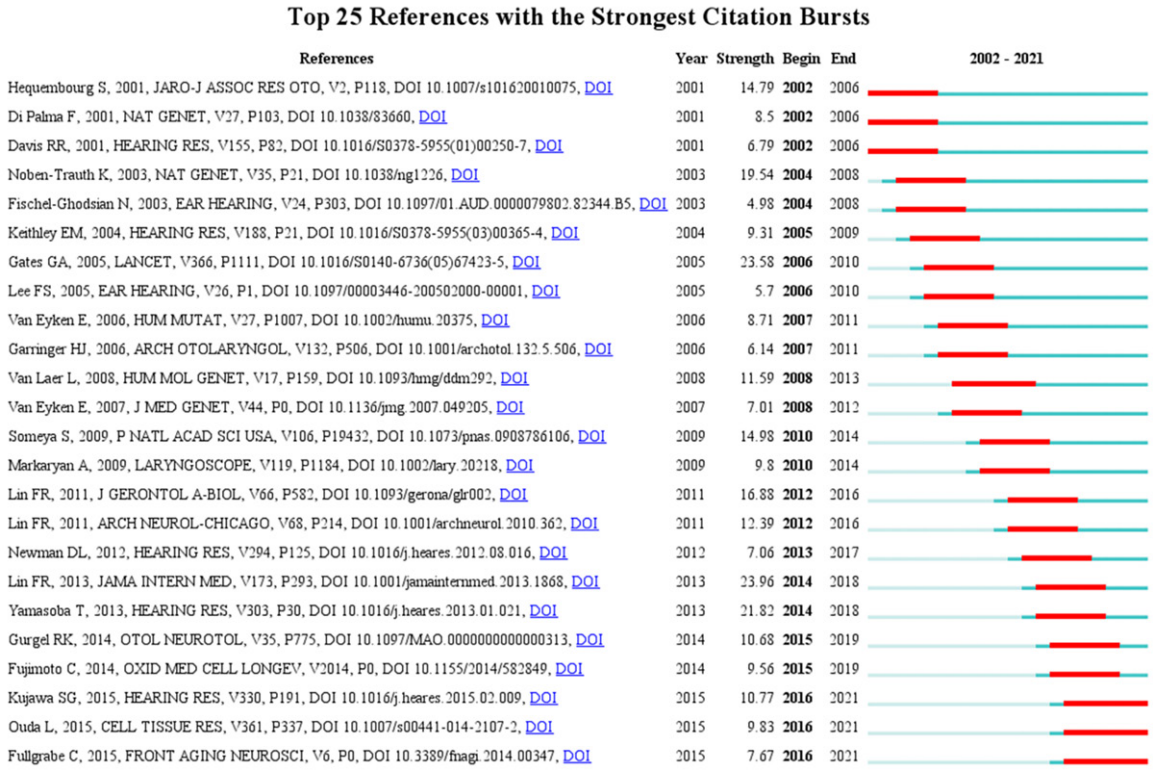

Figure 9. Top 25 references with the strongest citation bursts on presbycusis research between 2002 and 2021.

cations. It is worth noting that the vast majority of the top 10 prolific countries are developed countries. This may be attributed to the level of economic development and financial investment in scientific research by these countries. Among the top 10 countries, the USA (0.20) did not produce the highest centrality scores. Rather, Germany had a maximum centrality score of 0.36, followed by Italy (0.31), indicating that they had a crucial role in fostering international cooperation on presbycusis research.

Among the top 10 institutions, nine were located in the USA, whereas one was located in China, indicating a distinct advantage of the USA in the field. The University of California was the most productive institution. As illustrated in the collaboration network map, while many institutions were active in collaboration, some were not. It is therefore recommended that countries and institutions engaged in this field promote cooperation and collaborate to develop and expand this area.

Scholars may benefit from identifying the contributions of leading authors in a particular field to progress along the path and provide guidance [21]. Researchers such as Frisina DR, Van Camp G, and Dubno JR have made outstanding contributions to this field through the quality and the large number of their publications. It is thus likely that these scholars and their research groups will publish impactful papers on presbycusis in the future. Further, these leading researchers are also ideal candidates for collaboration and academic exchange. However, the network density showed a lack of active collaboration among top authors.

Analyses of journals revealed that Hearing Research was the most influential journal in the field, with the highest number of publications and citations. Overall, the top 10 journals on presbycusis research were primarily in the fields of audiology, otorhinolaryngology, and neurosciences. This suggests that presbycusis is a major concern for audiologists, otolaryngologists and neurologists worldwide. In addition, we also found that the top 10 co-cited studies were published in highly influential academic journals such as *Nature*, *Cell*, and *The Lancet*.

