

R E V I E W

A bibliometric analysis of the impact of COVID-19 vaccines on the immune system (2020-2024)

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Abstract. *Background and aim:* The rapid development and deployment of COVID-19 vaccines have been pivotal in mitigating the global pandemic, yet the long-term impact of these vaccines on the immune system remains an area of ongoing investigation. *Methods:* This bibliometric analysis aims to provide a comprehensive evaluation of global research trends and key findings related to the effects of COVID-19 vaccines on immune function, drawing on data from the Scopus and Web of Science Core Collection (WOS-CC) databases. Data merging, statistical analyses, and visualizations were conducted using RStudio and the Bibliometrix R package. *Results:* We analyzed 377 research and review articles published between 2020 and 2024, identifying trends in publication volume, citation metrics, and keyword frequency. Our findings highlight the complexity of vaccine-induced immunity, including the duration of immune responses, interactions with other vaccines, and potential alterations in immune surveillance. The analysis also underscores the importance of collaborative research efforts, with significant contributions from leading institutions and countries. *Conclusions:* This study offers valuable insights into the evolving landscape of COVID-19 vaccine research, emphasizing the need for continued investigation to optimize vaccination strategies and address emerging public health challenges. (www.actabiomedica.it)

Key words: COVID-19 vaccines, immune system, bibliometric analysis, vaccine-induced immunity, global research trends, vaccination strategies

Introduction

The COVID-19 pandemic has dramatically reshaped global public health priorities, with the rapid development and deployment of vaccines being a cornerstone of the response (1). While considerable attention has been paid to the immediate efficacy and safety of these vaccines, understanding their long-term impact on the immune system is of great interest (2). As we transition into the post-pandemic era, the focus has shifted toward evaluating the extended effects of COVID-19 vaccines (3), including their

influence on immune function (4), vaccine-induced immunity (5), and potential interactions with other aspects of immune health (6). Recent studies have revealed an evolving landscape of SARS-CoV-2 variants, underscoring the importance of ongoing immune system research. For instance, variants such as Delta and Omicron have shown varying levels of vaccine resistance, which has raised questions about the duration and breadth of vaccine-induced immunity (7). Moreover, some studies suggest that certain variants may interact with immune responses differently, complicating the long-term prediction of vaccine efficacy

(8). Incorporating these findings highlights the urgent need to continue researching the immune system's response to vaccination in the face of such dynamic challenges. COVID-19 vaccines have proven effective in reducing severe disease and death (9), but emerging evidence suggests that their effects on the immune system are complex and multifaceted (10). Recent studies indicate that these vaccines may influence various immune parameters, including the duration of immune responses (11), interactions with other vaccinations (12), and potential alterations in immune surveillance (13). For example, research has shown that the duration of immune memory varies across different population groups, suggesting the need for tailored vaccination strategies (14). Exploring these factors is essential for several reasons:

- a. **Public health impact:** A comprehensive understanding of the long-term effects of COVID-19 vaccines can help in optimizing vaccination strategies, ensuring sustained protection against COVID-19, and addressing any unintended consequences on overall immune health (15).
- b. **Guidance for future vaccination:** Insights gained from ongoing research will inform the design of future vaccines and vaccination schedules, potentially improving their efficacy and safety profiles (16).
- c. **Addressing emerging challenges:** As new variants of SARS-CoV-2 emerge and global vaccination rates increase, evaluating how vaccines interact with the immune system will be crucial for adapting public health policies (17) and vaccination programs (18).

This bibliometric analysis provides a detailed review of recent studies published between 2020 and 2024, focusing on the impact of COVID-19 vaccines on various aspects of the immune system. By synthesizing data from diverse research efforts, this article aims to highlight key findings, identify trends, and address gaps in the current understanding of vaccine-induced immune responses. The novelty of this review lies in its comprehensive analysis of new evidence, including the evolving dynamics of SARS-CoV-2 variants, and its implications for both immediate and long-term public health strategies.

Materials and methods

Article selection strategy

In August 2024, data were collected from the Scopus and Web of Science Core Collection (WOS-CC) databases for a detailed analysis of research and review articles examining the effects of COVID-19 vaccines on the immune system. The search strategy was meticulously crafted to cover a wide range of topics related to this area. Table 1 details the search queries employed in the databases.

To guarantee the precision and relevance of the data, specific inclusion criteria were applied. These criteria included: (1) articles published from 2020 to 2024, (2) articles written in English, and (3) the exclusion of conference proceedings, book chapters, and editorial content. Figure 1 provides a flowchart that visually represents the process of data extraction and selection.

