Experimental and Applied Medical Science, 6,3: 241-258, 2025. DOI: 10.46871/eams.1622524
Clinical Research

Trends in Biodefense Strategies: Confronting Emerging Infectious Diseases and Bioterrorism Threats

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Abstract

Purpose: *This study analyzes publication trends and co-authorship networks in biodefense and emerging infectious diseases research from 2000 to 2024 using data from the Scopus and PubMed databases.*
Method: *Data were collected from Scopus and PubMed databases to identify research articles related to biodefense and emerging infectious diseases over the period 2000–2024. Using Vos-viewer software a bibliometric approach was applied to evaluate publication trends, key contributing entities (organizations, countries, and authors), and co-authorship networks. The analysis was complemented with insights into the relationship between research productivity and major global health emergencies.*
Result: *The results of the study demonstrate a significant increase in research productivity following major health crises such as the 2001 anthrax attacks in the U.S., and the H1N1 and COVID-19 pandemics. Key contributors include leading organizations such as the Centers for Disease Control and Prevention (CDC), Harvard Medical School, and the World Health Organization (WHO). Countries like the United States, China, and Australia were identified as the most active in fostering collaborative efforts. However, disparities in funding and the existence of research silos were identified as persistent challenges.*
Conclusion*: The study highlights the responsive nature of biodefense research to global health emergencies, emphasizing the necessity of interdisciplinary and international collaboration. Opportunities for advancing biodefense research include expanding partnerships across nations and disciplines to build a resilient and inclusive framework for addressing global health threats. Additionally, the research underscores the importance of proactive and collaborative strategies to strengthen global preparedness for emerging health challenges.*

Key words*: Biosecurity, bio-surveillance, biothreat, bioweapons, global health, pandemic,.*

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Introduction

The apprehension and anxiety around biological threats become more significant in the 21st century, arising from both naturally occurring diseases and deliberate acts of bioterrorism. The disease's potential to disseminate to other countries is a consequence of the increasing interconnectedness of the world. Biotechnology advancement has also sparked concerns about probable misuse of biological materials (1). In the light of these dynamics, biodefense strategies and programs now encompass a multi-layered system that includes scientific studies, research, diagnosis, and others.

In this context, biodefense, the preparation for and response to biological threats, has become increasingly critical to countries' global health security. For instance, the 2001 anthrax attacks in the United States, during which many recipients received envelopes containing anthrax spores, are considered the most significant bioterrorism incident in history. This incident resulted in five fatalities and 22 infections, causing significant fear and panic nationwide (2). Following this incident, bioterror-related pathogen research received extensive funding (3).

Biodefense refers to a range of preventive initiatives in public health responses that play a crucial role in controlling, preventing, and reducing the impact of bioterrorism and infectious diseases (4). Therefore, developed countries consistently strive to advance their studies on bioterrorism and biological threats. Biodefense measures are essential for safeguarding communities from many biological dangers, including diseases and bioterrorism agents. These techniques include several methods, ranging from immune system stimulation to the formulation of antiviral treatments and policy structures. For instance, effective biodefense programs must include early identification and prioritization of threats, the development and stockpiling of targeted antibodies and vaccines, and thorough planning and cooperation across public health and security authorities (4- 6).

Historical Background and Current Biodefense Strategies

The term biosecurity or biodefense, including strategies for addressing biological threats, has its historical roots in agricultural methodologies and biological warfare since ancient times (Table 1) (7).

Table 1. Instances of Biological Warfare Throughout the Last Centuries.

Event	***Year***
Emperor Barbarossa contaminates water wells with human corpses in Tortona, Italy.	1155
Mongols launch corpses of plague victims over the fortifications of Caffa on the Crimean Peninsula.	1346
Spaniards mix wine with the blood of leprosy sufferers to sell to their French adversaries in Naples, Italy.	1495
Polish military uses rabid dogs to project saliva at adversaries.	1650
German and French troops establish an initial agreement to refrain from using "poison bullets."	1675
The British distribute blankets contaminated with smallpox to Native Americans.	1763
Napoleon floods fields around Mantua, Italy, to facilitate the spread of malaria.	1797
Confederates sell garments from patients with yellow fever and smallpox to Union forces in the United States.	1863

A successful biodefense strategy requires vigorous scientific research and development to provide diagnostic tools, medicines, and vaccines to counter bioweapons agents (9). Significant milestones influencing modern biodefense measures originated during World War I, when many nations investigated biological weapons, but without extensive deployment. During World War II, research on biological warfare intensified, as both Axis and Allied troops engaged in studies that increased worldwide awareness of the danger. Several agents are recognized for their historical use as bioweapons, with occurrences ranging from the First World War to more contemporary instances, like the anthrax assaults in the USA in 2001. Particular pathogens, such as Bacillus anthracis and Yersinia pestis, are elucidated, emphasizing their involvement in diverse outbreaks and military uses (Table 2).