Knowledge base

The evolution of references with citation bursts may reflect dynamic changes in a given field [16]. The strongest citation burst was produced by the article of Lin et al. [25] (23.96, 2014-2018). This observational prospective study was the first to report hearing loss as an independent risk factor for incident cognitive impairment and accelerated cognitive decline among older people. It is worth noting that the citation burst of three papers is currently ongoing. The study by Kujawa and Liberman [26] published in *Hearing Research* (10.77, 2016-2021) showed that the degeneration of cochlear synapses occurred before threshold elevation and hair cell loss in ARHL. Ouda et al. [27] (9.83, 2016-2021) comprehensively reviewed major age-related changes occurring in the central part of the auditory system, and they suggested that primary neural degeneration exerts important effects on sensorineural hearing loss. The results of Füllgrabe et al. [28] (7.67, 2016-2021) showed that age-related changes in audiometric sensitivity were unrelated to decreased speech perception ability in older adults.

A collection of co-cited references can partially represent a knowledge base [17]. Cluster analysis of the reference co-citation network revealed that recent presbycusis studies mainly focused on “cochlear synaptopathy”, “oxidative stress”, and “dementia”.

Recent evidence shows that hearing loss may also occur without loss of hair cells through a pathology phenomenon termed “cochlear synaptopathy” (CS), in which hair cell abundance remains unchanged but cochlear neuronal synapses between auditory nerve fibers and inner hair cells decrease [29]. Animal and human studies confirm that CS is the earliest contributor to presbycusis. A study on guinea pigs and mice demonstrated that decreased numbers of cochlear synapses precede threshold elevation and hair cell loss in ARHL [26]. Furthermore, the number of spiral ganglion cells in the human temporal bone has been observed to decrease with aging despite normal hair cell abundance [30]. In fact, elderly people with presbycusis frequently suffer from impaired speech perception, especially under challenging listening conditions, even when auditory thresholds are normal [12]. Noise exposure is known to cause CS and, ultimately, neuronal degeneration; however, the lack of sensitivity of standard audiological tests complicates the assessment of CS in humans [31]. Therefore, the general understanding of the individual and combined effects of CS on human presbycusis should be improved through behavioral and objective tests.

The results of numerous studies implicate oxidative stress in the pathogenesis of presbycusis [32-34]. Oxidative stress impairs the peripheral and central auditory systems in animal models of ARHL. Excessive levels of free radicals and oxidative damage were observed in the cochlea, stria vascularis, spiral ganglion neurons, cochlear nucleus, inferior colliculus, and auditory cortex [32]. Antioxidant supplements have been shown to be effective in preventing or decelerating ARHL in most animal studies [34]. In aging rats, the administration of antioxidants such as vitamins A, C, and E, alpha-lipoic acid, acetyl-L-carnitine, and melatonin increased hearing sensitivity and reduced hair cell loss [34]. In addition, an antioxidant-enriched diet delayed the progression of ARHL in mice and dogs [35]. However, few studies on antioxidant therapy for presbycusis in humans are available, and their results are contrary. A three-year double-blind randomized placebo-controlled trial conducted by Durga et al. [36] showed that hearing loss at speech frequencies in elderly persons with ARHL was decelerated following folic acid supplementation. Polanski et al. [37] evaluated the therapeutic effects of various antioxidants treatment schemes on presbycusis, including papaverine chlorhydrate plus vitamin E, α-lipoic acid plus vitamin C, and ginkgo biloba dry extract. The results showed that six months of treatment with antioxidants did not improve the hearing threshold in patients with presbycusis.

Dementia is a common form of cognitive disorder in older adults and represents a global health challenge [38]. Numerous epidemiological and laboratory studies showed that presbycusis is strongly associated with dementia [7, 8, 39]. A case-control study by Uhlmann et al. [40] published in the 1980s reported a link between hearing impairment and dementia, which was the first paper on this topic. Their results demonstrated that in cases with Alzheimer’s-type dementia, the prevalence of hearing loss of 30 dB or greater was twice as high as that in the controls. Further, hearing