Performance analysis

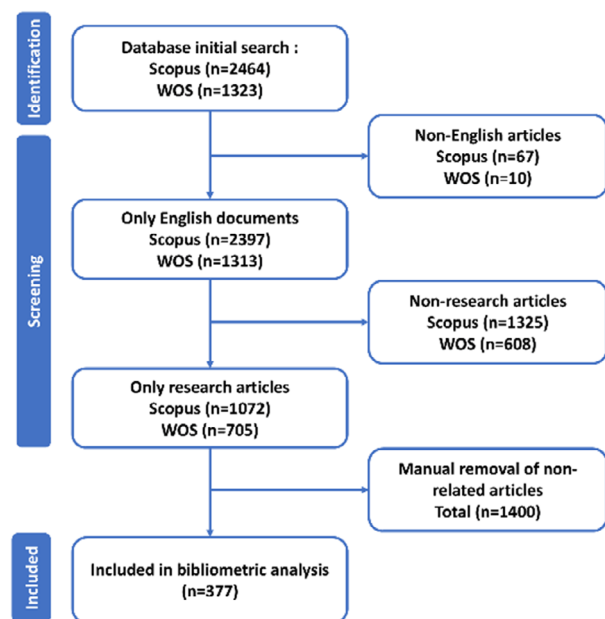
In this study, performance analysis and science mapping were carried out using specialized software tools. RStudio v.4.3.1, along with the bibliometric R-package (<http://www.bibliometrix.org>; accessed on 20 August 2024), was utilized for these analyses (16). Additionally, Biblioshiny was employed for data analysis due to its web-based capabilities. This software operates with two databases, and WOS and Scopus data were merged in excel file using Table 2 codes in R-studio and then non-related data were removed manually. Biblioshiny was selected because it offers comprehensive and detailed citation information, which is particularly useful for conducting in-depth bibliometric analyses and evaluating research impact.

Analysis of keyword frequencies

A timeline analysis was carried out to monitor the frequency of specific keywords over time. A TreeMap was generated to visually display the distribution and significance of the top 10 most frequently occurring keywords. Additionally, thematic analysis was conducted to discern the primary trends and topics in the

Table 1. Scopus and WOS queries for bibliometric analysis of the impact of COVID-19 vaccines on the immune system

No.	Queries
#1	“2019 nCoV Disease” Or “2019 nCoV Infection” Or “2019 Novel Coronavirus” Or “2019 Novel Coronavirus Disease” Or “2019 Novel Coronavirus Infection” Or “2019 Novel Coronaviruses” Or “2019-nCoV” Or “2019-nCoV Disease” Or “2019-nCoV Diseases” Or “2019-nCoV Infection” Or “2019-nCoV Infections” Or “Coronavirus 2, SARS” Or “Coronavirus Disease 19” Or “Coronavirus Disease 2019” Or “Coronavirus Disease 2019 Virus” Or “Coronavirus Disease-19” Or “Coronavirus, 2019 Novel” Or “Coronavirus, Wuhan” Or “COVID 19” Or “COVID 19 Pandemic” Or “COVID 19 Virus” Or “COVID 19 Virus Disease” Or “COVID 19 Virus Infection” Or “COVID19” Or “COVID-19” Or “COVID-19 Pandemic” Or “COVID-19 Pandemics” Or “COVID19 Virus” Or “COVID-19 Virus” Or “COVID-19 Virus Disease” Or “COVID-19 Virus Diseases” Or “COVID-19 Virus Infection” Or “COVID-19 Virus Infections” Or “COVID19 Viruses” Or “COVID-19 Viruses” Or “Disease 2019, Coronavirus” Or “Disease, 2019-nCoV” Or “Disease, COVID-19 Virus” Or “Infection, 2019-nCoV” Or “Infection, COVID-19 Virus” Or “Infection, SARS-CoV-2” Or “Novel Coronavirus, 2019” Or “Pandemic, COVID-19” Or “SARS Coronavirus 2” Or “SARS Coronavirus 2 Infection” Or “SARS CoV 2 Infection” Or “SARS CoV 2 Virus” Or “SARS-CoV-2” Or “SARS-CoV-2 Infection” Or “SARS-CoV-2 Infections” Or “SARS-CoV-2 Virus” Or “SARS-CoV-2 Viruses” Or “Severe Acute Respiratory Syndrome Coronavirus 2” Or “Severe Acute Respiratory Syndrome Coronavirus 2 Infection” Or “Virus Disease, COVID-19” Or “Virus Infection, COVID-19” Or “Virus, COVID19” Or “Virus, COVID-19” Or “Virus, SARS-CoV-2” Or “Viruses, COVID19” Or “Wuhan Coronavirus” Or “Wuhan Seafood Market Pneumonia Virus”
#2	“Vaccine” Or “Vaccines”
#3	“Immune Systems” Or “System, Immune” Or “Systems, Immune” Or “Immune System”
#4	#1 AND #2 AND #3

**Figure 1.** The flow chart of the screening process using PRISMA.

selected articles. Yearly assessments of local publication trends and the average total citations per article were performed. To identify the most prolific journals, publication counts were analyzed, and Bradford’s Law was

used to identify core journals—those few journals that contribute significantly to citations in the field (19).

Identification of leading institutions, sources, authors, and collaborating countries

The top 10 most productive institutions and authors were ranked based on their share of published papers. Collaboration patterns were visualized to elucidate the relationships between institutions and authors. In the country analysis, countries were ranked by the proportion of articles they contributed, and the extent of multi-country collaborations was assessed for the top 10 countries. A network of country collaborations was mapped according to the number of publications from each country.

