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# A bibliometric analysis of the Fasting-Mimicking Diet

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The Fasting-Mimicking Diet (FMD) is a nutritional strategy that involves significantly reducing calorie intake for a specific period to mimic the physiological effects of fasting while still providing the body with nutrition. Our study aimed to conduct a bibliometric study to explore the latest publishing trends and areas of intense activity within the sphere of FMD. We extracted data on FMD publications from the Web of Science Core Collection (WOSCC) database. The bibliometric analysis was conducted by WOSCC Online Analysis Platform and VOSviewer 1.6.16. In total, there were 169 publications by 945 authors from 342 organizations and 25 countries/regions, and published in 111 journals. The most productive country, organization, author, and journal were the United States, the University of Southern California, Valter D. Longo, and *Nutrients*, respectively. The first high-cited document was published in *Ageing Research Reviews* and authored by Mattson et al. In this study, they discuss the various health benefits of FMD including improved metabolic health, weight management, and even potential effects on delaying aging processes and reducing the risk of chronic diseases. In conclusion, our study is the first bibliometric analysis of the FMD. The main research hotspots and frontiers were FMD for cancer, FMD for metabolic-related diseases, and FMD for cognitive improvement. FMD may have some potential benefits for multiple diseases which should be further investigated.

## KEYWORDS

**Fasting-Mimicking Diet (FMD), bibliometric analysis, research hotspots, human health, adaptation**

## 1 Introduction

The Fasting-Mimicking Diet (FMD) is a dietary regimen designed to replicate the effects of traditional fasting while still allowing for food intake. This approach typically involves a significant reduction in calorie intake, with a specific focus on a low-protein, low-carbohydrate, and high-fat composition, rich in nutrients. FMDs are generally followed for short periods, typically ranging from 3 to 7 days, and are often repeated cyclically, such as monthly, to achieve ongoing benefits. The primary goals of an FMD are to trigger beneficial cellular and metabolic responses similar to those obtained through water-only fasting, such as improved metabolic health, reduced inflammation, and potential longevity benefits. FMD is recommended to be undertaken with medical supervision, particularly for individuals with existing health conditions or those on medications (1–16).

In recent years, FMD become more and more popular since it may have potential benefits for human health, including cancer and diabetes. However, there lacks a bibliometric analysis that consolidates existing publication patterns and forecasts emerging research focal points in

this domain. Bibliometric Analysis refers to the quantitative assessment and interpretation of scientific literature (17–19). It uses statistical methods to analyze articles, books, and other publications to provide insights into the patterns, structures, and trends in scientific research. Essentially, bibliometrics play a crucial role in deciphering the influence, distribution, and development of research across diverse fields. By employing bibliometric Analysis, one can gain clarity on pivotal articles, the trajectory of research trends, and the progressive unfolding of scientific concepts throughout history. In light of this, our study aimed to undertake an exhaustive bibliometric analysis to identify the leading edges and areas of concentrated research activity in the FMD field.

## 2 Methods

### 2.1 Data collection

Relevant literature pertaining to the FMD was systematically sourced from the Web of Science Core Collection (WoSCC). Recognized for its comprehensiveness and authority, WoSCC served as the primary database for this study. The search was delimited to documents published between 1 January 2000 and 15 September 2023. The specific search terms employed for this literature hunt were: “Fasting-Mimicking Diet” OR “Fasting-Mimicking Diets” OR “Fasting-Mimicking” OR “Fasting mimicking Diet” OR “Fasting mimicking Diets” OR “fasting mimicking.” The publications was exported in TXT format with “Full Record and Cited References.”

### 2.2 Bibliometric analysis and visualization

Once the data was compiled, the WoSCC Online Analysis Platform facilitated a detailed bibliometric analysis. This analysis centered around annual publication numbers, the top 10 in terms of productive countries/regions, authors, organizations, and journals, and spotlighted the top 20 high-citation publications. For a more visual representation and understanding of the data, VOSviewer 1.6.16 software was employed. The software enabled the mapping and visualization of several facets, such as co-authorships across institutions, countries/regions, and authors; citation patterns across journals and references; and co-occurrence patterns of keywords. The resultant visualizations, presented in the form of detailed maps and figures, were subsequently exported for further analysis and interpretation. In the analysis of keyword co-occurrence, we consolidated the synonyms “fasting mimicking diet” and “mimicking diet” under the single term “fasting-mimicking diet” for uniformity and clarity.