loss was independently and significantly correlated with cognitive dysfunction severity. Similar results were observed in subsequent studies. ARHL was considered the most promising modifiable risk factors for dementia [41]. It was estimated that up to 9% of dementia cases could be prevented by addressing midlife hearing loss [38]. Recent national longitudinal studies have shown that hearing aids may decelerate the cognitive decline and reduced dementia onset in older adults [42, 43]. Currently, several plausible hypotheses have been proposed to explain the hearing-cognition relationship. First, an uneven reallocation of neural resources and depletion of cognitive reserve in individuals with ARHL was observed, which may result in the clinical presentation of dementia [44]. In addition, it was proposed that ARHL puts older adults at increased risk for social isolation, which may in turn lead to dementia [44]. A further hypothesis is that ARHL may alter the structure and function of the brain, thereby increasing the risk of dementia. Compared to older adults with normal hearing, older adults with ARHL exhibit accelerated brain volume decline [45]. It should be emphasized that any causal association between ARHL and dementia must be thoroughly investigated before any definitive recommendations concerning treatment can be made.

Emerging topics

Presbycusis was conventionally attributed primarily to damage to the peripheral auditory system, particularly the structure and function of the cochlea [13]. Recently, however, pathophysiological alterations in the auditory cortex have been shown to play an important role in the pathogenesis of presbycusis [39]. Neuroimaging studies have shown that variations in the morphology of the auditory cortex are associated with presbycusis [46, 47]. Erick et al. [48] found that atrophy of the auditory cortex was closely associated with high-frequency hearing impairment in patients with presbycusis. An arterial spin labeling magnetic resonance imaging (MRI) study conducted by Ponticorvo et al. [49] showed that patients with presbycusis exhibited a significantly decreased cerebral blood flow to the right auditory cortex, which was negatively correlated with audiogram steepness. In addition, functional MRI research has shown that altered functional connectivity of the auditory cortex may cause cognitive dysfunction in patients with presbycusis [50]. Electrophysiological evidence from aged animals suggests the presence of increased spatial tuning and reduced temporal fidelity of responses in the auditory cortex [51]. Moreover, deficits in temporal and spatial processing may contribute to the predominant complaint of patients with presbycusis, i.e., the difficulty in understanding speech. Numerous molecular-level alterations in the auditory cortex have been identified in animal models of presbycusis. Youn et al. [52] found that mitophagy impairment in the auditory cortex was associated with presbycusis in mice. Cytosolic mtDNA in the auditory cortex may contribute to the pathogenesis of presbycusis through the activation of the cGAS-STING pathway, which elicits type I interferon and inflammatory responses in mice [53]. In addition, Li et al. [54] reported that compared to 3-month-old rats, 24-month-old rats exhibited significantly lower expression of G9a (a histone methyltransferase) in the auditory cortex, which was associated with hair cell loss and significant hearing threshold elevation. Thus, an in-depth exploration of the molecular mechanisms by which the auditory cortex contributes to age-related deafness will help identify improved therapeutic avenues.

Alzheimer's disease (AD) is the most common cause of dementia in the elderly population [55]. As discussed above, epidemiological studies have closely linked ARHL to AD [40]. This strong association has also been confirmed by a growing body of clinical and molecular evidence. A recent prospective cohort study showed that early ARHL was associated with a higher β-amyloid burden in patients with AD [56]. Xu et al. [57] reported a link between ARHL and the atrophy of entorhinal cortex and elevated cerebrospinal fluid tau levels, however, the nature of the association between these two diseases remains unclear. Patients with AD frequently exhibit hearing impairment at an early stage, however, hearing loss is considered to be an independent risk factor for AD [41]. A recent genetic driver analysis by Abidin et al. [58] showed that ARHL and AD were associated not through a shared genetic architecture but through a shared vulnerability in molecular pathways. In a recent review, Shen et al. [59] examined the molecular links between ARHL and AD and suggested that mitochondrial

dysfunction and alterations in some signaling pathways including the ROS/VEGF, SIRT1/PGC-1α (or FNDC5), and CaMKKβ/AMPK pathways, may be the key cause. Furthermore, shared metabolic dysregulation was proposed to contribute to the development of both diseases. Llano et al. [60] found that AD patients with hearing impairment exhibited significantly lower levels of serum phosphatidylcholine than AD patients without hearing impairment. In conclusion, the relationship between ARHL and AD requires further research.

Limitations

Due to the nature of bibliometrics, this study has several limitations. First, only studies from the WoSCC database were included, which may have resulted in bias and incompleteness. In addition, only articles and reviews in English language were included in the present study; thus, our findings may not be entirely comprehensive. Last, our search results may differ with regard to the current amount of literature available due to the continuous updating of WoSCC data. However, adjustments can be made to address these limitations in the future.

