Title

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Journal

Expert Opinion on Drug Safety, 21(8)

ISSN

1474-0338

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Publication Date

2022-08-03

DOI

10.1080/14740338.2022.2091543

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Article *in* Expert Opinion on Drug Safety · June 2022

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To cite this article: Gul Saeed, Jillian C. Kohler, Raphael E. Cuomo & Tim K Mackey (2022): A systematic review of digital technology and innovation and its potential to address anti-corruption, transparency, and accountability in the pharmaceutical supply chain, Expert Opinion on Drug Safety, DOI: 10.1080/14740338.2022.2091543

To link to this article: https://doi.org/10.1080/14740338.2022.2091543

Published online: 28 Jun 2022.

EXPERT OPINION ON DRUG SAFETY
https://doi.org/10.1080/14740338.2022.2091543

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REVIEW

A systematic review of digital technology and innovation and its potential to address anti-corruption, transparency, and accountability in the pharmaceutical supply chain

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ABSTRACT

Introduction: The urgent need to acquire medical supplies amidst the COVID-19 pandemic has led to bypassing of controls that govern the global pharmaceutical supply chain, increasing the risk of corruption. Hence, promoting anti-corruption, transparency, and accountability (ACTA) in supply chain and procurement has never been more important. The adoption of digital tools, if designed and implemented appropriately, can reduce the risks of corruption.

Areas Covered: Following PRISMA guidelines, we conducted an interdisciplinary systematic review of health/medicine, humanities/social sciences, engineering, and computer science literature, with the aims of identifying technologies used for pharmaceutical supply chain and procurement optimization and reviewing whether they address ACTA mechanisms to strengthen pharmaceutical governance. Our review identified four distinct categories of digital solutions: e-procurement and open contracting; track-and-trace technology; anti-counterfeiting technology; and blockchain technology.

Expert Opinion: Findings demonstrate an increase in research of technologies to improve pharmaceutical supply chain and procurement functions; however, most technologies are not being leveraged to directly address ACTA or global health outcomes. Some blockchain and RFID technologies incorporated ACTA mechanisms and mentioned specific policy/governance frameworks, but more purposeful linkage is needed. Findings point to the need for targeted policy development and governance to activate these innovative technologies to improve global health .

KEYWORDS

Access to medicines; accountability; corruption; e-procurement; global health; good governance; improved health outcomes; pharmaceutical procurement; supply chain; technology; transparency; COVID-19

1. Introduction

1.1. Background

Corruption, defined as "the misuse of entrusted power for private gain" [1], is a particular risk in the global supply chain generally and the pharmaceutical sector specifically. Corruption risks are always present in the health system, but they substantially increase during public health crises, such as the ongoing COVID-19 pandemic [2–4]. Specifically, the urgent need to acquire essential health products that are limited in supply can lead to gaps in procurement practices, suppliers engaging in price gouging, government officials engaging in bribery to bypass regulatory controls and procedures, theft of supplies within distribution systems, and "increased circulation of falsified products" [2,4–6]. Governments, even those with historically robust national health regulatory systems, have rushed to secure essential medicines, vaccines, personal protective equipment, and ventilators amidst the pandemic, with concerns of fraud and abuse in these programs beginning to emerge [5,7–9].

The pharmaceutical supply chain and particularly the pharmaceutical procurement process are vulnerable to a lack of transparency, accountability, and heightened risks of corruption given they are complex, multi-party, cover many jurisdictions, and are transnational parts of the global health ecosystem. There are several stages involved in the pharmaceutical supply chain (manufacturing, distribution) and the procurement cycle (pre-bidding, bidding, and post-bidding) [4], with each stage having its own vulnerabilities to corruption. The following corrupt activities may take place during each procurement phase: (1) pre-bidding: rigged needs assessments and circumvention of tender procedures; (2) bidding: bribery and kickbacks during bid evaluation and collusion or market division in bidding; and (3) post-bidding: false invoicing, inflated invoicing, changing contract agreements, and failure to deliver products procured [10,11]. The deployment of products, from manufacturing to service delivery, is also highly vulnerable to corruption risks [4]. Corruption risks during the transportation of supplies include theft of items from the public supply chain for personal use, diversion, or selling in the black market [4].

Globally, an estimated US$500 billion in public health spending is lost to corruption each year; consequently, the health system as a whole suffers from inadequate access to

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Table 1. ACTA definitions (adopted from Vian T. 2020 [23]).

Term	Definition
Corruption	Abuse of entrusted power for private gain. This includes bribes, embezzlement, misappropriation, diversion of government property, trading in influence, abuse of function, and illicit enrichment.
Transparency	Transparency is a public value that requires that citizens be informed about how and why decisions are made, including procedures, criteria applied by government decision makers, the evidence used to reach decisions, and results. Often transparency refers to access to information.
Accountability	Accountability is a public value that requires government institutions to explain and make understandable their performance in achieving goals and addressing the needs of the public, in comparison to standards and commitments. It requires visible, responsive action if standards and commitments are not met.

public health goods and services [12,13]. The impact of corruption on certain at-risk populations can also be deadly, for example, as many as 140,000 child deaths (under the age of five) annually are estimated to be caused by corruption [12,14,15]. Of equal importance, corruption can hinder the government's ability to deliver on government led programs that guarantee certain health services and constitute a social contract, diminishing the public's trust in these services [16]. As such, there is a critical need for anti-corruption, transparency, and accountability (ACTA) mechanisms (see Table 1 for description) in the pharmaceutical procurement, supply, and distribution processes. ACTA principles can help ensure better access of populations to essential health products and advance shared global goals of improving the health and wellbeing of all populations as envisioned in the UN Sustainable Development Goals (SDGs) Goal #3 [17–19].

1.2. Challenges faced during COVID-19 and potential for technology advances

The unprecedented challenges on health systems and global supply chains caused by COVID-19 and the damaging impacts of corruption emphasize the need for enhanced global efforts to create resilient health supply chains to safeguard medicines, vaccines, and other health products needed to arrest the spread of this novel and evolving disease [2,20]. Publicly funded health programs that supply these goods are especially vulnerable to corruption if there is already weak governance in the country, generally characterized by a lack of transparency and poor accountability in existing government and regulatory systems [21,22]. Still, when there is effective oversight and strong ACTA mechanisms in health systems management, corruption risks are reduced [23–25]. For example, higher levels of transparency in the pharmaceutical procurement process may help prevent price gouging and manipulation, via public disclosure of information that allows comparison of prices paid by different facilities for the same health product [26]. Further, accountability mechanisms (e.g. citizen report cards and whistleblowing mechanisms) may reduce corruption by ensuring public actors and institutions are answerable to the people they serve and that they comply with existing standards and procedures, as well as by imposing sanctions when corruption is identified [23,26].

To advance ACTA and further facilitate anti-corruption initiatives and partnerships, there has been increasing attention by governments, international organizations, and procurement agencies on the evaluation and adoption of different forms of technology to identify corruption risks and promote ACTA in the health sector, with a specific focus on the pharmaceutical sub-sector [27,28]. Notably, COVID-19 has compelled various industries to invest in "digital transformation" initiatives, including the pharmaceutical sector, that now uses a multitude of digital solutions to address challenges related to supply chain disruptions, increase the speed and scalability of drug discovery, optimize operation of biomedical and clinical research, and implement systems to ensure the integrity of medicine supply and distribution [29]. Specific to ACTA areas, advancements in information and communication technologies (ICT), web and cloud-based platforms, and big data and artificial intelligence (AI), including machine learning, have led to the development and implementation of digital solutions that have improved transparency in the management of public sector health funds (e.g. e-government initiatives), enhanced oversight and reporting mechanisms (e.g. websites for whistleblowing), and increased adoption of supply chain technologies (e.g. digital track-and-trace systems); and ultimately, have a strong potential to reduce corruption in the pharmaceutical sector [27,30–32].

Nonetheless, there are several ethical implications of using digital technologies, including security and privacy concerns (e.g. violation of privacy rights) [32,33]. What is more, gaps remain in laws and policies that aim to protect human security and privacy as they struggle to keep apace with the quick advancements in digital technology [33]. For example, amidst COVID-19, the rapid development and adoption of digital solutions, such as mobile applications for contact tracing, have triggered privacy concerns [34]. As such, there is a need for concerted efforts at national and international levels to ensure that the relationship between digital technologies and users they seek to benefit is ethical, particularly under unprecedented circumstances, such as pandemic response measures enacted for COVID-19. Anti-corruption and supply chain security digital technologies promoting ACTA principles will equally need to be developed with ethical and privacy considerations in mind given the sensitive, potential life-saving, and complex nature of addressing both corruption and access to essential health commodities.

However, existing published research indicates that initiatives to promote ACTA in the pharmaceutical supply chain/procurement have primarily focused on non-technological solutions, such as multi-stakeholder initiatives (e.g. Medicines Transparency Alliance and the Good Governance for Medicines Programme) and policy frameworks [23,25,32,35]. To date, there have been few studies that focus on assessing whether ACTA principles have been purposefully developed into technology-based solutions specific to the pharmaceutical supply chain, and if in turn, they promote good pharmaceutical governance and help in the fight against global health corruption. Hence, this study conducts a systematic review of the literature focused on identifying, characterizing, and assessing the application of different forms of technology used or

investigated for the pharmaceutical supply chain and procurement and how they can advance ACTA goals.

2. Methods

The aims of this systematic review are twofold: (1) to identify digital technologies employed for pharmaceutical supply chain and procurement optimization; and (2) to determine whether these technologies address ACTA mechanisms to curb corruption in the pharmaceutical supply chain or procurement process. This research builds on prior review articles and provides a systematic update of studies that specifically focus on existing and emerging digital technologies to optimize the functions of and promote ACTA in the pharmaceutical supply chain and procurement [23,36,37]. Herein, we define "digital technology" as concepts, tools, and solutions that are internet-based information and communication systems, including online portals and management systems, supply chain tools, cloud-based platforms, and electronic databases.

2.1 Search strategy

In accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [38], we carried out an interdisciplinary review in May 2021. Specifically, we reviewed journal articles, original research, conference papers, case reports, technology reviews, commentaries and news reports that were indexed in four scholarly databases: PubMed (Medline), JSTOR, IEEE Xplore, and ACM Digital Library (see summary of review methodology in Figure 1). We selected these databases based on the interdisciplinary nature of the study aims which required a review of the science/health literature (from PubMed-indexed journals that cover life sciences and biomedical topics); research in the areas of humanities, social sciences, and natural sciences (from JSTOR which indexes peer-reviewed papers, abstracts, and conference proceedings that are multidisciplinary ranging from economics, political science to health and science); studies on information, communication, and engineering technologies (from IEEE Xplore-indexed articles that focus on scientific and technical content published by the IEEE); and research on advances in computing sciences (from ACM Digital Library, which indexes various journals, conference proceedings, technical magazines, newsletters and books in the computing literature).

The four databases were searched for articles published in the English language between January 2011 and May 2021, using the Medical Subject Headings (MeSH) unique ID term "Pharmaceutical Preparations/supply and distribution" (ID: D004364), "Technology" (ID: D013672), "technology, pharmaceutical" (ID: D013678), and Materials Management, Hospital" (ID: D008421). Other non-MeSH key search terms included "pharmaceuticals," "pharmaceutical supply chain," "medicines supply chain," "medicines procurement," "purchasing," "open contracting" in combination with "e-procurement" (short for electronic procurement) or "technology." Keywords were queried in the Title/Abstract field using the advanced search function settings for PubMed, JSTOR, IEEE Xplore, and ACM Digital Library databases. We chose a 10-year literature review period as this review is focused on relatively new or innovative technologies.

