Review article

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Mapping the landscape of immunonutrition and cancer research: a comprehensive bibliometric analysis on behalf of NutriOnc Research Group

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Abstract

The ongoing global health challenge of cancer is driving the pursuit of innovative avenues for prevention, treatment, and enhanced outcomes. The convergence of nutrition and immune modulation, known as immunonutrition, is ready to act as a catalyst for transformative change in cancer research and therapy. Our study employs a bibliometric analysis to uncover the evolving trends within immunonutrition and cancer research across the past 25 years. Bibliometric data, including authors, journals, affiliations, and countries, were analyzed using the Bibliometrix R package. Clustering algorithms were applied to keywords to identify thematic areas and their evolution. A total of 489 documents were analyzed, showing an annual growth rate of 8.7%, with a collaboration index of 5.41, highlighting comprehensive multidisciplinary involvement within this landscape. Core authors demonstrated sustained productivity, while occasional authors indicated widespread interest. The Medical University of Warsaw led in institutional contributions. Country-wise, Italy, France, and the USA emerged as forerunners in fostering research productivity. Key journals like 'Clinical Nutrition' served as beacons, emphasizing the multidimensional nature of this topic. The analysis highlighted growing research output and several collaborations, indicating the importance of immunoenriched nutrition in cancer treatment. The interplay of core authors and diversified engagement harmoniously accentuates the cross-disciplinary nature of this burgeoning field. International collaboration facilitated knowledge exchange. Prominent documents shaped the field, emphasizing the significance of nutritional interventions. Thematic clusters revealed varied focuses, including pharmaconutrients, surgical approaches, inflammation, and specific cancers. The expanding research output suggests further development, particularly in exploring immunoenriched nutrition's impact on cancer types and patient populations. The multidisciplinary nature and international collaborations enhance the field's progress. Gaps in research underscore the need for original studies and personalized approaches. This study guides future research, informing evidence-based nutritional interventions and advancing cancer care practices.

Keywords: bibliometric analysis, cancer, immune system, immunonutrition, nutrition

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Introduction

Cancer remains a remarkable global health challenge, demanding continuous exploration of novel approaches to prevention, treatment, and improved patient outcomes[1]. While conventional treatments such as surgery, chemotherapy, and radiation therapy have shown effectiveness, they often lead to significant side effects and exhibit limited success rates, particularly in advanced stages[2]. As a result, a notable attempt has arisen to explore supplementary strategies that regulate the intrinsic immune defenses for targeted interaction and control of neoplastic cells[3]. Immunotherapy, a paradigm that leverages the immune system's capabilities to specifically target and destroy cancer cells, has shown remarkable promise, but its efficacy can be variable due to factors such as tumor heterogeneity and the suppression of immune responses within the tumor microenvironment[4]. Simultaneously, this variability has prompted researchers to investigate the role of nutritional factors in modulating immune responses, with the aim of enhancing the effectiveness of anticancer therapies[5], and, in recent years, the intriguing nexus between immunonutrition and cancer has raised considerable scientific attention[6,7]. Immunonutrition, an emerging field at the interface of immunology and nutrition, focuses on the impact of specific nutrients on immune system modulation[8]. Understanding the profound influence of immunonutrition on cancer development, progression, and therapeutic interventions holds exceptional promise in revolutionizing cancer research and clinical practice[9–11].

Immunonutrition is grounded in the recognition of the immune system's pivotal role in cancer surveillance, response to treatment, and overall disease trajectory[12–14]. Accumulating evidence suggests that dietary factors, such as omega-3 fatty acids, arginine, nucleotides, and antioxidants, are thought to enhance immune cell function, modify the tumor microenvironment, reduce inflammation, and support tissue repair, thereby potentially improving cancer outcomes[15–17]. This realization has captivated the attention of the scientific community, leading to extensive investigations into the potential of immunonutrition as a complementary approach to conventional cancer therapies[12,18–20]. However, the evidence-based recommendations of these nutritional formulas in clinical practice are still scarce and limited to specific populations.

Bibliometrics is an essential quantitative tool for evaluating research output, trends, and impact. It achieves this by exploring publication patterns, the geographical distribution of research endeavors, key contributors, collaborative networks, citation trends, and original works[21]. As no bibliometric investigations have yet explored global trends regarding immunonutrition and cancer, the aim of this study is to uncover essential insights into this dynamic and flourishing field over the past 25 years[22]. This pioneering analysis carries immense value for scientists, clinicians, and policymakers alike, as it presents a comprehensive overview of the existing scientific advancements, identifies knowledge gaps, and highlights potential routes for future research[23,24]. Additionally, by systematically evaluating the current state of immunonutrition and cancer research, this analysis is essential to provide a solid foundation for informed decision-making and facilitate collaborations between disciplines, promoting groundbreaking advancements in cancer prevention, treatment, and patient care.

HIGHLIGHTS

- Immunonutrition's impact on cancer outcomes offers groundbreaking potential.
- In 25 years, immunonutrition and cancer research boosted, emphasizing multidisciplinarity.
- Thematic analysis reveals surgical approaches and specific cancers as clusters for the future.
- Addressing gaps can optimize the efficacy of immunonutrition for improved cancer outcomes.

