Delay Management in Pharmaceutical Cold Chain Logistics: A Systematic Literature Review

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Abstract

The global pharmaceutical cold chain logistics is vital for preserving the efficacy of temperature-sensitive products such as vaccines and biologics. Nevertheless, inefficiencies and delays persist, leading to substantial losses of pharmaceuticals annually and reducing access to life-saving treatments. This study presents a thematic analysis of the literature by employing a systematic literature review methodology to investigate the root causes and develop key thematic dimensions of delays within the pharmaceutical cold chain logistics, with a particular focus on vaccine and blood supply chains. Analyzing 80 peer-reviewed studies published between 2007 and 2024, the review reveals that delays are not limited to last-mile delivery challenges but occur throughout the supply chain, particularly in upstream stages such as production and international logistics. The study underscores the need for innovative, context-specific strategies to address production bottlenecks, cross-border logistics issues, and decision-making inefficiencies and calls for increased empirical research on digital technologies and sustainability practices to enhance resilience and reduce environmental impacts. Future research should prioritize exploring strategies to mitigate upstream delays in production and cross-border logistics, as these areas represent critical bottlenecks. There is also a pressing need for empirical studies on the implementation and effectiveness of digital technologies, including IoT, blockchain, and AI, in enhancing cold chain efficiency and responsiveness. This study thus advances both theoretical understanding and empirical knowledge of pharmaceutical cold chain logistics, paving the way for more resilient and efficient healthcare delivery networks ultimately improving public health outcomes.

Keywords: Pharmaceutical cold chain logistics, Cold chain logistics, City Logistics, Thematic analysis, Delay Management.

1. Introduction

The global cold chain logistics market is driven by the increasing demand for temperature-sensitive goods, particularly within the pharmaceutical and food industries (Aung & Chang, 2023; Lutzmayer, 2024). An astonishing 70% of biopharmaceutical products require temperature-controlled handling, underscoring the vital importance of the market. Despite its critical importance, significant challenges persist, as approximately 35% of pharmaceuticals are wasted each year due to inefficiencies in the cold supply chain. Recently, cold supply chain has become an increasingly important aspect of the urban logistics and health-care industry with the growing demands of biologics and precision medication. The pharmaceutical cold chain logistics is the term given to the temperature-controlled supply chain that encapsulates production, storage and distribution to maintain quality and safety from bench to bedside (Lutzmayer, 2024). It is an uninterrupted process of maintaining, transporting and storing temperature-sensitive medical products, such as blood and vaccines, under optimal conditions from the manufacturing site to the point of care (Lutzmayer, 2024). In 2019, cold chain logistics accounted for 26% of the pharmaceutical logistics market (Turan & Ozturkoglu, 2022). In 2020, the global healthcare cold chain logistics market was valued at 11.3 billion U.S. dollars. It is anticipated to experience significant growth in the coming years, with projections suggesting the market will expand to 17.4 billion U.S. dollars by 2026. As of 2021, cold chain logistics represented approximately 30% of the global pharmaceutical logistics market (Lutzmayer, 2024). This figure is projected to rise, driven by the escalating demand for temperature-sensitive biologics and the widespread distribution of vaccines, including those for COVID-19.

Healthcare sector supply chains are riddled with delays (Green, 2014; Van Zyl-Cillié et al., 2023), with these issues becoming even more critical in the pharmaceutical cold chain logistics supply chains due to strict temperature and timing constraints (Dai et al., 2020; Dai et al., 2021). For example, a major obstacle in the global response to COVID-19 has been the significant production delays of leading vaccine manufacturers such as BioNTech, Moderna, and AstraZeneca (Alam et al., 2021; Karakaya & Balcik, 2024). These delays have affected the timely delivery of vaccines across the world due to a limited number of vaccine production companies which has created bottlenecks supply chain (Haidari et al., 2013). The pharmaceutical cold chain logistics faces a range of delays, from, production, logistical slowdowns and regulatory hold-ups to technology-related issues, all of which are frequently encountered (Assi et al., 2012). Delays occurring at any point within the pharmaceutical cold chain logistics can have a cascading effect, ultimately leading to delays in the final stage of vaccine administration (Haidari et al., 2013; Karakaya & Balcik, 2024). Each stage, from production to transportation and storage, is critical in ensuring timely vaccine delivery (Karakaya & Balcik, 2024; Preiss et al., 2016).

A delay in the pharmaceutical cold chain logistics can have serious negative consequences for public health and economic development (Ashok et al., 2017; Karakaya & Balcik, 2024). When vaccines are exposed to temperatures above or below the recommended range, they may lose their potency and efficacy, resulting in reduced immunization coverage and increased risk of disease outbreaks (De Boeck et al., 2020). Moreover, a delay in the pharmaceutical cold chain logistics can also cause financial losses due to the wastage of expensive vaccines and the need for revaccination (Lin et al., 2020). Therefore, it is crucial to minimize the delay in the pharmaceutical cold chain logistics and ensure timely and consistent delivery of vaccines to the target populations (Lin et al., 2020).

Current research on pharmaceutical cold chain logistics focuses on medical research and public environmental health, with only a limited number of studies examining vaccine supply chains from an operations management and operations research perspective (Fahrni et al., 2022; Green, 2008). Additionally, very few researchers have explored the delays within the channel system, specifically time delays in the pharmaceutical cold chain logistics (Green, 2008). Existing studies often overlook the reality that pharmaceutical cold chain logistics systems and decision-makers do not operate instantaneously but are subjected to considerable delays. In reality, these systems typically experience considerable delays at various stages, and decision-making processes are frequently delayed by information transmission lags (Comes et al., 2018). Incorporating these time delays into pharmaceutical cold chain logistics models would provide a more accurate representation of real-world scenarios.

Drawing from ongoing discussions, it is evident that there is a consensus among researchers and industry professionals on the urgent need to refine the logistics associated with the pharmaceutical cold chain, particularly in terms of more effectively managing delays within the cold chain network (Haidari et al., 2015; Hosseini Bamakan et al., 2021). This imperative is driven by the dual goals of mitigating financial losses from discarded medications and exploring strategies to reduce or even eliminate the need for extensive refrigeration. Addressing these gaps not only promises significant improvements in cost-effectiveness but also enhances the sustainability of supply chain operations. To address these issues, this research aims to identify the common causes of delays in the pharmaceutical cold chain logistics through a thematic analysis of the literature. The rest of this paper is structured as follows. Section 2 describes the methodology. Section 3 shows the descriptive analysis. Section 4 examines the themes in pharmaceutical cold chain logistics. Section 5 presents the main findings and gaps in the literature. Section 6 proposes future research directions, and Section 7 concludes the paper.

2. Methodology

We developed our SLR following the general principles for conducting a structured systematic literature review, as suggested by Durach et al. (2021) and Seuring et al. (2021). Figure 1 illustrates our systematic review process. The following subsections describe the steps of the SLR methodology we conducted to identify articles and extract trends in the literature.

