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SYSTEMATIC REVIEW

Bibliometric analysis and network visualization mapping of global research in Q fever vaccine [version 1; peer review: 1 approved with reservations]

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Abstract

Background: Query fever (Q fever), caused by Coxiella burnetii, is a highly infectious zoonotic infection to humans and livestock. Despite extensive efforts to develop effective vaccines against this disease, only one vaccine is licensed and available. The aim of this study was to investigate the global research trends, keystone bibliometric parameters, and network visualization mapping in Q fever vaccine from 1941 to 2021.
Methods: A retrospective bibliometric followed by a visualized study was conducted. The searches were conducted in the Science Citation Index Expanded (SCI-E) Edition of Web of Science Core Collection (WoSCC). The following keywords were used: "Q fever" OR "Query fever" OR "Coxiella burnetii" OR "Coxiella-burnetii" OR "C.

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1. **Carrie Mae Long** [ID], National Institutes of Health, Hamilton, USA

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burnetii" (Topic) AND "Vaccin*" OR "Immuniz*" OR "Immunis*" (Topic) without any limitation. The data were plotted for co-authorship countries, co-occurrence keywords plus, and bibliographic coupling sources network visualization mapping. The VOSviewer version 1.6.17 was used for network visualization.

Results: The bibliographical search resulted in a total of 478 publications which were included in this study. The publications were mainly published in English (n=436), while the major document types were articles (n=391). The most productive year was 2014 (n=33), while the most cited year was 2020 (n=1026). The extensively studied research areas were immunology and veterinary science, and the most used keywords plus were Q-fever and Coxiella-burnetii. Kazar J (n=17) was the leading author, while the famous journal was Acta Virologica (n=23). The most active institution was the Slovak Academy of Sciences (n=32), and the leading country was the US (n=129).

Conclusion: A rapid increase has been observed in Q fever vaccine publications and citations in the past 20 years. This study might be of great interest to provide standard bibliographic information and keystones parameters in Q fever vaccine research.

Keywords
Q fever, Q fever vaccine, Bibliometric analysis, Web of Science, Visualization mapping

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Introduction

Query fever (Q fever) is a highly infectious zoonotic infection to humans and livestock caused by the etiological agent *Coxiella burnetii*, an intracellular gram-negative bacterium widespread throughout the world.[1,2] Domestic ruminants are believed to be the primary source of Q fever in humans.[3,4] In humans, the infection is primarily transmitted via inhalation of aerosols from contaminated soil and animal excrement, most notably parturient fluids.[4–9] Consumption, particularly raw milk, is also likely a route of *C. burnetii* transmission. Although *C. burnetii* has been isolated from arthropods, primarily ticks, it is unlikely that arthropod-borne transmission of Q fever is significant in humans.[5,10] However, *C. burnetii* can infect other animal species, including pets and birds and cause human cases of Q fever.[3,6,8,11] The majority of animal species infected with *C. burnetii* exhibit no symptoms.[4,6] However, in goats and sheep, Q fever's most common clinical manifestations are abortion and stillbirth. Q fever has been linked to sporadic abortion, infertility, and metritis in cattle.[6,12] Abortion epidemics in livestock have been reported in endemic regions, resulting in severe economic consequences.[1,13,14] Abortion can result in the excretion of up to 1 billion *C. burnetii* per gram of placenta.[15]

In humans, the disease presents as an acute flu-like illness with a debilitating headache and cyclic fever as its hallmark symptoms.[1,5] The typical signs and symptoms of symptomatic infection include headache, pyrexia, and respiratory tract infection, including atypical pneumonia; hepatitis is also a possibility.[16] Chronic infection is well-known, most commonly manifesting as Q fever endocarditis.[5,16–18] Correlations between *C. burnetii* infections and the onset of atherosclerosis, chronic fatigue syndrome, and other cerebrovascular events also have been suggested.[1,5,18,19] Despite extensive efforts to develop an effective vaccine against human Q fever, only Q-Vax® is commercially available, and its licensed use is limited to Australia.[20–22] Thus, the current study was conducted to explore the global research outputs, research areas, and frontiers, and to establish the visualization mapping of research in the Q fever vaccine.