Materials and methods

In 2020, young members of the Italian Association of Medical Oncology (AIOM), Italian Association of Radiotherapy and Clinical Oncology (AIRO), Italian Society of Surgical Oncology (SICO) and the Italian Society of Parenteral and Enteral Nutrition (SINPE) planned common research goals and founded the NutriOnc Research Group, aimed at implementing multidisciplinary strategies to improve patient quality of life[18]. The Scopus database was systematically searched between 1 January 1998 and 15 May 2023, in order to retrieve the worldwide literature concerning immunonutrition in relation to cancer, with the keywords 'immunonutrition' and 'cancer'. Studies in languages other than English were excluded. Search fields included article title, abstract, and keywords. Bibliographic attributes included data on citation information (authors; document title; year; source title; volume, issue, pages; citation count; source and document type; DOI), bibliographical information (affiliations; serial identifiers; PubMed ID; publisher; editors; correspondence address), abstract, and author keywords. Bibliographic metadata were exported from Scopus using the BibTex file format and exported in the R environment (R-Studio 0.98.1091 software). The Bibliometrix R package was used for the extraction and generation of bibliometric illustrations[25]. The 'summary ()' function was used to summarize the main information about the collection: the total number of documents, the documents per year, the annual growth rate (the progression ratio of the scientific production over the time-period), the number of documents per author, the collaboration index (calculated as total authors of multiauthored articles divided by total multiauthored articles), the most relevant sources (source clustering was analyzed through Bradford's Law[26]), the most relevant authors (per number of authored documents), the author's production over time, the author productivity (through Lotka's law[27]), the corresponding author's country, the most relevant affiliations (by number of documents with affiliation name disambiguation parameter), the multiple countries publication (the measure of the international collaboration intensity of a country based on the number of documents, for each country, in which there is at least one co-author from a different country), the number of documents per country (based on authors' nationality), the most global cited documents. The top keywords were represented by a tree map. By applying a clustering algorithm on the keyword network, it was possible to highlight the different themes of a given domain on a thematic map. The x-axis referred to the centrality (the importance of the theme in the entire research field) and the y-axis referred to the density (the measure of the theme's development). Each bubble represented a network cluster and the bubble size was proportional to the cluster keyword occurrences.

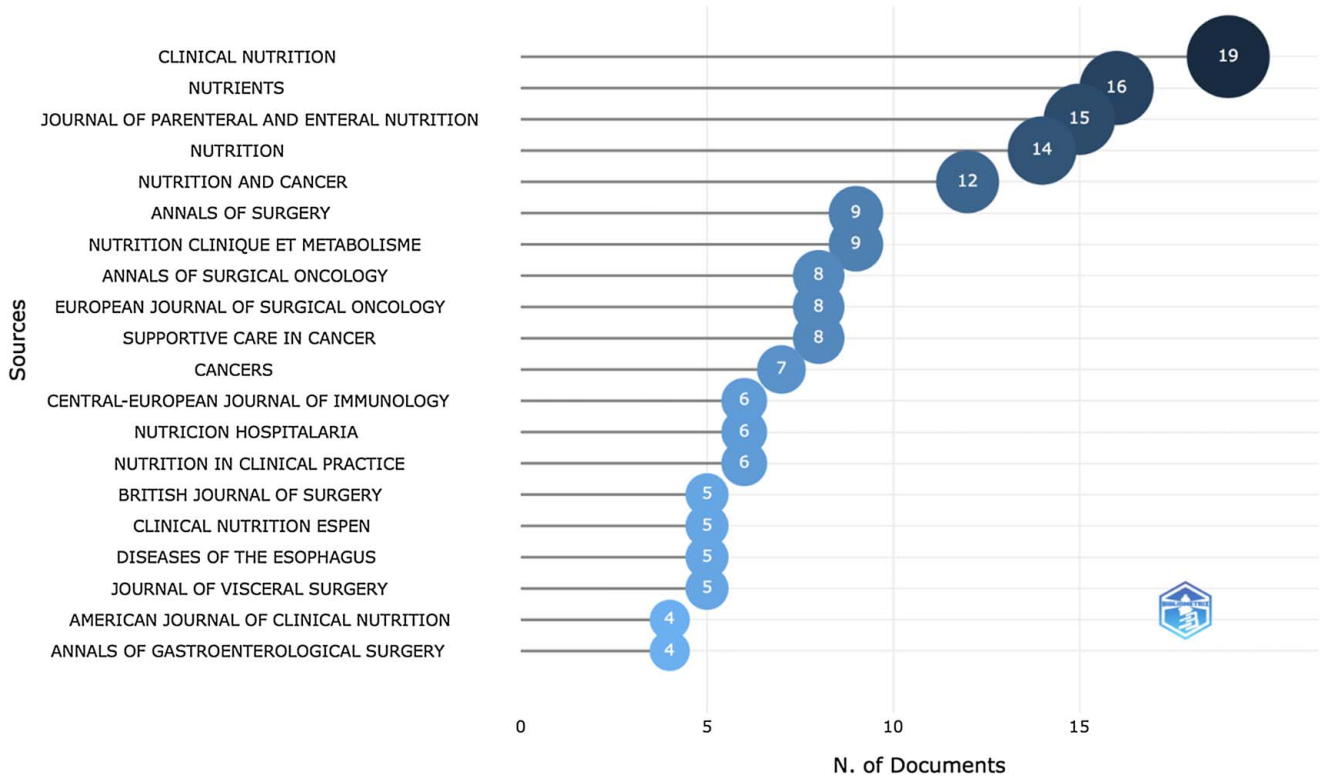


Figure 1. Most relevant journals. The most relevant journals (*y*-axis) are stratified based on the number of documents (*x*-axis).

