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The 100 Most Cited Publications in Aging Research: A Bibliometric Analysis

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ABSTRACT

Aim: The basic aim of this analysis was to evaluate the 100 most cited publications in aging research.

Methods: On January 17, 2021 Web of Science Core Collection database was searched for aging research publications. The studied parameter includes; publication year, authorship, publication type, keywords, journal name, institution, country, and visualization mapping. HistCite™ application for citation analysis and VOSviewer software was used for visualization mapping.

Results: The top 100 most cited papers were published in 52 journals, authored by 537 authors. The most cited paper was "The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease," which received 6039 citations (2013 average citations per year). *Nature* was the most attractive journal (n=13). Aging was the most dominant used keyword. The maximum number of papers were published in 2005 (n=8). Harvard University was the leading institute (n=13), while the United States of America (USA) was the most productive country (n=76).

Conclusion: The highly cited papers were published in developed countries, and no study was published in low-income countries.

Keywords: aging or ageing, bibliometric analysis, VOSviewer

INTRODUCTION

Biological aging (evry living organism) involves a broad range of life changes that negatively impact all fundamental biological processes and ultimately lead to loss of organismal homeostasis and eventually death [1,2]. Human aging (related to human lives) annexes the macroscopic changes, including grinding of the skin, wrinkling, loss of muscle, and physical weakness. They are more vulnerable to a wide range of diseases when individuals get older. In particular, cardiac diseases, cancer, and stroke are the most common age-related disorders, including chronic lower respiratory disorders, type 2 diabetes, and neurodegeneration, representing the leading cause of death among the aged [1,3]. The burden of human aging in all nations worldwide is enormous social, medical, and economical. It is crucial and urgent to develop effective interventions to ensure healthy aging [4]. Age-dependent molecular damage accumulates lower DNA or protein stability, energy production, utilization failure, and homeostasis disruption leading to structural and functional decline. Mutations that offer an overall health benefit over a lifetime of the organism are also expected to increase the population frequency, although their phenotypic action in older ages is detrimental [1,2]. The evolutionary aging theory predicts that the average life span is higher in organisms where fertility increases with age, and the intrinsic rate of aging develops in response to extrinsic hazards [5].

Model organisms were used extensively to discover the retained aging pathways and assess interventions that improve longevity and aging. Laboratory mice, insects, and rats are commonly used in aging research in laboratory mice with strong genetic backgrounds, short life, ease of feeding, defined genetic manipulation, and environmental risks [4]. All living things age somehow, and it has proven surprisingly difficult to explain why despite years of research [6,7]. Why, for example, do our repair mechanisms appear to degrade with age, resulting in the loss of youth natural resilience to minor physical injury and physical stress [8]? The enzyme telomerase is a hot topic in ageing research at the moment, as it is responsible for maintaining the protective "seal" at the end of each chromosome [9]. Telomeres are the names given to these ends [10], and they prevent chromosomes from fusing and causing abnormalities and protecting the chromosome ends from being nibbled away by cell enzymes [7,10,11]. Chromosomes are extremely valuable and must last a lifetime

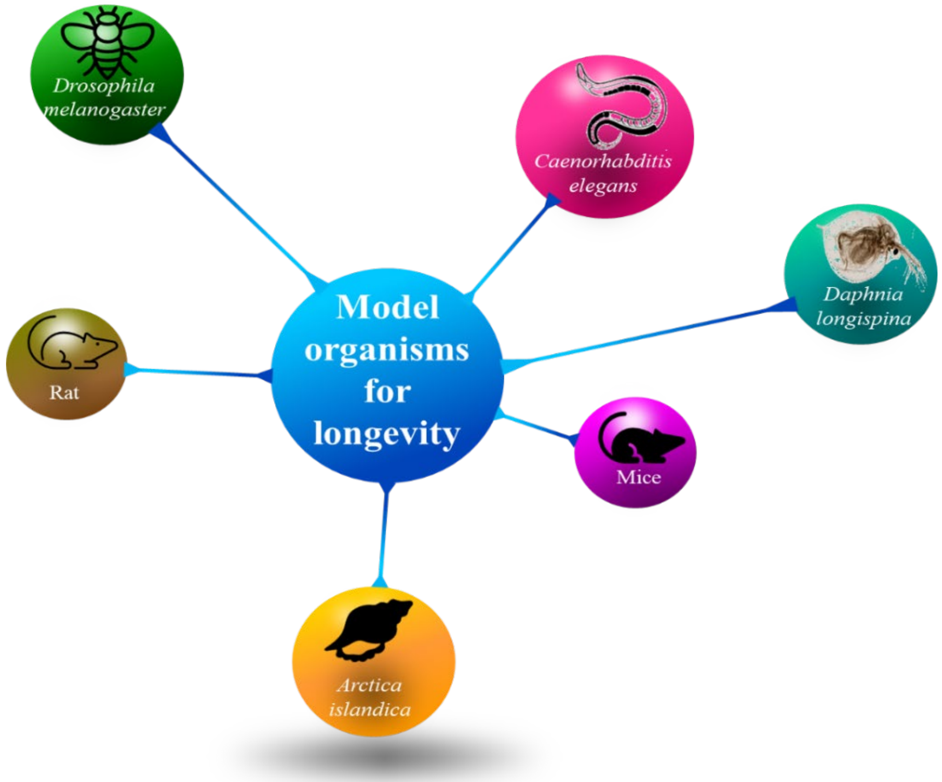

Figure 1. Model organisms for longevity research

[12]. They replicate themselves with each cell division, but this also means that any damage sustained during the division process is passed on to the new cells [13]. The lives of animals are limited from a few weeks (*Drosophila melanogaster*, *Caenorhabditis elegans*, and *Daphnia longispina*) to centuries (*Arctica islandica*) (**Figure 1**). Lifespan extension has been of interest for a long time, but longevity mechanisms remain mostly unknown. Invertebrates such as fruit flies or nematodes (fish and mice) with relatively short lifespans are excellent models to study longevity mechanisms. Interestingly, new animal models have been applied for longevity studies under technological developments such as Next-Generation sequencing (NGS) [14].

Bibliometrics analyses; a series of written publications, including journals, books, and scientific publications, using statistical and mathematical tools [15]. It evaluates quantitative research academic output and provides evidence of financing [16]. Bibliometric analysis provides insight into a subject, field, or discipline. It assesses authors, institutions, and countries performance by mapping the structure and dynamics of disciplines utilizing databases [17]. A map understands the information produced in a given field and helps develop public health policies by monitoring its development [15]. Social network analysis for scientific collaboration and co-citation relations is used in bibliometric studies [18]. The international citation indexes, Science Citation Index Expanded (SCI-E), Social Sciences Citation Index (SSCI), and Arts and science quote index are the most critical data sources (A & HCI). The Web of Science Core Collection (WoSCC) database provides access to these indexes [15,19-20]. Thus, the current study was conducted to identify and characterize the 100 most cited publications in aging research.

