Internet of Things Applications for Cold Chain Vaccine Tracking: A Systematic Literature Review

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Abstract

The COVID-19 pandemic has led to an immense effort by laboratories, governments, and non-governmental organizations to develop vaccines in record time. According to the World Health Organization (WHO), one of the major challenges for global immunization is to keep the temperature conditions of these supplies in remote areas, especially in underdeveloped countries. Monitoring the cold chain, the supply chain specializing in refrigerated goods, such as food and health items, becomes critical to their preservation. Technologies inherent to the Internet of Things, like RFID and temperature sensors, are commonly used to identify and detect physical changes in the environment in which they are embedded. This survey presents a Systematic Literature Review (SLR) conducted to identify the most relevant studies on this topic from digital libraries. Through this SLR, 23 primary studies were selected from which important data were extracted and analyzed. The presented results in this study should explain which and how the key technologies are used to control the delivery of vaccines in the cold chain, focusing on remote regions.

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Keywords

Internet of things · Ubiquitous and pervasive computing · IoT applications · Transport · Cold chain · Vaccine · COVID-19 · Pandemic preparedness · Systematic literature review · Survey

37.1 Introduction

COVID-19 is a respiratory disease caused by the SARS-CoV-2 virus, which was characterized as a pandemic by the World Health Organization (WHO) on March 11, 2020, after the number of cases increased by 13 times and the number of affected countries tripled in the 2 weeks before that date [1]. Since this disease's emergence, governments and Non-Governmental Organizations (NGOs) have joined forces to help pharmaceutical companies develop effective vaccines to fight this disease in record time.

The control of temperature conditions for the storage of these vaccines is vital for their usefulness and controlling the disease itself, being a challenge mainly for underdeveloped and emerging countries [2, 3]. According to [3], by February 2021, most prominent vaccine candidates required storage between 2 and 8 °C and later proven high-effective vaccines [4], such as Pfizer-BioNTech and Moderna, even needed lower temperatures: −70 °C and − 20 °C, respectively.

The management of the Cold Chain, a term that refers to the production, storage, and distribution of products sensitive to variations in temperature and humidity, has been explored by the WHO since 2007 to facilitate the distribution of vaccines outside the conventional range temperature, which is from 2 °C to 8 °C. This endeavor culminated in the development of an innovative approach called the Controlled Temperature Chain (CTC) [5]. A vaccine

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with the CTC label can withstand up to 40 °C for at least 3 days before its application, which makes it possible to immunize populations in remote areas, besides making its handling cheaper, as it does not require refrigeration and facilitates transport because of the reduction in weight of the container.

Making Cold Chain management unnecessary for these biological complexes would be the most effective solution to address the difficulties imposed, but this is still one of the significant challenges of pharmaceutical research [6]. Vital supplies such as antivenom for venomous snakebites, commonly applied in remote areas of the Amazon region, also face challenges of effectiveness and safety because of the use of different modes of transport and susceptibility to failure of refrigeration equipment [7]. A similar challenge is confronted by the food sector, where it is estimated that 30% of food produced for human consumption is wasted because of failures in Cold Chain management, caused mainly by insufficient refrigeration [8].

As stated by [8], several technologies have been applied to monitor changes in the conditions of the Cold Chain, highlighting Radio Frequency Identification (RFID) and Wireless Sensor Networks (WSN). While the first refers to object identification, for example, by reading tags, the second mentions networks capable of collecting and centralizing physical data from an environment through sensors. Both technologies are part of the Internet of Things (IoT), a term coined by Kevin Ashton in 1999, according to which objects common to our daily lives, called "things", with integrated technologies capable of identifying, observing, intervening, and understanding the world, communicating via the Internet [9]. IoT has gained significant relevance, especially in the last decade, when there was an average annual growth of publications above 85% between 2015 and 2019 [10].

To investigate, evidence, and report the significant studies related to IoT applications for vaccine logistics in the cold chain, a Systematic Literature Review (SLR) was carried out and is detailed throughout this survey. We describe the dominant technologies found and their usage in different contexts, aiming to help researchers who may face the same problems due to the challenges imposed by diverse environments and locations during transportation.

This paper is further structured: Section 37.2 details the method applied to search and select relevant documents; Section 37.3 presents in a structured way the results through the extracted data; Section 37.4 shows discussions about the results to answer the research questions correctly; finally, Section 37.5 summarizes the relevant findings and highlights future work in regarding of this topic by the authors.