Results

Summary of the papers

A total of 377 research and review articles were examined, sourced from 246 different journals. The analysis included contributions from 4,079 authors,

Table 2. Codes were used to merge Scopus and Web of Science exported data in RStudio

```
library(bibliometrix)
library(openxlsx)
## importing web of science dataset
web_data<-convert2df("abs.txt")
## importing scopus dataset
scopus_data<-convert2df("abs.
bib",dbsource="scopus",format="bibtex")
##combined both datasets
combined<-mergeDbSources(web_data,scopus_
data,remove.duplicated=T)
##exporting file
write.xlsx(combined,"combinedabs.xlsx")
```

yielding an average of 15.16 citations per document over the past decade. Key findings related to the impact of COVID-19 vaccines on the immune system are summarized in Table 3, which lists the most-cited documents in this field over the last ten years. The Annual Growth Rate for this research area was calculated at 26.26%, indicating a steady increase in publications during the study period. The substantial volume of research is further highlighted by the presence of 917 unique author keywords. It is noteworthy that a relatively small proportion of authors (11.67%) participated in collaborative studies.

Trend of publication and citation

The annual number of publications varied, with the peak in 2022 (N = 118) and the lowest in 2020 (N = 24). The trend of publications over the years is illustrated in figure 2A. Furthermore, the average total citations per article also showed considerable fluctuation. A significant increase was observed in 2020, with the mean citations per article reaching 16.12, whereas 2024 recorded the lowest average at 0.44 (Figure 2B).

By utilizing Bradford's Law, which describes how scientific articles are distributed among journals, we identified 24 core journals that are preferred by researchers (Figure 3). These core journals collectively produced a significant share of the total publications on the impact of COVID-19 vaccines on the immune system. Our analysis showed that "Frontiers in Immunology" was the most prolific journal, with 27 articles, representing about 7.16% of all publications during

the study period (Table 4). Furthermore, we assessed the local citations of these core journals within our dataset, "Frontiers in Immunology" received the highest number of local citations (in total 206).

Most productive authors, institutions, countries, and their collaboration network

Harvard University (USA), Tel Aviv University (Israel), and the University of Pennsylvania (USA) were the top contributors, with 21, 20, and 20 publications, respectively. Prominent authors in this area included Li Y. and Zhang Y., each with 13 articles, followed by Li J. and Liu Y. with 11 articles. The Three-Fields Plot maps the connections among authors, journals, and keywords, offering a detailed view of the research and review activities concerning the impact of COVID-19 vaccines on the immune system from 2020 to 2024 (Figure 4).

Over the past decade, the USA and China dominated global scientific output, with 226 and 134 publications, respectively. Italy and Iran followed with 126 and 95 publications, respectively (Table 5). In terms of publication trends, both the USA and China showed a strong preference for single-country publications, contributing 53 each. The majority of collaborative efforts also centered around the USA and China.

Co-occurrence, hotspots and emerging keywords

Author keywords were analyzed using Biblioshiny, with a focus on those frequently associated with COVID-19, vaccines, and immunity (Figure 5A). A notable upward trend was observed in keywords related to antibodies (Figure 5B). Timeline analysis of significant keywords indicates that seven keywords in Figure 6 experienced peak citations during the pandemic.

In summary, this study comprehensively reviewed the impact of COVID-19 vaccines on the immune system, identifying top journals, impactful articles, collaborations between institutions, authors, and countries, as well as important and emerging keywords. The findings provide valuable insights into the research landscape and highlight potential areas for future studies.

Table 3. The top 10 most cited documents on the impact of COVID-19 vaccines on the immune system (2020–2024)

Rank	Study ID [References]	Title of the Document	Journal Name	Total Citations	DOI
1	Wu Y, 2020 (17)	A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2	Science	759	10.1126/science.abc2241
2	Carreño J, 2022(18)	Activity of convalescent and vaccine serum against SARS-CoV-2 Omicron	Nature	333	10.1038/s41586-022-04399-5
3	Poh C, 2020(20)	Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralising antibodies in COVID-19 patients	Nat Commun	287	10.1038/s41467-020-16638-2
4	Vanderheiden A, 2020 (21)	Type I and Type III Interferons Restrict SARS-CoV-2 Infection of Human Airway Epithelial Cultures	J Virol	205	10.1128/JVI.00985-20
5	Beharier O, 2021(22)	Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine	J Clin Invest	175	10.1172/JCI150319
6	Kiyotani K, 2020(23)	SARS-CoV-2 genomic variations associated with mortality rate of COVID-19	J Hum Genet	100	10.1038/s10038-020-0771-5
7	Poduri R, 2020(24)	Drugs targeting various stages of the SARS-CoV-2 life cycle: Exploring promising drugs for the treatment of COVID-19	Cell Signal	94	10.1016/j.cellsig.2020.109721
8	Spencer A, 2021(25)	Heterologous vaccination regimens with self-amplifying RNA and adenoviral COVID vaccines induce robust immune responses in mice	Nat Commun	91	10.1038/s41467-021-23173-1
9	Lyons-Weiler J, 2020 (26)	Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity	J Transl Autoimmun	84	10.1016/j.jtauto.2020.100051
10	Lederer K, 2022 (27)	Germinal center responses to SARS-CoV-2 mRNA vaccines in healthy and immunocompromised individuals	Cell	81	10.1016/j.cell.2022.01.027

