

# On the exploitation of the blockchain technology in the healthcare sector: a systematic review

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## Abstract

The blockchain is a disruptive technology born in the last few years, which possible applications in different domains are being extensively studied. In this context, healthcare appears to be a very attractive application domain for the blockchain because, due to its characteristics, it can provide the necessary guarantees on the secure processing, sharing and management of sensitive patient data. In this paper, we perform a systematic review of the literature on the adoption of the blockchain technology in healthcare, focusing on applications implemented in real contexts. Our goal is to investigate the current state of the art in this specific field, emphasizing limitations and possible future developments.

Publications extracted from Scopus, PubMed and Web of Science that satisfy some pre-determined search criteria were collected by means of appropriate queries. These papers were analyzed and classified into five main categories, based on the specific sub-domain on which the applications were projected.

The performed analysis highlighted that research activities are currently focused on data security and on the implementation of electronic health records through the Blockchain. On the other hand, some other areas are still under-explored, including that related to IoT or to the implementation of automated diagnosis systems.

## Keywords

Healthcare, Blockchain, Smart Contracts

## 1. Introduction

In 2008, Satoshi Nakamoto proposed a solution to the double spending problem (Satoshi Nakamoto, 2008), that refers to the possibility of spending a digital currency multiple times, due to its inherent ease to be duplicated. Nakamoto's innovative idea was to use the blockchain, and proposed the specific blockchain nowadays known as Bitcoin, together with its native cryptocurrency.

A blockchain is a database of sequential blocks containing transactions, distributed in a peer-to-peer network, where each node of the network owns its own copy. The Bitcoin blockchain, like other blockchains subsequently proposed, is *public*. The main advantages of public blockchains are the transparency, the immutability, the traceability and, therefore, the reliability of the stored data. These characteristics make the blockchain applicable in many contexts besides the storage and verification of cryptocurrency transactions.

One of the most interesting applications of the blockchain technology, on which companies and researchers are focusing their efforts, is that of the healthcare. In this context, research activities are being conducted on the design of proper processes to share data, such as records, reports and images, between healthcare institutions without involving third parties that may possibly alter it (Rakic, 2018). Other lines of research include archiving patient health data (Shahnaz et al. (2019)), enforcing transparency and verifiability of medical experiments (Bell et al., 2018), and supporting the traceability of drugs to prevent counterfeiting issues (Kuo et al., 2017).

In this scenario, the goal of our work is to perform a systematic review of blockchain applications in healthcare that have been proposed in the literature and/or have been actually

23 implemented in real contexts. The motivations of this work live in the need of assessing the  
24 current state of the art, outlining challenges and opportunities, as well limitations of current  
25 solutions, in order to pave the way for future research activities in this field.

26 Existing works in the literature have been selected using the PubMed PubReminer tool<sup>1</sup>,  
27 focusing on Scopus, PubMed, and Web of Science, using *blockchain* as a seed keyword in  
28 the title of the articles. We refined the set of identified paper by eliminating duplicates  
29 (since copies of the same article can be found in different repositories), and by removing  
30 papers without an abstract, a DOI, or keywords provided by the authors. This step was  
31 followed by a manual selection based on the abstracts and/or the full content of the articles.  
32 In particular, a paper has been included in this review if it describes an application in the  
33 healthcare sector that is actually implemented, even through a small prototype. Therefore,  
34 papers describing purely theoretical ideas were excluded. This manual selection led to a  
35 total of 64 articles, that were subsequently been categorized into research areas, in order to  
36 provide researchers with some clues about the challenges, the opportunities and the gaps  
37 for which further research activities are needed. The details of the methodology adopted to  
38 refine the query are reported in Section 4.

39 The rest of the paper is organized as follows: Section 2 provides a brief introduction on the  
40 blockchain technology; in Section 3, we describe the specific challenges arising while adopting  
41 the blockchain for healthcare applications, briefly review existing surveys, and outline the  
42 contribution of this paper; in Section 4, we define the methodology we followed to conduct our  
43 systematic review; in Section 5 we discuss the outcome of our review, specifically focusing on  
44 the identified categories; in Section 6, we outline possible research directions; finally, Section  
45 7 concludes the paper and outline some possible future work.

## 46 2. Background on blockchain technology

47 A blockchain is a database of sequential blocks, stored in multiple decentralized and  
48 independent nodes. Chaining is implemented by injecting some information about a given  
49 block into the following block. More specifically, the hash of the previous block in the chain  
50 is added to the header of the current block (Vujicic et al., 2018). Hashes are strings, of fixed  
51 or variable length, generated by an algorithm (SHA256 in the case of the Bitcoin blockchain)  
52 which goal is to produce a non-reversible bit sequence that uniquely identifies/represents the  
53 entire block data. The peculiarity of hashing algorithms is that the change of a single bit in  
54 the input data results in a significant (and unpredictable) change of the returned hash. The  
55 *immutability* comes specifically from such hash values. Indeed, it is impossible to alter or  
56 tamper any data stored in a previous block, without changing the hashes stored in the next  
57 block, which accordingly would alter the hashes of all the subsequent blocks. Therefore, any  
58 malicious change to the data in a block would be easily detected by the participant nodes of  
59 the blockchain, that would mark such a change as invalid.

60 When someone submits a transaction (see Figure 1 for a graphical overview), it is broad-  
61 casted to the network, and enters into the so-called *transaction pool*, that contains all the  
62 unconfirmed transactions. The validation of transactions is based on the process of the gen-  
63 eration of blocks, called *mining*. This process is performed by special nodes of the network,

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<sup>1</sup><https://hgserver2.amc.nl/cgi-bin/miner/miner2.cgi>

64 called *miners*, and consists of *i*) the selection of a subset of transactions from the transaction  
65 pool; *ii*) the calculation of a *valid* hash value for the block that is being generated; *iii*) the  
66 broadcast of the mined block to the network. Note that the complexity is only in step *ii*),  
67 that is based on the identification of a value to assign to a given variable (called *nonce*) in  
68 the block header, such that the hash value of the obtained block is less than a given threshold  
69 defined by the protocol. This means that miners proceed by performing several attempts,  
70 by varying the value of the nonce, hoping to find a valid hash value. Accordingly, the more  
71 computational power a miner allocates to solving such a cryptographic puzzle, the higher  
72 the probability to find a valid hash and be able to propagate the block to the network. This  
73 process is called Proof-of-Work - PoW (Gervais et al., 2016), and is currently adopted in  
74 Bitcoin, in the current version of Ethereum and in several other blockchains.

75 One may wonder why a miner would spend so many resources to solve such a puzzle and  
76 generate a new block. The answer comes from the incentivization mechanism put in place  
77 in the blockchain, that rewards a given amount of cryptocurrency to miners who succeed  
78 in finding the solution. Note that, due to the decentralized nature of the blockchain, it is  
79 possible that two or more miners find a solution at the same time. In this case, a fork of  
80 the blockchain is created, where different versions of the chain temporarily live simultane-  
81 ously. However, each miner continues working on one of the versions, and once a new block  
82 is broadcasted, the longest chain<sup>2</sup> is considered as the true one by all the nodes, solving  
83 the temporary inconsistency caused by the fork. This strategy, although expensive from a  
84 computational viewpoint, is effective against several kinds of attacks (Gervais et al., 2016).

85 Besides Proof-of-Work consensus algorithm, other approaches have been proposed in  
86 other blockchains, including:

- 87 • Proof of Stake (PoS), that introduces the concept of cryptocurrencies at *stake* and *coin*  
88 *age*, through which the probability that a miner solves the puzzle and creates a new  
89 block depends on the amount of cryptocurrency put at stake, and the amount of time  
90 it is at stake (Cao et al., 2020a). PoS will be adopted by the next version of Ethereum.
- 91 • Delegated Proof of Stake (DPoS) derives from PoS and consists in delegating the right  
92 to create a new block to a subset of representative nodes (Yang et al., 2019). DPoS is  
93 currently implemented in Cardano, EOS, and TRON.
- 94 • Ripple Protocol Consensus Algorithm (RPCA), that is adopted by Ripple and follows  
95 a different approach based on three iterative phases (Chase & MacBrough, 2018).

96 In general, the goal of a consensus protocol is to keep the status of the blockchain consistent  
97 and genuine, avoiding possible attacks, while possibly keeping the needed resources under  
98 control. Of course, if the majority of the computational power (in the case of PoW) is in  
99 the hands of malicious miners, there is still the possibility of compromising the chain (Saad  
100 et al., 2020). This is the motivations behind the need to maximize the decentralization, i.e.,  
101 the number of nodes acting as miners.

102 The above-mentioned characteristics make the blockchain a suitable tool for storing not  
103 only cryptocurrency transactions, but general-purpose data, without the need of a trusted

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<sup>2</sup>This approach is adopted by Bitcoin, but other criteria can generally be used.

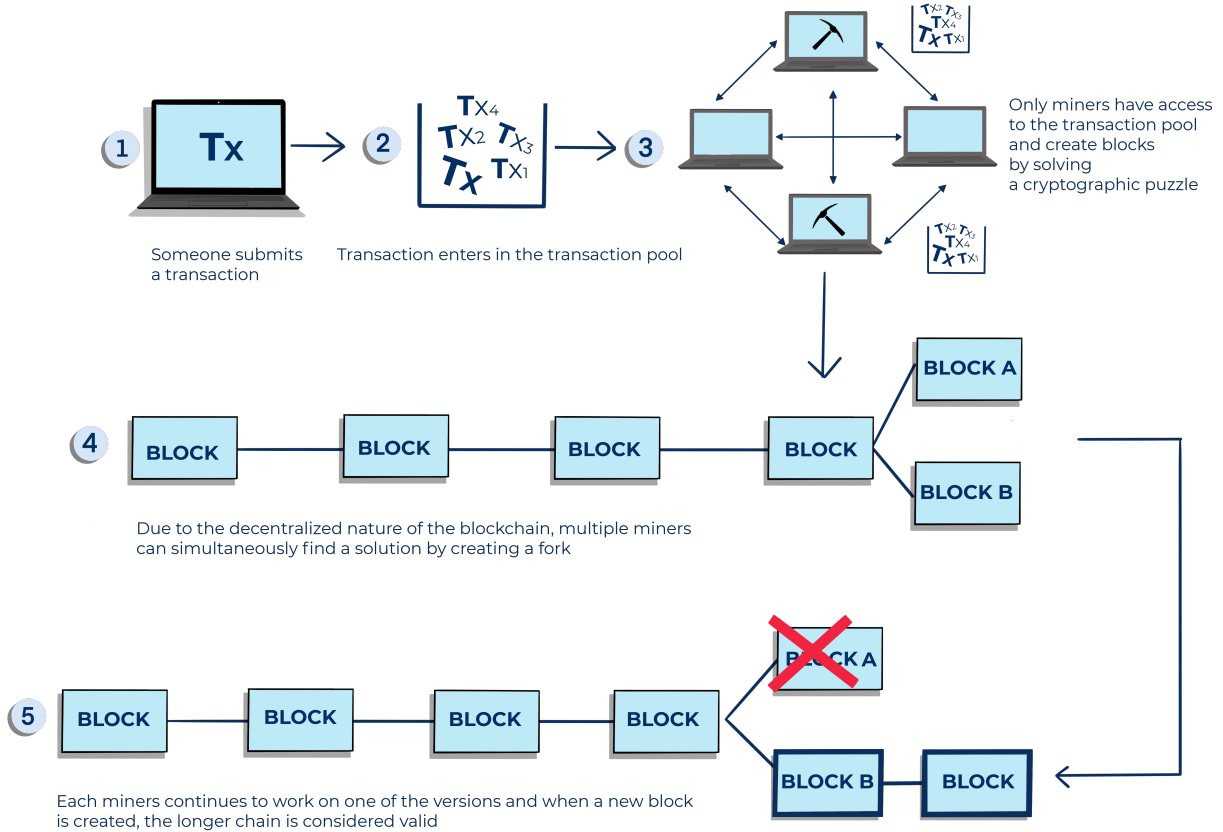


Figure 1: Graphical representation of the general workflow followed to mine new blocks in Bitcoin.

104 third party, and with strong guarantees in terms of immutability and transparency. This  
 105 led other blockchain developers to also focus research and development activities on ad-  
 106 vanced mechanisms to persist data and execute code, through the so-called *smart contracts*  
 107 introduced in Ethereum.

108 A smart contract is a collection of functions and data, that define its state, residing at  
 109 a specific address on the blockchain. In Ethereum, smart contracts represent a specific type  
 110 of account, with its own balance (in terms of amount of cryptocurrency - ETH), which can  
 111 also send transactions over the network. However, differently from standard accounts, called  
 112 Externally Owned Accounts (EOAs), they are not controlled or owned by any user, but act  
 113 autonomously as they have initially been programmed to. Their functions can be called  
 114 through a transaction starting from an EOA, or by other smart contracts, provided that the  
 115 initial trigger comes from an EOA. Smart contracts can define rules and authorizations, and  
 116 store data in a decentralized manner. The interaction with them is irreversible.

