



Review

Global research landscape of health care-associated infections among immunocompromised people before and after the start of the COVID-19 pandemic



Chidozie Declan Iwu

School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria 0001, South Africa

ARTICLE INFO

Keywords:

Health care-associated infections
 Immunocompromised individuals
 COVID-19
 Prevention strategies
 Patient outcomes

ABSTRACT

Health care-associated infections (HCAIs) pose a substantial threat to immunocompromised individuals and represent a frequent adverse event in health care delivery. The aim of this study was to evaluate the global research landscape of HCAIs among immunocompromised populations before and during the COVID-19 pandemic. A systematic search of articles published between 2013 and 2022 in the Web of Science Core Collection database was conducted, and content analytics and integrated science mapping were used for data analysis and interpretation. The review identified 1,473 articles. Only 633 articles authored by 4,151 individuals and published in 366 journals were included. The average citation rate was 14.27 per document, and research production grew annually by 9.07% peaking in 2021 during the COVID-19 pandemic but declining in 2022. The United States emerged as the most productive country, with 743 publication appearances and 2,485 citations. Keywords such as “epidemiology,” “infection,” “mortality,” and “risk factors” were frequently encountered in the analyzed literature. The main research themes, including “mortality,” “sepsis,” “immunosuppression,” “expression,” and “pneumonia,” underscored the focal points of importance within this domain. This study highlighted the growing interest regarding HCAIs in immunocompromised populations, especially during the COVID-19 pandemic. The study findings underscore the need to advance research efforts to understand different immunocompromised states, develop tailored infection prevention measures, and address health care disparities to mitigate the burden of HCAIs among immunocompromised individuals.

1. Introduction

Health care-associated infections (HCAIs) pose a substantial global public health challenge, with serious implications for patient well-being and health care costs [1]. These infections lead to increased morbidity, mortality, prolonged hospital stays, and elevated expenses, particularly in intensive care units (ICUs) where invasive procedures and devices are extensively used [2].

HCAIs account for more than 140,000 global deaths each year [3], with approximately 30% occurring in ICUs [4]. Factors contributing to the occurrence of HCAIs are multifaceted, encompassing pathogen characteristics, host factors, treatment-related aspects, health care pro-

cesses, and environmental conditions [5]. Although endogenous sources are the primary origin of pathogens, transmission from human and environmental sources during health care delivery is also a concern [6].

In the 21st century, hospital-acquired infections have become more alarming owing to factors such as the presence of a large number of immunocompromised patients, increased outpatient treatments leading to a higher acuity level among hospitalized individuals, invasive medical procedures bypassing natural protective barriers, potential pathogen spread facilitated by health care personnel, inadequate sanitation protocols, and the emergence of drug-resistant microorganisms owing to routine antimicrobial use [7].

Abbreviation: HCAIs, Health care-associated infections; WoS, Web of Science; ICUs, Intensive Care Units; BIA, Bibliometric Index Analysis; SNMA, Scientific Network Map Analysis; AGR, Annual Growth Rate; TC, Total Citations.

E-mail address: chidoziedecan@gmail.com

<https://doi.org/10.1016/j.imj.2024.100127>

Received 31 December 2023; Received in revised form 23 March 2024; Accepted 4 August 2024

2772-431X/© 2024 The Author(s). Published by Elsevier Ltd on behalf of Tsinghua University Press. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

HCAIs affect both adult and pediatric patients, with bloodstream infections, pneumonia, and urinary tract infections being common manifestations [8]. Among pediatric populations, infants under 1 year of age, those with extremely low birth weight, and children in the ICU are particularly vulnerable [2,9]. Effective containment strategies include instrument disinfection, hand hygiene for hospital staff and visitors, and stringent infection control practices [10]. Given that a considerable proportion of HCAIs are preventable through intensive hygiene and control programs, it is crucial to prioritize preventive measures [7].

Existing evidence lacks a comprehensive understanding of the global research landscape concerning HCAIs among immunocompromised individuals. Whereas previous studies have primarily focused on individual risk factors [11], a gap remains regarding the specific context of HCAIs in this vulnerable population. Therefore, the aim of this study was to assess the current state of research on HCAIs among immunocompromised individuals, exploring research trends, key contributors, and the geographic distribution of publications. By mapping the existing knowledge and research output, this analysis can provide a comprehensive overview and identify research gaps that require further exploration.

2. Methods

2.1. Study approach and data source

Following the description of Aria et al. [12], a systematic review and bibliometric analysis was used to evaluate the research landscape of HCAIs among immunocompromised individuals globally. This approach was chosen to substantially enhance the quality of the literature review using a transparent, systematic, and replicable method. This holistic approach to the literature review process ensures a comprehensive and objective evaluation of the HCAI research landscape among immunocompromised populations [13]. This method included bibliometric index analysis (BIA) and scientific network map analysis (SNMA). Whereas BIA provides insights into publication trends and major sources of research publications, SNMA can be used to visualize the conceptual structure of the landscape including the keyword co-occurrence network and thematic maps of the landscape [12].

Relevant research publications on HCAIs among immunocompromised individuals were collected from the Web of Science (WoS) core collection database and its various indexes. These indexes include the Science Citation Index Expanded, Social Sciences Citation Index I, Arts & Humanities Citation Index, Conference Proceedings Citation Index-Science, Conference Proceedings Citation Index-Social Science & Humanities, Book Citation Index-Science, Book Citation Index-Social Sciences & Hu-

manities, and Emerging Sources Citation Index. We chose the WoS database as our primary data source owing to its extensive coverage of scholarly literature across multiple disciplines. WoS serves as a comprehensive repository of citation data and has become a widely recognized and utilized source for conducting bibliometric analyses. The database also provides essential bibliometric indicators that are crucial for bibliometric analysis [14].

2.2. Search and data retrieval

A systematic search was conducted in the WoS database on June 24, 2023 to identify relevant publications on HCAIs among immunocompromised individuals. The “title search” strategy was used owing to its proven effectiveness in retrieving substantial and relevant publications with increased sensitivity and specificity [15]. The search and retrieval process followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16]. A comprehensive set of search terms was used, comprising keywords related to HCAIs (“health care-associated infection*” OR “cross infection” OR “nosocomial infections” OR “nosocomial infection” OR “hospital acquired infection” OR “hospital acquired infections” OR “hospital-acquired infection” OR “hospital-acquired infections” OR “health care associated infection” OR “health care associated infections” OR “health care-associated infection” OR “health care-associated infections”) and immunocompromised individuals (“immunocompromised” OR “immunodeficient” OR “immunosuppressed” OR “transplant recipients” OR “Immunodeficienc*” OR “immunocompromis*” OR “Immunosuppres*”). To refine the search results, specific criteria were applied. These included limiting the publication years to the period from 2013 to 2022, focusing only on research articles as the document type, and selecting English as the language for inclusion. The retrieved data from the databases were exported in BibTeX format and imported into the Mendeley referencing software where they were de-duplicated. To ensure the relevance and appropriateness of the included articles, a validation process was conducted. This included abstract and full-text screening. Only relevant articles with the desired date of publication and written in English were included in the final analysis.

2.3. Data analysis

A descriptive approach was used, encompassing data visualization and contextual scientific mapping. This analysis was performed using the biblioshiny application of the bibliometrix package in RStudio version 4.2.2 (The R Project for Statistical Computing, Vienna, Austria). Various bibliometric parameters were examined, including

prominent sources of publications, keywords and trending topics, production by country, and conceptual structures of the landscape. The annual growth rate of publications was estimated using Poisson regression models owing to the applicability in modeling count data, which is aligned with the discrete nature of annual publication counts. The average age of the included documents was estimated by calculating the difference between the publication year of each document and the current year at the time of analysis, as shown in Eq. (1).

$$\text{Average Age} = \sum_{i=1}^n \left(\frac{\text{Current Year} - \text{Publication Year}(i)}{n} \right) \quad (1)$$

where Current Year is 2022 (the final year of the study period), Publication Year(*i*) = publication year of each individual document within the dataset, and *n* = total number of included documents.

3. Results and discussion

3.1. Retrieved publications

A total of 1,473 publications were retrieved from the literature. After the first refinement, 652 publications were excluded because their publication dates fell outside the specified period of 2013–2022. The remaining 821 publications underwent further refinement based on article type, and only original articles were retained, resulting in a final selection of 633 publications, which were validated and finally included in subsequent analysis (shown in Fig. 1).

3.2. Characteristics of included studies

Systematic analysis of the included studies on HCAs among immunocompromised individuals can provide important insights into the research landscape in this field. A total of 633 documents from 366 different sources, including journals and books, were identified and analyzed (shown in Table 1). The analysis covered a timespan from 2013 to 2022, capturing the most recent advancements in understanding and management of HCAs among immunocompromised individuals, including advancements in infection prevention and control practices, emerging pathogens, and changes in the landscape of disease burden.

The annual growth rate of 9.07% indicates a continuous and increasing interest in studying HCAs among immunocompromised populations. These findings reflect the evolving nature of research in this area and growing recognition of the importance of HCAs in the context of immunocompromised individuals. The average age of the included documents was 4.74 years, indicating

Table 1
Global summary of data on HCAs among immunocompromised people (2013–2022).