Additionally, select case studies and technical reports providing additional details on the specific application of reviewed technology at international and national levels were derived from sources in the gray literature, including international organization, non-governmental organizations,

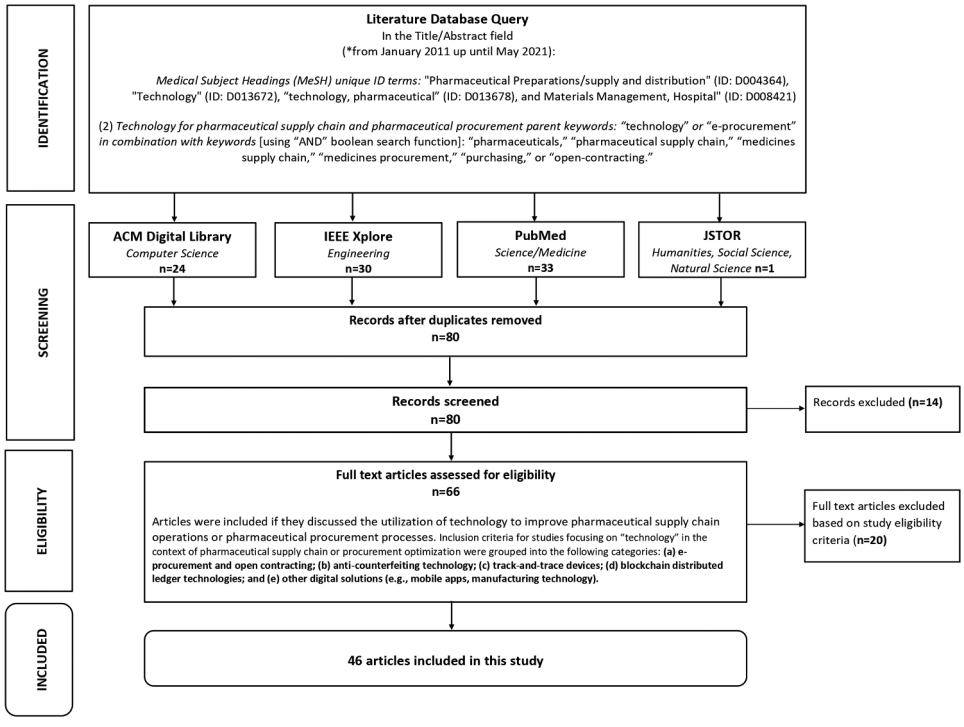

Figure 1. Summary of systematic review methodology.

and solution provider websites for the purposes of reporting real-world case studies illustrative of technology utilization.

2.2 Study selection

To minimize errors and reduce potential biases in study selection, authors GS and TM independently applied inclusion and exclusion criteria that filtered results by initially reviewing abstracts and subsequently, full text of all extracted articles. Any discrepancies regarding study eligibility were resolved through discussion among the authors to reach a final consensus.

2.3 Inclusion criteria

Articles were included in this review if they discussed or examined technology in the context of pharmaceutical supply chain and/or pharmaceutical procurement, including articles specific to e-procurement methods or supply chain optimization. Research articles, review articles, case studies, commentaries, technical reports, and conference papers were all included for the purposes of identifying key technology modalities and characteristics and whether the technology addresses ACTA mechanisms.

2.4 Exclusion criteria

Initially, articles were excluded if they did not discuss the application of technology to optimize the pharmaceutical supply chain or procurement process (e.g. discussed other fields of study such as pharmaceutical manufacturing, commodity procurement in another industry, or public procurement generally). Subsequently, articles that included pharmaceutical supply chain or pharmaceutical procurement but did not discuss forms of technologies (e.g. non-digital and solely field-based solutions) were excluded. We did not exclude literature based on specific content types or study designs.

2.5 Bias assessment

If any randomized controlled trials (RCTs) were selected, the Cochrane Collaboration's tool for assessing risk of bias should be used [39]. The influence of publication bias should be assessed vis-à-vis a funnel plot in the case that comparable quantitative measures were identified across studies. For all other types of studies, the influence of biases was qualitatively evaluated by the authors, which is a technique previously employed in systematic reviews and indicated as being influential in health policy research [40].

3. Results

3.1 Search results

Based on our review of study databases, we reviewed a total of 88 results. After the initial screening process, including excluding duplicates and reviewing titles/abstracts, we conducted a full-text review of 66 articles for relevance to the study inclusion and exclusion criteria. Subsequently, **46 articles** were deemed eligible for inclusion (See Figures 2 and 3 for study characteristics). Type of articles included research articles, conference papers, book chapters, and case studies, which came from authors in 21 different countries. Notably, the academic literature in health, engineering, and computational sciences addresses the use of technology in different ways based on the 46 articles retrieved and examined. Specifically, searches on IEEE Xplore and ACM Digital Library resulted in studies mainly focused on the technical aspects of existing and emerging technologies used for improving the pharmaceutical supply chain and procurement performance. However, most of these articles lacked specific discussion on the implications of implementing technology for population health and health systems. In contrast, the health literature retrieved in PubMed mainly focused on examining the effectiveness of technologies and their implications for health-care institutions and population health outcomes, though often lacked technical details. Meanwhile, economics and political sciences literature on JSTOR did not yield relevant results.

The major technology types identified in these studies were grouped as follows: (a) e-procurement and open contracting; (b) anti-counterfeiting technology; (c) track-and-trace solutions; (d) blockchain technology; and (e) a broad category for other digital solutions that did not fit into the other categories. The vast majority of retrieved studies focused on evaluation of track-and-trace and anti-counterfeiting technologies and relatively unproven systems, such as blockchain, with fewer articles discussing more established systems, such as e-procurement. A full summary of extracted articles is available in the Supplementary File (See Appendix).

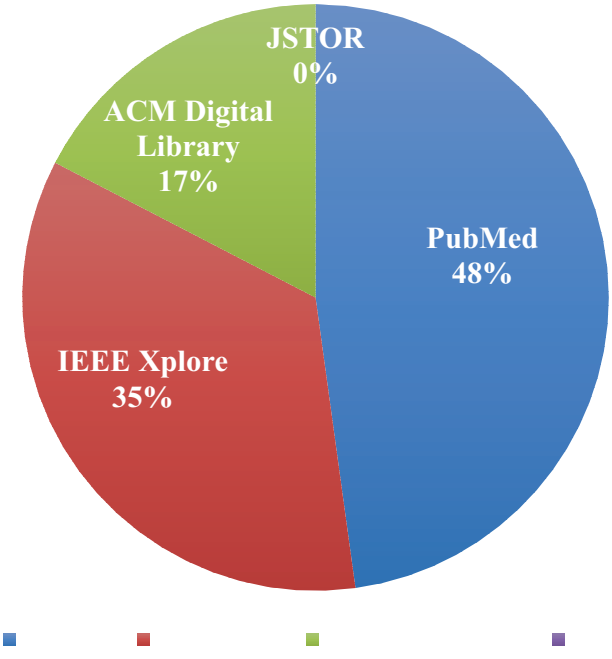

Figure 2. Breakdown of Databases that Indexed Publications Meeting Study Eligibility Criteria

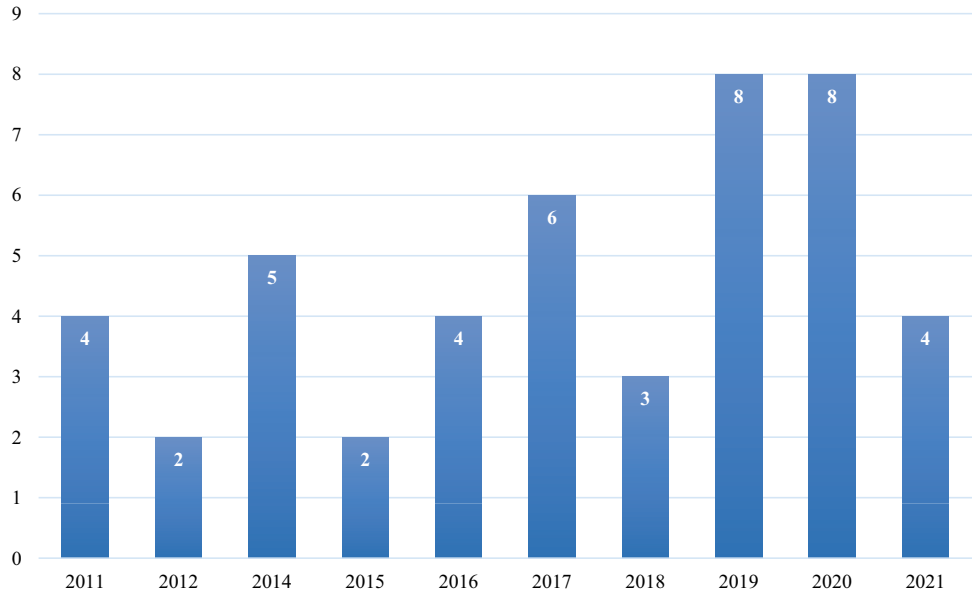

Figure 3. Number of Publications Retrieved from Academic Databases By Year

3.2 Risk of bias

Previous research [40] suggests that several biases may be relevant to health policy research and should be taken into account where applicable, including publication bias [41], surveillance bias [42], context bias [43], and omission bias [44]. However, in the context of our systematic review, it was not possible to employ these conventional bias assessment techniques. More specifically, this review did not detect any RCTs; thus, Cochrane Collaboration's tool for assessing risk of bias was not used. Additionally, studies included in this review did not report quantitative measures associated with outcomes or interventions, and thus, assessing the influence of publication bias was not possible. Nonetheless, consistent with previous studies, it is important to consider that biases may have potentially influenced the overarching findings of this review as follows: (1) there may have been unpublished literature, especially during COVID-19 given it is a recent event, describing the use of digital solutions to promote ACTA in the pharmaceutical supply chain and procurement; and (2) given the sensitive nature of the topic, the pharmaceutical sector and other organizations may not always publish evaluations or reports about using technology to combat corruption as that can potentially reveal internal corruption activities, compliance gaps, or proprietary/confidential methods.

3.3 Technology features

3.3.1 E-procurement and open contracting

E-procurement refers to the use of internet-based technology platforms to procure commodities, including healthcare and pharmaceutical goods [37,45]. More broadly, e-procurement can be described as an end-to-end solution that takes place entirely online, as well as integrates and streamlines the entire procurement process, including search, sourcing, negotiation, ordering, and receipt. Although this form of procurement is relatively new compared to paper-based procurement, advances in internet use, e-procurement software, and cloud-computing have enabled healthcare and pharmaceutical sectors to more readily adopt e-procurement systems [37,46]. The use of e-procurement has also marked a shift from private digital networks, in particular 'Electronic Data Interchange,' to public, internet-based networks. Employing e-procurement solutions has considerable added values and benefits for stakeholders (e.g. bidders, suppliers) involved in the procurement process, including potential cost reduction, competitiveness enhancement, efficient supply chain functions, minimization of corruption risks by creating equal opportunity, optimizing workflow, increasing transparency [26,45–48], and enabling greater automation of procurement processes [37].