In the *first phase*, we conducted a pilot review of the literature and analysed the main theoretical contributions in the field. We aimed to synthesise the extant literature focusing on delay management in pharmaceutical cold chain logistics using a structured approach. In the *second phase*, we identified papers from the Scopus database. This database was selected because it encompasses a comprehensive range of refereed journals from major publishers. The key selection criterion was peer-reviewed published scientific articles written in English that addressed delay management in pharmaceutical cold chain logistics. To identify relevant papers, we used a combination of keywords (e.g., *Cold Chain Logistics, Vaccine Supply Chain*, *Delay, Postponement, etc.*) using Boolean operators (AND, OR) to query the title, abstract, and keyword fields. In the *third phase*, we retrieved and selected relevant literature using the databases and keywords identified earlier. After conducting a comprehensive search, we removed duplicates and screened the remaining papers by reviewing titles, abstracts, and full texts to ensure they met our research focus. This systematic sampling process is detailed in Figure 2, showing the progression from search results to final paper selection.

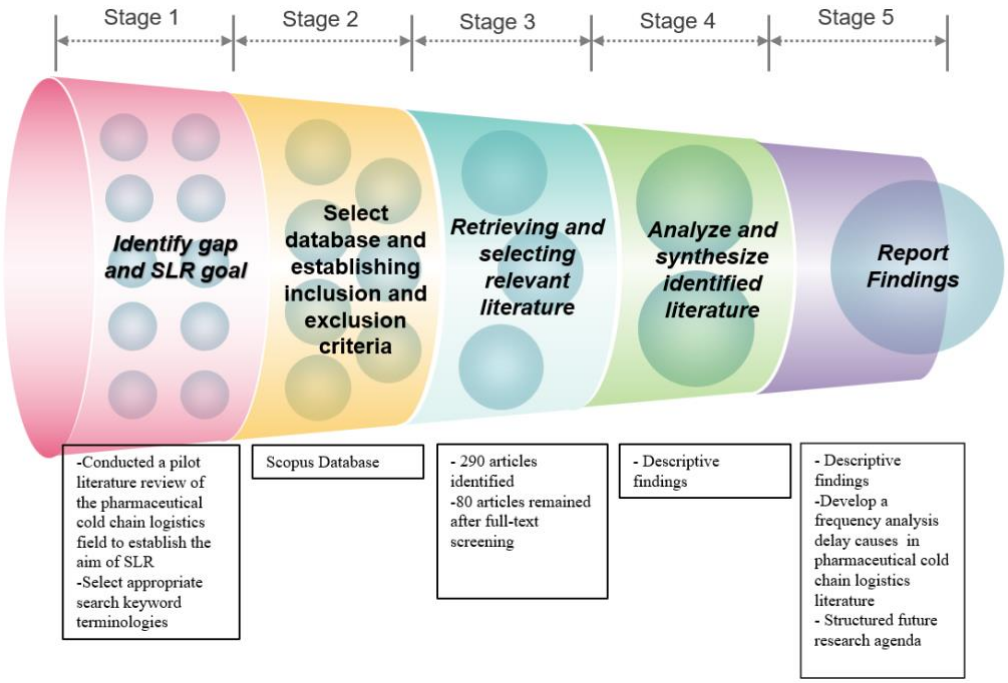

Figure 1. Systematic literature review process

We identified 290 papers using our developed keyword in the Scopus Database. By eliminating duplicate entries, we narrowed the selection down to 289 papers. After screening the titles and abstracts, we further removed 157 papers that were not related to delay management in pharmaceutical cold chain logistics and were left with 132 papers. Finally, we analysed the full text of the remaining articles and removed 43 papers because they did not have a clear focus on delay management and pharmaceutical cold chain logistics. This final sample consisted of 80 studies published between 2007 and 2024. We did not select 2024 as the start date for our selection of papers; this year simply corresponds to the first published study that satisfies our SLR criteria.

In the *fourth phase*, we collated the descriptive findings. This descriptive analysis was intended to describe the literature development trend by frequency analyses of our selected articles according to year, journal publisher, academic institution, and key author. We then categorised the identified papers according to different dimensions. We developed the dimensions and categories of our classification framework through a combination of inductive and deductive reasoning (Seuring & Müller, 2008). The *last stage* involved discussing the overall SLR outcomes and research gaps and developing future research directions.

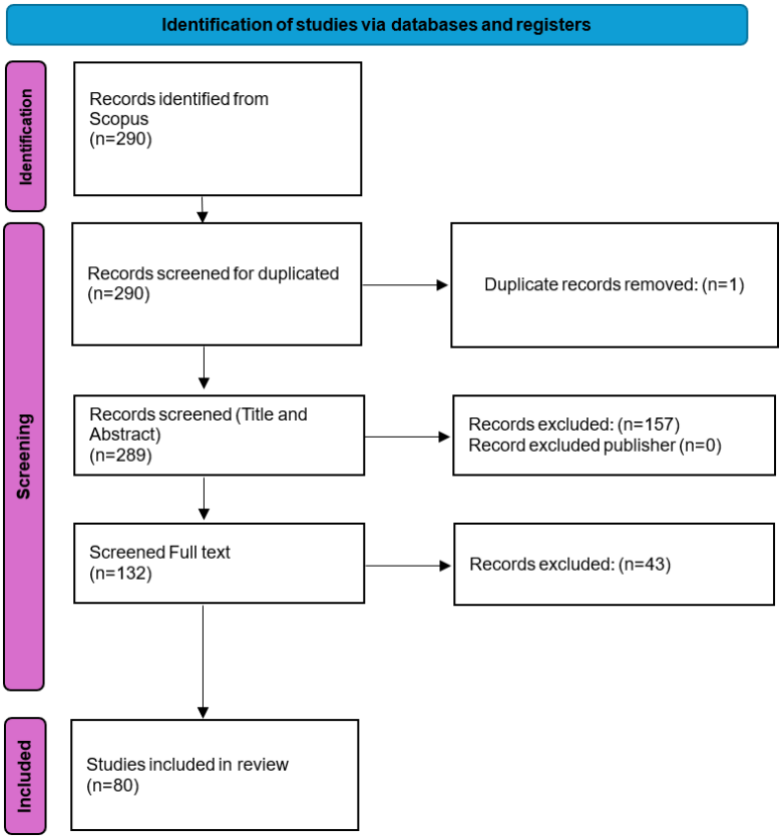

Figure 2. Sampling process

3. Descriptive analysis

3.1. Distribution of reviewed papers over time

The distribution of publications in the pharmaceutical cold supply chain research field over time reveals an increase in interest and contributions from 2007 through 2024 as shown in Figure 3. The development of research in pharmaceutical cold chain logistics can be contextualized alongside the COVID-19 pandemic timeline. From 2007 to 2012, the initial stage was characterized by limited activity and sporadic contributions, with only 1-3 publications per year and cumulative growth below 10%, indicating a nascent stage of interest in the field. The steady development stage spanned from 2013 to 2019, during which research activity gradually increased, with consistent yet modest contributions that laid the groundwork for further exploration. By 2020, cumulative growth had reached 22%, just as the COVID-19 pandemic emerged, highlighting the early recognition of logistics and supply chain issues in pharmaceutical cold chain logistics.