Description	Results
Main information about the data	
Timespan	2013:2022
Sources (Journals, Books, etc)	366
Documents	633
Annual Growth Rate (%)	9.07
Document Average Age	4.74
Average citations per document	14.27
References	21112
Document contents	
Keywords Plus (ID)	1704
Author's Keywords (DE)	1676
Authors	
Authors	4151
Authors of single-authored documents	10
Authors collaboration	
Single-authored documents	10
Co-Authors per document	7.29
International co-authorships (%)	16.03
Document types	
Article	633

the incorporation of up-to-date knowledge. This demonstrates the relevance of the findings and highlights the continuous efforts to understand and address HCAs in this vulnerable population. Furthermore, the average citations per document, which amounted to 14.27, suggested a considerable level of recognition and impact for the studies in the field of HCAs among immunocompromised individuals. This metric indicates that, on average, each document included in the analysis has been referenced or cited approximately 14.27 times in other scholarly works. This is much higher than that observed in a study that carried out a similar analysis [17]. The analysis of references in the included studies revealed substantial use of the existing literature, with a total of 21,112 references cited. This demonstrates that researchers in the field of HCAs among immunocompromised individuals have drawn extensively upon a wide range of sources to inform their studies. By referencing many publications, researchers have established a strong foundation of knowledge and have integrated previous findings into their own work. This also implies a robust foundation for future research and emphasizes the need to build upon these impactful studies, addressing emerging challenges and further advancing the understanding and management of HCAs in immunocompromised individuals.

Collaboration among authors was evident, with a total of 4,151 authors involved in the included studies. Among these studies, there were 10 single-authored documents, indicating that few studies were conducted by individual researchers. These single-authored documents reflect the input of independent researchers who have made contributions to the field, demonstrating their expertise and specialization in studying HCAs among immunocompromised individuals. The prevalence of co-authorship, with an average of 7.29 co-authors per document,

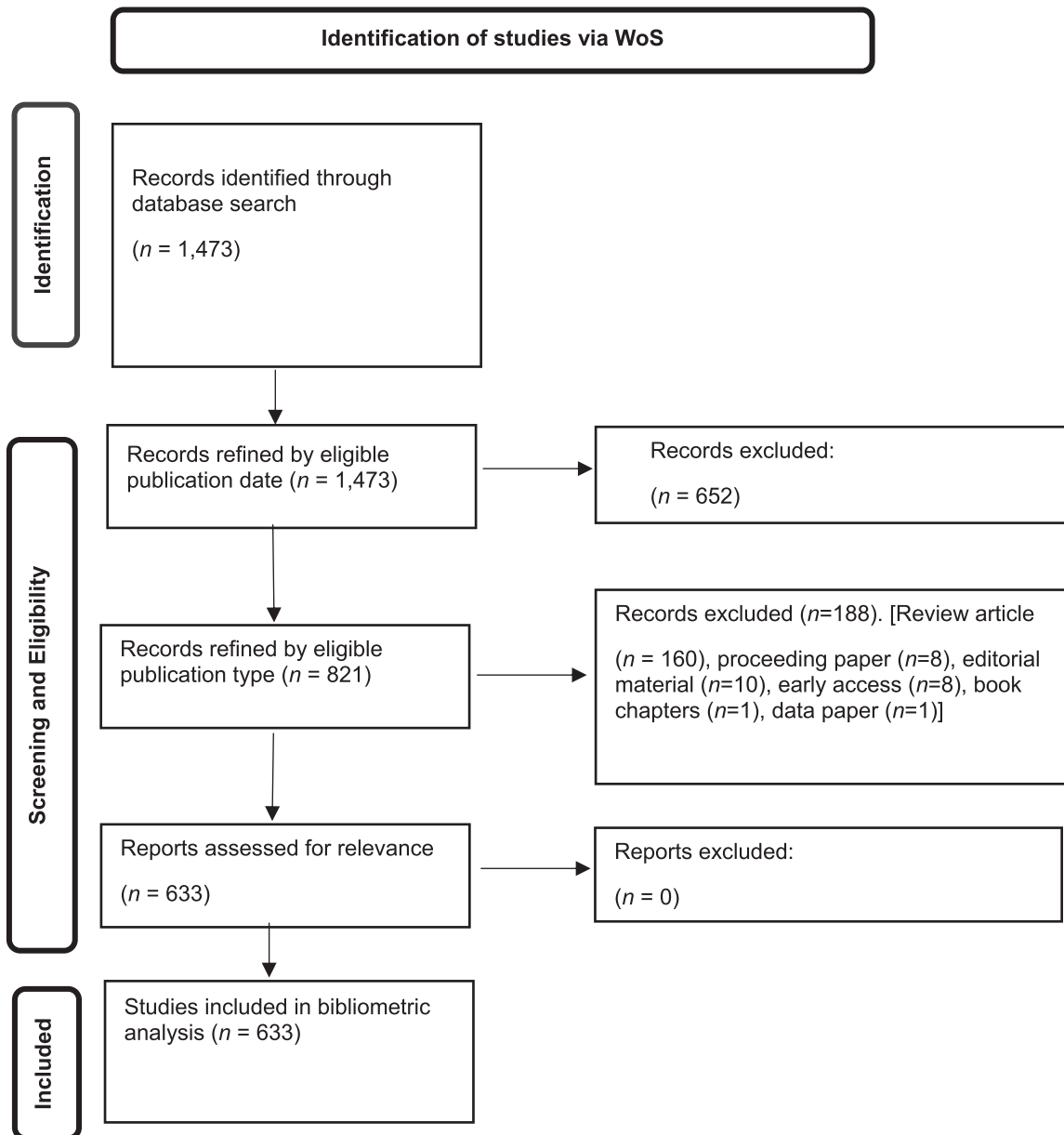


Fig. 1. PRISMA flow diagram of the study selection process.

signifies the collaborative nature of research in this field. The presence of international co-authorships, accounting for 16.03% of collaborations, indicates a global engagement and the exchange of knowledge and expertise in addressing HCAs among immunocompromised individuals.

The included studies encompassed a wide range of topics, as indicated by the numerous Keywords Plus (ID) and Author's Keywords (DE) identified. This reflects the multidimensional nature of HCAs and highlights the need for a comprehensive approach that considers various factors such as infection prevention strategies, antimicrobial resistance, patient outcomes, and health care policies. The diversity of topics covered provides a rich knowledge base for further exploration and intervention development.

3.3. Annual growth rate (AGR) of research on HCAs among immunocompromised people (2013–2022)

The AGR and mean total citations (TC), as shown in Fig. 2, provide important insights into the research trends and impact of studies on HCAs among immunocompromised people from 2013 to 2022. The AGR shows the progress and development of research in this field [18]. The AGR of 9.07% indicates a continuous and steady increase in research activity in this field over the specified period. Although this is lower than the AGR previously reported in a similar study focused only on Asian countries [19], our finding highlights the growing interest and recognition of the importance of studying HCAs among immunocompromised populations. The positive AGR sug-

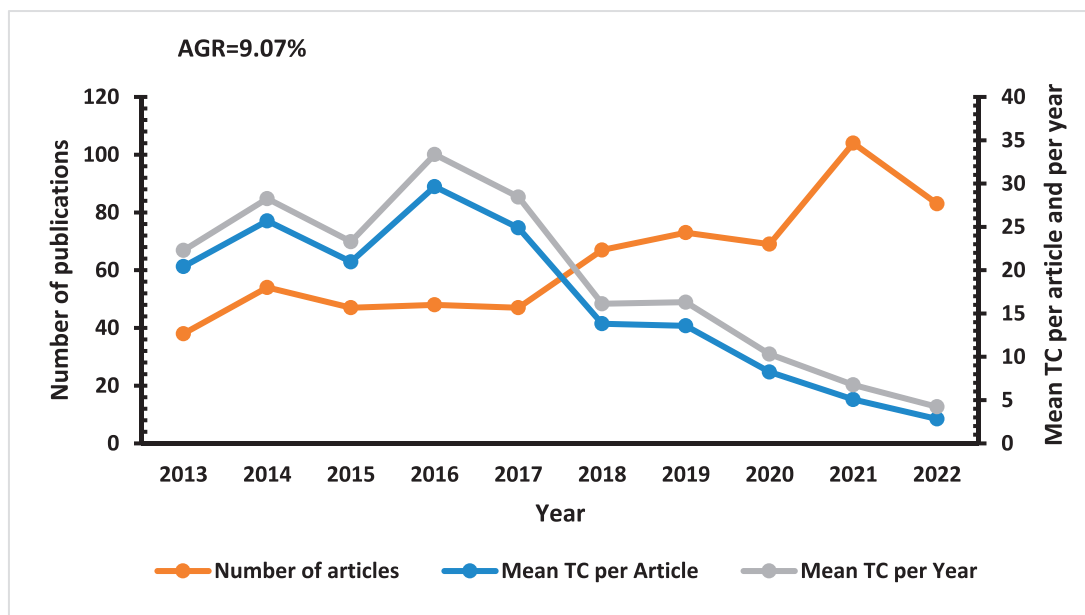


Fig. 2. Distribution, mean total citations (TC) per article and mean TC per year of annual publications on HCAs among immunocompromised people (2013–2022). AGR: annual growth rate; HCAs, health care-associated infections.

gests that researchers are actively engaged in addressing the challenges and complexities associated with HCAs in this vulnerable population. This calls for collaborative research initiatives and knowledge exchange to comprehensively address the complexities associated with infections in this vulnerable population.