Generally, e-procurement systems comprise components that can digitize information and create electronic records for each pharmaceutical procurement phase [37,45], allowing the procurement process to be well documented and more transparent to parties involved. Studies reviewed illustrated that a key advantage of e-procurement is its ability to enable electronic bidding/tendering, where multiple suppliers can upload tenders on web-based platforms and bidders can more easily access health product information (e.g. quality and price) and supplier information (e.g. whether a supplier is reliable) [26], increasing their chances of selecting the best supplier. Other research described automated multi-criteria decision-making frameworks based on the fuzzy expert system in MATLAB to help bidders in selecting the most suitable supplier [49]. Electronic bidding also increases price competition by improving access to information, reducing participation costs for bidders, and allowing procurement agencies to get better prices via open-tender procurement (i.e. suppliers

from across the world can be invited to give quotes for specific products on the market) [26,45,46].

Furthermore, e-procurement enables automation of the procurement and transaction processes, making it both cost and time efficient. Unlike paper-based procurement, there is no paperwork and postage fee involved for sending tender documents, and it also enables faster amendment of documents compared to paper or mail-based updates [45,46]. Internet-based medicine transactions may also reduce transaction costs and improve work efficiency as they can be carried out electronically, which addresses potential human resource constraints [47]. These platforms can also establish secure payment systems, utilize electronic contracts and electronic signature seals, as well as issue digital certificates [50]. Moreover, Miniati et al. examined the use of health technology assessments (HTAs) to evaluate different procurement planning technology approaches, particularly in the context of medical devices in hospital systems [50]. This research highlighted that procurement planning should take into consideration specific "user profiles" (e.g. clinical, economic, technological priorities) to allow health facilities to procure medical devices that are specific to their needs.

Additionally, a few studies noted that e-procurement systems can integrate additional data from other types of digital solutions, such as anti-counterfeiting and ICT technologies, to further optimize the supply chain and procurement processes [37]. For example, patient wristbands with barcodes in combination with scanners and existing software systems can help collect data about type, dosage, and time of administration of medications. Not only do these records aid medical staff in getting the right quantity of the right medication to patients, but they can also help the procurement department identify what the demand of a particular medicine is at a specific hospital ward [50]. As a result, this can reduce wastage and related costs.

Finally, e-procurement in tandem with open contracting initiatives may further improve pharmaceutical supply chain management [26,51]. For example, electronic records retrieved from e-procurement systems can facilitate the process of open contracting, which refers to publicly disclosing and monitoring procurement information, including who the buyer and seller are, what is being purchased and at what price, and information about the expiry of contracts and unsuccessful bids/bidders [51,52]. While a major critique of e-procurement systems has been that governments primarily use supply-side models and do not make information accessible to all stakeholders, the Open Contracting Data Standard (OCDS) attempts to address this challenge by providing a common set of guidelines on how and when to publish data throughout the contract process for goods and services [53]. Specifically, OCDS includes standards for data transparency, from planning (e.g. budgets, procurement plans), tenders (e.g. tender notices, value), award (e.g. bid evaluation, bidder information), contract (signed contract, amendments), to implementation (e.g. payments, progress updates, completion, or termination details) [51,53].

Importantly, several international organizations have implemented features of e-procurement systems, including the UN Global Marketplace [54] and the Global Fund's wambo.org, an online purchasing platform for health commodities that extended its scope to include COVID-19 products to ensure their availability amidst supply shortages and hoarding [55]. Other international organizations have created guidelines on how to adopt these systems, for example, the UNDP e-Tendering: User Guide for Bidders [56]. E-procurement systems have also been implemented domestically in health procurement systems (see Table 2 for examples).

Table 2. Case Studies of E-procurement Systems.

Ukraine's E-procurement System ProZorro
The Ukrainian government implemented ProZorro, a centralized e-procurement system guided by OCDS that made market data publicly available [57]. As a result, over 2,000 health organizations saved an average of 15% on all of their procurement. In particular, by making detailed market data readily available to organizations, the government encouraged greater competition and fairness in bidding for contracts [51].
Bionexo's Purchasing Platform at Benito Menni hospital
In April 2008, Benito Menni hospital near Barcelona implemented Bionexo's purchasing platform to optimize and streamline the processes of managing and purchasing medical and non-medical supplies. This platform enables requests of quotes and the evaluation of suppliers who respond to the requests electronically. Results between June 2008 and April 2010 show that Benito's electronic purchasing platform is cost-efficient, provides access to a wider supplier base, enables an up-to-date, global overview of all products on the market, and simplifies the purchasing process by centralizing it. Notably, this electronic platform also facilitates internal transparency when managing purchases, provides insights on the reasons for product changes, improves traceability of the purchasing process, as well as enables the integration of other digital solutions such as barcodes [46].

3.3.2 Track-and-trace

Several papers described the use of non-digital and digital track-and-trace solutions within the pharmaceutical supply chain, with a majority focusing on Radio-frequency identification (RFID) based technologies [58–63]. Track-and-trace solutions provide visibility into the status of and activities within the pharmaceutical supply chain [58,60,63]. Specifically, track-and-trace methods can provide information about the object of interest, known as the Traceable Resource Unit (TRU), throughout its life cycle via the use of recorded identification [58,64]. Musamih et al. [64] elucidate that the objectives of traceability are twofold: (1) "to track the history of transactions" and (2) "track the real-time position of the TRU." In our review, non-digital track-and-trace techniques included laboratory or field test kits that used various taggants (micro-taggants, chemical, biological, silicon); nuclear quadrupole resonance (NQR) spectroscopy (e.g. using NQR-sensitive elements as extrinsic tags, which can generate unique watermarks); and isotope ratios using laser fluorescence or resonance techniques [58,65].

Existing digital track-and-trace solutions within pharmaceutical supply chain management included generic machine-readable solutions, namely barcodes and Quick Response (QR) codes [60]; wireless communication tools, such as SmartPoints [66]; RFID technologies [36,59–62,67,68]; and electronic pedigree (e-pedigree). Barcodes are commonly used to facilitate tracking of goods throughout the different stages of the pharmaceutical supply chain. A barcode is an optical one-

dimensional label encoded in one direction (horizontally) by modifying the widths and spacings of parallel lines. Although the cost of using barcodes is low, research consistently shows that barcodes are vulnerable to counterfeiting, do not have encryption capabilities, and have restricted data storage capacity and limited ability to track products in real-time [36,60,61,66–69]. In contrast to barcodes, a QR code, an optical two-dimensional label, utilize encoding for greater security and larger data storage capacity because they can store information in two directions (horizontally and vertically) [60]. With the exception of these features, QR codes share similar limitations as one-dimensional barcodes.

Compared to machine-readable solutions (e.g. barcodes and QR codes), wireless communication tools were reported as more effective for track-and-trace purposes. Firstly, wireless sensor networks can be used for real-time monitoring of pharmaceutical products throughout the supply chain, particularly to avoid quality degradation and spoilage during transport and storage [63]. Bijwaard and colleagues [63] described a system called SmartPoints that can enable real-time quality monitoring of perishable goods, such as medicines, using a combination of RFID and wireless mesh networks that can host multiple sensors to detect temperature, humidity levels, and actuators, among other aspects of products, while also configuring each SmartPoint with encryption key(s). In this sense, the SmartPoints system is described as not only improving drug traceability, but also enabling proactive monitoring by detecting weaknesses in the distribution process and increasing consumer safety. Relatedly, Najlae et al. [70] proposed a model to mitigate product expiry issues in the supply chain using a proactive replenishment system.

Specific to digital track-and-trace, many papers focused on RFID-based technology, which is a wireless digital tool that uses electromagnetic fields, in particular, radio waves, to automatically track and identify products that have been affixed with RFID tags [36,69]. Typically, RFID-based technologies comprise three main components at the front end, a tag, reader and antenna, and a database at the back end [61,71]. Yang et al. [60] refer to RFID technologies with this structure as 'integrated circuit (IC)–based RFID,' which they differentiate from chipless RFID on the basis that the latter does not contain microchips with digital data. Unlike barcodes, major advantages of RFID-based technologies include that RFID tags can be read without the need for a direct line of sight, the tags are rewritable and reusable up to a thousand times, the RFID reader can read multiple tags simultaneously, and they can reduce expenses related to lost and stolen equipment [61,68,69,71]. Some authors also highlight that the industry is only able to realize the full benefits of RFID when all stakeholders of the supply chain integrate RFID-based solutions and when there is support from the government and legislation [59,71].

RFID technologies also have several limitations worth noting, including high scanning and communication costs and limited privacy, security, interoperability, and scalability [36,37,67,72]. The performance of the tag may also considerably decrease when tracing products containing a significant amount of metal or liquid due to the RFID signals passing through these materials [61,62].

Table 3. Proposed Solutions to Overcome Limitations of RFID-based Technologies for Track-and-Trace and Anti-counterfeiting Purposes.

Limitation of RFID-based Technology	Proposed Solution
Limited ability for item-level identification	• Catarinucci et al. [62] proposed the use of Ultra-high Frequency (UHF) RFID tags (both near field and far field tags), noting that they are the most promising technology for serialized item-level identification. Notably, the UHF near field tag has demonstrated optimal performance for different drug types even in the presence of liquid and metal which is not achievable by a regular RFID tag.
Low efficiency due to high processing times	• To further improve efficiency, Schapranow et al. [69] proposed an architecture for processing location-based event data of tagged items within a distributed RFID infrastructure to reduce processing time. Specifically, their system incorporated an in-memory computing engine that only loads attributes needed to answer a particular query and stores and retrieves captured electronic product code (EPC) events, resulting in faster response times when querying a specific EPC. • Rahman and Ahamed [73] proposed using batch authentication to improve process efficiency, especially for large-scale applications to detect counterfeit drugs.
High costs and less effective in harsher environments	• Yang et al. [60] proposed the use of chipless RFID tags as they are less costly and more advantageous in harsher environments (e.g. higher temperatures) than the regular IC-based RFID tag.
Poor on-dose authentication*	• Yang et al. [60] described a hybrid tool combining a non-digital and digital technique, known as a QR coded microtaggant, which can be used for on-dose authentication. • Wazid et al. [71] proposed using near field communication (NFC) tags to authenticate medicine dosage forms using mobile phones and secure mutual authentication between the NFC tag and server. While its basic architecture is similar to RFID technology, NFC-based solutions can be more conducive to the mobile environment. Specifically, they require no reader and only need an NFC-enabled mobile device to scan the NFC tag attached to the medicine package, which allows the customer to verify the authenticity or the origin of the drug [71].
Limited security*	• Some studies discussed how to attenuate serious security threats against data transmission (e.g. tag cloning and spoofing, eavesdropping of tag reader communication, impersonation attack, modification attack, replay attack) and protect anonymity. For example, Schapranow et al. [69] suggested using mutual authentication (e.g. one-time passwords) to prevent involvement of unauthorized third parties. • Zanetti et al. [66] proposed a "tailing" method to detect cloned RFID tags in supply chains by using RFID readers to write random values ("tails") to each tag as it travels through the supply chain and subsequently, using a centralized detector to identify cloned tags.

Note: Limitations denoted with are specific to anti-counterfeiting*

Table 4. Case Study for Track-and-trace Technology: Kit Check - Coral Gables Hospital and COVID-19 Case Study 2020.

Kit Check provides automated drug tracking solutions to help hospital pharmacies improve their operational efficiency, increase patient safety, and enhance visibility into the medicines inventory. Pharmacists and technicians can use the original Kit Check comprising a RFID reader, RFID tags attached to medications, and cloud services to check the quality, contents, and age of medications in kits which typically include 150 different drugs that are used in hospitals. This automated tracking solution reportedly reduces manual processing time from 30 minutes to three minutes and, in turn, cuts labor costs at hospitals by $180,000 or more annually [74].
During COVID-19, Coral Gables Hospital in Florida used Kit Check's drug tracking solution to gain insights into medication usage in order to ensure that essential COVID-19 medications were in stock and to keep track of medications that were running low in supply. Specifically, the hospital attached RFID tags to medications that were used for treating COVID-19 symptoms and intubation. This allowed the hospital to automatically record the usage of these medications into the Kit Check system. The Kit Check system provided medical staff with information related to the amount of drug supply available and where medications were located throughout the hospital, as well as allowed them to determine when they needed to use alternative treatments for COVID-19 [76].