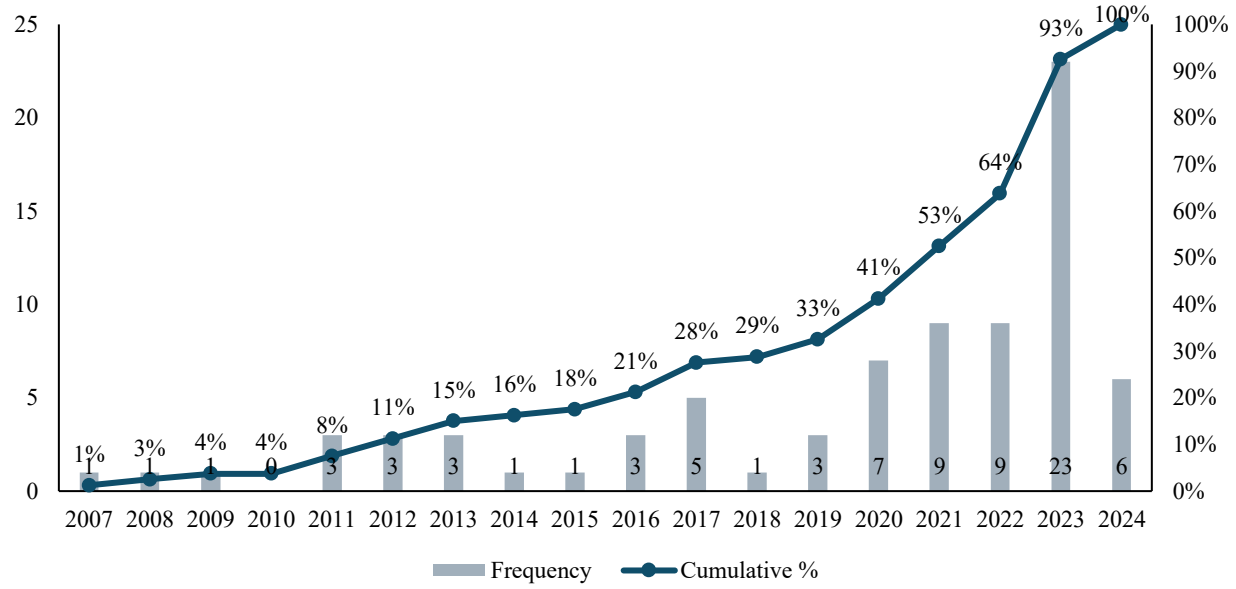

Figure 3. Distribution of reviewed papers over time

The growth stage in 2021 and 2022 reflected a response to the global challenges posed by the pandemic, with more frequent contributions as researchers and institutions sought to address urgent pharmaceutical cold chain logistics needs. This surge in activity highlighted increased recognition of the field's critical role in vaccine distribution and cold chain logistics. The surge stage occurred in 2023, with 23 publications representing 93% of cumulative research activity, underscoring an intense focus likely driven by lessons learned from pandemic-related disruptions and a push to strengthen cold chain systems.

3.2. Distribution of papers by journal and country

Table 1 presents the distribution of journals that contributed multiple articles on the pharmaceutical cold chain logistics. Of the 80 journals included in the review, 27 journals were found to have published more than 2 articles on the topic. The distribution of papers per journal illustrates the dissemination of research related to pharmaceutical cold chain logistics across various scholarly outlets. Among the journals, " " had the highest number of articles, totaling 14 publications, reflecting significant interest and contributions in this area. Following closely, " " published 7 papers, indicating a focus on immunization logistics and cold chain dynamics. Other journals, such as " " and " " each had 3 publications, suggesting diverse but less concentrated attention across different fields. This distribution demonstrates a multidisciplinary interest in pharmaceutical cold chain logistics issues, spanning areas such as public health, operational research, sustainability, and supply chain management. The concentration of articles in these journals reflects the growing scholarly interest in the pharmaceutical cold chain logistics within operations research and related fields.

Table 1. Number of papers per journal (included if n>2)

Journal	Number of papers
Vaccine	14
Annals of Operations Research	7
Journal of Humanitarian Logistics and Supply Chain Management	3
Transportation Research Part E: Logistics and Transportation Review	3

Figure 4 illustrates the geographical distribution of studies included in the systematic review on the pharmaceutical cold chain logistics. The majority of the studies are concentrated in the United States, with 27 publications, indicating a strong focus on cold chain logistics in this region. Following the U.S., Iran emerges as another significant contributor with 17 studies. This distribution highlights that while pharmaceutical cold chain logistics is a global concern, research efforts are largely concentrated in specific regions, suggesting the potential for expanding research efforts in other areas to address regional challenges.