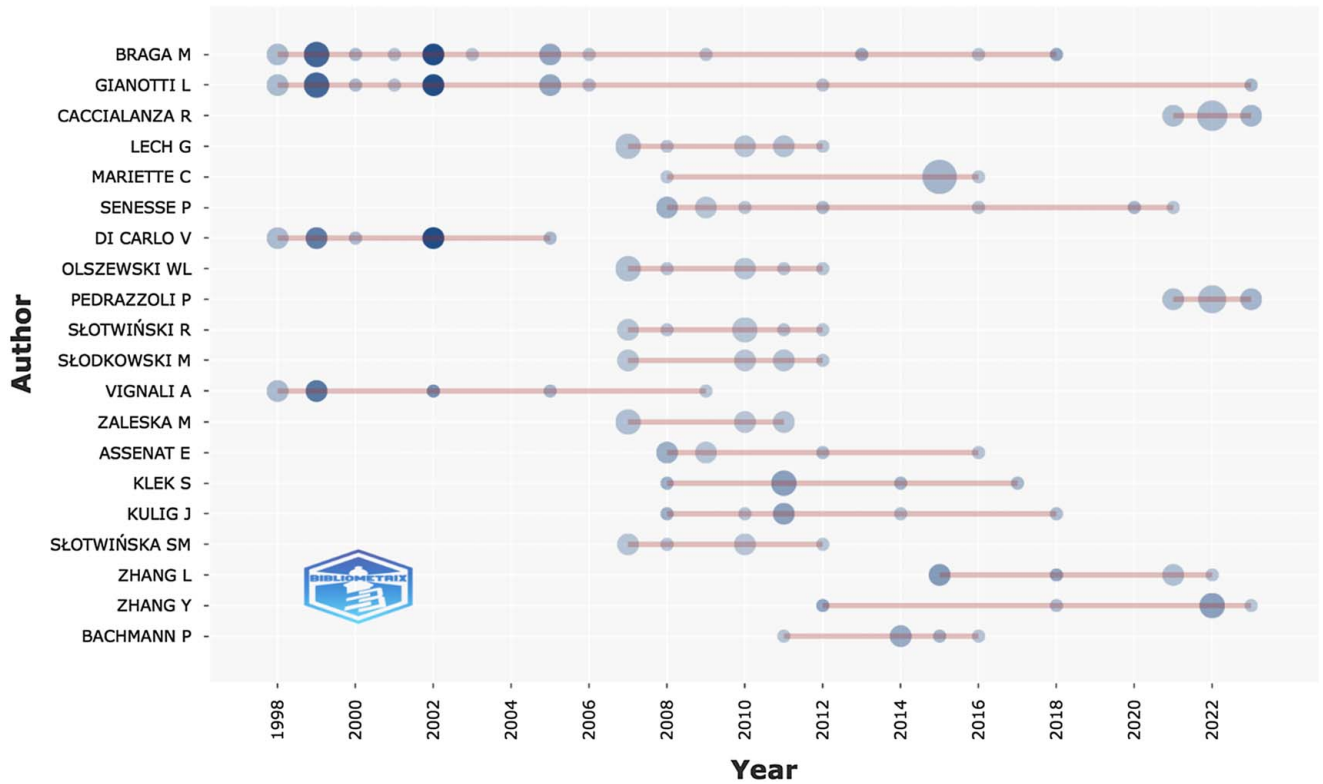


Figure 2. Top authors' production over time. The line represents author's timeline; the bubble size is proportional to the number of documents; the color intensity is proportional to the total citations per year.

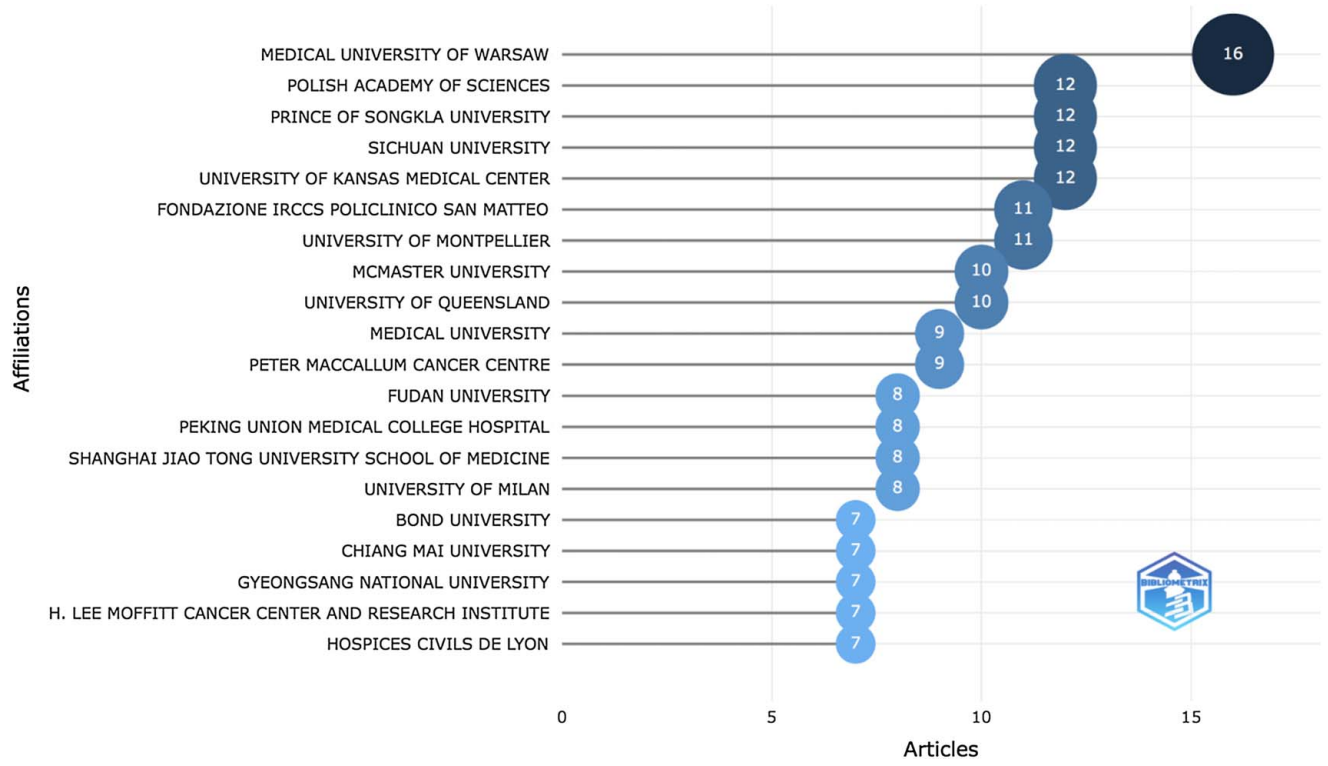
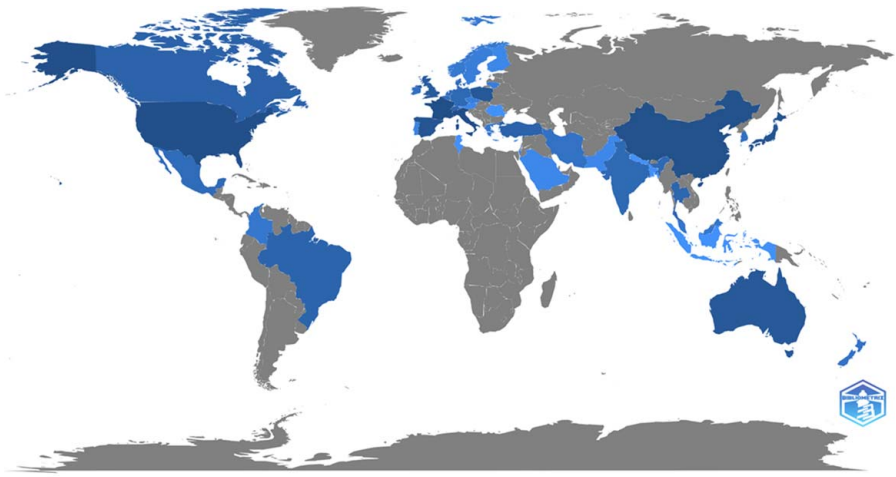


