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Review

Review

Biomedical blockchain with practical implementations and quantitative evaluations: a systematic review

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Abstract

Objective: Blockchain has emerged as a potential data-sharing structure in healthcare because of its decentralization, immutability, and traceability. However, its use in the biomedical domain is yet to be investigated comprehensively, especially from the aspects of implementation and evaluation, by existing blockchain literature reviews. To address this, our review assesses blockchain applications implemented in practice and evaluated with quantitative metrics.

Materials and Methods: This systematic review adapts the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework to review biomedical blockchain papers published by August 2023 from 3 databases. Blockchain application, implementation, and evaluation metrics were collected and summarized.

Results: Following screening, 11 articles were included in this review. Articles spanned a range of biomedical applications including COVID-19 medical data sharing, decentralized internet of things (IoT) data storage, clinical trial management, biomedical certificate storage, electronic health record (EHR) data sharing, and distributed predictive model generation. Only one article demonstrated blockchain deployment at a medical facility.

Discussion: Ethereum was the most common blockchain platform. All but one implementation was developed with private network permissions. Also, 8 articles contained storage speed metrics and 6 contained query speed metrics. However, inconsistencies in presented metrics and the small number of articles included limit technological comparisons with each other.

Conclusion: While blockchain demonstrates feasibility for adoption in healthcare, it is not as popular as currently existing technologies for biomedical data management. Addressing implementation and evaluation factors will better showcase blockchain's practical benefits, enabling blockchain to have a significant impact on the health sector.

Key words: blockchain; biomedical; electronic health records; implementation; evaluation.

Introduction

As the landscape of healthcare and biomedical research continues to evolve, the acquisition and utilization of biomedical data provide unprecedented opportunities for research, personalized care, and the implementation of artificial intelligence (AI) for healthcare applications. As medical and biomedical research centers navigate the increasing volume of data, there also comes the need for robust data-sharing solutions across institutions. However, problems occurring within a conventional, centralized data repository can allow a single point of failure.[1,2] Specifically, traditional solutions rely on the availability of a central server,[3] which could be impacted by network downtime or system maintenance.[4,5] Furthermore, potential alterations of a central audit trail can hinder data handling within the growing healthcare sector.[6–8] Finally, the difficulty in ensuring data provenance could impact the trustworthiness of the sharing framework.[9]

Although there are existing data-managing alternatives to traditional database infrastructures, such as cloud storage,[10,11] distributed databases,[12,13] and gossip algorithms,[14–16] *blockchain*[17,18] has emerged as a promising technology to address the aforementioned challenges. Blockchain is a decentralized data-sharing platform where all participating institutions maintain local copies of a data transaction ledger.[5] Initially popularized as the underlying technology behind cryptocurrencies such as Bitcoin,[17] blockchain has continued to be developed for various applications outside of the financial sector, such as supply chain management, food tracing, and wholesale.[19–25]

In the realm of healthcare and biomedical data sharing, blockchain offers a range of benefits. At its core, blockchain provides a decentralized platform for sharing biomedical data,[5,9,26–28] and thus, avoids the issue of a single point of failure.[1,7,29] Also, the immutability of blockchain reduces the risk of errors, as well as unauthorized data modifications and deletions.[1,2,4–6,9,27,29,30] Moreover, the source of the data stored on the blockchain is verifiable, which increases the confidence of the data-accessing institutions.[1,7,27,29] Additionally,

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smart contracts (ie, computer programs stored and executed on the blockchain) can further streamline processes and reduce the need for intermediaries in data sharing.[1,2,4–7,9,30] With these desirable technical features, blockchain has the potential to facilitate the efficient sharing of biomedical research and trial data for accelerating the development of innovative medical technologies, as well as to foster better-coordinated care among healthcare providers for enhancing patient outcomes and the overall quality of healthcare services. Although blockchain has the potential to transform healthcare, there has yet to be a "killer application" in the biomedical field compared to centralized databases. Despite many biomedical blockchain proposals, many of them were still in the ideation stage.[31] Also, as a new technology, the cost of implementing and maintaining a blockchain-based system could be high, as indicated by the rarity of blockchain developers (only ~2% in a recent online survey[32]). While the potential of blockchain in healthcare and biomedical data sharing is becoming more widely recognized, understanding the practicality of the technology is of interest to biomedical informatics researchers and technicians. Therefore, a review of existing implementations with evaluation results may help provide a high-level overview of the current status of this emerging field.

Several existing studies provide a general survey of research advances regarding medical blockchains but do not focus on implementations or evaluations.[4,27,29,30,33–39] Other reviews focus on more specific aspects such as medical internet of things (IoT) data management,[23,40–42] cloud computing,[22] and fog computing,[40] all while not requiring a more developed implementation and thorough evaluation. However, practical implementation and quantitative evaluation are imperative to understand the real need for blockchain and to provide more insight into the progress of blockchain adaptation in medical applications. In this article we systematically review biomedical blockchains with implementation details and evaluation results.

Objective

In this study, we identify and summarize practically implemented blockchain applications that were evaluated with quantitative performance metrics.

Materials and methods

We adapted the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework to perform this systematic review. We aim to investigate the following research questions in this review:

1) What practical implementations for blockchain technology exist for healthcare and biomedical data sharing?
2) How well do these implementations perform—in simulation or deployment?
3) What limitations for blockchain performance and overall adoption still exist?
4) What are the gaps and future research directions for applying blockchain technology to healthcare?