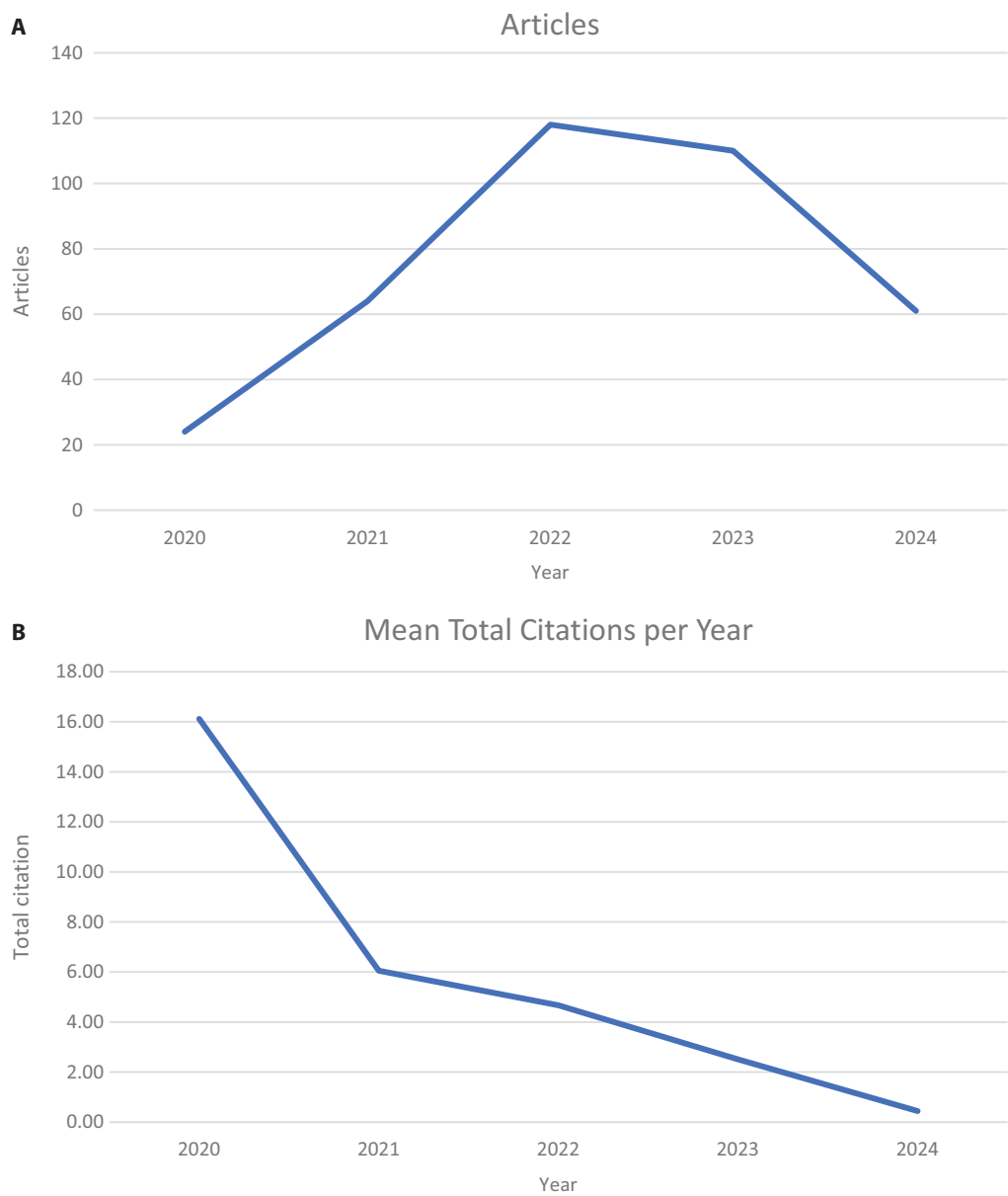


Figure 2. Global yearly trends in (A) publications and (B) citations related to the effects of COVID-19 vaccines on the immune system.

