AN E-PRESCRIPTION SYSTEM FRAMEWORK TO LOWER PRESCRIBING AND MEDICATION DISPENSING ERRORS USING BLOCKCHAIN, MACHINE LEARNING, AND NEAR FIELD COMMUNICATION (NFC)

by

Bader M. Aldughayfiq

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To my beloved parents, Munif and Fahadh, to my moonlight, my wife, Agharid, and my rising stars Jawf and Munif, who were with me every step all the way. I love you all.

Table of Contents

List of Tables

List of Figures

Abstract

Medication errors are among the most significant risks facing the pharmaceutical industry. These errors can result from various issues such as a heavy workload, the misinterpretation of a prescriber's handwriting, or dispensing the wrong medication to the wrong patient. Hence, many countries have implemented e-prescription systems trying to reduce medication errors. In addition, researchers have proposed several mobile apps that use near-field communication (NFC) to manage patients' medication intake instructions and remind patients about intake times. We conducted a comparative review involving eight countries implementing e-prescription systems. One of the challenges and limitations of the reviewed systems is the availability of medication histories to the parties involved in the system. Moreover, the clinical decision support (CDS) systems are not part of the e-prescription system, and they do not provide quality, valuable alerts that would help avoid potential harm from the prescribed medication.

The objective of the thesis is to develop a framework for an e-prescription system that aims to enhance the security, privacy, availability, and reliability of the ePrescription information while prescribing and dispensing medication. Therefore, the framework benefits from the characteristics, features, and advantages of the technologies blockchain, Machine Learning (ML), Near Field Communication (NFC).

The framework will use blockchain technology to make the patient's information secure, private, and available to the involved parties. Moreover, to enhance medication safety, we proposed using machine learning (ML) to detects any serious outcome caused by anomalies in the e-prescription before submitting it. Finally, using a mobile application enabled with NFC technology to transfer the patient's token Id to the pharmacy management system will verify the patient's identity and control the access to the patients' ePrescription information. The application will help to manage and display the ePrescription information when needed to the patients. We developed a proof-of-concept and evaluated the reliability and performance of the blockchain and ML modules. Further, we conducted a user study of the NFC mobile application to evaluate its usability. Lastly, we conducted a survey study to understand better the strengths and shortcomings of the proposed features in the framework (i.e. blockchain and ML). The results are promising that the framework might help mitigate medication errors at different levels, starting from prescribing until dispensing the medications to the patients.

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Chapter 1

Introduction

1.1 Overview of Medication Errors

In 2016, a tragic incident [18] led to the death of an eight-year-old boy. The boy's parents gave him what they thought was his sleep medication; however, the medication was not what the doctor had prescribed. The pharmacist gave them Baclofen, a muscle relaxant. The coroner found that the high dosage of Baclofen administered was fatal for a boy of that age. Moreover, according to [3], the insurance group CAN and the Healthcare Providers Organization (HPSO) in their analysis of ten years of claims data. They reported that 75.3% of closed claims are because of either a wrong dose or the wrong drug. Moreover, from the already-closed claims, injuries resulted from 13.6% of these overdoses, and 11.7% of these led to death [3, 4]. See figure 1.1. Moreover, a descriptive analysis study of the quality-related events reported by community pharmacies in Nova Scotia constructed by [19]. According to their study, which reports between 2010-2017, they define the quality-related events as medication errors (e.g., wrong drug, dose, or incorrect instructions)that either reached the patient or were prevented before dispensing. In the study, they analyzed nearly 130 thousand reported events; almost 98 thousand were quality-related events. Out of the 98 thousand, 0.95%(i.e., equals to 928 events) were events that patients got harmed.

In 1999 the Institute of Medicine (IOM) stated that almost 45,000- 98,000 deaths in the United States (US) were medical errors [20]. Furthermore, a more recent study [21] estimated medical errors would be the death cause of almost 251,000 each year in the US. Medical errors are the third leading cause of death in the US after heart disease, and cancer [21]; also, medication errors are the third leading cause of death in Canada after heart disease and cancer [22–24]. According to the 2007 report from the Canadian Institute for Health Information, in the past two years, 1 of 10 patients was given the wrong medication, or the wrong dose [25].

A systematic review of the studies about prescribing errors published between

1985 to October 2007 was conducted by [26] to investigate the prevalence rate and nature of prescribing errors in hospital inpatients. Most of the reviewed studies were conducted in the US and Uk. The authors found that prescription errors occur commonly, which cause almost 50% hospital admission. In addition, a Commonwealth survey study [27] that surveyed 700-750 patients in Australia, New Zealand, and Canada and approximately 1500 adults in the US, UK, and Germany. Found almost 30% of Canadian patients reported medical, medication and/or laboratory errors. By comparison, only 22% of UK patients reported errors. Moreover, The study found the errors increased when more physicians were involved from 15% to 40%. Therefore, several Information Technology (IT) systems are designed to help minimize medication errors, (i.e. the most common type of medical errors) [28].

However, medication errors also occur in the community and commercial pharmacies. A descriptive analysis study of the quality-related events reported by community pharmacies in Nova Scotia, Canada, between 2010-2017 defines the quality-related events as medication errors that either reached the patient or medication errors prevented before dispensing. The authors define medication errors as a wrong drug, dose, or incorrect instructions [19]. In the study, they analyzed nearly 130 thousand reported events; almost 98 thousand were quality-related events. Out of the 98 thousand, 0.95%(i.e., equals to 928 events) were events that patients got harmed [19].

1.2 Solutions to Overcome the Medication Errors

Therefore, to address the above issues, the authors in [1] introduced ten strategies. These strategies mainly focused on minimizing medication dispensing errors but did not reduce the time required to prepare a prescription, affecting the provided service's quality. Also, one of the strategies suggests adding more staff to reduce the increased work rate, increasing pharmacy costs. To elaborate further, dispensing the wrong medication or taking the wrong dosage might be caused by many reasons. However, most errors are related to pharmacies' work strategies, such as using paper prescriptions. Paper prescriptions have many flaws, such as difficulties in reading the handwriting of a prescriber. This issue may cause dispensing the wrong medication or giving incorrect instructions on medication intake.

According to [29], patient identity confirmation is needed to dispense the medication. However, they did not specify any methods of confirming the identity of the patient. The common practice verifies the patient by home address and name verbally to the authors' best knowledge. This practice will raise security and privacy issues where any person (i.e. knows address and name) could pick up the medication. Also, sharing an address and a name verbally and publicly could raise security and privacy matters.

A critical factor in improving the quality of the service provided by drugstores is to make the process of dispensing medication efficient, accurate, and effortless. Therefore, automating getting prescriptions and dispensing medications will help minimize the risk caused by receiving the wrong medication or the wrong dose. The Internet of Things (IoT) is described as various devices and systems in where they connect and exchange information by using many wireless and wired network technologies. One of the wireless network technologies used in the IoT is known as Near Field Communication (NFC) technology and is available on smartphones. This technology has been used to open several opportunities to optimize services' quality, such as tap-to-pay

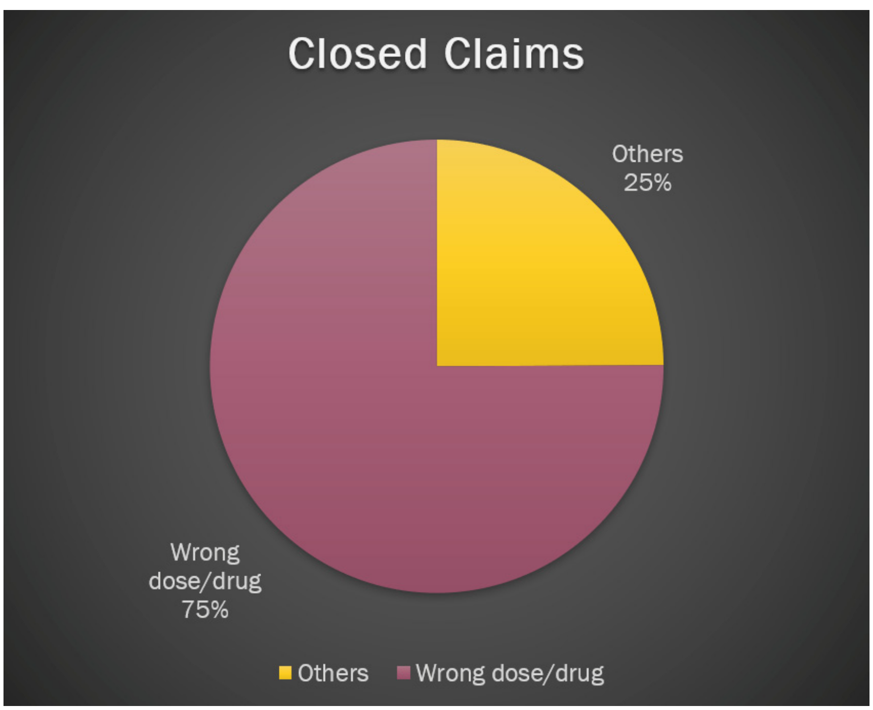


Figure 1.1: Shows the percentage of the closed claims related to medication dispensing errors [3, 4]

services. Also, various fields (e.g. healthcare, access control) use NFC to gather and transmit information securely.

1.3 Research Gap

According to [29], patient identity confirmation is needed when dispensing medication. However, they did not specify any methods for confirming the identity of a patient. The most common practice is to verify patients using their home address and name to the best of our knowledge. This practice raises security and privacy issues, as anyone (i.e., someone who knows the patient's address and name) could pick up the medication. Also, stating a patient's address and name in public could implicate the individual in other matters.