Table 2. Classification of Biological Agents and Historical Instances of Use.

Caused Disease	Pathogen	Used
Category A (Major Public Health Hazards):		
Anthrax	*Bacillus anthracis* (B)	First World War Second World War Soviet Union, 1979 Japan, 1995 USA, 2001
Botulism	*Clostridium botulinum* (T)	–
Haemorrhagic Fever	Marburg virus (V)	Soviet Bioweapons Programme
	Ebola virus (V)	–
	Arenaviruses (V)	–
Plague	*Yersinia pestis* (B)	Fourteenth-Century Europe Second World War
Smallpox	Variola major (V)	Eighteenth-Century N. America
Tularemia	*Francisella tularensis* (B)	Second World War

Category B (Public Health Hazards):

Brucellosis	*Brucella* (B)	–
Cholera	*Vibrio cholerae* (B)	Second World War
Encephalitis	Alphaviruses (V)	Second World War
Food Poisoning	*Salmonella, shigella* (B)	Second World War USA, 1990s
Glanders	*Burkholderia mallei* (B)	First World War Second World War
Psittacosis	*Chlamydia psittaci* (B)	–
Q Fever	*Coxiella burnetti* (B)	–
Typhus	*Rickettsia prowazekii* (B)	Second World War
Various Toxic Syndromes	Various bacteria	Second World War

The Cold War era saw a surge in biological weapons development, especially by the United States and the Soviet Union, prompting the first worldwide efforts to regulate biological weapon proliferation (10). This resulted in the formation of the

Biological Weapons Convention (BWC) in 1972, the first international convention prohibiting the creation, manufacturing, and stockpiling of biological weapons, serving as a cornerstone for contemporary biodefense policy and practice (10).

Collaborations in economics and health across countries represent a primary domain susceptible to spread, threats, and exploitation by bioterrorism. Combating these threats requires comprehension of the many and varied facets of the issue. This depends on the ability to comprehend and do research. Therefore, each country adopts their own unique strategies for biodefense based on their priorities and resources. For instance, the U.S. national biodefense strategy utilizes a multi-faceted strategy to mitigate biological threats via preventive, defense, and response mechanisms. Preventive measures emphasize biosafety standards and the “One Health” paradigm to mitigate zoonotic threats and enhance global health security. The U.S. bolsters early threat identification via integrated bio-surveillance and diagnostics, addressing both natural and intentional threats. The policy facilitates swift mobilization via vaccine development as well as coordinated recovery initiatives to manage crises and bolster community resilience, highlighting the need of worldwide cooperation to reduce biological threats (11). China's biodefense plan includes policy modifications and legal structures that align biological research with national security, restrict certain overseas partnerships, and implement stringent biosecurity and criminal legislation (11). Furthermore, China's biotechnology industry has dual-use capabilities for military and potential bioweapons applications, accompanied by stringent export regulations to regulate this duality. Notwithstanding China's adherence to international accords like the BTWC and Geneva Protocol, apprehensions persist about possible undisclosed bioweapons endeavors (10 and 12).

These days, the threat terrain in biodefense is increasingly complicated, caused not only by emerging zoonotic pathogens but also because of serious biosafety lapses in laboratories. For instance, in July 2022, Ghana confirmed its first-ever outbreak of Marburg Virus Disease; three cases were confirmed, two of which were fatal, with a case-fatality rate of 67% by the end of the outbreak in mid-September (16). Just a few months later, Equatorial Guinea saw its first-ever Marburg outbreak from February to June 2023; 17 laboratory confirmed cases, and 23 probable cases culminated in 12 confirmed deaths and other variant fatalities, making way for national and WHO-led response measures until closure of the outbreak in June (17).