Study design

Articles about biomedical blockchain applications were first identified through a keyword-based search. After identifying relevant keywords and a specific search query, a search was performed using 4 prominent science database search platforms, PubMed,[43] Scopus,[44] Embase,[45] and Web of Science,[46] adapting each search query to the syntax used by each database's search tool. Citations for all resulting papers were extracted and entered into EndNote, a citation management tool.[47] Following deduplication, 2 screenings were performed based on relevant inclusion and exclusion criteria. Finally, the remaining papers were examined in full, and relevant information from each article was extracted.

Information sources and search strategy

A keyword-based search for academic articles related to blockchain applications in healthcare and biomedical research was performed on August 28, 2023. We summarize our search keywords in Table 1. Articles focusing on blockchain applications needed to include "blockchain" in the title. To limit the scope of our review to biomedical data-related articles only, we required that at least one of the following biomedical keywords or key phrases be present in the title: "healthcare", "medical data", "biomedical data", "electronic health record", "ehr", "electronic medical record", "emr", "patient health record", "phr", "clinical". To focus on papers that had quantitative evaluation metrics for their blockchain implementations, either "experiment" or "results" needed to be present in any field for the database entry of the paper. Lastly, reviews, editorials, and retracted papers were to be excluded, and therefore, we required that none of "review", "editorial", or "retracted" appear in any field of the database entries. Search queries were developed for the following databases: PubMed, Scopus, Embase, and Web of Science. We summarize our search queries in Table 2.

Selection process and eligibility criteria

Following querying, all citations were exported from each database and imported into EndNote to deduplicate this list, and the resulting citations were then exported to a shared sheet for review. The resulting papers were screened twice by 2 authors, RL and YY, independently. Authors discussed any papers they had uncertainty about with a third author, T-TK, to reach a consensus on the final inclusion or exclusion.

Table 1. Keywords and fields that were searched.

Number	Keyword	Field searched	Requirement
1	Blockchain	Title	Required
2	Medical data		One of 2–10 required
3	Biomedical data		
4	Clinical		
5	Electronic health record		
6	Electronic medical record		
7	Patient health record		
8	EHR		
9	EMR		
10	PHR		
11	Results	All fields	One of 11–12 required
12	Experiment		
13	Review		Exclusion required
14	Editorial		
15	Retracted		

Table 2. Search queries for each database.

Database	Search query
PubMed	(blockchain[TI]) AND ((healthcare[TI]) OR (biomedical data[TI]) OR (medical data[TI]) OR (clinical [TI]) OR (electronic health record[TI]) OR (electronic medical record[TI]) OR (patient health record[TI]) OR (ehr[TI]) OR (emr[TI]) OR (phr [TI])) AND ((results) OR (experiment)) NOT (review) NOT (editorial) NOT (retracted)
Scopus	TITLE(blockchain) AND (TITLE(healthcare) OR TITLE("biomedical data") OR TITLE("medical data") OR TITLE(clinical) OR TITLE("electronic health record") OR TITLE("electronic medical record") OR TITLE("patient health record") OR TITLE(ehr) OR TITLE(emr) OR TITLE(phr)) AND (results OR experiment) AND NOT review AND NOT editorial AND NOT retracted
Embase	((blockchain and (healthcare or biomedical data or medical data or clinical or electronic health record or electronic medical record or patient health record or ehr or emr or phr)).ti. and (results or experiment).af.) not review.af. not editorial.af. not retracted.af.
Web of Science	TI=(blockchain) AND TI=(healthcare OR "biomedical data" OR "medical data" OR clinical OR "electronic health record" OR "electronic medical record" OR "patient health record" OR ehr OR emr OR phr) AND ALL=(results OR experiment) NOT ALL=(review OR editorial OR retracted)

First screening

The first screening was performed using strictly the title and abstract. The screening eliminated papers that utilized blockchain to a minimal extent in biomedical and healthcare data-sharing applications. As we wanted to focus on articles that analyzed the blockchain aspect specifically, therefore papers were excluded if they did not include an indication for blockchain evaluation. For example, to determine if a blockchain application was developed, we looked for language similar to "uses a blockchain-based selective sharing mechanism"[48] and "we use … a blockchain implementation to securely transfer the data"[49] within the abstract. To determine if the blockchain was evaluated, we looked for language similar to "we performed experiments on the system to evaluate its performance,"[50] "we develop a prototype … experimental results show,"[51] or "this work develops a comprehensive blockchain framework, with simulations."[52] Abstracts with language indicative of both of these qualities were included through the first screening. Abstracts focusing primarily on other technologies such as the performance of a deep-learning model that uses blockchain, or otherwise suggested a review-style or non-evaluative blockchain article, were excluded.

Second screening

Following the first screening, a second screening was performed using more stringent inclusion and exclusion criteria. This screening was performed using primarily the methods and results section of articles. For an article to be included, the following inclusion criteria were required: a multi-site blockchain implementation, nodes (computers that contribute to creating/maintaining blockchain) running in different physical environments, the hardware and environment specifications needed to be present, the blockchain platform needed to be specified, the blockchain had to be evaluated on real or otherwise publicly available patient health data, and the evaluation needed to use quantitative benchmark metrics. If full access to the article was not available, the article was not written in English, or any of the previously listed inclusion criteria were not present within the article, the article was excluded. In practical healthcare settings, a fully functioning blockchain application would consist of multiple nodes running in separate sites storing real-world health data. While full deployment in the current healthcare or biomedical research system was not a necessary inclusion criterion, implementations needed to incorporate at least 2 nodes running in separate environments with either real or publicly available healthcare or biomedical data to be considered sufficiently viable. Furthermore, the specifics of the platform and the computing resources that were used were required since they provide insight into the security, viability, and performance of the implementation. The blockchain platform was needed to ensure the security of biomedical data. The computing resources (ie, the hardware and cloud platform) are necessary to participate in the creation/viewing of blocks and transactions. Either multiple machines, multiple cloud environments, or multiple Internet Protocol (IP) addresses are required for each node. Computing information helps confirm the status of a blockchain as multi-nodal, as well as provides insight into the diversity of environments and resources used across different institutions for developing blockchain technologies and impacting their performance metrics.

