nutrición clínica y Dietética Hospitalaria

Artículo Original

Nutr Clín Diet Hosp. 2024; 44(3):131-141
DOI: 10.12873/443murillo

Worldwide research on calorie restriction in aging. A bibliometric study

Antonio Fernando MURILLO-CANCHO[1], David LOZANO-PANIAGUA[1], Francisco MANZANO-AGUGLIARO[2], Bruno José NIEVAS-SORIANO[1]

1 Department of Nursing, Physiotherapy, and Medicine, University of Almeria.
2 Department of Engineering, University of Almeria.

Recibido: 31/mayo/2024. Aceptado: 17/junio/2024.

ABSTRACT

Background: Human aging is often associated with diseases that limit quality of life. Therapeutic anti-aging interventions, such as calorie restriction, can slow its progression. Analyzing the main areas of interest in the scientific literature allows us to understand the trends in research on calorie restriction in aging. This research aimed to conduct a comprehensive bibliometric analysis to determine the approaches and areas of research activity related to studying calorie restriction in aging and its use as a therapeutic intervention to slow its development.

Methods: A bibliometric analysis was conducted based on publications deposited in Scopus using its API and VOSViewer.

Results: A total of 5565 published documents were reviewed. The main keywords were analyzed and grouped into five study groups: risk factors and pathological consequences, biochemical mechanisms linked to caloric restriction and aging, experimental issues and clinical studies, functional aspects of the cell and caloric restriction, and his experimental study. The study shows the trend of increasing publications. Most of these articles are written in English and published in the United States.

Conclusions: Calorie restriction in aging is a topic of interest to researchers, and more research is needed to improve its understanding and therapeutic application.

KEYWORDS

Calorie restriction; aging; bibliometric, medicine antiaging, worldwide research.

INTRODUCTION

Human longevity is increasing globally, particularly in more developed countries. It is essential to ensure that people live longer and enjoy a high quality of life. The "anti-aging medicine" field aims to implement various studies to develop effective strategies for clinically slowing or limiting the aging process[1].

One of the most effective therapeutic interventions for delaying aging is dietary-metabolic modulation. This method generally involves restricting energy or nutrient intake while ensuring the individual does not experience malnutrition. This aspect is a priority, as it could negatively affect the individual's health[2].

The support for these strategies is based on their impact on various metabolic pathways studied to promote longevity in experimental models[3]. These pathways are responsible for the different physiological adaptations related to improvements in health.

Calorie restriction, a dietary intervention that involves reducing energy intake without causing malnutrition, holds immense potential. It is a well-researched non-genetic, non-pharmacological approach that has been shown to extend lifespan and promote health in experimental animals, sparking curiosity about its potential in humans.

Implementing energy restriction offers a ray of hope to individuals, providing enhanced protection against pathophysiological changes[4] to aging. This includes heart and metabolic health, neurodegeneration, obesity, and cancer, instilling opti-

Correspondencia:
Antonio Fernando Murillo Cancho
afmurillo@ual.es

mism about the potential of calorie restriction as a therapeutic intervention.

The aging process affects the long human lifespan, various lifestyle habits, and non-physiological factors such as customs, culture, and socioeconomic conditions. However, it is challenging to assess the effectiveness of calorie restriction as a therapeutic tool for extending life. However, it is possible to improve overall health by following a diet with moderate energy restriction and balanced nutrients.

While there is limited and recent clinical research on controlled calorie restriction in humans, it is crucial to emphasize the need for more comprehensive and long-term studies. This urgency is underscored by the fact that certain important epidemiological aspects, such as mortality and longevity, have not been clearly defined yet.

Several clinical trials are being developed to evaluate various aspects of energy re-striction and its benefits in slowing the progression of age-related pathologies. Other factors related to good health have also been confirmed, including improved sleep quality, better mood, and increased sexual appetite. However, a lower mineral density in the bones was observed[5,6].

Caloric restriction and other dietary modifications have gained popularity for their potential health benefits. To date, no bibliometric analysis has examined the patterns of scientific literature in this area, which could help guide the development of future research. Bibliometric analysis is a valuable tool for quantitatively evaluating and interpreting literary production across various fields of study. This study method uses statistical techniques to analyze multiple publications, extracting useful information about patterns and trends in scientific research. Using bibliometric analysis makes it possible to obtain quality information on relevant publications, the direction of re-search trends in that field, and even the discovery of gaps or potholes in the development of research that are not detectable in any other way.

This research aimed to conduct a comprehensive bibliometric analysis to determine the approaches and areas of research activity related to studying calorie restriction in aging and its use as a therapeutic intervention to slow its development.

MATERIALS AND METHODS

To conduct this study, we searched the Scopus database and used its API to locate the articles published up to March 2024. Our research strategy was ((TITLE-ABS-KEY ("caloric restriction") AND TITLE-ABS- KEY (aging)). The data was recovered in April 2024.

The scientific clusters were analyzed based on keywords and the connections between countries or authors using the VOSViewer software version 1.6.20, which allows the construction of graphic representations of the relative distribution of bibliometric elements.

The software allows the analysis of the coexistence of keywords by graphically representing the relationships between keywords in a set of data or texts of the same type, such as selected scientific articles.

The processing of the information carried out makes it possible to identify different re-search groups and point out elements of high research productivity that make it possible to mark trends in research and its direction, providing interesting information.

The possibility of having a representation between keywords facilitates the identification and analysis of the most important themes of a set of texts, which, among other things, can serve to focus new research.

RESULTS

The search retrieved 5565 publications, which were analyzed in various aspects: research trends, distribution by countries and institutions, types of documents and languages, thematic category, sources and authors, country collaboration network, and keywords.

Research trends

The search for documents initially had a limited amount of time on production (Figure 1a). Research results on the subject were published regularly from 1998 onwards.

There has been a clear publishing trend since 2000, with the highest number of publications reached in 2013: 285. This trend has been consistent, with more than 200 literary contributions produced each year from 2006 to 2023, indicating that this is an emerging area of research.

The slight decrease in the years 2022 and 2023 is not very significant. This is especially true when considering that 86 articles were published in the first quarter of 2024 alone. This suggests that there may have been an extensive literary contribution throughout this year, confirming the positive trend in research interest in this subject.

3.2. Distribution by countries and institutions

The data we extracted indicates that at least 73 countries and 160 institutions have participated in contributing literature on the topic of study. Figure 1b shows the 15 nations that have published the most articles.