117 Note that each interaction with the blockchain, both in terms of cryptocurrency transfers  
 118 and in terms of invocations of smart contract functions, requires a fee (in cryptocurrencies)  
 119 to be paid to miners, which depend on the complexity of the operations performed and on  
 120 the amount of data stored/accessed. For this reason, the storage of large amount of data  
 121 (e.g., images, videos, large textual documents, etc.) on the blockchain is discouraged, and

122 existing solutions generally rely on either centralized/hybrid architectures, or on specific  
123 decentralized file systems, like the InterPlanetary File System (IPFS)<sup>3</sup>. IPFS provides a  
124 decentralized mean for storing and accessing data, enabling the possibility to download them  
125 from multiple locations that are not managed by a single organization. It also improves the  
126 resiliency, by distributing data worldwide in multiple nodes owned by multiple entities and  
127 individuals. On the contrary, attacks to specific servers of an organization, or accidents (e.g.,  
128 a fire in a datacenter), may easily compromise centralized data. IPFS also makes censorship  
129 actions harder to be applied, since data from IPFS can come from multiple locations. In  
130 general, IPFS promotes the possibility to make data permanently available, without the  
131 control of a centralized authority. This characteristic made it the most adopted file system  
132 for managing large amounts of data in combination with blockchain-based solutions, also in  
133 the context of health data.

134 Another important peculiarity of the blockchain is the possibility of freely taking part to  
135 the network: anybody can act as a simple node or as a miner, submit transactions, or read  
136 the full history of past transactions, provided that the performed operation conforms to the  
137 protocol. This characteristic is specific of the so-called *public* (or *permissionless*) blockchains,  
138 like Bitcoin and Ethereum. Note that public blockchains may not be the right solution for all  
139 the application domains. This is the case of health data, which, in most cases, are personal  
140 and sensitive, and need to be protected and accessed selectively. Therefore, *permissioned*  
141 blockchains have been proposed, starting from (the permissioned version of) Ethereum and  
142 Hyperledger Fabric. Among permissioned blockchains, we can mainly distinguish two sub-  
143 categories, namely, *private* and *consortium* blockchains. Private blockchains, also known  
144 as *managed* blockchains, are controlled by a single organization, which decides who can  
145 act as a node, possibly granting different authorizations. On the other hand, consortium  
146 blockchains are governed by a group of organizations, rather than one single entity. Con-  
147 sortium blockchains, therefore, are more decentralized than private blockchains, resulting in  
148 higher levels of security. However, setting up consortiums can be problematic because of the  
149 initial required cooperation and trust among the participants.

150 Of course, different hybrid variants of the mentioned types of blockchain are possible,  
151 as well as hybrid architectures that put together a private/consortium blockchain with a  
152 public blockchain, to identify the best trade-off between data privacy/protection and secu-  
153 rity/transparency, according to the application scenario at hand.

154

### 155 3. Challenges and contributions

156 In this section, we briefly discuss the challenges raised by the adoption of the blockchain  
157 technology in healthcare. Indeed, although several advantages can be provided by the  
158 blockchain technology to different application scenarios in healthcare, mainly due to its inher-  
159 ent reliability, verifiability, and robustness to tampering, it also introduces some criticisms.  
160 Among them, the first aspect to consider is the fact that data related to health are gener-  
161 ally personal, and possibly sensitive, which introduces additional challenges in terms of data

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<sup>3</sup><https://ipfs.io/>

162 protection and security. In general, data protection regulations, like the General Data Pro-  
163 tection Regulation (GDPR), are considered not fully compatible with public blockchains<sup>4</sup>,  
164 mainly because of the impossibility to guarantee the right to be forgotten. Therefore, as  
165 mentioned in the previous section, the adoption of private/consortium blockchains or hybrid  
166 architectures are being considered the right solution. This is the motivation for which most  
167 of the works that we will present in Section 4 fall in this category.

168 The adoption of the blockchain may also introduce inefficiencies in terms of costs and  
169 delays. Indeed, while centralized systems may easily (and cheaply) perform complex data  
170 consistency checks, perform security checks, store large amounts of data, and provide near  
171 real-time responses, the adoption of the blockchain introduces the need to properly check for  
172 access authorization in a decentralized manner, as well as storage limitations and latencies,  
173 due to the block validation process. Moreover, as mentioned in Section 2, complex trans-  
174 actions may be expensive in terms of miners' fee (in cryptocurrencies), making the whole  
175 technology inapplicable in some contexts due to the unacceptable increases of costs.

176 As a result, the research activities on the adoption of the blockchain in the healthcare  
177 sector mainly focused on addressing the above-mentioned challenges. Such challenges have  
178 also been considered in other surveys that reviewed existing approaches. A relevant example  
179 is the survey by Agbo et al. (2019), where the authors adopted a generic query to select  
180 publications including keywords such as *blockchain*, *ledger* or *medic*, without specifically  
181 focusing on works presenting implemented solutions. Agbo et al. (2019) classified blockchain  
182 applications in healthcare according to different use cases, focusing on commonalities and  
183 differences among the existing approaches, without providing specific details about them.  
184 Together with the challenges related to the limited speed and scalability, mainly due to  
185 the large amount of involved data and the need for short response times, the authors also  
186 emphasized an additional issue, namely, the lack of interoperability, as there is no standard  
187 for the development of blockchain-based applications for healthcare.

188 Another relevant survey is the work by Chukwu & Garg (2020). Similarly to the survey  
189 by Agbo et al. (2019), the query used to select publications was very generic and without a  
190 specific focus on available implementations. The authors analyzed the selected works along  
191 three different viewpoints, namely:

- 192 • *bibliometric distribution*, i.e., how many works have been published for each type,  
193 where the considered types include, for example, studies proposing frameworks, studies  
194 discussing prototyping models, or studies implementing real applications;
- 195 • *functional distribution*, i.e., the use case considered in the publication, such as the  
196 management of electronic medical records, or access control with identity management;
- 197 • *technical analysis*, performed only on works actually proposing prototypes and imple-  
198 mentations, which focused on the categorization of technical aspects, such as architec-  
199 tures, blockchain platforms, storage schemes, and consensus algorithms.

200 As stated by the authors, papers proposing models without a working prototype or im-  
201 plementation account for 2/3 of the total number of selected papers. Also in this survey,

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<sup>4</sup>[https://www.cnil.fr/sites/default/files/atoms/files/blockchain\\_en.pdf](https://www.cnil.fr/sites/default/files/atoms/files/blockchain_en.pdf)

202 communication, scalability and speed issues are emphasized as strong limitations coming  
203 from the adoption of the blockchain.

204 Finally, it is worth mentioning the recent survey by Tandon et al. (2020). The authors  
205 used the same search query adopted by Agbo et al. (2019), but did not follow the PRISMA  
206 methodology like the previously mentioned surveys. On the contrary, the authors adopted  
207 specific selection criteria to determine quality, relevance and robustness (Webster & Watson,  
208 2002), while a meta-ethnographic approach (Noblit & Hare, 1988) was used to review and  
209 summarize the studies that qualified for inclusion. Overall, four major families were iden-  
210 tified: *i*) conceptual evolution, *ii*) technological advancements (in terms of faced technical  
211 challenges, and developed applications), *iii*) efficiency enhancement, and *iv*) data manage-  
212 ment, including data security and privacy.

213 As already mentioned, existing surveys did not specifically focused on actually imple-  
214 mented solutions, and mostly collected quantitative statistics along different dimensions of  
215 analysis, without providing details on each specific work. Although this strategy may provide  
216 a wide overview, it does not allow the reader to focus on ready-to-use (or at least prototyped)  
217 solutions. In this respect, in this paper, we provide the following contributions:

- 218 • we focus on actually available implementations of blockchain solutions for healthcare;
- 219 • we describe the selected publications, providing a clear idea about the contribution  
220 they provide to solve typical challenges;
- 221 • based on the implemented solutions, as well as on their advantages and limitations, we  
222 outline additional research directions.

## 223 4. Methodology

224 We conducted a systematic review of major applications of blockchain technologies in  
225 healthcare by performing a set of queries on 3 different repositories, i.e., Pubmed, Web  
226 Science and Scopus. We performed the queries in July 2022, and adopted the well-established  
227 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement  
228 (Moher et al., 2009). In the following, we briefly describe the main steps that we followed,  
229 according to the PRISMA statement.

230 **Identification.** In order to build a collection of papers to consider, it is first necessary  
231 to identify the keywords to define the search query.

232 At this purpose, we adopted the PubMed PubReminer tool<sup>1</sup> by entering the term *blockchain*  
233 as the first word in the title of the articles to be retrieved. The tool returned a total of 353  
234 results, together with a list of the most frequently used words in the abstracts of Pubmed  
235 publications, in descending order of occurrence. This list was used to identify additional  
236 keywords to refine the query, avoiding general terms like *provide* or *paper*. Specifically, we  
237 required the presence of the words *application*, *develop* or *system* (and their variants) to  
238 focus on paper discussing actual implementations of blockchain technologies, and added the  
239 condition of the presence of at least one of the keywords *clinical*, *doctor*, *patient* and *health*  
240 (and their variants), to narrow down the search to the healthcare sector. No time-based filter  
241 was imposed on the query, since the blockchain technology has received a huge attention only



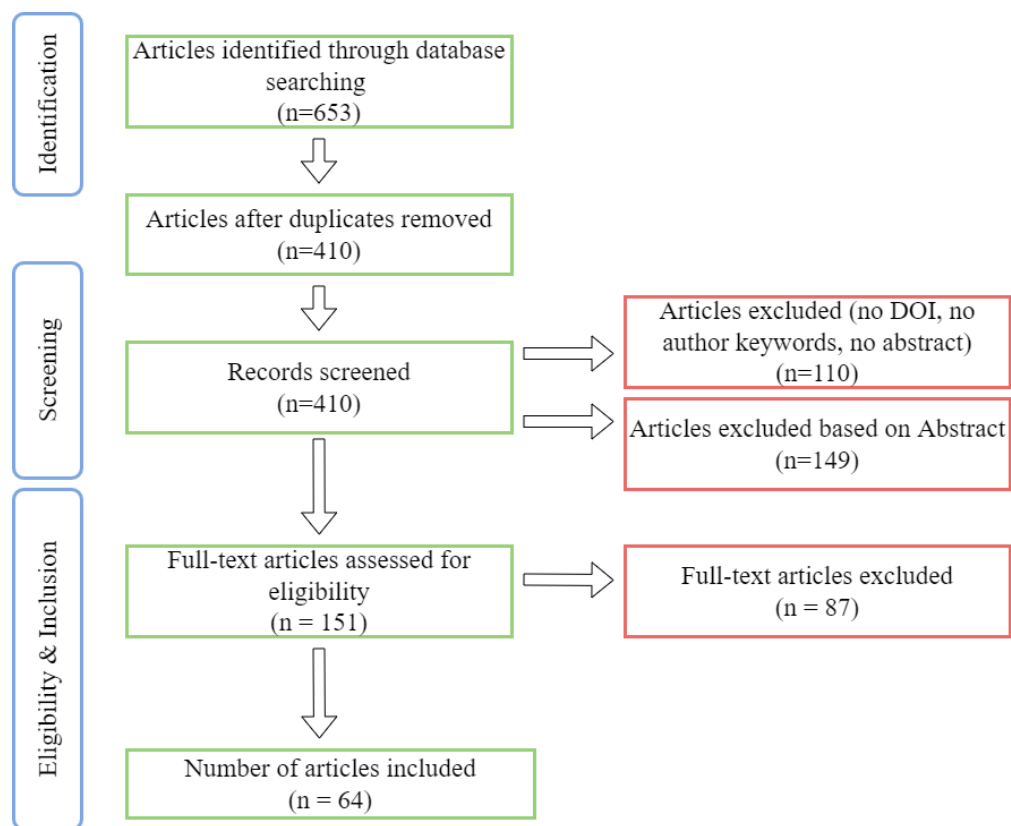


Figure 2: The followed PRISMA flow diagram.