A critical factor in improving the quality of the services provided by drugstores is to make the process of dispensing medication efficient, accurate, and effortless. Therefore, automating getting prescriptions and dispensing medications will help minimize the risk caused by receiving the wrong medication or the wrong dose. The IoT offers the ability to exchange information securely and efficiently by using wireless and wired network technologies. Such technology is known as NFC technology and is available on smartphones. This technology has been used to create several opportunities to optimize services such as tap-to-pay services. Also, a variety of fields (e.g., healthcare, access control) use NFC to gather and transmit information securely.

Thus, we propose a secure system to optimize the medication dispensing process by benefiting from the technologies because of their advantages to reduce medication errors at multiple levels during the prescribing and dispensing process. Although the framework aims to reduce medication errors, the despising and prescribing of the medication process involve several steps that might cause errors. The framework does not solve nor reduce the errors that occur during the whole process. Although the framework aims to reduce medication errors, the dispensing and prescribing of the medication process involve several steps that might cause errors. The framework does not solve nor reduce the errors that occur during the whole process. The framework focuses at the prescriber's office on the submission process and detecting any serious outcome caused by anomalies in the prescription. At the pharmacy, the framework focus relies on receiving the e-prescription, verifying the prescriber and the patient, and finally, handing the patient the medication at the end of the dispensing process. Through this thesis, we will be using the terms the prescribing and dispensing process as explained above.

The framework introduces a more reliable and secure method to confirm the patient's identity and reduce dispensing errors. We use NFC technology in smartphones to securely transfer information (e.g., insurance ID numbers, prescription IDs) between the patient's smartphone app and the pharmacy. We used NFC because of its proximity requirements since the user has to be within 4 cm from the reader to transfer information, thus ensuring the user's physical presence. We also use NFC technology to able the pharmacists to check the prescribed medication before handing the medication to the patient at the final stage of the dispensing process to avoid dispensing the wrong medication to the wrong patient. In addition, we use biometric information (i.e., fingerprints) to grant the patient access to the application services. Then, the patient will be able to transfer the needed information to the pharmacy using NFC technology during the medication dispensing process. However, in the final framework design, the patient provides a token Id, which can be used in a future design with different methods not specific to NFC. Different sharing methods will help other users who can not use NFC or can not pick up the medications.

Furthermore, we use the blockchain to securely manage the process of sharing patient medication and prescription information and control access to preserve the confidentiality of patient information. Blockchain will allow us to ensure that only the participants can access the information in the chain. Lastly, we use machine learning algorithms to give the prescriber alerts during the prescribing process to ensure no errors are made from drug interactions or drug suitability to the patient's health condition. Therefore, enhancing patient safety and ensuring no harm is anticipated to a patient during the prescribing process. Although the proposed system will not prevent human errors, we believe it will mitigate medication dispensing errors. One of these human errors might affect the efficiency of the framework is if the prescriber ignores the alerts from the machine learning algorithm. Also, because the framework does not cover the whole dispensing process at the pharmacy, another human error is if the pharmacists filled the wrong medication in the bottle or compound the wrong medications.

1.4 Report Organization

The organization of the report is as follows. In chapter 2, we explore and discuss the recent literature regarding the use of NFC technology in health care systems and the current systems for e-prescribing technology. Furthermore, we will discuss the ePrescription systems that use blockchain technology and machine learning techniques. Chapter 3 we explore the comparative review we conducted on countries that implemented ePrescription systems. Chapter 4 will discuss the previous framework. Chapter 5 discuss the usability study of mobile application in the previous framework and the study results. Chapter 6 will discuss

. Last, in chapter 7, we will discuss the proposed application analyses and the system's proposed security and the prescribing method features. Finally, we will conclude this report in chapter 11 and discuss future work associated with this research.

Chapter 2

Background and Literature Review

This section will explore the proposed systems in healthcare or medication-related services that use NFC technology or mobile apps. Some proposed systems also use both NFC and mobile apps. We also explored some of the current systems and services that use the e-prescription approach.

2.1 NFC technology

NFC is a wireless communication technology is used to exchange data within the distance of less than 4 Centimetre (cm) [30, 31]. Moreover, NFC uses the frequency of 13.56 Megahertz (MHz) to transfer the data [32]. NFC comes in several forms. The first, is an NFC reader or NFC chip (e.g. a card, or bracelet). The NFC chip can store a small amount of data, such as a unique identification (ID) (e.g. Social Insurance Number). Third, which is most commonly used these days, is the NFC-enabled smartphone, where the smartphone can act as an NFC reader and an NFC card (i.e. Host Card Emulation (HCE) mode)[33, 34]. One advantage of using smartphones over chips is the larger amount of storage and resources available, which allow the NFC card to perform more complicated processes [32].

2.1.1 NFC Security Threats

NFC inherits many similarities from Radio-frequency identification (RFID). Therefore, NFC is vulnerable to the same security threats as RFID, such as relay attack. In this type of attack, the aim is to authenticate the rogue device to the NFC reader. The attack will start to initiate communication with the user device using the NFC reader and will challenge it to authenticate itself for the transaction. Once the user device gives the credentials, the attacker NFC-reader will transfer the information to another device controlled by the attacker. The second device will act as the victim's NFC device. In this step, the attacker will provide the authentication information to the legitimate NFC reader to gain access to the services provided by that NFC reader [35, 36]. See Figure 2.1.

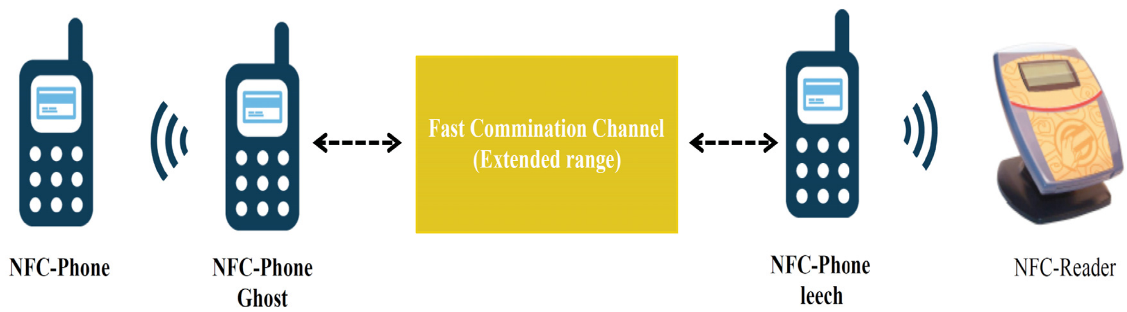


Figure 2.1: Relay attack process on NFC

2.2 NFC systems and mobile apps systems for health care

Healthcare services is a vast research area to be covered. Therefore, we will only mention the most recent relevant proposed systems to our application.

The German electronic health card is an example of health- care systems that support the NFC cards. The developers of that card designed a centralized technical structure, where healthcare providers, such as pharmacies, hospitals, and healthcare centers. It can connect to the health insurance company with centralized services. This structure allows communication between various healthcare field stakeholders to provide better service to the patient [37].

The use of mobile apps and NFC in healthcare has been the primary interest of many researchers. According to [38], there is an app to make ultrasound available through smartphones. The app called Mobisante [39] is developed to provide doctors with a portable ultrasound device using their smartphones. The app also offers a lower cost and ease of use for this industry. The app works with an ultrasonic transducer connected to the smartphone through a USB port.

Health monitoring apps aim to provide an increasing number of patient health monitoring services. These apps monitor different vital signs, such as heart rate, blood pressure, and others. An example of this type of apps is what AirStrip Technologies [40] has developed. They developed three apps to collect patient information during hospitalization and help doctors and healthcare professionals offer better healthcare services. Moreover, the app has a real-time data transmission feature. This feature will help the physicians analyze the data on their mobile apps. They will then act upon that real-time feed [38, 40].

In [41], the authors proposed a health care monitoring system. Their system aims to collect information about the patient's vital signs. One of the system's features is monitoring the patient's status and sending emergency alerts to the doctor's device.

In [42], the authors developed an application for monitoring Alzheimer patients' activities in health centres and homes. The application will provide an efficient way for caregivers to manage data and enhance the quality of service they provide to patients [43].

2.3 NFC systems and mobile apps systems for health care (medication-related services)

In this section, we will review related work focusing on medication management apps. Medication management refers to either organizing medication for patients or detecting medication interactions.

S.Fan et al. proposed a mobile app called the HealthPal [5]. This app aims to help elderly individuals by reminding them about and managing their health tasks, such as doctor appointments, exercise times, taking blood pressure, pulse rates, and medication intake times. Reminders use audio and visual alerts. The app will prevent patients from forgetting their medication time and type. Moreover, visual alerts will help patients avoid mixing or taking the wrong medication.

In [6, 7], the authors presented Wedjat, a mobile app that helps patients remember medication intake instructions. Wedjat also keeps the patient's intake records, and updates a user database or a personal health records system [8]. In [44], the authors describe the possibilities of utilizing NFC technology in smartphones to help elderly individuals with vision impairment manage their medication. The authors proposed two scenarios of medication management and organization. In the first scenario, a pharmacist will attach an NFC tag to the medication packaging, containing information about that medication. Then, the user will have to touch the tag with their smartphone to enable the NFC reader mode in the application. An audio interface

Figure 2.2: HealthPal application interfaces [5]

Figure 2.3: Wedjat application interfaces [6, 7]

will convert the information so that the user can listen to information about that medication. In the second scenario, the application will manage the medication intake instructions. A home care service provider operates a back-end system to store the intake instructions. The home care service provider will also provide an NFC tag for the medication with the intake schedule information, such as required doses and medication intake times. The NFC tag will be attached to the medication packaging with all the required above information [8].