Seven countries published over 250 articles: the United States, Italy, and the United Kingdom were the most productive, contributing 2,925, 420, and 398, respectively. They comprise 52.6%, 7.54%, and 7.15%, over half of all global publications.

The most surprising thing about these results is China's remarkable capacity for literary production, which, in the first four months of 2024, has published practically half of the articles it produced throughout 2023.

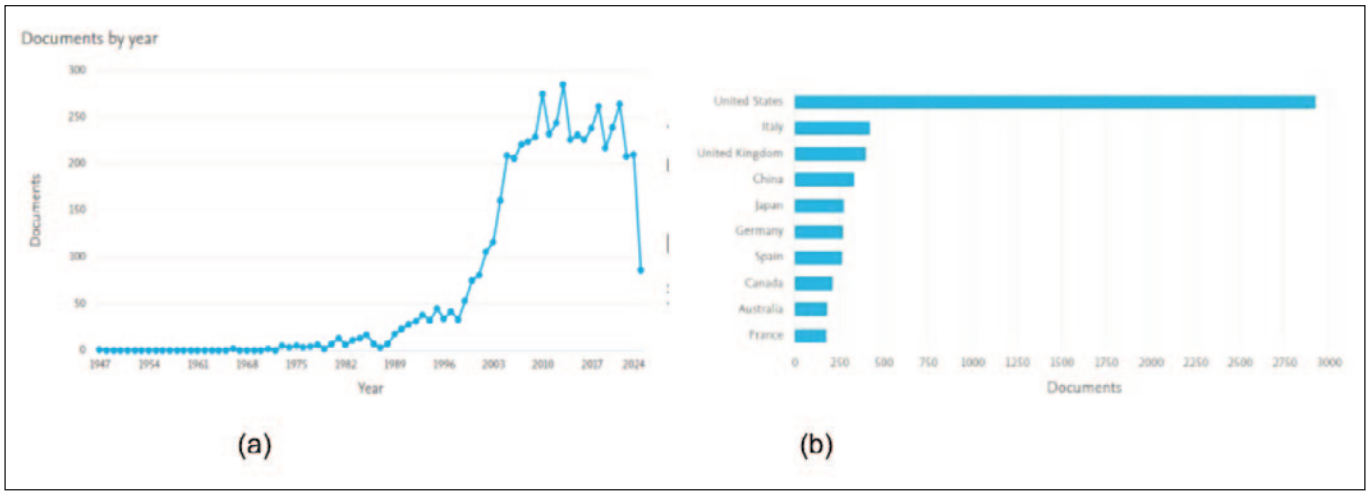

Figure 1. a) The trend over time in publications on calorie restriction in aging
b) Publications by country (15 most productive countries)

The top 15 institutions that have published the most on this subject are in North America. Specifically, the institution with the highest affiliation contributing to the literature is the National Institute on Aging (NIA) (4%), followed by the University of Texas Health Sciences Center at San Antonio (3.45%) and the National Institutes of Health (NIH) (3.36%).

The first non-American institution that appears in the ranking of the most literary productive on the subject in question is The University of Sydney, which is in 21st place in the ranking above.

Regarding citations, it's important to note that a group of authors from various European institutions has the most significant citations, totaling 10,875.

Table 2 displays the top ten most cited documents analyzing calorie restriction. Interestingly, none of them belong to the institutions with the most publications on the subject.

Table 1. Publications made by the institutions

Affiliation	Documents
National Institute on Aging (NIA)	224
University of Texas Health Science Center at San Antonio	192
National Institutes of Health (NIH)	187
Joe R. & Teresa Lozano Long School of Medicine	164
University of Wisconsin-Madison	161
University of Wisconsin School of Medicine and Public Health	139
Harvard Medical School	129
Pennington Biomedical Research Center	120
William S. Middleton Memorial Veterans Hospital	102
Washington University School of Medicine in St. Louis	94
Others	4.053

Types of documents and languages

The analysis of the published documents (Table 4) reveals that articles (55.5%) are the most frequently occurring document type, followed by reviews (29.8%). Conference papers (3.6%), book chapters (3.0%), editorials (2.7%), short surveys, (2.5%), notes (2.2%) and other document types collectively represent less than 0.7% of the analyzed records, indicating their lower frequency.

The analyzed documents have been written in 19 different languages. English is the most frequent language (97.2%). However, many publications appear in other languages, mainly French, Japanese, German, Chinese, and Spanish (1.9%). The remaining languages (<1%) include Russian, Italian, Ukrainian, Czech, Hungarian, Portuguese, Polish, Korean, Swedish, Persian, Malay, Greek, and Croatian. This diversity is not an issue for indexing in Scopus since it only requires that the title, abstract, and keywords be published in English, which is necessary for locating the publications.

Thematic category

The analysis considered various thematic areas within literary production on the subject. Most publications were in the field of biochemistry (40.0%), followed by medicine (28.6%). Other thematic areas such as were also represented although

Table 2. Most cited documents that analyze calorie restriction

Title	Authors	Year	Citations	Country
Free radicals and antioxidants in normal physiological functions and human disease	Valko, N. et al.	2.007	10,875	EUR
Oxidants, antioxidants, and the degenerative diseases of aging	Ames, B.N. et al.	1.993	5.573	USA
Resveratrol improves health and survival of mice on a high-calorie diet	Baur, J.A. et al.	2.006	3,802	USA
Mitochondria, oxidants, and aging	Balaban, R.S. et al.	2.005	3.576	USA
Small molecule activators of sirtuins extend Saccharomyces cerevisiae lifespan	Howitz, K.T. et al.	2.003	3.301	USA
Nutrient control of glucose homeostasis through a complex of PGC-1α and SIRT1	Rodgers, J.T et al.	2.005	2.715	USA
Oxidative stress, caloric restriction, and aging	Sohal, R.S., Weindruch, R.	1.996	2.694	USA
Extending healthy life span from yeast to humans	Fontana, L. et al.	2.010	2.287	USA
The human intestinal microbiome in health and disease	Lynch, S.V., Pedersen, O.	2.016	2.185	USA
Oxidative damage and mitochondrial decay in aging	Shigenaga, M.K., Hagen, T.M., Ames, B.N.	1.994	1.875	USA

to a lesser extent, neuroscience (6.8%), nursing (5.4%), and pharmacology (3.5%). Mathematics and engineering had the lowest participation.