242 recently. These conditions resulted in the following query, written according to the query  
 243 language used by Scopus:

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244 TITLE (blockchain AND (application OR develop OR system) AND ((clinic OR
245 clinical OR clinically OR clinics) OR (medic OR medical) OR (patient OR
246 patients) OR health OR healthcare)) AND (LIMIT-TO (LANGUAGE, "English"))
  
```

247 The query returned 479 papers from Scopus, 128 from Web of Science and 46 papers from  
 248 PubMed, for a total of 653 records. We finally removed 243 duplicate records, leading to a  
 249 total of 410 articles belonging to the initial database.

250 **Screening.** Starting from the 410 selected articles, a first screening step was performed  
 251 by excluding the documents that did not contain the basic necessary information to perform  
 252 a descriptive analysis, such as the abstract (12 records excluded), the author’s keywords  
 253 (67 records excluded) and the DOI (31 documents excluded), resulting in 300 articles. The  
 254 second step was performed through a critical reading of the abstracts. Specifically, we ex-  
 255 cluded papers describing conceptual models, protocols, or algorithms for which there was no  
 256 contextual implementation, even through prototypes. Additionally, articles that focus only  
 257 on the implementation of user interfaces were discarded. At the end of both the screening  
 258 steps, we obtained 151 eligible articles.

259 **Eligibility & Inclusion.** Finally, we critically read all eligible papers, and screened  
 260 out 87 additional records. The adopted criteria are basically the same as those adopted in

261 Screening phase, but applied on the entire text of the publication. At the end of the whole  
 262 process, a final database consisting of 64 articles was obtained.

263 In Figures 3, 4 and 5 we graphically depict some basic statistics related to three main as-  
 264 pects of the selected papers: the adopted blockchain or tool (based on an existing blockchain),  
 265 the consensus algorithm, and the blockchain type.

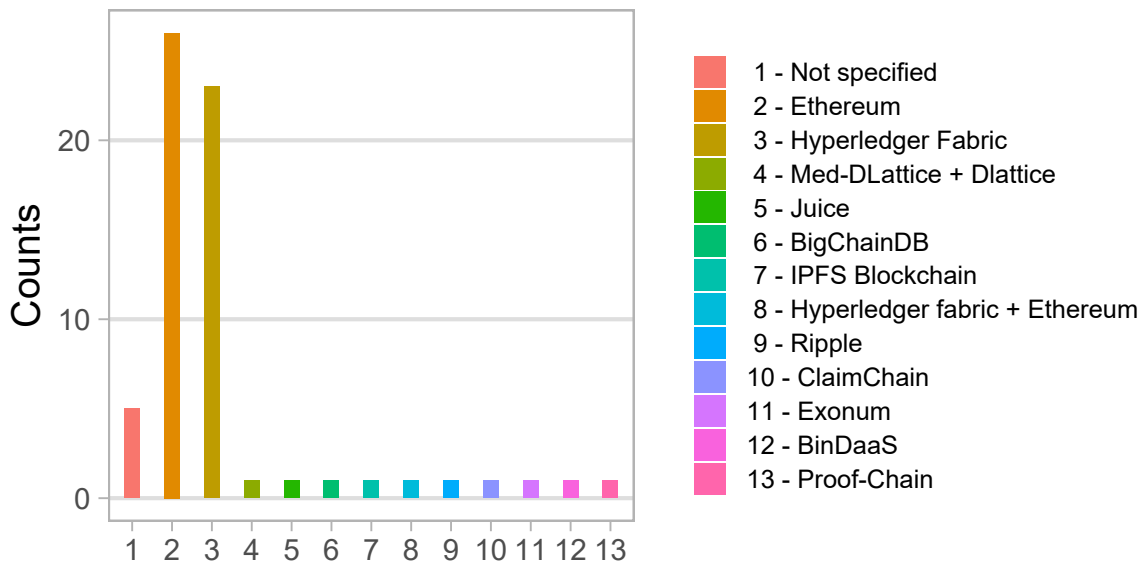


Figure 3: Number of selected papers for each blockchain or blockchain platform.

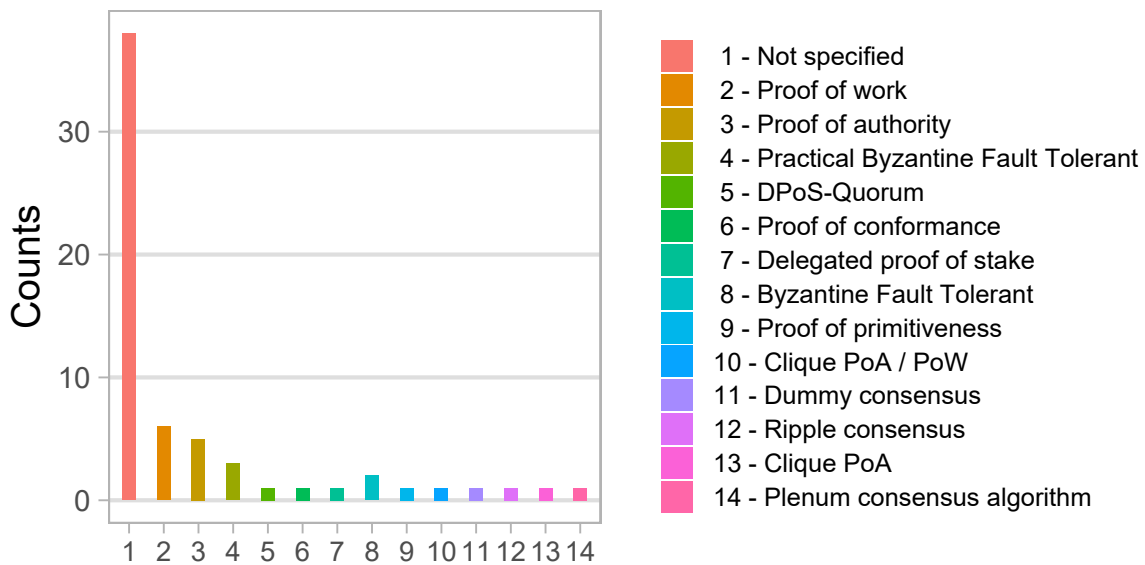


Figure 4: Number of selected papers for each consensus algorithm.

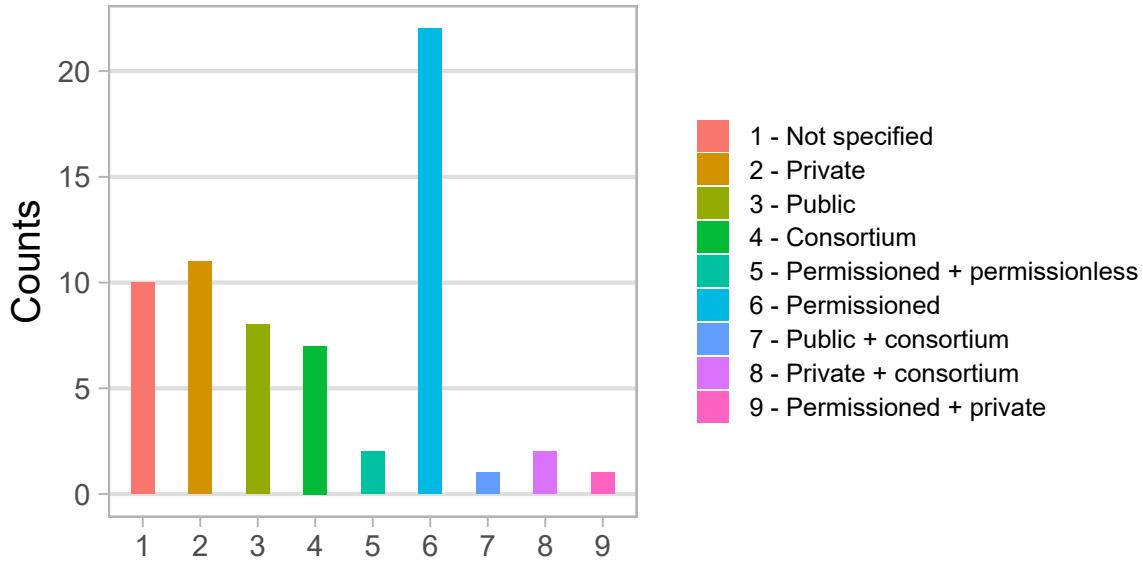


Figure 5: Number of selected papers for each blockchain type.

## 266 5. Blockchain-based applications in healthcare

267 In this section, we present the selected papers. We first classify them according to  
 268 their main topic, namely according to the specific domain the described applications were  
 269 designed for. Our ultimate goal is to understand the aspects where blockchain research and  
 270 development has focused most, achieving interesting results, and to highlight the main gaps  
 271 where challenges have still to be solved.

272 In Figure 6, we graphically depict the identified categories, while in Figure 7, we depict  
 273 the total number of papers appearing yearly for each of them.

274 In the following subsections we discuss in detail the articles falling into each category.

### 275 5.1. Electronic Medical Records

276 Electronic Medical Records (EMRs) or Electronic Health Records (EHRs) contain private  
 277 and sensitive patient data and are usually held by hospital systems. It is often difficult for pa-  
 278 tients to access their own health data, which may also be distributed among different actors.  
 279 To alleviate this difficulty, Toshniwal et al. (2019) proposed PACEX, a blockchain-based  
 280 system that allows patients to have complete control over their EMR. PACEX records all  
 281 EMR exchanges, stores the hash values of EMRs on the blockchain for integrity verification,  
 282 while minimizing on-chain data storage. The implementation exploits the Ethereum private  
 283 blockchain and consists of three main components: the application for patients, the appli-  
 284 cation for hospitals, and the blockchain. The first grants users full authority to access their  
 285 data and allows for the management of EMRs distributed across multiple hospitals. The  
 286 second can be adopted by each hospital to process requests of access, or to retrieve EMRs  
 287 from other hospitals. Each hospital will run an Ethereum node to connect to the private  
 288 blockchain network. The blockchain records all the interactions that take place between the

289 parties via Smart Contracts. The authors performed a qualitative analysis that proved that  
290 the proposed system can meet the requirements of authentication, integrity, access control  
291 and traceability. Moreover, the system is user-friendly, as it does not require the patient to  
292 have any knowledge related to the blockchain. The main drawback is that PACEX is not  
293 able to handle simultaneous multiple requests.

294 Koushik et al. (2019) developed a decentralized medical service for patients and healthcare  
295 providers, based on blockchain. The authors propose a web application that can interact with  
296 the blockchain network via REST API calls, providing an easy way for participants to share  
297 and/or view medical data. Essentially, the application works as follows: when a doctor visits  
298 a patient, prescriptions are added to the user’s record along with the necessary observations.  
299 When the patient is visited by other doctors, they can easily access the patient’s data about  
300 previous visits. The application has been implemented using Hyperledger Composer, which  
301 enables the creation of a permissioned blockchain network.

302 The uniqueness of this implementation is the use of Hyperledger Composer, since imple-  
303 mentations of medical records management systems prior to this work adopted the Ethereum  
304 framework, a public blockchain network that natively cannot preserve the confidentiality of  
305 health-related data.

306 Huang et al. (2019) proposed MedBloc, a blockchain network that consists of multiple  
307 nodes which actors are the patients, the healthcare providers, the network administrator, the  
308 certificate authority, the authentication service provider, and the client. Since all data on the

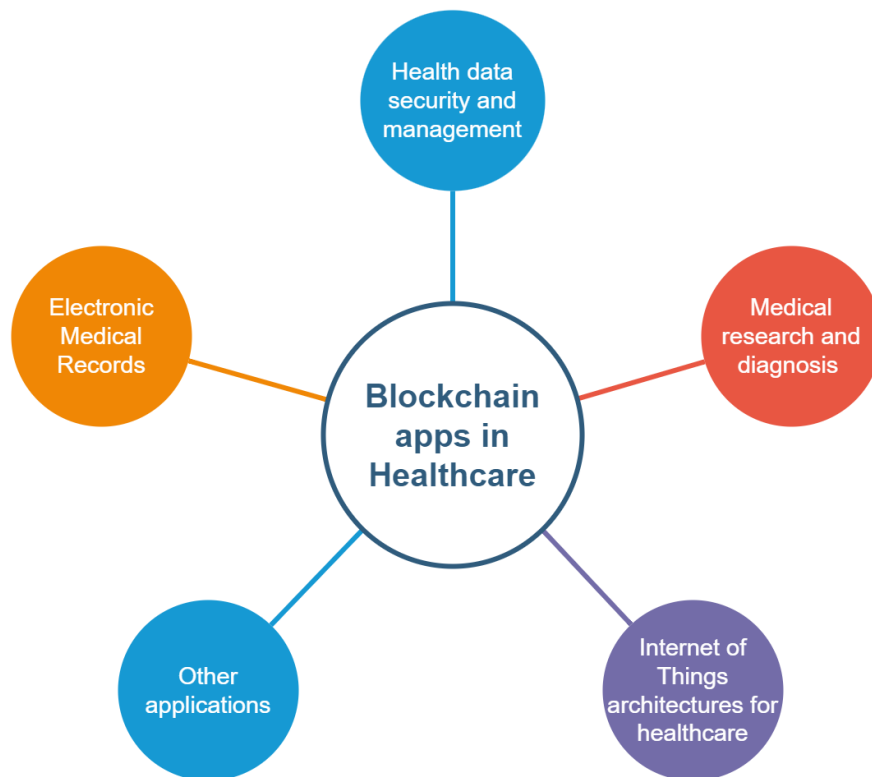


Figure 6: Categorization of the selected papers.

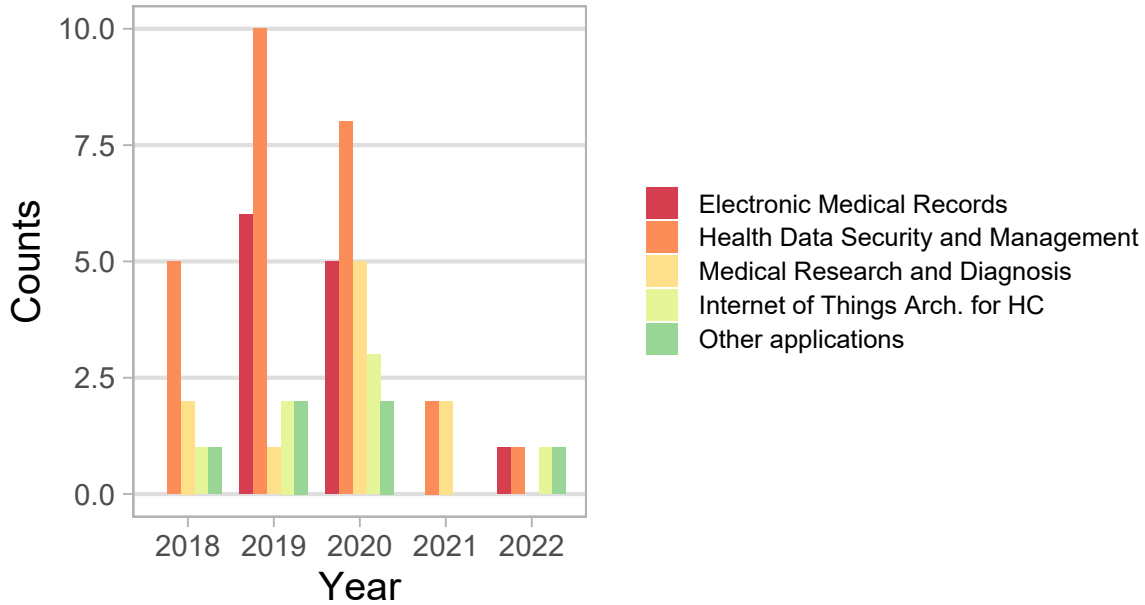


Figure 7: Number of papers appearing each year per category.

309 blockchain is transparent, the authors proposed to use non-traditional blockchain entities,  
 310 such as authentication servers and certificate authorities, to provide means for issuing digital  
 311 identities and protecting the keys used to encrypt all the data on the blockchain. Finally,  
 312 smart contracts are used to enforce access control rules and protect patients' privacy.

313 In general, sharing medical records between patients and healthcare facilities, and inte-  
 314 grating all EHRs of a group of clinical centers can be achieved using cloud technology. In this  
 315 context, Rahman et al. (2019) tried to show if it is possible to integrate the blockchain with  
 316 a traditional cloud-based EHR management system to take advantage of its security and  
 317 immutability features, and how to choose a specific blockchain network so that the control  
 318 over the data is fully decentralized. In their paper, they propose a system architecture based  
 319 on the Ethereum public blockchain. The originality of this study lies in the introduction  
 320 of the blockchain *handshakers*: every time a transaction is sent to the public blockchain  
 321 network, it is anonymously validated by them against smart contracts.

322 Daraghmi et al. (2019) designed the system *MedChain* to improve existing systems by pro-  
 323 viding interoperable, secure and efficient access to medical records. To reduce the data sent  
 324 to the blockchain, they are stored in centralized databases while the Ethereum blockchain is  
 325 used to store all accesses to EMRs, so that the events that happened on EMRs are tracked.  
 326 The authors propose a new incentive mechanism that is not based on a monetary value, but  
 327 is welfare-oriented and integrated with the Proof-of-Authority (PoA) consensus algorithm.  
 328 Specifically, the nodes of the network are associated with a grade indicating the quantity and  
 329 quality of their medical records in terms of readability, completeness, consistency, correct-  
 330 ness and non-redundancy. This grade is assessed by a special tool called *Records Evaluation*  
 331 *Manager*. Healthcare providers' nodes with low grades are more likely to be selected to cre-  
 332 ate new blocks, while nodes with higher grades than the average are *voting* nodes, that are

333 responsible for the validation process. The proposed scheme rewards the block creator with  
334 an incentive that reduces its probability of creating the next block, thus achieving fairness  
335 among providers. Data integrity is ensured by using the SHA-256 hash algorithm, while  
336 security is ensured by adopting the distributed ElGamal re-encryption schema (Zhou et al.,  
337 2005).

338 In order to prevent a medication incident in advance, comprehensive management of  
339 individual medication history is essential. Kim et al. (2019) has developed a patient-centric  
340 medication history recording system using blockchain that captures the QR code printed on  
341 the envelope directly based on the prescription. All information is stored in blockchain using  
342 the hash value of the data, preventing data tampering.

343 BiiMed (Jabbar. et al., 2020) is a Blockchain framework, implemented using a private  
344 Ethereum blockchain, to improve interoperability and data integrity regarding EHR sharing  
345 that is part of a Health Information System (HIS). In the HIS, the data access management  
346 module exploits Smart Contracts to support medical facility authentication and authoriza-  
347 tion. A unique aspect of this work is the introduction of the Trusted Third-Party Auditor  
348 (TTPA) based on Blockchain technologies, which validates and stores the shared medical  
349 data. Once a medical facility is added to BiiMED, it can add patient records, that are  
350 hashed and submitted to the Blockchain framework. The smart contract associated with the  
351 TTPA allows records to be added, updated, and removed. The access management system  
352 verifies the medical provider’s access request and sends a key that enables the communica-  
353 tion with the HIS medical provider, i.e., the access to read/write operations on the patient’s  
354 medical record.

355 An alternative solution to share EMRs across different systems is proposed by Cao et al.  
356 (2020b) in the system HB-EMRS, which adopts a hybrid scheme that combines permissioned  
357 and permissionless blockchains for EMR management. Specifically, sensitive parts of EMRs  
358 are recorded on the permissioned blockchain, accessible only by the members of the consor-  
359 tium, while non-sensitive data of EMRs are stored on the permissionless blockchain. The  
360 participants of the consortium are connected through a set of predefined rules and smart con-  
361 tracts. HB-EMRS also integrates on-chain and off-chain storage to enable the management  
362 of large amounts of data. The data is encrypted and stored in a distributed storage system,  
363 namely the Inter-Planetary File System (IPFS). The framework also provides backup func-  
364 tionalities: if the EMR data on the consortium blockchain is maliciously tampered with, the  
365 full data stored on the IPFS can be used for secure recovery and tracing, ensuring the security  
366 of the HB-EMRS solution. The proposed system has been implemented using Hyperledger  
367 Fabric and Ethereum, and the latency and throughput tests under different configurations  
368 have shown good performances.

369 It is noteworthy that blockchain-based systems generally lack scalability and require  
370 large storage space. Abdul Rahoof & Deepthi (2020) try to solve this problem in the  
371 HealthChain system, which provides a health record management system with scalability  
372 and small storage space. The system is organized using the so-called *regions*, i.e., subsets  
373 of users. HealthChain adopts two types of blockchain networks: a private blockchain for  
374 intra-regional communication, and a *consortium* blockchain for inter-regional communica-  
375 tion. This system significantly reduces the storage on the ledger since transactions are only  
376 stored in the region they belong to. HealthChain is implemented using Ethereum and uses  
377 smart contracts to manage information exchanges among all the components.

378 Fu et al. (2020) developed a novel nesting algorithm for a healthcare-oriented blockchain,  
379 to preserve the privacy of the EMR data. It consists in partitioning the  $l$  bits of the original  
380 EMR into  $t$  groups, each having  $l/t$  bits. A message sharing scheme splits such  $t$  parts  
381 into  $n$  shares, where  $1 \leq t \leq n$ . Such shares are then transferred to different nodes in the  
382 blockchain, which differs from traditional blockchains since data is not shared by all nodes.  
383 Specifically, all nodes can add blocks, that also store hashes that identify the pieces of the  
384 EMRs. In the recovery process, authorized data users can collect a set of EMR shares and  
385 then reconstruct the EMR, even if a few shares are tampered with or discarded. The security  