Data collection process, data items, and synthesis of results

For the 11 papers that met all criteria, a sheet was created to extract 20 data items, which are listed in Table 3. Two authors, RL and YY, extracted information from these papers independently and consulted T-TK regarding any disagreements about the articles. The overall screening process and data collection methods were reviewed and guided by a fourth author, LO-M.

Results

Study selection, selected article, and comparison of results

We summarize the search process results in Figure 1. Following the query, a total of 523 papers were identified. After deduplication, 415 papers remained. The distribution of publication years for these 415 papers is displayed in Figure 2. After the first screening, there were 199 papers left. Lastly, after the second screening, 11 papers remained for analysis that fulfilled our inclusion criteria. The publication year distribution of these 11 articles is shown in Figure 3, and the breakdown by country of origin is shown in a map using Google Maps[53] in Figure 4. The full comparison results for the extraction of data items (Table 3) are outlined in Tables 4, 5, 6, and 7. Basic information regarding the article and its specific blockchain application is outlined in Tables 4 and 5. Blockchain implementation details and evaluation metrics are summarized in Tables 6 and 7.

Selected article characteristics

The following is a brief description of the 11 articles included in this review. Basic information collected from each article is summarized in Table 4. The 11 articles spanned a range of

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Table 3. Data items collected from the final set of papers.

Category	Data item	Description
Basic information	Title	Title of the article
	Author	Authors of the article
	Date published	Date when article was published online
	Document type	The type of academic paper that the article is (eg, journal article, conference paper)
	Publication source	Journal or conference where article was published
	DOI	DOI of the article
	Reference	Full citation of the article
Biomedical application	Application	Application of blockchain in the healthcare space
	Blockchain need	Advantage that blockchain provides over currently available technologies
	What type of data is used?	Raw data that blockchain is being applied for
	What is stored on the blockchain?	What specifically is stored on the blockchain—how the data is pre-processed and in what format
	Data source	Source for data that blockchain uses (if available)
Implementation details	Platform	Blockchain platform (eg, Ethereum, Hyperledger Fabric)
	Network permission	Dictates who has access to the blockchain (eg, public, private[a])
	Number of nodes	Number of separate data center blockchain nodes
	On-chain language	Coding language used to develop the blockchain
	Off-chain language(s)	Coding language(s) used to develop non-blockchain components (eg, data handling, user interface)
	GitHub link	GitHub link for code repository
	Hardware	Computing machines used for each node
	Cloud platform	Cloud platform used for each node (if applicable)
Evaluation metrics	Available metrics	Benchmark metrics used to evaluate the blockchain performance

[a] Public blockchains are accessible to everyone (permissionless), while private blockchains only grant permission to an authorized group of people (permissioned).