METHODS

On January 17, 2021 the WoSCC database was searched using the search keywords (“Aging” OR “Ageing”) in title field without restrictions. The 100 most cited papers were included based on the number of citations (**Figure 2**). The following data were extracted; year of publications, authors, type of publications, journals name, frequently used keywords, institutions, and countries. The data were exported in to HistCite™ and VOSviewer software for windows for citations count and network visualization mapping respectively. The retrieved data were plotted for co-authorship countries and, co-occurrence author keywords. In this study, no human or animal subjects were involved directly, therefore no ethical consideration was needed.

RESULTS

The top 100 most cited papers were published in 52 journals with 6716 cited references, 407 keywords, and 537 authors. Among them, 63 were research articles (15996 global citations), and 29 were reviews articles (53923 global citations) (**Table 1**). The most cited paper was “The diagnosis of dementia due to Alzheimer’s disease: Recommendations from the National Institute on Aging-Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease” published by McKhann et al. (2011) received 6039 citations (2013 average citations per year) [21] (**Table 2**). The most productive year was 2005 (n=8), while the most cited year was 2011 (n=20041 global citations), as shown in **Figure 3A** and **3B**, respectively. The leading country in aging research was the

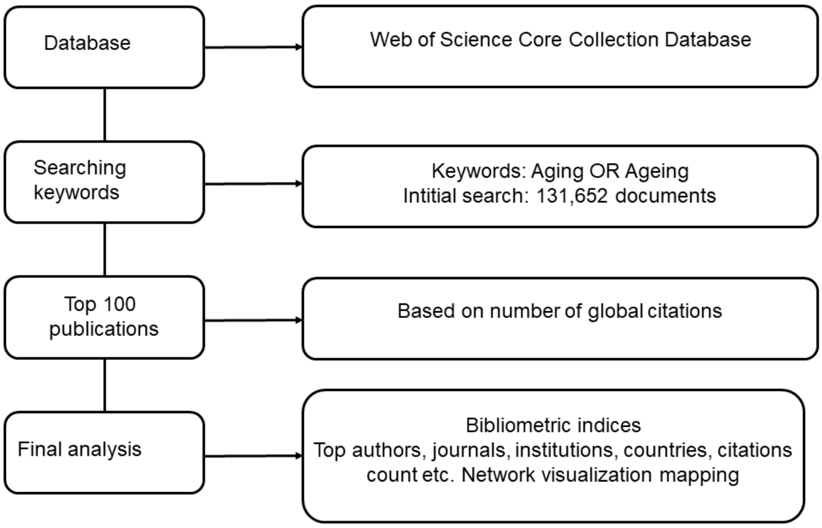

Figure 2. Flow chart of the included publications in final analysis

Table 1. Type of documents

Document Types	Number	Percent	LCS	GCS
Articles	63	63	96	115996
Reviews	29	29	29	53923
Proceedings Papers	4	4	1	5380
Book Chapters	3	3	2	4453
Notes	1	1	3	979

LCS: Total local citation score, GCS: Total global citation score

Table 2. Top 100 most cited studies in aging research

Rank	Study reference	Local citations	Per year	Global citations	Per year
1	McKhann GM, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers & Dementia. 2011 May; 7(3): 263-269.	4	1.33	6039	2013.00
2	Finkel T, Holbrook NJ. Oxidants, oxidative stress and the biology of ageing. Nature. 2000 NOV 9; 408(6809): 239-247.	1	0.07	6025	430.36
3	Harman D. Aging - a theory based on free-radical and radiation-chemistry. Journals of Gerontology. 1956; 11(3): 298-300.	8	0.14	5430	93.62
4	Dimri GP, et al. A biomarker that identifies senescent human-cells in culture and in aging skin in-vivo. Proceedings of The National Academy of Sciences of The United States of America. 1995 SEP 26; 92(20): 9363-9367.	6	0.32	4903	258.05
5	Hall EO. The Deformation and ageing of mild Steel .3. Discussion of results proceedings of the Physical Society of London Section B. 1951; 64(381): 747-753	0	0.00	4723	74.97
6	Ames BN, Shigenaga MK, Hagen TM. Oxidants, antioxidants, and the degenerative diseases of aging. Proceedings of the National Academy of Sciences of The United States of America. 1993 Sep 1; 90(17): 7915-7922	3	0.14	4638	220.86
7	Lopez-Otin C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging cell. 2013 Jun 6; 153(6): 1194-1217	0	0.00	4489	4489.00
8	Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers & Dementia. 2011 May; 7(3): 270-279	4	1.33	4338	1446.00
9	Harley CB, Futcher AB, Greider CW. Telomeres shorten during aging of human fibroblasts. Nature. 1990 May 31; 345(6274): 458-460	5	0.21	4142	172.58
10	Sperling RA, Aisen PS, Beckett LA, Bennett DA, Craft S, et al. Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease Alzheimers & Dementia. 2011 May; 7(3): 280-292	4	1.33	3335	1111.67
11	Good CD, Johnsrude IS, Ashburner J, Henson RNA, Friston KJ, et al. A voxel-based morphometric study of ageing in 465 normal adult human brains. Neuroimage. 2001 Jul; 14(1): 21-36	4	0.31	3296	253.54
12	Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, Mckinlay JB. Impotence and its medical and psychosocial correlates - Results of the Massachusetts male aging Study. Journal of Urology. 1994 Jan; 151(1): 54-61	1	0.05	3177	158.85
13	Beckman KB, Ames BN. The free radical theory of aging matures. Physiological Reviews. 1998 APR; 78(2): 547-581	2	0.13	2684	167.75
14	Zoncu R, Efeyan A, Sabatini DM. mTOR: from growth signal integration to cancer, diabetes and ageing. Nature Reviews Molecular Cell Biology. 2011 Jan; 12(1): 21-35	0	0.00	2640	880.00
15	Balaban RS, Nemoto S, Finkel T. Mitochondria, oxidants, and aging Cell. 2005 FEB 25; 120(4): 483-495	1	0.11	2630	292.22
16	Berlett BS, Stadtman ER. Protein oxidation in aging, disease, and oxidative stress. Journal of Biological Chemistry. 1997 Aug 15; 272(33): 20313-20316	1	0.06	2418	142.24
17	Greicius MD, Srivastava G, Reiss AL, Menon V. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: Evidence from functional MRI Proceedings of The National Academy of Sciences of The United States of America. 2004 Mar 30; 101(13): 4637-4642	0	0.00	2407	240.70
18	Sohal RS, Weindruch R. Oxidative stress, caloric restriction, and aging Science. 1996 Jul 5; 273(5271): 59-63	6	0.33	2318	128.78
19	Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR. Signal abnormalities at 1.5-T in Alzheimer dementia and normal aging. American Journal of Roentgenology. 1987 Aug; 149(2): 351-356	0	0.00	2292	84.89
20	Kuroo M, Matsumura Y, Aizawa H, Kawaguchi H, Suga T, et al. Mutation of the mouse klotho gene leads to a syndrome resembling ageing Nature. 1997 Nov 6; 390(6655): 45-51	1	0.06	2193	129.00
21	Fearnley JM, Lees AJ. Aging and Parkinsons-disease - Substantia-Nigra Regional Selectivity Brain. 1991 Oct; 114: 2283-2301.	0	0.00	2153	93.61
22	Wallace DC. A mitochondrial paradigm of metabolic and degenerative diseases, aging, and cancer: A dawn for evolutionary medicine. Annual Review of Genetics. 2005; 39: 359-407	2	0.22	2126	236.22