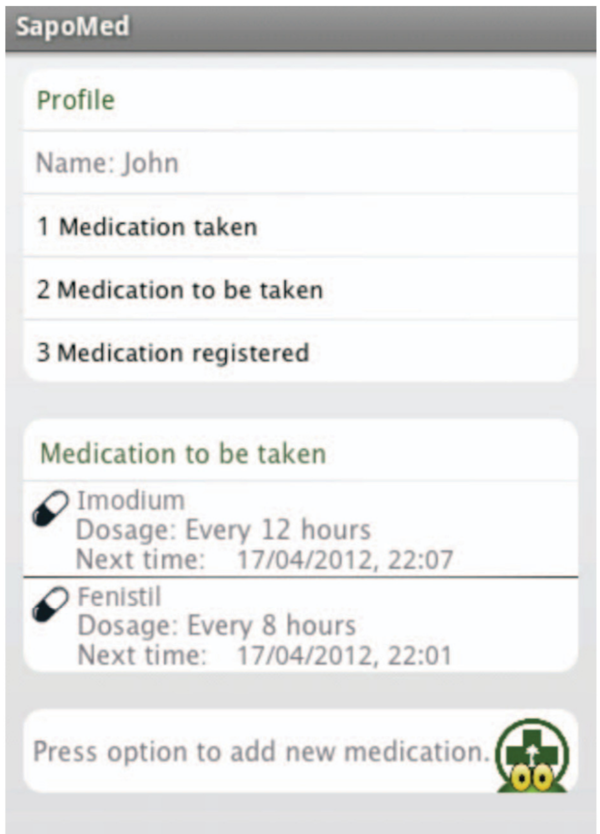


Figure 2.4: SapoMed application interface [8]

Silva et al. presented SapoMed, a mobile application designed for medication management and monitoring. The focus of their work is to prevent medication intake errors by tracking and managing all prescribed medication. The user has two options to input the medication and intake information: inputting the information manually or scanning the medication barcode. For the second choice, the application will obtain the required information from a web server. The web server will store all medication information and past intake information in a medication database [8].

Most medication-related applications are management applications such as [45]. This application helps to remind elderly patients to take their prescriptions at the correct times. The application will also provide information for the doctors to help them monitor whether their patients are taking their prescriptions.

SemTag [46] is an application that uses NFC to facilitate access to medical emergency information securely. An NFC tag will contain the necessary emergency information of a patient. The tag will be placed in a high, visible place in the patient's home for the caregivers. Once an emergency occurs, the caregivers will scan the tag to gain basic emergency information about the patient from the servers using a unique ID stored in the tag. Jara et al. [47, 48] use NFC in pharmaceutical Information System (PIS) to ensure that the nurse will give the right medication to the right patient. The nurse will need to scan the patient's tag using NFC, and the server will check for drug interactions in the patient's historical records.

2.4 Blockchain

2.4.1 Overview

Blockchain is a decentralized network that includes a distributed chain of blocks. The blockchain network is a peer-2-peer network. Each block in the chain includes information about a transaction in the chain. All transactions are recorded in the blocks. These blocks are linked to each other by storing a hash value to the previous block data. The user verifies the block by calculating the hash value and matching it with other blocks' hash in the network. If the verification process is successful, then the new block will be added. One of the well-known examples of blockchain is the Bitcoin network. Bitcoin is a finance network used to organize and monitor the participating peers' financial transactions [9]. Figure 2.5 shows the blockchain architecture. The blockchain network in its distributed architecture ensures the privacy of transaction information and the ability to share the blocks in the network securely [49–51].

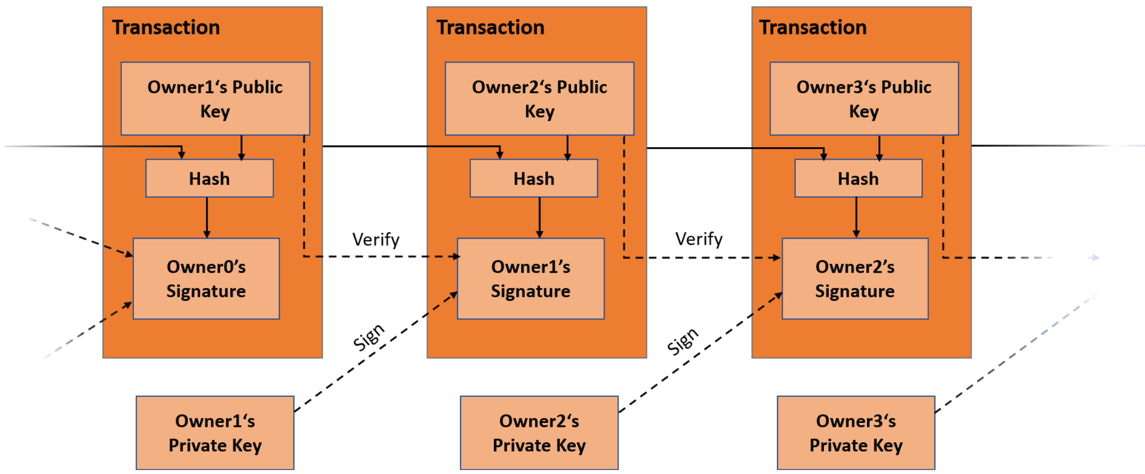


Figure 2.5: blockchain architecture [9]

2.4.2 Blockchain Uses In e-Prescription and Medication Management System

Many researchers have proposed the use of a blockchain network in the healthcare sector. We will explore some of the proposals in this section.

The authors in [50] proposed the use of blockchain to manage and secure a patient's health data gathered from wearable devices. They proposed a framework with two blockchain networks: personal health care (PHC) and external record management (EMR). The patient will control the PHC blockchain network, and it will manage and maintain the health data generated by wearable devices. Moreover, the PHC network will store data in an external cloud database to facilitate sharing a patient's health data with the doctor. Meanwhile, the EMR blockchain network will manage the patient's health data while visiting a healthcare centre. The EMR network is controlled and managed by the healthcare centres. Insurance companies will have access to patient data on the EMR network. Lastly, the authors proposed using a machine learning module to detect any severe outcome caused by anomalies in the patient health data generated by the patient.

In [49], the authors develop a cryptocurrency called RxCoin to be used to prescribe a medication using the principles of blockchain electronically. The authors developed a proof of concept of their system to demonstrate the blockchain principles using the proposed RxCoin. Furthermore, they used the smart contracts concept to create the prescription and store it to trace the blockchain's medication transaction histories.

In their paper, they explain the process of creating RxCoin during the prescribing process. The prescriber will issue a new prescription, thus creating a new RxCoin. This coin will later be transferred to the pharmacist to start the process of filling the prescription. Then, the pharmacist will create a new transaction with that RxCoin, informing the system that the prescription was filled. Creating and transferring the RxCoin will issue a transaction for each process. The blockchain will store the transactions, and after each process (i.e. creating and transferring the RxCoin), the system will announce the new stored transaction. The authors believe the use of blockchain could help deal with the opioid crisis in the US [49, 52, 53].

Another proposed system was introduced by [51]. It is called the decentralized medication management system (DMMS). The system aims to improve patient medication histories' security and privacy while sharing and transferring data between healthcare centers. The system utilizes a blockchain network to achieve the mentioned goals. In this system, the prescription is encrypted with the patient public key after the prescriber issues it. The patient will have full access to the medication history across the health care centres and will be able to decrypt it using their private key. Moreover, the prescriber can view the medication history from other healthcare centers with the patient's approval.

MedRec is an MIT research project that aims to utilize the Ethereum blockchain as a solution for managing Electronic Health Record (EHR) and giving the patient agency over their medical record. The authors believe that MedRec will address fragmented medical data, slow access to medical data, system interoperability, and patient agency over their data. They believe it will improve the quality and quantity of data for medical research. MedRec will handle authentication, confidentiality, and accountability when sharing sensitive medical information. MedRec uses a smart contract to trace the patient's health record shared in the network to achieve the system's goals. Finally, MedRec gives the patient full access to their health record history. Furthermore, MedRec allows the patient to store their medical record at their local database (e.g. local PC or mobile phone) [49, 54]. Relying heavily on the patient to manage their health record might make data vulnerable to privacy breaches at the patient end.

Similarly, Health Nexus is developing a blockchain network based on Ethereum.

They aim to solve the same issues faced by MedRec except for the patient agency. Health Nexus focuses on providing a secure method for sharing health information between health care providers [49, 55].

As can be seen, most of the proposed blockchain networks focus on transferring patient information securely and preserving their data privacy. Moreover, only one proposal suggests giving the patient control over their medical information. As mentioned above, the patient agency might lead to privacy breaches at the patient end since they will store their private key to decrypt the block on their local device. Moreover, the other proposals will allow pharmacists to create a new transaction stating that the prescription filling process has finished. Thus, this process might create the opportunity to misuse the prescribed medication. Furthermore, this system does not confirm that the patient has received the medication. Therefore, the blockchain network must have a confirmation stage that can be issued from the patient end. Moreover, confirmation of the validity of that prescription can be done by other participants in the network.

2.5 Machine Learning

2.5.1 Overview

Machine learning algorithms are used broadly in various healthcare systems as a decision-supporting application. These applications help improve the service quality of care provided to the patients. Moreover, the applications benefit from the data collected in healthcare centres. Therefore, both preparing data for processing and the collected data quality have a significant role in driving quality results that help improve the decision-making process. Nowadays, most of the data collected are processed in different healthcare applications to deliver good services. The following are examples of machine learning uses in the healthcare sector in general and prescribing medication in particular.