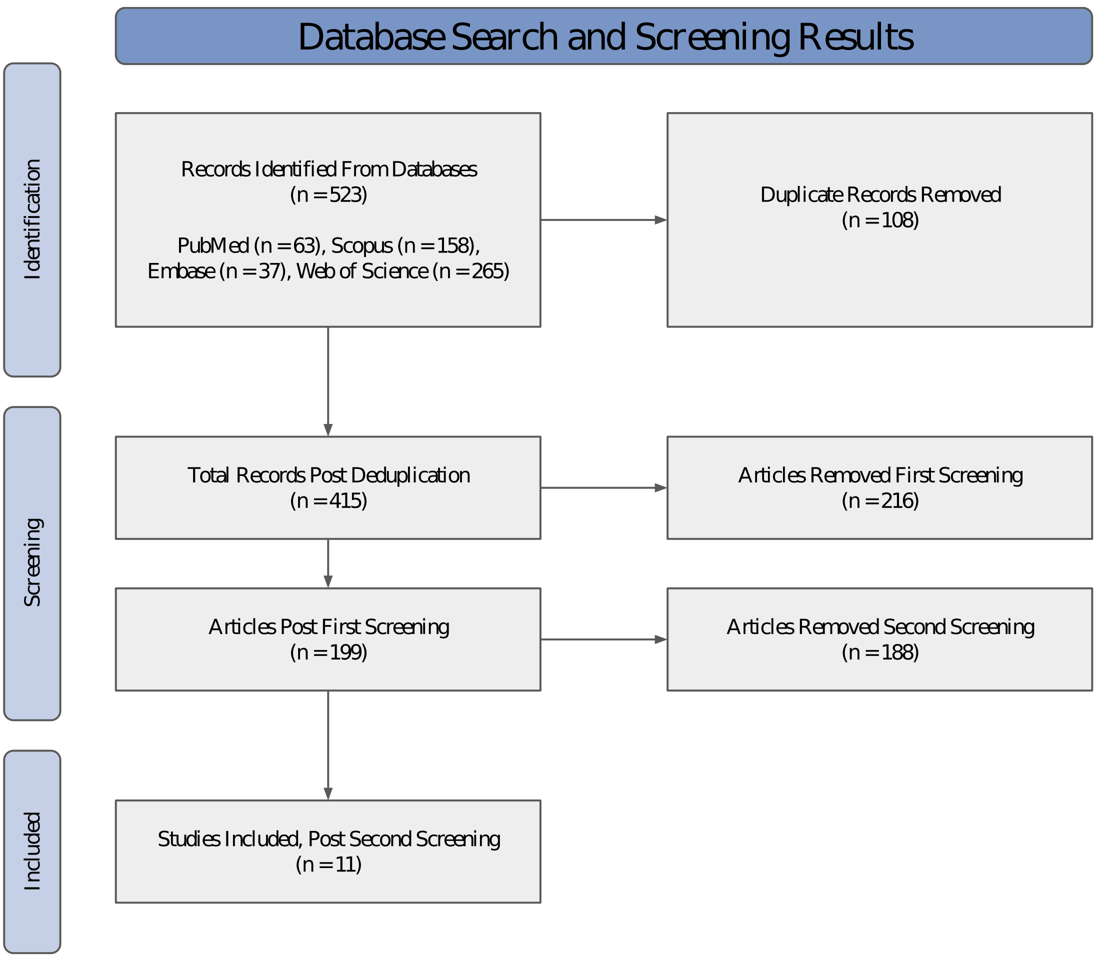

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart-based study selection process.

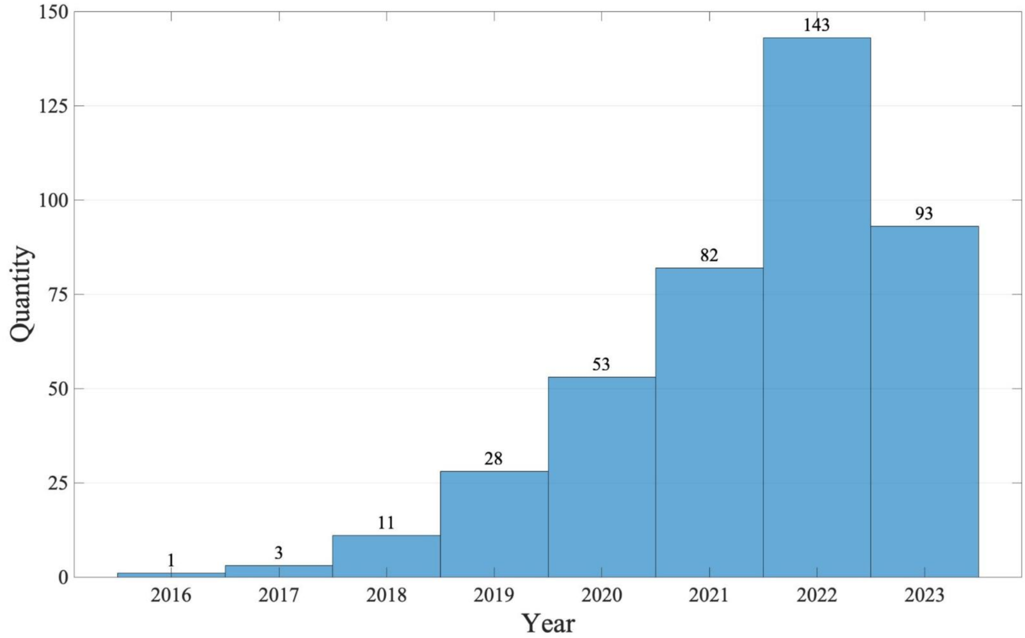

Figure 2. Number of unique articles post querying published per year.

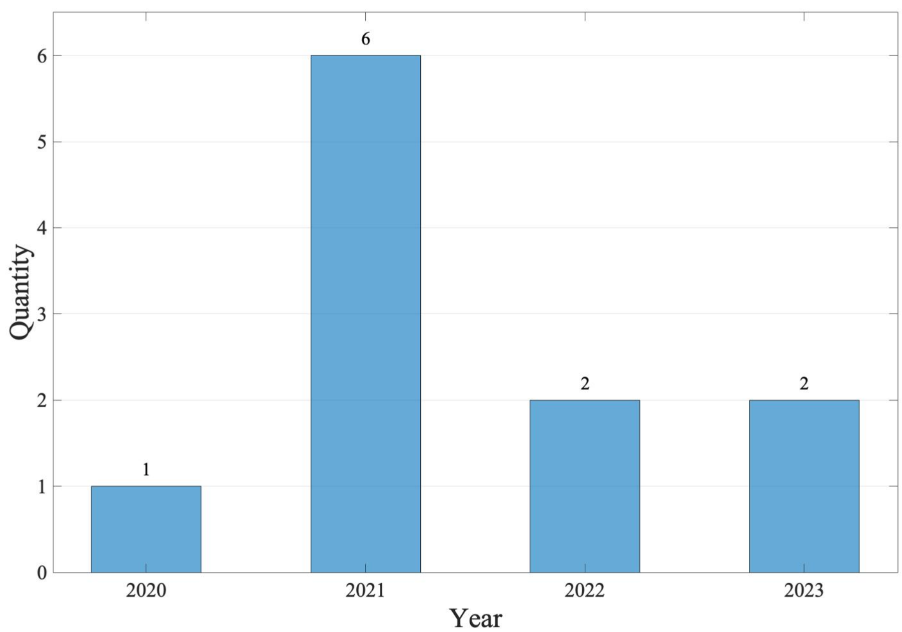

Figure 3. Publication year distribution of 11 articles included for review.

healthcare applications including COVID-19 medical data sharing, decentralized medical IoT data storage, clinical trial management, medical certificate storage, electronic health record (EHR) data sharing, and federated learning. Blockchain was proposed to solve concerns like immutability, availability, security, privacy, auditability, automation, decentralization, and interoperability. Information on the specific blockchain application for the 11 articles is presented in Table 5.