Discussion

The results of this bibliometric analysis provide a comprehensive overview of the global research landscape concerning the impact of COVID-19 vaccines on the immune system. By examining 377 research and review articles published between 2020 and 2024, this study sheds light on several critical trends

and emerging themes that have defined the research in this field. The substantial increase in publications over the study period, particularly the peak in 2022, underscores the intense focus and urgency in understanding the immunological effects of COVID-19 vaccines. This surge in research activity likely reflects the global scientific community’s response to the immediate need for vaccine-related knowledge to combat

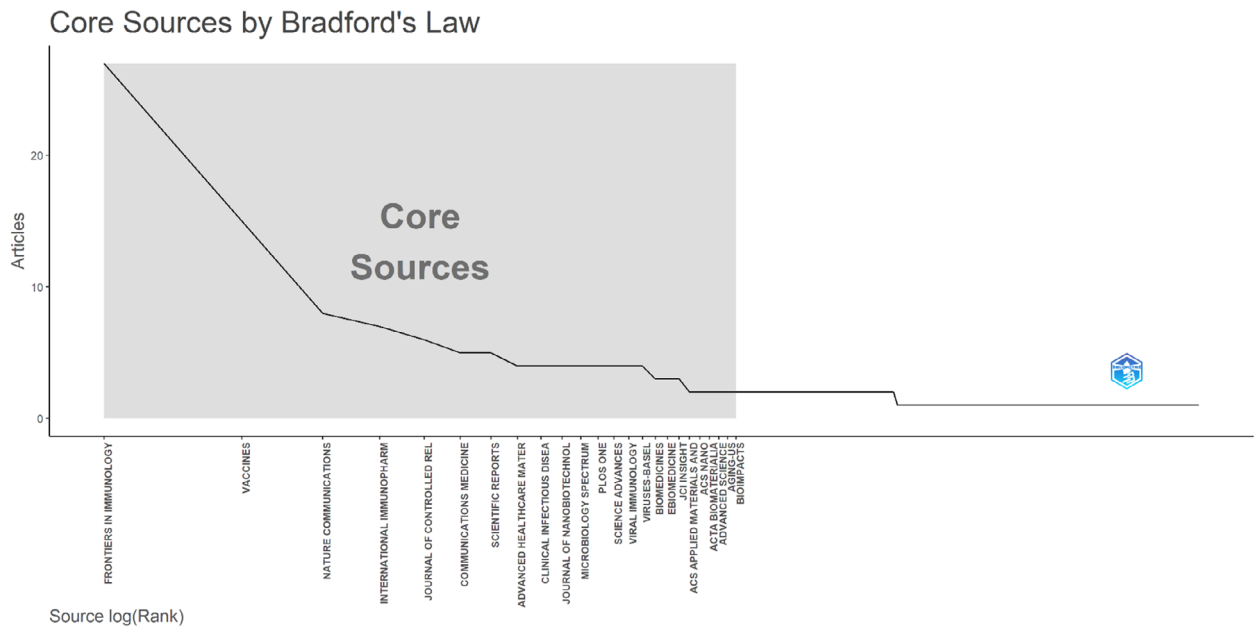


Figure 3. The Bradford’s Law analysis identified 24 core journals focused on the impact of COVID-19 vaccines on the immune system from 2020 to 2024.

Table 4. The top 10 journals published more article on the impact of COVID-19 vaccines on the immune system

Sources	Articles
Frontiers in Immunology	27
Vaccines	15
Nature Communications	8
International Immunopharmacology	7
Journal of Controlled Release	6
Communications Medicine	5
Scientific Reports	5
Advanced Healthcare Materials	4
Clinical Infectious Diseases	4
Journal of Nanobiotechnology	4

the ongoing pandemic(9). The high average citation count per document (15,16) suggests that the research outputs in this domain are not only abundant but also influential, with significant contributions to the broader scientific debate (28). One of the most critical aspects highlighted by the analyzed literature is the complexity of vaccine-induced immune responses(29). The duration of these responses, as reflected in highly

cited studies, remains a key area of interest. This focus is vital, given the evolving nature of SARS-CoV-2 and the emergence of new variants. The literature suggests that while COVID-19 vaccines are effective in inducing robust immune responses, the longevity and breadth of these responses can vary depending on factors such as vaccine type, dosing intervals, and population demographics (30). Studies that examine the transfer of immunity, such as maternal to neonatal antibody transfer, also add valuable insights, particularly in vulnerable populations(31). Another significant theme is the interaction of COVID-19 vaccines with other vaccines and their potential effects on overall immune surveillance(32). The research indicates a nuanced landscape where heterologous vaccination regimens and pre-existing immune conditions may influence vaccine efficacy and safety. For example, studies exploring the use of self-amplifying RNA and adenoviral vaccines demonstrate that different combinations can induce varied immune responses, which could inform future vaccine design and public health strategies(33). The bibliometric analysis also highlights the global nature of research in this field, with significant contributions from institutions across multiple