## 3 Results

### 3.1 Trends in global publications

Based on the provided data related to the FMD, a total of 169 documents were identified. Figure 1 illustrates the trend in publications, the variety of publication types, and the categories of

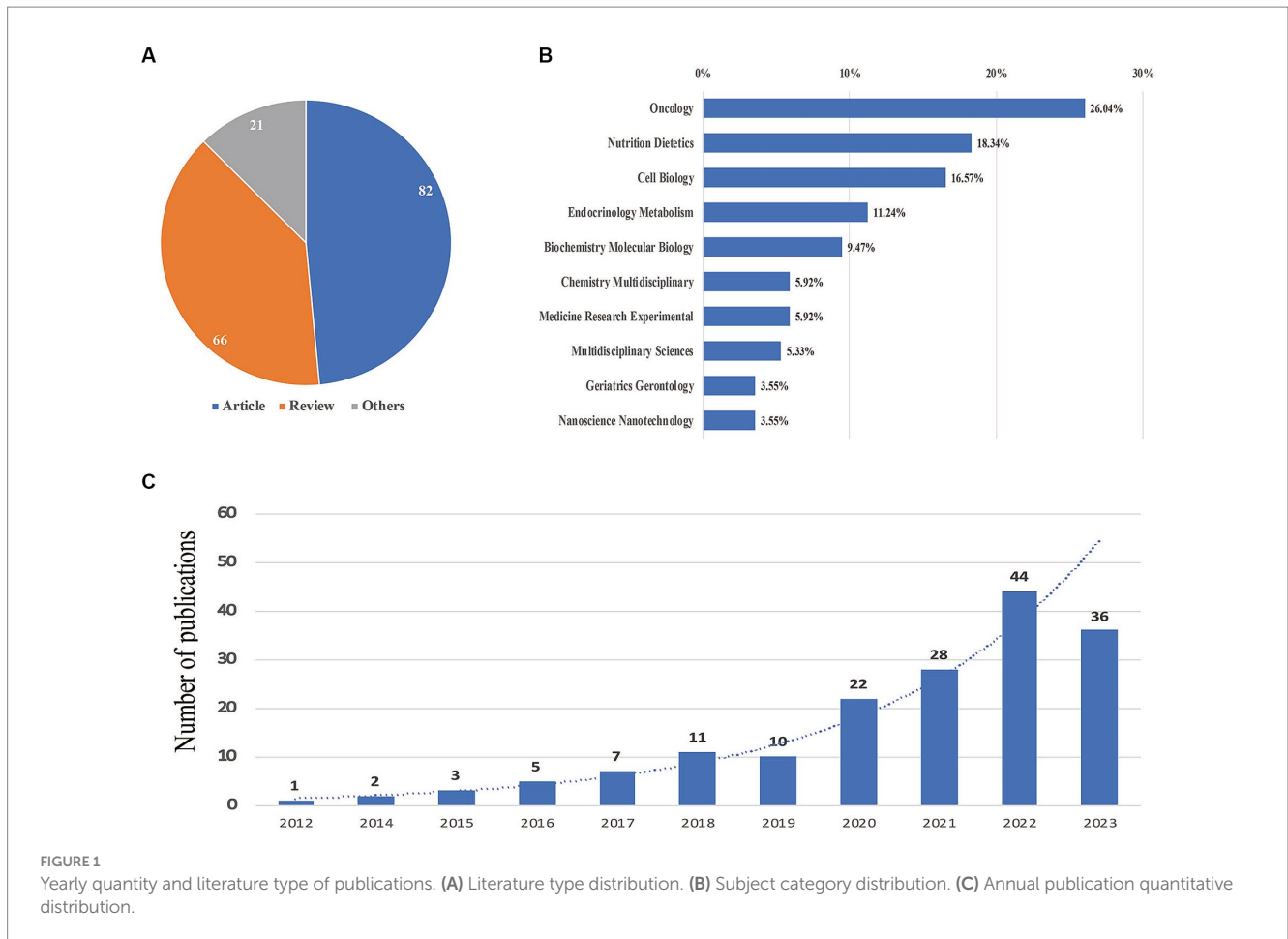
subjects being explored. Analyzing the time frames, the literature can be grouped into two primary phases: in the initial phase, which spans from 2012 to 2016, there was a modest number of publications, never surpassing 10 annually. This phase reflects the emerging interest and early research conducted on FMD. The subsequent phase from 2017 to 2023 represents a significant uptick in research intensity and focus. During this period, the yearly number of documents consistently increased, peaking at 44 publications in 2022. This increasing trend suggests a growing recognition of the relevance and significance of FMD in the scientific community. Projecting from current patterns, it is anticipated that publications related to FMD will continue on an upward trajectory due to the heightened interest and perceived importance of the topic. Diving into the specifics of publication types, the pie chart in Figure 1A reveals that out of the 169 publications, 82 were articles (representing 48.5% of the total), 66 were reviews (accounting for 39.1%), and the remaining 21 (or 12.4%) fell into other categories. As for the subject areas covered by these documents, Figure 1B presents a detailed breakdown: Oncology leads the chart with 26.64% publications, followed closely by Nutrition Dietetics at 18.34% and Cell Biology at 16.57%. The bar chart in Figure 1C offers a clear visualization of the yearly growth in FMD-related publications, emphasizing the exponential rise in research output from 2017 onwards.