Conclusion

Over the past 20 years, presbycusis has received increasing research attention worldwide, as evidenced by the proliferation of publications in this field. The USA is predominant in presbycusis research. As research in this area has developed, several different topics have emerged. Recent research hotspots included “cochlear synaptopathy”, “oxidative stress”, and “dementia”, which constitute substantial research fields. “Auditory cortex” and “Alzheimer’s disease” are emerging as new research frontiers. In summary, this is the first bibliometric analysis to provide objective and systematic insights into presbycusis research, which will serve as a valuable guide for future research in this area.

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Disclosure of conflict of interest

None.

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References

[1] Gates GA and Mills JH. Presbycusis. Lancet 2005; 366: 1111-1120.
[2] Löhler J, Cebulla M, Shehata-Dieler W, Volkenstein S, Völter C and Walther LE. Hearing impairment in old age. Dtsch Arztebl Int 2019; 116: 301-310.
[3] Patel R and McKinnon BJ. Hearing loss in the elderly. Clin Geriatr Med 2018; 34: 163-174.
[4] Tian R, Almeida OP, Jayakody DMP and Ford AH. Association between hearing loss and frailty: a systematic review and meta-analysis. BMC Geriatr 2021; 21: 333.
[5] Rutherford BR, Brewster K, Golub JS, Kim AH and Roose SP. Sensation and psychiatry: linking age-related hearing loss to late-life depression and cognitive decline. Am J Psychiatry 2018; 175: 215-224.
[6] Mick P, Kawachi I and Lin FR. The association between hearing loss and social isolation in older adults. Otolaryngol Head Neck Surg 2014 150: 378-384.
[7] Slade K, Plack CJ and Nuttall HE. The Effects of age-related hearing loss on the brain and cognitive function. Trends Neurosci 2020; 43: 810-821.
[8] Chern A and Golub JS. Age-related hearing loss and dementia. Alzheimer Dis Assoc Disord 2019; 33: 285-290.
[9] Stucky SR, Wolf KE and Kuo T. The economic effect of age-related hearing loss: national, state, and local estimates, 2002 and 2030. J Am Geriatr Soc 2010; 58: 618-619.
[10] Elliott KL, Fritzsch B, Yamoah EN and Zine A. Age-related hearing loss: sensory and neural etiology and their interdependence. Front Aging Neurosci 2022; 14: 814528.
[11] Bowl MR and Dawson SJ. Age-related hearing loss. Cold Spring Harb Perspect Med 2019; 9: a033217.
[12] Tawfik KO, Klepper K, Saliba J and Friedman RA. Advances in understanding of presbycusis. J Neurosci Res 2020; 98: 1685-1697.