37.2 Method

An SLR was elaborated to search for primary studies about the addressed topic in an organized and auditable way. According to [11], an SLR is a secondary study capable of identifying, evaluating, and interpreting relevant research. It is divided into three phases: planning, conducting, and reporting. In the first phase, the objective and protocols are defined. Afterward, the studies are collected and refined during the conduction. Finally, the results are reported in the last step.

Many tools are designed to perform an SLR within the context of Software Engineering [12]. In our case, the Parsifal (https://parsif.al) tool was chosen because it covers most of the stages of the systematic review process; it is open-source and online available, which enables collaborative work even if the researchers are geographically distributed.

We conducted our SLR by applying [11] guidelines through the Parsifal tool. In the planning phase, we have defined the Research Protocol (RP), the Quality Assessment Checklist (QAC), and the Data Extraction Form (DEF). During the review conduction, studies were searched, imported, selected, and qualified, with their relevant data extracted and analyzed, following the previously defined RP. Afterward, all the data collected was organized so that we could show the most relevant results of the reporting phase.

37.2.1 Planning the Review

The RP defines the objective of the SLR, the research questions that guide it, the search string used for querying papers, the chosen search sources, and the inclusion and exclusion criteria applied for selecting studies.

To inspect the main issues and their current solutions involving IoT applications for cold chain vaccine tracking, our SLR sought to answer the following **Research Questions** (RQ):

- RQ1 – What are the main IoT technologies used in cold chain vaccine logistics?
- RQ2 – Which of these technologies are applied in remote areas?

The **Search String** was defined aiming to answer both RQs, combining keywords and their synonyms with "AND" and "OR" logical operators:

("internet of things" OR" IoT" OR" pervasive computing" OR" ubiquitous computing") AND ("cold chain" OR" logistics" OR" SCM" OR" supply chain") AND" vaccine".

Pertinent **digital libraries and databases** of Computer Science and Health areas have been chosen as search sources of the RP: ACM Digital Library, IEEE Digital Library, PubMed Central: PMC, Scopus, and Springer Link.

To keep only topic-related manuscripts, the RP **inclusion criteria** were determined in such a manner:

1. Title, abstract, or keywords refer to cold chain vaccine logistics;
2. Title, abstract, or keywords are related to IoT, Ubiquitous and Pervasive Computing;
3. Study published between 2010 and 2021.

Dealing with the RP **exclusion criteria**, the following were defined to avoid outdated and secondary articles, besides keeping only those focused on IoT applications:

1. Book, chapter, or secondary study;
2. Complete article unavailable;
3. Absence of IoT application for cold chain vaccine logistics.

In addition to the RP, the **Quality Assessment Checklist** was specified in the planning phase, intending to rate the selected manuscripts containing five items. For each question of the QAC, there were three answers with their respective weight: Yes (1.0), Partially (0.5), and No (0.0). Thus, an article's maximum Quality Assessment Score (QAS) would be 5.0.

- Are the research aims specified?
- Is the study compared to related work?
- Is there hardware and/or software specification?
- Is there an IoT application detailed?
- Are the data collection and results adequately detailed?

37.2.2 Conducting the Review

The SLR was conducted in July 2021 as illustrated in Fig. 37.1. In total, 575 studies were retrieved by submitting the aforementioned search string to the digital libraries and databases. All of them were introduced to the Parsifal tool, totaling 514 papers after 61 were classified as duplicated.

The first step of selection was reading the title and abstract of the non-duplicated manuscripts while applying the RP inclusion and exclusion criteria, which ended up in a list of 46 articles for the complete analysis. Finally, the full reading with the same criteria was employed in the final round, with 23 selected papers for data extraction.

37.2.3 Reporting the Review

The most relevant information from the selected studies, i.e., sensors and protocols used, the local storage capability, the countries where they were carried out, and the QAS are presented in Table 37.1. All the manuscripts employ temperature sensors, while humidity is a secondary concern applied in 60.9%, and only 30.4% detect lighting. The communication protocol was not specified in the applications of the S14, S17, and S20 papers. Local storage was employed in 43.5% of these articles, enabling their applications to operate without an Internet connection.

