



Review

Physical activity and immunity in obese older adults: A systematic bibliographic analysis

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ABSTRACT

Extensive research has been conducted on the roles of physical activity in immune functioning. However, reviews on the effect of physical activity on immune function among obese older adults are scarce. This study aimed to map the trend and development of the key terms and prominent sources to identify potential research opportunities through a systematic bibliographic analysis. A systematic search was conducted in the Scopus database on the following query: (sport* OR "physical activity" OR exercise) AND (elderly OR "older adult*" OR aging) AND (immun*) AND (obes*) AND NOT (animal), in March 2023. Publication timing and citation were descriptively analyzed, followed by the bibliographic coupling and the term co-occurrence analyses for generating network and overlay visualization mapping using the VOSviewers software. The search resulted in 426 articles dating back from 1991 to the present and were dominated by authors from Western countries. Three thematic clusters of this research area were generated, covering (1) the impact of physical activity or inactivity on health, (2) physical activity assessments and the use of association and cross-sectional study as the primary type of research, and (3) the physical activity impacts at the population level. For future research, more intervention studies are needed to understand how exercise affects immune response in older obese adults and to explore optimal duration, type, and intensity of the exercise, using a multi-omics approach. Studies in non-Western populations and systematic reviews are recommended to complement this bibliographic analysis.

Introduction

A tendency toward a constant growth of the elderly population in the recent and coming years is evident.^{1,2} In 2020, there were 727 million people aged 65 or older worldwide, which is expected to be more than double by 2050.³ This aging population has become a major public health concern due to increases in health care costs,^{4,5} required for managing the age-associated weakening of physiological functions such as cardiorespiratory, endocrine, and musculoskeletal systems in older adults.⁶ The decline in physiological function in the aging population is often exacerbated by obesity,⁷ which has also become a global pandemic in these recent years, affecting more than 600 million adults,⁸ and contributing to 70.7 and 77.0 million disability-adjusted life years (DALYs) in females and males,⁹ and an estimated 2.19% of global gross domestic product (GDP) globally. Obesity induces proinflammatory

cytokine, leading to chronic low-grade inflammation that contributes to the development of chronic diseases.⁶ Obesity also increases oxidative stress that damages cells and impairs immune function, thus, increasing susceptibility to infections and cancer.¹⁰ The public health problems related to aging and obesity, thus, are alarming.

Excessive adipose tissue masses in obesity serve as an underlying pathology of obesity-related metabolic diseases,⁷ since the adipose tissue is not only an energy reservoir but also a multifunctional endocrine organ secreting a range of bioactive peptides and proteins affecting the immune system.¹¹ The immune cells in the innate and adaptive immune systems tend to infiltrate visceral adipose tissue as insulin-responsive tissues that can incite inflammatory responses.^{11–13} It further leads to local and systemic increases in pro-inflammatory molecules, such as tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6, interferon (IFN)- γ , inflammatory adipokines, chemokines, and free fatty acids (FFAs).^{7,12} The accumulation effect on the alterations of these adipokines and cytokines

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Abbreviation list

csv	Comma-separated value
DALYs	Disability-adjusted life years
FFAs	Free fatty acids
IL	Interleukin
IFN	Interferon
GDP	Gross domestic product
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TNF	Tumor necrosis factor
TGF- β	Transforming growth factor-beta
US	United States

further contributes to the increases of low-grade systemic inflammation in obese individuals.^{7,14}

Similar to obesity, with the increase of age, the immune system undergoes a remodeling process, which is coined as ‘*immunosenescence*’,¹⁵ and characterized by declines in both innate and adaptive immunity. *Immunosenescence* induces considerable shifts in leukocyte subpopulations,¹⁵ declines in various immune cell functions,¹⁵ and increases in the predisposition to chronic activation of immune cells, resulting in local and systemic inflammations, a significant risk factor for morbidity and mortality.^{13,16–18} Aging and obesity, thus, share numerous biological similarities as both induce a state of low-grade chronic inflammation, which is coined as ‘*inflammaging*’, an inflammation state due to aging, or ‘*adipaging*’, an alteration of adipocyte tissue due to aging, responsible to numerous comorbidities such as metabolic syndrome and cardiovascular diseases.¹⁹ The inflammation in aging and obesity also contributes to the development of muscle loss (sarcopenia), which further exacerbates the inflammation state, creating a vicious cycle of metabolic and immunological dysfunctions.²⁰ The superimposition of aging with obesity, thus, drastically increases chronic systemic low-grade inflammation.^{6,10} Strategies to offset these deleterious impacts of aging and obesity on health, therefore, are required, and one of the key strategies in managing this problem is through physical activity.^{15,21,22}