2.5.2 Machine Learning Uses In e-Prescription and Medication Management System

In [56] the authors propose to find any non-medical use of drugs by applying an unsupervised machine learning algorithm on Twitter data. The authors collected 11 million tweets using the names of three commonly abused opioid drugs as filters. They then applied an unsupervised machine learning algorithm to find themes of abusing the mentioned drugs. The machine learning model they used was called a biterm topic model (BTM) [57], which was proposed to detect patterns in short texts like tweets. The authors found 2.3 million tweets that had one of the extracted patterns from the used model.

The authors in [58] proposed the use of machine learning to predict antibiotics that could be used to treat urinary tract infections (UTIs). The ML algorithm measures the antibiotic's resistance level based on the patient's clinical history. They used data on more than 700,000 UTIs from almost 315,000 patients. They divided the data into two sets for training and testing the developed ML model. They found that the accuracy of the model is 95%, which is higher than the accuracy of prescribing antibiotics by physicians, which is 91% [58, 59].

Another study [60] developed an outlier CDS system based on ML to predict any medication prescribing errors for inpatient settings. The proposed system was integrated into an existing EHR system for a healthcare centre. The system aims to detect prescriptions that are outliers based on the patient's health condition. An example of these outliers is when a medication is never or rarely prescribed to a patient with a specific condition (e.g. a birth control drug being prescribed to a baby.) The system collected and analyzed data on prescribed medications for 16 months. More specifically, it recorded all the drug alerts in real-time for all the drugs prescribed by physicians. Then, the alerts were assessed for accuracy, validity, and usefulness. The authors found that their system generated a low rate of alerts for 0.4% of all the prescribed drugs, which is not a high burden for physicians. Out of all the generated alerts, only 80% were accurate and clinically useful alerts.

Chapter 3

E-prescription Systems Jurisdiction Comparison Review

3.1 Materials and Method

In this review, we investigate e-Prescription systems using a jurisdiction comparison method. We will discuss the systems that are implemented and outline their features. We selected the countries with an ePrescription system from each content. The selection process of countries was as follows:

1 We choose the leading countries that have deployed e-Prescription systems from each continent. In Europe, many countries have adopted the digital health approach in the past decade. However, few considered the leading countries that fully implemented the ePrescription system. This approach is part of the national electronic-health strategy in the European Union (EU) countries [61, 62]. Moreover, we explored the other content to select the countries.

2 In the second stage, we considered the availability of the ePrescription system to community pharmacies and whether the system is nationwide or statewide in the selection process. We excluded e-Prescription implemented only within hospitals.

3 At this stage, a key factor in our selection process is the security and privacy protocols. We compared the e-Prescription systems from a technical and security aspect.

4 Finally, the countries that resulted from the selection process were four EU countries (UK, Spain, Sweden, and Denmark), two North American countries (US and Canada), Australia, and Japan.

We based the data collection process on the main components of the ePrescription system model [63–66]. The collected data from the countries included:

- The ePrescription system architecture components. Such components are the architecture type (i.e. centralized or decentralized system), prescription database, medication database, medication history database, clinical decision support (CDS) features, issuing a paper prescription, electronic prescribing types, medical records, and ePrescription for controlled medicine.

- The systems security and privacy protocols in place such as using HL7 protocol, patient consent, and patient's identity verification. Also, the system components identifiers (Pharmacy ID, Prescriber ID, Medication ID, Prescription ID, and Patient ID).

- The process of ePrescription system (the ePrescription information availability to the involved parties, the availability of Drug-Drug Interactions (DDI) information based on the patient health record, storing the ePrescription information for future uses, and the electronic transfer of the prescription to a pharmacy)

This review was retrieved by searching for keywords or/and a combination of keywords from the search engines Google, Google Scholar, PubMed, IEEE, ACM, Dalhousie University library electronic resources, and official digital health websites of the selected countries. The keywords used for the search are "Eprescription", "e-prescription", "electronic prescription", "e-Rx", "eDispensing", or "electronic dispensing" with the name of each of the selected countries. Then, we examined all the retrieved papers and related documents. Besides, we compared all the retrieved data with the official website of the systems used in this review to remove any outdated or false information. Finally, we compared the systems' countries and the data. We present the results using comparative tables.

3.2 e-Prescription systems

3.2.1 PrescribeIT: Canada's e-Prescription System

PrescribeIT is a government-established system for e-Prescriptions service. The system has been partially implemented in some of the provinces and fully in others. The system aims to expand across the nation in all the provinces shortly. A workshop [10] was conducted in 2016 with several prescribers and pharmacists to explore issues in the paper prescription system. Therefore, the system's main purpose is to act as a medium to transfer and exchange prescription information between prescribers and pharmacists. According to [67], the following are the main requirements that resulted from the study for PrescribeIT:

- Secure communication between the pharmacy and the prescriber.
- Effective Drug Information System (DIS) to detect drug interactions for both the pharmacy and prescriber.
- Integration with an Electronic Medical Record (EMR) management system.
- e-Prescription status and alert to the prescriber.
- Security and privacy in accessing patient information.

PrescribeIT defines e-Prescription as the process of transmitting a prescription between a prescriber and a pharmacy with the condition of not affecting the clinical workflow [10]. Therefore, PrescribeIT's primary focus is to enable transmitting e-Prescriptions securely between the involved parties. Besides, PrescribeIT met the requirements by integrating the system with existing health care systems (e.g. DISs, and EMR) available in care provider software [68].

The system will encrypt and send the prescription information from a prescriber to a patient's pharmacy of choice. Moreover, in terms of security, the system provides access control. Figure 3.1 illustrates the architecture of the system. PrescribeIT aims to connect the involved parties by enabling them to exchange prescription information. The system will not replace the current management system in the pharmacies or the prescriber's office. Instead, the system helps monitor the prescription by storing the prescription information of a patient. Figure 3.2 shows the complete architecture and features to be deployed in the future.

Patients' Data Security and Privacy Besides the system is encrypting the patients' prescriptions information while transferring between systems, the user of PrescribeIT (i.e. a prescriber or a pharmacist) must use multi-factor authentication to access the patient's prescription information. The system uses an access control process to grant and revoke accounts on the system. The user is required to use

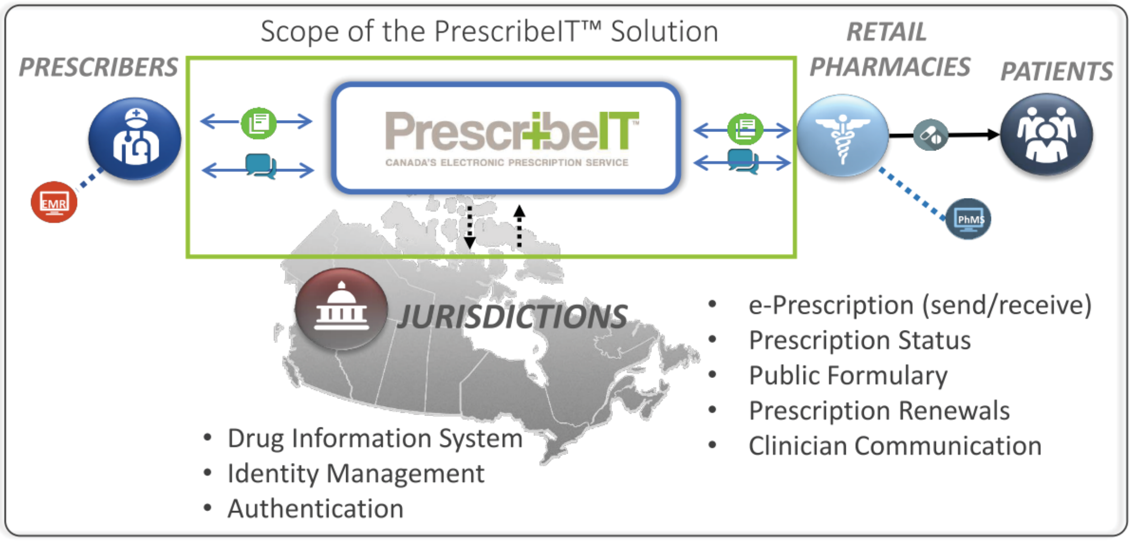


Figure 3.1: PrescribeIT overall structure [Used with the permission of Canada Health Infoway [10]].

password authentication to access the assigned levels in the system. Moreover, for security, all transactions in the system are logged and audited [69, 70].

3.2.2 Surescripts: Private e-Prescription System in the US

Surescripts is an e-Prescription network where the stakeholders in the system can communicate and exchange data. Surescripts is a decentralized e-Prescription network. The parties in the network can communicate with each other using peer-to-peer communication [71]. Surescripts provides the prescriber with the patient's medication history and formulary and benefit information from participating insurers and pharmacy benefit managers (PBMs) [72–74]. Figure 3.3 illustrate the key features of the Surescripts system.