To overcome common limitations of RFID-based technologies, several papers proposed changes including having a tag with adequate shape, frequency, size, and reading range (see Tables 3 and 4 for additional examples) [60,62,69,71].

Incorporating many of these track-and-trace principles, the concept of e-pedigree has also emerged as a digital track-and-trace solution. E-pedigree builds an accurate, auditable electronic record to track and trace every step of a pharmaceutical product as it moves through the supply chain, from manufacturer to dispenser [77]. Hence, mandating e-pedigree and track-trace requirements as a form of ensuring integrity of the pharmaceutical supply chain, while also optimizing processes is now being pursued by several countries [58]. These track-and-trace solutions can also extend to more purposeful use as an anti-counterfeiting solution such as detection of substandard and falsified medicines [36].

3.3.3 Anti-counterfeiting technology

Anti-counterfeiting solutions comprised both digital and field-based and/or physical/hardware non-digital tools that were primarily used for drug quality control in the pharmaceutical supply chain. Several articles focused on non-digital anti-counterfeiting strategies including field-based hand-held scanners such as the TruScan Raman spectrometer (e.g. for conducting spot checks) and the United States Food and Drug Administration (FDA) Counterfeit Detection Device 3 (CD3+); portable testing kits, including Global Health Pharma Fund (GPHF) Minilab®; microscopic fingerprinting techniques, such as physical chemical identifiers and nanotechnology/nanoparticles; a chemometric passport approach using NQR spectroscopy; tamper-evident packaging (e.g. breakable cap, flexi-cap, induction sealing, roll-on pilfer-proof screwcap, self-adhesive seal); anti-counterfeit medicines packaging labels using nano- or micro-structured materials; and product serialization (i.e. using unique printed codes to identify medicines) [36,58,60,71,75,78].

Importantly, some of these anti-counterfeiting technologies incorporate mobile and RFID-based solutions as previously discussed, as well as online pharmacy verification. RFID-based technology has been recognized across the pharmaceutical industry as a means of enabling anti-counterfeiting approaches [36,61]. Several studies show that RFID technology is an effective tool to prevent counterfeit drugs from infiltrating the supply chain by improving visibility level in supply chain management [36,61,62,69,71]. However, RFID anti-counterfeiting technology comes with certain security limitations, including that RFID tags do not guarantee the authenticity of a particular drug as they can be cloned [36,37,67,72]. Given the limitations of RFID-based technologies previously outlined, several articles proposed modifications to optimize their use specifically for anti-counterfeiting (see Table 3 for examples) [66,69,71,73].

Relatedly, anti-counterfeiting solutions that focus on e-pedigree mediated by mobile devices are gaining attention. For example, mPedigree and Sproxil developed digital systems that leveraged the growth of mobile phones allowing manufacturing organizations to use labels containing an encrypted code under a scratch off panel on the medicine packaging [71]. While purchasing a medicine, a patient can check if a medicine is legitimate by scratching off the label and texting the encrypted code to the company's system, which responds with a text message stating whether a drug is authentic [71]. With labels on over 500 million medicine packages and its convenience for tracking and authenticating pharmaceutical supply chain data, mPedigree has used its system to detect counterfeit malaria medication [79].

Finally, three studies discussed online store verification techniques to combat sales of illicit drugs via online venues [36,80,81]. Technologies such as website seals, website verification services, and top-level domain names can serve as verification tools for online pharmacies [36]. For example, in the United States, the National Association of Boards of Pharmacy serves as a registry operator of the ".pharmacy" domain to ensure pharmacies who obtain this top-level domain are safe, comply with United States laws, and sell United States FDA-approved medications [36,80]. These digital solutions work in tandem with non-digital solutions, such as educational strategies that aim to equip consumers with the knowledge to identify illicit online pharmacies (e.g. pharmacy personnel can tell consumers to look for the ".pharmacy" domain when purchasing medicine online) and to make them more aware of the dangers of purchasing medications online [36,80]. Other strategies identified in our systematic review were machine learning algorithms and web crawling to better identify and classify illicit online pharmacies through data/text mining and content analysis. For instance, Der et al. [81] identified affiliate programs behind online storefronts, which is a critical step for tracking illicit e-commerce, by extracting features that revealed when Web

Table 5. Blockchain technology case studies.

The Modum Company's Blockchain-based Tracking Solution
The Modum company is a startup based in Zurich, Switzerland that uses a IoT and blockchain-based supply chain logistics solution to assist European companies in complying with the European Commission regulations for pharmaceutical transport. Their digital tracking solution checks if European companies are meeting specific transport standards to ensure the quality of the drugs is maintained until they arrive at the destination. Specifically, Modum leverages the blockchain Ethereum platform to create a drug sharing network and through a smart contract, it checks if the condition of the drug conforms to specific standards during different stages. The system integrates IoT concepts to oversee the condition of drugs [90,91]. If issues are detected during monitoring, the drug will be refused and the control panel will be alerted to take action [83].
IBM Rapid Supplier Connect Solution
Blockchain has also shown promise amidst the COVID-19 pandemic. For instance, IBM developed a blockchain based network, Rapid Supplier Connect, to address the issue of medical equipment shortages by connecting buyers to suppliers outside their traditional supply chain while ensuring integrity via its blockchain-based Trust Your Supplier identity platform [92].

pages linked to the same affiliate program shared a similar underlying structure and subsequently, using those features to profile the websites of illegal online pharmacies and their affiliate networks.

3.3.4 Blockchain technology

The last technology category identified in this review made up a large volume of studies but remains a relatively newer technology solution. This group of articles discussed the potential role for blockchain-based solutions that use distributed ledger technology to optimize the pharmaceutical supply chain and procurement process [37,64,72,82–89] (see Table 5 for examples). Blockchain is an emerging technology type, with its primary popularity in Fintech, cryptocurrency, and non-fungible token (NFT) applications, but has also seen widespread interest for business and private network applications, including from the pharmaceutical sector [86].

Blockchain systems are primarily composed of a distributed ledger that records transactions and is shared and agreed upon by all parties as the sole record of transactions (with agreement on transactions established through a process known as a consensus mechanism); a cryptographic hash function (used to generate a value to cryptographically linked series of "blocks" of data to ensure their security and near immutability); and a series of nodes (e.g. computers in a Peer-to-Peer network) that make up the distributed network that runs the blockchain [89]. In a blockchain, each block can represent a collection of data about a transaction and every new block containing the hash of the former block creates a "blockchain" of timestamped data establishing the agreement, provenance, and finality of the history of a transaction [82,85].

What makes blockchain a promising technology for the healthcare and pharmaceutical sectors is its ability to establish a distributed trust environment and automate processes on the blockchain through the execution of smart contracts (i.e. programs stored on a blockchain that self-execute when certain conditions are met) [87–89]. Blockchain design can be beneficial when parties want to move away from dependence on a centralized authority and decentralize control and management to a peer-to-peer network. Blockchain technology employs different types of consensus protocols (e.g. Proof of Work, Proof of Stake, Proof of Authority, Proof of Elapsed Time, etc.) that ensure mutual consent between all authorized nodes about what data is written to the blockchain, better ensuring data integrity about what is written on a shared ledger [84,87]. Additionally, blockchain can employ the aforementioned smart contracts to manage transactions according to the terms and conditions set out between parties, potentially reducing the need for intermediaries and introducing process improvement and cost savings [64,72,84].

Reflecting this increased interest, blockchain technology has been widely discussed as a potential tool for the pharmaceutical sector to improve supply chain management and pharmaceutical governance [67]. There are several characteristics of blockchain that make it particularly useful for the pharmaceutical system, including decentralization, fault tolerance (i.e. failure of one or more components of the blockchain network does not cause the entire system to fail), and immutability (i.e. the ability of the blockchain ledger to be permanent and maintain an unalterable history of transactions, security, transparency, and traceability) [64,82–85,88,89]. Some specific use cases that have emerged are monitoring and establishing provenance of medicines supply chain transactions, possibly enabling detection of counterfeit medicines, verifying products, detecting fraud and abuse in procurement and claims reimbursement, and enabling saleable returns as well as other regulatory solutions, such as post-market surveillance, addressing medicines shortages, and recall management [37,56,64,72,84,87–89,93]. Most studies in our review underscored that blockchain-based drug traceability solutions could be a critical future tool for safeguarding the pharmaceutical supply chain from counterfeit products, as blockchain can identify the origin of data, as well as track, authenticate, and manage products throughout the supply chain while recording all the necessary information that is viewable to stakeholders operating in the supply chain [37,64,67,82,83,88,89,93–95].

Furthermore, it has been argued that pharmaceutical procurement can be substantially improved by blockchain technology [37,88]. In particular, this technology can create an immutable record of procurement decisions, including procurement pricing, legal tendering requirements, and historical records of supplier performance, all data critical to enable contracting authorities to make procurement decisions and further advance e-government and open procurement initiatives. Ultimately, this could allow bidders to verify potential suppliers and conditions of tenders, which can inform their decision to select the right supplier and enable better fraud detection [37,88]. Other benefits of blockchain include cost and time efficiency that could be enabled by the use of smart contracts that automatically execute the terms and conditions of a request for proposal throughout the various procurement stages [72,87].

Blockchain technology also can integrate existing digital solutions to provide more comprehensive supply chain management [67,83], meaning that it acts as an enabling architecture for other established technologies, many of which were previously described. To illustrate, Alkhoori et al. [87] proposed a blockchain powered smart shipping container for vaccine distribution that has built-in sensors that capture data (e.g. temperature for cold-chain management, GPS location) to monitor products with data sent to the cloud via a real-time exchange mechanism. If a supply chain violation or spoilage is detected, it is registered on the blockchain which uses its peer-to-peer network to prevent any single entity from modifying the record and notifies relevant authorized nodes/stakeholders. Kumar and Tripathi [94] describe a Blockchain approach using encrypted QR code security with Public Keys to improve drug safety from manufacturer to the end-user. Subramanian et al. [96] propose the use of a mobile application, QR codes, cryptocurrency, Internet-of-Things (IoT) devices, and a hybrid blockchain design (e.g. working with both public and private blockchain networks) to enable transparency and better validate medicine distribution to patients while also addressing counterfeits. de Aguiar et al. [83] and Fiorentino et al. [84] show that integrating IoT with distributed ledger technologies can enhance the performance of both technologies in the context of managing the pharmaceutical supply chain. Particularly, the authors state that the security of cryptography and immutability of records can make IoT data more secure, with sensors for IoT devices enabling monitoring of medicines throughout the supply chain and mobile applications making supply chain data more accessible to end-users (e.g. using mobile applications to read bar codes and medicines). Sylim et al. [95] proposed a protocol for a Pharmacosurveillance Blockchain System that uses RFID tags and e-pedigrees as additional data collection sources that could be secured on a blockchain for enhanced supply chain security.