Regular moderate-intensity physical activity has been found to attenuate the pathophysiology of ‘*adipaging*’ by reducing the production of pro-inflammatory cytokines and increasing the production of anti-inflammatory cytokines, which can help to reduce chronic inflammation.²³ Moderate-intensity physical activity improves systemic inflammation.²⁴ The anti-inflammatory properties of exercise are mediated through multiple pathways associated with the role of muscular contraction in increasing the release of anti-inflammatory cytokines (e.g., IL-10 and transforming growth factor-beta (TGF- β)) and suppressing the pro-inflammatory cytokines (e.g., IL-1, IL-2, IL-12, IL-18, IFN- γ , and TNF- α).¹² These effects are varied depending on the volume of contractile muscle mass involved, duration, type and intensity of the exercise.¹² The optimal exercise prescription for improving the immune system particularly for this target population, thus, needs to be determined by further research.

Both aerobic and resistance trainings are reported to improve immune responses.^{23,25} Regular moderate-intensity exercise also improves insulin sensitivity and glucose metabolism,²⁶ which can help to reduce inflammation associated with obesity and metabolic disorders and prevent sarcopenia.²⁷ On the other hand, high-intensity practices without sufficient recovery can trigger decreases in cellular immunity that promotes systemic inflammation propensity, thus, increasing the susceptibility to infectious diseases.^{12,24} Furthermore, while studies have suggested that acute exercise is an essential immune system adjuvant that improves defense activity and metabolic health,^{7,15} and that regular moderate-intensity physical exercises provide optimum stimulation in overcoming systemic inflammation,^{7,12} the effects of longitudinal

exercise on ‘*immunosenescence*’, however, are still inconclusive.²⁸ The specific mechanisms through which physical activity influences inflammation, thus, warrant more investigation. Nonetheless, growing evidence from previous research has supported an inverse relationship between moderate exercise training and illness risk.^{7,23} Thus, physical activity (i.e., exercise therapy) has been frequently prescribed as a practical and non-invasive approach to treating several metabolic diseases.^{24,29}

A systematic review reported that exercise immunology is a relatively new area of research, with 90% of papers published after 1990, although some of the earliest studies were published over a century ago.²³ The review also summarizes four major areas of exercise immunology, covering acute and chronic effects of exercise on the immune system, clinical benefits of this exercise-immune relationship, nutritional influences on the immune response to exercise, and the exercise effect on immunosenescence.²³ The first period (1900–1979) focused on changes in primary immune cell function caused by exercise. The second period (1980–1989) focused on the increasing evidence that vigorous exercise was linked to transitory immunological dysfunction, heightened inflammatory biomarkers, and a higher risk of upper respiratory tract infections. The third period (1990–2009) focused on the interaction between diet, immune system aging, and inflammatory cytokines. Lastly, the current period (2010–present) emphasizes technological advancements in mass spectrometry to apply biomolecular approaches to exercise immunology studies.^{23,30} It is further anticipated that the field of exercise immunology will investigate these technologies to offer perspectives on the relationships between physical activity, dietary intake, and immunological response, with applications to the individual level and how the immunological alteration caused by exercise lowers the risk of prevalent chronic diseases.^{23,30}

While growing evidence has, to some extent, elucidated common biological alterations in the immune system caused by physical activity in immunosenescence,²³ the development of research on physical activity in obese older adults in the literature needs to be explored. This study, therefore, aimed to map the trend and the development of the key terms and prominent sources related to the roles of physical activity in modulating immune systems among obese older adults, through a systematic bibliographic analysis, for identifying potential and recommended research areas for advancing the research.