386 analysis and the simulation results have shown that this architecture makes the EMR storage  
387 and sharing processes secure and efficient.

388 Tith et al. (2020) proposed a decentralized system implemented using Hyperledger Fabric  
389 to solve the problem of sharing medical data between EHRs without relying on a centralized  
390 system. The key features of the system are a trusted repository of patient data in EHRs  
391 that ensures access as well as integrity of the data itself, and enhanced security in handling  
392 patient data by using a special encryption scheme in which the data is encrypted with an  
393 appropriate symmetric key. Then, the symmetric key is asymmetrically encrypted with the  
394 patient’s public key and linked to the encrypted data. This hybrid encryption makes the  
395 process efficient in terms of both speed and convenience, as encryption of large data can be  
396 done faster with the symmetric key than with the asymmetric key, while the latter is more  
397 convenient when encrypting smaller data.

398 Huang et al. (2021) proposed the BCES system, a blockchain-based eHealth system able  
399 to ensure that the manipulation of EHRs can be verified. In BCES, every data manipulation  
400 is logged on the blockchain as a transaction for permanent storage. Specifically, the authors  
401 proposed the adoption of a so-called Proof-Chain to store data manipulation logs, and an  
402 attribute-based proxy encryption to achieve fine-grained access control of medical data.

403 Finally, it is worth mentioning the work by Akhter Md Hasib et al. (2022), who aimed at  
404 improving the intelligence and the security of electronic health management. The authors  
405 proposed an architecture that provides data immutability and complete transparency of  
406 the transactions through the Ethereum blockchain. The main users are the patients, the  
407 doctors, and the hospitals. Patients share personal data through a portal, which front-end  
408 is implemented using ReactJS, HTML and CSS, while the back-end is represented by smart  
409 contracts implemented using the Solidity language. The hospital administration can control  
410 the process but cannot access the detailed data. Doctors can access a patient’s medical  
411 records by submitting a request to the patient. At the end of the consultation, the doctor  
412 can update the patient’s data and, after a verification step performed by the hospital, the  
413 blockchain network is updated.

414 Table 1 summarizes the main characteristics of the papers described in this section.

<b>Ref.</b>	<b>SC</b>	<b>Blockchain</b>	<b>Major strenghts</b>	<b>Cit.</b>
Toshniwal et al. (2019)	Yes	Ethereum	This work develops PACEX, an application that allows patients to share and have complete control over their data using the Blockchain	5
Koushik et al. (2019)	Yes	H. Composer	The authors propose a patient-centered medical record management system	6
Huang et al. (2019)	Yes	H. Fabric	It proposes a key storage framework that aims to improve usability by leveraging an authentication server for storing the cryptographic material	17
Rahman et al. (2019)	Yes	Ethereum	The authors introduce the use of blockchain handshakers that enable the validation of the submitted transactions	13
Daraghmi et al. (2019)	Yes	Ethereum	It proposes a new incentive mechanism that leverages the degree of health providers regarding their efforts on maintaining medical records and creating new blocks	47
Kim et al. (2019)	-	IPFS	It describes a medication history record system that captures the QR code printed on the envelope directly based on the prescription	4
Jabbar. et al. (2020)	Yes	Ethereum	The originality is the introduction of the Trusted Third-Party Auditor that validates and stores shared data	2
Cao et al. (2020b)	Yes	H. Fabric, Ethereum	It adopts a hybrid scheme that combines permissioned and permissionless blockchains	10
Abdul Rahoof & Deepthi (2020)	Yes	Ethereum	The authors propose a system to solve the scalability problem of blockchain-based systems	2
Fu et al. (2020)	-	-	It proposes a lightweight privacy-preserving cross-institution EMR sharing scheme based on the blockchain technique and a lightweight (t,n)-threshold message sharing scheme	19
Tith et al. (2020)	Yes	H. Fabric	The authors adopt the AES algorithm for symmetric-key encryption of patient data and the Elliptic Curve ElGamal algorithm for asymmetric-key encryption of the symmetric key in the proxy reencryption scheme	15
Huang et al. (2021)	Yes	Proof-Chain	The BCES system adopts the so-called Proof-Chain to store users' manipulations of medical data	16
Akhter Md Hasib et al. (2022)	Yes	Ethereum	The proposed system improves the transparency and the security of electronic health records management, involving patients, doctors and hospitals.	4

Table 1: Summary of the characteristics of the works falling under the category *Electronic Medical Records*. The column *SC* indicates the adoption of Smart Contracts (“-” means that it is not specified). The column *Cit.* refers to the number of citations in Scopus on 19/07/2022.



## 5.2. Health data security and management

Health information mostly consists of sensitive data, which protection is fundamental. Research activities focused on finding solutions to ensure reliability and privacy, despite the need of sharing information over the network using blockchain and its inherent features.

The system proposed by Zhang & Lin (2018) exploits a combination of two permissioned blockchains. Medical providers' private blockchain stores patients' original medical information (encrypted for security reasons), while the consortium's blockchain only contains index entries to such data. The authors also proposed a secure and privacy-preserving personal health information sharing protocol (BSPP) based on the proposed architecture. Although patient identities are encrypted, authorized doctors can still search for relevant patient indexes using pseudo identities. Furthermore, the doctor can only access the patient's medical history, i.e. the past, while he may not access future data without re-obtaining the patient's consent.

Li et al. (2018) designed a novel blockchain-based data storage system (DPS). Applications mainly interact by submitting, manipulating, querying, and verifying data. Users can submit the data to be stored on the DPS, and can query it and verify its authenticity, based on the so-called concept of *proof of primitiveness*. This system is effective against tampering and deletion, can detect illegal/invalid transactions and report them to users, but needs improvements and optimizations in terms of image management and storage data structures.

Ramani et al. (2018) proposed a system based on 5 main phases to ensure confidentiality, integrity, and authentication. Specifically, the proposed phases are: *i) Registration*: the patient provides his/her data using a mobile device before a visit. *ii) Data appending/adding request*: a doctor requests the update of the patient's data with his/her consent. The doctor encrypts the data using a common key that can be derived from the patient, who ultimately verifies and signs the data. Finally, the doctor approves the patient's signature and transfer the data to the blockchain. *iii) Data appending/adding operation*: before actually storing the data, the blockchain checks the timestamp, looks for the patient's public key and checks the validity of the signature against the declared involved patient and doctor. *iv) Data retrieval request*: the doctor submits a retrieval request to the blockchain at a given time point by attaching the identity of the patient and the identity of the doctor. *v) Data retrieval operation*: the blockchain, upon receiving a request, checks the freshness of the request through the value of  $T_p$ , the validity of the signature and whether the patient has given the doctor permission to access the data. Then, it returns patient's data corresponding to that time period.

Peña et al. (2019) focused on protecting patient data in mobile health systems by developing a model for secure data collection, sharing, and integration. The model, which allows patients to access to their data, manages three phases: *i) data collection* through apps or wearable devices, *ii) data processing* on the blockchain and cloud-based systems to ensure privacy and security, and *iii) a monitoring system* to track the system performance. The proposed architecture exploits Hyperledger Composer and, according to the performed tests, ensures authentication, confidentiality, integrity, and availability of data.

Ghaffaripour & Miri (2019) described a framework that improves access control mechanisms in privacy-sensitive medical data management systems. The authors envisioned two levels of privacy preservation in their system. The first is the adoption of a variant of attribute-based encryption, namely Key-Policy Hierarchical Attribute-Based Encryption

460 (KP-HABE) (Deng et al., 2017) to encrypt user data outside the blockchain. The second  
461 level is the benefits brought by the use of blockchain, with Hyperledger Fabric as a reference  
462 model.

463 Recently, there have been several ransomware attacks through which attackers installed  
464 malwares on servers of medical organizations, making data inaccessible. To alleviate this  
465 problem, Reen et al. (2019) proposed a model that provides absolute privacy and security  
466 using cryptography, blockchain and IPFS. The main advantage of using the blockchain in  
467 this scenario is the fully decentralized and immutable system of storage, where access con-  
468 trols make possible misuse of data easily identifiable. IPFS ensures immutability of patient  
469 records, while the blockchain ensures immutability of recorded transactions. Biometric-  
470 based encryption ensures that even in a scenario where patients are in a critical condition  
471 and cannot provide access to their records, the latter can be accessed using their fingerprints.  
472 However, there are a number of drawbacks that still need to be addressed, such as the limited  
473 scalability of the blockchain, and the inability to delete all copies in an IPFS-based network.

474 Nguyen et al. (2019) analyzed the performance of a different model for sharing patients'  
475 data using the blockchain and IPFS. The system is based on a smart contract running  
476 on Ethereum, through which authentication and user identification mechanisms are imple-  
477 mented to ensure system integrity. The authors also provided a security analysis and a  
478 comprehensive evaluation in terms of several performance metrics to highlight the advan-  
479 tage of the proposed framework over existing solutions.

480 Andola et al. (2019) proposed the SHEMB system, in which the patient is the sole  
481 authority who has complete control over his/her data. Doctors and departments have a  
482 common distributed ledger based on Ethereum to share patients' data. However, doctors and  
483 patients are not required to store a full copy of the ledger. On the contrary, they coordinates  
484 with other departments of the hospital to have access to the full set of patients' data.  
485 Moreover, to increase the efficiency of the patient search, symmetric searchable encryption  
486 was integrated into the record retrieval component.

487 In another work (Figueroa et al., 2019), the authors proposed to combine the blockchain  
488 technology with RFIDs to support tracking, identification, and communication. However,  
489 in order to preserve also privacy and security aspects, the authors rely on an attribute-  
490 based access control systems (ABAC). Specifically, Figueroa et al. (2019) implemented a  
491 decentralized blockchain-based ABAC model on Ethereum, and considered a specific supply  
492 chain for healthcare, where surgical instruments with RFID tags can only access specific  
493 areas. A physical node consists of an RFID Reader Control (RFID-RC), a DApp and a  
494 Smart Contract. When an RFID-tagged instrument attempts to enter a room, the RFID-  
495 RC sends an access request to the DApp, which forwards it to the blockchain, calling the  
496 smart contract passing some attributes related with the asset, such as the product type and  
497 the serial number. Then, the DApp exploits these attributes to check against the ABAC  
498 security policies, that determine whether the access is authorized or not.

499 A particular scenario can be found in a traditional emergency access system, when the pa-  
500 tient cannot give consent to emergency personnel to access their personal health information.  
501 Rajput et al. (2019) proposed an emergency access control management system (EACMS)  
502 based on a permissioned blockchain built through hyperledger fabric. In EACMS, the pa-  
503 tient defines a-priori the access control policy for *non-emergency* doctor and the *emergency*  
504 doctor. Experimental results confirmed that this structure ensures the security of sensitive

505 PHR patient data, and a time-efficient access that also provides privacy, accessibility and  
506 granular access control.

507 Zhou et al. (2019) proposed the system Med-PPPHIS, that exploits a combination of a  
508 permissionless blockchain and a permissioned blockchain. The permissioned blockchain is  
509 called Med-DLattice and its nodes store and protect data, together with data fingerprint  
510 on the chain, and periodically anchor snapshots of the data to the public blockchain. Each  