Table 2 (continued). Top 100 most cited pulications in aging research

Rank	Study reference	Local citations	Per year	Global citations	Per year
23	Brenner BM, Meyer TW, Hostetter TH. Dietary-protein intake and the progressive nature of kidney-disease - The role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, Renal Ablation, and Intrinsic Renal-Disease. New England Journal of Medicine. 1982; 307(11): 652-659	0	0.00	2101	65.66
24	Franceschi C, Bonafe M, Valensin S, Olivieri F, De Luca M, et al. Inflamm-aging - An evolutionary perspective on immunosenescence Molecular and Cellular Gerontology. 2000; 908: 244-254	1	0.07	2051	146.50
25	Ames BN, Cathcart R, Schwiers E, Hochstein P. Uric-acid provides an antioxidant defense in humans against oxidant-caused and radical-caused aging and cancer - A hypothesis. Proceedings of The National Academy of Sciences of The United States of America-Biological Sciences. 1981; 78(11): 6858-6862	1	0.03	2020	61.21
26	Cadenas E, Davies KJA. Mitochondrial free radical generation, oxidative stress, and aging. Free Radical Biology and Medicine. 2000 Aug; 29(3-4): 222-230	1	0.07	1933	138.07
27	Vetter J, Novak P, Wagner MR, Veit C, Moller KC, et al. Ageing mechanisms in lithium-ion batteries. Journal of Power Sources. 2005 Sep 9; 147(1-2): 269-281	0	0.00	1915	212.78
28	Rowe JW, Kahn RL. Successful aging. Gerontologist. 1997 AUG; 37(4): 433-440	0	0.00	1808	106.35
29	Fries JF. Aging, natural death, and the compression of morbidity. New England Journal of Medicine. 1980; 303(3): 130-135	2	0.06	1788	52.59
30	Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. Lancet. 2009 Oct 3; 374(9696): 1196-1208	0	0.00	1771	354.20
31	Wardlaw JM, Smith EE, Biessels GJ, Cordonnier C, Fazekas F, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurology. 2013 Aug; 12(8): 822-838	0	0.00	1766	1766.00
32	Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. American Review of Respiratory Disease. 1983; 127(6): 725-734	0	0.00	1734	55.94
33	Stadtman ER. Protein oxidation and aging. Science. 1992 Aug 28; 257(5074): 1220-1224	3	0.14	1704	77.45
34	Sapolsky RM, Krey LC, Mcewen BS. The neuroendocrinology of stress and aging - The glucocorticoid cascade hypothesis. Endocrine Reviews. 1986 Aug; 7(3): 284-301	1	0.04	1689	60.32
35	Rowe JW, Kahn RL. Human aging - Usual and successful. Science. 1987 Jul 10; 237(4811): 143-149	1	0.04	1671	61.89
36	50 Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. Journal of Clinical Endocrinology & Metabolism. 2001 Feb; 86(2): 724-731	1	0.08	1663	127.92
37	Trifunovic A, Wredenberg A, Falkenberg M, Spelbrink JN, Rovio AT, et al. Premature ageing in mice expressing defective mitochondrial DNA polymerase. Nature 2004 May 27; 429(6990): 417-423	6	0.60	1659	165.90
38	Shigenaga MK, Hagen TM, Ames BN. Oxidative damage and mitochondrial decay in aging. Proceedings of The National Academy of Sciences of The United States of America. 1994 Nov 8; 91(23): 10771-10778	2	0.10	1646	82.30
39	Cottrell AH, Bilby BA. Dislocation theory of yielding and strain ageing of iron. Proceedings of The Physical Society of London Section A. 1949; 62(349): 49-62	1	0.02	1630	25.08
40	Lakatta EG, Levy D. Arterial and cardiac aging: Major shareholders in cardiovascular disease enterprises Part I: Aging arteries: A “set up” for vascular disease. Circulation. 2003 Jan 7; 107(1): 139-146	0	0.00	1613	146.64
41	Huttenlocher PR. Synaptic density in human frontal-cortex - Developmental-changes and effects of aging. Brain Research. 1979; 163(2): 195-205	1	0.03	1612	46.06
42	Raz N, Lindenberger U, Rodrigue KM, Kennedy KM, Head D, et al. Regional brain changes in aging healthy adults: General trends, individual differences and modifiers. Cerebral Cortex. 2005 Nov ; 15(11): 1676-1689	1	0.11	1562	173.56
43	Campisi J. Senescent cells, tumor suppression, and organismal aging: Good citizens, bad neighbors. Cell. 2005 Feb 25; 120(4): 513-522	1	0.11	1549	172.11
44	Kenyon CJ. The genetics of ageing. Nature. 2010 Mar 25; 464(7288): 504-512	3	0.75	1549	387.25
45	Baker DJ, Wijshake T, Tchkonia T, LeBrasseur NK, Childs BG, et al. Clearance of p16(Ink4a)-positive senescent cells delays ageing-associated disorders. Nature. 2011 Nov 10; 479(7372): 232-U112	2	0.67	1486	495.33
46	Harman D. The aging process. Proceedings of The National Academy of Sciences of The United States of America-Biological Sciences. 1981; 78(11): 7124-7128	3	0.09	1481	44.88
47	Hastie ND, Dempster M, Dunlop MG, Thompson AM, Green DK, et al. Telomere reduction in human colorectal-carcinoma and with aging. Nature. 1990 Aug 30; 346(6287): 866-868	1	0.04	1412	58.83
48	West RL. An application of prefrontal cortex function theory to cognitive aging. Psychological Bulletin. 1996 Sep; 120(2): 272-292	3	0.17	1369	76.06
49	Wood JG, Rogina B, Lavu S, Howitz K, Helfand SL, et al. Sirtuin activators mimic caloric restriction and delay ageing in metazoans. Nature. 2004 Aug 5; 430(7000): 686-689	1	0.10	1353	135.30
50	Savill JS, Wyllie AH, Henson JE, Walport MJ, Henson PM, et al. Macrophage phagocytosis of aging neutrophils in inflammation - Programmed cell-death in the neutrophil leads to its recognition by macrophages. Journal of Clinical Investigation. 1989 Mar; 83(3): 865-875	0	0.00	1342	53.68
51	Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, et al. The loss of skeletal muscle strength, mass, and quality in older adults: The health, aging and body composition study. Journals of Gerontology Series A-Biological Sciences and Medical Sciences. 2006 Oct; 61(10): 1059-1064	0	0.00	1339	167.38
52	Poeggeler B, Reiter RJ, Tan DX, Chen LD, Manchester LC. Melatonin, hydroxyl radical-mediated oxidative damage, and aging - A hypothesis. Journal of Pineal Research. 1993 May; 14(4): 151-168	0	0.00	1330	63.33
53	Parfitt AM, Mathews CHE, Villanueva AR, Kleerekoper M, Frame B, et al. Relationships between surface, volume, and thickness of Iliac Trabecular bone in aging and in osteoporosis - Implications for the microanatomic and cellular mechanisms of bone loss. Journal of Clinical Investigation. 1983; 72(4): 1396-1409	0	0.00	1311	42.29
54	Lexell J, Taylor CC, Sjostrom M. What is the cause of the aging atrophy - total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15-year-old to 83-year-old men. Journal of the Neurological Sciences. 1988 Apr; 84(2-3): 275-294	2	0.08	1310	50.38
55	Kujoth GC, Hiona A, Pugh TD, Someya S, Panzer K, et al. Mitochondrial DNA mutations, oxidative stress, and apoptosis in mammalian aging. Science. 2005 Jul 15; 309(5733): 481-484	3	0.33	1304	144.89
56	Chan DC. Mitochondria: Dynamic organelles in disease, aging, and development. Cell. 2006 Jun 30; 125(7): 1241-1252	0	0.00	1250	156.25
57	Goldberger AL, Amaral LAN, Hausdorff JM, Ivanov PC, Peng CK, et al. Fractal dynamics in physiology: Alterations with disease and aging. Proceedings of The National Academy of Sciences of The United States of America. 2002 Feb 19; 99: 2466-2472	0	0.00	1248	104.00
58	Park DC, Reuter-Lorenz P. The adaptive brain: Aging and neurocognitive scaffolding. Annual Review of Psychology. 2009; 60: 173-196	0	0.00	1211	242.20
59	Cabeza R, Anderson ND, Locantore JK, McIntosh AR. Aging gracefully: Compensatory brain activity in high-performing older adults. Neuroimage. 2002 Nov; 17(3): 1394-1402	2	0.17	1191	99.25