Material and methods*Study design*

This study was a systematic review and bibliographic analysis on bibliographic data retrieved from the Scopus data based in March 2023 on the topic of physical activity concerning immunity among obese older adults.

Search strategy

The search was conducted in March 2023 since the time of inception on the following search query (TITLE-ABS-KEY (sport*) OR TITLE-ABS-KEY (“physical activity”) OR TITLE-ABS-KEY (exercise) AND TITLE-ABS-KEY (elderly) OR TITLE-ABS-KEY (“older adult*”) OR TITLE-ABS-KEY (aging)) AND (TITLE-ABS-KEY (immun*) AND TITLE-ABS-KEY (obes*) AND NOT TITLE-ABS-KEY (animal)).

Bibliographic metadata management

The results from the query were managed based on a guideline from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Abstracts were retrieved from the Scopus database and were reviewed based on PRISMA recommendations. Studies were excluded when the study was not conducted on humans or were irrelevant to the topic of physical activity and immune systems in obese older adults. The exclusion was based on the review of the title and abstract. The data from

the Scopus database were then downloaded in the comma-separated value (csv) format and were imported to and analyzed with Microsoft Excel and VOSviewers.³¹

Data collection and analysis

Publication Timing and Citation

Analysis of the bibliographic metadata was conducted to identify the progression of publication in time and the growth of citations along the publication period. The analysis was conducted on the raw bibliographic data from the Scopus database in the csv format using Microsoft Excel software.

Bibliographic analysis

The bibliographic analysis was conducted using the VOSviewers software on the csv bibliographic metadata file from the Scopus database. The bibliographic coupling assigned ‘countries’ as the selected unit of analysis with the counting method of ‘full counting’. The limit of the maximum number of countries per document and the minimum number of citations were not assigned. The limited minimum number of documents of a country, however, was set to ‘one’. We then maximize the number of countries to be selected to include all the results. Manual cleaning was conducted on the results before the network, and overlay visualization proceeded for clustering and identifying the trend regarding sources and timing.

The term co-occurrence was conducted in the title and abstract fields. We assigned the ‘ignore the structured abstract label and the copyright statements’ and ‘full counting’ as the counting method. We assigned 25 words as the minimum number of term occurrences in the document. All terms that met the threshold were displayed and followed by manual cleaning to ensure that all the terms were relevant to the research topic. The general layout for the network and overlay visualization for the bibliographic analysis is illustrated in Table 1.

Results

Search results

Fig. 1 illustrates the PRISMA 2020 flow diagram for systematic search. As shown in the figure, 467 studies were obtained from the initial search. No study was removed in the initial screening, which included

Table 1
Lay out Assignment.

Parameter	Value
Normalization	Association Strength
Lay out	
Attraction	2
Repulsion	0
Random starts	1
Maximum iterations	1,000
Initial step size	1.00
Step size reduction	0.75
Step size convergence	0.001
Random seed	0
Clustering	
Resolution parameter (detail of clustering)	1
Minimum cluster size [N]	1
Random starts	10
Iteration	10
Random seed	0
Visualization	
Scale	1.00
Weights	Document/Occurrences
Labels size	0.50
Maximum number of lines	1 000

duplication-checking, nor after checking the relevance based on the title. However, 41 records did not contain abstract data, therefore, were removed from the result list leaving 426 studies. No further exclusion was conducted after reviewing the abstract. Thus, 426 bibliographic data from the Scopus database were retrieved for further analysis.

Publication Timing and Citation

Fig. 2 summarizes the growth of publications and citations on this research topic. The earliest publication was published in 1991 which increased slowly in the next two decades until 2019. In 2020 the number of publications on this topic almost doubled from the previous year. The increased trend persisted in the following year. There was a decline in the number of documents in 2023. However, the data were retrieved in the first quartal of the year. Thus, the total number of documents at the end of the year is expected to rise. Fig. 2 also illustrates the number of citations. As depicted in Fig. 2, the yearly citations fluctuated in numbers.