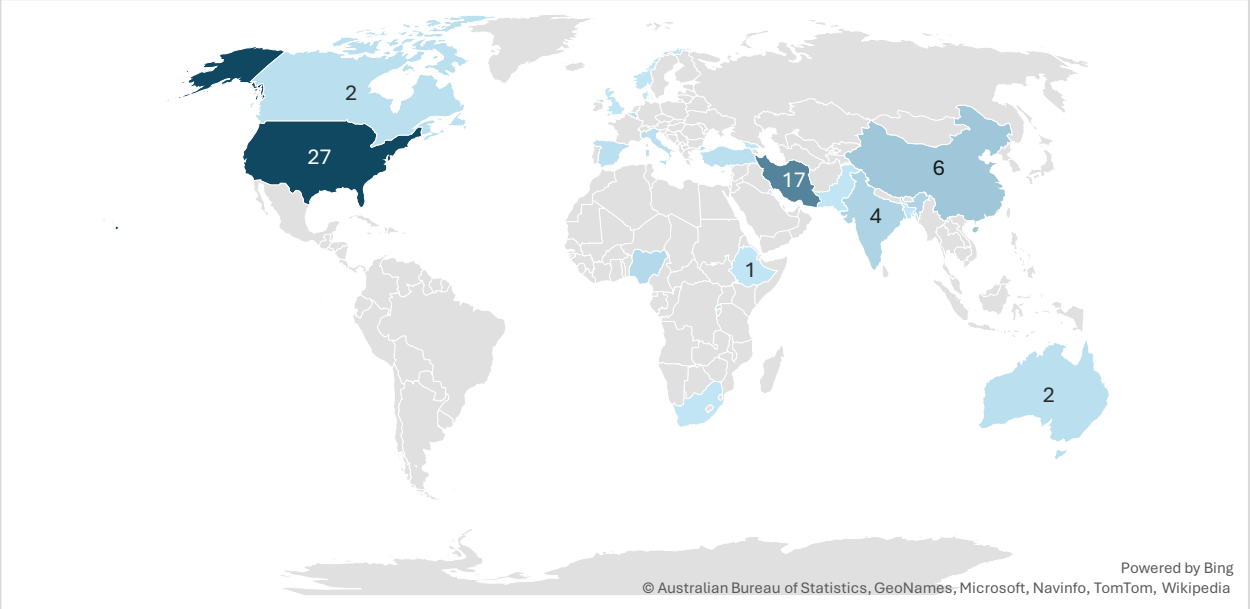

Figure 4. Number of papers published per country

Table 2 highlights the top contributing authors in the field of pharmaceutical cold chain logistics research, focusing on those with more than one published article. The leading contributors include Hosseini-Motlagh, S. M., Lee, B. Y., and Samani, M. R. G., each with four publications. The contributions of the top authors reflect two prominent research trends that have evolved in the pharmaceutical cold supply chain literature over recent years. Hosseini-Motlagh, S. M. and Samani, M. R. G. have focused extensively on the design and optimization of blood and plasma supply chains, emphasizing robustness, flexibility, and risk management to mitigate disruptions—particularly during health emergencies such as the COVID-19 pandemic. Their work spans themes such as resilient network design, capacity-sharing mechanisms, and strategies for maintaining supply continuity under uncertainty. In parallel, B. Y. Lee and L. A. Haidari have concentrated on vaccine supply chains, with research evolving from traditional cold chain logistics toward innovative solutions, including the use of thermostable vaccines and redesigning distribution systems to improve access in low- and

middle-income countries. Over time, these two streams of research demonstrate a clear trend toward building resilience and adaptability in pharmaceutical cold supply chains, integrating technological and strategic innovations to address both ongoing challenges and acute disruptions in global health delivery systems.

Table 2. Top contributing authors (included if n > 1)

Author	Country	Affiliation	Number of published articles
Hosseini-Motlagh, S. M.	Iran	School of Industrial Engineering, Iran University of Science and Technology, University Ave	4
Lee, B. Y.	USA	Public Health Computational and Operations Research (PHICOR), University of Pittsburgh	4
Samani, M. R. G.	Iran	School of Industrial Engineering, Iran University of Science and Technology, University Ave	4
Dai, D.	China	School of Management Science and Engineering, Anhui University of Finance and Economics,	2
Haidari, L. A.	USA	Public Health Computational and Operational Research (PHICOR) Group, School of Medicine and Graduate School of Public Health, University of Pittsburgh	2

3.3. Distribution of papers per category for each structural dimension

Table 3 presents the distribution of papers across key structural dimensions in the pharmaceutical cold chain logistics literature. In terms of supply chain focus, the majority of studies (70%) concentrate on the vaccine supply chain, reflecting its critical role in global health, particularly during mass immunization campaigns like those for COVID-19. The blood supply chain accounts for 24% of the papers, emphasizing concerns with ensuring timely and safe delivery of blood products, while other pharmaceutical cold chains represent only 6%, suggesting an underexplored area in the literature. The predominance of vaccine supply chain studies within the reviewed literature is not merely a reflection of scholarly interest but signals the global health priority vaccines have commanded—particularly under the intense scrutiny and logistical demands posed by the COVID-19 pandemic. This focus highlights how vaccines have become emblematic of the cold chain challenge, offering clear case studies for issues like last-mile delivery, cold chain equipment, and maintaining product integrity in varied settings.

Table 3. Number of papers per structural dimension

Dimension	**Categories**	**Number of papers**	**Percentage**
Supply chain focus	Blood supply chain	19	24 %
	Vaccine supply chain	56	70 %
	Pharmaceuticals	5	6 %
Geographical focus	Developed countries	18	23 %
	Developing countries	49	61 %
	Global	13	16 %
Theories	Game theory	7	9 %
	Contingency	18	23 %
	Stakeholder theory	9	11 %
	Systems Theory	69	86 %

The geographical emphasis on developing countries (61%) indicates a prioritization of regions where cold chain vulnerabilities are most acute. The relative paucity of studies focusing on developed countries (23%) and global frameworks (16%) suggests that the field has yet to fully explore systemic cold chain challenges that transcend regional disparities. Theoretical engagement within the field appears notably narrow. The overwhelming reliance on Systems Theory (86%) reflects a strong inclination toward holistic and structural analyses of cold chain networks—valuable for mapping complexity but often insufficient for explaining behavioral, strategic, or adaptive dimensions. The limited application of Stakeholder Theory, Game Theory, and Contingency Theory signals a missed opportunity to explore power dynamics, negotiation processes, and strategic decision-making between actors across the cold chain ecosystem.

3.4. Scientometric analysis: Keyword Co-occurrence

This section presents a co-occurrence network analysis aimed at identifying the conceptual structure and evolving research trends within the pharmaceutical cold supply chain literature. This analysis offers a complementary perspective by examining the relationships between frequently used keywords across the selected studies. Using VOSviewer software (Van Eck & Waltman, 2013), we extracted 895 keywords from 80 peer-reviewed articles and visualized their co-occurrence patterns to detect clusters of related research topics. We present two interrelated visualizations that serve distinct but complementary purposes. The co-occurrence network (Figure 5) provides a structural mapping of the conceptual contributions in the field, while the overlay visualization (Figure 6) reveals the temporal dynamics of emerging research themes. The rationale for this approach lies in its ability to capture both the dominant themes in literature and the shifts in scholarly focus over time. Together, the figures support a more informed and context-sensitive interpretation of the field's development and evolving research priorities.

Figure 5 presents a visualization of the co-occurrence network of the most frequently used keywords in the articles included in our systematic review. It highlights the interconnections among keywords related to medical supply chain delays. This analysis extracted a total of 895 keywords from 80 research papers, which were classified into three distinct clusters, each represented by a different color. These clusters reflect the interrelated research areas within the field of medical supply chain delays and are categorized as follows: 1. Cluster A (Blue) - Keywords related to "vaccines". 2. Cluster B (Red) - Keywords associated with "supply chain management" 3. Cluster C (Green) - Keywords pertaining to "decision-making", and "information systems". Among these, "Vaccines" emerges as the central keyword, serving as the focal point that connects various research themes within the study of medical supply chain delays. Below, we provide a brief summary of each cluster to further illustrate the thematic distinctions and their relevance to the field.

a) Cluster A: Blue Cluster

Cluster A primarily focuses on vaccine-related topics, with key terms such as "*vaccine supply chain*", "*human*", "*influenza vaccine*", and "*immunization*". The high density of this cluster (represented in blue) indicates a significant research emphasis on vaccine supply chain and immunization, suggesting a substantial body of literature dedicated to the study of vaccine supply chains.

b) Cluster B: Red Cluster

Cluster B centers on blood supply chain management. Key terms in this cluster include "*blood supply chain*", "*blood*", "*supply chain management*", and "*disasters*". This cluster highlights the critical importance of supply chain management in the distribution of medical resources, particularly blood, and underscores the potential disruptions caused by disasters that can significantly impact the efficiency and resilience of blood supply chains

c) Cluster C: Green Cluster

The green cluster emphasizes key terms related to decision-making, which is interconnected with both the vaccine supply chain and the blood supply chain. Cluster C includes keywords such as "*information management*", "*global supply chain*", and the "ambidexterity", reflecting research focused on decision-making in data management and the application of technology and innovation in the supply chain systems for blood and vaccines.