Meanwhile, in early 2025, Nigeria experienced a striking spike in Lassa fever cases, with finally 535 confirmed cases and 98 deaths spread over 14 states and a remarkable surge of 76 cases and 12 deaths in the fourth epidemiological week of January alone, representing a sharp rise of near 12.4% in cases and 10.4% in deaths with respect to 2024 (18). These outbreaks bring out the twin challenges of emergent infectious diseases; finding ways to deal with the sudden appearance of zoonotic events and endemic viral surges that altogether threaten the sustaining power of a national health system-even as the greater global response is now increasingly turning to technology-based tools such as genomic surveillance, AI-aided predictive modeling, and speedy mobile diagnostics for better preparedness in the future.

The purpose of this study is to examine literature trends around biodefense and bioterrorism, focusing on the evolution of global research initiatives in response to increasing infectious diseases and bioterrorism threats. By utilizing a bibliometric analysis of the Scopus and PubMed scientific databases the study aims to analyze scientific publication patterns across countries, institutions, and thematic areas to identify key contributors to the field of biodefense literature and underscore cooperative efforts that support global readiness.

Methodology

Using VOS-viewer software for bibliometric mapping is considered crucial in identifying current publications and collaborative networks, which in turn informs future research paths (13). A systematic approach toward literature analysis often includes extensive databases like Scopus or Web of Science (14) which yield enduring results for both quantitative and qualitative research (15). This study retrieved data on Nov. 1st, 2024, from the Scopus and PubMed databases and utilized VOS-Viewer software version 1.6.20 to create a bibliographic map of the countries, institutions, and authors.

The study narrowed the literature search results to include four areas of literature to obtain a comprehensive compilation of pertinent articles. The categories include (1) articles, (2) conference papers, (3) reviews, and (4) conference reviews. The search results displayed the relevant page of any phrase that appears in the title, abstract, or keywords of any literature in the Scopus and PubMed databases between the years 2000 and 2024. A unique search strategy was employed for this study (Table 3).

Table 3. Advanced Search Strings for Biodefense Research in Scopus and PubMed.

Database	Search String	Description
Scopus	TITLE-ABS-KEY (biodefence OR biothreat OR bioterrorism OR biosecurity) AND PUBYEAR > 1999 AND PUBYEAR < 2025 AND PUBYEAR > 1999 AND PUBYEAR < 2025 AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMIT-TO (DOCTYPE , "cp") OR LIMIT-TO (DOCTYPE , "cr"))	Searches for terms “biodefense,” “biothreat,” “bioterrorism,” or “biosecurity” in the title, abstract, or keywords of articles published from 2000 to 2024.
PubMed	(((((((Biodefense[Title/Abstract]) OR (biothreat[Title/Abstract]))) OR (biosecurity)) OR (bioweapons)) OR (pandemic)	Searches for terms “biodefense,” “biothreat,” “biosecurity,” “bioweapons,” or “pandemic” in the title or abstract of publications between 2000 and 2024.

The search results were acquired from both databases and then exported as documents in PubMed and CSV format. The documents included information such as the

author(s), title, year, source title, citation count, source and document type, affiliations, publisher, communication address, author keywords, and indexing keywords. The documents were then imported into the VOS-Viewer application, and the bibliographic mapping of each was conducted separately, which included the co-authorship analysis of organizations (Scopus and PubMed) and co-authorship analysis of countries (Scopus).

This enabled network visualization, overlay visualization, and density visualization. The layout and clustering settings were modified to improve visualization, considering the content and data. Larger nodes often signify enhanced connectedness, suggesting more importance. Some certain statistical charts were generated with Microsoft 365.

To ensure the quality and relevance of the dataset, a rigorous data cleaning process was applied. The initial search results consisted of publication types such as articles, reviews, conference papers, and conference reviews. Editorials, letters, errata, and duplicates were removed to preserve academic integrity and organs for original research publications. Review articles were included because of their ability to analytically synthesize trends, while systematic reviews and meta-analyses were retained only if their focus pertained directly and solely to biodefense, bioterrorism, or emerging infectious diseases within the confines of the search terms. Actress papers not directly addressing the focus of this study (e.g., some tangential topics in unrelated medical fields) were also rejected. Publications without full bibliographic data, such as the absence of author affiliations or publication years, were filtered out before the analysis process since they could not be incorporated into VOS-viewer.

