



Global Research on Centenarians: A Historical and Comprehensive Bibliometric Analysis from 1887 to 2023

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Received: February 17, 2024 Revised: March 19, 2024 Accepted: March 27, 2024 Background: Centenarians are considered the most successful human biological aging model. However, the characteristics and patterns of research among centenarians have not been described or analyzed. Thus, this study aimed to disclose the historical landscape of global research on centenarians. Methods: This bibliometric study investigated historical evidence on centenarian research published in the Scopus database. The bibliometrix package in R was used to perform visual and quantitative analyses of research metrics, trends, and patterns. Results: Of the 2,061 documents included between 1887 and 2023, 84.2% (n=1,736) were published as articles with primary data. We identified international collaboration and annual growth rates of 21.4% and 3.15%, respectively. The United States published the highest number of papers on centenarians (n=786), whereas the publications from Italy had the highest impact (h-index of 90). Based on the frequency of keywords, mortality, genetics, dementia, Alzheimer's disease, and immunosenescence are a few of the most studied topics among centenarians, with emerging research related to mitochondrial DNA and comparison of results between nonagenarians and centenarians. Italy, the United States, and China lead the global research collaboration network, collaborating most frequently with Japan and European countries. Conclusion: Global research on centenarians has grown over the last 20 years, primarily led by Italy, the United States, and China. Latin American and African countries have conducted little or no research on centenarians. The most widely studied topics include mortality, cognition, immunosenescence, and genetics.

Key Words: Centenarians, Longevity, Aged, Research, Bibliometrics

INTRODUCTION

The world is currently facing a critical demographic transition with the acceleration of population aging, which is linked to an increase in the incidence and prevalence of age-related chronic diseases.¹⁾ These conditions result in a substantial disease burden and high healthcare costs.^{2,3)} Therefore, international consensus recommendations emphasize designing and implementing health strategies and plans to promote healthy aging.^{4,5)} This emphasis aims to optimize healthy lifespans in the older adult population, along with other health indicators such as functional capacity, quality of life,

and self-satisfaction during aging.⁶⁾

Centenarians are the most successful biological aging model in humans.⁷⁾ This population is characterized by a low prevalence of age-related chronic diseases, favorable functionality and independence, adequate social resilience, and life satisfaction.^{8,9)} Studying this population is important for understanding the physiological and pathophysiological mechanisms of aging and the determinants associated with these outcomes.^{7,10,11)} Various studies have used centenarians as super-control groups for comparing clinical phenotypes, biomarker expression, and immunological resilience.¹²⁾ These results, based on precision medicine, show promising out-

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comes, such as the identification of genetic polymorphisms that protect against certain diseases or conditions.¹³⁾

Despite the notable advantages provided by research on populations, what has been studied regarding the centenarian population, how it has been studied, and where, has not been examined. The heritability of extreme longevity is approximately 30%.¹⁴⁾ Therefore, lifestyle, environmental factors, and social determinants of health are crucial for understanding the evolution and health phenotypes of centenarians.¹⁵⁾ These characteristics vary between regions, making the study of centenarians tailored to social and cultural contexts essential for understanding the risks and benefits of specific signatures in each population.¹⁶⁾

Globally, just over 2,000 or 3,000 articles related to centenarian research have been published.⁸⁾ However, this scientific production has never been characterized, highlighting a significant gap in knowledge regarding what has been researched and what remains to be investigated in centenarians. This limitation hinders the development of evidence-based road maps. To address this and provide useful and actionable data for researchers in longevity, healthy aging, and centenarian studies, we aimed to describe the historical landscape of global research on centenarians, highlighting their characteristics and future priorities.

MATERIALS AND METHODS

Study Design

Bibliometric cross-sectional study.

Source Database

We performed a broad search of the Scopus database, which is the largest peer-reviewed literature database and provides access to numerous metrics related to authors, citations, and scientific articles. Currently, Scopus includes > 15,000 indexed medicine journals and has been previously used to perform bibliometric analyses.^{17,18}

Search Strategy

Our search identified all scientific articles on centenarians published worldwide. We used Medical Subject Headings terms and synonyms to construct the search. After pilot testing, to identify the largest amount of related evidence, we used the following search: TITLE-ABS-KEY (centenarian) OR TITLE-ABS-KEY (centenarians) OR TITLE-ABS-KEY (centenar*).