Table 2 (continued). Top 100 most-cited studies in aging research

Rank	Study reference	Local citations	Per year	Global citations	Per year
60	Lu T, Pan Y, Kao SY, Li C, Kohane I, et al. Gene regulation and DNA damage in the ageing human brain. Nature. 2004 Jun 24; 429(6994): 883-891	0	0.00	1189	118.90
61	Price JL, Morris JC. Tangles and plaques in nondemented aging and "preclinical" Alzheimer's disease. Annals of Neurology. 1999 Mar; 45(3): 358-368	1	0.07	1174	78.27
62	Zecca L, Youdim MBH, Riederer P, Connor JR, Crichton RR. Iron, brain ageing and neurodegenerative disorders. Nature Reviews Neuroscience. 2004 Nov; 5(11): 863-873	0	0.00	1171	117.10
63	Rubinsztein DC, Marino G, Kroemer G. Autophagy and aging. Cell. 2011 Sep 2; 146(5): 682-695	1	0.33	1171	390.33
64	Hedden T, Gabrieli JDE. Insights into the ageing mind: A view from cognitive neuroscience. Nature Reviews Neuroscience. 2004 Feb; 5(2): 87-U12	1	0.10	1168	116.80
65	Drachman DA, Leavitt J. Human memory and cholinergic system - Relationship to aging. Archives of Neurology. 1974; 30(2): 113-121	0	0.00	1167	29.18
66	Lee CK, Klopp RG, Weindruch R, Prolla TA. Gene expression profile of aging and its retardation by caloric restriction. Science. 1999 Aug 27; 285(5432): 1390-1393	2	0.13	1157	77.13
67	Beal MF. Aging, Energy, and oxidative stress in neurodegenerative diseases. Annals of Neurology. 1995 Sep; 38(3): 357-366	1	0.05	1138	59.89
68	Kirkwood TBL. Evolution of aging. Nature. 1977; 270(5635): 301-304	1	0.03	1132	30.59
69	Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurology. 2012 Nov; 11(11): 1006-1012	0	0.00	1118	559.00
70	Campisi J. Aging, Cellular Senescence, and Cancer. Annual Review of Physiology, 2013; 75: 685-705	0	0.00	1116	1116.00
71	Wallace DC. Mitochondrial genetics - A paradigm for aging and degenerative diseases. Science. 1992 May 1; 256(5057): 628-632	3	0.14	1104	50.18
72	Hoeijmakers JHJ. Molecular origins of cancer DNA damage, aging, and cancer. New England Journal of Medicine. 2009 Oct 8; 361(15): 1475-1485	1	0.20	1102	220.40
73	Robinson AL, Donahue NM, Shrivastava MK, Weitkamp EA, Sage AM, et al. Rethinking organic aerosols: Semivolatile emissions and photochemical aging. Science. 2007 Mar 2; 315(5816): 1259-1262	0	0.00	1100	157.14
74	Kurosu H, Yamamoto M, Clark JD, Pastor JV, Nandi A, et al. Suppression of aging in mice by the hormone Klotho. Science. 2005 Sep 16; 309(5742): 1829-1833	0	0.00	1097	121.89
75	Franceschi C, Capri M, Monti D, Giunta S, Olivieri F, et al. Inflammaging and anti-inflammaging: A systemic perspective on aging and longevity emerged from studies in humans. Mechanisms of Ageing and Development. 2007 Jan; 128(1): 92-105	0	0.00	1084	154.86
76	Salat DH, Buckner RL, Snyder AZ, Greve DN, Desikan RSR, et al. Thinning of the cerebral cortex in aging. Cerebral Cortex. 2004 Jul; 14(7): 721-730	1	0.10	1076	107.60
77	Feldman HA, Longcope C, Derby CA, Johannes CB, Araujo AB, et al. Age trends in the level of serum testosterone and other hormones in middle-aged men: Longitudinal results from the Massachusetts Male Aging Study. Journal of Clinical Endocrinology & Metabolism. 2002 Feb; 87(2): 589-598	0	0.00	1075	89.58
78	Riggs BL, Wahner HW, Dunn WL, Mazess RB, Offord KP, et al. Differential changes in bone-mineral density of the appendicular and axial skeleton with aging - Relationship to spinal osteoporosis. Journal of Clinical Investigation. 1981; 67(2): 328-335	0	0.00	1072	32.48
79	Smith CD, Carney JM, Starkereed PE, Oliver CN, Stadtman ER, et al. Excess brain protein oxidation and enzyme dysfunction in normal aging and in Alzheimer-disease. Proceedings of The National Academy of Sciences of The United States of America. 1991 Dec; 88(23): 10540-10543	4	0.17	1072	46.61
