

COVID-19 Vaccine Cold Chain Research: A Bibliometric Analysis

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Abstract: Current worldwide COVID-19 pandemics have resulted in global demand for vaccine supply chain management. These vaccines require efficient cold chain logistics, which are critical to the success of mass vaccination campaigns. In this study, a bibliometric review process is utilized to analyze the state of vaccine cold chain research for the years 2020-2021, the period during which the current COVID-19 pandemics began. Publication data for this period were collected from the Dimensions and the Web of Science databases, and the results were compared using bibliographic coupling and co-citation analysis using the VOS technique by Van Eck, et al. (2014) and the Bibliometrix software package provided by Aria, et al. (2017). This research isolates and identifies the most relevant thematic clusters and publications within the vaccine cold chain literature. The results of this study provide direction for future vaccine cold chain research and demonstrate the importance of developing effective vaccine delivery systems. Furthermore, research trends in closely related topics such as vaccine production, storage, and transport are highlighted.

Keywords: Vaccines, Cold Chain, Bibliometric Analysis, COVID-19, Supply Chain Management

1. Introduction

Pandemic response and control of viral diseases requires high vaccination coverages and large quantities of supplies to be quickly made available. The rapid manufacture and distribution of WHO-approved COVID-19 vaccines requires long term storage at low temperatures to prevent microbial contamination and loss of potency over the course of time. This is traditionally achieved using thermos-stabilization approaches that maintain stability at lower temperature, reducing overall costs associated with the logistics of vaccine delivery to ensure the highest level of vaccine coverage to populations.

Accordingly, this literature study may benefit researchers seeking confirmation on the most relevant research questions concerning vaccine cold chain research in the context of COVID-19. The study seeks to systematically answer three questions: (1) What are the most cited current publications, (2) What sources do these publications cite, and (3) under what common topics can these publications and their references be classified? To address these questions, bibliometric coupling and co-citation analysis are used. A brief diagram of these two techniques are shown in Figure 1; two publications are bibliographically coupled if they cite the same source, while two references are co-cited if they are cited by the same publication.

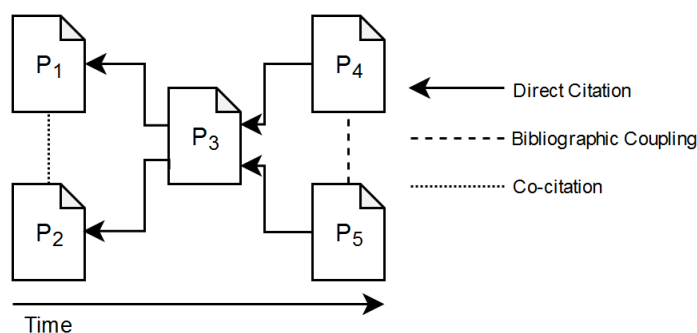


Figure 1. Bibliographic coupling and co-citation analyses

2. Methodology

As of this study, WHO has approved 6 vaccines that have passed Stage III clinical trials; they are: Astrazeneca, Johnson & Johnson, Moderna Therapeutics, Pfizer/BioNTech, Sinopharm, and SinoVac (WHO, 2021). The specific names of these vaccines, as well as the institutions that produced them, were added to the search. Vaccine cold chain search terms were adapted from an extensive literature review by (Matthias, 2007), and COVID-19 search terms were adapted from (Kousha & Thelwall, 2020). Furthermore, the search results were limited to results published in 2020-2021. The structure of this search can be seen in Figure 2.