The number of articles published each year exhibited an increasing trend, indicating a growing interest and research activity in the area of HCAs among immunocompromised people. The graph (Fig. 2) shows a relatively steady rise in the number of publications, with a peak in 2021. This suggests that researchers are actively contributing to the knowledge base on HCAs in immunocompromised populations and addressing the associated challenges. The peak in the number of articles published in 2021 may also be attributed to the influence of the COVID-19 pandemic. The pandemic had an enormous impact on global health, leading to increased awareness and research focus on infectious diseases, including HCAs [20]. The urgency to understand and mitigate the spread of COVID-19 may have prompted researchers to investigate the intersection between immunocompromised individuals and HCAs. Additionally, the COVID-19 pandemic shed light on the vulnerabilities of immunocompromised populations and the increased risk faced by these groups in health care settings [21]. This heightened awareness may have stimulated research interest and funding in the field, resulting in a surge of publications in 2021.

The mean TC per article shows some fluctuations over the years, as shown in Fig. 2. There was a peak in 2016, with a higher citation impact compared with other years. However, there were variations in the citation im-

act during subsequent years, with a decline from 2017. This indicates that certain articles published in 2016 had a greater impact and were more frequently cited by the scientific community. The mean TC per year provides an overview of the overall citation impact of the research. The line graph illustrates some variations in the citation impact, with higher values in certain years, such as in 2016 and 2017. This suggests that the articles published in those years had a greater overall impact and received more citations by the scientific community. The subsequent decline in citation impact highlights the evolving nature of research and the need for ongoing contributions to maintain a sustained impact. For future studies, this underscores the importance of not only producing high-impact research but also ensuring continuous relevance and engagement with the scientific community to comprehensively influence and advance the field.

3.4. Main sources of research publications on HCAs in immunocompromised people, 2013–2022

Analysis of the main sources of research publications on HCAs in immunocompromised individuals provides insights into the landscape of scholarly output in this field. Among the identified sources, *PloS One* had the highest number of articles (15 publications), indicating its considerable contribution to HCAI research, as shown in Fig. 3. This is in contrast to results of a similar study in which the *Journal of Hospital Infection* was the most productive source of publications [19]. In the present study, *BMC Infectious Diseases* followed *PloS One* closely, with 14 publications. The *Journal of Hospital Infection*

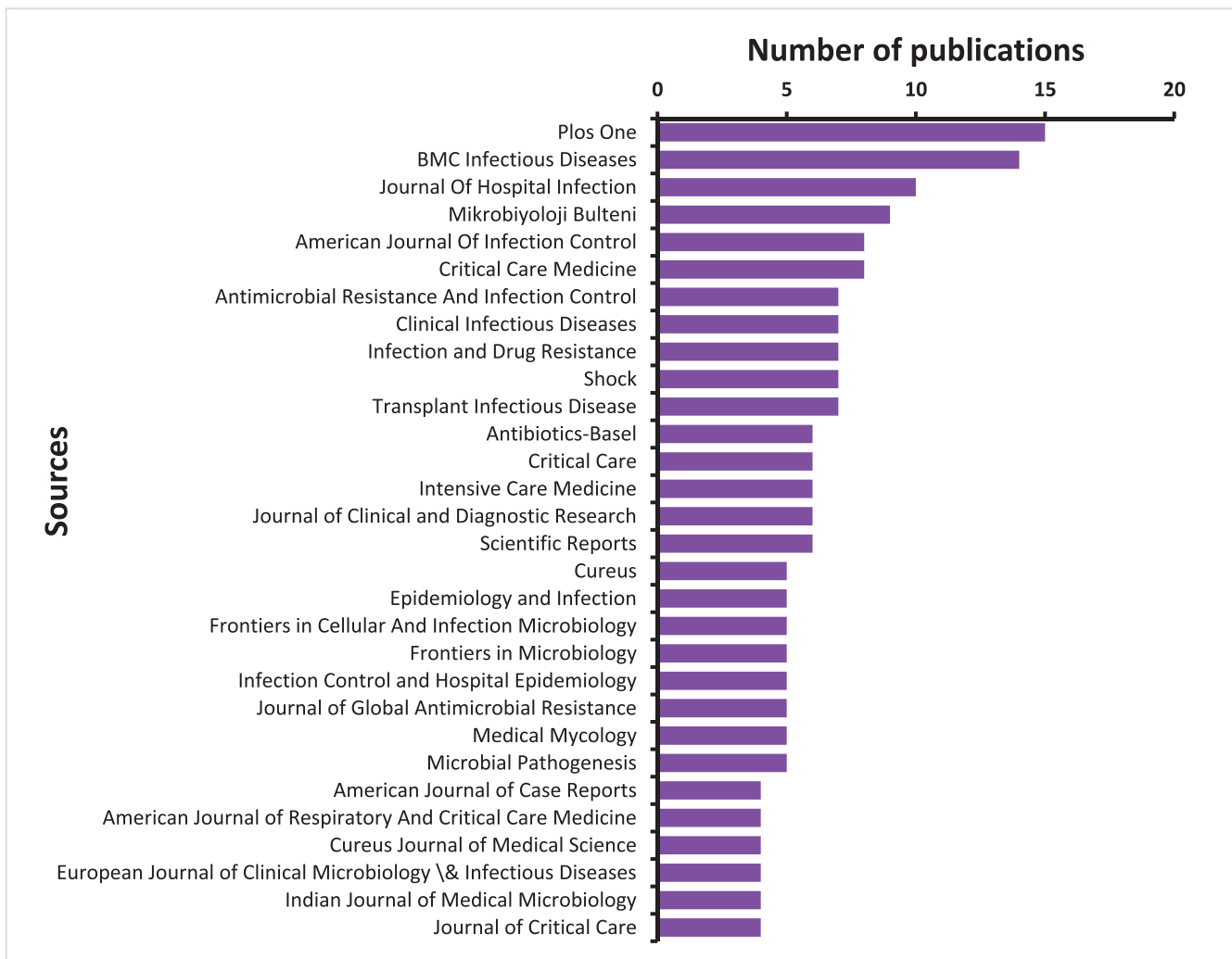


Fig. 3. Thirty main sources of research articles on health care-associated infections among immunocompromised people, 2012–2013.

and *Mikrobiyoloji Bulteni* also emerged as notable sources, with 10 and 9 publications, respectively. Other sources namely the *American Journal of Infection Control*; *Critical Care Medicine*; *Antimicrobial Resistance and Infection Control*; *Clinical Infectious Diseases*, *Infection and Drug Resistance*; *Shock*; and *Transplant Infectious Disease*, each had seven publications. The remaining sources had varying numbers of publications ranging from four to six.

The distribution of research publications across these diverse sources highlights the multidisciplinary nature of HCAI research in immunocompromised populations. This signifies the engagement of researchers from various fields, including microbiology, infectious diseases, critical care, and epidemiology. These sources serve as platforms for sharing knowledge, disseminating research findings, and facilitating collaboration among researchers working on HCAs. The prominence of certain sources, such as *PloS One* and *BMC Infectious Diseases*, suggests their recognition as reputable outlets for HCAI research. These sources attract researchers interested in studying HCAs among immunocompromised individuals and play a crucial role in advancing knowledge in the field.

Researchers, health care professionals, and policymakers can benefit from exploring these relevant sources, which provide access to a wealth of valuable information, evidence-based findings, and updates on advancements in preventing, diagnosing, and managing HCAs in immunocompromised populations.

3.5. Country scientific production of research on HCAs in immunocompromised people, 2013–2022

The analysis of country scientific production on HCAs among immunocompromised individuals from 2013 to 2022, based on the number of countries contributing to each publication, revealed diverse international contributions, as shown as in Fig. 4A. A total of 73 countries were identified as active participants in research related to HCAs in these vulnerable populations.