Figure 3. Most relevant affiliations.



Country	Documents	Country	Documents
ITALY	198	CANADA	37
FRANCE	196	BRAZIL	31
USA	175	SWITZERLAND	31
CHINA	158	THAILAND	27
SPAIN	113	INDIA	22
JAPAN	109	GERMANY	21
POLAND	86	MEXICO	18
AUSTRALIA	78	DENMARK	17
UNITED KINGDOM	66	NETHERLANDS	17
TURKEY	38	BELGIUM	14

Figure 4. Country scientific production map. Blue intensity is proportional to the number of publications (dark blue = high productivity; gray = no documents). The nationality of each author in a document was considered.

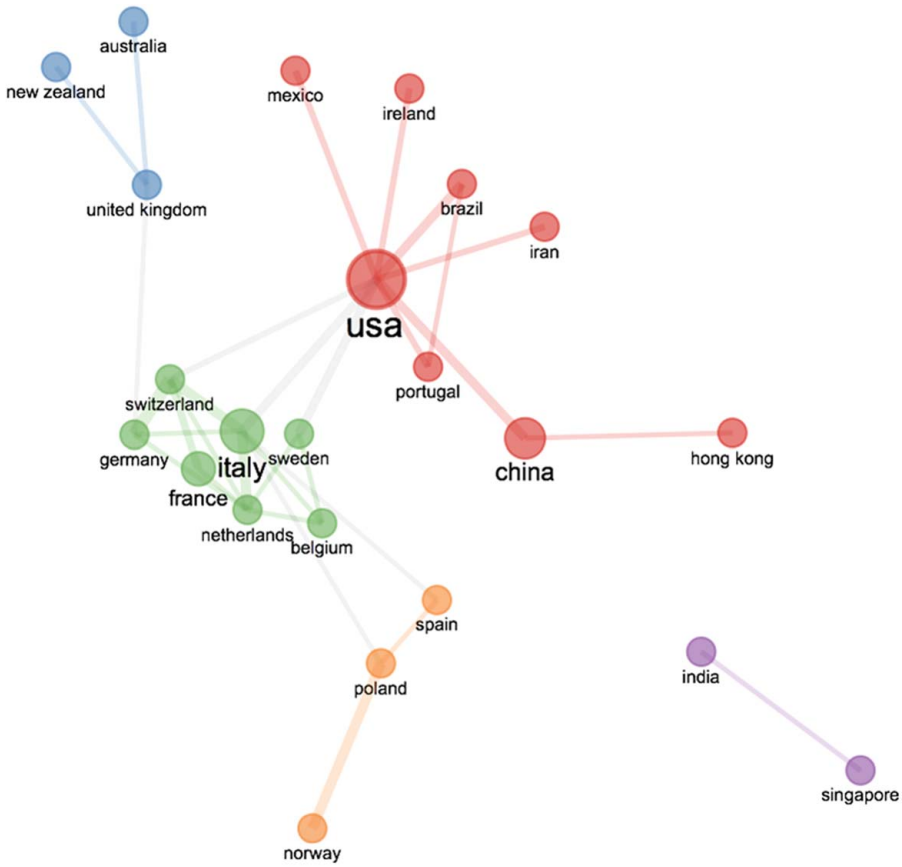


Figure 5. Collaboration network. Each node represents a country, and its size reflects the number of articles published by researchers from the country. Connecting lines represent co-occurring relationships between the countries.

Dividing the time span in three different time slots (1998–2006, 2007–2014, and 2015–2023), it was possible to study and plot the thematic evolution.

The country collaboration network showed countries relationships in the field of the scientific research. Each node indicated a country and the size of the node represented the number of documents; the links between nodes represented the co-occurrence relationships and their size referred to the frequencies.

Results

Main information

Between 1998 and 2023, a total of 489 documents were published, including, as defined by Scopus, 292 (59.7%) original articles, 15 (3.1%) book/book chapter, 5 (1.0%) conference papers, 8 (1.6%) editorials, 2 (0.4%) erratum, 12 (2.5%) letters, 4 (0.8%) notes, 147 (30.1%) review articles, and 4 (0.8%) short surveys.

Global publication trend

Over time, an increased number of documents was recorded, with an annual growth rate of 8.7%. Before 2000, only a limited number of papers were issued. Then, from 2001 to 2015, a slow and intermittent increase in annual publication were registered. The most rapid and notable increases occurred in 2020s, with over 50 documents per year published on the topic ($n = 53$ in 2020, $n = 58$ in 2021, $n = 58$ in 2022). Thirty-six of the 489 documents contained a single author and the remaining 453 contained multiple authors. The collaboration index was 5.41.

Analysis of sources

Overall, 270 journals published one or more documents included in the analysis. Eighteen journals represent the *core zone*, having published one-third of all the retrieved documents ($n = 163$; 33.3%). The most relevant journals are listed in Figure 1. Although each journal had a different publisher, the proposed aim and scope were similar, with a strong focus on generating evidence-based findings in immunonutriton and cancer research. The top source was 'Clinical Nutrition' with 19 articles published between 1998 and 2023.