### 3.2 Evaluation of countries/regions, academic organizations, authors, and journals

In total, 945 authors from 342 institutions and 25 countries/regions contributed to the field of FMD in 111 journals. The most productive country was USA with 86 publications, followed by Italy (61 publications) and the People's Republic of China (33 publications). For institutions, the University of Southern California tops the list with 45 publications, followed by the Ifom Fire Institute of Molecular Oncology with 42 publications, and the Chinese Academy of Sciences with 15 publications. In terms of individual researchers, Valter D. Longo stands out with 47 publications, showcasing him as a leading expert in this area. The concept of FMD was developed and popularized by he and his colleagues at the University of Southern California. Sebastian Brandhorst and Filippo De Braud follow with 17 and 14 publications, respectively. The most productive journal is *Nutrients* with 12 publications, and followed by the *Nature Communications* with 5 publications and *cancers* with 4 publications. Overall, this analysis underscores the importance and growing interest in the FMD in the global scientific community. Tables 1, 2 compile the 10 most prolific authors, organizations, countries/regions and journals in the FMD research arena. Figures 2, 3 present network visualization maps depicting citation interconnections among journals, countries/regions, institutions, and authors.

### 3.3 Analysis of highly-cited publications

The visualized citations of references are depicted in Figure 4, and the attributes of the 20 most-cited documents are encapsulated in Table 3 (1, 2, 4, 6, 7, 10, 13, 15, 20–31). The first high-cited document



was published in *Ageing Research Reviews* and authored by Mattson et al. (27). In the context of the FMD, the article may discuss how intermittent fasting, such as the FMD, can potentially promote various health benefits. These benefits may include improved metabolic health, weight management, and even potential effects on delaying aging processes and reducing the risk of chronic diseases. The second high-cited document was published in *Cell Metabolism* by Longo et al. (26). In this review, they explored the relationship between time-restricted feeding and fasting including the FMD and circadian rhythms, and their potential impacts on a healthy lifespan. These benefits might include improved metabolic health, cellular repair processes, and even longevity. The article likely delves into how aligning fasting periods with the body's natural circadian rhythms and limiting food intake to specific time windows may positively impact health and longevity. The third high-cited document was published in *Aging Cell* by Longo et al. (25). The article may explore specific dietary intervention involving FMD, can influence aging processes, with the potential benefits of periodic fasting for promoting longevity and improving age-related health markers. The fourth high-cited document was published in *Science Translational Medicine* by Wei et al. (30). In this article, they investigate the effects of a FMD on various markers and risk factors associated with aging, diabetes, cancer, and cardiovascular disease, and explores how this diet can impact biomarkers related to these health conditions. It may discuss the potential benefits of the FMD in terms of improving these markers

and reducing the risk factors associated with age-related diseases. The fifth high-cited document was published in *Cell Reports* by Choi et al. (13). They explore the effects of FMD on tissue regeneration, autoimmunity, and symptoms of multiple sclerosis (MS). They discuss the potential benefits of the FMD in promoting tissue regeneration and reducing autoimmunity, ultimately leading to a reduction in MS symptoms. This suggests that this specific dietary approach may hold promise in managing multiple sclerosis.

### 3.4 Analysis of keywords

Figure 5 displayed the network visualization maps of co-occurrence of keywords, including five clusters and key terms: Fasting and Diet Clusters: The central and prominent cluster revolves around "fasting-mimicking diet," "caloric restriction," "intermittent fasting," and "ketogenic diet." This is indicative of a core research area focused on dietary interventions and their impacts. Cancer and Treatment Cluster: On the left side, terms like "cancer," "chemotherapy," "cancer therapy," and "breast cancer" are connected, suggesting research on how fasting or dietary interventions might affect cancer and its treatment. Metabolic Processes Cluster: Terms like "metabolism," "glucose metabolism," "insulin resistance," and "oxidative stress" suggest a focus on the metabolic impacts of fasting

TABLE 1 The top 10 productive authors, institutions and countries based on publications.