Methods

Study design and database searches

A bibliometric review followed by a visualized study was conducted (See underlying data).[23] The review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping review (PRISMA-ScR) guidelines.[23] The Science Citation Index Expanded (SCI-E) Edition of Web of Science Core Collection (WoSCC) was used to search for relevant publication on the Q fever vaccine as of October 16, 2021. The Web of Science (WoS) is the world's oldest database belonging to the commercial provider.[24,25] Currently, the WoS is hosted by Clarivate Analytics.[26] The WoSCC database is a selective citation index of scholarly and scientific publishing covering books, data compilations, proceedings, and journals.[25] The WoSCC is a commonly used database for bibliometric studies.[27–33] Previously published bibliometric studies conducted in medical and health sciences and other areas used SCI-E Edition of the WoSCC.[34–37] Therefore, in the current study, SCI-E Edition was utilized.

Searching keywords

The following keywords were used: "Q fever" OR "Query fever" OR "Coxiella burnetii" OR "Coxiella-burnetii" OR "C. burnetii" (Topic) AND "Vaccine*" OR "Immunize*" OR "Immunis*" (Topic). The searches were performed without any limitation in the topic field. The Topic field searches title, abstract, author keywords, and keywords plus.

Data extraction and analysis

We extracted many attributes such as author name, year of publication, journal, document type, institution, and country. The data were downloaded both in Comma-separated value and Tab delimited files. The collected information was entered into a Microsoft Excel spreadsheet, and the values were presented in frequencies and percentages.

Network visualization mapping

The data were exported in Tab delimited file into VOSviewer software version 1.17.1 for macOS for network visualization mapping. VOSviewer is a widely available tool for network visualization, overlay visualization, and density visualization mapping.[38] The retrieved data were plotted for co-authorship countries, co-occurrence keywords plus, and bibliographic coupling sources network visualization mapping. After plotting the data, clusters were formed, and each color designates a different cluster. The minimum cluster size for co-authorship countries was fixed at 10. The countries with zero total link strength (TLS) were excluded from the plotting. The thicker line between the countries represents the stronger collaboration, while the larger node or label represents the higher the weight vice versa.[39] The co-occurrence of a keyword plus was selected at 5. The keywords plus terms are generated from the titles of articles/documents cited by the author of the article being indexed. The articles/documents whose references are not linked to source items will not have keywords plus.[40] The data were further plotted for bibliographic coupling sources based on the cited references. The minimum number of items of a source was selected at 5. Alongside network visualization, the density visualization mapping was generated. In density visualization, same as network and overlay visualization, the items are represented by their label. In density visualization, each point has a color that represents the density of items at

that point. In the neighborhood of a point in density visualization, the larger the number of items, and the weights of the neighboring items, the closer the color of the point is to yellow color.[39]

Results

Characteristics of the studies

The initial search retrieved a total of 478 documents, and all the documents were included in the final bibliometric analysis and visualization mapping. The documents were published in nine languages: English (n=436), German (n=20), French (n=11), Czech (n=3), Dutch (n=3), Russian (n=2), Italian (n=1), Polish (n=1), and Slovak (n=1).