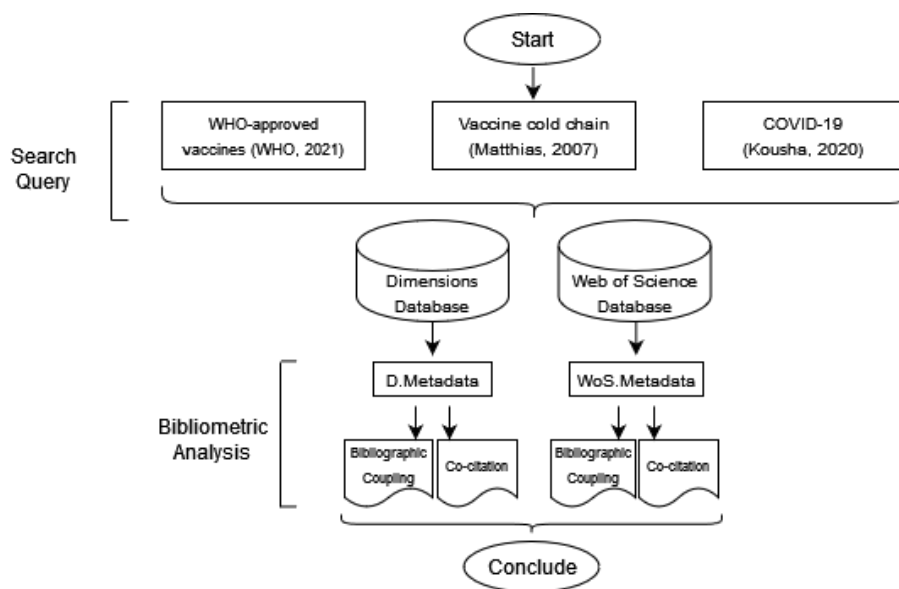


Figure 2. Query and analysis methodology for the bibliometric study

Accordingly, the following search terms in Table 1 were used for the Dimensions and Web of Science Core Collection databases:

Table 1. Adapted search query strings

Database	Query	Publications
Dimensions Analytics	Full data: ("pfizer" OR "biontech" OR "bnt162b2" OR "jnj-78436735" OR "johnson" OR "janssen" OR "ad26.cov2.s" OR "moderna" OR "mrna-1273" OR "astrazeneca" OR "chadox1 ncov-19" OR "azd1222" OR "sinopharm" OR "sinovac" OR "coronavac" OR "picovacc") AND ("supply chain" OR "logistics" OR "distribution" OR "vaccination strategy" OR "vaccination program" OR "allocation") AND ("cold chain" OR "thermostability" OR "refrigeration") AND ("2019-nCoV" OR "COVID-19" OR "SARS-CoV-2" OR "HCoV-2019" OR "hcov" OR "NCOVID-19" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome corona virus 2" OR "coronavirus disease 2019" OR ("coronavirus" OR "corona virus") AND (Wuhan OR China OR novel)))	99
Web of Science	TS=(((("pfizer" OR "biontech" OR "bnt162b2" OR "jnj-78436735" OR "johnson" OR "janssen" OR "ad26.cov2.s" OR "moderna" OR "mrna-1273" OR "astrazeneca" OR "chadox1 ncov-19" OR "azd1222" OR "sinopharm" OR "sinovac" OR "coronavac" OR "picovacc") AND ("supply chain" OR "logistics" OR "distribution" OR "vaccination strategy" OR "vaccination program" OR "allocation" OR "administration" OR "vaccine cold chain" OR "vaccine refrigeration")) AND ("2019-nCoV" OR "COVID-19" OR "SARS-CoV-2" OR "HCoV-2019" OR "hcov" OR "NCOVID-19" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome corona virus 2" OR "coronavirus disease 2019" OR ("coronavirus" OR "corona virus") AND (Wuhan OR China OR novel))))	146

Subsequently, these metadata obtained from these results were analysed with VOSViewer software and by the Bibliometrix R package.