Bibliographic coupling

The bibliographic coupling query yielded 71 countries. However, three were removed from the list (‘Universitat Greifswald’, ‘health’ and ‘center’) as those terms were not qualified as the name of a country. Of the 68 countries, only 60 countries were connected by bibliographic coupling with each other and, thus, were processed in the network and overlay visualization. The list of the 60 countries, along with the strength of the links are provided in Appendix A. Fig. 3A shows that the publications were dominated by publications from the United States (US), and they were categorized into 9 clusters. The complete list of countries in each cluster, along with their occurrence and relevance, is available in Appendix A. In addition to the US, most of these countries were in Europe. Only a few countries in Asia (e.g., China, Cambodia and South Korea) and Africa (e.g., South Africa and Cote Divoire) contributed as the sources of the document published on this research topic.

Fig. 3B further indicate that authors from the US and most European countries were the pioneer in this research topic, followed by smaller countries such as Brazil, Greece, Poland, Singapore, and Romania.

Term co-occurrence

There were 6 477 terms resulting from the initial term co-occurrence query. Of those, 124 terms met the threshold of the assigned minimum number of occurrences. All items were retained and processed in the data visualization and were presented in Fig. 4. As seen in Fig. 4A, all terms were classified into three clusters. The complete list of terms, their occurrence, and relevance within each cluster are available in Appendix B. The three clusters in Fig. 4a are codes with red, blue, and green colors. The red cluster primarily represents the impacts of physical activity and inactivity (e.g., obesity, disease, covid, immune system, muscle mass, tissue). The blue cluster mainly codes physical activity types and assessments (e.g., exercise, strength, week/month, baseline) and study design on the topic (e.g., cross-sectional studies, association, relationship, factor). Finally, the last cluster, represented by green color appears to cover physical activity level at the population level (e.g., risk, population, prevalence, risk factor).

Fig. 4B illustrates the overlay visualization of the trend of terms connected with physical activity in the published documents from 2016 to the present. As seen in the figure, prior to 2016, most studies focused on the impact of physical activity on health, disease (risk factor), and function (physiology). The topic then refocused on its role in obesity, body mass index, and inflammation and its impact on older adults. Intervention studies on this topic emerged around 2016, while association and relationship studies gained more interest afterwards. Studies on the immune system, serum, and cellular parameters also increased during this period. Data from Appendix B indicate that the occurrence and relevance levels of physical activity correlate (i.e., association and cross-