Result and discussion

Utilizing the Scopus database over the past 24 years (2000-2024), reveals that the search string employed in this study (Table 3) yielded a total of 19,015 literature items. The literature types included Articles (n=12,072, 75.9%), Conference Papers (n=851, 5.3%), Reviews (n=2968, 18.7%), and Conference Reviews (n=21, 0.1%) respectively.

Results demonstrate that notable fluctuations in publication volumes highlight shifts in scientific focus over time, likely influenced by global health events and bioterrorism concerns. Initially, from 2001 to around 2006, document output was relatively low across all journals, indicating either limited research focus or fewer biodefense concerns at that time (Figure 1) However, in the mid-2000s, a steady increase in publications began, especially

for journals like Biosecurity and Bioterrorism and Transboundary and Emerging Diseases, suggesting growing interest and awareness in these fields.

A significant peak in publication counts is also observed around 2009-2011 for Biosecurity and Bioterrorism, which aligns with global discussions on pandemic preparedness post-H1N1 influenza. Other journals, such as Transboundary and Emerging Diseases and Frontiers in Veterinary Science, also show increased publications in the late 2010s and early 2020s, reflecting intensified research, possibly spurred by events like the COVID-19 pandemic. Preventive Veterinary Medicine and Plos One have shown more moderate and consistent contributions, with some peaks in recent years that could relate to cross-species disease transmission studies. These trends underscore a reactive pattern, where global disease events and security threats drive spikes in academic research output within biodefense and related fields.

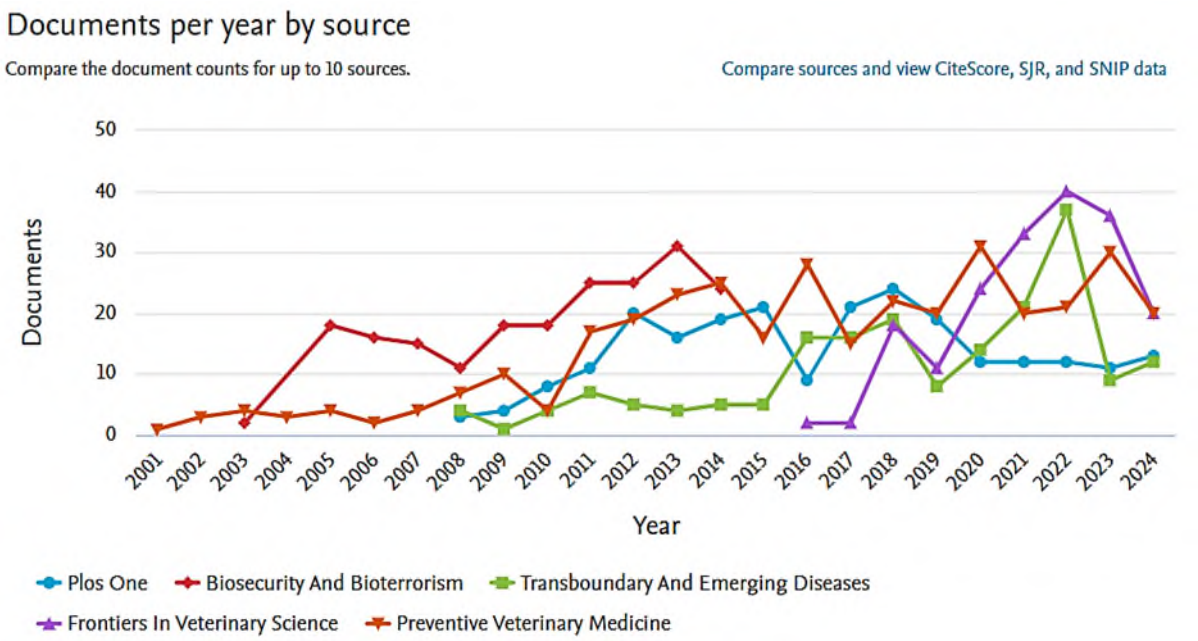

Figure 1. Annual Publication Trends in Biodefense and Emerging Infectious Disease Research Across 5 Key Journals in Scopus Database (2001–2024).