The United States (US) demonstrated the highest scientific production, with 743 publication appearances, indicating a strong research focus and expertise in addressing HCAs among immunocompromised individuals. Other countries in the Americas, such as Brazil with 71 pub-

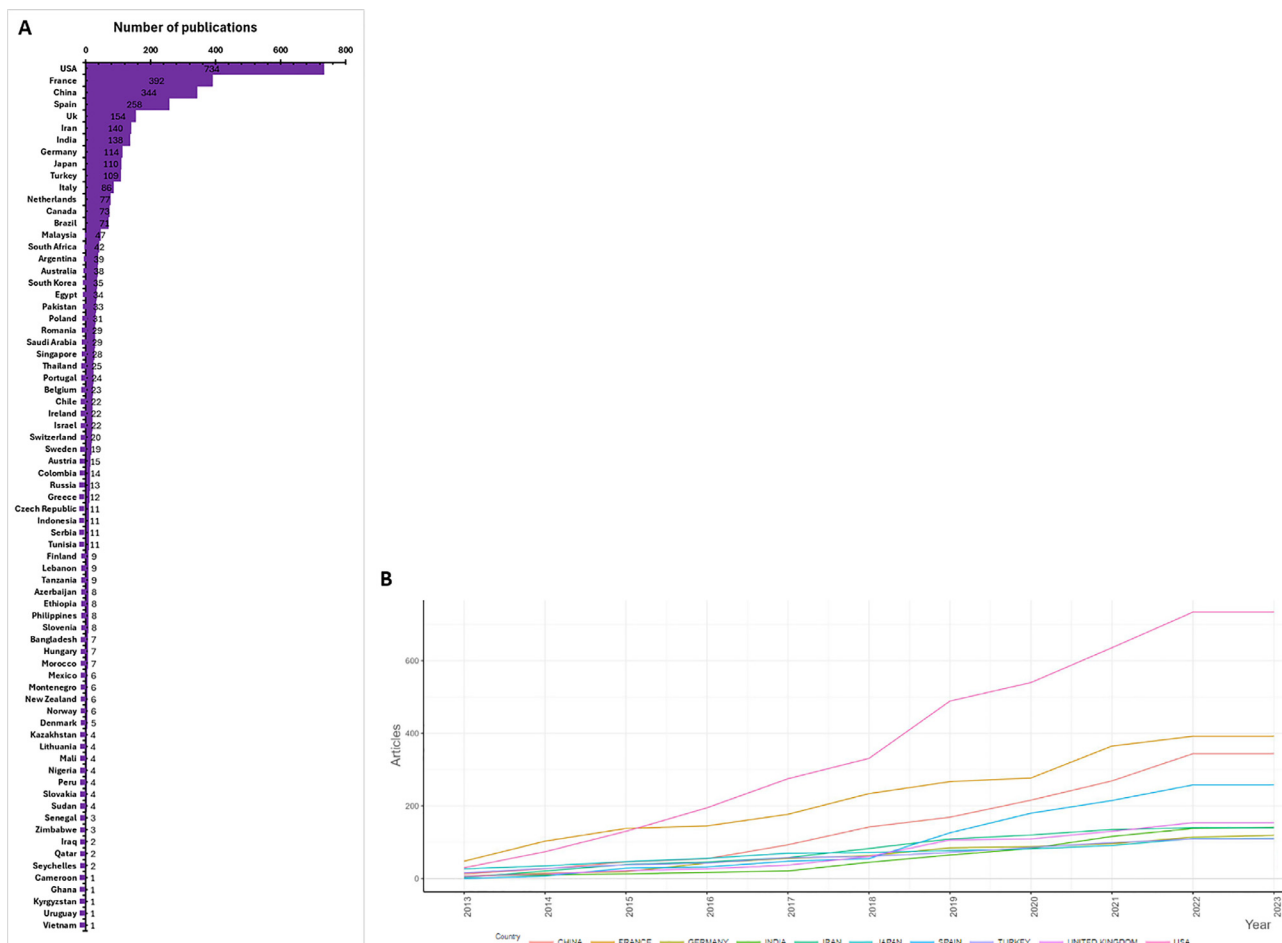


Fig. 4. (A) Country-scientific production of research on health care-associated infections in immunocompromised people, 2013–2022. (B) Time trend of the 10 leading countries producing research on health care-associated infections in immunocompromised people, 2013–2022.

lication appearances and Argentina with 39 publication appearances, also showed notable research outputs, highlighting the commitment to understanding and managing HCAs in the region.

In Europe, France emerged as a key contributor to HCAI research with 392 publication appearances, highlighting the nation's commitment to understanding and combating these infections among immunocompromised individuals. Other European countries, including Spain with 258 publication appearances, the United Kingdom (UK) with 119 publication appearances, and the Netherlands with 77 publication appearances, demonstrated substantial research outputs, reflecting a collaborative effort in the region.

Asian countries made noteworthy contributions as well, with China leading with 344 publication appearances, indicating the country's dedication to understanding HCAs and finding effective interventions for immunocompromised populations. India, with 141 publication appearances, showed active involvement in research, reflecting the growing recognition of HCAs as a critical health care issue in the country.

Africa also contributed to the research landscape, with several countries making valuable contributions. South Africa demonstrated notable research output with 42 publication appearances, highlighting the efforts to address HCAs among immunocompromised individuals in the region. Other African countries, including Egypt with 34 publication appearances, Tunisia with 11 publication appearances, and Morocco with 7 publication appearances, also actively participated in research related to HCAs.

The wide geographic representation of research publication appearances reflects a global commitment to addressing HCAs in immunocompromised populations. Also, the varying number of publication appearances per country could be attributed to the population size of the country and the number of hospitals per country. The findings emphasize the importance of regional and international collaboration, knowledge exchange, and capacity building to tackle the challenges associated with these infections on a global scale. By leveraging the collective expertise and experiences of researchers from various regions, advancements can be made in preventing and managing HCAs, ultimately improving the outcomes and quality of life for immunocompromised individuals.

Additionally, the distribution of research outputs across regions highlights variations in research focus and expertise. Whereas some regions may exhibit higher production, it is important to acknowledge and encourage collaborative efforts among researchers worldwide to address the challenges of HCAs among immunocompromised populations, including those in Africa.

Time trend analysis of country-specific scientific production from 2013 to 2023 in the field of HCAs among immunocompromised individuals reveals consistent and often impressive growth for the 10 leading contributing countries, as shown in Fig. 4B. Notably, China, France, Germany, India, Iran, Japan, Turkey, the UK, the US, and Spain all demonstrate substantial increases in research output over the analyzed period. The steady growth observed in these countries suggests a sustained and heightened global interest in understanding and addressing HCAs in immunocompromised populations. This trend may be attributed to several factors, including increased awareness of the clinical importance of HCAs, advancements in medical research, and a growing recognition of immunocompromised individuals as a vulnerable population. The implications of these findings are multi-fold. First, the consistent growth in research output signifies a global commitment to addressing the challenges associated with HCAs among immunocompromised individuals. The increasing number of publications reflects a collective effort to improve preventive strategies, patient outcomes, and overall health care delivery for this vulnerable population. Second, the variations in growth patterns among countries highlight regional differences in research focus and expertise. Collaborative efforts could bridge these gaps, fostering knowledge exchange and capacity building globally. Third, the sustained interest in HCAs research is indicative of a shared recognition of the importance of this field in public health. By leveraging the collective expertise and experiences of researchers worldwide, advancements can be made in preventing and managing HCAs, ultimately improving outcomes and the quality of life for immunocompromised individuals.

3.6. Most citations on HCAs, by country

Analysis of the most cited countries in research on HCAs among immunocompromised people provides valuable insights into the global impact and quality of scientific output. The most-cited countries in terms of the scientific production of research HCAs in immunocompromised populations from 2013 to 2022 is shown in Fig. 5. Two metrics, including TC (Fig. 5A) and average number of article citations (Fig. 5B), were used to evaluate the impact and quality of research output by different countries. These metrics provide distinct insights into the impact and quality of research outputs. TC reflects the overall recognition and influence of a country's research, and

average article citations shed light on the impact and influence of individual research articles.

The US emerged as the country with the most cited publications, with a total of 2,527 citations, indicating its significant contributions to the field of HCAs in immunocompromised populations. This also indicated that the US has a strong research infrastructure, potentially influencing global practices in managing HCAs among immunocompromised individuals. France also exhibited a strong research impact with a total of 1,106 citations, demonstrating its substantial presence in the scientific community. China demonstrated notable growth in this area, garnering 682 citations, which showcase its increasing research contributions.

In terms of the average number of article citations, the Netherlands stood out with the highest value at 63.5 (Fig. 5B), highlighting the exceptional impact and recognition of its research output. Spain, Japan, the UK, and Germany also displayed noteworthy average article citations of 13.6, 21.8, 23.3, and 15.6, respectively, underscoring the contributions and influence of these countries in advancing knowledge in this field. Engaging with researchers from these nations will not only enhance the quality of studies but also influence health care strategies globally, particularly in managing HCAs among immunocompromised individuals.

3.7. Research keywords on HCAs in immunocompromised people, 2013–2022

The frequently occurring keywords shown in Fig. 6A provide valuable insight into the current research landscape of HCAs in immunocompromised populations. These findings can guide future research directions and inform health care practices, emphasizing the importance of epidemiological studies, infection control measures, antimicrobial resistance management, accurate diagnosis, and tailored management strategies to improve patient outcomes and reduce the burden of HCAs in vulnerable populations [22].