511 consensus node in Med-DLattice is a National Physique Monitoring Station (NPMS), that  
512 stores a shared ledger for token assets and medical data of each user. The nodes of Med-  
513 DLattice are able to reach consensus efficiently using the proposed DPoS-Quorum algorithm.  
514 In the consensus process, NPMSs could use Verifiable Random Functions to check whether  
515 they have valid consensus identities to participate in the consensus committee and decide  
516 the proposal according to the sum of voting rights they own and represent. If their identities  
517 are valid, the consensus vote will be taken. When the number of votes collected by NPMS  
518 exceeds the *legal* threshold, consensus is reached and the consensus process ends.

519 Chenthara et al. (2020) proposed the system HealthChain, a framework that consists of  
520 a Distributed Application (dApp), built using Angular, that interacts with the Hyperledger  
521 Composer Rest server to show the state of the data stored on a CouchDB database. This  
522 application supports four types of users, namely doctors, patients, pharmacists and recep-  
523 tionists. The *Fabric-CA* component provides public key certificates for all the applicants.  
524 The *Membership Service Provider* component abstracts all cryptographic mechanisms such  
525 as identity validation, signature generation and verification, certificate issuance, and authen-  
526 tication of healthchain users. The user can submit queries through the Fabric SDK, that  
527 checks the global state of the permissioned blockchain, built with Hyperledger Fabric, and  
528 forward the query to the blockchain. HealthChain also requests the consent to other peers  
529 before actually submitting the transaction to the blockchain. Smart contracts are executed  
530 during every user interaction to identify the request, validate it, secure the interaction with  
531 the doctors, and grant access permissions. The implementation have shown that the pro-  
532 posed architecture also provides a tamper-proof mechanism, thanks to the storage of hash  
533 values for each transaction in the blockchain.

534 Arunkumar & Kousalya (2020) proposed a novel secure decentralized cloud-based med-  
535 ical blockchain (CMBC) to address privacy and security issues in sharing patient health  
536 data among different medical organizations. The CMBC architecture adopts a lightweight  
537 authentication encryption algorithm to upload encrypted health data to the decentralized  
538 cloud-based blockchain. The proposed architecture also adopts a separate key distribution  
539 center to generate and exchange the public keys along with the secret keys, used to encrypt  
540 and decrypt the data, over an unsecured channel.

541 Tanwar et al. (2020) proposed an access control system, implemented using Hyperledger  
542 Fabric, to improve data accessibility for healthcare providers. In the designed architecture  
543 there are 4 main actors: Patient, Clinician, Lab and System administrator. Different activ-  
544 ities within the architecture are regulated by different Smart Contracts, that also manage  
545 the users' roles and the access to resources according to the permissions associated with the  
546 defined roles.

547 The specific topic of supporting access control has also been considered by other works.  
548 Lately, Kumar & Tripathi (2021) emphasized that the adoption of the blockchain for access  
549 control introduces scalability issues, due to the tracking of the entire history. To solve this

550 problem, they propose an enhanced Bell-LaPadula model (Liu et al., 2016), according to  
551 which access control is based on Smart Contracts and on the categorization of peers with  
552 different levels of authorizations and security. It is not required that each peer maintains the  
553 complete transaction history, but only the portion satisfying the access control policies. The  
554 proposed model is implemented using Hyperledger Fabric, while smart contracts are imple-  
555 mented using Hyperledger Composer, in order to manage access control rules dynamically,  
556 overcoming the originally static nature of the Bell-LaPadula model.

557 The security measures adopted in the implementation of blockchains may not be enough  
558 with the advent of quantum computing, which is based on the concept of Q-bits, that  
559 provide an overlay state in addition to the values 0 and 1 such that a bit can take on  
560 both values simultaneously. This aspect exponentially increases the computational power,  
561 introducing additional risks on systems based on traditional encryption strategies. Bhavin  
562 et al. (2021) considered these potential issues, and implemented a blockchain for healthcare  
563 management via Hyperledger Fabric, managing data access via smart contracts and using  
564 quantum blind signature (Lin et al., 2014) for distributing keys. The experimental results in  
565 terms of transaction throughput, resource consumption, and network traffic showed that the  
566 proposed scheme improves the performance of the blockchain.

567 Shah & Rajagopal (2022) proposed an extension of the DPS architecture (Li et al., 2018),  
568 called M-DPS. The proposed architecture is based on the Ethereum blockchain and a set of  
569 smart contracts. Moreover, contrary to the original DPS architecture, it also exploits the  
570 IPFS. The authors compared M-DPS with DPS, showing interesting benefits of the proposed  
571 architecture in terms of reduced transaction costs and storage space.

572 Tang et al. (2018) proposed the system MedImgShr, implemented in Ethereum, which  
573 main innovation is the a credit score scheme implemented through a smart contract. When  
574 patients or hospitals share medical images, their score changes, influencing their permission  
575 to operate.

576 Upadhyaya et al. (2018) proposed a blockchain-based secure healthcare system specifi-  
577 cally for developing countries. Based on various literature reviews, the authors conducted a  
578 feasibility study (technical, economic, operational, programmatic) on an automated secure  
579 health system in an outreach clinic (ORC) in Chapagaun (Lalitpur) and in the Children Eye  
580 ENT and Rehabilitation Service (CHEERS), in Bhaktapur (Nepal). The authors designed  
581 the architecture for an optimal health system using the proposed blockchain model, and  
582 developed a pilot prototype. Its effectiveness was validated with the balanced scorecard, i.e.,  
583 a tool usually adopted to evaluate the organization’s success according to different aspects.

584 Ni et al. (2019) proposed Healchain, a consortium blockchain-based architecture consist-  
585 ing of three layers. Each node in Healchain is run by private servers belonging to trusted  
586 authorities such as hospitals. These servers are used to validate health records by verifying  
587 linked authorization information. Big data can be stored in an off-chain system like IPFS.  
588 The hash of data provided by IPFS along with authentication information is packaged into  
589 transaction records on Healchain. By using blockchain, the system has a number of advan-  
590 tages such as confidentiality, integrity and traceability. Moreover, a formula is proposed to  
591 determine the computational power by trying to maximize the individual economic benefit,  
592 i.e. the difference between rewards and costs.

593 While the idea of using blockchain technology in healthcare is not new, there are still  
594 barriers that need to be overcome in order for blockchains to be used on a large scale. One

595 possible solution is the use of the so-called *sidechains*, which are secondary chains connected  
596 to the main blockchain. One of the advantages of using sidechains in healthcare is the ability  
597 to record transactions and mine blocks simultaneously, as there may be a large amount of  
598 patient transactions at the same time. The nature of blockchains requires multiple nodes  
599 in the network to reach consensus before a block is created, which in this context can lead  
600 to potential bottlenecks. Using secondary chains that are specific to a person/patient on  
601 the network can prevent the aforementioned bottlenecks on the main blockchain for the  
602 following reasons: *i)* fewer transactions are actually sent on the main chain; *ii)* transactions  
603 involving different patients are actually independent of each other, and can be safely added  
604 to the sidechain of the respective patient; *iii)* more transactions per seconds can generally  
605 be handled. Based on these considerations, Donawa et al. (2019) implemented the so-called  
606 Patient-Healthchain architecture, which is based on the use of sidechains.

607 Another example of a generic three-tier architecture for blockchain-based data manage-  
608 ment, private in this case, is proposed by Zhuang et al. (2020). The basic idea is to create  
609 a generalized architecture that provides functions for data coordination, permission grant-  
610 ing, and data sharing. From the bottom to the top, the layers are: *i)* *transaction* layer,  
611 that consists of two smart contracts that specify a metadata model for medical records, and  
612 methods that govern data access rights, permission policies, and data encryption; *ii)* *inter-*  
613 *facing* layer, that provides four methods for obtaining health data from different facilities,  
614 storing the encrypted data securely, sending metadata or data requests to the blockchain  
615 via smart contracts in the transaction layer, and sending the encrypted data to the recipient  
616 who obtained the necessary permissions from the data owner; *iii)* *application* layer, that  
617 consists of the healthcare applications that, based on the interfacing layer, securely collect  
618 data and analyze it. Using this architecture, the authors developed two example applications  
619 for health information exchange that demonstrate the feasibility of adopting blockchain for  
620 data management in healthcare.

621 Among the challenges that need to be addressed when adopting the blockchain, there are  
622 the integration, the migration and the synchronization with centralized healthcare systems.  
623 Biswas et al. (2020) proposed an architecture based on a unified blockchain network across  
624 the country. The central elements are *i)* the certificate authority, which is responsible for  
625 registering all the elements that interact in the network by generating certificates and signa-  
626 tures; *ii)* the peers; *iii)* the smart contracts, through which the access and privilege control  
627 of the different users is defined in order to maintain the medical records; *iv)* the authorizer,  
628 i.e. the main person responsible for creating the blocks, the ledger and the communication  
629 channel. The data structures involved are the blocks of the chain and the tables of relational  
630 databases, that are adopted to store large data outside the chain.

631 Thwin & Vasupongayya (2019) proposed a blockchain-based system for managing per-  
632 sonal medical records. Considering both the potential benefits and the limitations of the  
633 blockchain technology, Thwin & Vasupongayya (2020) focused on analyzing the performance  
634 of such a system in a real-world scenario to ensure its usability in practice. The performance  
635 of the proposed architecture was evaluated at different request rates, including 1.9, 3.8, and  
636 15.2 per second, which correspond to 165,000, 330,000, and 1,320,000 accesses per day, re-  
637 spectively. The results showed that the system can respond to 165,000 daily accesses within  
638 4 minutes. However, when increasing the rate to 3.8 requests/s, the response time can reach  
639 20 minutes, while 50% of these responses are provided within the 8 minutes. The results

640 with an arrival rate of 15.2 requests/s shows that only 30% of the responses are provided  
641 within the 8-minute emergency requirement.

642 Seo & Cho (2020) proposed a system which involves building a private blockchain for  
643 sharing images and supports some rewards for providers. The proposed system is also able  
644 to extract the regions of interest of the input images, using some preprocessing algorithms.

645 Medical data usually include images such as photographs, X-rays, and ultrasound im-  
646 ages, which by their nature represent large amounts of data. This aspect clashes with the  
647 characteristics of the blockchain, since each block has fixed limited size. Therefore, the chal-  
648 lenge is to figure out how to manage image data on the blockchain taking advantage of the  
649 guarantees of reliability and immutability that it offers.

650 Jabarulla & Lee (2021) proposed a new proof of concept for a distributed patient-centric  
651 image management (PCIM) system that enforces security without using a centralized struc-  
652 ture, exploiting Ethereum and IPFS, as well as an access control protocol based on smart  
653 contracts. Each block containing PCIM data is approved and registered by a patient, while  
654 transaction validation is performed by the selected consortium and approved by the health-  
655 care ecosystem. Authorized participants follow a protocol based on a smart contract to  
656 manage image requests. The network consists of protocol called *Patient-Centric Access*  
657 *Control protocol using a Smart Contract* (PCAC-SC) and a blockchain ledger to manage  