Blockchain implementation specifics, including the development platform, network permission, number of nodes, on- and off-chain programming languages used, GitHub link, hardware specifications, and cloud platform specification are included in Table 6. Speed and other blockchain evaluation metrics used to assess blockchain performance in each article are presented in Table 7. Each of the articles is briefly summarized below:

Article #1 develops a cross-cloud blockchain system (on Amazon, Google, Microsoft clouds) and application for potential use in federated data analysis. The authors apply an Ethereum-based, private blockchain implementation (ie, participating nodes require permission, as opposed to public blockchain which is permissionless) with an off-chain infrastructure developed in Java to store COVID-19 reports, and they evaluate their system using run-time efficiency of contract deployment, network transaction speed,

Maps Data: Google ©2024

Figure 4. Country of origin for 11 included articles plotted on a map using Google Maps.[53]

and accuracy of recorded logs compared to a standard centralized solution. Their implementation achieves proficient deployment, search, and query speeds compared to centralized frameworks. Note that the author list overlaps with the one in this systematic review.

Article #2 uses blockchain and interplanetary file storage (IPFS) as a secure distributed decentralized storage system (DDSS) for medical IoT data, specifically collecting data from hospital biometric sensors. Their private blockchain implementation is developed in Hyperledger Fabric and uses React and Node.js to develop a user API. They evaluate the performance of their DDSS system using performance metrics such as hash function, transaction decoding, encryption, and decryption speeds. Additionally, they benchmark their system using upload, download, and whole system transaction speeds. They then compare the system's performance to previous solutions. Furthermore, they also observe the effect of increasing the number of nodes on performance. Outside the scope of this review, they apply their blockchain implementation for distributed machine learning training for decision-making tasks.

Article #3 implements a clinical trial management system using a Quorum blockchain by JP Morgan. They use the Quorum blockchain for its security, scalability, and efficiency. They evaluate their blockchain implementation using data upload time, data query time, average transaction latency, and transaction speed. Their work demonstrates the feasibility of blockchain use in clinical trial management.

Article #4 creates a blockchain for handling biomedical certificates for training auditing and records. The blockchain stores certificate PDFs and relevant metadata on the chain. Their implementation uses a private Ethereum blockchain and a Java-based user interface. The authors evaluate their implementation primarily through storage speed metrics such as storage time with respect to the number of certificates added, storage time with respect to the number of nodes, and the average time taken to add 100 certificates. They also adapt their private blockchain implementation to a public blockchain to test on the Ropsten test network. They evaluate the time it takes to add one certificate to the public blockchain. Note that the author list overlaps with the one in this systematic review.

Article #5 develops a blockchain-based dynamic access control framework to ensure privacy for electronic medical record (EMR) data sharing. They implement their framework using ChainSQL, a blockchain that supports database functions and leverages the XRP blockchain by Ripple. They evaluate their framework on 200,000 EMRs and test performance by observing how key-value pair speed and transaction delay are affected by write size. Additionally, they record the transactions per second (TPS) for operations like ledger search, historical transaction query, account creation, counting the number of transactions, and contract execution.

Article #6 designs a hybrid edge cloud and blockchain framework for biometric IoT sensor data offloading and sharing. They build their implementation using a private

Table 4. Basic information from included articles.

#	Authors	Title	Date published	Document type	Publication source	DOI	Ref.
1	Kuo et al.	Blockchain-enabled immutable, distributed, and highly available clinical research activity logging system for federated COVID-19 data analysis from multiple institutions	Mar 14, 2023	Journal	*JAMIA*	10.1093/jamia/ocad049	54
2	Egala et al.	Fortified-chain 2.0: intelligent blockchain for decentralized smart healthcare system	Feb 22, 2023	Journal	*IEEE IoT*	10.1109/JIOT.2023.3247452	48
3	Zhuang et al.	Re-engineering a clinical trial management system using blockchain technology: system design, development, and case studies	Jun 27, 2022	Journal	*JMIR*	10.2196/36774	55
4	Tellew and Kuo	CertificateChain: decentralized healthcare training certificate management system using blockchain and smart contracts	Mar 14, 2022	Journal	*JAMIA Open*	10.1093/jamiaopen/ooac019	50
5	Wu et al.	Privacy-preserved electronic medical record exchanging and sharing: a blockchain-based smart healthcare system	Oct 29, 2021	Journal	*IEEE JBHI*	10.1109/JBHI.2021.3123643	51
6	Nguyen et al.	A cooperative architecture of data offloading and sharing for smart healthcare with blockchain	Jun 24, 2021	Conf.	IEEE ICBC	10.1109/ICBC51069.2021.9461063	56
7	Vangipuram et al.	CoviChain: a blockchain based framework for nonrepudiable contact tracing in healthcare cyber-physical systems during pandemic outbreaks	Jun 20, 2021	Journal	*SNCS*	10.1007/s42979-021-00746-x	49
8	Chen et al.	A blockchain-based preserving and sharing system for medical data privacy	May 27, 2021	Journal	*FGCS*	10.1016/j.future.2021.05.023	57
9	Kanagi et al.	Efficient clinical data sharing framework based on blockchain technology	May 12, 2021	Journal	*MIM*	10.1055/s-0041-1727193	58
10	Zhuang et al.	Development of a blockchain framework for virtual clinical trials	Jan 25, 2021	Conf.	AMIA	N/A	52
11	Kuo et al.	EXpectation Propagation LOgistic REgRession on permissioned blockCHAIN (ExplorerChain): decentralized online healthcare/genomics predictive model learning	May 2, 2020	Journal	*JAMIA*	10.1093/jamia/ocaa023	59