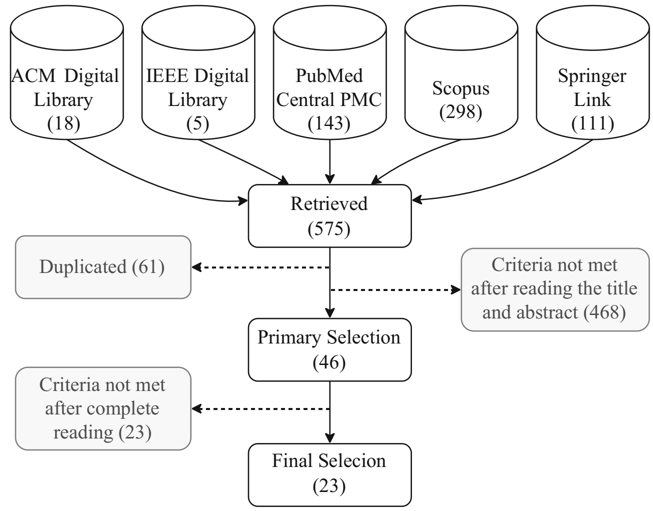

Fig. 37.1 Summary of the SLR conduction

The extracted data through the DEF is described in detail in the Results section, while the complete list and the detailed information of these papers, including the Digital Object Identifier (DOI), title, and authors' names, can be accessed via https://bit.ly/3VTY6Cb.

37.3 Results

The main characteristics raised from the selected studies were: the year of publication for indicating the trend of the subject; the employed technologies for identifying, monitoring, and tracking vaccines during transport, mainly the used sensors and protocols; and the places where these studies were carried out. The SLR results for each one of these characteristics are reported in the sequel.

37.3.1 Time-Spreading of Selected Studies

This SLR was conducted from May to July 2021, focusing on the last 10 years. The distribution per year of the selected studies handling IoT applications for vaccine logistics is shown in Fig. 37.2.

From 2011 to 2017, the average of papers addressing this SLR subject was less than one per year. From 2018 to 2021,

Table 37.1 Summary of extracted sensors, local storage, protocols/technologies, countries, and score from the selected studies

	Sensors				Communication		
Study	Temperature	Humidity	Light	Local Storage	Protocols/Technologies	Country	Quality Score
S1	✓				6LoWPAN, RFID	Spain	4.0
S2	✓	✓		✓	GSM	Albania	4.0
S3	✓	✓	✓	✓	GSM	Laos	3.5
S4	✓			✓	RFID	Brazil	3.0
S5	✓				Bluetooth	Taiwan	5.0
S6	✓			✓	3G, 4G, BLE	Colombia	5.0
S7	✓	✓	✓	✓	Bluetooth	Hong Kong	5.0
S8	✓	✓	✓		GSM, WiFi, ZigBee	India	3.5
S9	✓				LoRaWAN	Congo	4.0
S10	✓	✓			WiFi	India	3.0
S11	✓	✓			Bluetooth 3G	Taiwan	4.5
S12	✓				SigFox	Colombia	4.0
S13	✓	✓		✓	3G, 4G	United Arab Emirates	4.5
S14	✓				–	South Africa	4.5
S15	✓	✓			GSM	Bangladesh	4.0
S16	✓	✓		✓	BLE, 3G, 4G, WiFi	Hong Kong	5.0
S17	✓				–	Denmark	5.0
S18	✓	✓		✓	BLE, WiFi	Italy	3.5
S19	✓	✓			RFID	China	5.0
S20	✓			✓	–	China	4.5
S21	✓	✓	✓		BLE	Portugal	5.0
S22	✓	✓	✓		4G, WiFi	United Arab Emirates	5.0
S23	✓	✓	✓	✓	GSM	Bangladesh	5.0

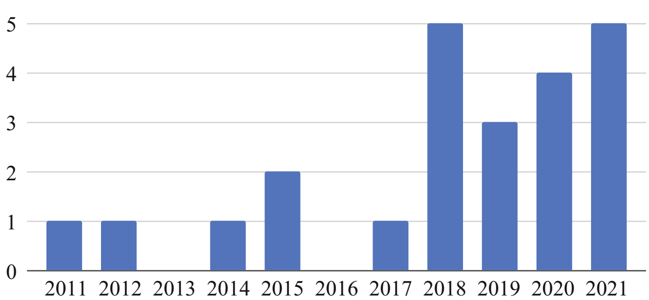

Fig. 37.2 Selected studies per year of publication

this average grew to 4,25, with peaks in 2018 and 2021. These two periods coincide, respectively, with the "development" and "rapid development" stages of the area defined by [10]. The former phase contains action plans and financing from Asian and European countries to promote the direction of the IoT, while the latter reaps the benefits of such investment.