80	Colcombe SJ, Erickson KI, Scalf PE, Kim JS, Prakash R, et al. Aerobic exercise training increases brain volume in aging humans. Journals of Gerontology Series A-Biological Sciences and Medical Sciences. 2006 Nov; 61(11): 1166-1170	0	0.00	1068	133.50
81	Hyman BT, Phelps CH, Beach TG, Bigio EH, Cairns NJ, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimers & Dementia. 2012 Jan; 8(1): 1-13	0	0.00	1067	533.50
82	Stadtman ER. Protein oxidation and aging. Free Radical Research. 2006 Dec; 40(12): 1250-1258	3	0.38	1063	132.88
83	Tyner SD, Venkatachalam S, Choi J, Jones S, Ghebranious N, et al. p53 mutant mice that display early ageing-associated phenotypes. Nature. 2002 Jan 3; 415(6867): 45-53	3	0.25	1062	88.50
84	Montine TJ, Phelps CH, Beach TG, Bigio EH, Cairns NJ, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease: a practical approach. Acta Neuropathologica. 2012 Jan; 123(1): 1-11	0	0.00	1061	530.50
85	Collado M, Blasco MA, Serrano M. Cellular senescence in cancer and aging. Cell. 2007 Jul 27; 130(2): 223-233	1	0.14	1049	149.86
86	Hannum G, Guinney J, Zhao L, Zhang L, Hughes G, et al. Genome-wide methylation profiles reveal quantitative views of human aging rates. Molecular Cell. 2013 Jan 24; 49(2): 359-367	0	0.00	1048	1048.00
87	Lupien SJ, de Leon M, de Santi S, Convit A, Tarshish C, et al. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. Nature Neuroscience. 1998 May; 1(1): 69-73	0	0.00	1044	65.25
88	Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, et al. Aging with multimorbidity: A systematic review of the literature. Ageing Research Reviews. 2011 Sep; 10(4): 430-439	0	0.00	1032	344.00
89	Sinclair DA, Guarente L. Extrachromosomal rDNA circles - A cause of aging in yeast. Cell. 1997 Dec26; 91(7): 1033-1042	2	0.12	1026	60.35
90	Brownlee M. Advanced protein glycosylation in diabetes and aging. Annual Review of Medicine. 1995; 46: 223-234	0	0.00	1017	53.53
91	Blasco MA. Telomeres and human disease: Ageing, cancer and beyond. Nature Reviews Genetics. 2005 Aug; 6(8): 611-622	1	0.11	1016	112.89
92	Rudolph KL, Chang S, Lee HW, Blasco M, Gottlieb GJ, et al. Longevity, stress response, and cancer in aging telomerase-deficient mice. Cell. 1999 Mar 5; 96(5): 701-712	3	0.20	1005	67.00
93	Doherty TJ. Aging and sarcopenia. Journal of Applied Physiology. 2003 Oct; 95(4): 1717-1727	1	0.09	1002	91.09
94	Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, et al. Prevalence of dementia in the United States: The aging, demographics, and memory study. Neuroepidemiology. 2007; 29(1-2): 125-132	0	0.00	999	142.71
95	Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: Burdens upon an aging, changing nation. Journal of Clinical Oncology. 2009 Jun 10; 27(17): 2758-2765	0	0.00	997	199.40
96	Mostoslavsky R, Chua KF, Lombard DB, Pang WW, Fischer MR, et al. Genomic instability and aging-like phenotype in the absence of mammalian SIRT6. Cell. 2006 Jan 27; 124(2): 315-329	1	0.13	995	124.38
97	Fisher GJ, Datta SC, Talwar HS, Wang ZQ, Varani J, et al. Molecular basis of sun-induced premature skin ageing and retinoid antagonism. Nature. 1996 Jan 25; 379(6563): 335-339	0	0.00	985	54.72
98	Guarente L, Kenyon C. Genetic pathways that regulate ageing in model organisms. Nature. 2000 Nov 9; 408(6809): 255-262	1	0.07	984	70.29
99	Alexander M. Aging, bioavailability, and overestimation of risk from environmental pollutants. Environmental Science & Technology. 2000 Oct 15; 34(20): 4259-4265	0	0.00	982	70.14
100	Linnane AW, Ozawa T, Marzuki S, Tanaka M. Mitochondrial-DNA mutations as an important contributor to ageing and degenerative diseases. Lancet. 1989 Mar 25; 1(8639): 642-645	3	0.12	979	39.16