In this study, the most frequently occurring keywords in research on HCAs among immunocompromised individuals included "epidemiology," "infection," "infections," "mortality," and "risk factors." These terms reflect the emphasis on understanding the spread and impact of infections, including their associated risks and outcomes, particularly in vulnerable populations. The keyword "bacteremia," which appears frequently in the literature, highlights the importance of bloodstream infections and their management in immunocompromised individuals. "Outbreak" and "resistance" were other frequent keywords, indicating the research focus on preventing and controlling outbreaks of resistant strains in health care settings.

The keywords "identification," "sepsis," and "intensive care unit" demonstrate the attention given to accurate

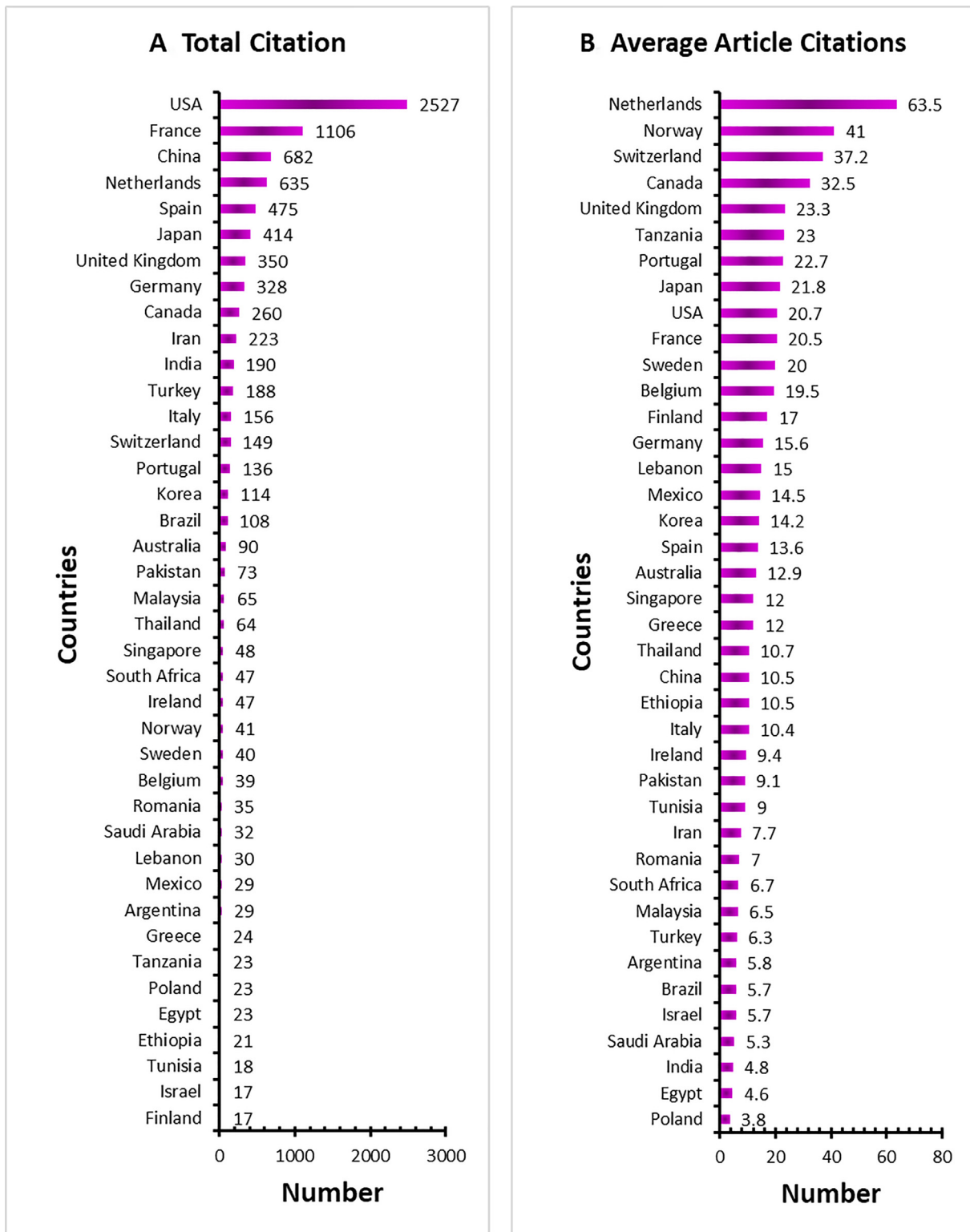


Fig. 5. Country scientific production of research on health care-associated infections in immunocompromised people, 2013–2022.

and timely diagnosis, as well as the management and outcomes of sepsis in immunocompromised patients, particularly in ICU settings. The keywords “nosocomial infections” and “bloodstream infections” underscore the interest in studying and preventing hospital-acquired infections, especially those related to the bloodstream. The

keyword “immunosuppression” reflects the critical aspect of studying the impact of compromised immune systems on the susceptibility to and management of HCAs. “Prevalence,” “surveillance,” and “expression” indicate the focus on understanding the scope of HCAs, implementing effective surveillance systems, and investigating

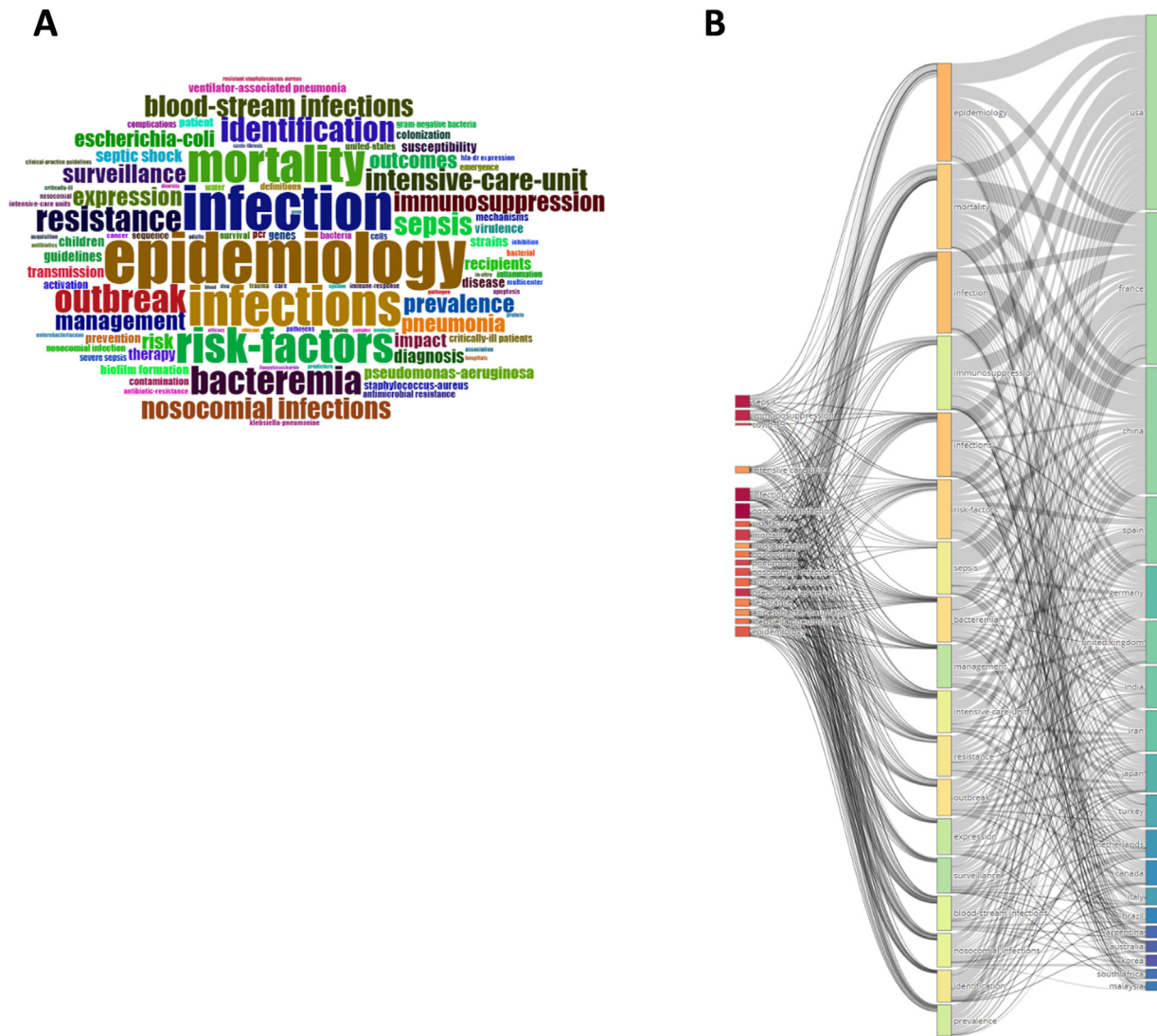


Fig. 6. (A) Word cloud of research on health care-associated infections in immunocompromised people, 2013–2022. (B) Three-field plot showing the distribution of keywords (1st and 2nd nodes) of research on health care-associated infections in immunocompromised people, 2013–2022 across countries (3rd nodes).

the molecular mechanisms and gene expressions associated with these infections.