Apart from the previously mentioned trend in the IoT field, the high number of articles in the last years can also be explained by the demand for monitoring vaccines during their storage and transport, given that such solutions are considered a Return on Investment (ROI) by the WHO CTC Workgroup in the strategic roadmap for priority vaccines [5].

37.3.2 Technologies of Selected Studies

The data relating to the employed technologies extracted from the selected studies allows us to answer RQ1. For a better explanation, the gathered technologies were divided based on the IoT three-layer architecture, i.e., devices, communication, and cloud, which, according to [13], is the most widespread Internet of Things architecture in the literature.

37.3.2.1 IoT Devices

The IoT devices in the cold chain, often called tags or data loggers, are composed of at least one microcontroller and linked sensors to monitor environmental conditions. Table 37.2 shows the studies, among the selected ones, that specify the employed hardware, i.e., microcontroller/board and/or sensor model.

Among the studies shown in Table 37.2, the most employed board family is Arduino (https://www.arduino.cc), mentioned in S11, S23, and S24. This open-source electronic platform abstracts low-level hardware programming and offers flexibility in prototyping, being widely adopted in the last decade [14]. It is worth mentioning the S18 cites the STM32L4 board, from STMicroelectronics (https://www.st.com), which is also compatible with Arduino and therefore can be classified as such.

Table 37.2 Studies and employed hardware

Study	Microcontroller/Board	Sensor model
S3	Fridge-Tag 30	–
S6	Raspberry Pi Family	K MAX6675
S7	SensorTag™ CC2650	–
S10	NXP LPC2148	LM35
S11	Arduino Family	DHT22
S12	PIC32MX130F064B	–
S13	Raspberry Pi Family	–
S14	–	PT-100
S18	STM32L4	–
S23	Arduino Family	–
S24	Arduino Family	–

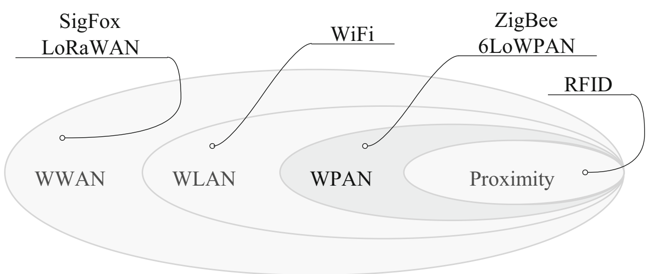

Fig. 37.3 Wireless technologies extracted and their geographic coverage. (Adapted from [13])

The applications of S6 and S13 use Raspberry Pi (https://www.raspberrypi.org), a single-board computer that runs Linux and provides a set of general-purpose input/output (GPIO). Together with Arduino, it is a highly popular platform for developing IoT applications [15].

NXP LPC2148, from NXP Semiconductors (https://www.nxp.com), is the microcontroller of the S10 application. It is small, has low power consumption, and is suitable for industrial control and medical systems. Finally, S3 and S7 embrace commercial solutions for continuous cold chain monitoring, including the data loggers Fridge-Tag 30 and SensorTag CC2650, respectively.

Only four sensor models were explicitly specified in the selected studies. The temperature sensors K MAX6675, DHT22, and PT-100 were employed in S6, S11, and S14 applications, respectively, while S10 used the LM35 sensor to track temperature and humidity.

37.3.2.2 Communication

The network plays a crucial role in IoT by enabling communication between devices and back-end applications. In Fig. 37.3, are illustrated the wireless communication technologies extracted from the studies and their respective geographic scope, while they are grouped by the publication's year in Fig. 37.4.

SigFox, LoRaWAN, and mobile networks are Wireless Wide Area Networks (WWAN), with regional or even nationwide coverage. The Global System for Mobile Communications (GSM) and the following generations (i.e. 3G and 4G) are present in over 40% of the selected papers, a fact that can be explained by their dominant role in the IoT area given the existing cellular infrastructure [13]. SigFox and LoRaWAN cited once in S12 and S8 respectively, are said low power WAN due to their low energy characteristic despite the long range. The former requires a subscription to a licensed wireless provider, while the latter permits owning the communication infrastructure [16].