Authors, affiliations, and countries

A total of 2479 authors contributed to these 489 documents with an average of 6.34 co-authors per publication. The frequency distribution of the scientific productivity identified several *core* authors ($n = 33$; 1.3%) who have written at least five documents and *occasional* authors ($n = 2088$; 84.2%) who published just one paper. As shown in Figure 2, the Braga Marco was ranked the first in number of documents (17 documents), followed by

Gianotti Luca (14 documents). This meant these authors might be leading figure in the explored field.

A total of 913 affiliations have contributed at least one paper in this topic. The most relevant affiliations (per number of documents) are listed in Figure 3. The research institution with the most publications was the Medical University of Warsaw with 16 articles. Among the top 20 institutions, 6 institutions are situated in Europe (Poland, Italy, France, the United Kingdom, and Spain) and 5 institutions in Asia (China). Country scientific production is shown in Figure 4, with a blue intensity scale denoting 1 to 198 records. The color intensity is proportional to the number of publications. All authors' nationality in each document is considered. Italy contributed the most publications in this field ($n = 198$; 40.5%), followed by France ($n = 196$; 40.1%) and United States of America ($n = 175$; 35.8%). A total of 23 countries were involved in the collaboration network (Fig. 5). There was an active collaboration in research between European countries. The USA had a strong connection mainly with China.

Documents

The most global cited documents are provided in Table 1. The top document was 'Nutritional approach in malnourished surgical patients. A prospective randomized study'[28] accounting 381 total citation and 17.318 citation per year.

Table 1

Most global cited documents.

Paper	DOI	TC	TC per year
Braga, 2002, Arch Surg[28]	10.1001/archsurg.137.2.174	381	17.32
Braga, 1999, Arch Surg[29]	10.1001/archsurg.134.4.428	341	13.64
Braga, 2002, Surgery[30]	10.1067/msy.2002.128350	303	13.77
Butt, 2009, Crit Rev Food Sci Nutr[31]	10.1080/10408390802145344	186	12.40
Marik, 2010, J Parenter Enter Nutr[32]	10.1177/0148607110362692	184	13.14
Heller, 2004, Int J Cancer[33]	10.1002/ijc.20291	160	8.00
Farreras, 2005, Clin Nutr[34]	10.1016/j.clnu.2004.07.002	153	8.05
Gianotti, 1999, J Parenter Enter Nutr[35]	10.1177/014860719902300631 4	151	6.04
Vanmeerbeek, 2020, Oncoimmunology[36]	10.1080/2162402X.2019.1703449	122	30.50
Fujitani, 2012, Br J Surg[37]	10.1002/bjs.8706	117	9.75
Grimble, 2005, Curr Opin Gastroenterol[38]	10.1097/01. mog.0000153360.90653.82	116	6.11
Pombo Antunes, 2020, ELIFE[39]	10.7554/eLife.52176	114	28.50
Xu, 2006, World J Surg[40]	10.1007/s00268-005-0756-8	113	6.28
McCowen, 2003, Am J Clin Nutr[41]	10.1093/ajcn/77.4.764	110	5.24
Di Carlo, 1999, Dig Surg[42]	10.1159/000018742	115	4.60
Sultan, 2012, Br J Surg[43]	10.1002/bjs.7799	106	8.83
Zheng, 2007, Asia Pac J Clin Nutr[44]	17392114[a]	106	6.24
Giger, 2007, Ann Surg Oncol[45]	10.1245/s10434-007-9407-7	100	5.88
Zhang, 2012, Surg Oncol[46]	10.1016/j.suronc.2012.01.002	99	8.25
Okamoto, 2009, World J Surg[47]	10.1007/s00268-009-0140-1	94	6.27

[a]PMID.

TC, total citations.

Conceptual analysis

The top keywords are represented by a tree map (Fig. 6). By applying a clustering algorithm on these keywords, a thematic map was generated. Based on the theme's relevance (centrality) and the theme's development (density), eight clusters were defined. Pharmaconutrients and surgical approach represented motor themes. The clusters in the basic themes' quadrant focused on inflammation and head and neck cancer. Lung carcinoma and prognostic nutritional index were isolated topics. Details are depicted in Figure 7.

Emerging trends

Changes in the main thematic areas and their relationship across years (time-period 1998–2006, 2007–2014, and 2015–2023) are shown in Figure 8. While in the first time-period most of the research focused on colorectal cancer, over time, increasing attention has been paid to other primary locations, such as esophageal, gastric, and head and neck cancers.

Discussion

In this study, we analyzed the research trends and hotspots over the past 25 years and explored the research frontiers in recent years in the field of immunonutrition and cancer research. The present bibliometric analysis provides a comprehensive overview of the focused scientific literature, shedding light on the current state of research and identifying potential avenues for future exploration. The findings from this analysis align with existing literature, revealing an increasing research output, multidisciplinary collaborations, and emerging thematic areas of investigation in this field[6,7]. The observed increase in the number of publications on immunonutrition and cancer over time is indicative of the growing recognition of the pivotal role that nutrition and immune function play in cancer biology and treatment[9–11]. This trend is consistent with the broader understanding of the complex interplay between host immune responses and cancer progression[12]. It highlights the scientific community's interest in exploring the potential of immunonutrition as an adjunctive therapy to conventional cancer treatments[19,20]. Moreover, the swift expansion of research in this field could reflect the principle of Price's theory[42], according to which the progression of scientific research can be categorized into four phases: the initial stage, the great development stage, the mature stage, and the completion stage. However, some disparities between actual development and the theoretical model might arise due to diverse factors like economic conditions, political influences, and policies. Drawing from the cumulative growth curve that has been obtained, it is plausible to postulate that the investigation into immunonutrition and cancer is presently positioned in a phase of great development, suggesting a likelihood of increased article output in the forthcoming period. Interestingly, substantial attention has been directed towards investigating the impact of immunonutritional support therapy on the prognosis of individuals with cancer. Customized immunoenriched nutritional assistance provided during a patient's hospitalization has shown the potential to reduce mortality rates and improve quality of life[3,6]. Conversely, an unfavorable nutritional status among cancer patients has commonly been associated with an adverse prognostic outcome[10].