The keywords “pneumonia,” “outcomes,” and “*Escherichia coli*” highlight the attention given to respiratory infections, the evaluation of treatment outcomes, and the specific role of *E. coli* in HCAs. “Risk,” “diagnosis,” and “impact” are terms that reflect the overall emphasis on assessing and managing the risks associated with HCAs, developing accurate diagnostic methods, and evaluating the broader impact of these infections on patients and health care systems. Other keywords such as “septic shock,” “*Pseudomonas aeruginosa*,” “recipients,” “therapy,” and “transmission” signify the research focus on understanding the complications, treatment approaches, transmission dynamics, and specific pathogens associated with HCAs in immunocompromised individuals.

Fig. 6B further explores the relationship between these keywords and countries, revealing a heterogeneous distribution across different nations. The observed variation

in the keyword distribution suggests diverse research priorities and emphases among countries, reflecting the distinct public health challenges faced by each nation. For example, publications from countries like the US, France, China, Spain, Germany, and the UK frequently used keywords like “epidemiology,” “mortality,” “infection,” “immunosuppression,” “risk factors,” “sepsis,” “bacteriemia,” “management,” “intensive care unit,” “resistance,” “outbreak,” “expression,” “surveillance,” “blood-stream infection,” “nosocomial infection,” “identification,” and “prevalence.” Publications from countries including South Korea and South Africa frequently used keywords such as “risk factors,” “sepsis,” “surveillance,” “blood-stream infection,” “nosocomial infection,” and “identification.” This indicates that although countries like South Korea and South Africa share some common keywords with the US, France, China, Spain, Germany, and the UK, they also exhibit distinct research priorities. This observation underscores the nuanced variations in public

health challenges and research focuses among different nations, highlighting the importance of recognizing and addressing country-specific needs in the global landscape of health care-associated infections among immunocompromised populations.

3.8. Trending topics on HCAs in immunocompromised people, 2013–2022

Trend topic analysis holds great importance as this can help to identify evolving research interests and areas of focus within a field. Tracking the frequency and distribution of keywords over time enables researchers to recognize emerging trends, assess research impact, and inform research strategies. Trend topic analysis also sheds light on knowledge diffusion, highlights research gaps, and guides researchers in aligning their work with current research interests. Overall, this approach provides valuable insights into the changing research landscape and aids in making informed decisions regarding resource allocation and research prioritization.

Between 2013 and 2014, the most frequently trending topics on HCAs in immunocompromised people included “acquired bacterial meningitis,” “acute gastroenteritis,” “kappa B,” “mononuclear cells,” “antibiotic therapy,” “bone marrow transplantation,” “antimicrobial susceptibility,” “dendritic cells,” “monocytes,” and “fluconazole,” as shown in Fig. 7. These findings suggest a focus on specific infections, treatment modalities, and the role of immune cells in combating HCAs during this period.

From 2015 to 2016, the attention shifted to topics such as “cytokine,” “diarrhea,” “invasive aspergillosis,” “hospitals,” “nosocomial infections,” “critically ill patients,” “PCR,” “activation,” “septic shock,” and “sepsis.” This indicates an increased emphasis on understanding the immune response, diagnostic methods, and the impact of health care settings on HCAs in immunocompromised individuals.

During the period from 2017 to 2019, the most frequently trending topics included “*Escherichia coli*,” “expression,” “surveillance,” “nosocomial infections,” “intensive care unit,” “bacteremia,” “mortality,” “infections,” “infection,” “epidemiology,” “outcomes,” “management,” “prevalence,” “resistance,” and “risk factors,” as shown in Fig. 7. These findings suggest a broader perspective on HCAs, encompassing surveillance, epidemiological studies, resistance patterns, and the overall management and outcomes of infections in immunocompromised populations.

From 2020 to 2022, the period coinciding with the COVID-19 pandemic, emerging topics included “water,” “sequence,” “mechanisms,” “susceptibility,” “cystic fibrosis,” “adults,” “critically ill,” “biofilm formation,” “therapy,” “hematological malignancies,” “recognition,” “antigen,” “COVID-19,” and “prediction,” as shown in Fig. 7.

The inclusion of COVID-19-related topics highlights the substantial impact of the pandemic on research priorities regarding HCAs. This finding underscores the need to understand the interplay between COVID-19 and immunocompromised states, the role of biofilm formation in infection persistence, and the development of predictive models for disease outcomes.

Overall, the landscape of research on HCAs in immunocompromised people has evolved over the years. From specific infections and treatment approaches, there has been a shift toward broader topics such as epidemiology, resistance, and risk factors. This suggests a growing understanding of the complex dynamics of HCAs and the need for comprehensive strategies in their prevention, diagnosis, and management. The inclusion of COVID-19-related topics reflects the adaptability of research priorities to address emerging challenges in infectious diseases. These findings contribute to a better understanding of the research landscape and can guide future studies aimed at improving patient outcomes and reducing the burden of HCAs in immunocompromised populations. Moreover, recognizing the specific topics trending during this period offers opportunities for researchers, clinicians, and policymakers to address pertinent issues in clinical practice, influence policy-making decisions, and strategize health care approaches, particularly in the context of health care emergencies like the COVID-19 pandemic.

3.9. Conceptual structure of research on HCAs in immunocompromised people, 2013–2022

The conceptual structure of research on HCAs in immunocompromised people using co-occurrence network analysis and thematic mapping provides a comprehensive understanding of the interconnectedness of concepts and the thematic trends within the literature. This analysis is invaluable for researchers and policymakers to identify key areas of focus, emerging trends, and potential research gaps, thereby informing future studies, resource allocation, and the development of effective interventions to address HCAs in immunocompromised populations.

In this study, co-occurrence network analysis revealed several important findings, as shown in Fig. 8A. The keyword “epidemiology” formed a cluster with related terms such as “infections,” “bacteremia,” “risk factors,” “blood stream infections,” and “prevalence.” This suggests a strong association between epidemiological aspects and the occurrence and transmission of infections in immunocompromised individuals. This finding emphasizes the need for robust epidemiological studies to inform infection prevention and control strategies targeting this vulnerable group. Additionally, the keyword “mortality” predominantly clustered with “pneumonia” and “infection,” highlighting the importance of these factors in under-

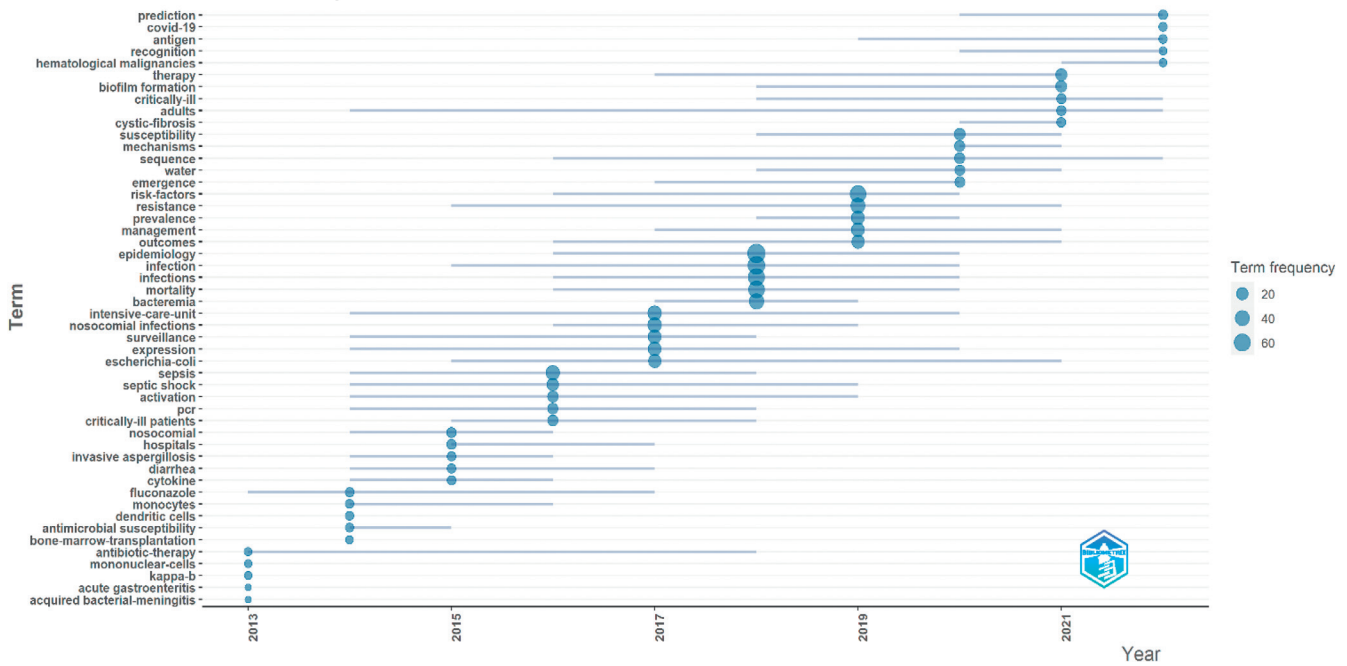


Fig. 7. Trending topics over time of research on health care-associated infections in immunocompromised people, 2013–2022.