Standardization and Data Collection

No language restrictions were applied regarding article inclusion. The database yielded results that encompassed diverse data, including the year of publication, article title and type, journal details, keywords, affiliations, author information, citations, and collaborations. We performed the search through November 26, 2023, with a focus on filters labeled "Journals." Subsequently, two authors performed a manual review using Microsoft Office Excel 2016 to eliminate duplicates and articles that did not meet the research scope (centenarians) based on their titles, abstracts, and keywords.

Subsequently, two authors performed another manual review to standardize the data. Then, a few variables were recategorized by article typology. We classified all original studies, regardless of their observational or experimental designs, as "original studies." The "review" category included narrative, systematic reviews, and meta-analyses. The "editorial" category comprised all articles published under that specific typology. In contrast, the "letter" category encompassed any other typologies distinct from the previous ones, including comments, correspondences, letters to the editor, etc. The same procedure was applied to study affiliations.¹⁸)

Indicators and Metrics

To assess the impact of the scientific production of authors, affiliations, and countries, we used the h-index, m-index, and g-index, along with the aggregate count of citations, when precise data were available for such calculations. The h-index is a quantitative bibliometric index that measures the impact of scientific output based on the number of citations in published articles.^{19,20)} For instance, an author has an h-index if h of their *p* papers have received at least *h* citations. Mathematically, this is expressed as follows:

$$h = \max_i \{C_i \ge i\}$$
 $i = 1, 2, ..., p \land C_i \ge C_i + 1$

where p is the number of documents published by the author and C_i denotes the number of citations for the *i*-th document, organized in descending order. Consequently, an h-index of 20 indicates no fewer than 20 articles, each with a minimum of 20 citations.

The m-index (also known as Hirsch's m-quotient) is a quantitative index that assesses the linear correlation of an investigator's impact over time.^{19,20} This value is calculated using the following equation:

$$m = h^N = h/Y_{aa}$$

where *h* denotes the h-index of the author and Y_{aa} represents the author's academic age, which is determined by subtracting the present year from the year of the author's first publication. Hence, in 2024, an author with an h-index of 20 with a first publication in 2020 would have an m-index of 5 (20/4 years [2024–2020]).

The g-index is an additional quantitative measure that emerges from the distribution of the accumulated citations of an author (the g-value), structured such that when positioned in descending order, they correspond to the g^2 ranking. A g-index of 10 requires at least 100 citations (g^2) from the ten most-cited articles (g), although not all must have a minimum of 10 citations.^{19,20)}

Data Analysis and Visualization

We applied bibliometric and network metrics. All the publications that satisfied the inclusion criteria were exported and downloaded. The bibliometrix package in R (version 4.3.1) was used to calculate the quantitative bibliometric indicators and perform visual analyses.²¹⁾ Owing to the potential for differences in names, spellings, or variants (e.g., plurals and synonyms) in the thesaurus.txt files, we performed manual standardization to integrate authors, institutions, and keywords. We used Microsoft Office Excel 2016 to calculate the frequencies and percentages of the qualitative variables.

We investigated scientific production and annual scientific growth and assessed the average number of citations per year, publication frequency, and impact indicators adjusted for journals. The most prolific authors were identified, and Lotka's law was employed to visualize the distribution of publications among the authors. Furthermore, we visualized the most-studied topics among centenarians worldwide, as well as collaborative networks among countries and affiliations.

Ethical Statement

Ethical approval was not required for this study as it did not include human subjects, animals, or clinical records. However, this study was part of the Coosalud EPS centenarian project.