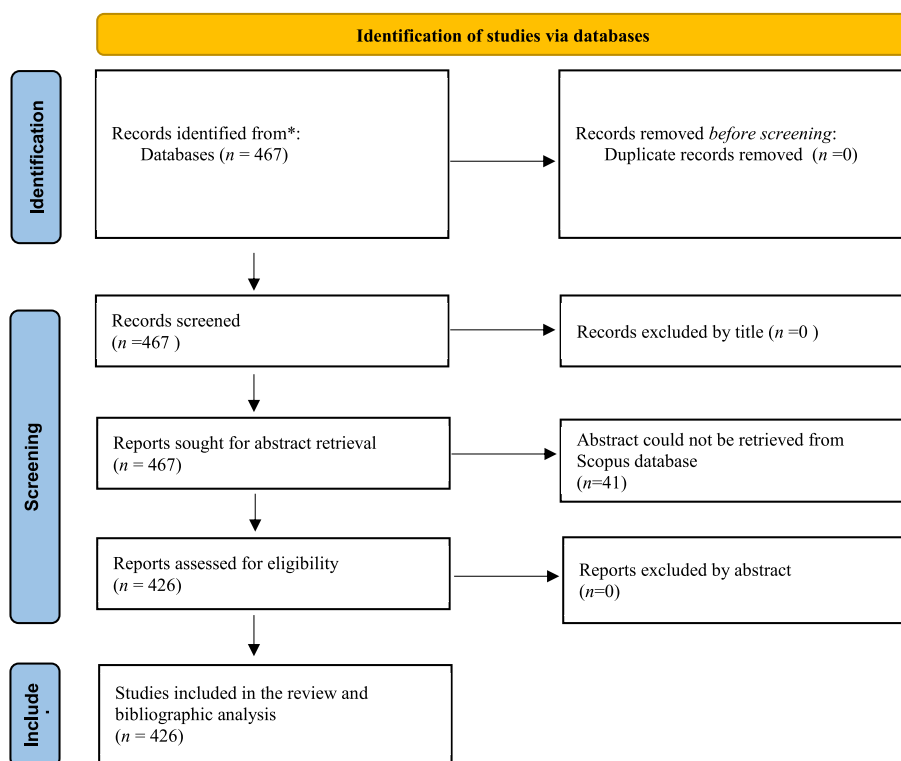


Fig. 1. Prisma Flowchart search.

sectional) are higher than those focusing on the intervention studies (i.e., intervention).

Fig. 4B is one of the myriads of overlay visualizations and timing that could be explored. However, Fig. 4A and B, in general, illustrate that physical activity, obesity, disease, and inflammation are the topic that gained the most interest as they are among those with the highest occurrence and relevance based on the term-occurrence analysis. Topic in the immune system and immune function unrelated to systemic inflammation only received little interest.

Discussion

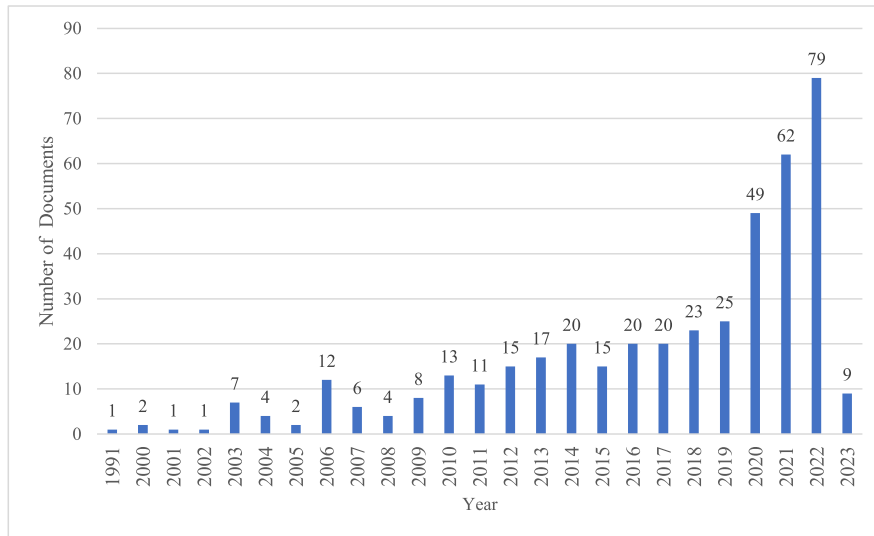
While extensive research has been conducted in the exercise immunology field of study,^{1,7,12} this current study is the first to map the trend, development, key terms, and prominent sources related to physical activity and the immune system in obese older adults through a systematic bibliographic analysis. The finding indicated that published documents in this research area date from 1990. Compared to the general exercise immunology studies,^{23,30,32} the published document on this field of study in obese older adults, however, is still limited. In light of the current tendency of the global ageing population and the growing obesity epidemic, and the potential roles of physical activity in improving the immune system in obese and aging populations, this area of research still needs further exploration.

The bibliographic coupling analysis further indicated that the documents and citation activities were dominated by researchers from Western countries, which has also occurred in other fields of science.³³ The Western domination in exercise immunology research may be attributed to several reasons. First, Western countries are generally more economically developed than other regions; thus, they tend to have well-established research infrastructures and funding sources that allow researchers to conduct high-quality research,³⁴ including in this field of study. Second, exercise immunology research has its roots in the Western world, thus, providing a strong basis for exercise immunology research compared to other regions.³⁵ Finally, Western countries have well-developed networks of researchers