Ethereum blockchain. While they evaluate the performance of the other non-blockchain components of their framework, they do not evaluate the blockchain speed performance, instead evaluating the cost of blockchain transactions.

Article #7 develops CoviChain, an IPFS and public blockchain data storage system that stores COVID-19 data hashes in the IPFS and stores hashes of these data hashes (two hashes applied to the COVID-19 data) in the blockchain, protecting the privacy of the stored data. They develop their blockchain using the Ethereum platform and user interface using ReactJS. They test their implementation using the Ropsten Testnet and evaluate it with metrics such as deployment time, mining time, and transaction costs for different file types.

Article #8 implements a blockchain for medical IoT data and patient health records for patients undergoing surgery. The authors develop their blockchain using Hyperledger Fabric. They provide a suite of speed-related metrics, evaluating TPS for varying storage and query request rates, as well as providing times for functions they use in their algorithms, such as encryption, decryption, key generation, and more.

Article #9 deploys a blockchain-based framework in a public hospital outside the US for patients to access their clinical data. The authors develop a private blockchain using the Ethereum platform and develop a decentralized application (DApp) for patients coded in Javascript, HTML, and CSS. They evaluate their framework through metrics such as the time to record a hash and reference pointer, the time to obtain an access token and decrypt and display a report, and the time to generate an access token for use.

Article #10 uses blockchain for virtual clinical trial management and data sharing. The authors implement their framework using the Ethereum platform. They evaluate the performance of their implementation using the time it takes for users to receive data and the time it takes for the system to alert a user when data with abnormal values have been detected by the blockchain system.

Article #11 develops ExplorerChain, a federated learning model developed using a private blockchain to share local machine-learning algorithm parameters. The blockchain was developed using the MultiChain platform and uses Java to integrate the blockchain within the ExplorerChain framework. This framework is

Table 5. Blockchain application data collected from included articles.

#	Application	Blockchain need	What types of data are used?	What is stored on the blockchain?	Data source (if available)
1	COVID-19 federated data analysis	Availability and decentralization for immutable analysis to avoid single-point-of-failure	COVID-19 Structured Query Language (SQL) code, summary statistics, and user activity logs	Log data and files	Private GitHub repository of the Reliable Response Data Discovery for COVID-19 (R2D2) Consortium
2	Medical IoT and EHR data sharing	Privacy and security for medical IoT data streaming and sharing	Medical IoT sensor data	Medical IoT sensor data pre-processed at edge nodes and encrypted	Publicly available EHR data to test DDSS behavior;[60] Heart disease dataset from Cleveland dataset[61]
3	Clinical trials management	Auditability, automation, immutability, and security for conducting and monitoring clinical trials	Trial master file and patient recruitment information	TMF encrypted at IPFS, decryption key stored on chain patient signature and some PHI on chain	User testing (no public data)
4	Biomedical research training certificates	Decentralized training certificate storage	Certificate PDF's and its metadata	PDF of the certificate and structured-formatted metadata	User testing[62]
5	EMR sharing	Privacy and security for EMR data sharing healthcare system	IoT sensor data and EMR	Medical IoT sensor data and EMR pre-processed at edge node and encrypted	SEER incidence data[63]
6	Medical IoT data security	Decentralization and security for medical IoT data sharing	IoT (Biokin Motion Sensor) data and EHR	Encrypted IoT data	Biokin Motion Sensor collected data
7	COVID-19 data hash storage	Decentralization, immutability, calculation efficiency, and security for COVID-19 data streaming	Medical IoT sensor data	Sensor data stored in different file types and encrypted	COVID-19 data folder
8	Anonymous medical data sharing	Anonymity, decentralization, and immutability for medical data sharing	IoT data during surgery	Encrypted IoT data	Unencrypted medical data files
9	Blockchain deployment in hospital for sharing health exam reports	Interoperability, privacy, and security for hospital exam reports	EHR	Encrypted prototype healthcare data (processed data)	Encrypted hash and reference pointer of a health examination report
10	Virtual clinical trials management	Decentralization and security for virtual patient recruitment, engagement, and monitoring	Patient health information (previous and device records) and patient recruitment information	Patient primary visiting history and patient-inputted health measurements	Synthetic data generated from MIMIC-III[64]
11	Federated learning	Decentralization for federated learning to avoid single-point-of-failure	Machine learning models	Machine learning models	Edited myocardial infarction and cancer biomarker data;[65] Length of hospitalization after surgery

evaluated based on iteration time for developing the model. Note that the author list overlaps with the one in this systematic review.