RESULTS

Among the 3,089 documents initially identified, we selected 2,061 published between 1887 and 2023. Of these, 84.2% (n = 1,736) were published as articles with primary data, followed by 8.4% (n = 173) as reviews. International collaboration and annual growth rates were identified at 21.4% and 3.15%, respectively, with an average document age of 15 years (Table 1). The first postmortem description of a centenarian was published in 1887.²²⁾ Subsequently, not until 1947 were two documents published describing the clinical and surgical histories of centenarians in the United States and the United Kingdom.^{23,24)} Since then, the number of publications related to research on centenarians has shown fluctuating growth, with a significant and sustained increase since the 1990s, peaking in 2020 (n = 116). In contrast, while citation be-

Table 1. General	characteristics	of globa	l researcl	n on	centenarians
(n=2,061)		-			

	Value
Document types	
Articles with primary data	1,736 (84.2)
Reviews	173 (8.4)
Editorials	22(1.1)
Letters	130 (6.3)
Authors	
Authorships	6,427
Authors of single-authored docs $(n = 6,427)$	199 (3.09)
Author collaboration	
Single-authored documents	228 (2.7)
Co-authors per document	6.49
International co-authorships (%)	21.4
Document contents	
Keywords	2,968
Journals	801
Annual growth rate (%)	3.15
Document average age (y)	15
Average citations per document	28.9

Values are presented as numbers (%).

havior has fluctuated over time, peaking in 1993 (average of 73 citations per article), we observed a noticeable decline in the last 20 years (Fig. 1). Applying Lotka's law, 72.3% of authors published only one document, followed by 12.7% with two publications.

Our analysis of the authors, affiliations, and countries with the highest scientific production related to research on centenarians revealed that the five most prolific authors were located in Italy, the United States, and Japan, with Claudio Franceschi (Italy) being the most prolific author with the highest impact to date (13,489 citations; h-index = 64, g-index = 75.5, m-index = 2.04). Regarding affiliations, four of the most prolific are located in Italy, and the remainder are located in the United States, with the Università di Bologna being the most prominent, with 207 documents related to research on centenarians. The United States had the highest number of articles published in the field (786 documents), followed by Italy (654 documents), although the latter had the highest impact (h-index = 90) (Table 2).

Regarding the behavior and impact of journals derived from publications on centenarians, *The Journal of Gerontology Series A: Biological Sciences and Medical Sciences* had the highest number of published articles (86) and the highest impact in all metrics (h-index = 36, g-index = 61, m-index = 1.38), including the number of citations (3,936) (Fig. 2A–2E). The number of articles published annually in the top five journals on centenarians varied, with significant peaks in different years, especially from *Archives of Gerontology and Geriatrics, Mechanisms of Aging and Development, and Experimental Gerontology*, which published at least 14 papers per

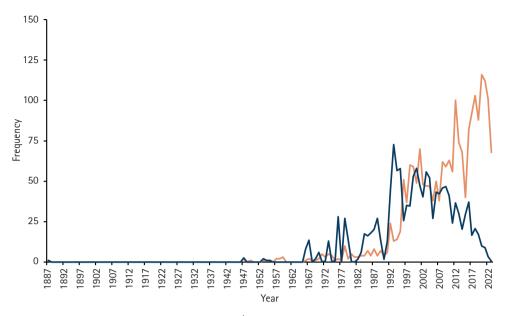


Fig. 1. Annual scientific growth of global research on centenarians (orange represents annual scientific production; blue, mean total citations per article per year).

Table 2. Production and impact of the most prolific affiliations and countries in global research on centenarians

	Documents over time				- Total documents ^{a)}	h-index	Country
	1887–1987	1988–1999	2000-2010	2011-2023	- Total documents	n-mdex	Country
Affiliation							
Università di Bologna	0	12	106	89	207	68	Italy
Istituto Nazionale Riposo e Cura Anziani	0	17	92	20	129	55	Italy
University of Giorgia	3	22	27	56	108	31	USA
Università degli Studi di Firenze	0	5	39	52	96	43	Italy
Università degli Studi di Palermo	0	5	37	47	89	37	Italy
Country							
United States	29	92	221	444	786	88	
Italy	1	103	243	307	654	90	
China	0	5	46	343	394	41	
Japan	15	53	79	127	274	48	
United Kingdom	9	14	39	80	142	37	

^{a)}Individual production was counted; therefore, a document might be counted multiple times according to research collaboration.

year (Fig. 2F).