standing mortality rates in this population. Comprehending the relationship between infections, pneumonia, and mortality can guide health care professionals in developing effective treatment and management approaches to improve patient outcomes and reduce mortality rates. The keyword “sepsis” showed an even distribution across the cluster, indicating its close association with concepts like “immunosuppression,” “septic shock,” and “expression.” This underscores the intricate relationship between sepsis and immunocompromised states. This finding suggests that exploring the underlying mechanisms and identifying biomarkers related to sepsis in immunocompromised individuals is crucial for early detection, intervention, and improved patient outcomes. Furthermore, the keyword “intensive care unit” mainly clustered with “*Pseudomonas aeruginosa*” and “outcomes,” emphasizing the relevance of these terms in the context of critical care and patient outcomes. This finding underscores the importance of understanding the specific challenges and considerations associated with managing HCAs in immunocompromised individuals receiving intensive care. This highlights the need for tailored interventions and infection control measures to mitigate the impact of *Pseudomonas aeruginosa* and improve patient outcomes in this setting. Finally, the keyword “management” had a specific connection only with “diagnosis,” suggesting a focused relationship between these two concepts. This finding suggests that effective management of HCAs in immunocompromised populations requires accurate and timely diagnosis. This emphasizes the importance of implementing appropriate diagnostic strategies to facilitate prompt treatment and prevent complications in this vulnerable patient group.

Thematic mapping further elucidated the conceptual structure by identifying four distinct themes, as shown in Fig. 8B. The Niche theme comprised a combination of topics such as “clinical outcomes,” “meta-analysis,” “antimicrobial interventions,” “decontamination,” and “protein secretion,” along with a group of concepts including “management,” “outcomes,” “diagnosis,” “guidelines,” and “prevention.” This suggests the existence of specialized areas of research within the broader field of HCAs in immunocompromised people, highlighting the need for targeted research efforts and the potential for advancements in these specific domains. The Major theme encompassed “mortality,” “sepsis,” “immunosuppression,” “expression,” and “pneumonia,” indicating their importance as major focal points in the area of study regarding HCAs in immunocompromised individuals. These concepts likely represent critical aspects of disease outcomes, treatment strategies, and pathogenesis, and their predominance indicates the importance of studying and addressing these factors in improving patient care and outcomes. The Emerging or Declining theme included “in-vitro,” “*Candida albicans*,” “blood stream infection,” “fluconazole,” and “mechanism.” This suggests evolving or shifting trends and priorities in the field, indicating the dynamic nature of research areas within the timeframe analyzed. Understanding these changes can guide researchers and policymakers in adapting their focus to address emerging challenges or redirecting efforts as certain areas become less prominent. Finally, the Basic theme represents a combination of keywords related to “epidemiology,” “infections,” “risk factors,” “intensive care units,” and “nosocomial infections,” as well as a group of

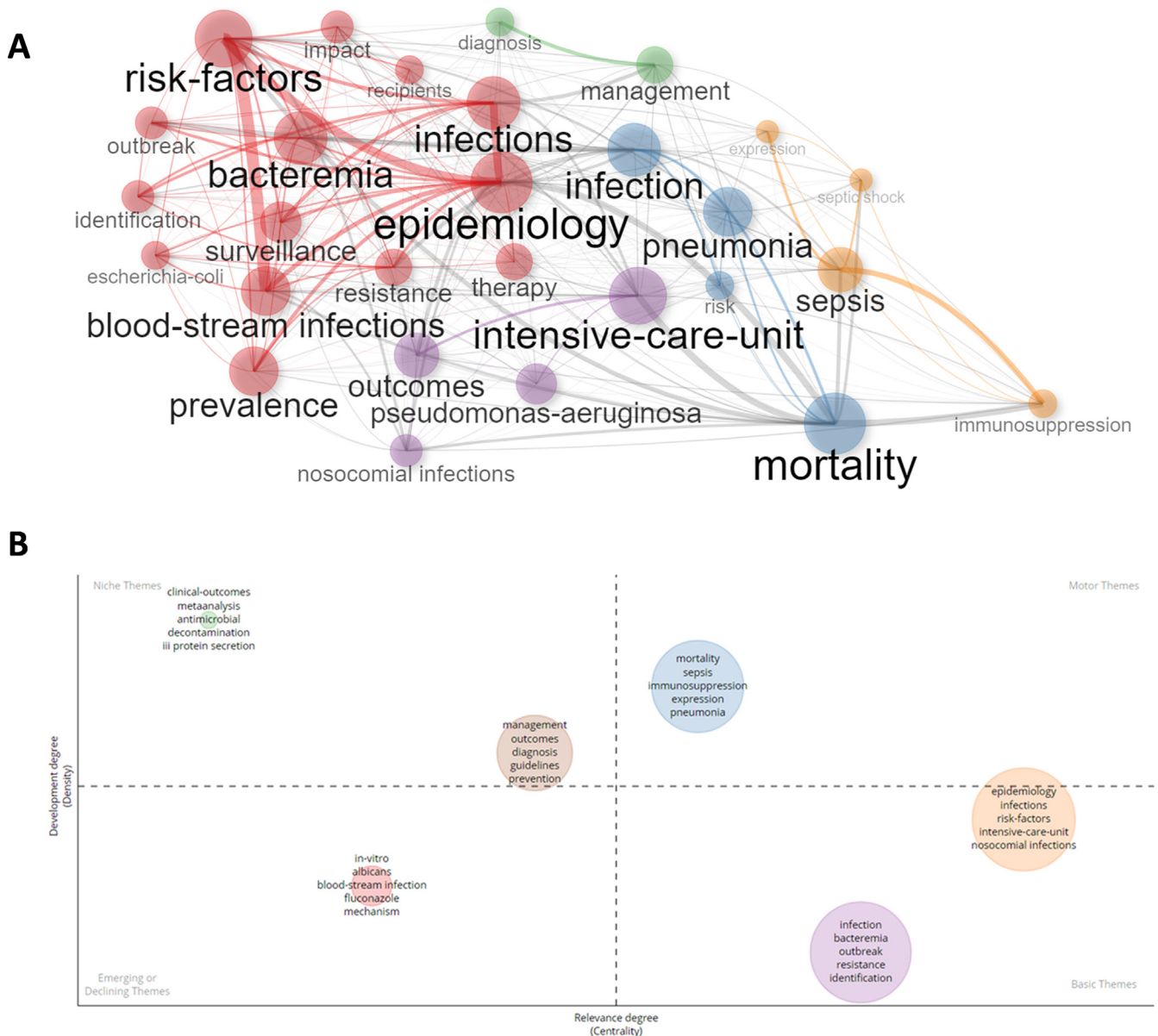


Fig. 8. Conceptual structure depicting co-occurrence network (A) and thematic map (B) of research on health care-associated infections in immunocompromised people, 2013–2022.

terms including “infection,” “bacteria,” “outbreak,” “resistance,” and “identification”, highlighting the foundational and fundamental aspects of research in this field. These concepts serve as building blocks for further investigations and provide a solid knowledge base for understanding and combating HCAs in immunocompromised individuals.

3.10. Future research directions and mitigation measures against HCAs among immunocompromised people

As HCAs among immunocompromised individuals continue to evolve, there are several key areas where future research efforts can make substantial contributions

to improving patient outcomes and reducing the burden of infections. Future research should focus on gaining a deeper understanding of different immunocompromised states, including the mechanisms underlying immune suppression and its impact on susceptibility to infection. Such understanding can inform targeted interventions to strengthen immune function and reduce the risk of HCAs. There is a need for innovative infection prevention and control strategies tailored specifically to immunocompromised individuals. This includes the development of guidelines for appropriate antimicrobial use, isolation protocols for patients with highly resistant pathogens, and the implementation of novel technologies for environmental disinfection. Given the increasing rates

of antimicrobial resistance [23], antimicrobial stewardship programs should be expanded and tailored to the unique needs of immunocompromised patients. This includes surveillance of antimicrobial resistance patterns, optimization of antimicrobial dosing regimens, and promotion of judicious antimicrobial use to minimize the development of resistance. Immunocompromised individuals often have impaired immune responses to vaccines, making them more susceptible to vaccine-preventable infections [24]. Future research should focus on developing alternative vaccination strategies, such as high-dose vaccines or novel adjuvants, to enhance vaccine efficacy in this population. There is a growing recognition of the heterogeneity among immunocompromised individuals, necessitating personalized treatment approaches based on individual risk factors, comorbidities, and immune status. Future research should explore the use of precision medicine techniques, such as genomics and immunophenotyping, to tailor treatment strategies and improve patient outcomes.