Patients' Data Security and Privacy Surescripts manages the security and privacy of the patient data based on the provided service. Benefit optimization is one of the services that Surescripts provides to caregivers. This service ensures that the patient's drug information is updated and accessible in real-time during patient visits. Surescripts works with the pharmacy benefit managers and the health care payers to acquire this information. Another service Surescripts provides is the medication history. This service provides the caregivers with medication-related information about the patient from the participating patient's community pharmacies and health

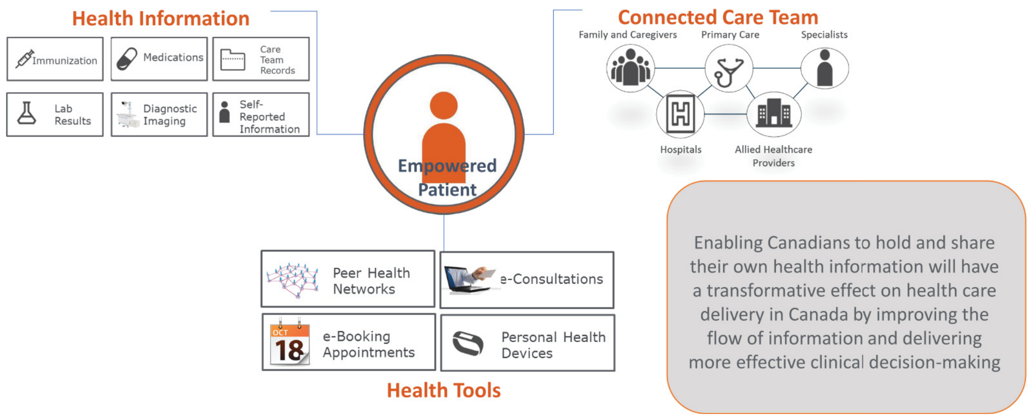


Figure 3.2: PrescribeIT future features[Used with the permission of Canada Health Infoway [10]].

insurance companies. This service requires the patient's consent to give the caregivers access to their medication history information. Clinical history is another service provided by Surescripts. In this service, the caregivers will request the previous care location the patient has attended. The service will cover the location of the past health record and the past prescribed and dispensed prescriptions. Surescripts handles the caregiver request for the medical record from the discovered location about the patient. Most importantly, the e-Prescription service allows the exchange of the prescription electronically. The network allows the prescriber and the pharmacy to exchange prescription information [11].

Electronic PA A prescriber asks for PA from a patient's health insurance before prescribing any medication. This requirement is the health insurance technique used for minimizing the cost of covered medications. Besides, the insurance will not pay any benefits for any medical care without Pre-approval. However, this is mostly the case for more expensive medication. Several drugs are subject to PA. The following is a list of the most frequent reasons why PA is required [75]:

- Brand medications that are available in a generic form
- Expensive medications
- Cosmetic medications
- Medications not usually covered by insurance companies

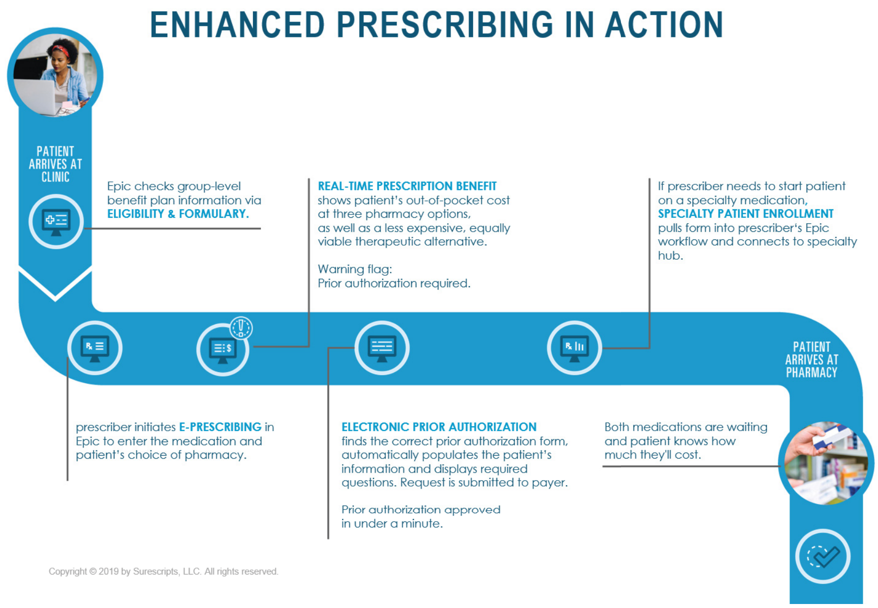


Figure 3.3: Key features of the Surescripts system[11].

Obtaining PA used to be a challenging process. In the past, prescribers needed to send the prescription to the pharmacy choice of the patient. Then, the pharmacist would start to process the prescription and find out if the prescription needed a PA usually through a phone call or by faxing a form. The patient would then be informed using the available channels, usually by phone. Following that, the pharmacist would start the PA approval process using phone calls or fax. This process would take days or weeks to finish. Finally, after getting approval, the patient would be notified that the prescription is ready to be picked up through a phone call. Besides, the increased use of expensive drugs that require PA approval made the process more complicated and time-consuming. The traditional process of obtaining PA eventually affected the quality of service at the prescriber's office. Finally, the prescriber's office had to meet all the different requirements from the insurance, based on the plan and the patient [76]. The PA approval process sometimes would take several days. According to [76], 69% of the patients had to wait several days to get their medications approved by the insurance company. Figure 3.4 illustrate the traditional process of PA.

Surescripts provides an ePA process. Using ePA simplifies the process and increases the efficiency of getting the prescription from the pharmacy without delay. During the e-prescribing process, the prescriber will start the process of obtaining

Figure 3.4: Traditional PA [11].

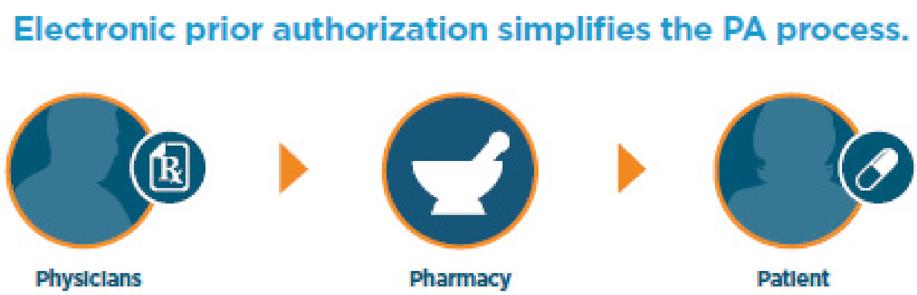


Figure 3.5: Electronic PA in Surescripts [11].

ePA approval. The system will notify the prescriber if there is a PA requirement or not. Then, the prescriber can select another medication option or send PA electronically using the EHR system. Following this, the system will transfer the prescription to the pharmacy, where it will be ready to be picked up [76]. Figure 3.5 illustrate the electronic PA process.

3.2.3 Australia's e-Prescription System

The Australian Digital Health Agency defines electronic prescription as an Electronic Transfer Prescription (ETP) service. The definition of ETP is transferring a prescription securely between a prescriber and pharmacy. The pharmacies and prescribers must use a Prescription Exchange Service (PES) system to communicate and exchange the prescription information securely. The PES system must be approved by the Commonwealth and meet specified security and privacy standards. In Australia, there are currently two PES systems: eRx Script Exchange and MediSecure. The involved parties (i.e. the pharmacy or the prescriber) may be connected to one or more PES systems. According to the Australian Digital Health Agency, the prescriber is responsible for registering their clinical practice with a PES. Also, the prescriber must have software with the ability to send e-prescriptions. Moreover, the prescriber is responsible for encryption key management. The e-Prescription must be encrypted when transferred to the pharmacy's PES. Moreover, both ETP and PES services are essential components for keeping records of the prescriptions and dispensing history. Each patient has a health record in the MyHealth Record system to store all the information generated by the parties in the health record. The patient can then view the prescription information and dispensing information using their portal in the MyHealth Record system. For that, the provider and the pharmacy must have the patient's consent to upload the information to the MyHealth Record system, and the patient must have an active MyHealth Record account. The authorized healthcare providers can view prescription and dispensing history through MyHealth Record system [77][78]. Figure 3.6 illustrates the Australian eRx architecture.

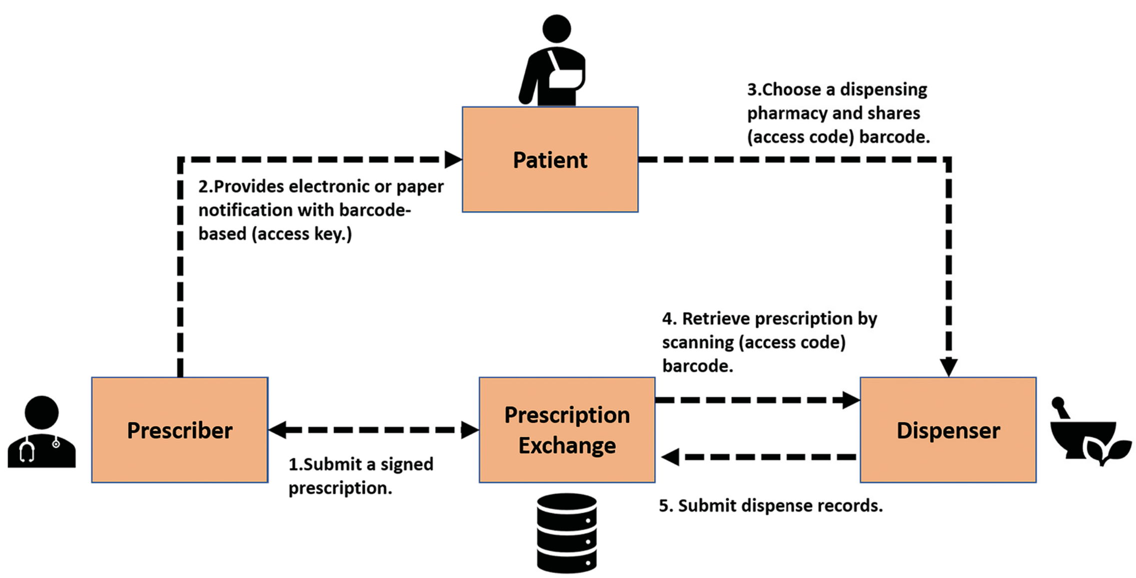


Figure 3.6: Australia eRx Architecture [12]

eRx meets all the legal privacy requirements described in the Privacy Act 1988 in Australia and the eAuthentication framework of the Australian government [12, 79]. According to eRx, all the prescription information is encrypted when transferred through the system. eRx acts as an electronic mail carrier, and only the prescriber and the pharmacist can access the prescription information [12]. eRx can only unlock the first layer of the three-layer encryption. The first layer has just the header information of the data package. This information is needed to send the right prescription corresponding with a scanned barcode in the paper prescription. The header information does not include any personal or medical information about the patient [80].