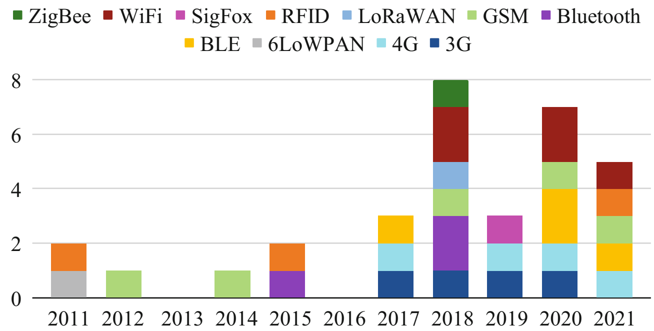

Fig. 37.4 Protocols per year

Cited in 15.9% of the chosen studies, WiFi, based on the IEEE 802.11 family [17], is the most widespread Wireless Local Area Network (WLAN), usually used within a home or a building. ZigBee and 6LoWPAN, correspondingly to S8 and S1, along with Bluetooth and its low-energy evolution (Bluetooth Low Energy – BLE) adopted by 21.9% of papers, are Wireless Personal Area Network (WPAN), which means they should work in the personal space from 10 up to 100 m [13].

Radio-frequency identification (RFID), mentioned by 9.4% of the gathered IoT applications, is usually composed of an RFID tag which can store an identification through transponders. When it has its own power source, it is considered an active tag, otherwise, it is a passive tag and can be activated by an electromagnetic signal emitted by an RFID reader [18]. Passive RFID tags are inexpensive and, along with the capacity of identifying something, it is a flashy technology in the IoT area.

Apart from the aforementioned Wireless Sensor Network (WSN) technologies, summarized by [13], the gathered manuscripts also mention the usage of the Hypertext Transfer Protocol (HTTP) and Message Queue Telemetry Transport (MQTT) as the application layer protocols [19]. S1, S3, S6, and S18–22 uses HTTP or its secure version (HTTPS) to exchange data between client and servers via its request and response model, while, S08, S14 and S22 employed the MQTT, a lightweight publish/subscribe messaging protocol, vastly adopted in the IoT industry [20].

37.3.2.3 Cloud

The National Institute of Standards and Technology (NIST) defines [21] Cloud Computing as *a model for enabling ubiquitous, convenient, on-demand network access to a shared pool of configurable computing resources*. Its cost-based model enables end-to-end services for users to access applications on demand from anywhere.

Among the selected papers, two of them explicitly specify the usage of cloud providers. Without providing further implementation information, the study S07 relies on the IBM Watson IoT service to register the IoT device and exchange real-time collected data. The authors of the S22 study stated the Microsoft Azure IoT Hub was selected because it can be integrated with other used Azure services seamlessly. It supports MQTT, HTTPS, and other application protocols.

37.3.3 Places of Selected Studies

The places stated in Table 37.1 were firstly defined whenever explicitly specified in the study, and secondly for being the leading country of the carried-out investigation. In Fig. 37.5, the countries painted in dark green speak for 2 studies each, while a light green painted country stands for 1 study. Asian countries were responsible for 56.5%, followed by 21.7% from Europe, 13% from South America, and 8.7% from Africa.

Regarding the remote area's issues, five papers explicitly cite the major challenges, which can be categorized as (a) lack of network connectivity and (b) energy outages. In S2 (Albania), the solution relies on the mobile phone battery against the common transitory power supplies. S23 (Bangladesh) focus on the low-energy consumption of the proposed prototype as its local storage capability to overcome power problems. S14 (South Africa) uses solar panels as the power source for their solution to monitor the vaccine box. S9 (Congo) applies solar energy as well, but it goes further and experiments with LoRaWAN to create a sequence of wireless devices to form arbitrarily large mesh networks, disconnected from the Internet.

37.4 Discussion

As presented in the results got with the SLR, a wide variety of technologies can be applied in cold chain vaccine logistics in different places throughout the world. Based on this information, this section aims to answer both research questions defined in this SLR.

37.4.1 RQ1: What Are the Main IoT Technologies Used in Cold Chain Vaccine Logistics?

A few sensor types are employed to gather the environmental conditions, especially for temperature. The collected input is usually processed in loco by the board, highlighting the choice of Arduino and Raspberry Pi. Hence, the data is transferred through wireless communication to a gateway or directly to the cloud. Mobile networks, such as GSM/3G/4G, are heavily employed throughout the years. SigFox and LoRa(WAN) are next-generation technologies employed for long-distance communication. Meanwhile, RFID, Bluetooth/BLE, and ZigBee are used for shorter-range communication. Cloud services such as IBM Watson IoT and Azure IoT Hub offer further data processing and analysis, supporting different application protocols for integration as HTTP/S and MQTT.