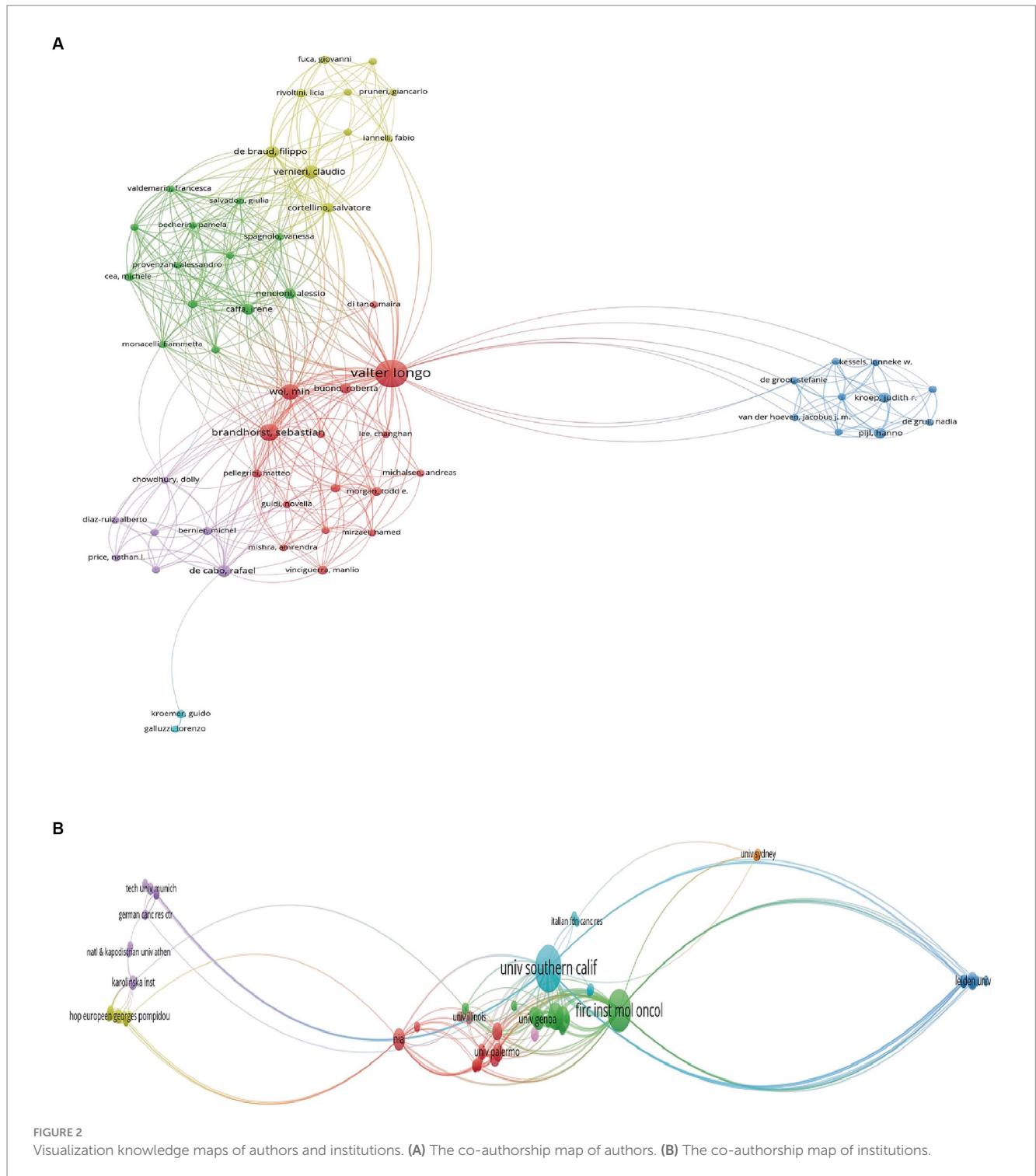
| Items       | Publications |  |        |           |         |
|-------------|--------------|--|--------|-----------|---------|
|             | Ranking      | Country  | Number | Citations | H-index |
| Country     | 1            | United States                                    | 86     | 4,619     | 30      |
|             | 2            | Italy  | 61     | 3,704     | 25      |
|             | 3            | Peoples R China                                  | 33     | 343       | 10      |
|             | 4            | Germany  | 12     | 1,066     | 5       |
|             | 5            | Netherlands                                      | 10     | 357       | 4       |
|             | 6            | Spain  | 10     | 177       | 7       |
|             | 7            | Australia  | 8      | 686       | 6       |
|             | 8            | England  | 6      | 961       | 4       |
|             | 9            | France   | 6      | 108       | 5       |
|             | 10           | Belgium  | 5      | 60        | 4       |
| Institution | 1            | University of Southern California                | 49     | 3,976     | 24      |
|             | 2            | Ifom Firc Institute of Molecular Oncology        | 42     | 3,321     | 22      |
|             | 3            | Chinese Academy of Sciences                      | 15     | 144       | 6       |
|             | 4            | Fondazione Irccs Istituto Nazionale Tumori Milan | 14     | 391       | 8       |
|             | 5            | University of Chinese Academy of Sciences        | 13     | 126       | 5       |
|             | 6            | University of California System                  | 12     | 763       | 6       |
|             | 7            | University of Milan                              | 12     | 391       | 8       |
|             | 8            | National Institutes of Health NIH USA            | 11     | 1,201     | 8       |
|             | 9            | University of Genoa                              | 11     | 617       | 8       |
|             | 10           | National Center for Nanoscience Technology China | 9      | 33        | 4       |
| Author      | 1            | Valter D. Longo                                  | 41     | 3,871     | 23      |
|             | 2            | Sebastian Brandhorst                             | 17     | 1,403     | 11      |
|             | 3            | Filippo De Braud                                 | 12     | 330       | 6       |
|             | 4            | Claudio Vernieri                                 | 11     | 384       | 8       |
|             | 5            | Valter Longo                                     | 8      | 29        | 3       |
|             | 6            | Alessio Nencioni                                 | 7      | 516       | 6       |
|             | 7            | Irene Caffa                                      | 7      | 516       | 6       |
|             | 8            | Wen Su   | 6      | 32        | 4       |
|             | 9            | Wenping Huang                                    | 6      | 18        | 2       |
|             | 10           | Roberta Buono                                    | 6      | 564       | 4       |