The included publications were cited 12,434 times (26.01 average citations per item) and 9,378 times without self-citations (19.62 average citations per item). The overall H-index value was 51 in the published documents. The most
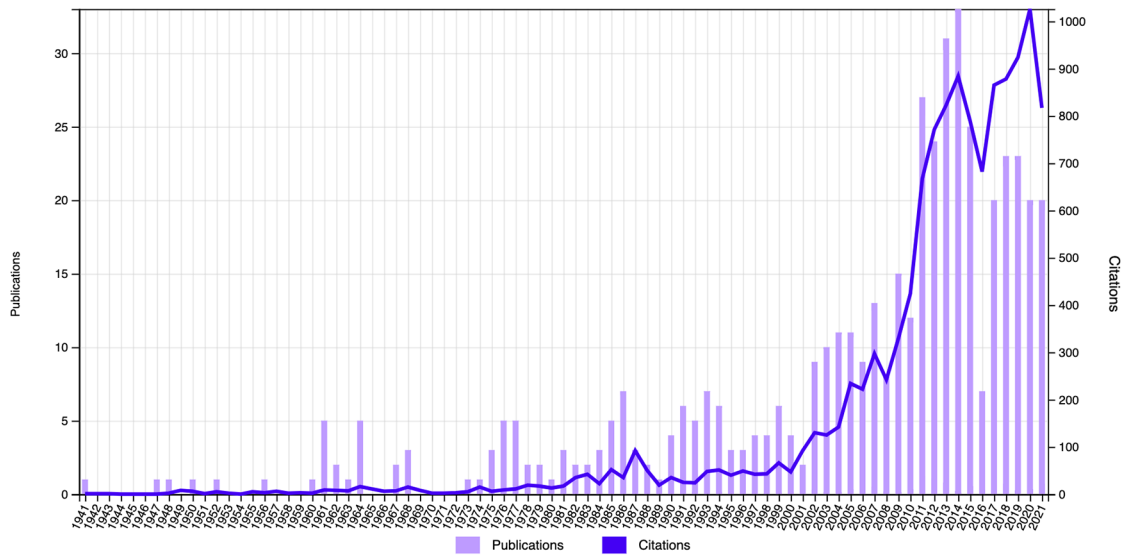
Figure 1. The number of publications and citations of studies in Q fever vaccine between 1941 to 2021.

Figure 2. Document types (A), top 10 most studied research areas (B), top 10 most prolific authors (C), and top 10 attractive journals (D) in Q fever vaccine research.

Figure 3. Top 10 active institutions (A) and top 10 leading countries in Q fever vaccine research (B).

Figure 4. Co-authorship countries visualization mapping: (A) Network visualization and (B) Density visualization.