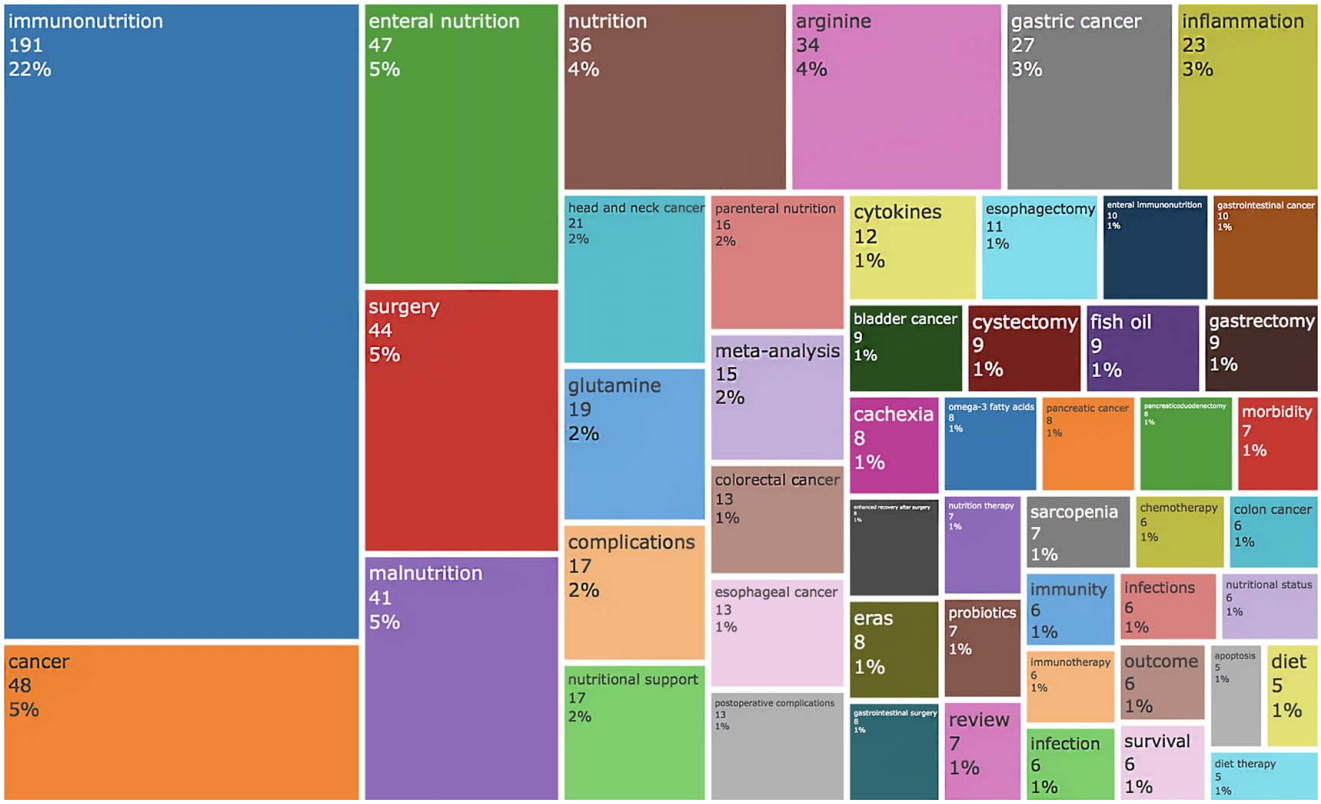


Figure 6. Tree map - Keyword frequency distribution.

The wide and different range of journals publishing on this topic, with 'Clinical Nutrition' emerging as the top source, indicates the multidisciplinary nature of immunonutrition research. This finding suggests that experts from various disciplines, including clinical nutrition, oncology, radiotherapy, and surgical oncology, are actively engaged in resolving the intricate connections between nutrition, immune function, and cancer outcomes[6,9–11,16]. Such collaboration enhances the breadth and depth of research conducted in this field.

The analysis of authorship patterns reveals the contributions of both core authors and occasional authors to the body of literature on immunonutrition and cancer. The presence of core authors, such as Braga Marco and Gianotti Luca, signifies their expertise and sustained productivity in this area of research. On the other hand, the large number of occasional authors suggests a broad engagement of researchers, emphasizing the widespread interest in studying the interface between nutrition, immune responses, and cancer. Examining affiliations provides valuable insights into the institutional landscape of immunonutrition and cancer research. The prominence of the Medical University of Warsaw as the leading institution in terms of publications indicates a concentrated effort in this field. Additionally, the involvement of institutions from Europe and China among the top contributors underscores the global nature of research in immunonutrition and cancer. This international collaboration fosters knowledge exchange and facilitates the pooling of resources and expertise.

The country-level scientific production analysis highlights Italy, France, and the United States of America as the leading contributors to the field of immunonutrition and cancer. These countries have made significant contributions to advancing knowledge in this area, demonstrating their research prowess and expertise. However, it is worth noting that other countries have also actively participated in the collaboration network, suggesting a collective global effort to tackle the challenges posed by cancer through the lens of nutrition and immune modulation. Recently, there has been a growing demand for collaborative efforts spanning various disciplines to address emerging challenges in the field of immunoenriched nutritional therapy for cancer. Some authors propose that nutrition therapy should be considered a primary treatment for cancer, on equal terms with surgery, radiotherapy, and chemotherapy. This position is particularly relevant when addressing prevalent malnutrition issues in cancer patients, notably sarcopenia and cachexia, for which appropriate nutritional support remains a fundamental intervention[28,30,31]. The most globally cited documents provide valuable insights into original works that have shaped the field of immunonutrition and cancer research[28,29,32–41,43–50]. The prominent document titled 'Nutritional approach in malnourished surgical patients: A prospective randomized study' stands out as the most cited and influential publication[28]. This underscores the significance of nutritional interventions in improving the outcomes of cancer patients, particularly those undergoing surgical procedures. However, it is important to consider that the analysis focused on citation count and did not assess the methodological quality or impact of individual studies.