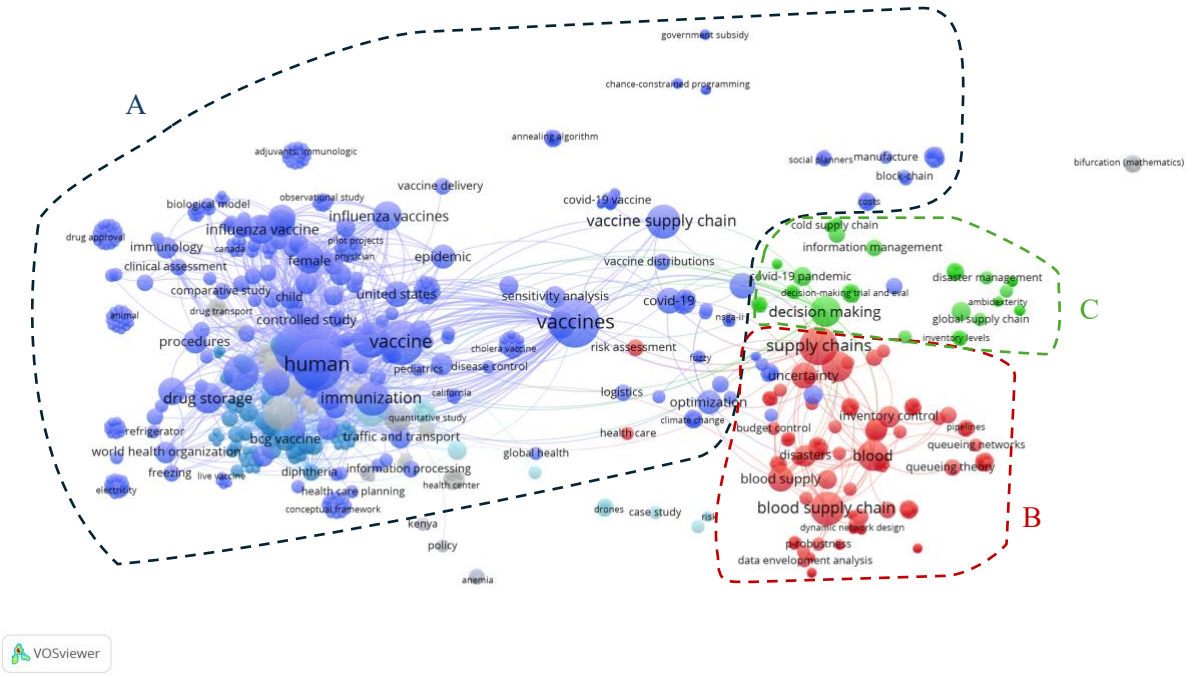

Figure 5. Co-occurrence network of keywords of the pharmaceutical cold supply chain

Figure 6 provides an overlay visualization of research trends based on keywords utilized from 2016 to 2024. A color gradient from purple to yellow is employed to indicate the chronological progression of research topics from past to present. The visualization reveals two distinct clusters of interconnected keywords. Notably, the keyword "*vaccines*" (2018–2021) occupies a central position, acting as a bridge between these two primary clusters.

The cluster A (blue, 2016–2018) comprises keywords related to health and vaccination, such as "*human*" "*vaccination*" "*preventive health service*" and "*controlled study*". This cluster reflects research primarily focused on disease prevention and the impact of vaccines on human health. In contrast, the cluster B (green-yellow, 2020–2024) includes keywords

associated with supply chain management, such as "*blood*", "*pharmaceutical supply chains*" and "*Covid-19*". This indicates a significant rise in studies on blood supply chain management and pharmaceutical logistics, particularly following the outbreak of COVID-19. The pandemic has underscored the importance of efficient global distribution of drugs and vaccines, drawing increased research attention to supply chain challenges.

The overlay visualization highlights the evolution of research priorities, shifting from an initial focus on vaccine effects on human health to a growing emphasis on blood and pharmaceutical supply chain management in recent years. Notably, since the onset of COVID-19 in 2020, the global healthcare system has faced unprecedented challenges in drug and vaccine distribution. Consequently, contemporary research has expanded beyond purely medical aspects to encompass resource management and supply chain logistics, aiming to enhance the efficiency of pharmaceutical and vaccine distribution worldwide.