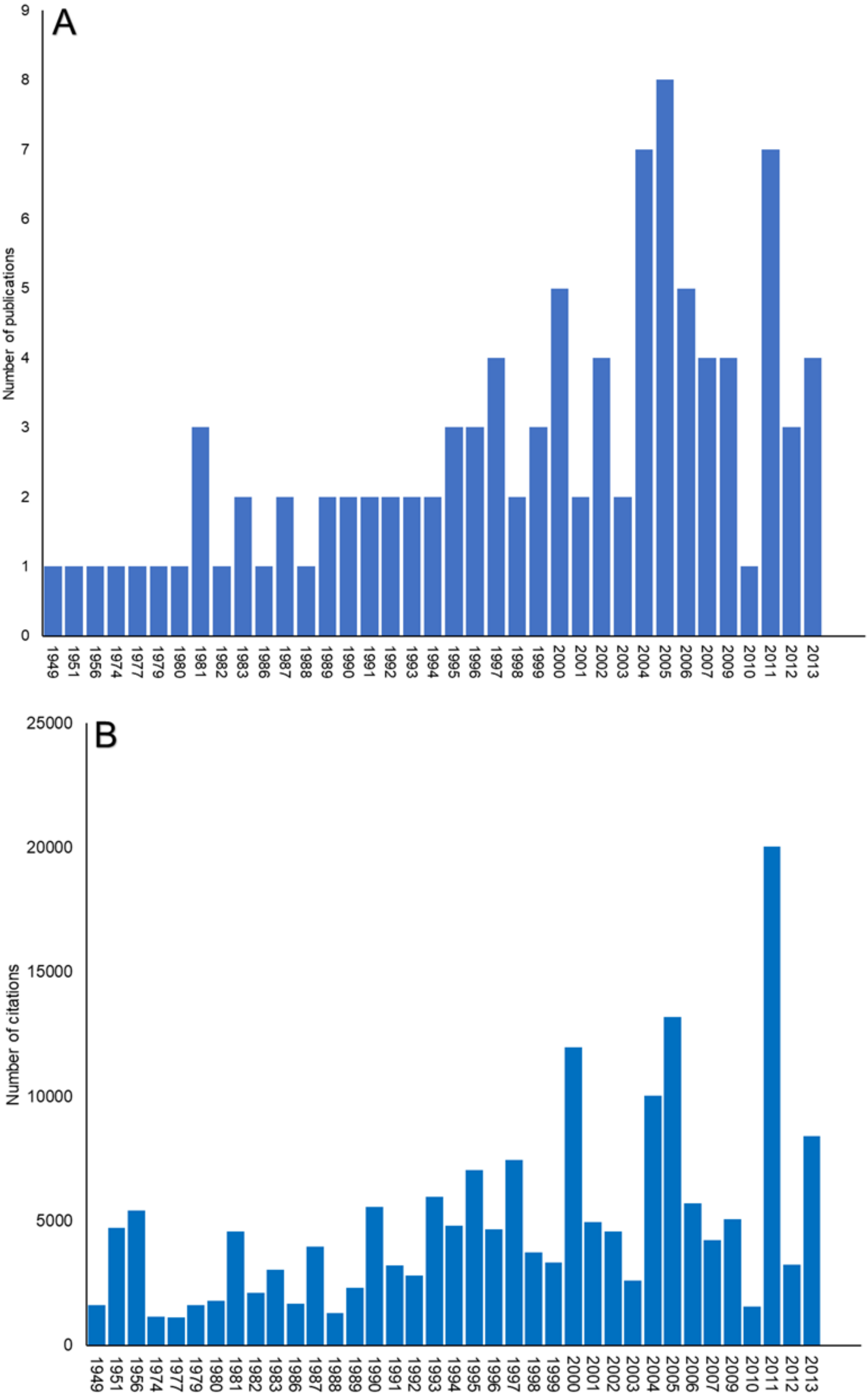

Figure 3. A) Year of publications (1949-2013) of the 100 most cited papers, B) Global citations of the 100 most cited publications

United States of America (USA) with 76 publications (**Table 3**). Aging (n=78), Ageing (n=22), and Disease (n=17) were the most frequently used keywords (**Table 4**). The most prolific author was Phelps CH (n=5) (**Table 5**). The most active institute was Harvard University, USA (n=13) (**Table 6**). Nature was the most attractive journal (n=13) (**Table 7**).

Table 3. Country with at least 3 publications

Country	Publications	Percent	LCS	GCS
USA	76	76	92	131441
UK	10	10	17	27068
Germany	9	9	4	15864
France	6	6	5	13892
Netherlands	6	6	7	12764
Canada	5	5	7	11042
Italy	5	5	1	7104
Japan	5	5	11	8908
Spain	4	4	5	7559
Sweden	4	4	8	5767

LCS: Total local citation score, GCS: Total global citation score

Table 4. The occurrence of a keyword at least 3 times

Word	Occurrences	Percent	LCS	GCS
Aging	78	78	103	139053
Ageing	22	22	28	41678
Disease	17	17	19	35176
Human	11	11	19	22500
Alzheimer	10	10	17	23903
Cancer	9	9	9	13071
Oxidative	8	8	15	18112
Stress	8	8	17	17830
Brain	7	7	7	8464
Mitochondrial	7	7	20	10751
Protein	6	6	11	9375
Association	5	5	12	15840
Diseases	5	5	12	9985
Dna	5	5	13	6233
Guidelines	5	5	12	15840
Institute	5	5	12	15840
National	5	5	12	15840
Radical	**5**	**5**	**12**	**13397**
Changes	**4**	**4**	**2**	**5980**
Cognitive	**4**	**4**	**8**	**7993**
Damage	**4**	**4**	**3**	**5267**
Degenerative	**4**	**4**	**11**	**8847**
Free	**4**	**4**	**12**	**11710**
Mice	**4**	**4**	**12**	**4823**
Normal	**4**	**4**	**8**	**8394**
Oxidation	**4**	**4**	**11**	**6257**
Theory	**4**	**4**	**14**	**11113**
Adults	**3**	**3**	**3**	**4092**
Caloric	**3**	**3**	**9**	**4828**
Cells	**3**	**3**	**9**	**7938**
Cellular	**3**	**3**	**1**	**3476**
Cortex	**3**	**3**	**5**	**4057**
Dementia	**3**	**3**	**4**	**9330**
Diagnostic	**3**	**3**	**12**	**13712**
Gene	**3**	**3**	**3**	**4539**
Healthy	**3**	**3**	**2**	**5632**
Humans	**3**	**3**	**1**	**4172**
Hypothesis	**3**	**3**	**2**	**5039**
Memory	**3**	**3**	**0**	**3210**
Men	**3**	**3**	**3**	**4048**
Oxidants	**3**	**3**	**5**	**13293**
Recommendations	**3**	**3**	**12**	**13712**
Restriction	**3**	**3**	**9**	**4828**
Results	**3**	**3**	**1**	**8975**
Senescent	**3**	**3**	**9**	**7938**
Volume	**3**	**3**	**0**	**4113**
Workgroups	**3**	**3**	**12**	**13712**

LCS: Total local citation score, GCS: Total global citation score

Table 5. The author with at least 3 publications

Author	Publications	Percent	LCS	LCS/t	GCS	GCS/t	LCR
Phelps CH	5	5	12	4	15840	5634.667	13
Ames BN	4	4	8	0.39816	10988	532.1193	16
Carrillo MC	4	4	12	4	14779	5104.167	10
Stadtman ER	4	4	11	0.7441	6257	399.1735	4
Thies B	4	4	12	4	14779	5104.167	10
Blasco MA	3	3	2	0.253968	6554	4751.746	17
Campisi J	3	3	7	0.426901	7568	1546.164	5
Guarente L	3	3	4	0.314076	3005	255.0137	8
Hyman BT	3	3	4	1.333333	8167	3077	9
Montine TJ	3	3	4	1.333333	5463	2175.667	9
Morris JC	3	3	6	1.5	8289	2198.867	4
Weindruch R	3	3	11	0.8	4779	350.8	9

LCS: Total local citation score, LCS/t: Total local citation score per year, GCS: Total global citation score, GCS/t: Total global citation score per year, LCR: Total local cited references.