Based on the frequency of keyword use, mortality, genetics, dementia, Alzheimer's disease, and immunosenescence were the most studied topics among centenarians (Fig. 3A). The main co-occurrence of these topics was related to (1) mortality, hip fracture, and risk factors; (2) immunosenescence linked to inflammation, inflammaging, and cytokines; (3) cognition related to dementia, neuropathology, personality, depression, and Alzheimer's disease; and (4) genetics related to Okinawa (a blue zone in Japan) (Fig. 3B). Thus, these constitute foundational topics, with emerging research related to mitochondrial DNA and the comparison of results between nonagenarians and centenarians (Fig. 3C). In the last 20 years, interest has increased in genetics, mortality, and dementia in centenarians (Fig. 3D). Compared to the 2000s, increasing studies have focused on genetic polymorphisms, inflammation, immunosenescence, and dementia. The last decade has seen an emerging interest in publishing on gut microbiota, quality of life, environment, nutritional status, resilience, and frailty (Fig. 3E, 3F).

Regarding research collaboration networks, we observed significant endogamous collaborations among Italian, American, and American-Japanese affiliations (Fig. 4A). The global research collaboration network is essentially led by Italy, the United States, and China, which collaborate most frequently with Japan and European countries (Fig. 4B). However, weak or no international collabo-

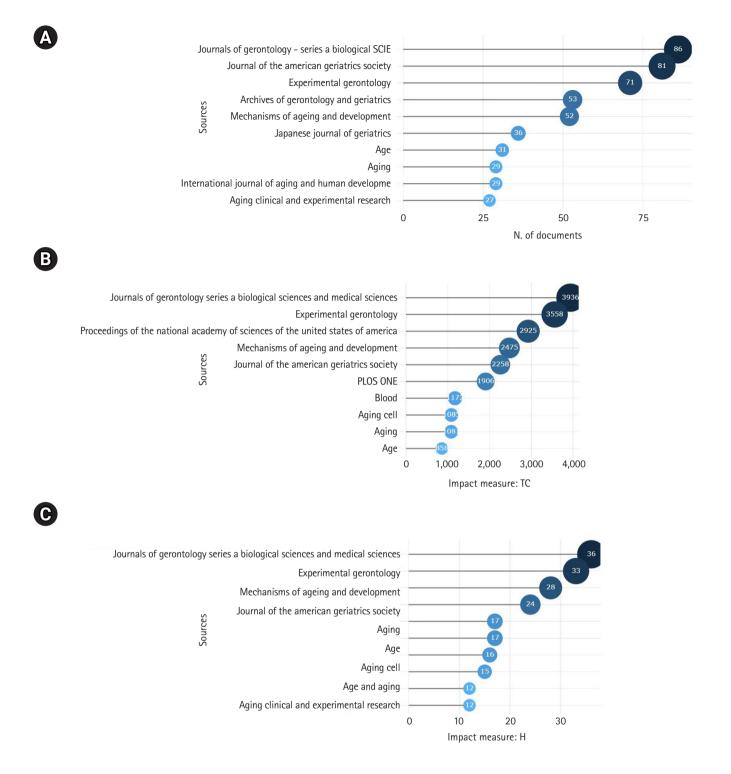


Fig. 2. Impact of journals and publication frequency on centenarians in the most popular journals. (A) Frequency of published articles. (B) Total citations received. (C) h-index derived from the articles. (D) g-index derived from the articles. (E) m-index derived from the articles. (F) Yearly frequency of articles published in most popular journals.