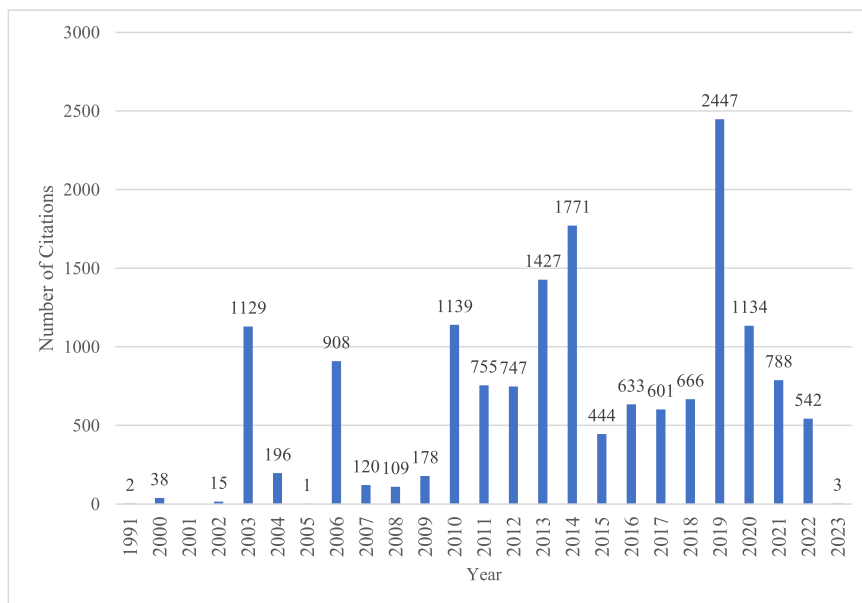
and institutions, which allows for collaboration and the sharing of resources and expertise,³⁴ thus, increasing the research productivity and outputs in this field of study. A shift toward more contributions from non-Western countries, thus, requires addressing factors such as research infrastructure, strong research tradition and networking. Encouraging research in non-Western countries is crucial for a comprehensive understanding of global issues and tailored solutions to address the impact of obesity and aging, which significantly challenge low- and middle-income countries with limited healthcare resources.³⁶

Concurrent to the major key topics that have been suggested in the previous reviews on exercise immunology,^{23,30,32} the co-occurrence key term analysis in this present study further mapped the indicated three thematic key terms on exercise immunology among older adults. The theme covered the impact of physical activity or inactivity on health, physical activity types and assessments, the use of the association and cross-sectional study as the primary type of research, and physical activity impacts at the population level. Cross-sectional observation studies in this regard are prevalent in this field, possibly because these studies are usually easier to conduct and require less time and resources compared to other study designs, particularly intervention studies.³⁷ Cross-sectional observational studies are also routinely conducted because they provide valuable insights into the relationship between physical activity and immune function and identify potential risk factors associated with the immune system and physical activity, which can further be confirmed by randomized control trials.³⁷ However, although cross-sectional observation is an important research design in this research field, they are limited in their ability to establish a causal relationship.³⁸ Moreover, most cross-sectional studies have focused on immune markers found in peripheral blood rather than in tissues where the primary immune functions occur.³⁹ Therefore, more interventions are required to increase the level of evidence in this research field, particularly at the tissue level.

The findings of this study also indicate that physical activity, obesity, disease, and inflammation are the topic that gained the most interest with the highest occurrence based on the term-occurrence analysis. On the



a. Number of Document by Year of Publication



b. Number of Citations by Year of Publications

Fig. 2. Publication timing and citation.

contrary, based on the term-occurrence analysis, topics in the immune system and immune function unrelated to systemic inflammation still received little interest. Nonetheless, several studies suggest several potential mechanisms by which regular moderate-intensity physical activity or exercise offset the deleterious effect of obesity and aging on the immune system, other than the increased production of anti-inflammatory cytokines.¹¹ Studies suggest that regular moderate-intensity exercise improves insulin resistance and impaired glucose metabolism, which contribute to immune dysfunction,¹⁹ and alters the gut microbiome, which could improve immune function.¹⁵ While several potential mechanisms of exercise in improving immune responses among obese older adults' immune have been proposed,^{7,23} further research is required to confirm and extend knowledge on possible mechanisms of exercise on immune response in older obese adults, the duration, type, and intensity of exercise required to exert positive

impacts on the immune system, with a particular focus on understanding the mechanisms underlying the transient alterations induced by acute exercise and the sustained adaptations induced by chronic exercise.³⁰