Table 6. The institution with at least 3 publications

Institution	Publications	Percent	LCS	GCS
Harvard Univ	13	13	15	23299
NIA	9	9	14	26480
Washington Univ	8	8	15	19652
Univ Calif San Diego	6	6	8	11893
Johns Hopkins Univ	5	5	12	14093
Mayo Clin	5	5	10	13991
NHLBI	5	5	9	12191
UCL	5	5	12	19928
Univ Calif Berkeley	5	5	14	14687
Univ Michigan	5	5	1	6674
Alzheimers Assoc	4	4	12	14779
MIT	4	4	4	5645
Univ Calif San Francisco	4	4	8	7207
Univ Tokyo	4	4	8	7929
Univ Washington	4	4	4	6538
Univ Wisconsin	4	4	11	5851
Brigham & Womens Hosp	3	3	1	4285
Brown Univ	3	3	8	6995
Northwestern Univ	3	3	0	3295
Rush Univ	3	3	4	5463
Univ Kentucky	3	3	4	3200
Univ So Calif	3	3	2	5001
Univ Texas	3	3	3	3731

LCS: Total local citation score, GCS: Total global citation score

Table 7. The 6 Journal with at least 3 publications

Journal	Publications	Percent	LCS	LCS/t	GCS	GCS/t	LCR
Nature	13	13	25	2.845374	25171	2337.56	11
Cell	9	9	10	1.14106	15164	5901.502	37
Science	8	8	18	1.109764	11455	819.357	13
Proceedings of the National Academy of Sciences of the United States of America	6	6	15	0.73256	15914	952.5185	7
Alzheimers & Dementia	4	4	12	4	14779	5104.167	10
Journal of Clinical Investigation	3	3	0	0	3725	128.4552	0
New England Journal of Medicine	3	3	3	0.258824	4991	338.6445	1

LCS: Total local citation score, LCS/t: Total local citation score per year, GCS: Total global citation score, GCS/t: Total global citation score per year, LCR: Total local cited references.

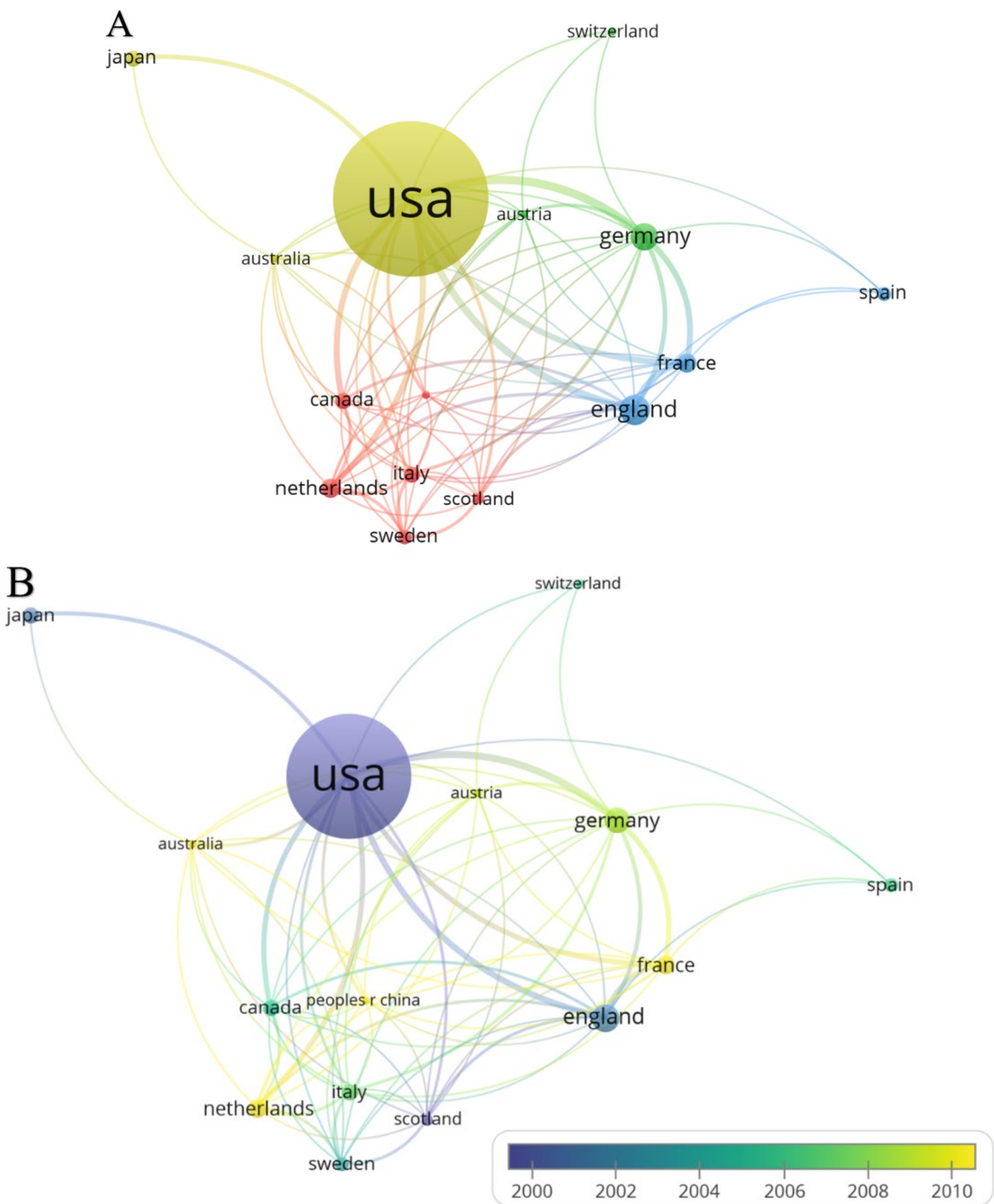

Figure 4. (A) Co-authorship and country network visualization mapping. (B) Overlay visualization mapping by time (year). There are four clusters formed; Red color designates cluster 1 (Canada, Italy, Netherlands, China, Scotland, Sweden), green color designates cluster 2 (Austria, Germany, Switzerland), blue color designates cluster 3 (England, France, Spain), and yellow color designates cluster 4 (Australia, Japan, USA)

Co-authorship and Country

The co-authorship and country mapping is presented in **Figure 4**. The minimum number of the document per country was set at 2. Of the 22 countries, 15 were included for visualization after network mapping. The USA had the highest total link strength (TLS) of 38, followed by England (TLS=24), and Germany (TLS=25).

Co-occurrences and Author Keywords

The minimum number of a keyword occurrence was fixed at 1. Minimum items included in a cluster were fixed at 5. Based on TLS, aging and dementia were the most widely used author keywords (TLS=49), and (TLS=16) respectively as shown in **Figure 5**.