The analysis of keywords and thematic clustering offers an intriguing insight into the current thematic areas of interest within the field. The identification of clusters related to

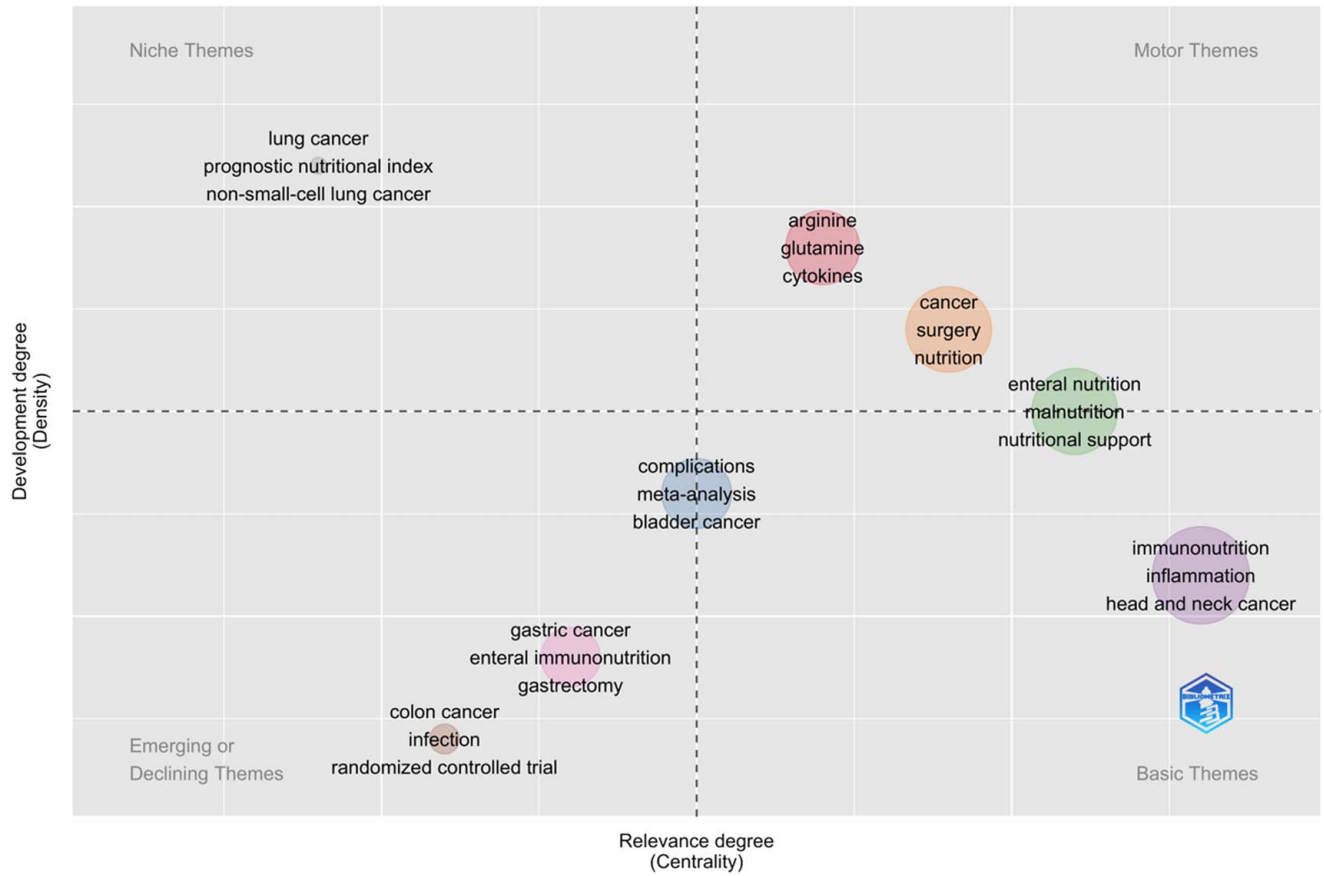


Figure 7. Thematic map. Each bubble represents a cluster, and its position is set according to the cluster Callon centrality (*x*-axis) and density (*y*-axis).

pharmaconutrients, surgical approaches, inflammation, and specific cancer types reflects the multifaceted nature of immunonutrition and its impact on cancer[6,51]. These clusters highlight the need to explore the fundamentals of immunonutrition, the effects of specific nutrients on immune cell function, and their influence on tumor microenvironments[17,52]. While the present bibliometric analysis provides valuable insights, several research gaps and future directions emerge from this analysis. Firstly, there is a need for further investigation into the specific mechanisms by which immunonutrition influences immune responses and cancer progression[53]. This necessitates conducting well-designed mechanistic studies, exploring the interactions between nutrition and the tumor microenvironment, and elucidating the molecular pathways involved[17,52]. Secondly, although the analysis identified prominent thematic areas, there is still much to be explored in terms of specific cancer types and patient populations[30]. Further research is warranted to investigate the effects of immunonutrition on different cancer types, considering the inherent heterogeneity in tumor biology and immune responses[54]. Moreover, personalized approaches that consider individual patient characteristics, such as genetic profiles and nutritional status, should be explored to optimize the efficacy of immunonutrition interventions.

Thirdly, while the analysis revealed the involvement of numerous institutions and countries, future research should focus on fostering more extensive and impactful international collaborations[31]. This would enable the sharing of resources, expertise, and diverse perspectives, facilitating the acceleration of research progress and the translation of findings into clinical practice.

It is essential to acknowledge that the selection procedure used in this study may introduce a degree of sampling bias. The exclusive reliance on English-language literature might have resulted in the oversight of valuable perspectives originating from non-English sources. Additionally, the informative nature of bibliometric analysis may not fully address specific research inquiries, potentially overlooking specific aspects of the topic. As a result, caution should be exercised when extrapolating our results to the wider population.