Furthermore, the use of a multi-omics approach is recommended to gain a more comprehensive understanding of the underlying molecular mechanisms in which exercise influences immune responses among obese older adults.³⁰

The present study has contributed to summarizing finding in exercise immunology in obese older adults through systematic bibliography analysis. The study carries some advantages inherent to the bibliographic method in that it can objectively and quantitatively summarize key terms and sources in publications efficiently using bibliometric indicators that are highly methodologically dependent.⁴⁰ However, several limitations need to be acknowledged. First, bibliographic analysis requires not only technical skill but critical sense and knowledge of the examined scientific domain to

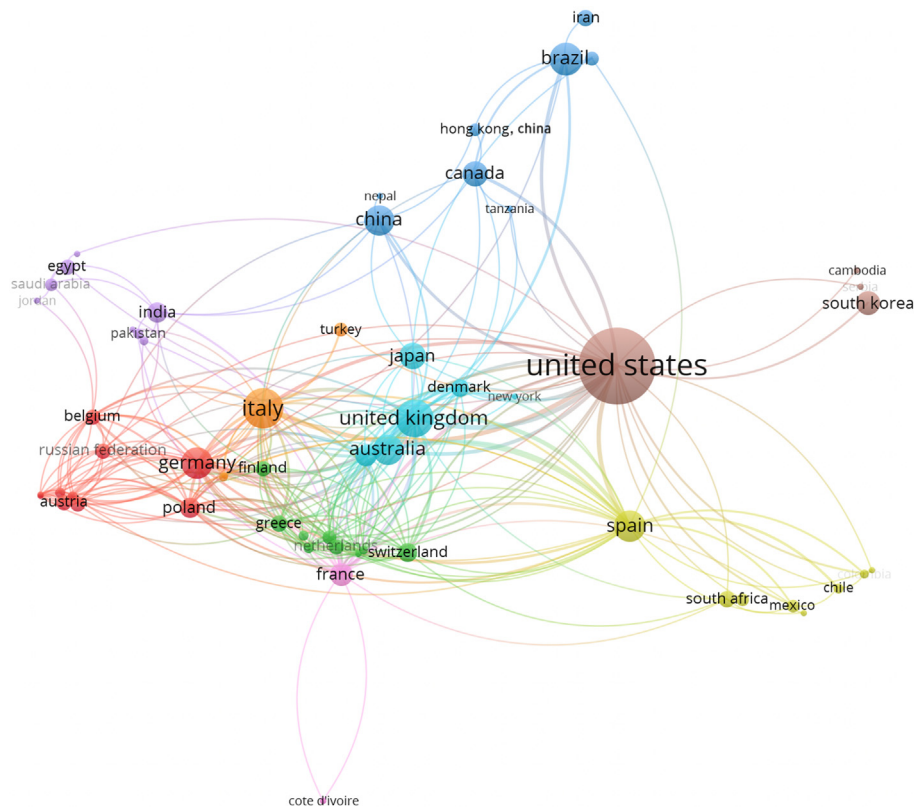


Fig. 3a. Bibliographic coupling with countries as unit of analysis (network visualization).