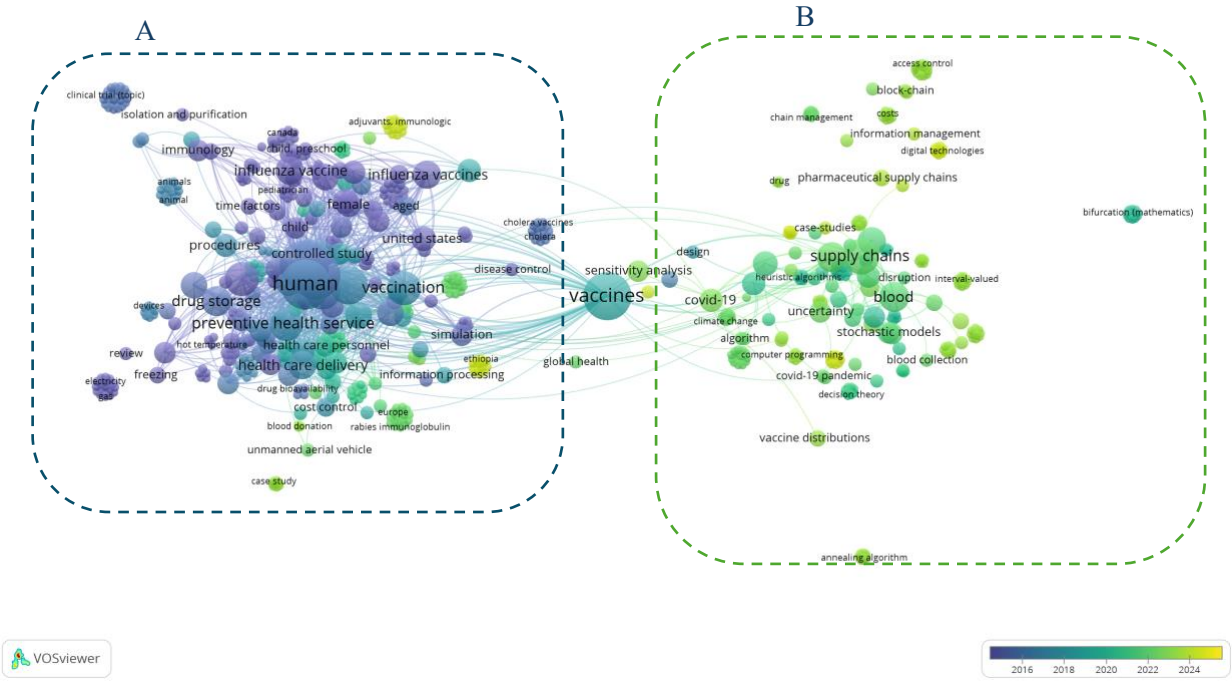

Figure 6. Overlay visualization of keyword trends

3.5. Frequency analysis of causes of delay observed in the literature

Figure 7 demonstrates the frequency analysis of main factors causing delay in pharmaceutical cold chain logistics. *Logistics and Supply Chain* issues emerged as the most frequent cause of delays, with a frequency of 68, underscoring the critical role of transportation and distribution challenges in vaccine supply chains. Closely following, *External Disruption* was also notable at 45 occurrences, capturing the impact of unforeseen events like pandemics or natural disasters. *Political, Social, and Geographic* factors contributed to 24 delays, indicating the influence of regulatory and regional challenges. At the same time as *Financial and Human Resource Constraints* and *Communication and Information Issues* were less frequent at 9 and 7, respectively. Lastly, "Infrastructure and Technological Constraints" had the lowest frequency at 6, suggesting that while technology poses challenges, it is less dominant compared to logistical and production issues in this context. This analysis emphasizes the need

for targeted strategies to address logistics, production, and external disruptions to enhance vaccine distribution efficiency.

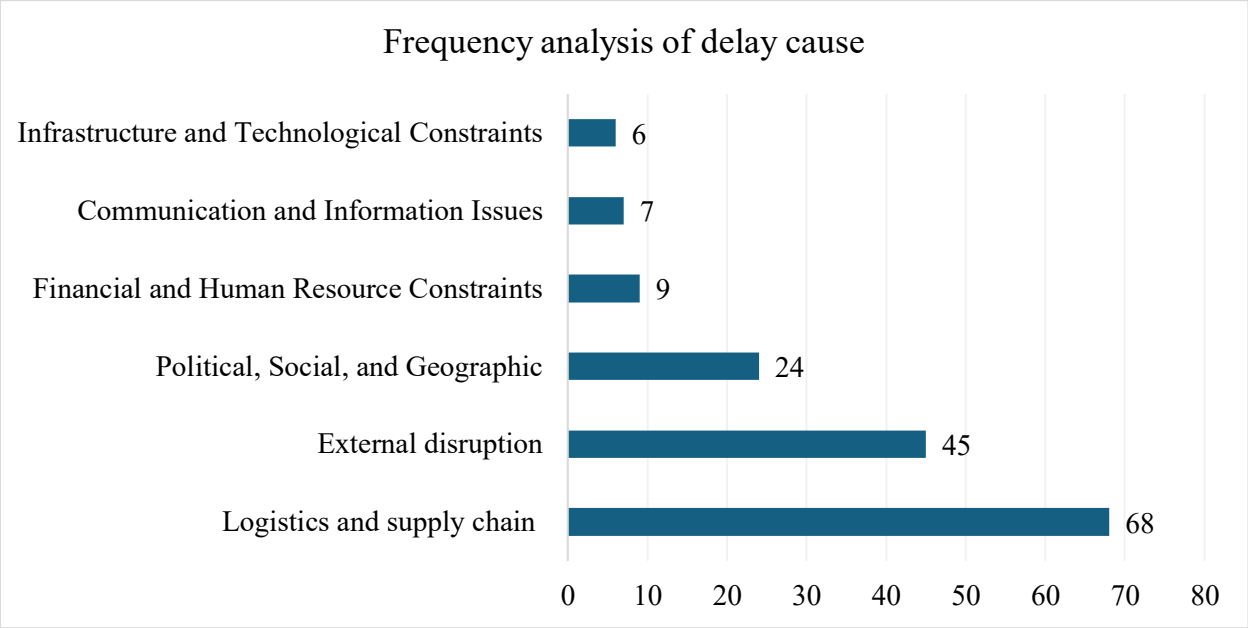

Figure 7. Frequency analysis of delay causes in pharmaceutical cold chain logistics

4. Key findings and future research direction

Despite an increasing attention on pharmaceutical cold chain logistics, significant gaps remain in addressing the complexities of delay management, supply chain disruptions, and operational inefficiencies. This study has identified multiple avenues for future research that can contribute to theoretical advancement and practical improvements in pharmaceutical cold chain logistics management.

First, our review finds that while research on cold chain logistics has expanded significantly in recent years, much of the focus remains on last-mile delivery and infrastructure challenges, particularly in developing regions (Cano-Marin et al., 2023; Correia et al., 2021). However, our findings reveal that delays occur across multiple stages of the supply chain, with a pronounced concentration in upstream operations, such as production and international shipping. Despite this, few studies have systematically examined these upstream delays or developed mitigation strategies to address bottlenecks in manufacturing and cross-border logistics. Future research should explore strategies for optimizing upstream processes and improving the responsiveness of supply networks.

Second, while digitalization and emerging technologies such as IoT, blockchain, and AI-driven predictive analytics are frequently cited as potential solutions for improving cold chain efficiency, empirical studies on their practical implementation remain scarce (Balachandar & Chinnaiyan, 2020; Goodarzian et al., 2023; Yadav et al., 2023). Existing literature primarily discusses these technologies at a conceptual level, with limited real-world case studies assessing their effectiveness in reducing pharmaceutical cold chain delays (Prosser et al., 2021). Future research should investigate the actual impact of digital interventions in cold chain management, examining how real-time tracking, automated temperature monitoring, and

machine learning-based forecasting can enhance supply chain responsiveness and reduce losses due to temperature excursions.

Third, sustainability remains an underexplored dimension in pharmaceutical cold chains (Rekabi et al., 2023; Turan & Ozturkoglu, 2022). While energy-intensive refrigeration and transportation processes contribute significantly to carbon emissions, only a small fraction of studies have examined low-carbon alternatives or the role of green logistics in cold chain management (Robertson et al., 2017). Given the increasing emphasis on sustainability in global supply chains, there is a pressing need for research on eco-friendly refrigeration technologies, renewable energy integration in cold storage, and the development of policies to encourage sustainable pharmaceutical logistics. Additionally, research should assess how sustainability initiatives can be balanced with the stringent regulatory and safety requirements of pharmaceutical cold chains.

Fourth, decision-making inefficiencies within cold chain logistics are often overlooked in the literature (Shahparvari et al., 2022). While many studies focus on physical and technological barriers, our review highlights the role of administrative and organizational delays, such as slow regulatory approvals, inefficient procurement processes, and fragmented coordination among supply chain stakeholders (Zhu et al., 2023). Future research should investigate how decision-making frameworks influence cold chain efficiency and explore strategies for streamlining inter-organizational coordination. This includes examining the role of centralized versus decentralized governance models in improving cold chain agility and responsiveness.