MediSecure offers the same service as eRx in terms of being an electronic medium used to transfer prescription information between the involved parties. Besides, MediSecure offers the DrShop service, which is a real-time prescription monitoring service. This service will provide the prescriber alerts if the prescribed medication could lead to an addiction [81]. In terms of privacy, MediSecure follows the same privacy methods as eRx [82]. However, MediSecure has a secure Script Vault where they will keep the encrypted prescription until the pharmacy retrieves the information [82]. Moreover, patient consent is required to send the prescription electronically through MediSecure [83].

3.2.4 United Kingdom's e-Prescription System

According to the health authorities in UK, the pharmacies process almost 1.5 million prescriptions are every day, and they expect this rate to increase by 5% every year [84]. 70% of those prescriptions are repeat prescriptions. Therefore, to provide more efficient and accurate service, electronic prescriptions are necessary [84]. The National Health Service (NHS) identifies that the most common users of the Electronic Prescription Service (EPS) are patients who get repeat prescriptions and patients who use one pharmacy to dispense all their prescriptions [13]. Furthermore, EPS is a more efficient method to send prescriptions securely to pharmacies. The EPS is sent through the NHS Spine system. Spine is a central system that allows the secure exchange of patients' health and care information between care provider organizations when needed [85, 86]. To participate in the EPS, patients must give their consent. Figure 3.7 shows the EPS overview system [87]. The system uses smart-cards authentication for the health care provider to access NHS Spine services such as EPS and the patient's Summary Care Record (SCR) [85, 86, 88, 89]. Spine has more than 800,000 smart-card users. Spine identifies the healthcare provider and their access levels for patient information using these smart cards [88, 89]. The system also provides the ability to choose the preferred pharmacy for the patient through the prescriber. This step is called nomination, and a patient's consent is required to participate in the EPS service. Moreover, the patient has the right to request a paper prescription at any time from the prescriber [13, 90, 91]. The system uses unique identifiers for the prescription form. When the prescriber issues a prescription, the system creates three identifiers: (1) the prescription form, (2) the short prescription form ID and (3) the prescription line item UUID. Identifiers 1 and 3 will not be visible for the end-users and only be used by the messaging protocol Health Level Seven International (HL7) [92, 93]. Identifier number 3 will be visible to the end-users and printed, and barcode in the paper prescription [91, 94]. NHS has allowed the use of EPS to prescribe a selected list of controlled drugs as of March 25, 2019. For the controlled drugs not on the selected list, the prescriber will need to use paper prescriptions [95].

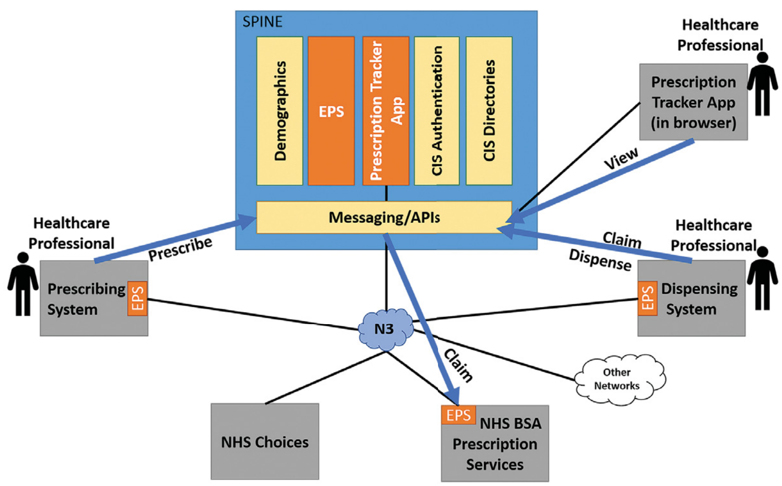


Figure 3.7: UK e-Prescription service architecture [13].

3.2.5 Spain's e-Prescription System

In Spain, the e-Prescription system's primary goal is to ensure the patient's safety and improve the patient's treatment care. According to the health authorities in Spain, the system must include a list of possible medications that the participating prescribers can prescribe. The medication list has a coding system for all the information about every medication approved on the list. The list will help detect drug interactions. Moreover, the system is connected to the patient's electronic health

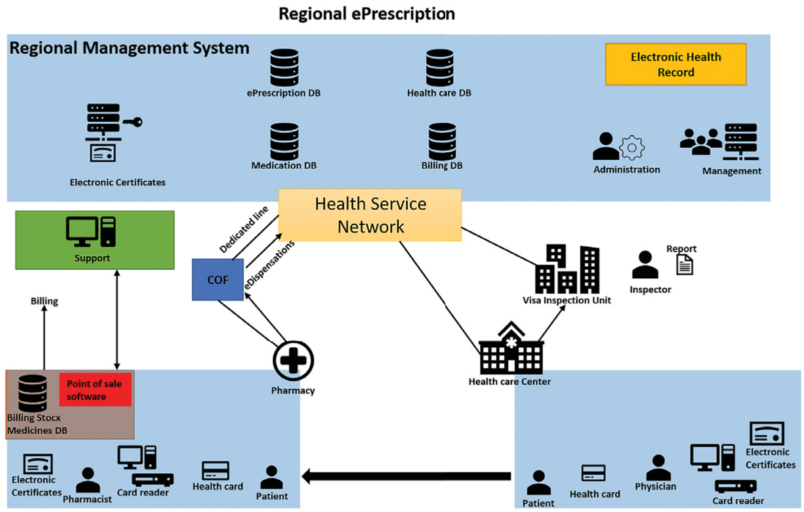


Figure 3.8: Spain e-Prescription system architecture [Adapted from [14]].

record to help identify any other interactions or allergies to the prescribed medicine. Besides, the prescription will be shared with any other prescriber treating the patient. Furthermore, the active prescription will be accessible by all pharmacies in the country. The patients will be able to pick up their medications at any pharmacy in the country or the surrounding countries using the eDispensation service, which is part of the e-Prescription system. Finally, the system uses Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT) to code all the information in the system [14, 96]. Figure 3.8 illustrates the Spanish ePrescribing system architecture.

3.2.6 Japan's e-Prescription System

The current prescription dispensing process in Japan is still in paper form. Figure 3.9 shows the flow of the dispensing process. The prescriber issues the paper prescription and delivers it to the patient. The patient then submits the prescription to the pharmacy of their choice. Next, the pharmacy prepares the medication and dispenses it to the patient. Finally, the pharmacy prepares the medication dispensing records. In addition, patients in Japan have a notebook where they keep a sticker for each dispensed medication. The pharmacy provides the stickers after dispensing. Some of the pharmacies provide an app that acts as a medication history notebook. This notebook acts as a medication database for each patient [15, 97, 98]. Even though Japan uses a paper prescription format, the government has proposed electronic prescription system guidelines in 2016 [16, 99, 100].

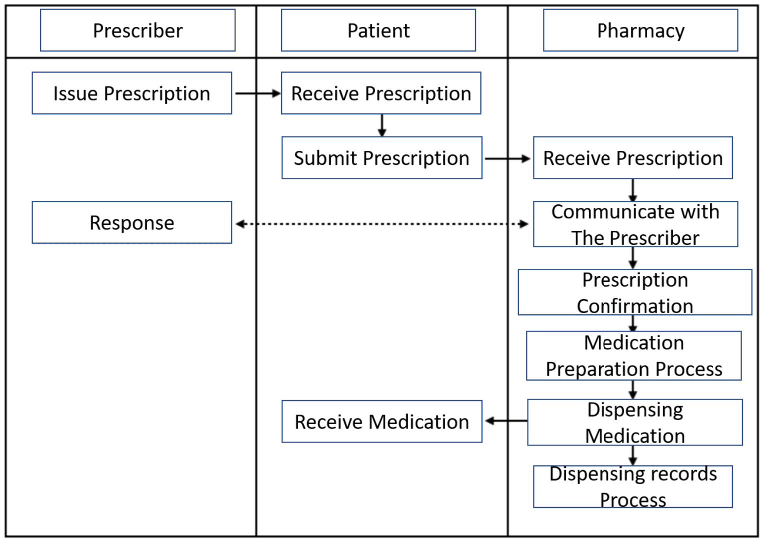


Figure 3.9: Japan current prescription process steps translated from [15].

Figure 3.10 shows the flow, as described in the guidelines published in 2016. The system proposes the use of a copy of the electronic prescription in paper form. The electronic prescription paper contains the prescription ID with the prescription contents. This version of the electronic prescription is carried by the patient and submitted by hand to the pharmacy. Two types of pharmacies can participate in this system. The first type is a pharmacy that can handle electronic prescriptions using the deployed management system to handle electronic prescriptions. The second type of pharmacies can accept only the paper prescriptions [15, 16, 97].