Other studies have evaluated and expanded upon the pros and cons of using different blockchain architectures for pharmaceutical supply chain applications [64,67,72,85], namely public (permissionless, anyone can join and participate), private (permissioned, only allow authorized and invited parties to join), and hybrid blockchains (can include elements of both private and public blockchains, including restriction of certain participation and choosing which data is public or private) [67,88,89,96]. Musamih et al. [64] proposed a blockchain-based solution for drug traceability in the supply chain on the popular Ethereum network and conducted a cost and security analysis, highlighting that their Ethereum-based system was efficient in terms of gas costs (e.g. the unit of cost that Ethereum uses to perform transactions on its network) of smart contract functions and had ample protection against malicious attempts targeting the integrity of transaction records. Uddin et al. [67] conducted a cross-comparison of Ethereum, Hyperledger Fabric (private), and Hyperledger Besu (semi-private) (i.e. Hyperledger is a popular umbrella open-source blockchain architecture and set of tools started by the Linux Foundation) and proposed that the latter two architectures were more beneficial for drug traceability because they allow companies to develop more customized rules, as well as fulfill key requirements and features that include secure communication, identity, and privacy. Finally, Kumiawan et al. [85] evaluated if a Hyperledger-based blockchain system's performance varies depending on the request type and number of clients on the network in the context of carrying out and recording medicine supply transactions and found that blockchain can improve overall throughput of network performance while minimizing latency and reducing computing resource costs.

Despite potential advantages of blockchain adoption for the pharmaceutical supply chain, stakeholders remain hesitant to adopt this relatively unproven technology because of issues related to concerns about having an adequate blockchain-trained workforce needed to fully implement and maintain a blockchain, lack of agreement on the potential architecture and governance of a pharmaceutical blockchain (e.g. private downstream supply chain models vs. multiparty consortium models), concerns about scalability and interoperability with existing supply chain management systems, and legitimate concerns of loss of competitive advantage, unknown costs, and incompatibility with existing laws and regulations [67,82,88,89]. Hence, despite a significant increase in interest and research in this area, the real-world application of blockchain to pharmaceutical supply chain and procurement remains in a stage of maturation.

3.3.5 Other digital solutions

Several other digital solutions that aimed to optimize pharmaceutical supply chain and procurement processes were also identified in our review, including mobile technologies, additive manufacturing (i.e. 3D printing), and other manufacturing technologies (e.g. high throughput screening, automated dispensing cabinets [ADCs]) [48,60,97–105]. Mobile technologies appeared to be among the most mature digital solutions for improving pharmaceutical supply chain management. Mobile technologies identified in this review leveraged mobile phone device platforms, wireless networks, and built-in cameras. For example, Seidman & Atun [48] described a mHealth application to improve data systems or processes to track and monitor drug inventory. Similarly, Nilseng et al. [98] assessed a drug management mobile app with healthcare workers in Tanzania that comprised an inventory management system used for viewing drug stocks and an ordering component for adding a new order or checking a prior one, with respondent participants reporting that they saw potential in the application to improve the drug ordering system and reduce drug stock outs.

To improve stock availability in resource-constrained settings, Ramanujapuram & Akkihal [99] described using a "Bulletin Board" (i.e. an HTML page on a web browser) that digitally captures the needs and availability of medicines and vaccines in real-time from any location, as well as detects abnormal activities (e.g. low stocks, out-of-stock, excess stock) using low-feature and affordable mobile phones, which then broadcasts this information to vendors

and managers who are upstream in the supply chain. An impact study of the "Bulletin Board" conducted in Karnataka, India, showed that vaccine stock availability for nine different vaccines increased to 99% and replenishment responsiveness improved by 64% [99].

Two studies highlighted that 3D printing, an additive manufacturing technology, should be leveraged within the pharmaceutical system due to its multipurpose characteristics [60,100]. 3D printing technologies include stereolithography; direct light processing; continuous liquid interface production; binder jetting; selective laser sintering; and nanoparticle jetting [100]. Awad and colleagues [100] described several opportunities to implement 3D printing in the pharmaceutical supply chain for applications including drug discovery, stock control, dispensing and digital dispensing, and on-demand manufacturing, among other use cases. For example, 3D printing can facilitate the transition of tablet production from being centralized (e.g. mass manufacturing at a warehouse) to decentralized (e.g. within local pharmacies, clinics), which may allow for greater medicine access, as well as personalization of medications while addressing local needs such as acute medicine shortages [100]. Yang et al. [60] highlight that printable electronic device (e.g. RFID tags, temperature sensor, humidity sensor, passive timer) can address the issue of high costs associated with the use of current hardware (e.g. RFID tags) affixed to pharmaceutical products while simultaneously improving pharmaceutical security and product quality.

Other digital-based technologies, such as automated medicine dispensers [102–104], automated prescription fillers [104], and isolators to minimize risk of cross contamination [105], can also improve efficiency and quality of the pharmaceutical distribution system. For example, Phimmasorn and Visitsattapongse [101] proposed an automated prescription drug dispensing machine for use by pharmacists, McCarthy and Ferker [103] focused on optimizing the use of an ADC at a large hospital, and Epstein et al. [102] described a real-time system to enhance the functions of ADCs that capture controlled drug transactions in real-time to reduce reconciliation errors (with an evaluation of its implementation in an Anesthesiology Department finding the reconciliation error rate was reduced from 8.8% to 5.2%). Given the ability of manufacturing technologies to improve pharmaceutical supply chain efficiency and accuracy, authors have argued that these technologies should be leveraged during normal times and not only when issues arise, in order to better prevent the risk of medicine shortages [105].

4. Discussion

Our systematic review conducted a multidisciplinary assessment of digital technologies that have been explored and adopted by the pharmaceutical sector to optimize the pharmaceutical supply chain and procurement process, with an emphasis of assessing whether such technologies address ACTA principles. Among the 46 studies included in our review, surprisingly most focused on emerging blockchain applications, followed by more established track-and-trace and anti-counterfeiting digital solutions (e.g. RFID-based technologies), with fewer studies discussing e-procurement systems. While our findings demonstrate an increase in research of technologies to improve pharmaceutical supply chain and procurement functions at national and international levels, most technologies are currently not being purposefully leveraged to directly address ACTA. Though some articles explicitly incorporated core ACTA mechanisms in the use of e-procurement systems and blockchain technologies, the majority did not reference these important principles, especially anti-corruption (see Table 6). Our findings also illustrate that design and ideation aligning technology features to core global health goals and existing policy frameworks appears to be lacking, necessitating more purposeful engagement to ensure technology is fit-for-purpose for social good and health equity. Notably, while some literature in this review discussed the technology's application to improve health systems by addressing the issue of medical supply shortages, including during COVID-19, most articles lacked tangible application of the technology's ability to measure impact on health outcomes. Below we discuss potential applications of technology to ACTA principles and some future recommendations.

4.1 Applicability of ACTA mechanisms

Anti-corruption "comprises actions taken to prevent, curb, or oppose corruption, and to mitigate its negative impacts" [23]. Most studies in this review did not directly link technology features to promoting anti-corruption efforts, though a few studies described that e-procurement systems can strengthen the governance of the pharmaceutical procurement process [26,37,45]. Specifically, the automation of the procurement process, ranging from communication between multiple stakeholders (e.g. bidders, suppliers) to electronic submissions of bids, enabled by e-procurement systems can reduce corruption risks as it minimizes human intervention, which is

Table 6. Technology Type and Associated ACTA Mechanism(s).

	ACTA Features Directly Linked			
Technology Type	Anti-corruption	Transparency	Accountability	Policy Alignment
e-Procurement Systems	Yes	Yes	Yes	Currently, no specific alignment with policy frameworks.
Blockchain	Yes	Yes	Yes	Mostly incompatible with recent laws and regulations regarding the pharmaceutical supply chain.
Anti-counterfeit	No	Yes	Yes	Compatible with some policies including the *Falsified Medicines Directive* in the European Union.
Track-and-trace	No	Yes	Yes	Compatible with several policies such as the *Drug Supply Chain Security Act (DSCSA)* and *FDA Safety and Innovation Act (FDASIA)* in the United States.

a critical facilitator of corrupt behavior in pharmaceutical procurement [106]. Additionally, the immutable, distributed ledgers in blockchain can be used to build incorruptible payment systems in low- and middle-income countries, where there are large inflows of money into the countries, which presents an opportunity for corruption [89]. Verification technologies affixed to medicine packages that also utilize blockchain technology for further validation can potentially minimize fraud and corruption in the pharmaceutical supply chain by creating a more multimodal trust environment [88]. However, despite their ability to serve as anti-corruption tools, e-procurement, and blockchain technology have primarily used for cost-saving purposes, with most users failing to directly link anti-corruption to enabling cost-savings [37,89]. More specifically, by preventing or detecting fraud throughout the supply chain and, in turn, improving health outcomes, anti-corruption efforts are an effective means for saving money and lives that can generate direct economic and social benefits [37]. As mentioned, nearly USD$500 billion — 7% of global healthcare expenditure — is lost to corruption annually: an amount estimated as sufficient to achieve Universal Health Coverage [107].

Transparency refers, amongst other definitions, to "the degree to which access to government information is available" [108]. Transparency necessitates public disclosure of information to ensure citizens are fully informed about how and why public policy decisions were taken [23,26]. In the context of both pharmaceutical procurement and supply chain, greater transparency can improve access to information and enable better consensus and informed decision-making [26]. Most technologies discussed in this review incorporated a transparency mechanism, though e-procurement and blockchain technologies emphasized its importance. Specifically, e-procurement systems' electronic record-keeping feature and blockchain's distributed immutable ledger technology can facilitate a transparent procurement process by creating audit trails that can be permanently and publicly available; ultimately, minimizing the risk for collusion and bid rigging [26,37,45,67]. For example, electronic documentation can improve subcontractor price visibility, which bidders can use to prevent price gouging, price manipulation, and overpayment [26]. This type of data can help detect corrupt activities (e.g. overpayments, collusion, kickbacks, etc.) within the procurement or supply chain processes by shedding light on any patterns or outliers, a feature highlighted in both e-procurement and blockchain solutions [26,89].

Notably, many of these technology features align with Article 9 of the United Nations Convention against Corruption (UNCAC), which expresses that procurement systems should be built on the principles of "transparency, competition, and objective decision-making" [106,109]. To further enhance transparency of the pharmaceutical procurement process, some studies suggested using e-procurement systems together with open contracting or blockchain [26,37,51]. Several articles that focused on RFID-based technologies, which are widely used for anti-counterfeiting and track-and-trace purposes, mention that RFID can enhance transparency in the pharmaceutical supply chain and, in turn, protect both suppliers and consumers against the growing counterfeiting problem [59,62]. A study on blockchain also highlighted that its integration of RFID technology could further increase transparency of the pharmaceutical supply chain and make it easier to audit, which can improve data resiliency and integrity [98].

Accountability requires institutions and individuals to be responsive

(e.g. explain and justify certain decisions and actions taken) to the public they serve [23,26,108]. While transparency can help identify if there is a potential corruption risk and reveal corrupt activities, accountability must go hand-in-hand with transparency mechanisms because it allows for consequences to be brought forward when corruption is identified. By making data publicly available, e-procurement systems that integrate OCDS principles allow all stakeholders involved across the pharmaceutical supply chain and procurement process to hold each other accountable [26,37]. Likewise, blockchain's near-immutable distributed record, use of consensus mechanisms, and smart contract execution layer also holds potential for stakeholders to be more accountable in a shared trust enviornment [36,64,87]. For example, greater access to procurement and supply chain information can increase compliance with policies/laws by creating audit trails and allowing for public scrutiny of decisions and actions.