From a baseline close to zero in 2000, there is a sharp increase in document counts, peaking around 750 by 2002, likely reflecting heightened interest and investment in biodefense following events like the anthrax attacks of 2001 and increased awareness of bioterrorism (Figure 2). After this early peak, there is a gradual decline until about 2008, followed by a stable period with counts ranging around 400-500 documents yearly up to around 2016. From 2016 onward, a steady upward trend is evident, with a notable surge after 2020, which could be attributed to the COVID-19 pandemic and renewed focus on emerging infectious diseases. Document counts reach a new high, peaking around 2022 at over 1,000 publications, then slightly decline in 2024, suggesting a possible stabilization or shift in focus. This trend indicates that major public health events and bioterrorism threats heavily influence research and publication activity in the field of biodefense.

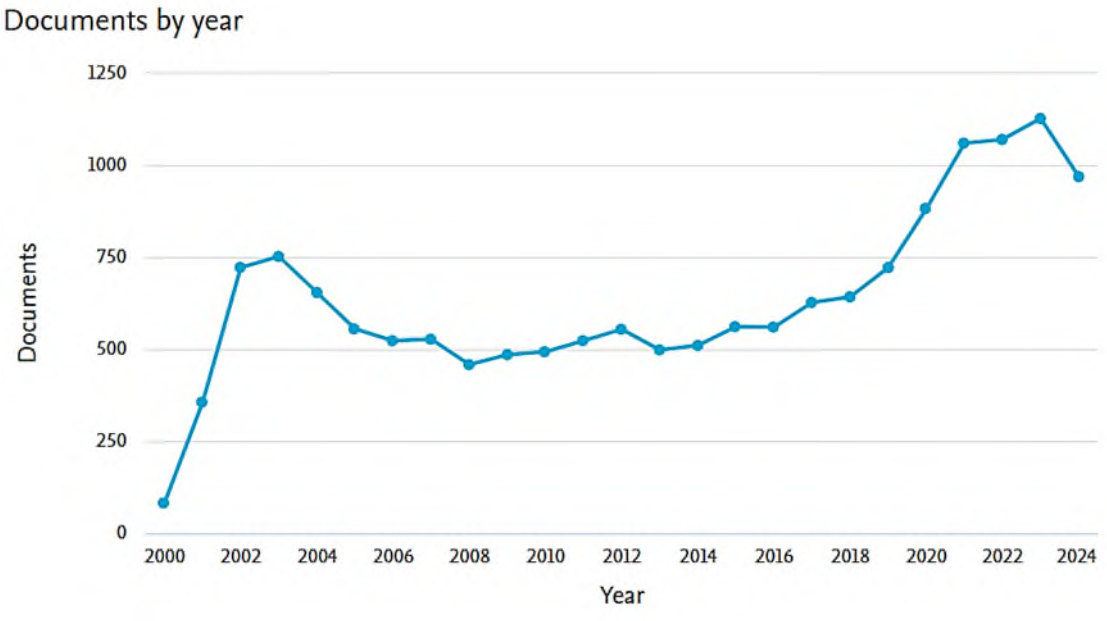

Figure 2. Annual Publication Trends in Biodefense Research in Scopus Database (2000-2024).

Co-authorship analysis of organizations (Scopus)

A minimum threshold was set to include only organizations with at least 25 documents and a minimum of 3 documents per organization. Out of a total of 43,227 organizations, 1,000 met these criteria. The largest connected component in this dataset comprises 484 items. Figure 3 indicates the collaboration of organizations from 2010 to 2025. Notable organizations like the Centers for Disease Control and Prevention (CDC), Los Alamos National Laboratory, and the Nuclear Threat Initiative appear as central nodes, reflecting their significant roles and partnerships in this field. The map highlights dense collaboration clusters, such as those around CDC and the Ministry for Primary Industries, indicating key partnerships in biodefense research. The color gradient shows that newer collaborations have emerged post-2020, likely due to increased global focus on infectious disease threats. Cross-national links, including institutions like CABI in Switzerland and various U.S.-based institutions, demonstrate the international scope and cooperative nature of recent research initiatives in biodefense and biosecurity.