Fifth, despite the significant challenges faced by pharmaceutical cold chains in low- and middle-income countries (LMICs), research remains heavily concentrated on high-income settings (De Boeck et al., 2022). Our review indicates that infrastructure deficiencies, unreliable power supply, and workforce constraints are major contributors to delays in LMICs, yet limited studies propose practical solutions tailored to these contexts (De Boeck et al., 2022). Future research should adopt a region-specific approach to studying pharmaceutical cold chains in LMICs, focusing on innovative, cost-effective solutions such as mobile cold storage units, decentralized vaccine distribution hubs, and community-driven cold chain management models.

Sixth, predictive analytics offers a promising avenue for delay prevention in pharmaceutical cold chains, yet its application remains largely theoretical (Nguyen et al., 2022). While some studies have explored simulation-based models for supply chain optimization, there is limited empirical work on the use of AI-driven predictive analytics in real-world settings (Nguyen et al., 2022). Future research should explore how big data and machine learning can be leveraged to anticipate potential disruptions, optimize routing decisions, and enhance inventory management, particularly in emergency response situations where timely vaccine and medication delivery is critical.

5. Conclusion

This study presents a systematic literature review of delay management in the pharmaceutical cold supply chain with a focus on vaccine and blood supply chains. We analyze 80 peer-reviewed studies published between 2007 and 2024. The review develops a frequency analysis of the most common causes of delays in the pharmaceutical cold supply chain particularly following the global disruption caused by the COVID-19 pandemic. The findings demonstrate that delays are not limited to last-mile delivery or infrastructure deficiencies, as often emphasized in earlier literature, but rather span the entire supply chain from upstream to downstream logistics and supply chain operations. Notably, upstream stages such as production

bottlenecks, international shipping, and cross-border coordination emerged as critical yet underexplored sources of inefficiency. The study also reveals a thematic concentration on vaccine supply chains and a geographical focus on developing countries, reflecting global health priorities. Although systems theory remains the dominant lens in current research, the underutilization of broader theoretical frameworks highlights a gap that future studies could explore to deepen conceptual understanding.

In addition to mapping the literature, this review identifies several critical areas for future exploration. These include developing targeted strategies for upstream delay mitigation, empirically assessing the impact of digital technologies on cold chain performance and integrating sustainability into cold chain operations. The review also highlights the need for improved governance models and decision-making frameworks particularly in multi-stakeholder environments, and emphasizes the importance of context-specific, low-cost solutions for resource-constrained settings. This study contributes to both theoretical advancement and practical understanding by synthesizing diverse strands of literature and proposing agendas for future research.

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References

Alam, S. T., Ahmed, S., Ali, S. M., Sarker, S., Kabir, G., & ul-Islam, A. (2021). Challenges to COVID-19 vaccine supply chain: Implications for sustainable development goals. *International Journal of Production Economics*, *239*, 108193. https://doi.org/https://doi.org/10.1016/j.ijpe.2021.108193

Ashok, A., Brison, M., & LeTallec, Y. (2017). Improving cold chain systems: Challenges and solutions. *Vaccine*, *35*(17), 2217-2223. https://doi.org/https://doi.org/10.1016/j.vaccine.2016.08.045

Assi, T.-M., Rookkapan, K., Rajgopal, J., Sornsrivichai, V., Brown, S. T., Welling, J. S., Norman, B. A., Connor, D. L., Chen, S.-I., Slayton, R. B., Laosiritaworn, Y., Wateska, A. R., Wisniewski, S. R., & Lee, B. Y. (2012). How influenza vaccination policy may affect vaccine logistics. *Vaccine*, *30*(30), 4517-4523. https://doi.org/https://doi.org/10.1016/j.vaccine.2012.04.041

Aung, M. M., & Chang, Y. S. (2023). *Cold Chain Management*. Springer Cham. https://doi.org/https://doi.org/10.1007/978-3-031-09567-2

Balachandar, S., & Chinnaiyan, R. (2020). Chapter 5 - Reliable pharma cold chain monitoring and analytics through Internet of Things Edge. In V. E. Balas, V. K. Solanki, & R. Kumar (Eds.), *Emergence of Pharmaceutical Industry Growth with Industrial IoT Approach* (pp. 133-161). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-12-819593-2.00005-4

Cano-Marin, E., Ribeiro-Soriano, D., Mardani, A., & Blanco Gonzalez-Tejero, C. (2023). Exploring the challenges of the COVID-19 vaccine supply chain using social media analytics: A global perspective [Article]. *Sustainable Technology and Entrepreneurship*, *2*(3), Article 100047. https://doi.org/10.1016/j.stae.2023.100047

Comes, T., Bergtora Sandvik, K., & Van de Walle, B. (2018). Cold chains, interrupted: The use of technology and information for decisions that keep humanitarian vaccines cool [Article]. *Journal of Humanitarian Logistics and Supply Chain Management*, *8*(1), 49-69. https://doi.org/10.1108/JHLSCM-03-2017-0006

Correia, D., Teixeira, L., & Marques, J. L. (2021). Last-mile-as-a-service (LMaaS): An innovative concept for the disruption of the supply chain [Article]. *Sustainable Cities and Society*, *75*, Article 103310. https://doi.org/10.1016/j.scs.2021.103310

Dai, D., Wu, X., & Si, F. (2020). Complexity Analysis and Control in Time-Delay Vaccine Supply Chain Considering Cold Chain Transportation. *Mathematical Problems in Engineering*, *2020*, 4392708. https://doi.org/10.1155/2020/4392708

Dai, D., Wu, X., & Si, F. (2021). Complexity analysis of cold chain transportation in a vaccine supply chain considering activity inspection and time-delay [Article]. *Advances in Difference Equations*, *2021*(1), Article 39. https://doi.org/10.1186/s13662-020-03173-z

De Boeck, K., Decouttere, C., Jónasson, J. O., & Vandaele, N. (2022). Vaccine supply chains in resource-limited settings: Mitigating the impact of rainy season disruptions [Article]. *European Journal of Operational Research*, *301*(1), 300-317. https://doi.org/10.1016/j.ejor.2021.10.040

De Boeck, K., Decouttere, C., & Vandaele, N. (2020). Vaccine distribution chains in low- and middle-income countries: A literature review. *Omega*, *97*, 102097. https://doi.org/https://doi.org/10.1016/j.omega.2019.08.004

Durach, C. F., Kembro, J. H., & Wieland, A. (2021). How to advance theory through literature reviews in logistics and supply chain management. *International Journal of Physical Distribution & Logistics Management*, *51*(10), 1090-1107. https://doi.org/10.1108/IJPDLM-11-2020-0381

Fahrni, M. L., Ismail, I. A.-N., Refi, D. M., Almeman, A., Yaakob, N. C., Saman, K. M., Mansor, N. F., Noordin, N., & Babar, Z.-U.-D. (2022). Management of COVID-19 vaccines cold chain logistics: a scoping review. *Journal of Pharmaceutical Policy and Practice*, *15*(1), 16. https://doi.org/10.1186/s40545-022-00411-5