4.2 Limitations

This review has a few limitations. First, though the published academic literature was retrieved from four different databases, the literature on this topic was likely incomplete and biased to certain topics and technology development given potential proprietary and confidentiality concerns regarding existing and emerging technology. Future studies should consider augmenting literature reviews with patent and intellectual property searches to better understand the innovation environment. Second, academic literature may not have captured technology adoption activities, particularly to combat corruption in the pharmaceutical sector as some companies may be reluctant to disclose or report their activities or compliance gaps. Third, while studies in the review discussed a breadth of potentially valuable digital tools that could address ACTA principles, most studies did not collect data related to specific ACTA outcomes. Future research should conduct qualitative research with key opinion leaders and greater discussion and engagement with local, national, and international organizations about their expectations for technology development in pharmaceutical governance and ACTA. Another potential limitation of the study was the focus on the pharmaceutical industry within the context of the overall health sector, which may have precluded certain other digital anti-corruption tools (e.g. general whistleblower systems that are not specific to drug procurement or supply chains) and were not examined in this study. General anti-corruption tools

that may be cross-sectorial should be carefully assessed in future studies.

5. Expert opinion

This systematic review updates and expands on prior reviews [23,36,37] while assessing whether technology addresses key ACTA principles. While challenges related to digital technologies' alignment with ACTA remain, it is clear they are critical tools for optimizing the pharmaceutical supply chain and procurement process and minimizing corruption risks. Thus, it is important for governments and policymakers to consider the role of digital solutions when forming new policies and regulations to encourage further investment, development, implementation, and evaluation of these technologies specific to ACTA goals. Results from this study also support the need for more robust stakeholder partnership on purposeful design of technology specific to ACTA. For example,there should be enhanced implementation of whistleblowing mechanisms in digital tools that are specific to the pharmaceutical sector to detect alleged incidents of corruption in the procurement process, especially considering that current policies and procedures governing the pharmaceutical system have not been sufficient for lowering the risk of corruption [110]. This should include appropriate engagement between public sector, private sector, and civil society to jointly develop tools that meet shared goals of ACTA and improve the efficiency, equity, and operation of pharmaceutical supply chains, a topic of elevated importance due to the COVID-19 pandemic. These solutions should also be contextual and culturally appropriate for local needs while taking into account the unique challenges faced by transnational cross-border supply chains, including for public health emergencies.

In response, we recommend a unique governance framework should be advanced by WHO, UNDP, UNCATD, and the UNODC to form a coalition of stakeholders to advance science and technology development specific to ACTA principles. These policy efforts should also integrate HTAs to include formal evaluation of existing and new technology to tackle corruption in the health sector and more specifically, in the pharmaceutical industry given its high-risk and direct impact on health outcomes. Importantly, the surge in cases of corruption and fraud during COVID-19 point to the urgent need to develop and enforce protocols on how to use digital solutions effectively and ethically during public health emergencies. While robust procurement protocols that can mitigate corruption risks exist, they are not specific to the use of digital technologies within the pharmaceutical supply chain and cannot be used during public health crises such as COVID-19. Protocols, such as the Compilation of Venice Commission Opinions and Reports On States of Emergency, should be adapted for the use of digital technologies within the pharmaceutical supply chain and procurement process to ensure that authorities follow best practices and due process in times of crisis [111]. Moreover, Radanliev et al. [34] propose that predictive, preventive, and personalized solutions should be used for pandemic management; wherein, different digital technologies are integrated to develop a solution that is based on individualized needs, as well as is strong in terms of security and privacy. Importantly, although evidence suggests that digital technologies, such as e-procurement systems, track-and-trace, anti-counterfeiting digital solutions, and blockchain, have immense potential to improve transparency and accountability, reduce costs, and potentially minimize corruption risks in the pharmaceutical sector, further research and advocacy is needed to catalyze technology for this critical social good, particularly in the context of ensuring a more equitable global drug supply chain.

Abbreviations

ACM	Association for Computing Machinery
ACTA	Anti-Corruption, Transparency, and Accountability
ADC	Automated Dispensing Cabinet
DLT	Distributed ledger technology
DSCSA	Drug Supply Chain Security Act
E-pedigree	Electronic pedigree
E-procurement	Electronic Procurement
HTAs	Health Technology Assessments
ICT	Information and Communication Technologies
IEEE	Institute of Electrical and Electronics Engineers
IoT	Internet-of-Things
JSTOR	Journal Storage
NFC	Near Field Communication
NFT	Non-fungible token
NGO	Non-governmental Organization
NQR	Nuclear Quadrupole Resonance
OECD	Organisation for Economic Co-operation and Development
OCDS	Open Contracting Data Standard
RFID	Radio-frequency Identification
UHF	Ultra-high Frequency
UN	United Nations
UNCAC	United Nations Convention on against Corruption
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UNODC	United Nations Office on Drugs and Crime
WHO	World Health Organization

Author contributions

G Saeed and TK Mackey contributed to methodology, data curation, formal analysis, writing – original draft. JC Kohler and TK Mackey contributed to supervision, project administration, and funding acquisition. All authors contributing to conceptualization, writing – review and editing of the manuscript.

Data availability

This systematic review is not registered.

Declaration of interest

TK Mackey is the CEO and co-founder of the startup company S-3 Research LLC, which is a company focused on data science solutions to address public health challenges and is currently funded by a National Institutes of Health – National Institute on Drug Abuse Small Business Innovation Research Contract. The company had no input, provided no funding, and otherwise had no involvement in the study. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Funding

This project was funded by the Connaught Global Challenge Award, grant number: 72060095.