3. Results and Discussion

The literature and database searches were completed on September 5, 2021 and yielded 99 and 146 articles for the Dimensions and Web of Science databases, respectively. The results for each search were first scanned for thematic relevance. Using Bibliometrix, a Thematic Map for the relevance of abstract terms from the Dimensions database was obtained in Figure 3:

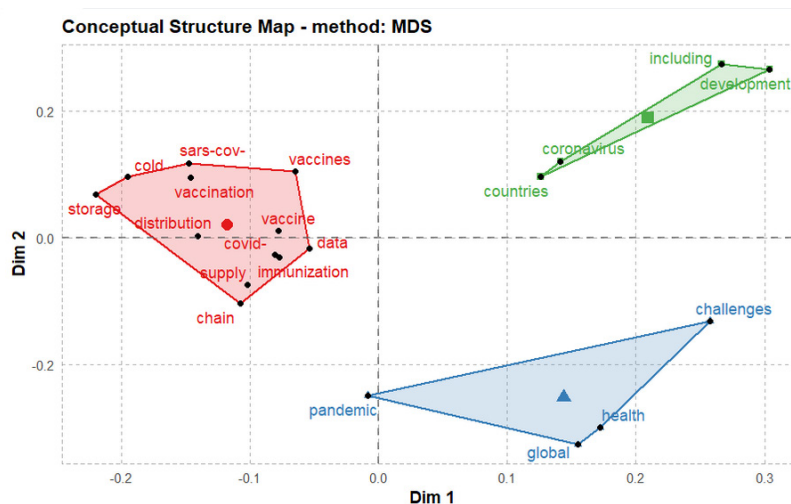


Figure 3. Multidimensional Scaling Analysis of the Dimensions abstracts

Subsequently, this was the result for the Web of Science database search in Figure 4:

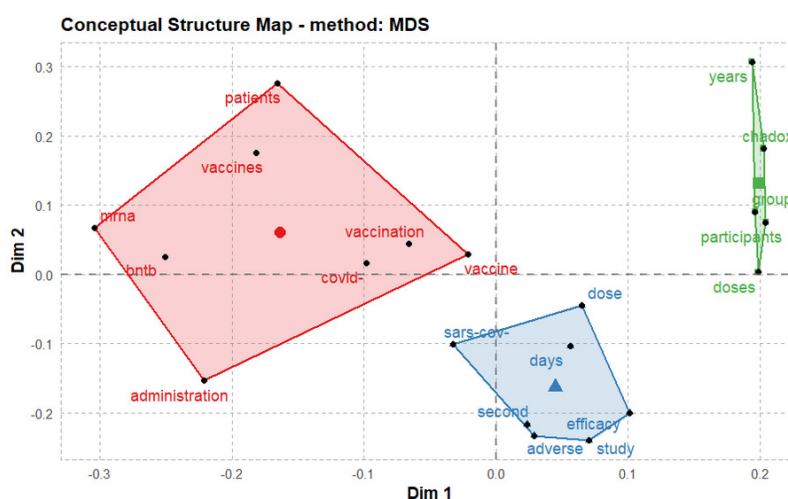


Figure 4. Multidimensional Scaling Analysis of the Web of Science abstracts

It appears that the latter Web of Science search deals mainly with efficacy studies, while the relevance of the Dimensions search seemed more thematically focused on distribution, logistics, and cold chain storage. To confirm this, bibliometric analysis was performed. As shown in Figure 5, VOSViewer graphically represents the relevance of publications on a coordinate plane; the more related two publications are, the closer they are. With a higher link strength, which is influenced by bibliographic coupling and co-citations cores, the larger the node:

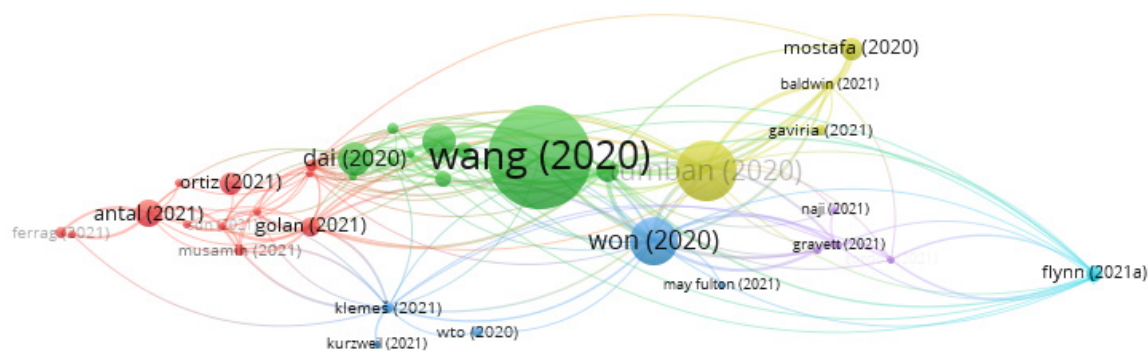


Figure 5. Publication bibliographic coupling network for the Dimensions database search

Table 2. Key Dimensions bibliographically coupled vaccine supply chain publications, n=25/36

Authors	Publication Title	Cluster	Link Strength
Reddy (2021)	COVID-19 mass vaccination campaign for healthcare workers in a low-resource setting: a clinician-driven initiative	1	2
Sun (2021)	A simulation-based analysis for effective distribution of COVID-19 vaccines: a case study in Norway	1	22
Ortiz (2021)	The potential effects of deploying sars-cov-2 vaccines on cold storage capacity and immunization workload in countries of the WHO African region	1	4
Golan (2021)	The vaccine supply chain: a call for resilience analytics to support COVID-19 vaccine production and distribution	1	33
Decouttere (2021)	Advancing sustainable development goals through immunization: a literature review	1	15
Shah (2021)	Blockchain for COVID-19: a comprehensive review	1	9
Musamih (2021)	Blockchain-based solution for distribution and delivery of COVID-19 vaccines	1	11
Ferrag (2021)	Fighting COVID-19 and future pandemics with the internet of things: security and privacy perspectives	1	7
Antal (2021)	Blockchain platform for COVID-19 vaccine supply management	1	20
Uddin (2021)	Energy analysis of a solar driven vaccine refrigerator using environment-friendly refrigerants for off-grid locations	1	13
Aboulotouh (2021)	Next-generation COVID-19 vaccines should take efficiency of distribution into consideration	2	73
Wang (2020)	The COVID-19 vaccine race: challenges and opportunities in vaccine formulation	2	38
James (2021)	Disrupting vaccine logistics	2	6
Dai (2020)	Who is running faster, the virus or the vaccine?	2	24
Dadari (2021)	How the use of vaccines outside the cold chain or in controlled temperature chain contributes to improving immunization coverage in low- and middle-income countries (lmics): a scoping review of the literature	2	10
Qi (2021)	Development of thermostable vaccine adjuvants	2	27
Mwendwa (2021)	COVID-19 and vaccines in Africa: a descriptive and thematic analysis of twitter content	2	5
Hinson (2021)	Critical prerequisites for COVID-19 vaccine acceleration: a developing economy perspective	2	19
Won (2020)	The current status of drug repositioning and vaccine developments for the COVID-19 pandemic	3	53
Klemeš (2021)	COVID-19 pandemics stage II – energy and environmental impacts of vaccination	3	23
Kurzweil (2021)	The ecological footprint of COVID-19 mRNA vaccines: estimating greenhouse gas emissions in Germany	3	2
Wto (2020)	Developing and delivering COVID-19 vaccines around the world	3	2
Gaviria (2021)	A network analysis of COVID-19 mRNA vaccine patents	4	3
Gordon (2021)	COVID-19 vaccines and vaccine administration	5	12
Maxwell (2021)	COVID-19 therapeutics for low- and middle-income countries: a review of re-purposed candidate agents with potential for near-term use and impact	5	16