Sources and authors

During the period under review, we analyzed various journals that have published articles on calorie restriction and aging to assess research trends. This analysis allowed us to obtain valuable information on the results approach, quality, and visibility. In total, 159 journals have published articles on this topic. Table 3a lists the top ten journals where scientific collaborations have been published.

The scientific journals included in this analysis have each published more than 70 articles on the topic being studied. The provided table displays the ranking of these journals based on the total number of publications and the citations received for their contributions. The table also presents the leading bibliometric indicators for the top ten journals under review. It is worth noting that 4 of the top 10 WoS-JCR journals in this field are in the first quartile, while another four are in the second quartile, underscoring the significance of the researched topic. Regarding the number of publications, Experimental Gerontology leads the way, with 25% more publications than the next journal in the ranking, Mechanisms Of Aging And Development.

The author who contributed the most published documents (as shown in Table 3b) was D.K. Ingram from the Pennington Biomedical Research Center in Baton Rouge, United States, followed by R. Weindruch from the University of Wisconsin School of Medicine and Public Health in Madison, United States. The author with the highest h-index (104) is Rafael De Cabo, who ranked sixth on the list of authors with the most published documents.

The analysis of the collaboration network among authors who have contributed more than 20 documents to the scientific literature is shown in Figure 4. The figure illustrates nine clusters, with the largest being red, including eleven authors, with Rafael De Cabo as a central member. The second most significant group is green, with five authors, followed by blue, yellow, and purple, each composed of four authors. Lastly, there are four groups - brown, cyan, orange, and light blue - each of 2 authors. Figure 2 displays the collaboration networks among authors with more than 20 documents on this topic.

Country Collaboration Network

A collaboration network has been established to show the countries of origin of the institutions responsible for the different research Figure 3 display the countries for each group and the leading country for each study.

The key countries in this collaboration network are the United States, United Kingdom, China, Spain, Italy, Germany, and South Korea. The largest group is led by the United Kingdom, which maintains strong connections with other Central European countries while being linked to other nations, particularly the United States.

Table 3a. Top ten journals where scientific collaborations have been published

Source Title	N	ISSN	SJR	SNIP	CS	JCR	IF
Experimental Gerontology	274	0531-5565	0.937	1.017	6.7	Q_2	3.9
Mechanisms of Ageing and Development	203	0047-6374	1.380	1.124	9.9	Q_2	5.3
Journals of Gerontology Series A Biological Sciences and Medical Sciences	194	1079-5006	1.703	1.522	9.9	Q_2	5.1
Aging Cell	182	1474-9718	2.738	1.580	15.0	Q_1	7.8
Ageing Research Reviews	109	1568-1637	3.007	2.673	17.5	Q_1	31.1
Biogerontology	104	1389-5729	0.907	0.969	8.3	Q_2	4.5
Age*	95	0161-9152			6.5	Q_1 (2018)	
Aging**	90	0394-9532					
Annals of The New York Academy of Sciences	73	0077-8923	1.626	1.878	11.0	Q_1	4.0
Rejuvenation Research	71	1549-1684	0.522	0.724	5.4	Q_3	2.6

* Since 2017, known as GeroScience ISSN: 2509-2715 CS 9.6 SJR 1,570 SNIP 1,199 Q2 1.26 IF.
** Since 1989 known as Aging clinical and experimental research ISSN:1594-0667 CS 7.3 SJR 0.982 SNIP 1.306 Q2 0.83 IF.

Table 3b. Top 10 authors on caloric restriction in aging research

Rank	Author	N	h-index	Affiliation, Country	Most contributed topics [2018-2022)
1	Ingram, D.K	99	83	Pennington Biomedical Research Center, Baton Rouge, United States	Caloric Restriction; Animals; Fasting
2	Weindruch, R.	97	78	University of Wisconsin School of Medicine and Public Health, Madison, United States	Caloric Restriction; Animals; Fasting
3	Bartke, A.	75	86	SIU School of Medicine, Springfield, United States	Somatotropin Receptors; Animals; Laron Syndrome
4	Roth, G.S.	69	64	Prolongevity Technologies LLC, Pylesville, United States	Caloric Restriction; Animals; Fasting
5	Leeuwenburgh, C.	62	89	University of Florida College of Medicine, Gainesville, United States	Intermittent Claudication; Ankle Brachial Index; Peripheral Arterial Disease
6	De Cabo, R.	59	104	National Institute on Aging [NIA) Bethesda, United States	Caloric Restriction; Animals; Fasting
7	Lane, M.A.	57	47	National Institute on Aging [NIA), Bethesda, United States	
8	Fontana, L.	52	70	Faculty of Medicine and Health, Sydney, Australia	Caloric Restriction; Animals; Fasting
9	Chung, H.Y.	51	79	Pusan National University, Busan, South Korea	Melanogenesis; Monophenol Monooxygenase; Extract
10	Yu, B.P.	49	60	University of Texas Health Science Center at San Antonio, United States	Signal Transduction; Group III Histone Deacetylasis; Srt1720