productive year of publications was 2014 (n=33, 884 citations), while the most cited year was 2020 (n=20, 1,026 citations), as shown in Figure 1. The documents published in 2021 (n=20) were cited 817 times.
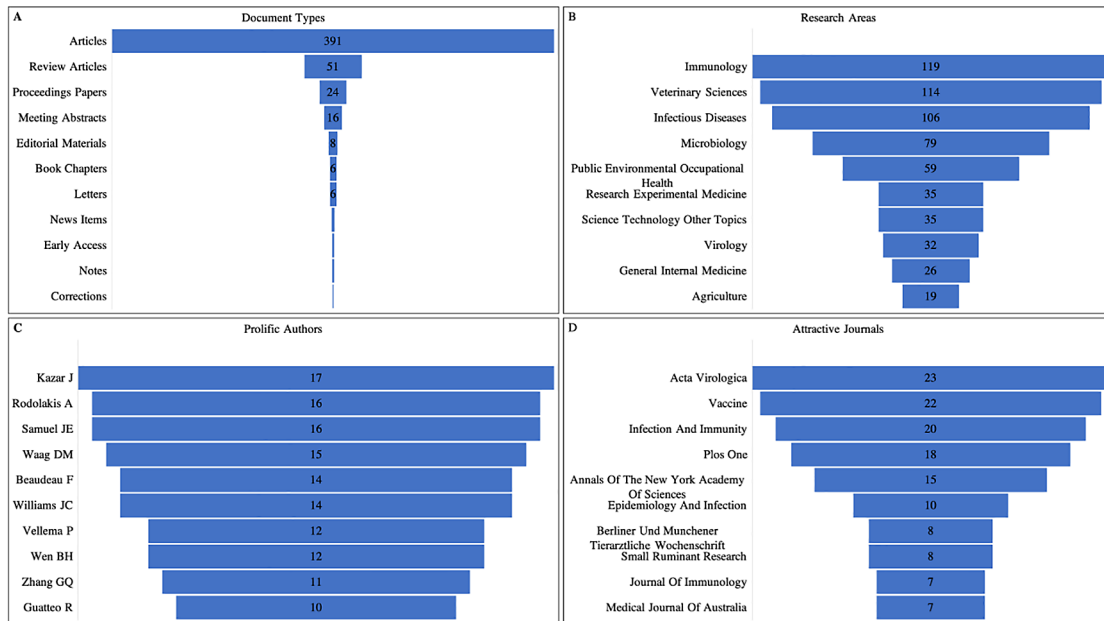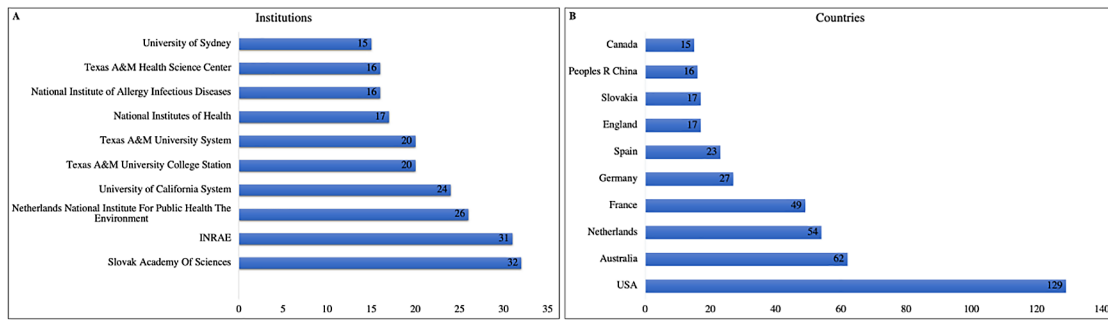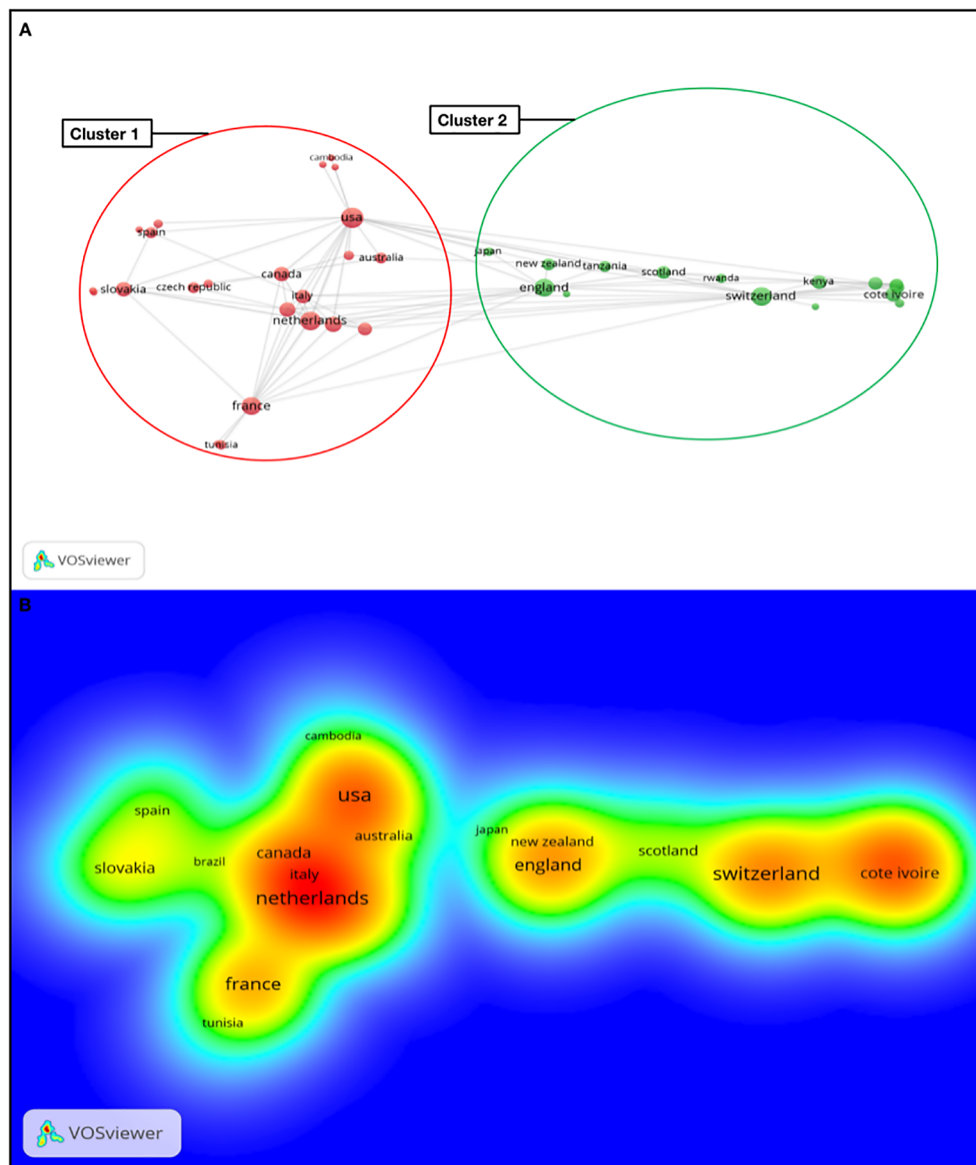
The majority of the documents were published as original/research articles (n=391), followed by review articles (n=51), and proceeding papers (n=24) (Figure 2A). The most studied research areas were immunology, veterinary sciences, and infectious diseases (Figure 2B). The most prolific author was Kazar J (n=17) (Figure 2C) and most of the article published in Acta Virologica (n=23) (Figure 2D).