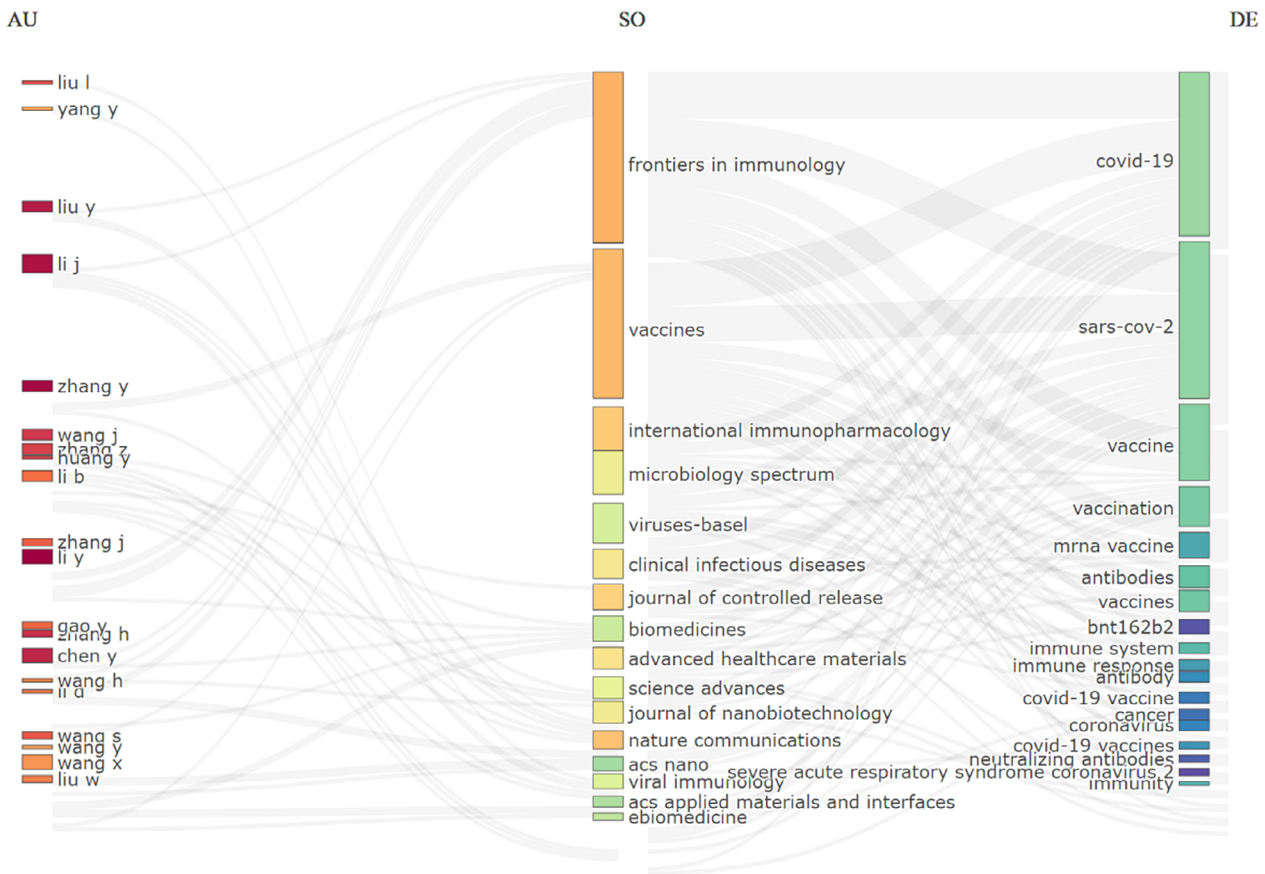


Figure 4. Three-Fields Plot representing the incoming and outgoing flows among authors, journals and author keywords contributing to the impact of COVID-19 vaccines on the immune system (2020-2024). *Abbreviations:* AU, authors; SO, Journals; and DE; author keywords.

Table 5. Top 10 publishing countries on the impact of COVID-19 vaccines on the immune system (2020-2024)

Country	Articles
USA	226
China	134
Italy	126
Iran	95
UK	68
Germany	64
Spain	47
Israel	44
Japan	42
South Korea	33

countries. This international collaboration is crucial in tackling the pandemic’s challenges and advancing our understanding of vaccine-induced immunity (34). The network of collaborations mapped in this study reflects a strong, coordinated effort to address pressing public health concerns, emphasizing the importance of shared knowledge and resources. Despite the wealth of research, certain gaps remain in our understanding of the long-term impacts of COVID-19 vaccines on the immune system (35). For instance, while there is considerable data on the immediate and short-term effects, fewer studies have focused on the long-term consequences of repeated vaccination or booster doses (36). Additionally, as new variants of SARS-CoV-2 continue to emerge, ongoing research will be needed to