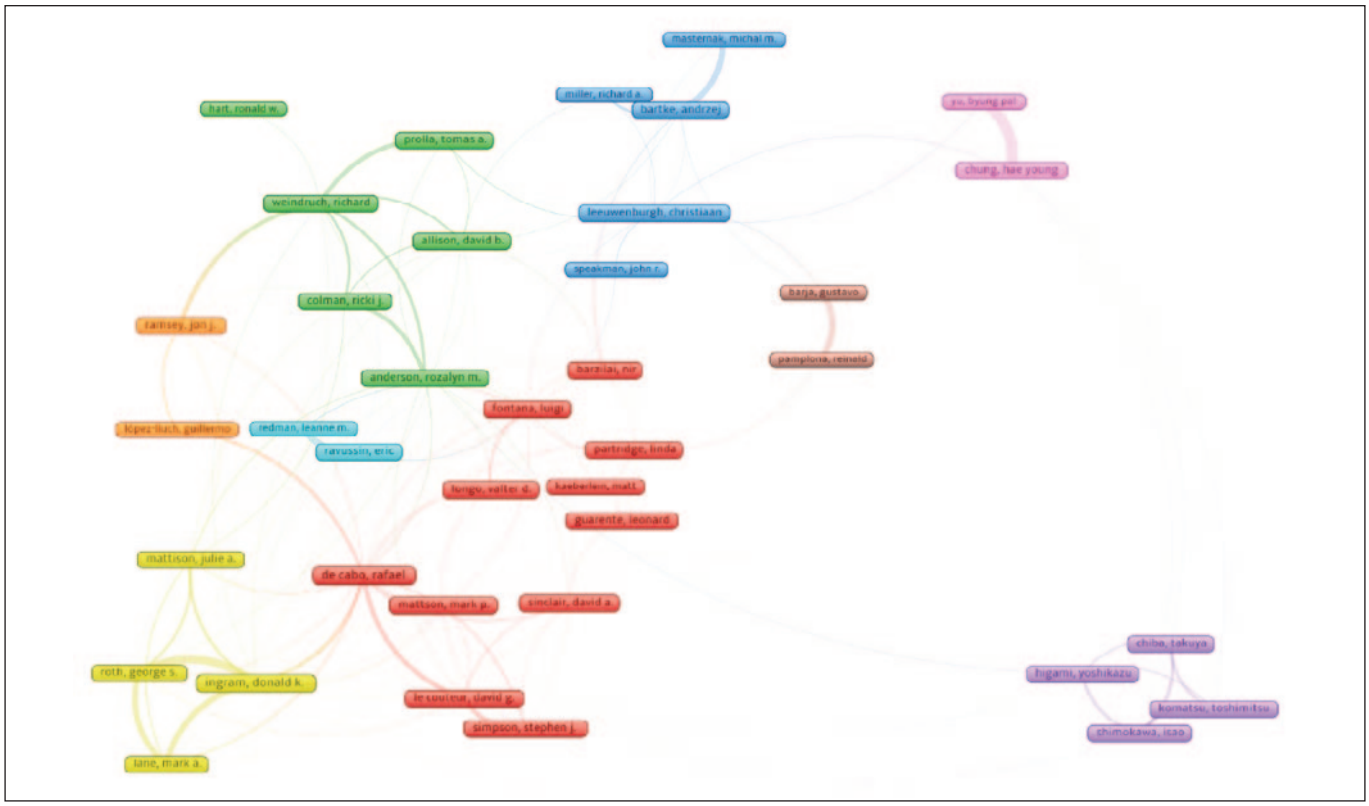

Figure 2. A network of authors who have published more than 20 articles on calorie restriction and aging

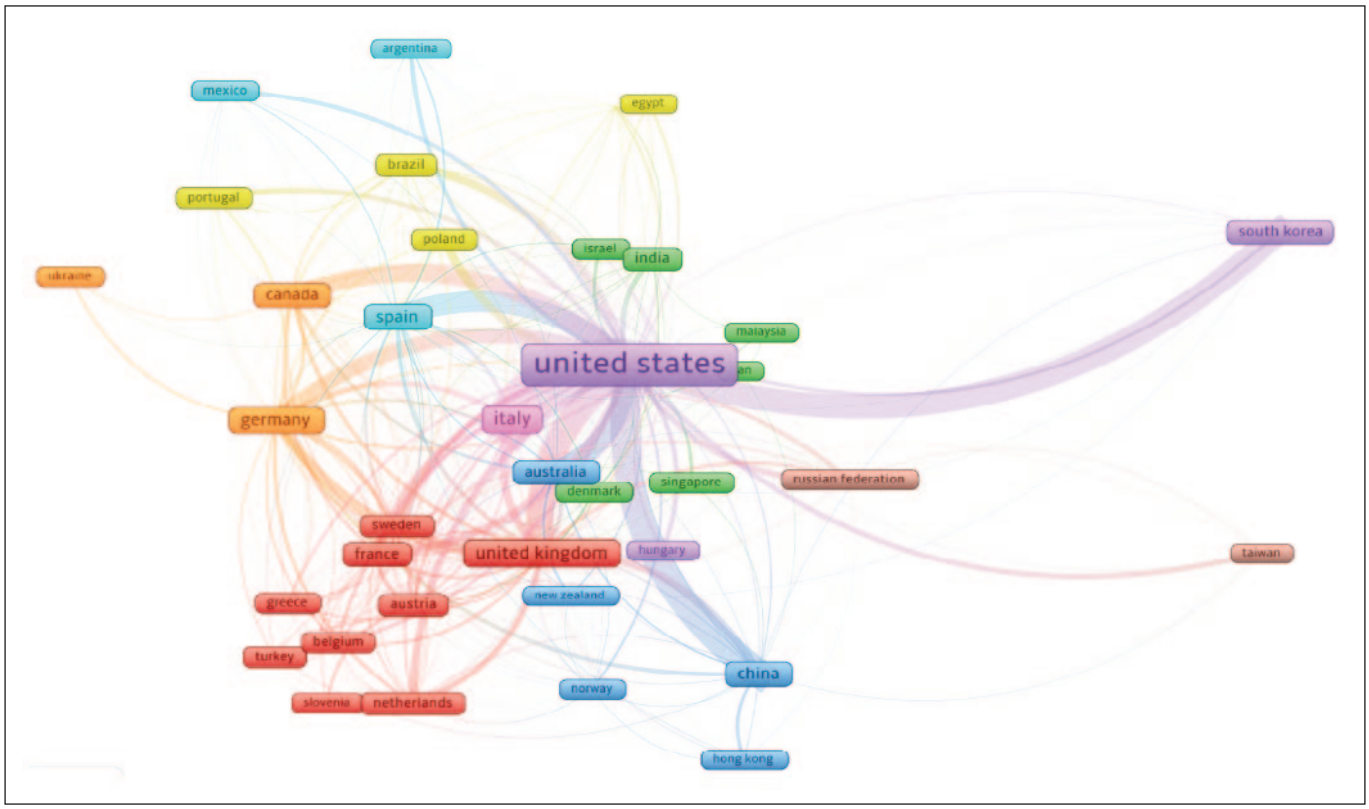

Figure 3. Countries network collaboration

The first group, led by China, cooperates with nearby countries such as Australia, New Zealand, and the United States. The second group, led by India, includes Israel, Malaysia, and Denmark. The third group, led by Germany, collaborates with Canada, the United States, and the United Kingdom. The fourth group, led by Spain, has connections with practically all the participating nations in this research.

However, the United States is the clear leader in directly connecting with the world's leading research nations. Also, to a lesser extent, there are small groups led by Russia and Italy.

Keywords

The primary keywords in the documents have been analyzed, including protein, aging, cell, calorie restriction, metabolism, longevity, priority, transcription, human, animal, and gene. A word cloud has been created to identify the most frequently used keywords in each topic efficiently. This approach has the potential to uncover areas within the field of research that need further attention and highlight those that are heavily researched from a bibliometric standpoint.