Vulnerable populations, including immunocompromised people, often face disparities in health care access and outcomes [25]. Future research should prioritize addressing these disparities through targeted interventions, community engagement, and policy changes aimed at improving health care equity and access to preventive services. The development of novel therapeutic approaches, such as immune-modulating therapies and phage therapy, holds promise for the treatment of HCAIs in immunocompromised individuals. Future research should focus on evaluating the safety and efficacy of these therapies in clinical trials and translating promising preclinical findings into clinical practice. Strengthening health systems, particularly in resource-limited settings, is essential for effective HCAI prevention and control. This includes improving infection surveillance systems, enhancing laboratory capacity for pathogen identification and antimicrobial susceptibility testing, and investing in health care infrastructure to support infection prevention and control efforts.

3.11. Study strengths and limitations

This study represents the first comprehensive and global overview of research trends on HCAIs among immunocompromised individuals. Our findings shed light on the current understanding of health care challenges and identify potential areas for future investigation. However, non-English articles were excluded, potentially missing valuable contributions. Despite this limitation, the present research provides valuable insights into the global research landscape of HCAIs in immunocompromised populations, as well as the impact of the COVID-19 pandemic on research outputs, and can guide further research efforts.

4. Conclusion

This study provides valuable insights into the research landscape of HCAIs among immunocompromised individuals from 2013 to 2022. The findings highlight the increasing attention and focus on HCAIs in this vulnerable population, particularly during the COVID-19 pandemic. *PloS One* emerged as a significant contributor to HCAI research, and the US demonstrated its leadership in scientific production and citation impact. Key research areas include epidemiology, infection, mortality, and risk factors. To further advance HCAI research in immunocompromised populations, it is recommended to promote international collaboration and interdisciplinary approaches. Encouraging partnerships among researchers from different countries and disciplines will foster knowledge exchange and innovative solutions. Research should be continued in this area, considering the evolving nature of HCAIs and the vulnerabilities of immunocompromised populations. Additionally, addressing emerging areas such as susceptibility, biofilm formation, and the impact of COVID-19 will contribute to staying ahead of evolving challenges. Strengthening surveillance and epidemiological studies is vital for understanding patterns of HCAIs and developing effective prevention strategies. By implementing these recommendations, we can enhance the prevention, diagnosis, and management of HCAIs, ultimately improving the health outcomes of immunocompromised individuals.

Funding

None.

Author contributions

CDI analyzed the data and prepared the first draft of the manuscript. CDI participated in the conception and design of the study, CDI constructively revised the manuscript; CDI participated in data collection and organization; CDI participated in and supervised the study throughout. The author commented on previous versions of the manuscript and approved the final version.

Acknowledgments

None.

Declaration of competing interest

The authors declare no conflict of interest.

Data available statement

The data that support the findings of this study are available on request from the corresponding author.

Ethics statement

Not applicable.

Informed consent

Not applicable.

References

- [1] K.E. Arnold, L. Aver, R. Bennett, et al. National and state healthcare-associated infections progress report 2014. <https://stacks.cdc.gov/view/cdc/22160> (accessed July 4, 2023).
- [2] L.A. Grohskopf, R.L. Sinkowitz-Cochran, D.O. Garrett, et al., A national point-prevalence survey of pediatric intensive care unit-acquired infections in the United States, *J. Pediatr.* 140 (4) (2002) 432–438, doi:10.1067/mpd.2002.122499.
- [3] W.H. Organization, in: *Report on the Burden of Endemic Health Care-Associated Infection Worldwide*, Libr. Cataloging Publ. Data, 2011, pp. 1–40.
- [4] S.S. Magill, J.R. Edwards, W. Bamberg, et al., Multistate point-prevalence survey of health care-associated infections, *N. Engl. J. Med.* 370 (13) (2014) 1198–1208, doi:10.1056/nejmoa1306801.
- [5] K. Blot, N. Hammami, S. Blot, et al., Seasonal variation of hospital-acquired bloodstream infections: a national cohort study, *Infect. Control Hosp. Epidemiol.* 43 (2) (2022) 205–211, doi:10.1017/ice.2021.85.
- [6] J.D. Siegel, E. Rhinehart, M. Jackson, et al., 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings, *Am. J. Infect. Contr.* 35 (10 suppl 2) (2007) S65–164, doi:10.1016/j.ajic.2007.10.007.
- [7] A.K. van der Bij, J.D. Pitout, The role of international travel in the worldwide spread of multiresistant Enterobacteriaceae, *J. Antimicrob. Chemother.* 67 (9) (2012) 2090–2100, doi:10.1093/jac/dks214.
- [8] M. Haque, M. Sartelli, J. McKimm, et al., Health care-associated infections - an overview, *Infect. Drug Resist.* 11 (2018) 2321–2333, doi:10.2147/IDR.S177247.
- [9] A.H. Sohn, D.O. Garrett, R.L. Sinkowitz-Cochran, et al., Prevalence of nosocomial infections in neonatal intensive care unit patients: results from the first national point-prevalence survey, *J. Pediatr.* 139 (6) (2001) 821–827, doi:10.1067/mpd.2001.119442.
- [10] P. Eckardt, R. Guran, J. Hennemyre, et al., Hospital affiliated long term care facility COVID-19 containment strategy by using prevalence testing and infection control best practices, *Am. J. Infect. Control.* 48 (12) (2020) 1552–1555, doi:10.1016/j.ajic.2020.06.215.
- [11] S.T. Micek, K.E. Kollef, R.M. Reichley, et al., Health care-associated pneumonia and community-acquired pneumonia: a single-center experience, *Antimicrob. Agents Chemother.* 51 (10) (2007) 3568–3573, doi:10.1128/AAC.00851-07.
- [12] M. Aria, C. Cuccurullo, Bibliometrix: an R-tool for comprehensive science mapping analysis, *J. Informetr.* 11 (4) (2017) 959–975, doi:10.1016/j.joi.2017.08.007.
- [13] H. Ejaz, H.M. Zeeshan, A. Iqbal, et al., *Rubella virus infections: a bibliometric analysis of the scientific literature from 2000 to 2021*, *Healthc. Basel* 10 (12) (2022) 2562, doi:10.3390/healthcare10122562.
- [14] Z. Xu, T. Lei, Y. Qin, An overview of probabilistic preference decision-making based on bibliometric analysis, *Appl. Intell.* 52 (13) (2022) 15368–15386, doi:10.1007/s10489-022-03189-w.
- [15] N. Sharma, M. Bairwa, B. Gowthamghosh, et al., A bibliometric analysis of the published road traffic injuries research in India, post-1990, *Health Res. Policy Syst.* 16 (1) (2018) 18, doi:10.1186/s12961-018-0298-9.
- [16] M.J. Page, J.E. McKenzie, P.M. Bossuyt, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, *BMJ* 372 (2021) n71, doi:10.1136/bmj.n71.
- [17] A. Ahmadvand, D. Kavanagh, M. Clark, et al., Trends and visibility of “digital health” as a keyword in articles by JMIR publications in the new millennium: bibliographic-bibliometric analysis, *J. Med. Internet Res.* 21 (12) (2019) e10477, doi:10.2196/10477.
- [18] M.Y. Tsay, Y.H. Yang, Bibliometric analysis of the literature of randomized controlled trials, *J. Med. Libr. Assoc.* 93 (4) (2005) 450–458.
- [19] A.W. Maula Cahyadin, A. Fuad, Healthcare-associated infections (HAI) research in Asian countries: a bibliometric analysis, *J. Thee Med. Sci. Berkala Ilmu Kedokteran* 50 (2018) 1–12, doi:10.19106/jmedsciesup005001201801.
- [20] S.D. Advani, E. Sickbert-Bennett, R. Moehring, et al., The disproportionate impact of coronavirus disease 2019 (COVID-19) pandemic on healthcare-associated infections in community hospitals: need for expanding the infectious disease workforce, *Clin. Infect. Dis.* 76 (3) (2023) e34–e41, doi:10.1093/cid/ciac684.
- [21] P.M. Macharia, N.K. Joseph, E.A. Okiro, A vulnerability index for COVID-19: spatial analysis at the subnational level in Kenya, *BMJ Glob. Health* 5 (8) (2020) e003014, doi:10.1136/bmjgh-2020-003014.
- [22] C.D. Iwu, T.C. Ekundayo, A.I. Okoh, A systematic analysis of research on *Arcobacter*: public health implications from a food-environment interphase perspective, *Foods* 10 (7) (2021) 1673, doi:10.3390/foods10071673.
- [23] C.D. Iwu, S.M. Patrick, An insight into the implementation of the global action plan on antimicrobial resistance in the WHO African Region: a roadmap for action, *Int. J. Antimicrob. Agents* 58 (4) (2021) 106411, doi:10.1016/j.ijantimicag.2021.106411.
- [24] L.F. Pittet, K.M. Posfay-Barbe, Vaccination of immune compromised children—an overview for physicians, *Eur. J. Pediatr.* 180 (7) (2021) 2035–2047, doi:10.1007/s00431-021-03997-1.
- [25] M. Leston, W. Elson, J.M. Ordóñez-Mena, et al., Disparities in COVID-19 mortality amongst the immunosuppressed: a systematic review and meta-analysis for enhanced disease surveillance, *J. Infect.* 88 (3) (2024) 106110, doi:10.1016/j.jinf.2024.01.009.