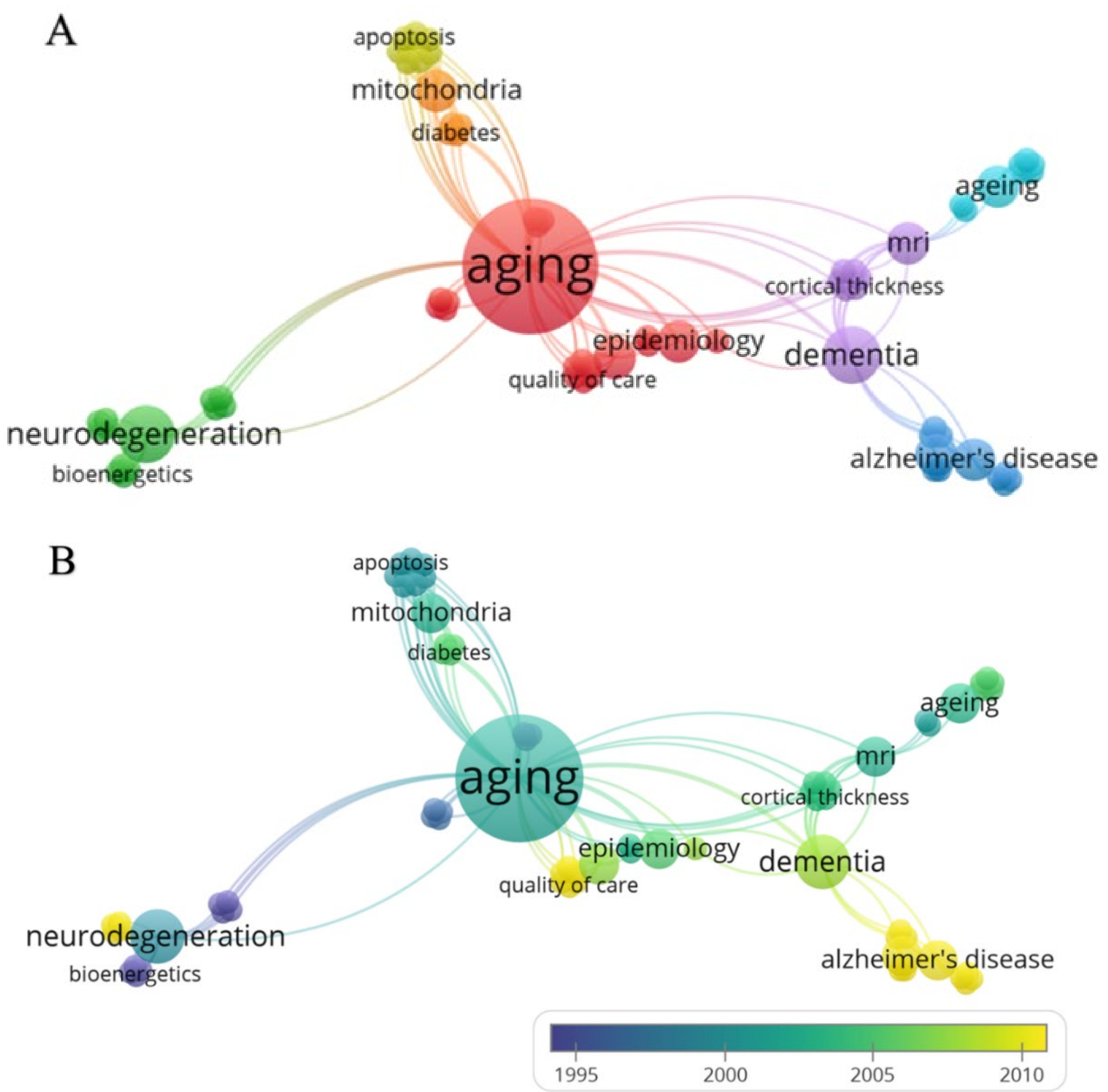

Figure 5. (A) Author keywords visualization mapping. (B) Overlay visualization by time (year). There are 7 clusters formed; cluster 1 red color (19 items), cluster 2 green color (13 items), cluster 3 blue color (11 items), cluster 4 yellow color (9 items), cluster 5 purple color (8 items), cluster 6 light blue (8 items), and cluster 7 orange color (5 items)

DISCUSSION

Bibliometric type studies are of great interest, providing an overview of the scientific published literature and other important parameters [22]. The number of bibliometric studies has been increased over the years [23]. This is the first comprehensive bibliometric analysis summarizing several features of the most influential studies on aging. Analysis of most cited studies on aging may be worthwhile to keep the young researchers and clinicians abreast of traditional knowledge. It may help clinicians, nutritionists and policymakers to decide based on results from influential previous studies.

Aging is an irreversible phenomenon that leaves multiple effects on the human body. Generally, it weakens muscles and all the body functions, leading to certain complications that ultimately burden the health system. In order to overview the research trends and most commonly addressed issues, the bibliometric is the most helpful strategy to reach the hot spot and analyze the research conducted in the field. By this, the researcher can easily identify the multiple studies on the same topic, select the best one, and summarize the best available evidence after critical analysis. This bibliometric study has selected 100 publications/papers out of 131,652 on aging published during the last century, i.e., from 1900-2021. During this period, the citation and publication pattern is not uniform. It keeps changing from year to year.

The top 100 papers were published in 52 different journals. Nature was the most frequent journal with 13 publications, followed by Cell (n = 9) and Science (n = 8). This trend depicts aging as a vast field with different dimensions that allow the authors to publish in well-reputed scientific journals. This study encompasses a wide variety of institutions, countries and authors involved in most cited publications. In this regard, Harvard University was on top, followed by NIA and Washington University, while the USA was the leading country, followed by United Kingdom (UK), Germany, and France. Among the most cited authors, Phelps CH was on top, which received 15840 citations.

All the included publications in this study were published in English, and 63% were research articles while 29% reviews, 4% proceeding papers, 3% were book chapters. This trend illustrates that English is a widely used language to exchange scientific findings, and a majority of the scientific results on aging are being published resulting from experimental work though the share of review and other articles are also countable. The most frequently used keywords and research areas linked with aging studies reflect the research focus.

More research is needed to be carried out in this field, and scientists, especially from developing countries, should be encouraged to conduct research and share the findings in peer-reviewed journals. Moreover, researchers and clinicians need to use the evidence summaries in clinical practices and update and develop new summaries based on their practices to use these approaches as well.

LIMITATIONS

This study has several limitations; a) a single database (WoSCC) was utilized; b) The citations count was based on WoSCC; c) The use of other databases like like Scopus and Google Scholar may alter the citations count or publications frequency.

CONCLUSION

This study provides a detailed, comprehensive overview of aging research. The USA was ranked the most productive and active country. The finding from 100 most cited publications in aging research may help the researchers, policymakers, and funding agencies for future research directions and hotspots. Low- and middle-income countries need to be supported through funding and by collaborating with them to upgrade the technical skills of researchers and clinicians.

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