and dietary restriction. Health Outcomes and Processes: “Regeneration,” “inflammation,” “resilience,” and “autophagy” point toward the potential health outcomes or cellular processes influenced by these diets. Other Dietary Patterns and Effects: There are terms like “body weight,” “weight loss,” and “energy restriction,” which relate to outcomes of dietary interventions and other dietary patterns.

## 4 Discussion

### 4.1 General information

To the best of our knowledge, this is the first bibliometric analysis related to the FMD. FMD is a specialized dietary regimen, has



attracted growing attention in the scientific community due to its potential health benefits. Numerous studies have explored its implications for metabolic health, weight management, and potential in influencing the course of various diseases, including cancer and diabetes. In our study, there were a total of 169 publications related to FMD. From a geographical standpoint, the USA emerged as the leading contributor with 86 publications. The most productive

institution and author are the University of Southern California and Valter D. Longo. The journal “Nutrients” was particularly noteworthy, with the highest number of FMD-related publications. Furthermore, the most highly cited work in this domain was published in Ageing Research Reviews by Mattson et al. (27), delving into the broader theme of intermittent fasting, encompassing FMD. In essence, the research on the FMD reflects a dynamic and growing field, with key



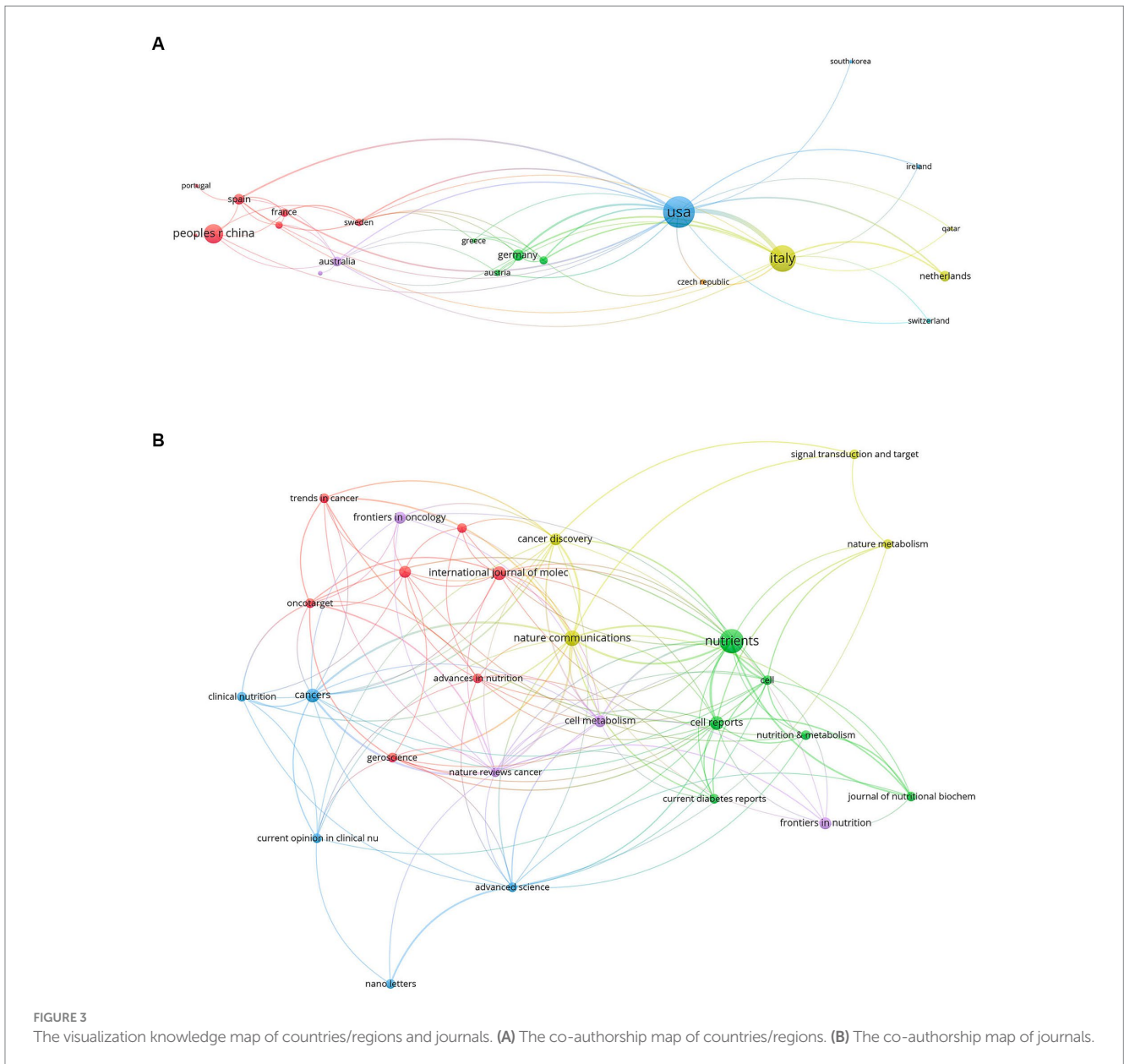
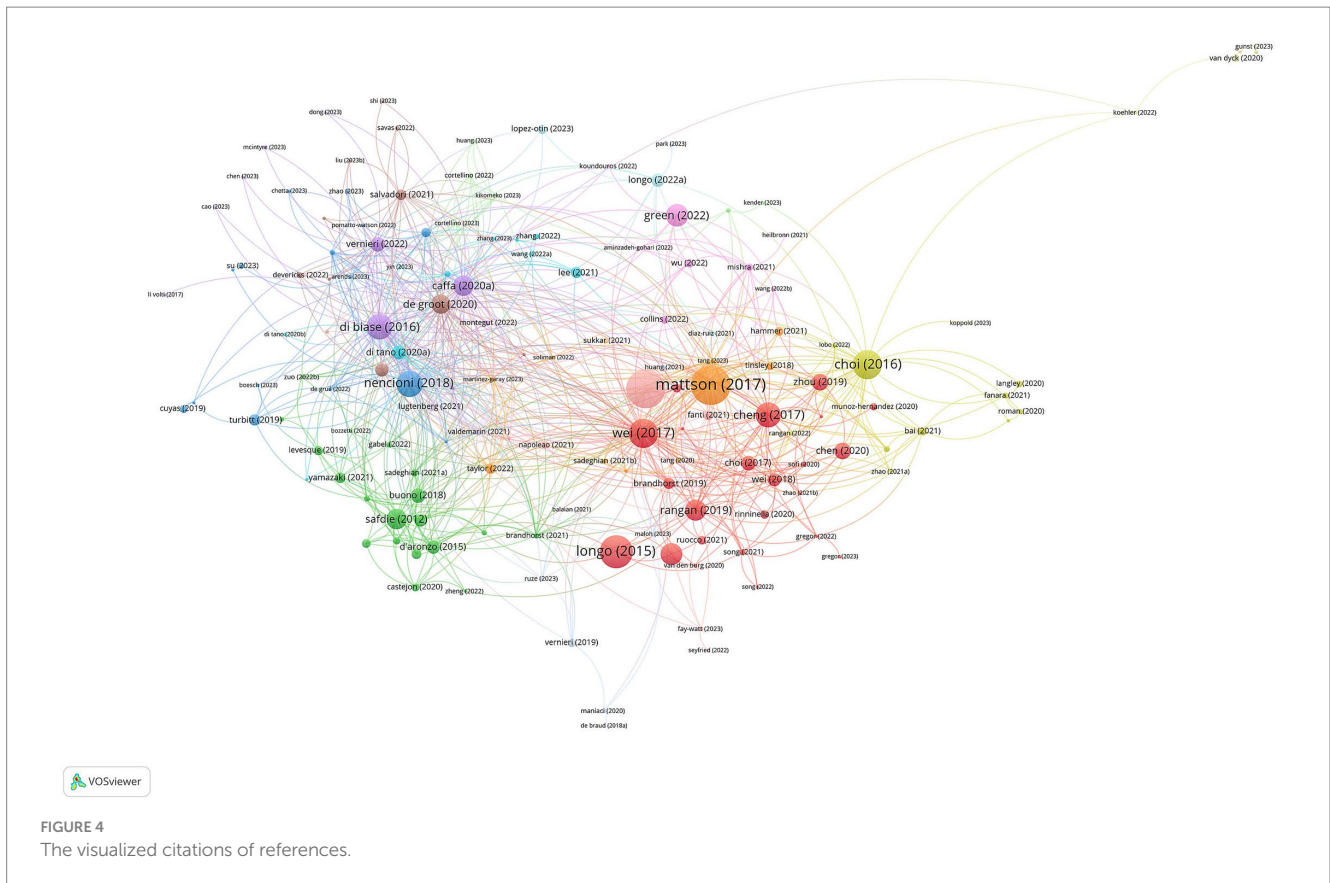