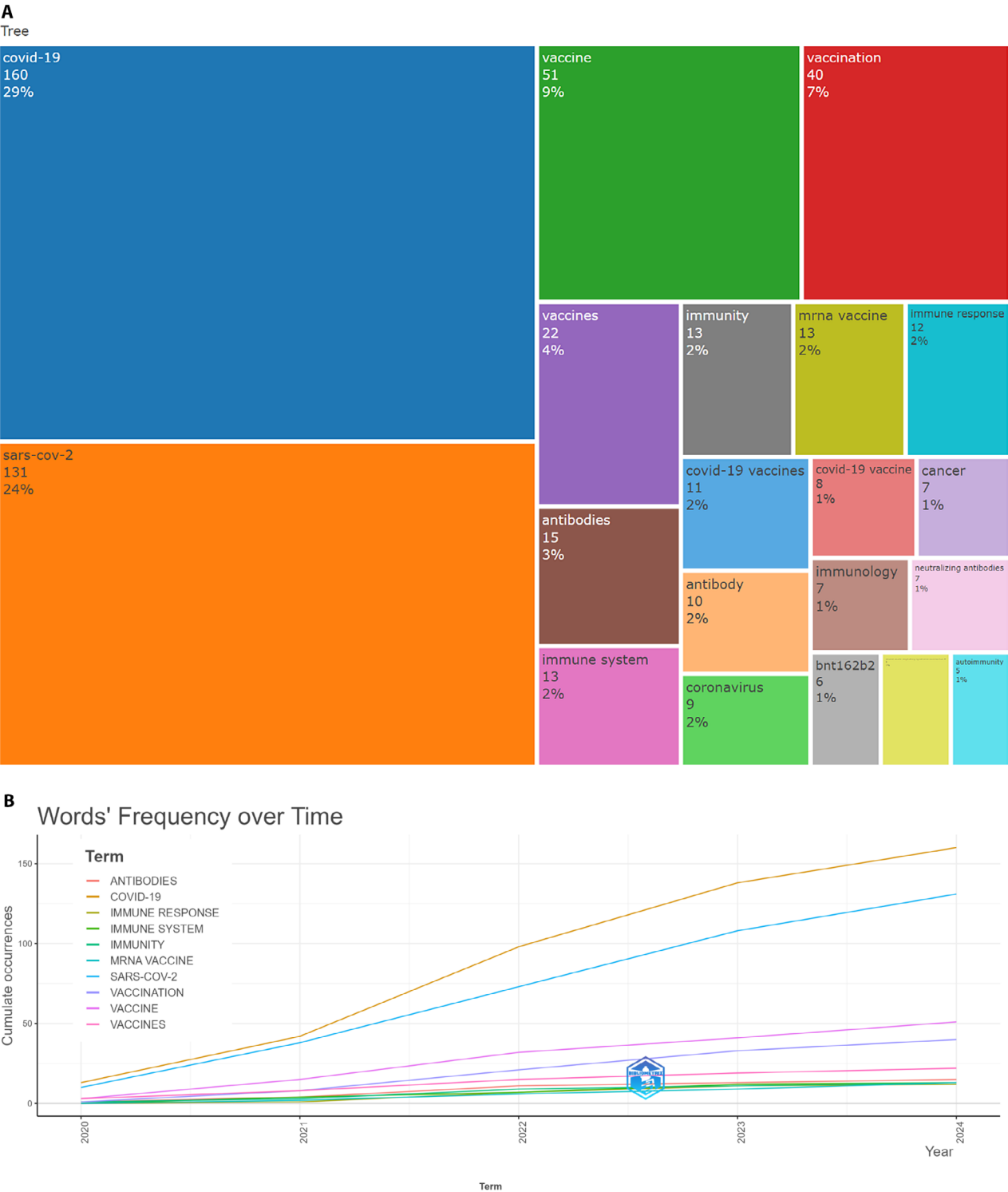


Figure 5. TreeMap (A) and frequency plot (B) illustrating the top ten keywords used by authors in publications examining the effects of COVID-19 vaccines on the immune system (2020-2024).

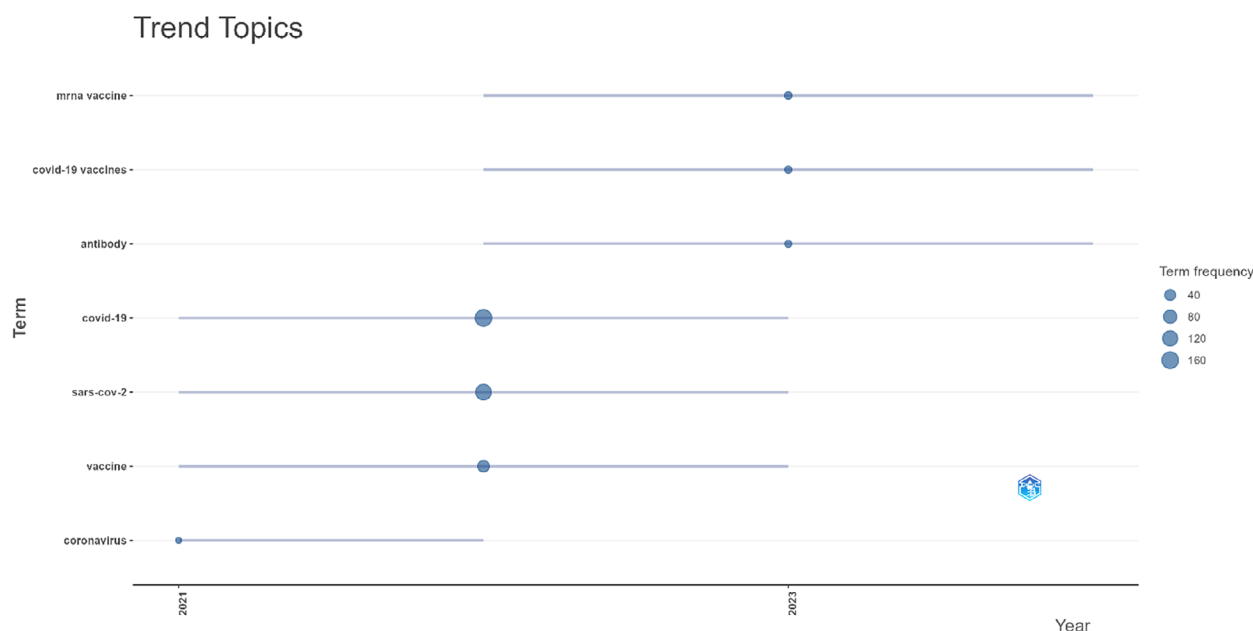


Figure 6. The timeline of the trend topics on the impact of COVID-19 vaccines on the immune system. Each bubble indicates the peak of frequency used for each, while the line indicates the years it was used.