The keywords related to the research analyzed here have evolved, as shown in Figure 4a. The graph uses the size of the term to indicate its occurrence in a certain period and the color it has. More guides about the occurrence were provided during the period studied.

Our research found that older documents often contain keywords like body weight, animal experiment, body fat, and diet reduction. In contrast, recent publications feature sirtuin, metformin, frailty, epigenesis, genetics, life extension, and intermittent fasting.

A network has been created with the main keywords used by the different research communities on the topic under study (Figure 4 b). In the graphic representation, the keywords are grouped into clusters of various colours depending on their defining keywords the green cluster groups terms related to the biochemical mechanisms linked to caloric restriction and aging. The blue cluster refers to words that point to aspects associated with experimental issues and clinical studies.

The red cluster is connected to topics related to risk factors and pathological consequences. The yellow cluster is associated with the functional aspects of the cell. Finally, the purple cluster encompasses words directly linked to calorie restriction and its study in experimental animals. A detailed description of the clusters with their keywords is shown in Table 4.

DISCUSSION

The main aim of this study was to analyze the scientific advances related to calorie re-striction and aging. The bibliometric analysis includes all scientific and literary pro-duction to provide information on research trends, institutions, and countries. A total of 5565 publications, including 3089 articles and 1658 reviews, were included in this study. Publications in this field showed an increasing trend starting in 1999, reaching peak production in 2013. As far as we know, this is the first bibliometric analysis study specifically focused on caloric (energy) restriction and its relationship with the biological aging process.

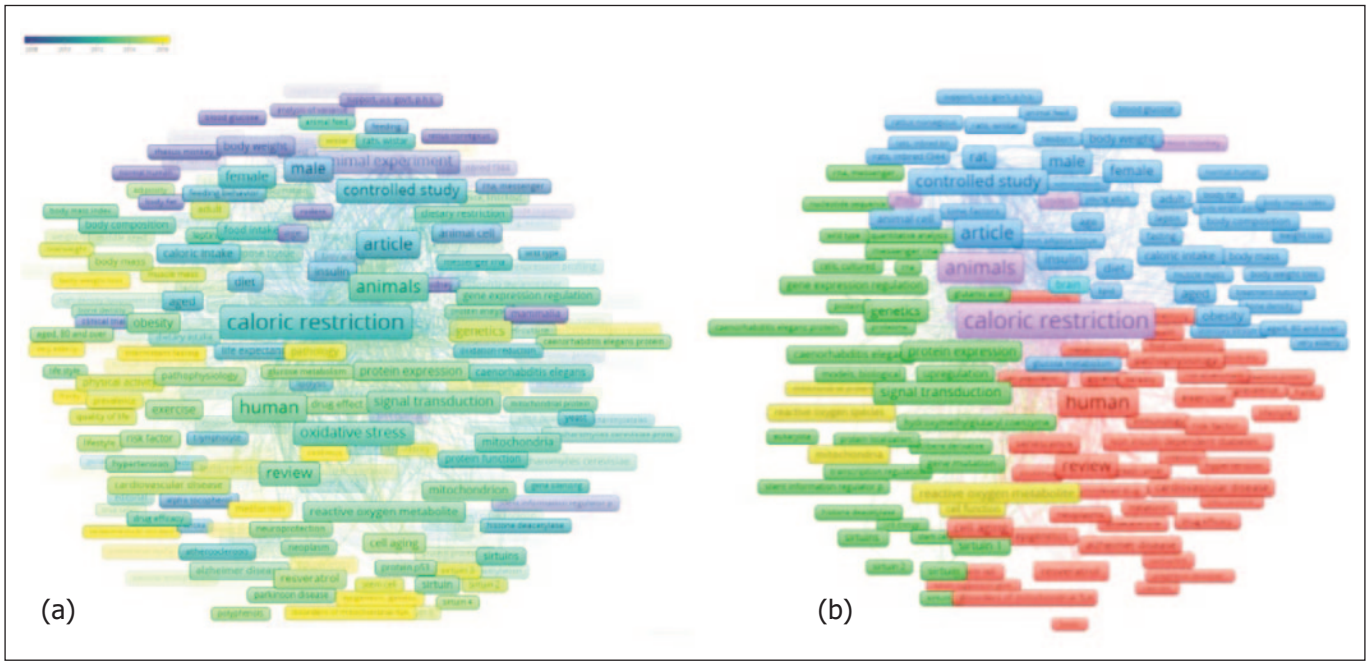

Figure 4. a) Evolution trend of keywords on calorie restriction in aging publications
b) Network of keywords on calorie restriction in aging publications

Table 4. The main keywords used by the communities detected the topic of calorie re-striction in aging

Colour Cluster	Keywords by cluster	Main Keywords	Topic
Red	382	Human/humans, review, inflammation, pathophysiology, senescence, degenerative disease	Risk factors and pathological consequences
Green	248	Signal transduction, protein expression, enzyme activity, gene expression, genetics	Biochemical mechanisms linked to calorie restriction and aging
Blue	216	Controlled study, male, female, article, animal cell, caloric intake, insulin, aged, animal experiment	Experimental issues and clinical studies
Yellow	82	Oxidative stress, reactive oxygen metabolite, mitochondria, reactive oxygen species	Functional aspects of the cell
Purple	67	Caloric restriction, priority journal, animals, nonhuman, longevity, life span, mouse	Calorie restriction and its experimental study

Most of the contributions consist of original articles in biochemistry and medicine written in English. The authors come from 160 different research centers in over 70 countries. The leading institutions in terms of literary production on this subject are the National Institute on Aging (NIA), the University of Texas Health Science Center at San Antonio, the National Institutes of Health (NIH), Joe R. & Teresa Lozano Long School of Medicine, University of Wisconsin-Madison, University of Wisconsin School of Medicine and Public Health, and Harvard Medical School. The most significant sci-entific production in this field comes from research centers in universities and medical schools, primarily in the United States. The United States publishes the most publications by a wide margin, leading to most institutions and citations related to this subject being from the United States.

A total of 159 authors contributed to this field. The most productive were Ingram, K., Weindruch, R., Bartke, A. Roth, G.S., Leeuwenburgh, C., and De Cabo, R., All with affiliations to American research centers.