In Japan, the Health Ministry later conducted multiple meetings with the involved parties, namely, prescribers and pharmacies. The results of the meetings are that the proposed system is more complex and requires the added cost of hiring more staff to manage different system components. Therefore, as a result, they proposed more simplified system guidelines. The system was supposed to be ready for use in late 2019 or early 2020 [15].

Figure 3.11 illustrates the newly proposed system where the patient gets an access code from the prescriber. The prescription system issues this access code after the prescriber submits prescription data. The patient has the choice of getting the access code in a paper form or an electronic form sent to their Personal Health Record (PHR) application. The system generates the access code using QR code technology. After the patient goes to the pharmacy to pick up the medication, the pharmacy scans the QR code to get the prescription information from the prescription system in the cloud. The pharmacy then starts the dispensing process. Finally, the pharmacy updates the prescription system with the prescription dispensing data. Furthermore, the patient's PHR application will be updated with the dispensing information to keep it in the electronic medication notebook [15, 97].

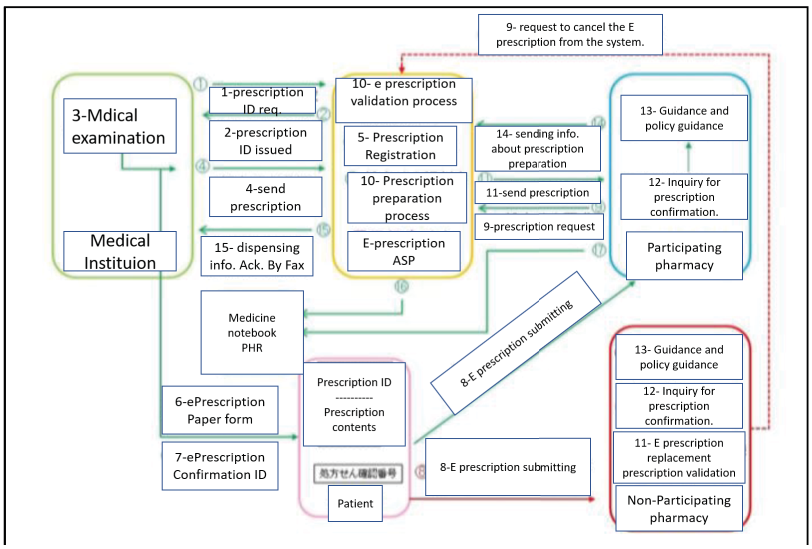


Figure 3.10: Japan e-Prescription system in the 2016 guidelines (translated) [16].

According to a news article [97], the Ministry of Health in Japan published its final report on the e-Prescription system design study results in March 2019. The system will connect the electronic medical record system with the pharmacies' databases using the HL7 standard Fast Healthcare Interoperability Resources (FHIR) [15, 93, 97, 101].

3.2.7 e-Prescription Overview in Sweden

Sweden's health care computerization started in the 1970s when the National Corporation of Swedish Pharmacies was the only pharmacy retailer in Sweden. They distributed minicomputers to all the offices in Sweden with built-in software from the Swedish branch of Data General. The pharmacies use the minicomputers to print medication labels to simplify safety checks in the pharmacies and at the patient's home. In addition, the minicomputers played an important role in developing the

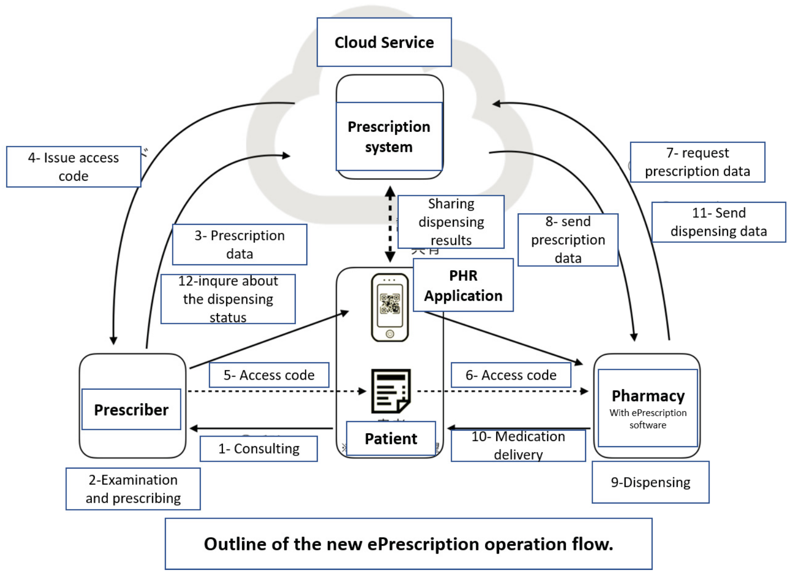


Figure 3.11: Japan new e-Prescription system expected in 2020 (translated)[15].

national prescription database in the early years of e-health compared to other countries. In the 1980s, health authorities introduced patients' smart cards to replace paper prescriptions. The patient's smart cards contain information about recently prescribed medications. After the prescriber writes the information on the card, the patient takes it to a pharmacy. Then, the pharmacist can access the information on the card with the help of the supporting system. Furthermore, the patient can take the card to any other prescriber, which holds their recent medication history. In the prescription writing process, the prescriber uses the support system to access all the information about medication from a national database generated from three sources:

- The product database was created and updated by the pharmacies.
- The medication database contains information about each medication, the recommended dose, and the side effects.
- The drug book contains information about diseases and the uses of medications to treat certain diseases.

The smart card developers made the patient's information only accessible by using the keys stored in the authorized caregiver card keys for access control. In the late 1990s, the use of electronic health record systems in outpatient clinics increased

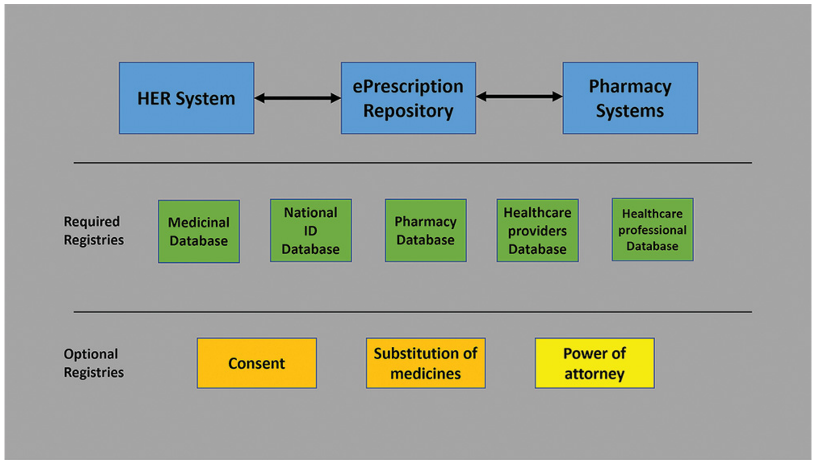


Figure 3.12: Sweden e-Prescription system components [17].

by 90%. Therefore, interest in the electronic transfer of prescriptions has greatly increased in recent decades. Sweden and Denmark were the world leaders in the adoption of electronically transferring prescriptions using the Electronic Data Interchange For Administration Commerce and Transport (EDIFACT) message format. In 2001, they replaced the message format with the XML message format based on the European pre-standard ENV 13607. In 2000, the National Corporation of Swedish Pharmacies replaced changed transferring prescriptions between the prescriber and pharmacies. Instead of using the patient's smart card, they requested that the prescribers transfer the prescriptions electronically to an e-Prescription repository. This evolutionary transition was feasible because the National Corporation of Swedish Pharmacies was the only pharmaceutical company in Sweden. In 2019, the Swedish eHealth Agency changed the system framework by managing the e-Prescription repository. This change was due to the increased number of pharmacy chains, which has led to an increased number of different systems at pharmacies [17, 102–105]. Figure 3.12 illustrates Sweden e-Prescription system components.

3.2.8 Denmark's e-Prescription system

Like Sweden, Denmark is one of the world leaders in the deployment of eHealth for the better care of patients [66, 96, 105]. In the 2000s, Denmark used an ongoing EHR system accessible by all caregivers in public hospitals. According to [106], nearly 85% of Denmark's population had health records in the EHR system by the year

2011. The centralized EHR system provided a robust infrastructure for establishing an e-Prescription system. Therefore, in 2002, Denmark introduced its e-Prescription system nationwide. The Danish Medicines Agency manages the system, and the system is responsible for managing and storing the electronic prescriptions issued by a prescriber. The e-Prescriptions can then be accessed by the patient as well as by prescribers and pharmacies. The e-Prescription records, when accessed by any of the above parties, will provide an overview of all the prescribed medications [66, 96, 106].

3.3 Results

This section will compare e-Prescription systems regarding their overall system architecture, privacy and security features, and medication history management.