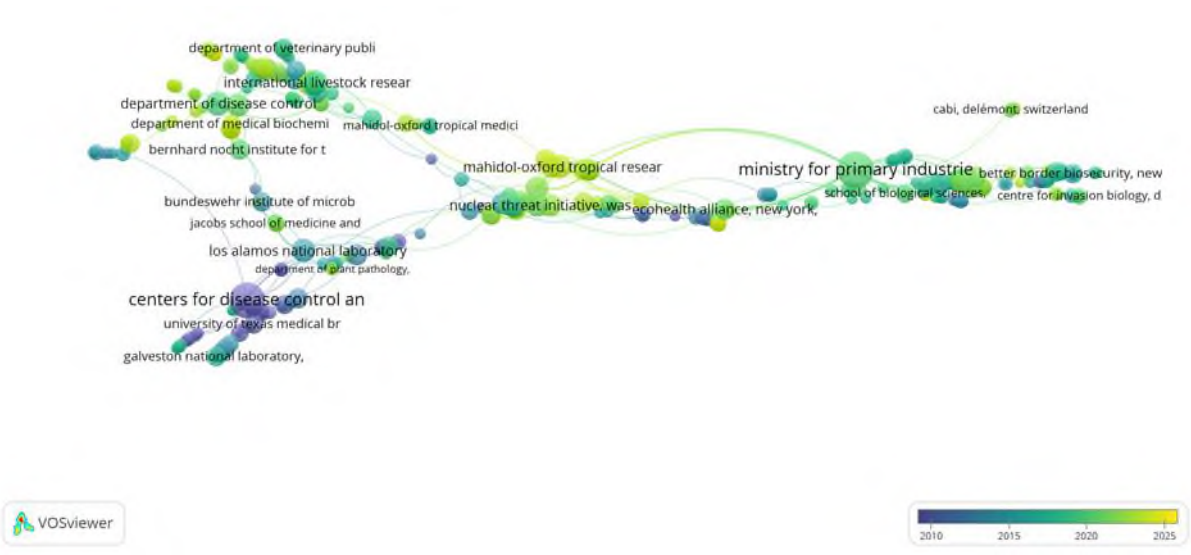

Figure 3. Co-Authorship Network of Organizations in Biodefense Research (2010-2025).

Co-authorship analysis of countries (Scopus)

In this analysis, the selection criteria were set to include a maximum of 25 countries per document, with a minimum threshold of 5 documents per country. These parameters led to the analysis of 132 countries. The analysis of co-authorship of countries shows that the United States, Australia, and China are prominent nodes, signifying their high involvement and central roles in global research networks in biodefense field (Figure 4). The dense cluster around these countries, involving France, Canada, the Netherlands, and New Zealand, among others, highlights active international collaboration. Countries like Bhutan, Puerto Rico, and some others are more isolated, with fewer collaborative connections. The color gradient shows that many collaborations have been more recent (post-2020), possibly reflecting increased global cooperation in response to recent infectious disease outbreaks, such as COVID-19. Overall, this map underscores the United States as a primary hub of global research partnerships in this field, with strong links to various regions worldwide.