TABLE 2 The top 10 productive journals.

| Ranking | Journal name                                | Country       | Counts |
|---------|---|---------------|--------|
| 1       | Nutrients                                   | Switzerland   | 12     |
| 2       | Nature Communications                       | England       | 5      |
| 3       | Cancers                                     | Switzerland   | 4      |
| 4       | Cell Reports                                | United States | 4      |
| 5       | International Journal of Molecular Sciences | Switzerland   | 4      |
| 6       | Annals of Oncology                          | Netherlands   | 3      |
| 7       | Cancer Discovery                            | United States | 3      |
| 8       | Cancer Research                             | United States | 3      |
| 9       | Cell Metabolism                             | United States | 3      |
| 10      | Frontiers in Nutrition                      | Switzerland   | 3      |
| 11      | Frontiers in Oncology                       | Switzerland   | 3      |
| 12      | Journal of Clinical Oncology                | United States | 3      |
| 13      | Trends In Endocrinology and Metabolism      | United States | 3      |



players and institutions paving the way for future explorations and discoveries.

## 4.2 Hotspots and frontiers

On the basis of publications of the FMD, highly-cited publications, and important keywords with high frequency, the key research areas within the field of FMD have been outlined as follows.

### 4.2.1 FMD for cancer

For this field, the FMD for cancer is the most popular topic. Many studies investigate the effects of FMD for cancer. For example, Caffa et al. (6) demonstrates the efficacy of combining a FMD (FMD) with hormone therapy to potentiate cancer treatment in hormone-receptor-positive breast cancers, which constitute roughly 75% of all breast cancer cases. In mouse models, the FMD synergistically improved the cancer-fighting impact of endocrine therapies, such as tamoxifen and fulvestrant, by significantly lowering systemic levels of IGF-1, insulin, and leptin, and impeding AKT–mTOR signaling pathways through the increased expression of EGFR1 and PTEN. This combination, particularly when a cycle of FMD was added to a regimen of fulvestrant and palbociclib (a CDK4/6 inhibitor), not only induced durable tumor regression but also countered the development of acquired resistance to the medications. Additionally, it prevented tamoxifen-induced endometrial hyperplasia, a common side effect of this drug. Encouragingly, early-phase clinical observations in human patients mirrored the metabolic alterations seen in mice and were

associated with prolonged anti-cancer benefits. These findings underline the potential of incorporating periodic FMDs as a complementary approach to enhance the effectiveness of hormone therapies in treating hormone-receptor-positive breast cancers (6).

Subsequently, the phase 2 DIRECT trial (7), which was the first randomized controlled study evaluating the effects of an FMD on toxicity and efficacy of chemotherapy in patients with cancer. In this study, they evaluated the effects of the FMD as an accompaniment to neoadjuvant chemotherapy in breast cancer patients. 131 HER2-negative stage II/III breast cancer patients participated, with half receiving an FMD and the other half their regular diet. Results showed no notable difference in toxicity levels between the two groups, even though one group did not receive dexamethasone with their treatment. The FMD group exhibited a higher likelihood of a significant or complete radiological response to chemotherapy. Importantly, DNA damage in T-lymphocytes was also reduced in the FMD group, hinting at the diet's protective qualities. Conclusively, the FMD displayed potential in enhancing the effects of chemotherapy in early-stage breast cancer patients, making it worthy of further exploration in cancer treatment protocols (7).

In addition, FMD may be also benefits for other types of cancer besides breast cancer, including lung cancer (32), colorectal cancer (3), and prostate cancer (33). There's been some benefits in the FMD for cancer: Protective effect during chemotherapy: Preclinical studies suggest that cycles of fasting or FMD can render cancer cells more sensitive to chemotherapy while protecting healthy cells. This is termed differential stress resistance (DSR). By enhancing the effects of chemotherapy on cancer cells and reducing side effects on normal





TABLE 3 The top 20 most highly cited references.