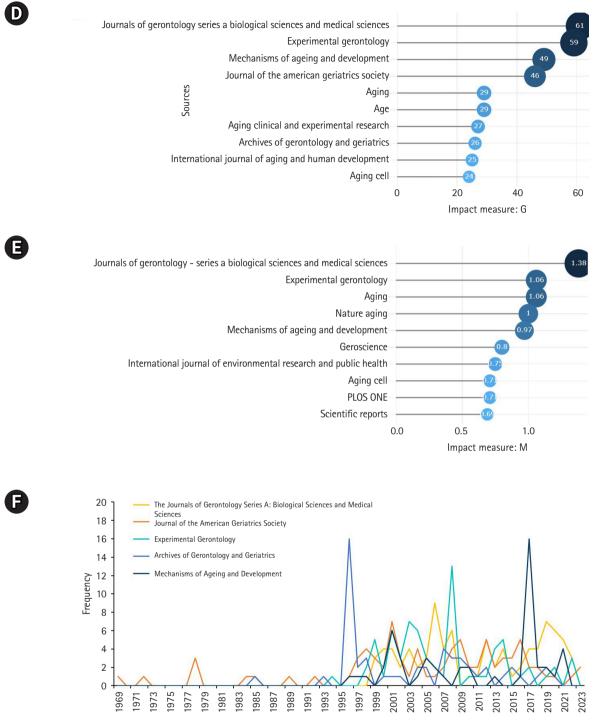


Fig. 2. Continued

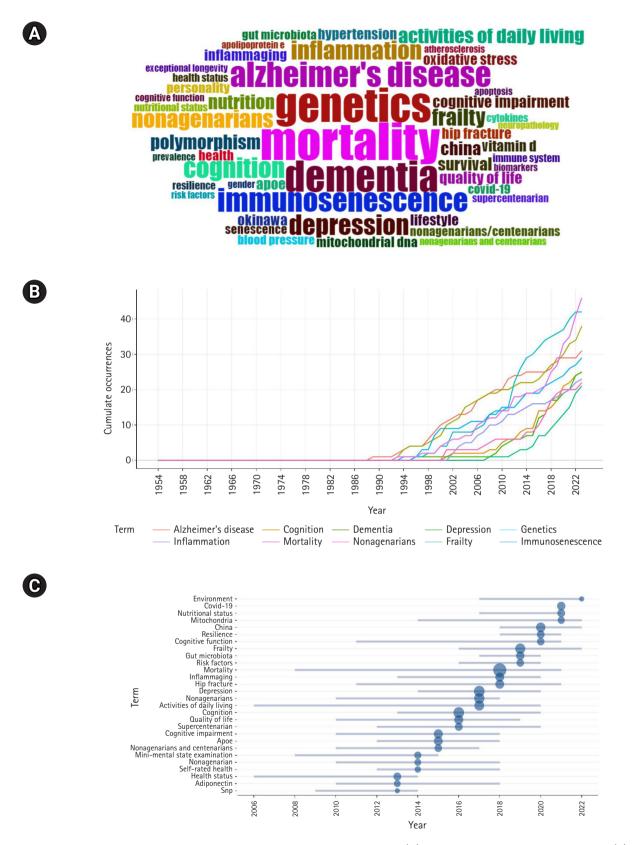


Fig. 3. Topics evolution and research patterns in global research on centenarians. (A) Wordcloud of most frequent keywords. (B) Co-occurrence network of keywords. (C) Thematic map with relevance and development degree of topics. (D) Frequency of occurrence of the most studied topics over time. (E) Trend topics from 2003 to 2012. (F) Trend topics from 2013 to 2023.