658 access control. Medical images are encrypted with the patient’s public key and stored in the  
659 IPFS network. When an authorized user wants to access the image, he/she simply down-  
660 loads it from IPFS. The patient, who owns the data, can provide his/her images to other  
661 requesters, by signing them with the requester’s public key obtained from the blockchain,  
662 and uploading them to IPFS and signing the transaction using the requester’s public key,  
663 his own private key, and the hash provided by IPFS.

664 Zaabar et al. (2021) proposed HealthBlock, a blockchain-based system for decentralized  
665 healthcare management. The HealthBlock architecture exploits the concept of decentralized  
666 storage and a permissioned blockchain network as an access control mechanism to monitor  
667 patient vital signs information. The authors also proposed the adoption of an OrbitDB  
668 database, which is based on IPFS. The HealthBlock users are patients, doctors, pharmacists  
669 and laboratory technicians, as well as the administrator of the blockchain network.

670 According to the GDPR, data must be removed after the agreed period, or whenever a  
671 user requests it. As mentioned in Section 3, this privacy regulation is generally incompatible  
672 with the blockchain technology, since (also personal) data cannot be deleted from the net-  
673 work once recorded. Kakarlapudi & Mahmoud (2021) presented a private data management  
674 system based on blockchain and cloud. The proposed system collects users’ consent and  
675 stores it on the blockchain network. The system allows users to store their data on a private  
676 cloud database, and to approve or revoke data requests. All such operations are recorded  
677 on the network through transactions. Moreover, users can keep track of the organizations  
678 accessing their data, making the proposed system completely transparent and traceable.

679 The outlined characteristics of the considered papers are summarized in Table 2.

<b>Ref.</b>	<b>SC</b>	<b>Blockchain</b>	<b>Major strenghts</b>	<b>Cit.</b>
Zhang & Lin (2018)	-	JUICE	The proposed system leverages a combination of two authorized blockchains plus a secure and privacy-preserving personal health information sharing protocol (BSPP)	230
Li et al. (2018)	Yes	Ethereum	It uses the concept of proof of primitiveness to verify the authenticity of the data	138
Ramani et al. (2018)	Yes	Ethereum	The authors focus on building a secure and efficient data accessibility mechanism using the blockchain technology	57
Peña et al. (2019)	Yes	H. Fabric	It proposes a security model to protect patient data on mobile health systems	1
Ghaffaripour & Miri (2019)	Yes	H. Fabric	The authors envisioned two levels of privacy preservation: the adoption of Key-Policy Hierarchical Attribute-Based Encryption(KP-HABE) and the use of blockchain	2
Reen et al. (2019)	Yes	Ethereum	The paper introduces the use of biometric encryption via fingerprints	7
Nguyen et al. (2019)	Yes	Ethereum	The paper proposes a EHRs sharing scheme enabled by mobile cloud computing and blockchain	161
Andola et al. (2019)	Yes	Ethereum	The system uses symmetric searchable encryption technique to speedup the access to the records	2
Figueroa et al. (2019)	Yes	Ethereum	The system is designed for a supply chain environment with a use case suitable for healthcare systems, so that assets such as surgical instruments containing an associated RFID tag can only access specific areas	17
Rajput et al. (2019)	Yes	H. Fabric	The case study considered is a specific healthcare supply chain, where surgical instruments with RFID tags can only access specific areas	59
Zhou et al. (2019)	Yes	Med-DLattice, DLattice	The authors propose the Med-PPPHIS system, which consists of a permissionless blockchain called DLattice and a permissioned blockchain called Med-DLattice	28
Chenthara et al. (2020)	Yes	H. Fabric	The blockchain is used to manage emergency access system	2
Arunkumar & Kousalya (2020)	Yes	Ethereum	The system adopts a lightweight authentication encryption algorithm to upload encrypted health data to the decentralized cloud-based blockchain	6
Tanwar et al. (2020)	Yes	H. Fabric	It proposes an algorithm for access control policy for participants to achieve privacy and security	264
Kumar & Tripathi (2021)	Yes	H. Fabric	The authors propose an enhanced Bell-LaPadula model to address the problem of scalability	9
Bhavin et al. (2021)	Yes	H. Fabric	The authors propose to use the Quantum blind signature to protect the traditional encryption system from quantum attacks	11
Shah & Rajagopal (2022)	Yes	Ethereum	The authors propose the M-DPS architecture, as an extension of the work by Li et al. (2018), to reduce transaction costs and storage space.	0

Tang et al. (2018)	Yes	Ethereum	The innovation is the credit scoring scheme implemented	12
Upadhyaya et al. (2018)	Yes	H. Fabric	Through the balanced scorecard, it has been shown that implementation of the proposed health system in a hospital results in 75% customer satisfaction and 63% financial gain	4
Ni et al. (2019)	Yes	-	The proposed system HealChain allows a decentralized and secure data management x	11
Donawa et al. (2019)	Yes	-	It introduces the use of sidechains	8
Zhuang et al. (2020)	Yes	Ethereum	The authors proposed a blockchain system that can be adapted to a wide range of healthcare applications for cross-site data coordination	4
Biswas et al. (2020)	Yes	H. Fabric	The authors propose a unified e-health system based on blockchain	16
Thwin & Vasupongayya (2020)	Yes	H. Fabric	The authors focused on demonstrating the usability of the proposed system in practice	4
Seo & Cho (2020)	Yes	H. Fabric	It covers image sharing and supports some rewards for providers	6
Jabarulla & Lee (2021)	Yes	Ethereum	It proposed a new proof of concept for a distributed patient-centric image management system	13
Zaabar et al. (2021)	Yes	H. Fabric	The authors proposed the system HealthBlock for decentralized health data management	14
Kakralapudi & Mahmoud (2021)	Yes	H. Fabric	The authors alleviated the GDPR-related issues by storing health data off-chain in a cloud database, and users' consent information on the blockchain	1

Table 2: Summary of the characteristics of the works falling under the category *Health data security and management*. The column *SC* indicates the adoption of Smart Contracts (“-” means that it is not specified). The column *Cit.* refers to the number of citations in Scopus on 19/07/2022.

### 680 5.3. Medical research and diagnosis

681 In this subsection, we discuss existing works dealing with the adoption of the Blockchain  
682 to *i)* support research activities, *ii)* facilitate the sharing of medical data to provide doctors  
683 with information for diagnoses and research, and *iii)* support emergency situations.

684 Wang et al. (2018) proposed a parallel health systems (PHS) framework to tackle the  
685 problem of sharing cross-border medical knowledge, since doctors usually turn out to be  
686 experts in only one field. The PHS framework consists of the physical healthcare system,  
687 which includes real doctors and patients, and the artificial system, which includes virtual  
688 doctors and patients. Computer-aided diagnosis experiments are conducted according to  
689 the principle of evidence-based medicine, which combines clinical knowledge, personal ex-  
690 perience, and real patient conditions. Artificial doctors are trained with some diagnostic  
691 standards extracted from medical publications, empirical diagnoses from major historical  
692 cases, and evidence-based medicine. For diagnosis, the artificial doctor relies on the actual  
693 symptoms, medical examination results, medical history, and family medical history. A par-  
694 allel execution takes place between real doctors and artificial doctors. On the one hand,  
695 when the artificial doctors conduct the experiments on computer-aided diagnosis and make  
696 the diagnosis of the disease, the real doctor confirms the result to make the final diagnosis.  
697 On the other hand, when the artificial doctor selects the best treatment scheme, the real



698 doctor will give his opinion on the result and provide the possible treatment scheme to the  
699 real patient. The blockchain is specifically exploited to store all the health data securely.

700 Medical research activities are strongly dependent on the available data, while patients  
701 are usually interested in protecting their privacy. To incentivize data sharing, contribution  
702 mechanisms and blockchain can be used. Park et al. (2018) followed this idea, by imple-  
703 menting the CORUS system, which uses crowdsourcing and blockchain to collect data, a  
704 cryptocurrency-based system to create research topics and stimulate continuous participa-  
705 tion, and cloud computing to evaluate health tools in citizen science fashion. On the same  
706 line of research, Lobo et al. (2020) proposed Exonum, an open-source blockchain-based sys-  
707 tem that facilitate patients' access to their data and encourage them to share it in exchange  
708 for some coins of a cryptocurrency, namely *LifeCoins*, to contribute to the research.

709 Fernández-Caramés et al. (2019) specifically focused on studies about the diabetes. Dia-  
710 betic patients can nowadays rely on a device called Continuous Glucose Monitor (CGM) that  
711 can continuously measure blood glucose levels. In order to share reliable data, the system  
712 proposed by Fernández-Caramés et al. (2019) involves the adoption of a decentralized stor-  
713 age system that receives, processes and stores the collected data. To motivate users to add  
714 new data, an incentive system based on a digital cryptocurrency called *GlucCoin* was also  
715 developed. Data storage is implemented using the decentralized database OrbitDB running  
716 IPFS, while Ethereum was chosen to be able to execute smart contracts.

717 Khezzr et al. (2020) proposed a solution to detect and track the daily activities of over  
718 65s, based on the energy consumption of home devices. To ensure that people's data is  
719 protected and accessible to authorized personnel within the healthcare ecosystem, blockchain  
720 technology is used as a mean to maintain and share daily activity patterns, discovered  
721 through a Bayesian model, with healthcare providers. These activity patterns are stored on  
722 the user profile and added to the Hyperledger blockchain. This allows healthcare providers  
723 to assess the daily activities of elderly people and make appropriate health assessments.

724 In the medical research and diagnosis field, the blockchain can be adopted to ensure the  
725 immutability of the collected data and the correctness of obtained results. Moreover, the  
726 wide adoption of wearable devices that collect real-time health information, such as heartbeat  
727 or blood saturation, opens up an infinite number of possibilities for potential applications.

728 In this context, Neto et al. (2020) implemented a proof of concept to analyze the use of  
729 blockchain technology in E-Health applications and, in particular, in genomic applications,  
730 like the manipulation of DNA sequence data. Their idea is to use the classical three-tier  
731 architecture for IoT devices. In this architecture, the first layer is the *data collection* layer,  
732 that is responsible for discovering information sent to the *data storage* layer, i.e. a blockchain-  
733 based database called BigchainDB, where only a few nodes are responsible for storing the  
734 sequences of transactions. Smart contracts are adopted to enforce access control policies  
735 and to ensure the privacy and security of the transmitted information. The final layer is the  
736 *application layer*, which access the data stored in the blockchain, using a digital signature  
737 which ensures the authentication, and on a relational database to provide services to users  
738 (i.e., doctors and patients). Specific applications can range from genomic analysis to real-  
739 time monitoring of patients' physiological data. The architecture also relies on a timeout,  
740 within which the validation of a block must be completed. Otherwise, if the timeout expires,  
741 an empty block is generated. The performed experiments emphasized how a sub-optimal  
742 parameter initialization of BigchainDB or a high latency introduced by the network may

743 lead to an excessive production of empty blocks. However, increasing the number of nodes  
744 alleviates this issue, even if the validation time can increase up to reach few seconds, that  
745 can still be considered reasonable for the adoption of the blockchain in this context.

746 Peral et al. (2020) proposed a blockchain-based architecture that allows patients to share  
747 their health data and organizations to access that data for a fee. The developed architecture  
748 uses two web applications: one to create the data for the blockchain, where each node  
749 corresponds to different users that participate in sharing the data, and the other to visualize  
750 the network created between the different users from an analytical point of view through  
751 dashboards. The authors considered the following use case: patients store their data in the  
752 blockchain via the system front-end. When a potential buyer decides to access some data,  
753 the system checks if he/she has permission to access it. If permission has not yet been  
754 granted, the system informs the patient about the buyer's request and the incentive offered.  