adapt vaccination strategies and ensure sustained immune protection (37). Moreover, the thematic analysis of keywords and research topics reveals areas that are still underexplored, such as the impact of vaccines on autoimmune conditions and the potential for immune escape in the face of viral mutations. Addressing these gaps will require continued, interdisciplinary research efforts, and possibly new methodological approaches, to provide a more holistic understanding of the immune landscape post-vaccination.

Conclusion

This bibliometric analysis underscores the complexity and importance of ongoing research into the impact of COVID-19 vaccines on the immune system. The findings emphasize the need for sustained, collaborative research efforts to address the evolving challenges posed by the pandemic. As we move forward, it will be crucial to build on the existing body of knowledge, focusing on long-term immune outcomes and adapting public health strategies to meet the needs of diverse populations worldwide.

Future perspectives

Improving Research on Long-lived immunity: Given the changing landscape of SARS-CoV-2 and worries about the duration of vaccine responses, future studies should place more focus on the long-term effects of COVID-19 vaccines on the immune system. Research should address the effects of repeated doses, including boosters, on the muted immune response which will help refresh immune memory over time in heterogeneous populations (e.g., older adults, immunocompromised patients). This will enable us to have actionable data to optimize future vaccination schedules, growing sustained immunity.

Examining interactions with other vaccines

An interaction between COVID-19 vaccines and other vaccines has been reported in the literature and merit further evaluation. The insights that heterologous vaccination regimens or co-administration of COVID-19 vaccines with other immunizations may shape immune responses should guide public health approaches. Future studies should define other vaccine

efficacy and safety implications in specific composition subgroups. Shrinking Box of SARS-CoV-2 Variants: As SARS-CoV-2 variants continue to emerge, public health strategies should have the ability to adapt. Data on the effects of this and future variants on vaccine-induced immunity should be prioritized so that vaccination policies can be adapted where necessary. An ability to tailor vaccines to target emerging variants may be key to ensuring high levels of protection around the world, particularly in areas with low uptake of vaccines or in groups of people who are vulnerable to severe disease.

Targeted strategies for vulnerable populations

More focus is required on the effects of COVID-19 vaccines in vulnerable groups, including people with autoimmune conditions, pregnant women, and the elderly. The studies should develop an understanding of the interactions between vaccines and those conditions, with an eye toward implications for vaccine safety and efficacy in these populations. This framework will provide equitable and personalized health strategies for those at the highest risk. Enhanced Research

Methodologies

The limitations of existing studies outlined above in this review particularly in regard to chronic/long-term sequelae of SARS-CoV-2 infection and autoimmune conditions, suggest that new methodologies may be needed or interdisciplinary approaches. To gain more precise insights into the long-term effects of COVID-19 vaccinations, future studies should adopt more rigorous longitudinal designs that include real-world data collection.

Impact on future vaccine design and public health initiatives

The knowledge gained through this study can directly inform future vaccine design with a focus on developing next-generation vaccines that optimize both durability and breadth of immune responses. Vaccine developers might need to widen their laboratory lens to consider other features of immune response — more than preventing severe disease, such as immune

surveillance, antibody transfer and emerging variants. This research can set the stage to help inform public health policies by emphasizing the importance of modifying vaccination programs to react to the virus' dynamic nature within the pandemic. However, it can also promote global health security by facilitating the development of vaccines against new variants of interest, or the adaptation of booster dose strategies against changing fitness landscapes. While leaders will already be scrambling to distribute COVID-19 vaccines, there are other policy implications of these findings, as well — integration of the COVID-19 efforts with broader vaccination campaigns will ensure a more comprehensive approach to population health.

Study limitations

This study focused solely on English-language articles indexed in WoC and Scopus, which could have resulted in language and database biases. Furthermore, the focus on keywords in article titles might have excluded relevant studies, limiting the scope of the analysis. Future research should incorporate broader search strategies and consider additional databases to gain a more comprehensive understanding of research trends.

Ethic Approval: We would like to inform you that ethical committee approval is not required for this study, as it is a bibliometric analysis. The research does not involve any studies with human participants or animals and therefore does not violate ethical principles for biomedical research.

Conflict of Interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: conception: SS, performance of work: AM, YB; interpretation or analysis of data: AM, YB, KB; preparation of the manuscript: SS, KB; revision for important intellectual content: YB, KB; supervision: SS, YB. All authors read and approved the final manuscript.

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