In total, 60 records did not contain institution names, while 34 records did not contain country names. The institution with the most publications (n=32) was the Slovak Academy of Sciences (Figure 3A). The top three leading countries in Q fever vaccine research were the USA (n=129), Australia (n=62), and the Netherlands (n=54), as shown in Figure 3B.
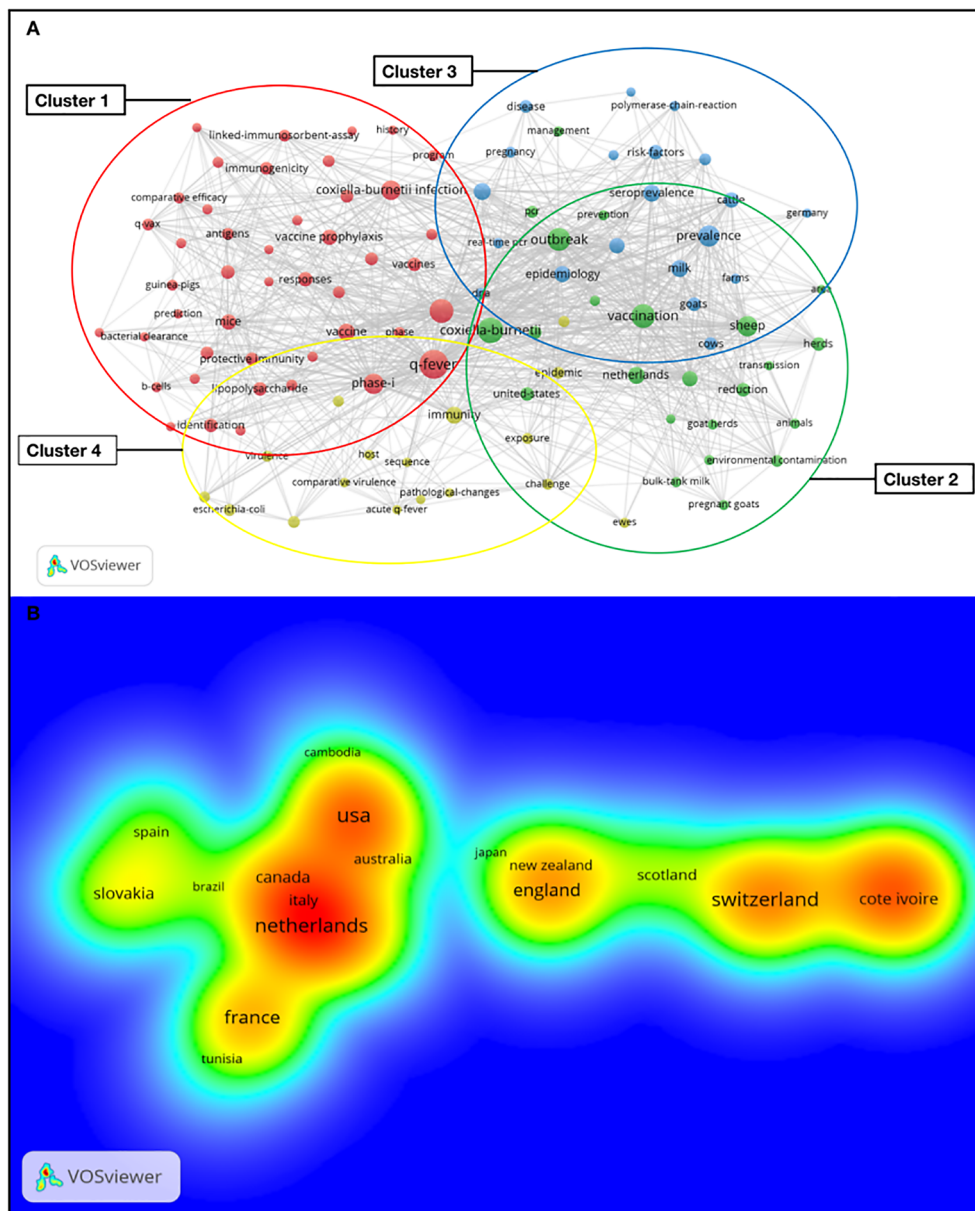
Figure 5. Co-occurrence keywords plus visualization mapping: (A) Network visualization and (B) Density visualization.