When studying the effects of calorie restriction on aging, it's interesting to observe how the keywords associated with this topic have evolved. The earlier studies focused on experimental methods and included terms like age, animal experiment, mammalian, rodent, and body weight. However, in more recent research, there is a shift towards using terms such as sirtuins, epigenesis, genetic intermittent fasting, and disorders of mitochondrial function. The recent publications show a significant change in focus. They are now more interested in the mechanisms of action of calorie restriction and its potential benefits in aging, such as the role of sirtuins[7]. Likewise, the documents focus on studying physiological factors related to cells, such as mitochondrial dysfunction in aging[8] or epigenetic effects[9].

One objective of a bibliometric study is to analyze the keywords used by researchers in published documents and identify any connections between them. This aspect helps determine the scientific groups into which the different subjects of a study can be categorized[10,11].

The study of calorie restriction in aging often involves research on experimental animals such as nonhumans, mice, Drosophila, or C. elegans. This finding can be explained because testing dietary interventions focused on aging in humans is complex due to the long duration of human life and other factors that can influence aging independently of diet. Therefore, conducting numerous tests on experimental animals is necessary for this research[12].

When studying the keywords associated with the leading countries that have made significant contributions to scientific literature in this field, it is evident that the most prevalent ones are Caloric Restriction, Aging, Nonhuman, Animals, and Human.

The analysis of keyword clusters enables their classification into distinct groups based on research trends[13]. The subjects are grouped into five categories in our study. The most important one is "red," linked to risk factors and pathological consequences in aging. The keywords used guide toward the indicated topic and include terms such as human/humans, review, inflammation, pathophysiology, senescence, and degenerative disease. Aging is a degenerative physiological process that originates from various biological factors[14] that imply the appearance of associated pathological problems due to different impairments in molecular and cellular functions[15,16] that represent a deterioration in the quality of life of individuals. In the literature produced by this group, we also observe the presence of keywords related to oncological processes and degenerative diseases[17,18], as these pathological events share some biological mechanisms[19,20].

The cluster highlighted in green is the second most important based on the number of publications contributed. These documents study the biochemical mechanisms related to

calorie restriction and aging. Within this cluster, keywords such as sirtuin, signal transduction, protein expression, and longevity are prevalent. Calorie restriction is an intervention that can modulate metabolic processes associated with aging, with sirtuins playing a prominent role, for example[21,22]. Understanding the mechanisms involved in the aging process and its associated diseases is essential for designing interventions to limit it, such as calorie restriction[23,24]. Metabolic signaling pathways[25,26] are a primary focus in understanding how to reduce the impact of aging on individuals.

The next most important group is the blue one related to experimental issues and clinical studies. The main terms that appear as keywords are controlled study, male, female, article, animal cell, caloric intake, insulin, aged, and animal experiment. The effects of potential interventions to limit the effects of aging, such as calorie restriction, can be measured and analyzed[27,28]. This group includes certain words, such as insulin, which are closely linked to the metabolic changes resulting from calorie re-striction[29], and caloric intake, which refers to the energy amount ingested through the diet[30,31,32]. We can expect new research on this topic in the coming years, as one of the most significant interests is to demonstrate the effectiveness of these dietary proposals in limiting the adverse effects of aging.

The fourth most important group, concerning the presence of keywords, has a much lower number than the previous ones. This group focuses on studying the functional aspects of the cell, including topics such as oxidative stress, reactive oxygen metabolite, mitochondria, and reactive oxygen species. Although this topic is related to the mechanisms of aging, which are primarily studied in another cluster, this group re-searches specific aspects of abnormal cellular functioning energy generation and the damage that can affect cells[33]. They also discuss the investigation of oxidative processes[26,34] as limiting factors in mitochondrial functionality that cause an abnormal metabolic response. Naturally, words related to antioxidant activity, such as manganese superoxide dismutase, are mentioned, as this action protects cells from damage caused by oxidizing agents that disturb mitochondrial functionality[35,36].

The purple group primarily researches caloric restriction and its impact on longevity, particularly in experimental animal models. The main keywords used in their research include caloric restriction, priority journal, animals, nonhuman, longevity, life span, and mouse. Since human life spans are too long to accurately measure the effects of different interventions on longevity and life expectancy, keywords such as mouse, animal, or nonhuman are used, as studies are conducted on much shorter-lived experimental animals, allowing for better evaluation of the interventions[37,38]. Relating caloric restriction to lifespan or longevity is another area of interest for this re-search group, as it seeks to assess the effectiveness of various dietary strategies in aging[39,40]. We understand that extensive knowledge will soon be generated in this regard due to the conclusion of clinical trials showing their results in this field for the blue group.

Limitations and strengths

This research has some limitations. Despite being methodologically precise, it is impossible to guarantee that all documents have been extracted for production. The key-words used have attempted to cover most of the literature, although we understand that it is only sometimes possible when it comes to a topic as specific as the one that is the object of the study. This search could have been expanded by modifying the equation for this purpose and introducing other terms such as treatment or anti-aging effect. Still, we have considered the formula valid because it better adapts to the true meaning of the intended bibliometric evaluation. Furthermore, it can sufficiently define the search, as other bibliometric studies have similarly proposed, providing ap-propriate information to establish research trends in the chosen area. The quality of the documents analyzed was not a primary focus as they were not the main subject of the study. However, we acknowledge that the database from which the publications were retrieved ensures their quality. The scientific impact of the obtained documents should have been explicitly considered. Still, efforts were made to demonstrate the significance of the leading publishing journals we collaborated with, as they are ranked in the first two quartiles (9 out of 10) in terms of impact.

This study also has some strengths. The methodology used is not only rigorous but also systematic, a standard approach employed in many other areas of knowledge and published after review by prestigious publishers. This systematic and rigorous approach, combined with the use of Scopus as a database for document extraction, ensures the quality and credibility of the results obtained. Therefore, we believe that this study could serve as a solid foundation for future analyses to observe the progress of research trends in the chosen subject.

CONCLUSIONS

Although scientific literary production has decreased slightly in the last two years, there has been exciting progression during the first quarter of this year, and this trend is expected to continue. Additionally, different studies and clinical trials in humans regarding the analyzed topic are being concluded, and the publication of their results is likely to lead to an increase in published documents in the coming months.

The bibliometric analysis of caloric restriction in aging identified several research groups with different approaches within the literature. The study of risk factors and pathological consequences, biochemical mechanisms linked to caloric restriction, functional aspects of the cell, and the study of experimental calorie restriction are the most prominent.