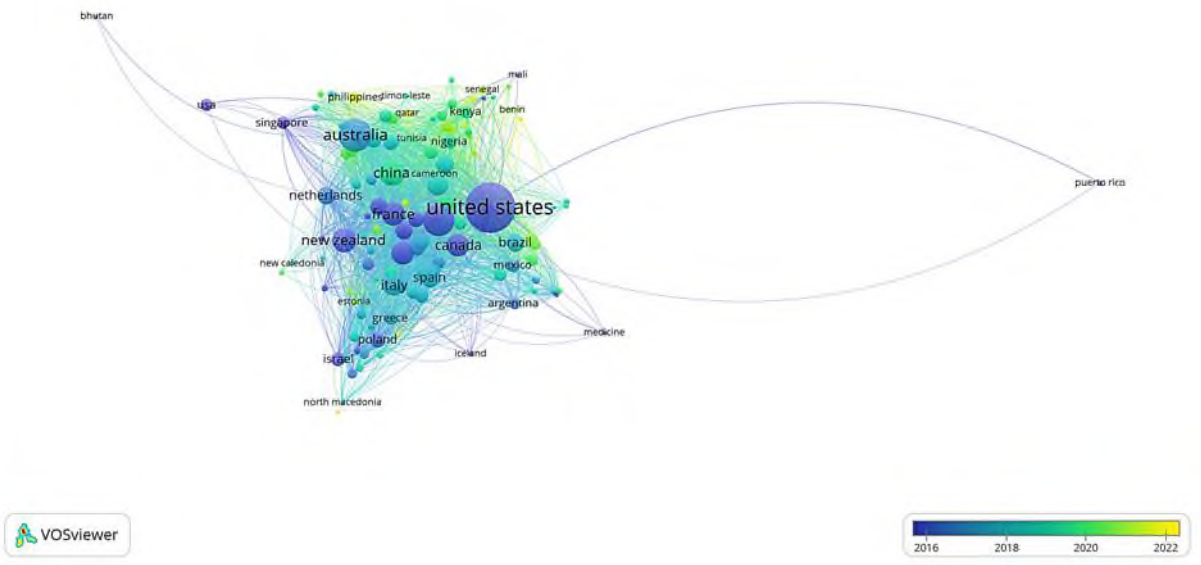

Figure 1. Co-Authorship Network of Countries in Biodefense Research (2016-2022).

Co-authorship analysis of organizations (PubMed)

The result of this analysis highlights certain key organizations as central figures in research collaborations. For instance, "Harvard Medical School, Boston" appears prominently, with larger node sizes and several connections, signifying its significant role in fostering research partnerships across multiple institutions. Similarly, organizations such as the "World Health Organization" and the "Dalla Lana School of Public Health" hold a central position in this network, demonstrating their significant contributions to research collaborations in the fields of public health and medicine. Other institutions such as "Georgetown University" and the "Saw Swee Hock School of Public Health" also play important roles, albeit with slightly fewer collaborations compared to Harvard (Figure 5). The presence of diverse international organizations, such as the "Heidelberg Institute of Global Health" and "GSK, Wavre, Belgium," illustrates the global nature of research partnerships in this field, reflecting an interconnected research ecosystem. This network provides insights into the collaborative dynamics in medical and public health research, where prominent institutions act as hubs of knowledge dissemination and partnership, linking other organizations within a global research framework. In this context, the findings emphasize the importance of academic and health institutions in driving collaborative research that likely spans multiple disciplines and geographical boundaries.

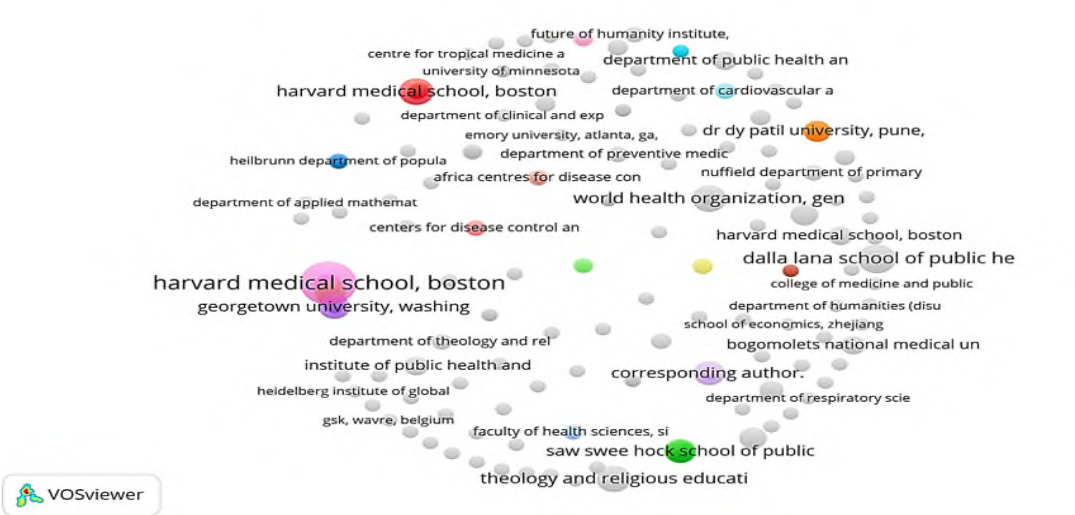

Figure 2. Co-Authorship Network of Organizations in the Field of Biodefense .

Discussion and Conclusion

The trends observed in biodefense and emerging infectious disease research reflect a reactive and dynamic field, closely linked to global health and security concerns. The spikes in publication volumes following events such as the anthrax attacks in 2001, the H1N1 influenza pandemic in 2009, and the COVID-19 pandemic in 2020 suggest that research efforts intensify in response to major health threats. This pattern illustrates a heightened awareness and prioritization of biodefense during periods of perceived vulnerability, leading to increased scientific output.