Co-authorship countries network and density visualization

Of the total countries, 18 countries with TLS zero were excluded from the mapping. For the rest of the countries, the TLS ranged from 1 to 36. USA was the leading country with the highest TLS with other countries (n=36), followed by Netherlands (n=28), Switzerland (n=27), France (n=21), and England (n=21). A total of two clusters were formed; cluster 1 consists of 23 countries, while cluster 2 had 16 countries (Figure 4).

Co-occurrence keywords plus network and density visualization

Of the total keywords plus, only 105 met the criteria. At the same time, the cluster size was fixed at 10. A total of four clusters were formed; cluster 1 consists of 45 keywords plus, followed by cluster 2 (n=23), cluster 3 (n=20), and cluster 4 (n=17) (Figure 5). The widely used keywords plus based on occurrence and TLS was Q-fever (n=110, TLS=402), followed by Coxiella-burnetii (n=77, TLS=266), infection (n=67, TLS=338), vaccination (n=64, TLS=287), and an outbreak (n=57, TLS=275).
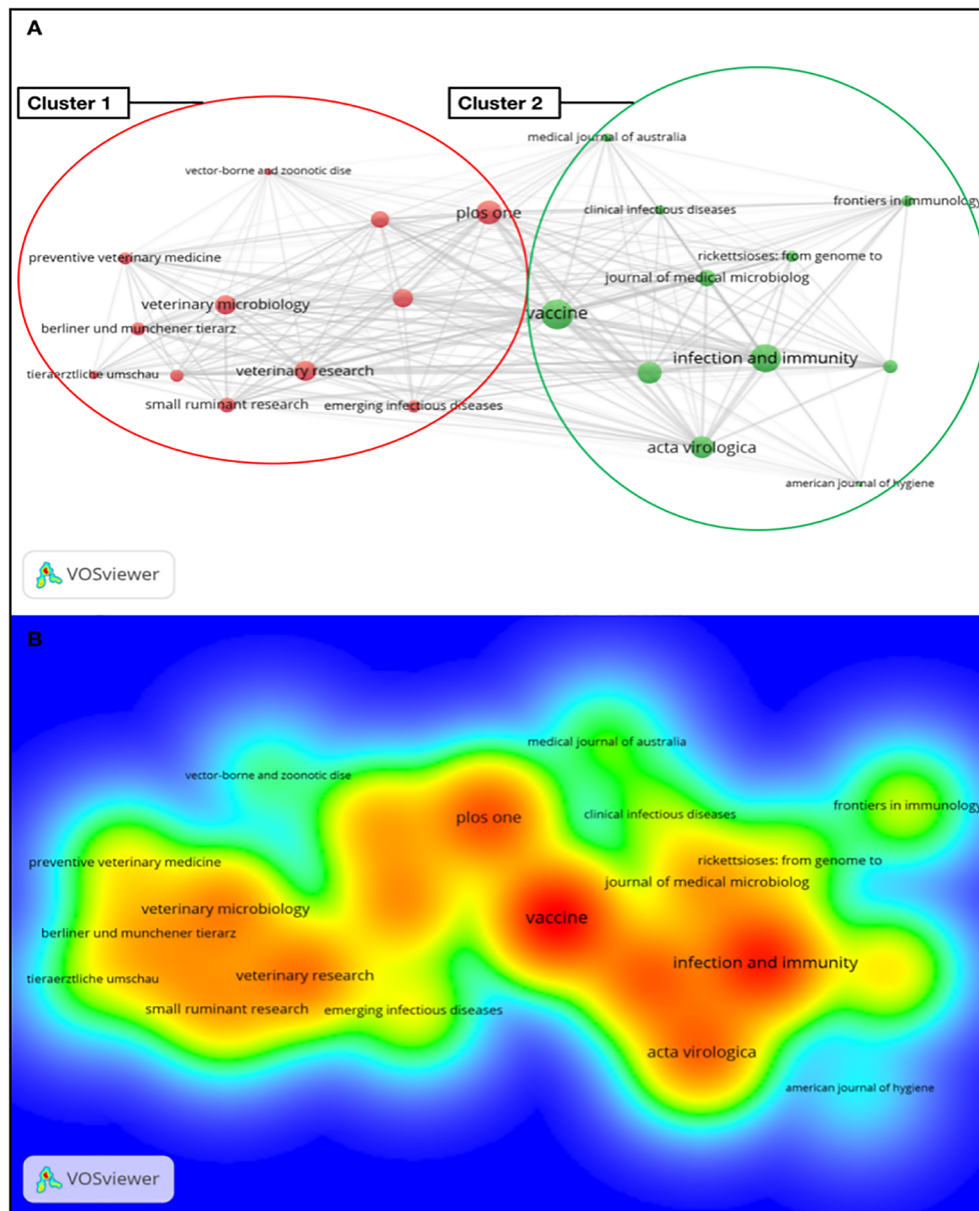
Figure 6. Bibliographic coupling sources visualization mapping: **(A)** Network visualization and **(B)** Density visualization.