Bibliographic coupling was first performed on the Dimensions search. A total of 36 linked publications were returned, of which the publications unrelated to the search topic were inspected and discarded. The 25 remaining publications were automatically clustered according to the VOS algorithm into 5 groups shown above in Table 2. Three primary clusters were detected for this search. The first few publications in Cluster 1 (red) deal primarily with the issue of vaccine cold chain logistics in several case countries. Subsequently, other publications in this cluster address creative approaches such as blockchain-based methods and IoT solutions for managing vaccine cold chain, vaccine storage, vaccine tracking, and vaccine administration. Cluster 2 (green) mainly investigates the specific attributes of the COVID-19 vaccines in development and their dependence on cold chain logistics. Perhaps most significantly, tradeoffs between the efficacy of ultra-cold chain vaccines such as Pfizer and Moderna were compared to the less stringent refrigeration temperatures of more conventionally refrigerated vaccines, such as Astrazeneca. This cluster also explores the possibility of “controlled temperature chains” outside the cold chain and vaccines adapted for higher temperatures as potential solutions. Cluster 3 (blue) expands the research direction to a global scale, investigating the sustainability implications of vaccine cold chain logistics both in terms of ecology and trade.

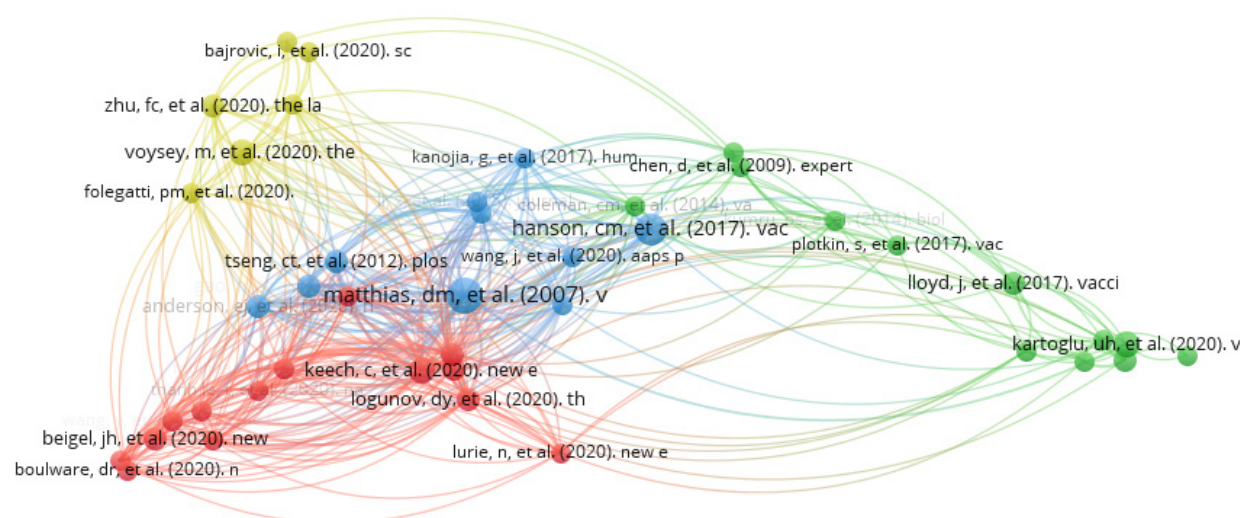


Figure 6. Reference co-citation network for the Dimensions database search, 3 minimum citations