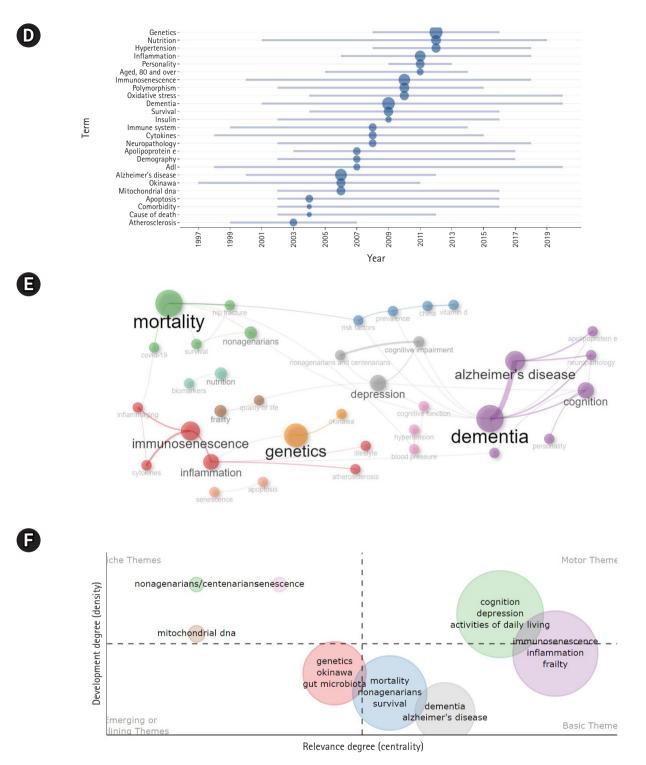
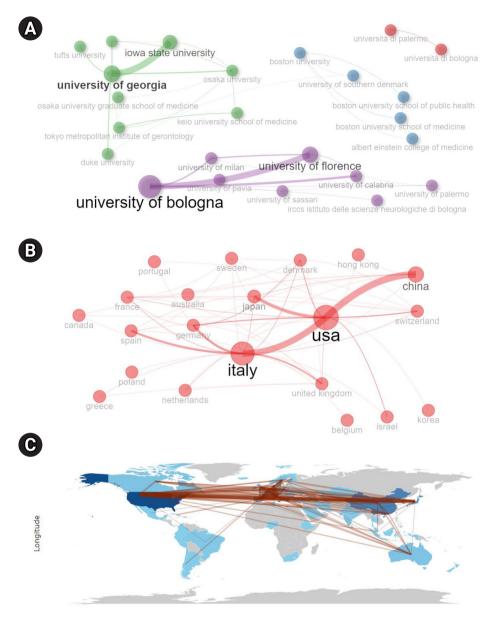


Fig. 3. Continued



Latitude

Fig. 4. Affiliations and countries collaboration network. (A) Affiliation collaboration network (with minimum number of five edges). (B) Countries collaboration network (with minimum number of five edges). (C) Countries' collaboration world map (with minimum number of two edges).

rations were identified between countries in Latin America, Africa, and the rest of the world (Fig. 4C).

Finally, the articles that have achieved the highest impact to date, based on the number of citations, were (1) "Through ageing and beyond: gut microbiota and inflammatory status in seniors and centenarians" (1,068 citations, published in *PLOS ONE* in 2010; https://doi.org/10.1371/journal.pone.0010667); (2) "Age-related changes in gut microbiota composition from newborn to centenarian: a cross-sectional study" (799 citations, published in *BMC Microbiology* in 2016; https://doi.org/10.1186/s12866-016-0708-5);

and (3) "Distinct DNA methylomes of newborns and centenarians" (583 citations, published in *Proceedings of the National Academy of Sciences* in 2012; https://doi.org/10.1073/pnas.1120658109).

DISCUSSION

The results of this study revealed the characteristics, trends, and collaborations in global research on centenarians. Previous bibliometric studies have addressed subtopics including physical exercise, ²⁵⁾ cognition during aging,²⁶⁾ and the scientific growth of re-

search on healthy aging,^{27,28)} but have not focused on centenarians.

The description of centenarians as a novel and infrequent finding in the general population occurred > 120 years ago.²²⁾ However, growth in research from 1887 to the 1950s was modest. Since then, compared with other medical disciplines,^{17,18)} the annual growth rate in this area of research has been low, primarily focusing on countries where blue zones have been described, possibly facilitating the design and execution of studies owing to access to the target population. Nevertheless, the research gap between regions is evident, as indicated by the distribution of publications according to Lotka's law, where 85% of the identified authors have published only up to two documents, suggesting occasional research or publication rather than massive centenarian research groups worldwide.

Italy, the United States, China, and Japan have led scientific research on centenarians, which may be linked to decades-old prospective centenarian cohorts such as the Italian Multicenter Study on Centenarians,²⁹⁾ Italian Longitudinal Study on Ageing,³⁰⁾ or the AKEA study³¹⁾ in Italy, the New England Centenarian Study,³²⁾ Georgia Centenarian Study³⁴⁾ in China, Okinawa Centenarian Centenarian Cohort Study³⁴⁾ in China, Okinawa Centenarian Study,³⁵⁾ and Tokyo Centenarian Study³⁶⁾ in Japan. These studies have allowed an extensive examination of this population in these countries. Many studies derived from these prospective cohorts have been published,^{12,37–39)} contributing significantly to our understanding of variables related to healthy aging, characteristics that confer properties to centenarians as super-controls, and the heritability of longevity that protects against certain diseases in centenarian offspring.⁴⁰⁾

This evidence suggests that the creation of large prospective cohorts characterizing variables specific to each region can help elucidate a few unanswered questions about centenarians, such as the absence of certain conditions despite decades-long exposures to risk factors or stressors, or proper proteodynamics, resilience, and immunological remodeling,⁴¹⁾ depending on the epidemiology and common microorganisms among different global regions.