Discussion

Summary of findings

From our results, Ethereum was the most commonly used platform for blockchain development, with 7 out of 11 implementations using Ethereum or an Ethereum-based platform. Other platforms used were Hyperledger Fabric (2 implementations), MultiChain (1 implementation), and Ripple (1 implementation). Of the 7 Ethereum-based implementations, 6 were private blockchains, and 1 was a public blockchain. The remaining 4 non-Ethereum implementations were all private. The prevailing use of private blockchain illustrated that a “circle of trust” could still be important for biomedical blockchain applications. Specific programming language details were not consistently present in all articles. Regarding smart contracts, 5 implementations used the Solidity

Table 6. Blockchain implementation data collected from included articles.

#	Blockchain information			Programming implementation			Node environment information	
	Platform	Network permission	# of nodes	On-chain language	Off-chain language(s)	GitHub link (if available)	Hardware (specification if available)	Cloud platform (if applicable)
1	Ethereum	Private	3	Solidity	Java, Bash	github.com/ChainSQL/chainsqld	3 VMs (2 vCPUs, 8 GB RAM, 100 GB disk)	Microsoft Azure (MA), Google Cloud Platform (GCP), and Amazon Web Services (AWS)
2	Hyperledger Fabric	Private	2	Unspecified smart contract	Javascript, Erlang	N/A	2 network computers (Intel i5 CPU @ 2.8 GHz, 64-bit Ubuntu 16.04 operating system)	N/A
3	Quorum	Private	6	Unspecified smart contract	R	N/A	1 laptop (16 GB of RAM, i5 processor, 1 TB hard drive); 5 Intel NUC machines, (16 GB of RAM, Intel i3 processor, 1.5 TB hard drive)	N/A
4	Ethereum	Private and Public[a]	2[a]	Solidity	Java	github.com/jefftellew/certificate-chain/tree/v1.0	2 VMs	AWS
5	Ripple	Consortium	8	C++	Javascript, Java, SQL	N/A	10 servers (Intel Xeon E5-2620 machine with eight cores, 32 GB RAM, connecting with 10 GB network)	N/A
6	Ethereum	Private	2	Solidity	N/A	N/A	2 VMs (Ubuntu 16.04 LTS)	AWS
7	Ethereum	Public	N/A[a]	Solidity	Javascript	N/A	Edge Intel Core i5-8250U CPU @1.60 GHz	N/A
8	Hyperledger Fabric	Private	7	Unspecified smart contract	N/A	github.com/nanodaemony/MedicalLedger	Host CPU (24 CPUs x Intel Xeon Gold 6136 CPU @ 3.00 GHz); VM (Intel Xeon Gold 6136 CPU @ 3.00 GHz 8 GB memory 20 GB disk); Android tablet (4 GB (memory), 64 GB SD card, Snapdragon 660AIE @ 2.2 GHz)	N/A
9	Ethereum	Private	4	Solidity	Javascript, HTML, CSS	N/A	4 servers (Intel core I3-8100 @3.60 GHz, 8 GB RAM and Ubuntu 16.04 LTS)	N/A
10	Ethereum	Private	6	Unspecified smart contract	N/A	N/A	6 Intel NUC machines	N/A
11	Multichain	Private	2, 4, 8	N/A	Java	github.com/tsungtingkuo/explorerchain	2, 4, 8 VMs (2 Intel Xeon 2.30 GHz CPUs, 8 GB RAM, 100 GB storage)	N/A

[a] Evaluated using Ropsten, a public test blockchain; this was determined to be a multi-node blockchain, but the number of nodes was dynamic and thus not specified.

programming language, and 1 used C++. For off-chain components, such as user interfaces for manual data entry, external data management, or statistical analyses, 4 used Javascript, 3 used Java, and 1 used R. Other programming languages supplemented these 3 for the various purposes listed, but these were the primary active coding languages to tie blockchain implementations to their respective applications. Of the 11 articles included, 8 contained storage speed-related metrics, 6 contained query speed-related metrics, 9 contained other speed-related metrics, and 2 contained other non-speed blockchain-related evaluation metrics.

The limitations outlined in the 11 papers provide valuable insights into the challenges of applying blockchain technology within biomedical healthcare contexts. These limitations include the need for more extensive comparative analyses of blockchain methods with current systems, scalability concerns tied to the size of datasets and users, and user acceptance and adherence. The inconsistency of information

Table 7. Categorization of blockchain-related evaluation metrics in each article.

#	Speed			Other metrics
	Storage	Query	Other	
1	Average recording time per log	Average query search time	Smart contract deployment time	N/A
2	Write transactions per second; update transactions per second; upload speed vs file size	Read transactions per second; download speed vs file size	Hash function time; decoding time; ECC encoding time; ECC decryption time	N/A
3	Data upload time	Data query time	Average latency (block time since last block); transaction per second (scalability)	N/A
4	Speed vs number of certificates added; Speed vs number of certificates added (# of nodes=1, 2); Average time to add 100 certificates (30 trials); Time to add 1 certificate to public blockchain using Ropsten	N/A	N/A	N/A
5	Key-value pairs per second vs write size; Transaction delay vs write size	Search in ledger speed Query speed	Account creation speed; counting number of transactions speed	N/A
6	N/A	N/A	N/A	Smart contract execution cost
7	N/A	N/A	Deploy time for different file types in Ropsten; mining time for different file types	Transaction cost
8	Throughput vs request rate (adding a record)	Throughput vs request rate for querying Medical Data Index Record (MDIR) and Data Usage Record (DUR) (message count=100, block size=512 KB)	Throughput vs request rate for querying Medical Data Index Record (MDIR) and Data Usage Record (DUR) (message count=100, block size=512 KB) Operation overhead (eg, encryption, decryption, etc.); throughput vs request rate for data sharing (message count=100, block size=512 KB) Average response time vs request rate for querying MDIR and DUR (message count=100, block size=512 KB)	N/A
9	Time to record hash and reference pointer to blockchain	Time to obtain access token, and decrypt and display report	Time to generate access token for use	N/A
10	Sponsor data receive time	N/A	Data response time on chain (alert)	N/A
11	N/A	N/A	Iteration time	N/A