Table 3. Key Dimensions co-citation vaccine supply chain publications, n=14/42

Authors	Publication Title	Cluster	Link Strength
Funk (2020)	A snapshot of the global race for vaccines targeting SARS-CoV-2 and the COVID-19 pandemic	1	38
Lurie (2020)	Developing COVID-19 vaccines at pandemic speed	1	19
Thanh le (2020)	The COVID-19 vaccine development landscape - Nature	1	37
Chen (2009)	Opportunities and challenges of developing thermostable vaccines	2	11
Chen (2014)	A planning model for the WHO-EPI vaccine distribution network in developing countries	2	15
Ivanov (2020)	Viability of intertwined supply networks: extending the supply chain resilience angles towards survivability. A position paper motivated by COVID-19 outbreak	2	16
Kartoglu (2020)	Logistical challenges for potential SARS-CoV-2 vaccine and a call to research institutions, developers and manufacturers	2	12
Kumru (2014)	Vaccine instability in the cold chain: mechanisms, analysis and formulation strategies	2	18
Lee (2017)	Economic impact of thermostable vaccines	2	12
Lin (2020)	Cold chain transportation decision in the vaccine supply chain	2	11
Lloyd (2017)	The origins of the vaccine cold chain and a glimpse of the future	2	14
Plotkin (2017)	The complexity and cost of vaccine manufacturing—an overview	2	14
Hanson (2017)	Is freezing in the vaccine cold chain an ongoing issue? A literature review	3	41
Matthias (2007)	Freezing temperatures in the vaccine cold chain: a systematic literature review	3	62

Co-citation analysis for the Dimensions search was also classified mainly in 3 categories, shown graphically in Figure 6 and tabulated in Table 3. Cluster 1 provides an analysis of current research progress toward COVID-19 vaccine development options. Cluster 2 addresses the historical issues, technical challenges, and innovative technologies associated with vaccine delivery, including topics such as cold-chain requirements and thermostability technologies. Lastly, Cluster 3 is commonly cited as a systematic study of multiple cases of failure points in the vaccine cold chain, including instances where vaccines were accidentally frozen during transport or storage.

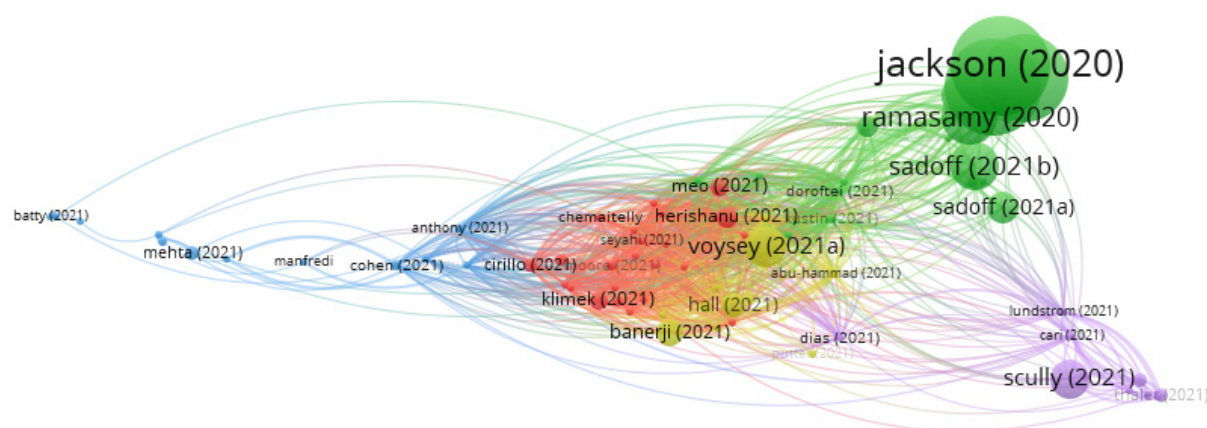


Figure 7. Publication bibliographic coupling network for the Web of Science database search, 1 minimum citation

Table 4. Key Web of Science bibliographically coupled vaccine supply chain publications, n=6/48