New approaches will likely appear in the investigation of calorie restriction in aging, providing new dietary formulas, supported or not, in the presence of nutraceutical supplements that facilitate the completion and development of this as an effective therapeutic intervention capable of limiting the incidence of pathological events typical of advanced age. This is relevant to reduce the morbidity and mortality that aging produces. This research aims to minimize the frailty of older adults, improve their quality of life, and reduce the economic and social costs associated with aging and the dependency that it causes in older people.

Direct research toward assessing the economic and social cost of interventions focused on reducing the effects of aging to understand their potential impact on society. More studies are needed to address specific gaps in our knowledge, such as applying optimal dietary-nutritional interventions about caloric restriction and assessing their long-term results in the human race.

These findings are essential for understanding the research on calorie restriction in aging and determining future study trends.

REFERENCES

1. Ok, S.-C. Insights into the Anti-Aging Prevention and Diagnostic Medicine and Healthcare. Diagnostics (Basel) 2022, 12, doi:10.3390/diagnostics12040819.
2. Ros, M.; Carrascosa, J.M. Current Nutritional and Pharmacological Anti-Aging Interventions. Biochim Biophys Acta Mol Basis Dis 2020, 1866, 165612, doi:10.1016/j.bbadis.2019.165612.
3. Green, C.L.; Lamming, D.W.; Fontana, L. Molecular Mechanisms of Dietary Restriction Promoting Health and Longevity. Nat Rev Mol Cell Biol 2022, 23, 56–73, doi:10.1038/s41580-021-00411-4.
4. Fukuoh, T.; Nozaki, Y.; Mizunoe, Y.; Higami, Y. [Regulation of Aging and Lifespan by White Adipose Tissue]. Yakugaku Zasshi 2024, 144, 411–417, doi:10.1248/yakushi.23-00165-4.
5. Most, J.; Gilmore, L.A.; Smith, S.R.; Han, H.; Ravussin, E.; Redman, L.M. Significant Improvement in Cardiometabolic Health in Healthy Nonobese Individuals during Caloric Restriction-Induced Weight Loss and Weight Loss Maintenance. American Journal of Physiology-Endocrinology and Metabolism 2018, 314, E396–E405, doi:10.1152/ajpendo.00261.2017.
6. Martin, C.K.; Bhapkar, M.; Pittas, A.G.; Pieper, C.F.; Das, S.K.; Williamson, D.A.; Scott, T.; Redman, L.M.; Stein, R.; Gilhooly, C.H.; et al. Effect of Calorie Restriction on Mood, Quality of Life, Sleep, and Sexual Function in Healthy Nonobese Adults. JAMA Intern Med 2016, 176, 743, doi:10.1001/jamainternmed.2016.1189.
7. Hall, J.A.; Dominy, J.E.; Lee, Y.; Puigserver, P. The Sirtuin Family's Role in Aging and Age-Associated Pathologies. Journal of Clinical Investigation 2013, 123, 973–979, doi:10.1172/JCI64094.
8. Madreiter-Sokolowski, C.; Sokolowski, A.; Waldeck-Weiermair, M.; Malli, R.; Graier, W. Targeting Mitochondria to Counteract Age-Related Cellular Dysfunction. Genes (Basel) 2018, 9, 165, doi:10.3390/genes9030165.
9. Hwangbo, D.-S.; Lee, H.-Y.; Abozaid, L.S.; Min, K.-J. Mechanisms of Lifespan Regulation by Calorie Restriction and Intermittent Fasting in Model Organisms. Nutrients 2020, 12, 1194, doi:10.3390/nu12041194.
10. Salmerón-Manzano, E.; Garrido-Cardenas, J.A.; Manzano-Agugliaro, F. Worldwide Research Trends on Medicinal Plants. Int J Environ Res Public Health 2020, 17, doi:10.3390/ijerph17103376.
11. Zupic, I.; Čater, T. Bibliometric Methods in Management and Organization. Organ Res Methods 2015, 18, 429–472, doi:10.1177/1094428114562629.
12. Ros, M.; Carrascosa, J.M. Current Nutritional and Pharmacological Anti-Aging Interventions. Biochim Biophys Acta Mol Basis Dis 2020, 1866, 165612, doi:10.1016/j.bbadis.2019.165612.
13. Niknejad, N.; Ismail, W.; Bahari, M.; Hendradi, R.; Salleh, A.Z. Mapping the Research Trends on Blockchain Technology in Food and Agriculture Industry: A Bibliometric Analysis. Environ Technol Innov 2021, 21, 101272, doi:10.1016/j.eti.2020.101272.
14. López-Otín, C.; Blasco, M.A.; Partridge, L.; Serrano, M.; Kroemer, G. Hallmarks of Aging: An Expanding Universe. Cell 2023, 186, 243–278, doi:10.1016/j.cell.2022.11.001.
15. Baechle, J.J.; Chen, N.; Makhijani, P.; Winer, S.; Furman, D.; Winer, D.A. Chronic Inflammation and the Hallmarks of Aging. Mol Metab 2023, 74, 101755, doi:10.1016/j.molmet.2023.101755.
16. Moskalev, A.A.; Shaposhnikov, M. V; Plyusnina, E.N.; Zhavoronkov, A.; Budovsky, A.; Yanai, H.; Fraifeld, V.E. The Role of DNA Damage and Repair in Aging through the Prism of Koch-like Criteria. Ageing Res Rev 2013, 12, 661–684, doi:10.1016/j.arr.2012.02.001.
17. Barzilai, N.; Ferrucci, L. Insulin Resistance and Aging: A Cause or a Protective Response? J Gerontol A Biol Sci Med Sci 2012, 67, 1329–1331, doi:10.1093/gerona/gls145.
18. Giunta, S. Exploring the Complex Relations between Inflammation and Aging (Inflamm-Aging): AntiInflammAging Remodelling of InflammAging, from Robustness to Frailty. Inflamm Res 2008, 57, 558–563, doi:10.1007/s00011-008-7243-2.
19. Hall, J.A.; Dominy, J.E.; Lee, Y.; Puigserver, P. The Sirtuin Family's Role in Aging and Age-Associated Pathologies. J Clin Invest 2013, 123, 973–979, doi:10.1172/JCI64094.
20. Szarc vel Szic, K.; Declerck, K.; Vidaković, M.; Vanden Berghe, W. From Inflammaging to Healthy Aging by Dietary Lifestyle Choices: Is Epigenetics the Key to Personalized Nutrition? Clin Epigenetics 2015, 7, 33, doi:10.1186/s13148-015-0068-2.
21. Wątroba, M.; Szukiewicz, D. The Role of Sirtuins in Aging and Age-Related Diseases. Adv Med Sci 2016, 61, 52–62, doi:10.1016/j.advms.2015.09.003.
22. Wątroba, M.; Dudek, I.; Skoda, M.; Stangret, A.; Rzodkiewicz, P.; Szukiewicz, D. Sirtuins, Epigenetics and Longevity. Ageing Res Rev 2017, 40, 11–19, doi:10.1016/j.arr.2017.08.001.
23. Lee, M.B.; Hill, C.M.; Bitto, A.; Kaeberlein, M. Antiaging Diets: Separating Fact from Fiction. Science 2021, 374, eabe7365, doi:10.1126/science.abe7365.