[13] Wang J and Puel JL. Presbycusis: an update on cochlear mechanisms and therapies. J Clin Med 2020; 9: 218.
[14] Eckert MA, Harris KC, Lang H, Lewis MA, Schmiedt RA, Schulte BA, Steel KP, Vaden KI Jr and Dubno JR. Translational and interdisciplinary insights into presbyacusis: a multidimensional disease. Hear Res 2021; 402: 108109.
[15] Chester J, Johnston E, Walker D, Jones M, Ionescu CM, Wagle SR, Kovacevic B, Brown D, Mikov M, Mooranian A and Al-Salami H. A review on recent advancement on age-related hearing loss: the applications of nanotechnology, drug pharmacology, and biotechnology. Pharmaceutics 2021; 13: 1041.
[16] Lei K, Wang X, Liu Y, Sun T and Xie W. Global research hotspots and trends of the Notch signaling pathway in the field of cancer: a bibliometric study. Am J Transl Res 2022; 14: 4918-4930.
[17] Cai M, Zhang Y, Chen S, Wu Z and Zhu L. The past, present, and future of research on neuroinflammation-induced mild cognitive impairment: a bibliometric analysis. Front Aging Neurosci 2022; 14: 968444.
[18] Tekin AM, Bahşi İ, Bayazit YA and Topsakal V. Global research on hereditary hearing impairment over the last 40 years: a bibliometric study. J Int Adv Otol 2021; 17: 482-491.
[19] Miao L, Ji J, Wan L, Zhang J, Yin L and Pu Y. An overview of research trends and genetic polymorphisms for noise-induced hearing loss from 2009 to 2018. Environ Sci Pollut Res Int 2019; 26: 34754-34774.
[20] Li L, Shi G, Yang Z and Shen Z. A bibliometric analysis of deafness gene literature from 2009 to 2018 based on web of science. J Int Adv Otol 2021; 17: 541-550.
[21] Zhou F, Zhang T, Jin Y, Ma Y, Xian Z, Zeng M and Yu G. Emerging trends and research foci in allergic rhinitis immunotherapy from 2002 to 2021: a bibliometric and visualized study. Am J Transl Res 2022; 14: 4457-4476.
[22] Synnestvedt MB, Chen C and Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. AMIA Annu Symp Proc 2005 2005: 724-728.
[23] van Eck NJ and Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics 2010; 84: 523-538.
[24] Aria M and Cuccurullo C. Bibliometrix: an R-tool for comprehensive science mapping analysis. J Informetrics 2017; 11: 959-975.
[25] Lin FR, Yaffe K, Xia J, Xue QL, Harris TB, Purchase-Helzner E, Satterfield S, Ayonayon HN, Ferrucci L and Simonsick EM; Health ABC Study Group. Hearing loss and cognitive decline in older adults. JAMA Intern Med 2013; 173: 293-299.
[26] Kujawa SG and Liberman MC. Synaptopathy in the noise-exposed and aging cochlea: primary neural degeneration in acquired sensorineural hearing loss. Hear Res 2015; 330: 191-199.
[27] Ouda L, Profant O and Syka J. Age-related changes in the central auditory system. Cell Tissue Res 2015; 361: 337-358.
[28] Füllgrabe C, Moore BC and Stone MA. Age-group differences in speech identification despite matched audiometrically normal hearing: contributions from auditory temporal processing and cognition. Front Aging Neurosci 2014; 6: 347.
[29] Parthasarathy A and Kujawa SG. Synaptopathy in the aging cochlea: characterizing early-neural deficits in auditory temporal envelope processing. J Neurosci 2018; 38: 7108-7119.
[30] Shehabi AM, Prendergast G and Plack CJ. The relative and combined effects of noise exposure and aging on auditory peripheral neural deafferentation: a narrative review. Front Aging Neurosci 2022; 14: 877588.
[31] Lokwani P and Prabhu P. Efficacy of behavioral audiological tests in identifying cochlear synaptopathy: a systematic review. Eur Arch Otorhinolaryngol 2022; 279: 577-594.
[32] Prasad KN and Bondy SC. Increased oxidative stress, inflammation, and glutamate: potential preventive and therapeutic targets for hearing disorders. Mech Ageing Dev 2020; 185: 111191.
[33] Alvarado JC, Fuentes-Santamaría V and Juiz JM. Frailty syndrome and oxidative stress as possible links between age-related hearing loss and Alzheimer's disease. Front Neurosci 2021; 15: 816300.
[34] Fujimoto C and Yamasoba T. Mitochondria-targeted antioxidants for treatment of hearing loss: a systematic review. Antioxidants (Basel) 2019; 8: 109.
[35] Tavanai E and Mohammadkhani G. Role of antioxidants in prevention of age-related hearing loss: a review of literature. Eur Arch Otorhinolaryngol 2017; 274: 1821-1834.
[36] Durga J, Verhoef P, Anteunis LJ, Schouten E and Kok FJ. Effects of folic acid supplementation on hearing in older adults: a randomized, controlled trial. Ann Intern Med 2007; 146: 1-9.
[37] Polanski JF and Cruz OL. Evaluation of antioxidant treatment in presbyacusis: prospective, placebo-controlled, double-blind, randomised trial. J Laryngol Otol 2013; 127: 134-141.
[38] Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, Ballard C, Banerjee S, Burns A, Cohen-Mansfield J, Cooper C, Fox N, Gitlin LN, Howard R, Kales HC, Larson EB, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L and Mukad-