Furthermore, the dominance of countries like the United States, China, and Australia in the co-authorship network underscores their critical role in shaping global biodefense strategies. These leading nations not only contribute substantial research but also foster international collaborations, positioning themselves as hubs within the research ecosystem. By doing so, they guide the research agenda, influence funding priorities, and provide expertise that helps to build resilience against future health threats.

The involvement of key institutions, such as the CDC, Harvard Medical School, and the World Health Organization, further reinforces the influence of well-resourced organizations in biodefense research. These institutions serve as central nodes within the co-authorship network, enabling the flow of knowledge and best practices across borders. Their roles are essential in coordinating research efforts, setting global standards, and responding rapidly to emerging threats. By driving collaborations across various sectors and disciplines, these institutions play an instrumental role in promoting a cohesive and coordinated approach to global health security.

Despite the growth and internationalization of biodefense research, several challenges persist. One primary challenge is funding disparities, with a significant concentration of resources in countries with advanced infrastructure and established institutions, while other regions receive comparatively limited support. This imbalance may hinder the development of a truly globalized biodefense strategy, as underfunded regions struggle to contribute to and benefit from collaborative research. Additionally, research silos present another challenge, where institutions may focus on specific aspects of biodefense or infectious diseases without sufficient integration across different fields, such as public health, veterinary science, and environmental health. This lack of interdisciplinary collaboration may limit innovation and prevent the holistic approach necessary for

effectively addressing complex, multifaceted threats.

However, these challenges also highlight potential opportunities for innovation and increased cooperation. Expanding international collaborations can help address funding disparities by pooling resources and sharing expertise across borders. Emerging digital technologies and open-access platforms can facilitate knowledge sharing and break down research silos, allowing institutions worldwide to contribute to and access biodefense research more equitably. Additionally, interdisciplinary partnerships could enhance understanding of cross-species disease transmission, environmental factors in disease spread, and biosecurity measures. Building strong, diversified research networks that include both well-funded and emerging institutions may provide a more resilient framework for addressing global health threats.

This research reveals significant key insights into how global health events and security concerns shape scientific output and collaboration. The surge in publications following events like the anthrax attacks in 2001, the H1N1 pandemic, and the COVID-19 pandemic highlights a reactive pattern in research focus driven by real-world crises. Notably, institutions such as the CDC, Los Alamos National Laboratory, and international partners play central roles in biodefense research, with a growing number of collaborations emerging post-2020. Additionally, the country-level co-authorship analysis underscores the United States as a key hub, fostering extensive global partnerships, particularly with Australia, China, and various European countries (table 4). This global, interdisciplinary research network underscores the essential role of academic and public health institutions in biodefense and public health preparedness. The co-authorship patterns, especially in prominent institutions like Harvard Medical School and the World Health Organization, demonstrate the interconnectedness of the research community. Together, these findings emphasize the collaborative, cross-national nature of biodefense research, underscoring the critical need for sustained partnerships and knowledge-sharing to address emerging global health threats effectively.

Table 4. Key Findings.

Aspect	Key Findings
Publication Trends	▪ Research output in biodefense and infectious diseases shows notable fluctuations, often increasing after global health events (e.g., anthrax attacks, H1N1, COVID-19).
Key Publication Peaks	▪ Early peak in 2001-2002 following the anthrax attacks. ▪ Significant increase in 2009-2011 following H1N1 pandemic. ▪ Surge in 2020-2022 driven by COVID-19.
Prominent Organizations in Co-Authorship	▪ Centers for Disease Control and Prevention (CDC), Los Alamos National Laboratory, and Nuclear Threat Initiative as central nodes. ▪ Other key institutions include Harvard Medical School, World Health Organization, and Dalla Lana School of Public Health.
International Collaboration	▪ Strong cross-national collaborations, with the U.S. as a central hub. ▪ Active partners include Australia, China, France, Canada, and the Netherlands.
Emerging Collaborations	▪ Increased global cooperation post-2020, possibly in response to COVID-19 and other health crises. ▪ Cross-national partnerships underscore a global response to emerging health threats.
Role of Academic and Health Institutions	▪ Academic and health institutions serve as hubs for knowledge dissemination and partnerships. ▪ Key in advancing multidisciplinary research in biodefense and public health.

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