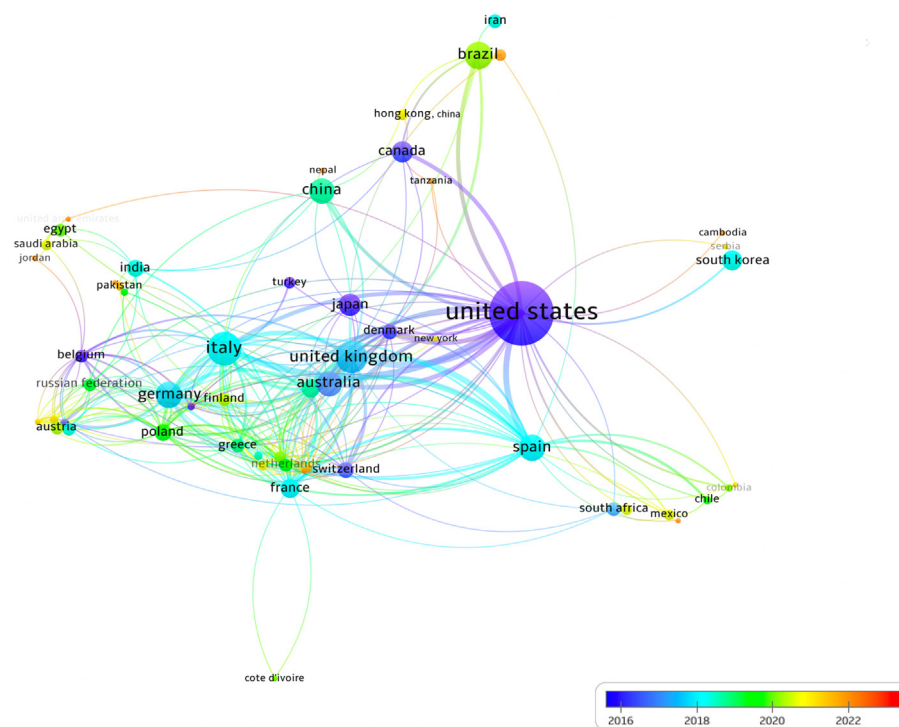


Fig. 3b. Bibliographic coupling with countries as unit of analysis (overlay visualization).

interpret the myriad of findings resulting from bibliometric investigations correctly and efficiently.⁴⁰ The interpretation and methodological skills are of utmost importance to arrive at a consistent and standardized set of indicators.^{31,40} The researcher in this study has reported the details of the

selected techniques in the bibliographic analysis for increasing accountability. However, the interpretation of the findings might be subjective. Secondly, this present study only employs ‘association strength’ as the standard normalization default to minimize the analysis’s complexity.³¹

Other normalization techniques such as ‘fractionalization’ and ‘LinLog/modularity’,³¹ thus, warrant further exploration in future studies. The exploration is required to minimize the risks of discrediting research that is important by the standards of its scientific discipline.⁴⁰ Thirdly, the bibliometric method is a quantitative method that attempts to transform unlimited quantities of publications into manageable entities, and its assertion of the research quality is limited.⁴⁰ Thus, this study should be followed by an in-depth analysis of the prominent document and sources through a systematic review.

Conclusions

The published documents in this research dated from 1990 and were dominated by Western countries. The three thematic key terms derived from the network mapping from the bibliographic analysis covering the impact of physical activity or inactivity on health, physical activity types and assessments, the association and cross-sectional study as the primary type of research, and physical activity impacts at the population level. Future research needs to focus on themes that still receive minor interest, such as the intervention studies of physical activity on immune functioning, at both individual and population levels. Further research is also required to corroborate and expand knowledge concerning the plausible mechanisms through which exercise affects immune response in older adults who are obese. Further investigation is also warranted to determine the optimal exercise parameters, including duration, type, and intensity, that elicit beneficial effects on the immune system, as well as to apply a multi-omics approach to comprehensively elucidate the underlying molecular mechanisms by which exercise influences acute or chronic immune responses in older adults with obesity. Studies for advancing this area of research in non-Western populations are also recommended to address the impact of obesity and aging, which significantly challenge low- and middle-income countries with limited healthcare resources. A further systematic review of this area of research is also highly recommended to complement this bibliographic analysis.

Submission statement

The manuscript has not been published previously, is not under consideration for publication elsewhere, is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere, including electronically in the same form, in English or any other language, without the written consent of the copyright holder.

Authors' contributions

All authors have contributed substantially to the analysis, interpretation, and drafting. All authors approved the final version and agreed to be accountable for all aspects of the work in ensuring the accuracy or integrity of the research and the manuscript.

Ethical approval statement

This study did not need ethical approval because no individual patient data was used.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.smhs.2023.07.001>.

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