Bibliographic coupling sources network and density visualization

Of the total publication sources, only 23 met the criteria and were plotted. Two clusters were formed; cluster 1 consisted of 12 items, while cluster 2 had 11 items. Based on TLS value, Vaccine, Infection and Immunity, and PLOS One were the leading sources of publication (Figure 6).

Discussion

This study has analyzed Q fever vaccine research trends and characteristics from 1941 to 2021. The key topics and research type in Q fever vaccine, main contributors and generators of knowledge in this field, and collaborations among researchers were presented. This study has shown an increase in publications and citations on Q fever vaccine research, especially for the last 20 years. This mirrors the trend of increasing vaccine-related publications throughout the years.[41] However, publications on Q fever vaccinations are lagging other infectious diseases such as Ebola and HIV.[42,43] This might be due to the status of Q fever as a neglected and understudied disease.[44]

The top research areas on Q fever vaccination include immunology, infectious disease, and microbiology. Furthermore, keyword analysis revealed that research areas include epidemiological surveys and pathophysiologic and genetic studies. This signifies the importance of fully understanding the disease entity to generate knowledge for vaccine production.[22] Also included in the top research areas are veterinary sciences, public environmental, occupational health, and agriculture. This relates to the importance of Q fever not only for human health but also for the industry, particularly agriculture and animal husbandry.[45]

The USA is the leading country in terms of the number of publications in Q fever vaccination. Furthermore, 8 out of the top 10 leading institutions in the field are from the USA. This is consistent with the high scientific productivity of the USA across different fields.[46] The USA is currently the country with the highest research expenditure and highest gross domestic product, which might explain its high productivity on research.[47,48] Moreover, we have shown that USA authors had the highest TLS with other countries, signifying its rich collaborations. Cooperation and collaboration have been shown to correlate well with increased research productivity.[49]

Notably, some countries with a high disease burden, including Morocco, Zimbabwe, and Nigeria, are not the countries with the highest research production.[44] This indicates an imbalance can be seen between research production and the burden of disease. Therefore, there is a need to increase research activities among these countries to provide more evidence on Q fever.