Authors	Publication Title	Cluster	Link Strength
Moghadas (2021)	Evaluation of COVID-19 vaccination strategies with a delayed second dose	1	114
Garcia-montero (2021)	An updated review of sars-cov-2 vaccines and the importance of effective vaccination programs in pandemic times	2	135
Younis (2021)	The era of the coronavirus disease 2019 pandemic: a review on dynamics, clinical symptoms and complications, diagnosis, and treatment	2	27
Nagy (2021)	An overview of current COVID-19 vaccine platforms	2	29
Krzysztofowicz (2021)	The use of GIS technology to optimize COVID-19 vaccine distribution: a case study of the city of Warsaw, Poland	3	2
Kumar (2021)	Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases	4	22

As the Web of Science database was constrained to a topic search, rather than a full text search, both the bibliographic coupling and co-citation analyses mainly returned results addressing clinical trials and efficacy. This can be observed in Figures 7 and 8, and the high node density and overlapping clusters supports this observation. However, the search also tended to return results that were more practical than theoretical, and often showed the specific distribution strategies and preparations used by various countries. These publications are listed in Table 4.

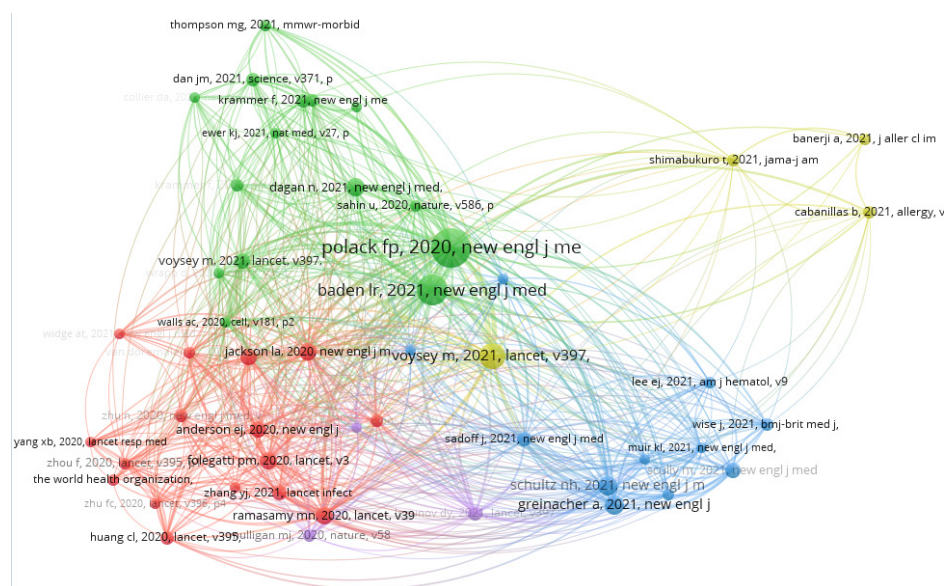


Figure 8. Reference co-citation network for the Web of Science database search, 5 minimum citations

4. Conclusion

This study provided a snapshot of the most relevant current vaccine cold chain publications in the context of the novel coronavirus COVID-19 pandemic response. It was concluded that: (1) the Dimensions search yielded the most bibliographically coupled results, (2) the Web of Science search mainly addressed clinical trials, and (3) the Dimensions search revealed the most thematically focused topics of cold chain innovation, logistics, and sustainability. It may be concluded that the search parameters and thematic classifications of this bibliometric approach may provide an efficient way to answer exploratory research questions on a particular subject area. It was also found that novel improvements are needed to achieve high coverage in the cold chain logistics required for rapid emergency vaccine deployment, such as in the face of pandemics. For example, more robust thermostability technologies and alternative vaccine forms were proposed in the literature, and the use of blockchain for data collection, transfer, management, tracking, and security is being explored to facilitate the creation and distribution of vaccine products. These recommendations should serve researchers seeking confirmation on the relevance of specific research areas to future work related to vaccine distribution. Future research might investigate the validity of bibliometrics as an evaluation method for assessing a particular topic's impact or priority, as well as exploring the utility of querying other databases.

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