Conclusion

In conclusion, this bibliometric analysis offers a comprehensive overview of the scientific literature concerning immunonutrition and cancer research spanning the last 25 years. It is noteworthy that the number of publications has increased since 2020, which means that there is a chance of further growth in research output in the near future. Additionally, the review of the clustering algorithm generated by the authors' keywords revealed promising perspectives for applying nutrition strategies to different types of cancer. The analysis also confirms the increasing multidisciplinary collaborations and emerging thematic areas within the field, underscoring the significance of nutrition and immune

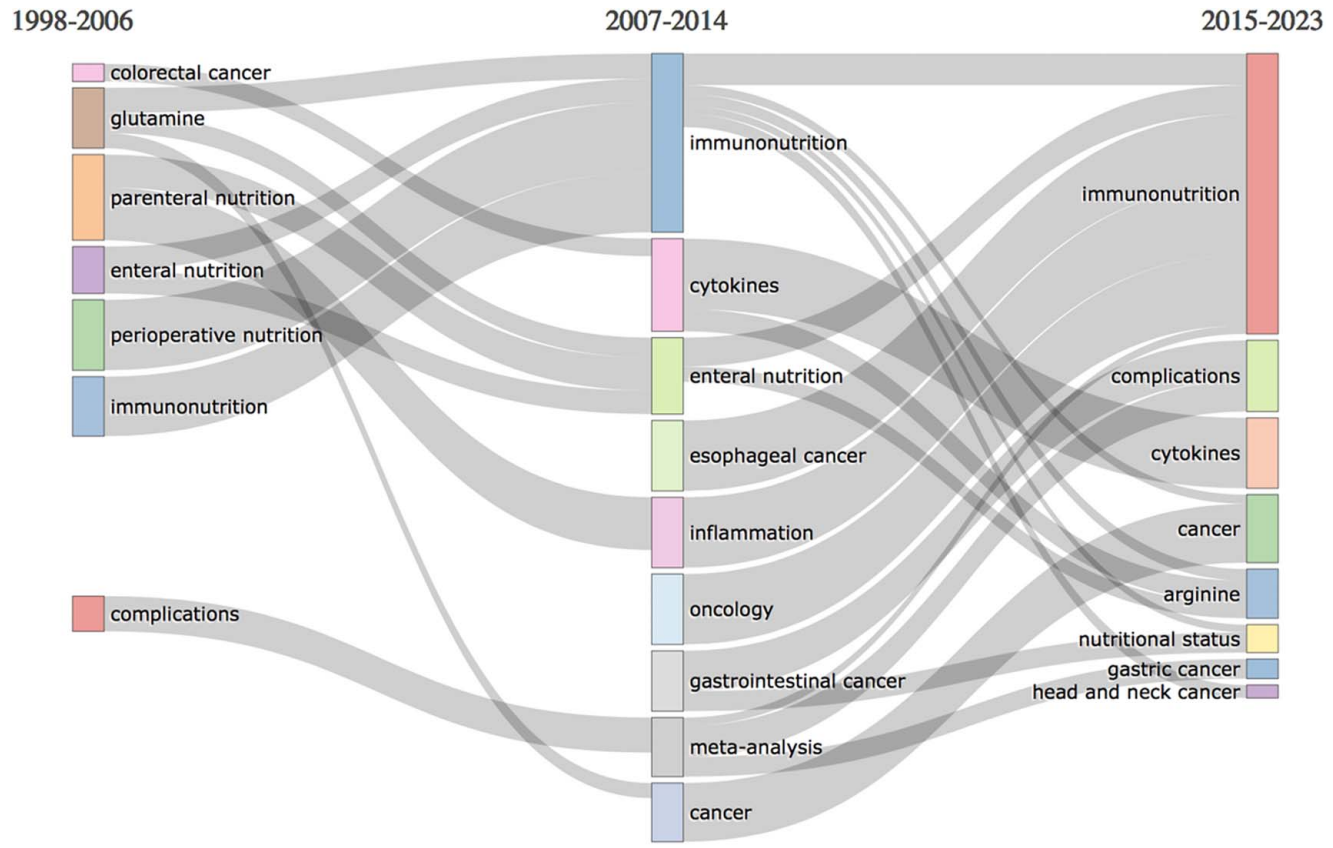


Figure 8. Thematic evolution. Thematic evolution analysis based on author's keywords. Each node width is generated by the keyword co-occurrence of the topics between two time slices. Colors are arbitrary.

function in cancer biology and therapeutic outcomes. On the other hand, current trends in publications highlights research gaps, emphasizing the need for more focused original studies, future investigations into specific cancer types as well as patient populations, and enhanced international collaborations. Through shedding light on potential research trajectories, this study provides guidance for improve cancer care practices through evidence-based nutritional solutions, which will contribute to the professional background of healthcare professionals.

Ethical approval

No ethical approval is needed as it is a bibliographic review.

Consent

No consent was obtained as it is a bibliographic review.

Sources of funding

The authors declare no source of funding.

Author contribution

F.D.F.: conceptualization, formal analysis, investigation, project administration, validation, and writing – original draft; C. G.C.: data curation, investigation, resources, supervision, and visualization; G.E.P.: data curation, formal analysis, validation, writing – original draft, writing – review and editing; C. A.: conceptualization, software, writing – review and editing; A.B.: investigation, resources, and supervision; O.B.: investigation, resources, and supervision; L.C.: data curation, investigation, methodology, and software; R.D.L.: conceptualization, methodology, project administration, and writing – review and editing; I.D.: formal analysis, project administration, and resources; L.I.: data curation, project administration, and validation. R.L.M.: conceptualization, formal analysis, and supervision; F.M.: conceptualization, formal analysis, software, and validation; D.P.: formal analysis, methodology, resources, and writing – review and editing; M.G.R.: conceptualization, investigation, project administration, and supervision; V.S.: data curation, project administration, and supervision; F.S.: conceptualization, investigation, supervision, writing – review and editing; K.P.: data curation, project administration, and supervision; L.M.: conceptualization, project administration, supervision, writing – original draft, writing – review and editing.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

It is a bibliographic review.

Guarantor

The guarantor is Dr Francesca Di Felice.

Data availability statement

Our article is a bibliographic review and bibliographic data were collected from Scopus database using 'immunonutrition' and 'cancer' as search strategy.

Provenance and peer review

Not commissioned.

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