| Rank | Title  | Journal                                     | Total citations | Year | First author      |
|------|--|---|-----------------|------|-------------------|
| 1    | Impact of intermittent fasting on health and disease processes   | Ageing Research Reviews                     | 506             | 2017 | Mark P. Mattson   |
| 2    | Fasting, Circadian Rhythms, and Time-Restricted Feeding in Healthy Lifespan  | Cell Metabolism                             | 500             | 2016 | Valter D. Longo   |
| 3    | Interventions to Slow Aging in Humans: Are We Ready?   | Aging Cell                                  | 359             | 2015 | Valter D. Longo   |
| 4    | Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease                              | Science Translational Medicine              | 276             | 2017 | Min Wei           |
| 5    | A Diet Mimicking Fasting Promotes Regeneration and Reduces Autoimmunity and Multiple Sclerosis Symptoms                              | Cell Reports                                | 272             | 2016 | In Young Choi     |
| 6    | Fasting and cancer: molecular mechanisms and clinical application  | Nature Reviews Cancer                       | 233             | 2018 | Alessio Nencioni  |
| 7    | Fasting-Mimicking Diet Reduces HO-1 to Promote T Cell-Mediated Tumor Cytotoxicity  | Cancer Cell                                 | 223             | 2016 | Stefano Di Biase  |
| 8    | Fasting-Mimicking Diet Promotes Ngn3-Driven $\beta$ -Cell Regeneration to Reverse Diabetes   | Cell  | 208             | 2017 | Chia-Wei Cheng    |
| 9    | Molecular mechanisms of dietary restriction promoting health and longevity   | Nature Reviews Molecular Cell Biology       | 162             | 2022 | Cara L. Green     |
| 10   | Protein and amino acid restriction, aging and disease: from yeast to humans  | Trends In Endocrinology And Metabolism      | 158             | 2014 | Hamed Mirzaei     |
| 11   | Fasting-Mimicking Diet Modulates Microbiota and Promotes Intestinal Regeneration to Reduce Inflammatory Bowel Disease Pathology      | Cell Reports                                | 144             | 2019 | Priya Rangan      |
| 12   | Fasting-mimicking diet and hormone therapy induce breast cancer regression   | Nature                                      | 143             | 2020 | Irene Caffa       |
| 13   | Fasting enhances the response of glioma to chemo- and radiotherapy   | Plos One                                    | 140             | 2012 | Fernando Safdie   |
| 14   | Fasting mimicking diet as an adjunct toneoadjuvant chemotherapy for breast cancer in the multicentre randomized phase 2 DIRECT trial | Nature Communications                       | 124             | 2020 | Stefanie de Groot |
| 15   | Neuroprotection of Fasting Mimicking Diet on MPTP-Induced Parkinson's Disease Mice via Gut Microbiota and Metabolites                | Neurotherapeutics                           | 94              | 2019 | Zhi-Lan Zhou      |
| 16   | Gut Microbiota Metabolites in NAFLD Pathogenesis and Therapeutic Implications  | International Journal of Molecular Sciences | 91              | 2020 | Jiezhong Chen     |
| 17   | Fasting-Mimicking Diet Is Safe and Reshapes Metabolism and Antitumor Immunity in Patients with Cancer                                | Cancer Discovery                            | 71              | 2022 | Claudio Vernieri  |
| 18   | Nutrition and fasting mimicking diets in the prevention and treatment of autoimmune diseases and immunosenescence                    | Molecular And Cellular Endocrinology        | 70              | 2017 | In Young Choi     |
| 19   | Starvation, Stress Resistance, and Cancer  | Trends In Endocrinology And Metabolism      | 68              | 2018 | Roberta Buono     |
| 20   | Synergistic effect of fasting-mimicking diet and vitamin C against KRAS mutated cancers  | Nature Communications                       | 65              | 2020 | Maira Di Tano     |

### 4.2.3 FMD for cognitive improvement

FMD has the potential effect on the improvement of cognitive functions in Alzheimer's disease (AD). Rangan et al. (16) investigated the effects of FMD on cognitive functions in Alzheimer's models, and found that FMD cycles demonstrated a reduction in cognitive decline and AD pathology in two mouse models, outperforming the effects of protein restriction cycles. In one particular mouse model, the FMD significantly reduced signs of AD, such as brain plaques and tau tangles, and fostered the growth of neural stem cells (16).

Moreover, FMD decreased the number of microglia and reduced the expression of neuroinflammatory genes, including the superoxide-producing Nox2. Improved cognition was observed in mice lacking Nox2 or those treated with a Nox2 inhibitor. Preliminary clinical data also suggest that FMD cycles are feasible and generally safe for a subset of AD patients. These findings underscore the potential of FMD cycles in delaying cognitive decline in AD (16, 45, 46).

There were some limitations in our study. We exclusively utilized the WoSCC database, as the VOSviewer software is incompatible with other databases like Embase and Pubmed for analyzing and visualizing co-citation maps. Furthermore, the volume of publications concerning FMD is still quite limited, and the pre-clinical and clinical data on both sexes and to elucidate potential differences are lacked, necessitating the imperative for additional research. Expanding this body of work is crucial to enhance our understanding of FMD's impacts on human health and to optimize the use of this method for health improvement purposes.

In conclusion, this is the first bibliometric analysis of the FMD. The main research hotspots and frontiers were FMD for cancer, FMD for metabolic-related diseases, and FMD for cognitive improvement. FMD may have some potential benefits for multiple diseases, including cancer, diabetes, and Alzheimer's diseases, which should be further investigated.

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## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Author contributions

XL: Data curation, Formal Analysis, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. YG: Formal Analysis, Funding acquisition, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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