24. Green, C.L.; Lamming, D.W.; Fontana, L. Molecular Mechanisms of Dietary Restriction Promoting Health and Longevity. Nat Rev Mol Cell Biol 2022, 23, 56–73, doi:10.1038/s41580-021-00411-4.

25. Madeo, F.; Carmona-Gutierrez, D.; Hofer, S.J.; Kroemer, G. Caloric Restriction Mimetics against Age-Associated Disease: Targets, Mechanisms, and Therapeutic Potential. Cell Metab 2019, 29, 592–610, doi:10.1016/j.cmet.2019.01.018.

26. Bárcena, C.; Mayoral, P.; Quirós, P.M. Mitohormesis, an Antiaging Paradigm. In; 2018; pp. 35–77.

27. Martin, C.K.; Bhapkar, M.; Pittas, A.G.; Pieper, C.F.; Das, S.K.; Williamson, D.A.; Scott, T.; Redman, L.M.; Stein, R.; Gilhooly, C.H.; et al. Effect of Calorie Restriction on Mood, Quality of Life, Sleep, and Sexual Function in Healthy Nonobese Adults: The CALERIE 2 Randomized Clinical Trial. JAMA Intern Med 2016, 176, 743–752, doi:10.1001/jamainternmed.2016.1189.

28. Velingkaar, N.; Mezhnina, V.; Poe, A.; Makwana, K.; Tulsian, R.; Kondratov, R. V. Reduced Caloric Intake and Periodic Fasting Independently Contribute to Metabolic Effects of Caloric Restriction. Aging Cell 2020, 19, doi:10.1111/acel.13138.

29. Cypser, J.R.; Kitzenberg, D.; Park, S.-K. Dietary Restriction in C. Elegans: Recent Advances. Exp Gerontol 2013, 48, 1014–1017, doi:10.1016/j.exger.2013.02.018.

30. Green, C.L.; Lamming, D.W.; Fontana, L. Molecular Mechanisms of Dietary Restriction Promoting Health and Longevity. Nat Rev Mol Cell Biol 2022, 23, 56–73, doi:10.1038/s41580-021-00411-4.

31. Martucci, M.; Ostan, R.; Biondi, F.; Bellavista, E.; Fabbri, C.; Bertarelli, C.; Salvioli, S.; Capri, M.; Franceschi, C.; Santoro, A. Mediterranean Diet and Inflammaging within the Hormesis Paradigm. Nutr Rev 2017, 75, 442–455, doi:10.1093/nutrit/nux013.

32. Weiss, E.P.; Racette, S.B.; Villareal, D.T.; Fontana, L.; Steger-May, K.; Schechtman, K.B.; Klein, S.; Holloszy, J.O.; Washington University School of Medicine CALERIE Group Improvements in Glucose Tolerance and Insulin Action Induced by Increasing Energy Expenditure or Decreasing Energy Intake: A Randomized Controlled Trial. Am J Clin Nutr 2006, 84, 1033–1042, doi:10.1093/ajcn/84.5.1033.

33. Harman, D. Origin and Evolution of the Free Radical Theory of Aging: A Brief Personal History, 1954–2009. Biogerontology 2009, 10, 773–781, doi:10.1007/s10522-009-9234-2.

34. Yee, C.; Yang, W.; Hekimi, S. The Intrinsic Apoptosis Pathway Mediates the Pro-Longevity Response to Mitochondrial ROS in C. Elegans. Cell 2014, 157, 897–909, doi:10.1016/j.cell.2014.02.055.

35. Tavallaie, M.; Voshtani, R.; Deng, X.; Qiao, Y.; Jiang, F.; Collman, J.P.; Fu, L. Moderation of Mitochondrial Respiration Mitigates Metabolic Syndrome of Aging. Proceedings of the National Academy of Sciences 2020, 117, 9840–9850, doi:10.1073/pnas.1917948117.

36. Chen, G.; Kroemer, G.; Kepp, O. Mitophagy: An Emerging Role in Aging and Age-Associated Diseases. Front Cell Dev Biol 2020, 8, doi:10.3389/fcell.2020.00200.

37. Hodge, B.A.; Meyerhof, G.T.; Katewa, S.D.; Lian, T.; Lau, C.; Bar, S.; Leung, N.Y.; Li, M.; Li-Kroeger, D.; Melov, S.; et al. Dietary Restriction and the Transcription Factor Clock Delay Eye Aging to Extend Lifespan in Drosophila Melanogaster. Nat Commun 2022, 13, 3156, doi:10.1038/s41467-022-30975-4.

38. Rana, A.; Oliveira, M.P.; Khamoui, A. V.; Aparicio, R.; Rera, M.; Rossiter, H.B.; Walker, D.W. Promoting Drp1-Mediated Mitochondrial Fission in Midlife Prolongs Healthy Lifespan of Drosophila Melanogaster. Nat Commun 2017, 8, 448, doi:10.1038/s41467-017-00525-4.

39. Speakman, J.R.; Mitchell, S.E.; Mazidi, M. Calories or Protein? The Effect of Dietary Restriction on Lifespan in Rodents Is Explained by Calories Alone. Exp Gerontol 2016, 86, 28–38, doi:10.1016/j.exger.2016.03.011.

40. Campanella, A.; Misciagna, G.; Mirizzi, A.; Caruso, M.G.; Bonfiglio, C.; Aballay, L.R.; Vas de Arruda Silveira, L.; Bianco, A.; Franco, I.; Sorino, P.; et al. The Effect of the Mediterranean Diet on Lifespan: A Treatment-Effect Survival Analysis of a Population-Based Prospective Cohort Study in Southern Italy. Int J Epidemiol 2021, 50, 245–255, doi:10.1093/ije/dyaa222.