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Appendix Supplementary File

Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Uddin et al.2021 [67]Blockchain for drug traceability: Architectures and open challenges.	*Health informatics journal*	Original research article	Drug traceability, supply chain, blockchain architectures, healthcare IT, Hyperledger	Blockchain technology has a strong ability to track and trace transactions. Hyperledger Fabric and Hyperledger Besu are two potential blockchain architectures that may be very effective for dug traceability.
Mackey & Cuomo 2020 [37]An interdisciplinary review of digital technologies to facilitate anti-corruption, transparency and accountability in medicines procurement.	*Global health action*	Peer reviewed article (interdisciplinary review)	Medicines procurement, corruption, technology, e-procurement, transparency, access to medicines	Various digital technologies can be utilized to promote ACTA in the procurement of medicines, including data transfer and/or e-procurement systems, as well as emerging digital solutions such as blockchain and machine learning.Digital technologies such as e-procurement systems show great potential in increasing transparency and accountability, as well as combating corruption but they are largely not being utilized for these purposes
Kohler and Dimancesco 2020 [26]The risk of corruption in public pharmaceutical procurement: how anti-corruption, transparency and accountability measures may reduce this risk.	*Global health action*	Narrative literature review	Procurement practices, good governance, accountability, transparency, health, open contracting, e-procurement	E-procurement systems are time and cost-efficient, as well as help reduce corruption risks in procurement and increase supplier compliance with contracts. For example, electronic bidding can help disseminate information about procurement procedures and results to all stakeholders involved in the procurement process and encourage price competition. E-procurement in tandem with open contracting is more effective in increasing transparency and accountability of the procurement process than either solution alone.
Abu-Elezz et al.2020 [82]The benefits and threats of blockchain technology in healthcare: A scoping review.	*International journal of medical informatics*	Scoping review	Blockchain technology, benefits, threats, healthcare	The traceability feature of blockchain technology has played a critical role in managing the pharmaceutical supply chain. When used, blockchain was reported to prevent incidents of counterfeit drugs given its characteristics of decentralization, immutability, transparency, and traceability.However, issues related to security, privacy, scalability and interoperability may influence the adoption of blockchain across the health sector.
Tan et al.2020 [89]Part 2: Blockchain technology in health care.	*ANZ Journal of Surgery*	Special article	Blockchain, computer security, electronic health records	Blockchain technology has the ability to integrate smart contracts which enable trusted transactions and agreements to be carried out among different, anonymous parties without the need for a central authority. The cryptographic hash linking the blocks of chain also guarantee that the chain is never broken and that each block is immutable; thus, it is near impossible alter past transaction records because that requires the subsequent blocks in the chain to be altered first. Blockchain allows transactions to be traceable and transparent by creating digital, immutable transaction records. This also helps build incorruptible payment systems.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Hertig et al. 2020 [80]Current Threats to Maintaining a Secure Pharmaceutical Supply Chain in an Online World.	*Hospital Pharmacy*	Literature review	Pharmaceuticals, online, quality assurance, safety, counterfeiting	Purchasing medicines online can be associated with a risk of receiving counterfeit medicines. Technology such as the National Association of Boards of Pharmacy's ".pharmacy" initiative, which provides legit online pharmacies with ".pharmacy" top-level domain, is a critical strategy to verify whether an online pharmacy is safe. Health professionals should educate patients about such initiative to help them detect fake online pharmacies.
Krezanoski et al 2019 [104]Comparison of traditional methods versus SAFEcount for filling prescriptions: A pilot study of an innovative pill counting solution in eSwatini	*PloS One*	Comparative study	Automated Dispensing Cabinet, medicines, pill counting	SAFEcount, an inexpensive automated handheld device for counting pills, can improve the accuracy and speed of pill-counting in resource-constrained settings. Among the 2,170 prescriptions counted using both the traditional method and SAFEcount, the proportion of prescription errors with traditional pill counting was 12.6% compared to 4.8% with SAFEcount.
da Silva & de Mattos 2019 [59]Critical Success Factors of a Drug Traceability System for Creating Value in a Pharmaceutical Supply Chain (PSC).	*International journal of environmental research and public health*	Literature review and expert interviews	Drug traceability systems, drugs, pharmaceutical supply chain management	Drug traceability systems are important for preventing fraud and counterfeit medicines from infiltrating the pharmaceutical supply chain. Critical success factors for developing and adopting drug traceability systems can be classified into three distinct categories: technology (the quality of the tracked information and the traceability system), organization (involvement of top management, supplier support, effective communication), and environment (legislation, government support, standards).Digital technologies, such as RFID-based solutions and IoT, have many benefits for supply chain management, including their potential to enhance transparency of the supply chain, as well as improve the authenticity of and access to medicines.
Radanović & Likić 2018 [88]Opportunities for Use of Blockchain Technology in Medicine.	*Applied health economics and health policy*	Current opinion	Blockchain, product authentication, drug supply chain, tracking pharmaceuticals, anti-counterfeiting	Blockchain systems can be used to track pharmaceuticals as they move through the supply chain and authenticate all products. More specifically, blockchain-based verification tags could be used to check the authenticity of the code and the medical product. For example, the company BlockVerify uses blockchain verification tags for anti-counterfeiting purposes.
Awad et al. 2018 [100]Reshaping drug development using 3D printing	*Drug discovery today*	Literature review	Additive manufacturing, 3D printing, rapid prototyping, drug discovery, pharmaceuticals	There is potential for 3D printing to cause a paradigm shift in the pharmaceutical sector in the context of drug development, manufacturing, and supply. 3D printing techniques can be classified into 7 main categories, including vat photopolymerisation, binder jetting, powder bed fusion, material jetting, direct energy deposition, sheet lamination, and material extrusion.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Sylim et al. 2018 [95]Blockchain Technology for Detecting Falsified and Substandard Drugs in Distribution: Pharmaceutical Supply Chain Intervention.	*JMIR research protocols*	Research proposal	Supply and distribution, information systems, counterfeit drugs, blockchain	The proposed pharmacosurveillance blockchain system comprises the blockchain ledger, smart contracts repository, a document repository (for storing pedigrees), and the drug distribution history comprising a list of participants who possessed the drug at any point during the deployment process and information on shipments. RFID tags and pedigrees are integrated for product authentication purposes. Additionally, consumers be able to scan a code printed on the receipt of their purchases to review the drug distribution history.
Mackey & Nayyar 2017 [36]A review of existing and emerging digital technologies to combat the global trade in fake medicines.	*Expert opinion on drug safety*	Literature review	Fake medicines, counterfeit medicines, substandard medicines, falsified medicines, health technology, anti-counterfeit, online pharmacies, supply chain	RFID-based solutions, advanced computational algorithms, online pharmacy verification, and blockchain technology are anti-counterfeiting technologies can be employed to effectively address the issue of counterfeit medicines.
Awodele & Fatoki2017 [75]Anticounterfeiting Strategies of Local Drug Manufacturers in Lagos, Nigeria: Implications for Public Health.	*Journal of population therapeutics and clinical pharmacology*	Descriptive study and experimental study	Anti-counterfeit, drug manufacturing, truscan analysis	Local drug manufacturers in Lagos, Nigeria employed spot checks using truscan analysis, a non-digital anti-counterfeiting strategy, to identify counterfeit malaria medicines. Results showed that antimalarials coming from manufacturing sources and open market passed the truscan spot checks, with an 83% and 78% pass rate respectively. To adequately address the issue of counterfeit medicines, the use of a combination of anti-counterfeiting technologies is recommended.
Panzitta et al. 2017 [105]The strategic relevance of manufacturing technology: An overall quality concept to promote innovation preventing drug shortage	*International journal of pharmaceutics*	Case study	Pharmaceutical technology, manufacturing technology, drug shortage,quality	Manufacturing technology, such as isolators or high containment connection, can improve the quality of the pharmaceutical distribution system by minimizing the risk of cross contamination. In addition to improving drug quality, manufacturing technology can be used to address the issue of drug shortages, which are often linked to poor drug quality or quantity, as well as advance drug discovery and development. Manufacturing technologies are key for the appropriate integration of manufacturing technology to effectively prevent drug shortages.
Seidman & Atun 2017 [][48]Do changes to supply chains and procurement processes yield cost savings and improve availability of pharmaceuticals, vaccines or health products? A systematic review of evidence from low-income and middle-income countries.	*BMJ global health*	Systematic review	Procurement, supply chain management, cost savings, pharmaceuticals, health products	Employing centralized procurement and tendering systems can decrease prices of various health products in low- and middle-income countries, as well as high-income countries.In the context of improving the supply chain management, there is no one-size-fits-all approach rather the context should be taken into account, including the root cause of inefficiencies) when selecting an approach.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
McCarthy & Ferker 2016 [][103]Implementation and optimization of automated dispensing cabinet technology	*American journal of health-system pharmacy: official journal of the American Society of Health-System Pharmacists*	Case study	Automated dispensing cabinet, cost reduction, prevention and control of medicine errors, hospital pharmacy service	The case study of the Pharmacy Department at the Center for Care and Discovery, University of Chicago Medical Centre showed that the implementation of automated dispensing cabinets increased the number and quantity of medications available at the point of care. Specifically, the automated dispensing cabinets improved the average medicine turnaround time as well as reduced the weekly stockout percentage and potential for product expiration. Automated dispensing cabinets were also found to be effective for increasing efficiency and reducing costs.
Epstein et al. 2016 [,102]Controlled Substance Reconciliation Accuracy Improvement Using Near Real-Time Drug Transaction Capture from Automated Dispensing Cabinets	*Anesthesia and analgesia*	Comparative study	Automated dispensing cabinets, controlled substance transactions, near real-time system	The proposed real-time system aims to enhance the functions of automated dispensing cabinets that capture controlled drug transactions in real-time in order to reduce reconciliation error. An evaluation of this system after its implementation in the hospital's Anesthesia Department showed that the controlled substance reconciliation error rate reduced from 8.8% to 5.2%, indicating that this near real-time system accurately captures the transactional data flowing over the hospital network.
Coustasse et al. 2016 [,61]Could the Pharmaceutical Industry Benefit from Full-Scale Adoption of Radio-Frequency Identification (RFID) Technology with New Regulations?	*Perspectives in health information management*	Literature review	RFID, cost savings, pharmaceutical supply chain, e-pedigree	RFID technology is a well-established and promising digital solution to quickly combat counterfeit drugs and ensure compliance with track-and-trace regulations. Most other technologies are not ready for full-scale implementation within the pharmaceutical supply chain.RFID technology can also help reduce costs pertaining to counterfeiting, patient safety, and inefficiencies. In particular, RFID makes the ordering of pharmaceutical products more precise as it can provide real-time information about the inventor, which can reduce the number of drugs that expire and are wasted. After the implementation of RFID asset-tracking technology, Mission Hospital in California reported that lost and stolen devices decreased from 13.8& to 0%, resulting in cost savings of $150,000 to $200,000.83 annually. RFID has also allowed the creation of e-pedigrees, which are auditable electronic documents that provide the distribution history of a drug.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Humphreys 2015 [,45]E-procurement in support of universal health coverage.	*Bulletin of the World Health Organization*	News article	E-procurement, Universal Health Coverage, electronic bidding, open-tender procurement	In efforts to improve procurement transparency, reduce medicine costs, and advance universal health coverage, Kenya is seeking to adopt electronic bidding for essential medicines' contracts. Paper bidding, a primary method used in the country, may not be impactful in terms of reducing bid rigging. Meanwhile, e-procurement increases competition as it reduces the participation cost for bidders, maximizes participation in the procurement process, and minimizes communication among the different bidders. Another major advantage of e-procurement systems is their ability for electronic record-keeping. E-procurement also facilitates the process of open-tender procurement, where suppliers from across the world can be invited to give quotes.Several Latin American countries have embraced e-procurement including Brazil, Chile, Colombia and Paraguay, and Mexico. Additionally, South Africa has utilized e-procurement for some time while Kenya is preparing to adopt this technology.
Nilseng et al. 2014 [,98]A cross-sectional pilot study assessing needs and attitudes to implementation of Information and Communication Technology for rational use of medicines among healthcare staff in rural Tanzania.	*BMC medical informatics and decision making,*	Cross-sectional pilot study	ICT, drug procurement, drug stock outs	Researchers provided a drug management mobile app to health workers in Tanzania and asked them if they found the app to be helpful for drug procurement. The mobile app comprised two parts: an inventory and an ordering part. The inventory part was used for viewing the drug stock, which listed the same drugs as the paper-based order forms used at the health facilities, after incoming or consumed supply. The ordering part was used for adding a new order or checking a past one. All participants reported that the mobile app had potential for drug management and improving the drug ordering system and reducing drug stock outs.
Catarinucci et al.2012 [,62]Enhanced UHF RFID tags for drug tracing.	*Journal of medical systems*	Original research article	Performance evaluation, RFID, supply chain, Ultra-high frequency, item level tracing	While the use of RFID technology is one of the most adequate candidates for item-level traceability, the performance of the RFID tag may considerably decrease when tracing products containing a significant amount of metal or liquid due to the RFID signals passing through these materials.Ultra-high frequency (UHF) RFID tags (both near and far field tags) are a promising alternative for item level tracing across the entire supply chain. The UHF near field tag, in particular, has shown optimal performance for different drug types even in the presence of liquid and metal which is not achievable by a regular RFID tag.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Hidalgo et al. 2011 [,46]E-procurement in hospitals.	*World hospitals and health services: the official journal of the International Hospital Federation*	Case study	E-procurement, purchasing in hospitals, purchasing management	Benito Menni, a psychiatric hospital in Spain implemented an e-procurement system which resulted in several financial and managerial improvements. These improvements included access to a wider supplier base, access to up-to-date global overview of each product on the market, ensuring internal transparency for managing purchases, ability to integrate technologies such as bar codes, streamlining the procurement process, as well as enhancing the traceability of the purchasing process, among others.
IEEE Xplore				
Alkhoori et al. 2021 [,87]Design and Implementation of CryptoCargo: A Blockchain-Powered Smart Shipping Container for Vaccine Distribution	*IEEE Access*	Original research article	Blockchain, IoT, cloud computing, supply chain, smart shipping, ethereum, trust	The proposed blockchain powered smart shipping container aims to provide an enhance supply chain management by providing real-time insights and increasing the visibility of the shipment process.This blockchain powered smart shipping container for vaccine distribution has built-in sensors that capture data (e.g. temperature, GPS location) to monitor products. Subsequently, the data is sent to the blockchain-based cloud system via a real-time exchange mechanism. When a violation is detected, it is registered on the blockchain. The blockchain uses its peer-to-peer network to prevent any single entity from modifying the record and all relevant stakeholders are notified of the violation.Blockchain has potential to ensure the integrity and safety of the items throughout shipment. An evaluation of the container showed that the success rate of transactions was over 99.6% and this solution demonstrated effectiveness in securely tracking the shipment.
Musamih et al. 2021 [,64]A Blockchain-Based Approach for Drug Traceability in Healthcare Supply Chain	*IEEE Access*	Original research article	Blockchain, drug counterfeiting, traceability, healthcare, supply chain, trust, security	Blockchain-based traceability systems ensure data security, transparency, immutability, as well as authenticated transaction records of pharmaceutical drugs. The proposed Ethereum blockchain-based approach leverages smart contracts, as well as decentralized off-chain storage to increase the efficiency of product traceability across the healthcare supply chain.A security and cost analysis of the blockchain-based traceability system found that the cost of utilizing this technique is very minimal and the key security goals of integrity, accountability, authorization, availability, and non-repudiation have a great potential to be achieved given the smart contracts were free from risks that may increase their susceptibility for exploitation and cyber-attacks.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Subramanian et al. 2021 [,96]Crypto Pharmacy – Digital Medicine: A Mobile Application Integrated With Hybrid Blockchain to Tackle the Issues in Pharma Supply Chain	*IEEE Open Journal of the Computer Society*	Original research article	Blockchain, counterfeit medicine, distributed ledger, mobile application, IoT, QR code	The proposed system integrates a mobile application with a hybrid blockchain design (working with both private and public blockchain networks) to identify substandard medicines across the pharmaceutical supply chain. It also leverages QR codes, IoT devices, and cryptocurrency to allow patients to verify the medicines being distributed to them. In this system, each transaction is appended to the blockchain, which is immutable and permanent; thus, the patient can gain confidence that the medicine they are consuming is authentic.
Fiorentino et al. 2020 [,84]Blockchain: Enabling Trust on the Internet of Things	*The Internet of Things: From Data to Insight, Wiley*	Book chapter	Blockchain, IoT, pharmaceutical supply chain management	Integrating blockchain with IoT may improve the performance of both technologies for the purpose of managing the pharmaceutical supply chain. The security of cryptography and immutability of records in blockchain can enhance the security of IoT data, where sensors for IoT devices can allow closer monitoring of medicines throughout the supply chain. IoT devices like mobile applications can improve access to supply chain for end-users (e.g. patients and health professionals can use mobile applications to read bar codes and medicines).The advantages of the trusted and immutability of records is critical for managing the pharmaceutical supply chain.
Kumiawan et al. 2020 [,85]Utilization of the Blockchain Network in The Public Community Health Center Medicine Supply Chain,	*21st Asia-Pacific Network Operations and Management Symposium*	Conference paper	Blockchain, medicine supply chain management, healthcare, Hyperledger fabric, performance analysis	The evaluation of the proposed Hyperledger-based blockchain system's performance in the context of carrying out and recording medicine supply transactions showed that its performance varies depending on the request type and number of clients on the network. The evaluation also showed that blockchain can improve overall throughput of network performance while minimizing latency and reducing computing resource costs. Regardless, blockchain can be utilized to effectively track the transactions throughout the supply chain. Overall, blockchain shows great promise for supply chain management as it ensures immutability, transparency, and decentralization of data.
Masna et al. 2019 [,58]Robust Authentication of Consumables With Extrinsic Tags and Chemical Fingerprinting	*IEEE Access*	Original research article	Nuclear Quadrupole Resonance, authentication, classification, extrinsic tagging, consumables, supply chain	Track-and-trace technologies offer an effective way to obtain information about an object of interest as it moves throughout the supply chain vis-à-vis recorded identification. Non-digital techniques such as nuclear quadrupole resonance (NQR) spectroscopy (e.g. using NQR-sensitive elements as extrinsic tags, which can generate unique watermarks) can also be used for track-and-trace purposes.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Hussain & Al-Junaid 2019[,49]Smart selection of vendors in health services	*2nd Smart Cities Symposium*	Conference paper	Pharmaceutical procurement, Multi-Criteria Decision Making	Automated multi-criteria decision-making frameworks based on the fuzzy expert system in MATLAB may be helpful for the optimization of conflicting objectives that arise during pharmaceutical procurement, and it can also assist bidders in selecting the most suitable supplier.
Shafique et al. 2019 [,68]The Role of Big Data Predictive Analytics and Radio Frequency Identification in the Pharmaceutical Industry	*IEEE Access*	Original research article	Big data predictive analytics, Internet of medical Things (IoMT), RFID, pharmaceutical logistic, supply chain management, supply chain performance	RFID technologies have been widely adopted to enhance the supply chain performance of organizations in the health and pharmaceutical sectors. For example, RFID has been used to track and trace counterfeit and outdated medical products, provision of medical transcriptions, as well as recording admission and discharge of patients. Using RFID-based technologies in combination with big data predictive analytics may further enhance supply chain performance, as RFID and the big data utilization concepts can be implemented to trace products in real-time to improve pharmaceutical organizational performance.
Kumar & Tripathi 2019 [,94]Traceability of counterfeit medicine supply chain through Blockchain.	*11th International Conference on Communication Systems & Networks*	Conference paper	Blockchain, drug safety, medical supply chain	The proposed blockchain approach integrates encrypted QR code security with Public Keys to improve drug safety from manufacturer to the end-user.
Raj et al. 2019 [,72]Anticounterfeiting in Pharmaceutical Supply Chain by establishing Proof of Ownership	*TENCON 2019 - 2019 IEEE Region 10 Conference*	Conference paper	Blockchain, supply chain, pharmaceutical, counterfeit, Hyperledger Fabric	While RFID technology is an effective anti-counterfeit measure for the supply chain, the RFID tags can be cloned easily which threatens the authenticity of the tags. Meanwhile, the proposed permissioned blockchain solution enhances security, authenticity, and visibility of the pharmaceutical supply chain by only allowing trusted parties to join the network, while preventing drug counterfeiting and traceability.
Wazid et al. 2017 [,71]Secure Authentication Scheme for Medicine Anti-Counterfeiting System in IoT Environment	*IEEE Internet of Things Journal*	Original research article	Anti-counterfeiting, authentication, IoT, RFID, near field communication	The proposed solution comprises near field communication (NFC) tags to authenticate medicine dosage forms using mobile phones and secure mutual authentication between the NFC tag and server in order to address the issue of poor on-dose authentication by RFID tags. Though its basic architecture is similar to RFID technology, NFC-based solutions are more conducive to the mobile environment as they require no reader and only need an NFC-enabled mobile device to scan the NFC tag attached to the medicine package, allowing the customer to verify the authenticity or the origin of the drug.
Najlae et al. 2016 [,70]Replenishment triggered by product to eliminate the expiry problem	*2016 3rd International Conference on Logistics Operations Management*	Conference paper	Expiry product, replenishment, smart product, product driven system	The proposed proactive replenishment system may be helpful in addressing product expiry in supply chain management, considering it is a very pertinent problem in the health and pharmaceutical sectors.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Chen et al. 2015 [,78]Authentication of Medicines Using Nuclear Quadrupole Resonance Spectroscopy	*IEEE/ACM Transactions on Computational Biology and Bioinformatics*	Original research article	Medicines authentication, counterfeit medicines, Nuclear Quadrupole Resonance	The unique medicines identifier (i.e. a different reference number for each package) and tamper-evident seals may be helpful for tracking and tracing medicines; however, these approaches focus on authenticating the package rather than the content. Conversely, Nuclear Quadrupole Resonance (NQR) spectroscopy, a non-invasive and non-destructive analytical technique, may be an effective way to verify contents of packaged medicines. Specifically, medicines are verified by comparing their measured spectra with references stored on the barcode of the product or a secure cloud-based database.
Miniati et al. 2014 [,65]Hospital-Based Expert Model for Health Technology Procurement Planning in Hospitals	*Annual International Conference of the IEEE Engineering in Medicine and Biology Society*	Conference paper	Health Technology Assessment, procurement, procurement planning	Health technology assessments (HTAs) were used to evaluate different procurement planning technology approaches, particularly for medical devices in hospital systems. Findings highlighted that procurement planning should take into account user profiles, such as their clinical, economic, and technological priorities, as this can help health facilities procure medical devices that fulfill their needs.
Dun et al. 2011 [,47]The opportunities and challenges of Internet medicine transaction services providers	*International Conference on Multimedia Technology*	Conference paper	Pharmaceutical e-commerce, Internet medicine transaction services provider, opportunity, challenge	Internet-based medicine transactions can used to reduce transaction costs and improve work efficiency because they can be carried out electronically. This ultimately addresses potential issues related to limited human resources.
Unver 2011 [,97]System Architectures Enabling Reconfigurable Laboratory-Automation Systems	*IEEE Transactions on Systems, Man, and Cybernetics, Part C Applications and Reviews*	Original research article	High throughput screening, laboratory automation systems, object-oriented design and development, reconfigurable automation, software patterns	High-throughput screening (HTS) is critical for delivering new drugs in a cost-efficient and quick manner. In particular, the automation feature of HTS makes it an ideal tool for drug discovery by improving efficiency and quality control which helps maintain integrity of the compounds being tested. Importantly, the authors highlight that flexibility and reconfigurability are two key features that facilitate the adoption of expensive equipment and instruments.
ACM Digital Library				
de Aguiar et al. 2020 [][83]A Survey of Blockchain-Based Strategies for Healthcare.	*ACM Computing Surveys*	Survey study	Distributed systems, blockchain, distributed ledger technology, healthcare, medical, survey	Blockchain integrated with IoT can better perform for the purposes of tracking health products throughout the supply chain. In particular, IoT can enable real-time monitoring and data transmission throughout the supply chain, while blockchain enhances the security and reliability of the products across the supply chain.
Phimmasorn & Visitsattapongse 2019 [,101]The Pharmacy Automatically Machine.	*Proceedings of the 2019 11th International Conference on Bioinformatics and Biomedical Technology*	Conference paper	Pharmacy, patient, drug, pharmacists	The proposed Pharmacy Automatically Machine is an automated prescription drug dispensing machine that may potentially help pharmacists order and dispense prescriptions in an easier and faster manner.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Yang et al. 2017 [,60]Hardware-Enabled Pharmaceutical Supply Chain Security.	*ACM Transactions on Design Automation of Electronic Systems*		Pharmaceutical supply chain, security, privacy, traceability, authentication	Integrating RFID-based technologies with other digital and non-digital techniques can help overcome limitations posed by RFID. The proposed hybrid tool called QR coded micro-taggant comprises non-digital and digital components that work together to address the poor on-dose authentication of RFID-based technologies. Additionally, the high costs associated with RFID-based solutions and their inability to operate effectively in harsher environments can potentially be addressed by using chipless RFID tags (i.e. do not contain microchips with digital data)as they are less costly and more advantageous in harsher environments (e.g. higher temperatures) than the regular integrated circuit-based RFID tag.This paper also highlights that printable electronic device may help overcome challenges related to high costs.
Der et al. 2014 [,81]Knock it off: profiling the online storefronts of counterfeit merchandise.	*Proceedings of the 20th ACM SIGKDD international conference on Knowledge discovery and data mining*	Conference paper	Security, web page classification, e-mail spam	Identification of affiliate programs behind online storefronts can potentially be a critical step toward tracking illicit e-commerce. The proposed process for identifying affiliate programs was carried out by extracting features that revealed when Web pages linked to the same affiliate program shared a similar underlying structure. Subsequently, those features were used to profile the websites of illegal online pharmacies and their affiliate networks.
Ramanujapuram & Akkihal 2014 [,99]Improving Performance of Rural Supply Chains Using Mobile Phones: Reducing Information Asymmetry to Improve Stock Availability in Low-resource Environments	*Proceedings of the Fifth ACM Symposium on Computing for Development*	Conference paper	Mobile phone application, bulletin board, supply chain management, information asymmetry, rural supply chain, public health	The proposed "Bulletin Board," a HTML page on a web browser, may potentially help address the issue of stock availability in low resource settings. Specifically, this technology digitally captures the needs and availability of medicines and vaccines in real-time from any location using low-end mobile phones, which are more affordable, and subsequently, broadcasts the acquired information to vendors and managers who are upstream in the supply chain. The "Bulletin Board" detects abnormal activities such as low stocks, out-of-stuck, or excess stock to ensure a balance in supply (availability) and demand (needs). Each activity logged on the Bulletin Board includes the event type (e.g. out-of-stock), event location, the time the activity took place, and a contact number to call. An impact study of the "Bulletin Board" from Karnataka, India found that vaccine stock availability for 9 different vaccines increased to 99% and replenishment responsiveness improved by 64%.