755 If the patient gives permission, the system stores it in the blockchain and notifies the buyer,  
756 who can view the data. The system stores the data access and deducts the payment from  
757 the buyer and credits it to the patient.

758 Gan et al. (2020) suggested storing the data on a Ethereum blockchain network to reduce  
759 or eliminate improper or unauthorized use of the information, that is under the total control  
760 of the patients. Patients are encouraged to use authentication and encryption protocols to  
761 ensure privacy through an incentive mechanism. In addition, the proposed system requires  
762 that big data is not stored in the blockchain but in the cloud, being encrypted if sensitive.

763 Diagnosis does not necessarily have to focus on current conditions, but can also involve the  
764 prediction of future diseases, based on indicators and patient characteristics. This concept  
765 led to the development of BinDaaS (Bhattacharya et al., 2021), a framework that integrates  
766 blockchain and deep learning, to securely protect patient data and make predictions about  
767 future diseases. BinDaaS exploits a lattice-based key and a signature verification scheme to  
768 resist quantum attacks. Experimental results proved the superiority of the proposed scheme,  
769 but also exhibited high communication costs, which can be considered a critical issue.

770 Along the same line of research, Shynu et al. (2021) proposed a secure and efficient  
771 blockchain-based health service for predicting diseases, such as diabetes and cardiovascular  
772 diseases in fog computing (Bonomi et al., 2012). The main components of the system are: the  
773 sensor devices that track human health parameters; the fog nodes, which can be computers  
774 or network devices; the blockchain used to monitor health data; the cloud, used for storage  
775 purposes; and the medical analyzer, who is the person authorized to access patients' health  
776 information to classify them as healthy or diseased. The authors adopted a rule-based  
777 clustering algorithm to group patients, and an adaptive neuro-fuzzy inference system based  
778 on feature selection (FS-ANFIS) to automatically classify patients.

779 Table 3 provides a summary of the characteristics of the papers discussed in this section.

#### 780 *5.4. Internet of Things architectures for healthcare*

781 Monitoring wearables and IoT devices are making patients' lives increasingly convenient,  
782 as they can collect, report, and analyze monitoring data, and transmit it to doctors in real  
783 time. Moreover, they can also be used to send instant notifications to people via mobile apps  
784 or other connected devices. In this context, Attia et al. (2019) designed and implemented a  
785 blockchain-based IoT architecture using Hyperledger Fabric to create a secure remote IoT  
786 monitoring system. In the proposed architecture, each peer can be part of one or more

Ref.	SC	Blockchain	Major strenghts	Cit.
Wang et al. (2018)	Yes	-	The authors propose an approach consisting of artificial systems-based parallel health care systems + computational experiments + parallel execution to improve the accuracy of diagnosis	120
Park et al. (2018)	Yes	H. fabric	It uses a cryptocurrency-based system to create research topics and stimulate continued participation	10
Fernández-Caramés et al. (2019)	Yes	Ethereum	The authors focus on building an application for the case study related diabetes treatment	53
Khezzr et al. (2020)	Yes	H. Fabric	It proposes a solution to track the daily activities of the over-65s in a smart home	5
Neto et al. (2020)	Yes	BigchainDB	This paper proposes an architecture with Blockchain for genomic applications	1
Lobo et al. (2020)	Yes	Exonum	The authors devised a system that encourages patients to share their data in exchange for cryptocurrency	3
Peral et al. (2020)	Yes	H. Fabric	It proposed an architecture that organizations to access patients' health data for a fee	4
Gan et al. (2020)	Yes	Ethereum	The system allows the management of patient data on the blockchain via an incentive-based approach	5
Bhattacharya et al. (2021)	Yes	BinDaaS	It combines blockchain and deep learning	45
Shynu et al. (2021)	Yes	-	It proposes an efficient blockchain-based secure health services for disease prediction	11

Table 3: Summary of the characteristics of the works falling under the category *Medical research and diagnosis*. The column *SC* indicates the adoption of Smart Contracts (“-” means that it is not specified). The column *Cit.* refers to the number of citations in Scopus on 19/07/2022.

787 channels. A proposal for a transaction, containing data received from the medical devices, is  
788 sent to the peers, that approve the proposal by executing the corresponding smart contract  
789 code to access the ledger. Then, based on the endorsement policy, certain peers decide  
790 whether a transaction is valid or not. If it is valid, the proposal is signed and a response  
791 is sent to the application SDK. Once the application SDK gets enough approvals for the same  
792 transaction according to the Practical Byzantine Fault Tolerance algorithm, the transaction  
793 is sent to the service which takes the validated transactions from the application SDK, creates  
794 blocks and sends them to the commit peers, that update the ledger.

795 Griggs et al. (2018) proposed the adoption of a consortium-authorized and managed  
796 blockchain to execute smart contracts that would evaluate information collected from a pa-  
797 tient’s IoT healthcare devices based on thresholds defined by experts. The smart contracts  
798 trigger alerts for the patient and healthcare providers when necessary, and store the trans-  
799 action details on the blockchain. The authors also published some demo smart contracts on  
800 a github repository ([https://github.com/ckohlhos/Healthcare\\_IoT\\_Blockchain](https://github.com/ckohlhos/Healthcare_IoT_Blockchain)).

801 To specifically address security issues in health information systems, Buzachis et al.  
802 (2019) proposed a Blockchain-as-a-Service-based solution for Electronic health Information  
803 Exchange (BaaS-HIE). This system is based on a private, consortium-driven blockchain,  
804 which means that only authorized users can read blocks and only specific nodes can execute  
805 smart contracts and verify new blocks. A typical application scenario is that of a patient

806 being monitored remotely by a doctor, equipped with various Internet of Medical Things  
807 (IoMT) devices, including a blood pressure monitor and a pulse oximeter. Each IoMT  
808 device must be authenticated with the patient (typically through a smartphone or a tablet)  
809 and then through its Identity-Based Signature (IBS) (Hess, 2002).

810 Therefore, the patient acts as an authority certifying that the node possesses the private  
811 key corresponding to its public key. The patient can also decide to share his/her health data  
812 with other doctors from different health centers, or deny further access to the doctor(s) once  
813 the treatment has been completed. The logic and state transition events are recorded as  
814 immutable data in the blockchain.

815 Another system proposed in this context by Zghaibeh et al. (2020) is Smart-Health  
816 (SHealth), a framework for a complete blockchain-based healthcare system, compatible with  
817 Hyperledger Fabric, consisting of four tiers. The first is the government layer, which is  
818 the highest authority in this system, having the main role of regulating the access to the  
819 blockchain. In the second layer we find the users who communicate with the system through  
820 *SHealth Wallet*, an application made available to them from trusted SHealth entities, such as  
821 providers and partners. The third layer is the IoT terminal layer, followed by the blockchain  
822 itself. According to the authors, SHealth is simple, robust, efficient, secure and able to cover  
823 all possible scenarios in healthcare systems, some of which are mentioned in the paper such  
824 as requesting further tests from a doctor or medication prescribing.

825 Abou-Nassar et al. (2020) proposed a decentralized and interoperable trust model that  
826 exploits the blockchain in healthcare IoT. The architecture consists of a first layer dedicated  
827 to information collection and processing, which includes sensors and actuators required for  
828 various functions such as retrieving location, temperature, blood pressure, weight, motion,  
829 vibration, humidity, etc. The second layer includes gateways and network paths required  
830 for the transmission of IoT data. The third layer is a middleware that consists of sub-  
831 layers (blockchain decision units, data analytics, and application support) lying between the  
832 technology layer and the application layer. According to the authors, the proposed model  
833 outperforms other similar approaches in terms of scalability, interoperability, availability,  
834 confidentiality and privacy. Moreover, as a future development, they propose to improve  
835 the system by using artificial intelligence and deep learning technologies, which will be used  
836 in the training phases to identify patterns indicative of specific symptoms from information  
837 acquired from wearable sensors.

838 Rahman et al. (2020) proposed a system with two types of human actors: the IoT provider  
839 and the homeowner who wants to safely combine a set of IoT devices. Before using the  
840 system, a blockchain profile and a digital wallet must be created for each actor. Multimedia  
841 IoT data such as images, audio, and video that cannot be stored on the blockchain due to  
842 limited block size are stored in a decentralized repository on IPFS, while a hash is store on the  
843 blockchain. After each IoT data transaction, the account balance is updated, notifications  
844 are generated, and the status of IoT devices is updated on the blockchain.

845 Azbeg et al. (2022) designed a healthcare system called BlockMedCare for the manage-  
846 ment of chronic diseases, and specifically diabetes. The system can collect and share patient  
847 data with medical teams. Each patient has a set of IoT medical and electronic wearable  
848 devices with embedded sensors. The patient's smartphone is used as intermediate device  
849 between the IoT devices and the medical team. Doctors, hospitals, pharmaceutical labora-  
850 tories and organizations are connected with patients through a blockchain network to access

Ref.	SC	Blockchain	Major strenghts	Cit.
Attia et al. (2019)	Yes	H. Fabric	It proposes an architecture for remote patient monitoring via IoT devices	29
Griggs et al. (2018)	Yes	Ethereum	The system uses smart contracts to assess patient health status by analyzing data collected from IoT health devices and comparing it to personalized threshold values. Available code.	359
Buzachis et al. (2019)	Yes	Ethereum	A platform suitable for overcoming security challenges via blockchain suitable for an EMRs-IoMT scenario has been realized	10
Zghaibeh et al. (2020)	Yes	H. Fabric	SHealth is a private multi-layered blockchain where each layer defines the privileges and permissions of entities in the system	13
Abou-Nassar et al. (2020)	Yes	Ripple	The authors propose a privacy-aware management framework and try to improve IoHT access control methods	102
Rahman et al. (2020)	Yes	H. Fabric	It presents the design of a prototype for secure gesture-based interaction with medical IoT devices in order to remotely protect the health of the elderly or patients with special needs	5
Azbeq et al. (2022)	Yes	Ethereum	It presents BlockMedCare, a system built for chronic disease management through daily data collection and sharing. Data are collected via IoT devices, stored on IPFS, and verified through hashes on the blockchain.	0

Table 4: Summary of the characteristics of the works falling under the category *Internet of Things architectures for healthcare*. The column *SC* indicates the adoption of Smart Contracts (“-” means that it is not specified). The column *Cit.* refers to the number of citations in Scopus on 19/07/2022.

851 their health data, which are encrypted and stored on the IPFS. The hospitals store an entire  
852 copy of the blockchain and participate to the consensus process.

853 A summary of the features of the described papers is provided in Table 4.  
854

### 855 5.5. Other applications

856 The healthcare system is an ecosystem in which not only medical data must be managed,  
857 but also a number of auxiliary data and activities that are necessary for the system to work  
858 properly.

859 Zhou et al. (2018) proposed MISStore, which adopts the blockchain to implement a health  
860 insurance billing system that can help insurance companies in obtaining the sum of the  
861 patient’s medical costs. In general, the process proceeds as follows: *i*) the hospital sends an  
862 initialization transaction to the blockchain network so that it can send the patient’s medical  
863 cost data to the blockchain network through *record-transactions*; *ii*) the insurance company  
864 can submit a *query-transaction* to the blockchain, to know the total amount of a patient’s  
865 cost data; *iii*) servers generate and send responses through *respond-transactions*.

866 Saeedi et al. (2019) implemented the system ClaimChain to show the potential benefits  
867 of adopting the blockchain for billing purposes between healthcare providers and insurance  
868 companies. In classical scenarios, an intermediary is responsible for sending invoices to avoid