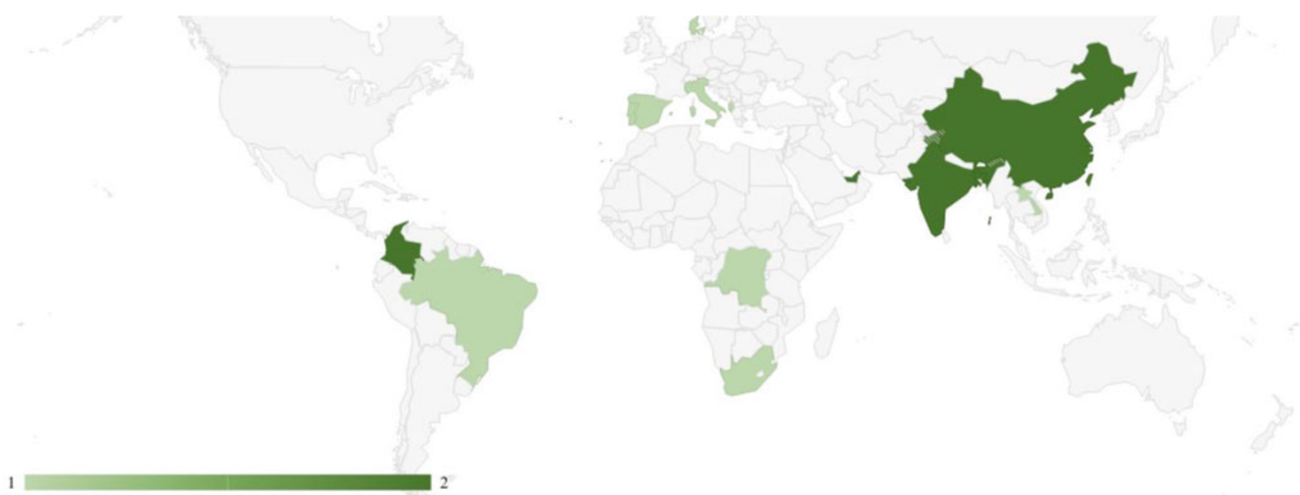

Fig. 37.5 Studies conducted worldwide: countries painted in dark green published 2 studies, while countries in light green contributed to 1 study each

37.4.2 RQ2: Which of these Technologies Are Applied in Remote Areas?

In rural or remote places, even nowadays cellular networks may be intermittent or do not exist at all [22]. In such scenarios, a hybrid solution using the device's local storage and WSN disconnect from the Internet is commonly applied, like SigFox and LoRa(WAN) for long-distance communication. Meanwhile, RFID, Bluetooth/BLE, and ZigBee are used for shorter-range link. Other key impact is the non-reliable power supply in such areas, which could be mitigated by employing low-power devices and protocols, besides batteries or sustainable power providers as solar panels.

37.5 Conclusion

This paper is focused on cold chain vaccine logistics by leveraging IoT technologies. The aim was to understand the key technologies and their correlation with remote places. In the elaborated SLR, the last decade's primary studies which addressed this problem via IoT applications were gathered and scrutinized via defined criteria.

It was possible to answer the RQ1 and RQ2 from the selected studies' information. Technologies-wise, following the three-layer IoT architecture, we highlighted the role of the IoT devices such as sensors, microcontrollers, and boards, a wide variety of wireless communication means, and cloud services when applied.

For remote areas' concerns, the lack of connectivity and the energy consumption of the solution were shown as the fundamental challenges. Strategies like local storage help to dodge the former, while next-generation and low-energy communications protocols address the former.

Policymakers can make decisions based on technologies and issues highlighted by this study, along with understanding the available vaccine's characteristics. Vaccines that require fine-grained temperature control may be suitable for urban areas, where power supply and connectivity are much more reliable. On the other hand, near real-time IoT solutions would improve the distribution of such goods in rural areas, mitigating the waste of resources and, most importantly, saving lives.

The presented SLR was performed during the Problem Investigation phase of the Master's degree project "System based on the Internet of Things for Intelligent Tracking applied to Cold Chain Logistics", under development by the first author of this paper. The co-author has guided the entire writing and reviewing processes for this article.

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