The frequency of keywords and research patterns demonstrates a significant mix of designs in centenarian studies. For example, the frequency of the keyword "mortality" related to hip fractures and risk factors suggests clinical research focused on the surgical field. However, hospital- or home-based research on cognition, dementia, and Alzheimer's disease has been reported. Additionally, the use of terms such as genetics and immunosenescence, which are related to inflammation, cytokines, and inflammation, suggests the need for basic or translational research.

As population genetics can influence up to 30% of the longevity mark,⁴²⁾ studies in regions where racial, ethnic, and cultural charac-

teristics differ significantly from those of countries with traditional cohorts (the United States, Europe, and Asia) are crucial. This highlights the absence of extensive research in Latin America and Africa, which show low frequencies of publications on centenarians and few collaborative networks. Multiracial research is critical for determining differences in race, ethnicity, and ancestry in genetics and genomics,¹⁶⁾ which are closely related to proteomic and metabolomic markers (whose signatures are unique to centenarians and reflect the favorable organic adaptive capacity during aging to reduce inflammation and promote a healthy lifespan).^{39,40,43)} Therefore, these data are the basis for proposing an innovative roadmap for these two continents to provide evidence to improve the care of this population and explore new biomarkers and protective factors for extreme longevity and healthy aging.

Despite the number of studies on longevity, healthy aging, comorbidities, sociodemographic characteristics, and a few biomarkers,⁴⁴⁾ more centenarian-specific studies are needed. Although existing research has shed light on various aspects of aging, evidence is required regarding how the environment affects centenarians, the type of care these individuals require, the public protection policies that affect them, and the health resources available to this population. Furthermore, understanding the social behaviors and cultural roles of centenarians and how these factors influence their health and well-being is essential. In this regard, normality parameters for specific biomarkers in this population must be established, and cognitive tests and functional constructs adapted to their unique needs and capabilities must be developed. The exploration of how centenarians relate to their environment, lifestyle, and interactions with the environment is essential, as these aspects can significantly impact their quality of life and ability to remain healthy and active at an older age. In short, focusing on specific studies of centenarians will enable us to better understand the factors contributing to their longevity and well-being and design more effective interventions to promote healthy aging in this unique population.

Finally, a hot topic in centenarian research is the absence of clinical practice guidelines and randomized controlled trials. To date, no registered clinical trials registered on ClinicalTrials.gov (http://tinyurl.com/5n875sx6) are related to pharmacological or non-pharmacological interventions in centenarians, and fewer than five registered studies are focused on nonagenarians. Considering the forecasted increasing life expectancy, advancing potential interventions for nonagenarians and centenarians who can maintain a good health phenotype and continue to play a useful role at the social and family levels is imperative. Therefore, despite progress in global research on centenarians, much work remains.

The major limitation of this study was the analysis of only the Scopus database. However, Scopus covers a wider journal range and provides help in keyword search and citation analysis.⁴⁵⁾ Additionally, the metadata recorded in the database is inherently biased. However, we standardized the analysis and performed manual reviews to reduce the margin of error.

In conclusion, global research on centenarians has grown over the last 20 years, primarily led by Italy, the United States, and China. However, research in Latin American and African countries is scarce. The most studied topics are mortality, cognition, immunosenescence, and genetics. Approximately 85% of the authors published up to two documents, indicating the absence of a continuous line of research on centenarians. Moreover, scientific collaboration is necessary to share data, create biorepositories, and robustly answer questions to identify the factors and determinants of successful and healthy aging.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, IDLM; Data curation, IDLM, MCDG; Investigation and Methodology, IDLM, SCT, JMA; Writing–original draft, IDLM, MCDG, SCT, JMA; Writing–review & editing, IDLM, MCDG, SCT, JMA.

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