869 fraudulent transactions. This process is generally inefficient and error prone, since requires  
870 manual operations. The proposed application, that aims to overcome these issues, consists  
871 of three main components: *Bill Generator*, *Bill Retrieval*, and the blockchain. Bill Generator  
872 is a web application for hospitals that allows authorized users to generate customer bills over  
873 the blockchain network. Bills over the blockchain can also be viewed by financial officials,  
874 that can approve them. On the other hand, Bill Retrieval is a web application that provides  
875 access to the billing information and generates reports to verify the budget submitted by  
876 healthcare providers. In this process, the blockchain replaces the middleman/agent, with  
877 the billing information being encrypted and hashed, and accessible only to the authorized  
878 insurance provider.

879 Another common function of the healthcare system is to transfer the care of a patient  
880 from one doctor to another, as needed. This process involves several steps that require  
881 provider-to-provider and provider-to-patient communication. In Taiwan, the National Health  
882 Insurance Administration (NHIA) has implemented a National Medical Referral (NMR)  
883 system that encourages doctors to refer their patients to different healthcare providers to  
884 avoid unnecessary hospital visits and financial burdens on the national health insurance  
885 system. However, this system lacks scalability and flexibility, and it cannot build trust  
886 relationships between patients, primary care doctors, and specialists. Therefore, Lo et al.  
887 (2019) developed a blockchain-based system to manage patient referrals. They also developed  
888 a decentralized, blockchain-enabled, framework-based personal health data app for patients  
889 to collect their data. The developed framework iWellChain has been deployed in an affiliated  
890 teaching hospital and four collaborating hospitals. Analysis of access logs revealed that  
891 patients were very interested in capturing health data, especially that from lab test reports.

892 Another context is that of medical procedures, that can be very complex nowadays. Here,  
893 the adoption of the blockchain to simplify them has been proposed by Khatoun (2020), who  
894 implements a framework with a decentralized application (DApp) supported by a private  
895 blockchain network with distributed file system (DFS). The author used Ethereum to im-  
896 plement the smart contracts that are used to create intelligent representations of medical  
897 records stored in the network and for various medical workflows, eliminating the need for a  
898 centralized control authority. To ensure high performance and efficiency, the data is stored  
899 in a local database, while the corresponding hashes are stored in the blocks. In this system,  
900 various processes such as issuing medical prescriptions, sharing lab tests, and automatic  
901 reimbursement of healthcare services have been implemented.

902 The Continuing Medical Education (CME) is necessary to ensure the ongoing education  
903 of medical staff. Certificates for these activities can sometimes be forged, and medical license  
904 renewal is also usually a very time-consuming manual process. By adopting the blockchain  
905 technology, the system may become inherently counterfeit-proof, and the management of  
906 medical licenses can be automated.

907 Rathod et al. (2020) proposed a workflow that includes registering users and events,  
908 receiving CMEs, and periodically verifying CMEs. When a doctor, organizer, or event needs  
909 to be registered, data must be submitted to the appropriate medical board, which stores all  
910 data in IPFS. Registering the account of a doctor or of an organizer consists in the invocation  
911 of a smart contract that maps the account address to an IPFS hash. If the entity is an event,  
912 the medical association assigns it a certain number of CME points after evaluating it. A  
913 smart contract is then invoked to verify the validity of the organizer, and to map the IPFS

Ref.	SC	Blockchain	Major strenghts	Cit.
Zhou et al. (2018)	Yes	Ethereum	The proposed system implements a health insurance billing system	91
Saeedi et al. (2019)	Yes	ClaimChain	The system allows you to manage the transition of a patient’s care from one doctor to another	0
Lo et al. (2019)	Yes	Ethereum	The system allows you to manage the transition of a patient’s care from one doctor to another	10
Khatoon (2020)	Yes	Ethereum	The system is capable of handling complex medical procedures such as surgery and clinical trials	100
Rathod et al. (2020)	Yes	Ethereum	The authors propose a robust system for managing doctors’ education certificates	1
Zou et al. (2022)	Yes	H. Fabric	The authors combined distributed identity identifiers (DIDs) and the verifiable credential (VC) using Hyperledger Indy, to build a distributed digital credit system for healthcare.	0

Table 5: Summary of the characteristics of the works falling under the category *Other applications*. The column *SC* indicates the adoption of Smart Contracts (“-” means that it is not specified). The column *Cit.* refers to the number of citations in Scopus on 19/07/2022.

914 hash of the event with the assigned credits and with the organizer’s address. The IPFS  
915 hash is provided as a QR code, which in turn is given to a doctor at the end of the event.  
916 The doctor’s scanning of the QR code invokes a smart contract, which, after verifying data  
917 validity, creates and assigns a certificate with a unique ID to the doctor. When the renewal  
918 period of the doctor’s license expires, a smart contract is invoked, which verifies the validity  
919 of the doctor’s data, calculates the number of CME credits accumulated and, if this value is  
920 sufficient, renews the license; otherwise, it may initiate sanctions or suspension of the license.

921 Zou et al. (2022) designed a healthcare consumer financing system based on a distributed  
922 digital identity architecture, organized in four layers: the *infrastructure* layer, which is re-  
923 sponsible for providing the necessary computing and storage resources to the higher layer;  
924 the *application support services* layer, which provides basic services such as identity authenti-  
925 cation, data encryption and decryption, and the underlying blockchain; the *application* layer,  
926 which provides protocols to realize functions, such as verifiable credential management and  
927 information maintenance, and an interface to let users interact with the network; the *user*  
928 layer, which implements several server-side interfaces that invoke functions of the applica-  
929 tion layer. The authors innovatively combined distributed identity identifiers (DIDs) and the  
930 verifiable credential (VC) model (Consortium, 2019), using the Hyperledger Indy toolkit<sup>5</sup>,  
931 to build a distributed digital identity credit system. The goal is to support healthcare con-  
932 sumers and healthcare institutions in the collection of credit information, thus simplifying  
933 the process of reviewing consumer information by financial institutions.

934 Table 5 summarizes the characteristics of the papers mentioned above.

935

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<sup>5</sup><https://www.hyperledger.org/use/hyperledger-indy>

## 936 6. Research Directions

937 As mentioned in Section 3, the adoption of the blockchain in healthcare can introduce  
938 additional challenges, some of which have not yet been fully addressed in the literature.  
939 Focusing on EMRs (see Section 5.1), the developed systems allow to store and selectively  
940 share patients' data, also taking care of their privacy. The main advantage over centralized  
941 systems appears to be the robustness to tampering operations, which may affect the pos-  
942 sibility to trace the full history of the patients and deeply understand the cause of disease  
943 conditions. However, the reluctance to share personal data (from the patient viewpoint) and  
944 the full transparency of each update to patients' data (from the medical personnel viewpoint)  
945 may discourage the adoption of the developed systems, which may appear as a *strict inspec-*  
946 *tor* ready to accuse of tampering anybody applies updates to data, rather than a tool to  
947 transparently and reliably track the full history of the patients. For this reason, more effort  
948 should be put on incentivization mechanisms, to promote data sharing and to let the medical  
949 personnel feel the technology as a supporting tool, rather than as a continuous inspector on  
950 the activities they conduct.

951 An analogous issue can be observed in the category of *Medical research and diagnosis* (see  
952 Section 5.3). In this case, indeed, the effectiveness of statistical analyses and the accuracy  
953 of descriptive/predictive models strongly depends on the availability of data, as well as  
954 on their correctness. While the latter is generally promoted by the blockchain, the poor  
955 availability of data, due to their personal/sensitive nature, may make some approaches totally  
956 inapplicable. A relevant example is that of deep learning methods, that, although can be  
957 considered the state of the art in several contexts, require a huge amount of data to build  
958 accurate models. In this respect, the research should move towards two parallel directions:  
959 *i)* the design of incentivization mechanisms to promote data sharing for research purposes;  
960 *ii)* the design of specific methods to learn predictive models for healthcare, that can work  
961 with small, incomplete and/or unlabeled datasets (e.g., learning methods that work in the  
962 semi-supervised setting (Mignone & Pio, 2018; Mignone et al., 2020; Pio et al., 2021)).

963 As regards *Health data security and management* (Section 5.2), the developed systems  
964 combine distributed file systems (e.g., IPFS) and off-chain storage with on-chain solutions  
965 for the certification of the data, and resort to hybrid architectures to balance between trans-  
966 parency and privacy preservation. However, considering the recent advances in quantum  
967 computing, we expect to see more effort in the research line of quantum encryption (Bhat-  
968 tacharya et al., 2021), which can be considered fundamental to preserve the current security  
969 characteristics of the blockchain also with the diffusion of quantum processors.

970 In the category of *Internet of Things architectures for healthcare* (see Section 5.4), the  
971 specific challenges that still need to be addressed are more related to possible communica-  
972 tion delays and miners' fees, introduced by the adoption of the blockchain. Indeed, while  
973 IoT devices usually need to communicate with low latencies, the validation process of the  
974 (specifically, public) blockchains may introduce unreasonable delays. For this reason, more  
975 attention should be put on the development of solutions based on specific blockchains that  
976 aim to solve these issues<sup>6</sup>

977 As regards other blockchain applications in healthcare (see Section 5.5), our systematic

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<sup>6</sup><https://www.iota.org/>.



978 review also highlighted that there are some areas where there is no solid research. Some  
979 relevant examples are the tracking and monitoring of the supply chain within hospitals, or  
980 the remote monitoring of fragile patients.

981 Finally, it is worth mentioning that the majority of the papers did not report a link to  
982 public repositories or websites. Although most of the algorithmic approaches are reported  
983 in the papers and are, therefore, reproducible, having the systems publicly available would  
984 facilitate the integration of contributions from the community and a quicker adoption of the  
985 blockchain technology in real-life scenarios in healthcare.

## 986 7. Conclusions and Future Work

987 The purpose of this study was to identify existing blockchain applications in the health-  
988 care sector, that have been implemented in a real-world environment. To achieve this goal,  
989 a systematic review was conducted by properly querying three among the major databases,  
990 namely Scopus, PubMed, and Web of Science. The results were used to identify current  
991 trends in academic research in this area. Specifically, we identified that the research is  
992 mostly focused on the exploitation of different blockchain characteristics, such as security  
993 and immutability, to protect and manage sensitive patient data. In fact, among the 64 most  
994 important publications identified, 28 deal with this topic, followed by 13 publications fo-  
995 cused on the implementation of electronic medical records. The remaining 23 papers were  
996 distributed among, Internet of Things architectures for healthcare, Medical research and  
997 diagnosis, and Other Applications.

998 For future work, we will investigate possible improvements of the blockchains from a  
999 technical viewpoint, to properly face the specific challenges raised by this domain, including  
1000 the issues related to costs, scalability and latency, that, as stated before, may compromise  
1001 the applicability of the proposed solutions in several health-related real scenarios.

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