provided across these articles makes it difficult to compare the efficacy of blockchain technologies (eg, only discussing smart contract execution costs without reference to other practical speed metrics). Moreover, many methods used in the studies reviewed simplify the handling of complex healthcare and biomedical data, for example, leaving data off-chain and only managing transactions or assuming uniform permissions.

Limitations

This systematic review has some limitations.

First, related to article selection, our review is limited to the data that we could collect from the 11 included articles, reflecting the apparent scarcity of articles with sufficiently developed implementations and evaluation results. The query terms used to select for blockchain-specific articles may have also excluded research that is relevant to this review. The written language and full-text accessibility criteria also reduced the number of considered papers. Additionally, 3 of the 11 articles included authors who are also authors of this systematic review (TTK and LO-M). More relaxed search criteria to cover more studies warrant future investigation.

Second, there was inconsistency in the information included in the articles. Critical information, such as the data used for the study and implementation-specific details, was often missing. We did not reach out to other authors to obtain the missing information.

Third, direct comparison of the results was not possible, due to differences in the evaluation metrics used and, in some cases, the lack of clear mathematical definitions.

Conclusion

While blockchain research has continued to progress within the past decade, the results of this systematic review suggest that further work is needed to motivate widespread blockchain adoption for biomedical applications. Blockchain has continued to demonstrate potential for deployment in the medical sector for applications such as decentralized file management, EHR sharing, IoT data storage and sharing, clinical trials management, and federated learning. Beyond the studies included in this systematic review, the broader challenge in biomedical healthcare blockchain implementations is to bridge the gap between theoretical or simulated concepts and real-world applications. Currently, there is yet to be a major transition to replace traditional databases with blockchain; most studies are still prototypes working in parallel with the centralized solution. For blockchain to be considered a deployable solution, it needs to be shown with higher confidence that it not only solves the problems that plague traditional systems, but also functions at a similar capacity and does not introduce its own debilitating drawbacks. This observation underscores the need for more implemented and evaluated solutions, consideration of more practical aspects during implementation, testing on real-world data, development of standardized evaluation metrics, comprehensive comparison with centralized solutions, and usability testing. These endeavors can endorse the technology, showcase blockchain's practical benefits, and fully harness its potential in the biomedical area. Today, use of blockchain in healthcare lags behind its use in other fields, following the pattern of delayed healthcare adoption of other "novel" technologies, such as relational databases,[66] EHR systems,[67] and predictive models.[68]

In the long run, the adoption of blockchain for improved biomedical data sharing could have a significant impact on the health sector, improving health research via various predictive tools and AI adoption (eg, auditability for performance monitoring, reproducibility), optimizing patient care (eg, facilitating information exchange for operations, volume prediction), enhancing EHR accessibility and privacy/security (eg, providing patients with an accurate log of who accessed each portion of their records for what purpose), and thus improving overall health outcomes. Although there are practical challenges in developing novel blockchain infrastructure, including the need for software engineers with blockchain development experience and for extra computing resources, with blockchain's desirable intrinsic properties, such as decentralization, immutability, ascertainment of data provenance, and smart contract automation, blockchain can serve as a valuable technology for data storage and sharing in the future. Most important, the decentralized aspect of blockchain is especially attractive for use in consortia of institutions, where there is a "trust but verify" approach to ensure that not only patient and institutional privacy is protected while data are shared, but also that no institution or entity exerts dominance over another (eg, a coordinating center that "holds hostage" a whole network of institutions). The transparency of the blockchain, where every authorized user (eg, a member institution or patient) can potentially view all transactions that involve them is a critical feature in this verification. For healthcare institutions, which tend to be very conservative with new technology, adoption of blockchain may take longer than for other industries, especially given constantly evolving underlying software, higher than average salaries for blockchain software engineers, and an unfortunate misconception that blockchain is for cryptocurrency only, and associated with questionable, illegal uses. For informaticians, blockchain technology is fascinating from the standpoint of combining technical and social aspects that must be considered when a "central bank" is not feasible or desired to handle transactions for a precious, highly sensitive asset such as health information. It takes time to understand how it works, why it works, and when it makes sense to deploy it. This systematic review shows some pioneering work in this area and highlights the need for more robust healthcare implementations and evaluations. It will be interesting to see how blockchain use in healthcare and biomedical research grows in the next decade.

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Author contributions

Roger Lacson contributed to conceptualization, data curation, formal analysis, investigation, methodology, visualization, and writing (original draft, review and editing). Yufei Yu contributed to conceptualization, formal analysis, investigation, methodology, validation, and writing (original draft, review and editing). Tsung-Ting Kuo contributed to conceptualization, formal analysis, methodology, supervision, and writing (review and editing). Lucila Ohno-Machado contributed to conceptualization, project administration, supervision, resources, funding acquisition, and writing (review and editing).

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Conflicts of interest

The authors declare no competing interests.

Data availability

No new data were generated or analyzed in support of this research.

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