Goodarzian, F., Navaei, A., Ehsani, B., Ghasemi, P., & Muñuzuri, J. (2023). Designing an integrated responsive-green-cold vaccine supply chain network using Internet-of-Things: artificial intelligence-based solutions. *Annals of Operations Research*, *328*(1), 531-575. https://doi.org/10.1007/s10479-022-04713-4

Green, L. V. (2008). Using Operations Research to Reduce Delays for Healthcare. In *State-of-the-Art Decision-Making Tools in the Information-Intensive Age* (pp. 1-16). https://doi.org/10.1287/educ.1080.0049

Green, L. V. (2014). Using Operations Research to Reduce Delays for Healthcare. In *State-of-the-Art Decision-Making Tools in the Information-Intensive Age* (pp. 1-16). https://doi.org/10.1287/educ.1080.0049

Haidari, L. A., Connor, D. L., Wateska, A. R., Brown, S. T., Mueller, L. E., Norman, B. A., Schmitz, M. M., Paul, P., Rajgopal, J., Welling, J. S., Leonard, J., Claypool, E. G., Weng, Y. T., Chen, S. I., & Lee, B. Y. (2013). Only adding stationary storage to vaccine supply chains may create and worsen transport bottlenecks [Article]. *Journal of Public Health Management and Practice*, *19*(5 SUPPL. 2), S65-S67. https://doi.org/10.1097/PHH.0b013e31828a83fe

Haidari, L. A., Wahl, B., Brown, S. T., Privor-Dumm, L., Wallman-Stokes, C., Gorham, K., Connor, D. L., Wateska, A. R., Schreiber, B., Dicko, H., Jaillard, P., Avella, M., & Lee, B. Y. (2015). One size does not fit all: The impact of primary vaccine container size on vaccine distribution and delivery [Article]. *Vaccine*, *33*(28), 3242-3247. https://doi.org/10.1016/j.vaccine.2015.04.018

Hosseini Bamakan, S. M., Ghasemzadeh Moghaddam, S., & Dehghan Manshadi, S. (2021). Blockchain-enabled pharmaceutical cold chain: Applications, key challenges, and future trends. *Journal of Cleaner Production*, *302*, 127021. https://doi.org/https://doi.org/10.1016/j.jclepro.2021.127021

Karakaya, S., & Balcik, B. (2024). Developing a national pandemic vaccination calendar under supply uncertainty. *Omega*, *124*, 103001. https://doi.org/https://doi.org/10.1016/j.omega.2023.103001

Lin, Q., Zhao, Q., & Lev, B. (2020). Cold chain transportation decision in the vaccine supply chain. *European Journal of Operational Research*, *283*(1), 182-195. https://doi.org/https://doi.org/10.1016/j.ejor.2019.11.005

Lutzmayer, S. (2024). *Pharma's Frozen Assets: Cold Chain Medicines*. IQVIA. https://www.astuteanalytica.com/industry-report/cold-chain-logistics-market

Nguyen, A., Samir, L., Robert, P., Simon, T., & and Lekens, B. (2022). Data analytics in pharmaceutical supply chains: state of the art, opportunities, and challenges. *International Journal of Production Research*, *60*(22), 6888-6907. https://doi.org/10.1080/00207543.2021.1950937

Preiss, S., Garçon, N., Cunningham, A. L., Strugnell, R., & Friedland, L. R. (2016). Vaccine provision: Delivering sustained & widespread use [Article]. *Vaccine*, *34*(52), 6665-6671. https://doi.org/10.1016/j.vaccine.2016.10.079

Prosser, W., Folorunso, O., McCord, J., Roche, G., Tien, M., Hatch, B., Spisak, C., Genovese, E., Pare, B., Donatien, K., Ibrahim, M., Abou-Charaf, E., Wright, C., & Dubourg, J. C. (2021). Redesigning immunization supply chains: Results from three country analyses [Article]. *Vaccine*, *39*(16), 2246-2254. https://doi.org/10.1016/j.vaccine.2021.03.037

Rekabi, S., Goodarzian, F., Garjan, H. S., Zare, F., Muñuzuri, J., & Ali, I. (2023). A data-driven mathematical model to design a responsive-sustainable pharmaceutical supply chain network: a Benders decomposition approach [Article]. *Annals of Operations Research*. https://doi.org/10.1007/s10479-023-05734-3

Robertson, J., Franzel, L., & Maire, D. (2017). Innovations in cold chain equipment for immunization supply chains [Review]. *Vaccine*, *35*(17), 2252-2259. https://doi.org/10.1016/j.vaccine.2016.11.094

Seuring, S., & Müller, M. (2008). From a literature review to a conceptual framework for sustainable supply chain management. *Journal of Cleaner Production*, *16*(15), 1699-1710. https://doi.org/https://doi.org/10.1016/j.jclepro.2008.04.020

Seuring, S., Yawar, S. A., Land, A., Khalid, R. U., & Sauer, P. C. (2021). The application of theory in literature reviews – illustrated with examples from supply chain management. *International Journal of Operations & Production Management*, *41*(1), 1-20. https://doi.org/10.1108/IJOPM-04-2020-0247

Shahparvari, S., Hassanizadeh, B., Mohammadi, A., Kiani, B., Lau, K. H., Chhetri, P., & Abbasi, B. (2022). A decision support system for prioritised COVID-19 two-dosage vaccination allocation and distribution [Article]. *Transportation Research Part E: Logistics and Transportation Review*, *159*, Article 102598. https://doi.org/10.1016/j.tre.2021.102598

Turan, C., & Ozturkoglu, Y. (2022). Investigating the performance of the sustainable cold supply chain in the pharmaceutical industry [Article]. *International Journal of Pharmaceutical and Healthcare Marketing*, *16*(3), 448-467. https://doi.org/10.1108/IJPHM-04-2021-0043

Van Eck, N. J., & Waltman, L. (2013). VOSviewer manual. *Leiden: Univeristeit Leiden*, *1*(1), 1-53.

Van Zyl-Cillié, M., Demirtas, D., & Hans, E. (2023). Wait!What does that mean?: Eliminating ambiguity of delays in healthcare from an OR/MS perspective. *Health Systems*, *12*(1), 3-21. https://doi.org/10.1080/20476965.2021.2018362

Yadav, A. K., Shweta, & Kumar, D. (2023). Blockchain technology and vaccine supply chain: Exploration and analysis of the adoption barriers in the Indian context. *International Journal of Production Economics*, *255*, 108716. https://doi.org/https://doi.org/10.1016/j.ijpe.2022.108716

Zhu, T., Yeo, N. T. B., Gao, S. Y., & Loke, G. G. (2023). Inventory-Responsive Donor-Management Policy: A Tandem Queueing Network Model [Article]. *Manufacturing and Service Operations Management*, *25*(4), 1585-1602. https://doi.org/10.1287/msom.2023.1228