Most of the top 10 journals in the Q fever vaccine field are international journals. Furthermore, 6 out of the top 10 journals have an impact factor greater than 3.0. Journal selection is influenced by different factors including journal ranking system, reliability of reviewing, university and national policies, usefulness of reviewers' feedback, and research funding bodies.[50]

Strengths and limitation

This is the first bibliometric study to summarize the global research output and trends in the Q fever vaccine indexed in WoSCC. The key bibliometric indices and visualization mapping were generated. This study used a single database WoSCC which may bias the results. Therefore, further studies are recommended to utilize multiple databases to evaluate the publication frequency and citation analysis.

Conclusion

This study used bibliometric analysis to provide an insight on the Q fever vaccine research, worldwide. In the past two decades, a rapid increase has been observed in Q fever vaccine publications and citations. USA was the leading country, and immunology was the most studied research in this field. The current study will provide standard bibliographic information and keystone parameters in Q fever vaccine research.

Data availability
Underlying data

Figshare: Bibliometric analysis and network visualization mapping of global research in Q fever vaccine.

DOI: https://doi.org/10.6084/m9.figshare.18316595.[23]

This project contains the following underlying data:

Q-fever data.text: (Data of the publications downloaded from the Web of Science that were used in this bibliometric analysis study)

Reporting Guidelines

Figshare: PRISMA-Scoping review checklist for "Bibliometric analysis and network visualization mapping of global research in Q fever vaccine"

DOI: https://doi.org/10.6084/m9.figshare.18316595.[23]

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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Version 1

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The submitted systematic review manuscript aims to investigate historic and modern Q fever vaccine-related publications. The authors conducted analysis of general research trends, global distribution, and other features related to these publications. The authors concluded that there has been a notable increase in Q fever vaccine-related publications in the past twenty years and that the presented study may provide utility as a bibliographic resource for researchers. The manuscript addresses an important and timely topic. The submitted work was easy to read and the data was presented in a concise matter. While the concept of the review is with merit, I have several concerns regarding the data inclusion criteria and the main figures.

Major comments:

The study design and database search were well-described and are suitable for replication. I have several concerns regarding the inclusion criterion for "Q fever vaccine research":

- The authors refer to the research of interest as "Q fever vaccine research" yet the criterion for this moniker does not appear to be well-defined. Given the wide breadth of studies that would be identified by the described search keywords, were publications identified based on type of manuscript (e.g. review, primary study) and level of relevance to C. *burnetii*/ Q fever vaccine research (e.g. ancillary association or study primary focus). I feel that these criteria need to be formally defined for the resultant data to be useful.

- Similarly, it might be prudent to refer to the manuscripts in question as "Q fever vaccine-related publications".

- Historically, C. *burnetii* has been referred to by a number of names, including *Rickettsia burnetii*, R*ickettsia burneti*, and C*oxiella burneti*. I am concerned that works published prior to

formal naming of the bacteria and disease may be excluded on the current basis of the search.

○ Figure 5B appears to be identical to Figure 4B.

○ I was unable to access the Q-fever data.text file. Access to this file is very important given that one of the main conclusions addresses the utility of this data.

Minor Comments:
○ The figure legends are very terse and could potentially be improved with the addition of relevant information. For example, in Figure 3 it is unclear how authorship and study country are defined (e.g. first author, last author, any author affiliation?). This could be outlined in the figure legend for clarity.

○ The authors state that "6 out of the top 10 journals have an impact factor greater than 3.0". How was impact factor determined? Some journals have chosen to refrain from self-reporting. [1] So I assume that impact factor was determined based on a third party source?

○ I suggest replacing words such as "attractive" and "famous" in reference to journals with less subjective alternatives.

References
1. Casadevall A, Bertuzzi S, Buchmeier M, Davis R, et al.: ASM Journals Eliminate Impact Factor Information from Journal Websites. *Antimicrobial Agents and Chemotherapy*. 2016; **60** (9): 5109-5110
Publisher Full Text

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Not applicable

Are the conclusions drawn adequately supported by the results presented in the review?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Coxiella burnetii, Q fever, vaccinology, immunology, bacterial pathogenesis, bacteriology, host-pathogen modeling

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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