am N. Dementia prevention, intervention, and care. Lancet 2017; 390: 2673-2734.
[39] Jayakody DMP, Friedland PL, Martins RN and Sohrabi HR. Impact of aging on the auditory system and related cognitive functions: a narrative review. Front Neurosci 2018; 12: 125.
[40] Uhlmann RF, Larson EB, Rees TS, Koepsell TD and Duckert LG. Relationship of hearing impairment to dementia and cognitive dysfunction in older adults. JAMA 1989; 261: 1916-1919.
[41] Ray M, Dening T and Crosbie B. Dementia and hearing loss: a narrative review. Maturitas 2019; 128: 64-69.
[42] Maharani A, Dawes P, Nazroo J, Tampubolon G and Pendleton N; SENSE-Cog WP1 group. Longitudinal relationship between hearing aid use and cognitive function in older Americans. J Am Geriatr Soc 2018; 66: 1130-1136.
[43] Strutt PA, Barnier AJ, Savage G, Picard G, Kochan NA, Sachdev P, Draper B and Brodaty H. Hearing loss, cognition, and risk of neurocognitive disorder: evidence from a longitudinal cohort study of older adult Australians. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2022; 29: 121-138.
[44] Uchida Y, Sugiura S, Nishita Y, Saji N, Sone M and Ueda H. Age-related hearing loss and cognitive decline - the potential mechanisms linking the two. Auris Nasus Larynx 2019; 46: 1-9.
[45] Johnson JCS, Marshall CR, Weil RS, Bamiou DE, Hardy CJD and Warren JD. Hearing and dementia: from ears to brain. Brain 2021; 144: 391-401.
[46] Lin FR, Ferrucci L, An Y, Goh JO, Doshi J, Metter EJ, Davatzikos C, Kraut MA and Resnick SM. Association of hearing impairment with brain volume changes in older adults. Neuroimage 2014; 90: 84-92.
[47] Eckert MA, Vaden KI Jr and Dubno JR. Age-related hearing loss associations with changes in brain morphology. Trends Hear 2019; 23: 2331216519857267.
[48] Eckert MA, Cute SL, Vaden KI Jr, Kuchinsky SE and Dubno JR. Auditory cortex signs of age-related hearing loss. J Assoc Res Otolaryngol 2012; 13: 703-713.
[49] Ponticorvo S, Manara R, Pfeuffer J, Cappiello A, Cuoco S, Pellecchia MT, Saponiero R, Troisi D, Cassandro C, John M, Scarpa A, Cassandro E, Di Salle F and Esposito F. Cortical pattern of reduced perfusion in hearing loss revealed by ASL-MRI. Hum Brain Mapp 2019; 40: 2475-2487.
[50] Fitzhugh MC, Hemesath A, Schaefer SY, Baxter LC and Rogalsky C. Functional connectivity of Heschl's gyrus associated with age-related hearing loss: a resting-state fMRI study. Front Psychol 2019; 10: 2485.
[51] Recanzone G. The effects of aging on auditory cortical function. Hear Res 2018; 366: 99-105.
[52] Youn CK, Jun Y, Jo ER and Cho SI. Age-related hearing loss in C57BL/6J mice is associated with mitophagy impairment in the central auditory system. Int J Mol Sci 2020; 21: 7202.
[53] Liu J, Chen H, Lin X, Yi J, Ye W, Wei F, Zhu X, Huang J and Su J. Age-related activation of cyclic GMP-AMP synthase-stimulator of interferon genes signaling in the auditory system is associated with presbycusis in C57BL/6J male mice. Neuroscience 2022; 481: 73-84.
[54] Li Q, Xiang YH, Liang XJ, Zhang Y, Zhao PP, Wang M, Bao XM, Zhu XB and Deng AC. Expression of G9a in auditory cortex is downregulated in a rat model of age-related hearing loss. J Mol Neurosci 2021; 71: 409-418.
[55] Pleen J and Townley R. Alzheimer's disease clinical trial update 2019-2021. J Neurol 2022; 269: 1038-1051.
[56] Golub JS, Sharma RK, Rippon BQ, Brickman AM and Luchsinger JA. The association between early age-related hearing loss and brain β-amyloid. Laryngoscope 2021; 131: 633-638.
[57] Xu W, Zhang C, Li JQ, Tan CC, Cao XP, Tan L and Yu JT; Alzheimer's Disease Neuroimaging Initiative 6. Age-related hearing loss accelerates cerebrospinal fluid tau levels and brain atrophy: a longitudinal study. Aging (Albany NY) 2019; 11: 3156-3169.
[58] Abidin FNZ, Wells HRR, Altmann A and Dawson SJ. Hearing difficulty is linked to Alzheimer's disease by common genetic vulnerability, not shared genetic architecture. NPJ Aging Mech Dis 2021; 7: 17.
[59] Shen Y, Ye B, Chen P, Wang Q, Fan C, Shu Y and Xiang M. Cognitive decline, dementia, Alzheimer's disease and presbycusis: examination of the possible molecular mechanism. Front Neurosci 2018; 12: 394.
[60] Llano DA, Issa LK, Devanarayan P, Devanarayan V; Alzheimer's Disease Neuroimaging Initiative (ADNI). Hearing loss in Alzheimer's disease is associated with altered serum lipidomic biomarker profiles. Cells 2020; 9: 2556.