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Reference	Journal	Content Type	Keywords	Key Findings
PubMed				
Rahman & Ahamed 2014 [,73]Efficient detection of counterfeit products in large-scale RFID systems using batch authentication protocols.	*Personal and Ubiquitous Computing*	Original research article	RFID, anti-counterfeiting, supply chain, batch authentication, security	Batch authentication (i.e. authenticating multiple users simultaneously) can improve process efficiency and enhance security, particularly in the context of detecting counterfeits in large-scale RFID systems.
Schapranow et al. 2012 [,69]Costs of authentic pharmaceuticals: research on qualitative and quantitative aspects of enabling anti-counterfeiting in RFID-aided supply chains.	*Personal and Ubiquitous Computing*	Original research article	RFID, pharmaceutical supply chain, anti-counterfeiting	The proposed digital architecture aims to process location-based event data of tagged items within a distributed RFID infrastructure to reduce processing time. This architecture incorporates an in-memory computing engine that only loads attributes needed to answer a particular query and stores and retrieves captured electronic product code (EPC) events, which results in faster response times when querying a specific EPC. Additionally, to address the issue of limited security posed by RFID-based technology, mutual authentication (e.g. one-time passwords) may be beneficial as they prevent involvement of unauthorized third parties.
Bijwaard et al. 2011 [][63]Industry: using dynamic WSNs in smart logistics for fruits and pharmacy.	*Proceedings of the 9th ACM Conference on Embedded Networked Sensor Systems*	Conference paper	Sensor Network, Logistics, RFID	The proposed system called SmartPoints aims to monitor the quality of perishable products, including medicines, in real-time. The system comprises RFID and wireless mesh networks that can host multiple sensors to detect temperature, humidity levels, and actuators, among other aspects of products. Additionally, this system can configure each SmartPoint with encryption key(s). Ultimately, the SmartPoints system improves drug traceability while enabling proactive monitoring by detecting weaknesses in the distribution process and increasing consumer safety.