3.3.1 Overall System Architecture

As we can see from Table 3.1, the systems are divided into two types, namely, centralized and distributed. First, in centralized systems, all the medical records are stored in centralized servers controlled by a federal regulatory body. The centralized systems help make all the medical records for a patient in all healthcare centres available for the caregiver at any of the health centres. Moreover, centralized systems offer better services for future research and studies. However, many researchers and medical institutions will argue that there is a loss of patient privacy and security when using centralized systems [107]. Many studies showed that centralized systems are vulnerable to Distributed Denial of Service (DDoS) Cyberattacks [107, 108] and social engineering attacks [107, 109, 110]. Moreover, the centralized systems will limit the patient's data privacy, as health records can be shared anywhere across the system [107, 111]. In the US, Surescripts [76] is an e-Prescription network that helps to connect and transfer e-prescriptions between a prescriber and a pharmacist. Therefore, the e-Prescription system is not centralized, and each health centre will store a piece of the patient information in their local systems. A recent update to Surescripts provides the ability to request any health information through the network; however, both parties who want to exchange it need to subscribe to Surescripts. Thus, each healthcare centre stores its EMR in its systems, and it is not accessible from other healthcare centres unless requested.

The decentralized systems offer more information privacy and more protection. However, the centralized approach improves the quality of the offered service and helps minimize the errors in that service. In terms of e-Prescription, one of the benefits of a centralized system is the availability of the patient's medication history to all parties. Thus, minimize medication interaction errors and Adverse Drug Reactions (ADR). As shown in the US case study, decentralized systems are also able to share medication history with other parties. However, this process is subject to in-place conditions, such as a health centre agreeing to share information with other parties or subscribing to the same e-Prescribing service. Other approaches, such as [97] propose that the medication history should be controlled by the patient and sent to the requesting parties. Moreover, other approaches [112–115] provide access to the patient using web portals to display relevant information about an e-Prescription in order to request medication delivery to the home. In [116], the authors propose an e-Prescription system in which the patient has the central role. This approach aims to give the patients priority in making decisions regarding their health.

One central aspect of the e-Prescribing systems is that they support prescriber decisions regarding prescribing medications to patients. These systems aim to help prescribers safely prescribe medications to patients. Such features are drug-drug interaction alerts, drug-allergy alerts, recommended doses, and drug information when prescribing any medication to a patient [117, 118].

From Table 3.1, only the Surescripts [71] (i.e. the US e-Prescription network) and Spain's e-Prescription [14] systems have Drug-on-Drug Interaction (DDI) alerts integrated in their systems. For other countries, to the best of our knowledge, there is no mention on the systems' websites about the description of their system; or the system architecture does not have the required CDS features. However, other survey studies suggest that most systems are likely to incorporate the CDS. For example, according to [117, 119, 120] in the UK, CDS systems are not a part of hospitals' systems or part of the e-Prescription system, but there is interoperability between the CDS systems and other systems to help with prescribing medications to patients safely. Moreover, according to [121] in their survey on the most common methods used to identify any case of Potential of Drug-Drug Interactions (PDDI), they found more than half tend to search for the drug name and use facts and comparisons to identify PDDI. They use various keyword strategies to search various databases and web resources.

The patient's medication history is an essential part of improving the safe prescribing of medication to a patient. This feature will help avoid any DDI and enhance the treatment process to lead to personalized care [122–124]. In Table 3.1, we see that not all the systems have this feature available to the prescriber. However, most of the systems incorporate this feature in EHR systems. For example, the UK system has this information in the patient record rather than in the e-Prescription service. The incorporation of medication history is different in some countries because of their definition of the e-Prescription system. In the UK, it is defined as a service for transferring electronic prescriptions from a prescriber to a pharmacy. While in Japan, the medication history information should be included in a patient's e-Prescription service application [16]. In [125], the authors propose a new approach for displaying patients' medication history in a timeline model. In their timeline, the medications will be displayed relevant to the time a patient took them. Their design aims to understand better a patient's complex medication history, which will help a prescriber reduce the work rate load of looking up the medication history and when the patient took those medications.

Issuing an e-Prescription for controlled medication is a significant limitation in all the systems mentioned above except Surescripts [126]. In the US, the e-Prescribing of controlled medication was permitted in 2010 [127], and the certification process was approved in 2013 [128]. In other systems, to the best of our knowledge, there is no available information about using e-prescriptions to dispense controlled medication. The e-Prescription service does not offer the prescription of controlled medication.

3.3.2 Patient Identity verification and e-Prescription Encryption

The need for a unique ID for all the involved parties in e-Prescription systems is crucial to make the systems fully automated. We can see in Table 3.2 that most of the systems have assigned unique IDs for the involved parties in the system, i.e., patient ID, prescriber ID, pharmacy ID. Assigning unique IDs for the mentioned above parties will help transfer e-Prescriptions efficiently and help avoid transferring or storing errors. Moreover, assigning unique IDs to each prescription and medication

Table 3.1: Comparison of the systems overall architecture

System	Surescripts	PrescribeIT	UK	Sweden	Denmark	Spain	Australia	Japan
Benefit Optimization	✓	✗	-	-	-	✓	✗	✗
Electronic Prescribing	✓	✓	-	-	-	✓	✓	✓
Prior Authorization	✓	✗	-	-	-	-	-	✗
Clinical History	✓	✗	✓	-	-	✓	-	✗
DDI Alerts [1]	✓	✗	-	-	-	✓	-	✗
Centralized System	✗	✓	✓	✓	✓	✓	✗	✗
Prescription Database	✗	-	✓	✓	✓	✓	✓	✓
Medication History	✓	✓	-	-	-	✓	Consent Required	✓
Medication Database	✗	-	✓	✓	✓	✓	✓	✓
Issuing Prescription	✗	✓	✓	✓	✗	-	✓	✓
e-Prescription(controlled Medicine)	✓	-	✗	✗	✗	-	-	✗

[1] The symbol (X) means that this feature does not exists in the reviewed system to the best of our knowledge.
[2] The symbol (–) means no information about the reviewed system's feature introduced or reported in the literature or the system's official website to the best of our knowledge
[3] DDI: The DDI alerts incorporated as part of the system.

Table 3.2: Comparison of the security and privacy features in the systems

System	Surescripts	PrescribeIT	UK	Sweden	Denmark	Spain	Australia	Japan
Pharmacy ID	✓	-	✓	✗	✗	-	✓	✗
Prescriber ID	✓	-	✓	✓	✓	-	✓	✗
Medication ID	✓	-	✓	✓	✓	✓	✓	✓
Prescription ID	✗	✓	✓	✗	✗	✓	✓	✓
Patient ID	Master Index	✓	✓	✓	✓	✓	✓	✓
Patient verification	-	-	-	-	-	Health card	-	✗
Participate consent	✗	✗	Choosing pharmacy	✗	✗	-	✓	✗
Using HL7 [1]	✓	-	✓	✗[2]	✗[3]	-	✓	✗

[1] The symbol (X) means that this feature does not exists in the reviewed system to the best of our knowledge.
[2] The symbol (–) means no information about the reviewed system's feature introduced or reported in the literature or the system's official website to the best of our knowledge.
[3] HL7 is a communication protocol to transfer the medical information from the ehealth service system to another. HL7 is used to encode the information to be readable to all the ehealth services systems [93, 129, 130].
[4] The Sweden eHealth systems uses a service-oriented communication end-point for the technical protocol, They uses ENV 13607 standard [113, 131, 132].
[5] The Denmark e-Prescription uses the MedCom communication standard nationwide. MedCom was established in 1994 in order to develop the communication standards for transferring medical records and information between health centres nationwide [102, 106].

will help manage each patient's prescription and all the prescribed medications in that prescription. As a standard practice, the system uses prescription IDs and medication IDs to keep a medication record for each pharmacy patient. Furthermore, prescriptions and medication records help manage the vast number of prescriptions a pharmacy had to manage.

Although no evidence is shown in the ePrescription systems' websites that they are using these IDs to verify patients' identities at the medication dispensing process, the existence of these IDs might suggest there is a verification process in place. For example, the pharmacists might swipe a patient's health card or asking the patient's Id verbally for verification. In Spain's e-Prescription system, the patient must show their health card to pick up their medication.

In terms of the communication protocol, most of the systems are using the HL7 protocol to encode and decode e-Prescription information between the involved parties [116, 130, 133–136]. For encryption, most of the systems use standard encryption methods such as public key infrastructure (PKI), such as in Australia and Canada [137, 138] or other standard authentication algorithms.

3.4 Discussion

After exploring the current e-Prescription systems, it is clear that they are different in applying this service. Due to several reasons, the difference is related to the countries' regulations and rules or the existing infrastructure [66]. However, several limitations might hinder improving the quality of the service provided to the patient.

3.4.1 Centralized or decentralized systems

Governments are progressing toward applying IoT solutions in health care services to enhance the quality of service and efficiency regarding the provided service. Moreover, an essential factor when handling patients' medical information is their privacy and security. E-Prescription and medication history are part of the patient's medical data. This part of medical data requires a critical level of privacy, and it should be stored securely due to the severe risks associated with it. One type of risk is tampering with a patient's medication intake instructions, which could cause the patient's death.

Therefore, many researchers [139–142] emphasize the need for security and privacy policies and protocols to use IoT solutions in health care.

One crucial challenge of e-Prescription systems is whether the system's overall architecture should be centralized or decentralized. As shown in Table 3.1, many e-Prescription services are centralized to connect to the EHR system of the patients. However, some countries have adopted the decentralized approach because of the existing infrastructure. For example, in the US, EHR systems are available at most hospitals and health care centres. Several approaches [51] have been proposed for decentralized systems for health records, medication histories, and e-Prescription to preserve patients' privacy and prevent any pointed attacks on medical information. However, many countries' regulations require a central physical location to control access to medical data. Therefore, an adaptable approach will help solve most architecture issues, such as a system designed to store, transfer, and share needed data (e.g. the patient's prescription history or medication history). Such a system can use any authentication protocol through a token handed to the patient, a key stored in a barcode, or a mobile application accessed by only the patient.

3.4.2 Medication History

Another challenging issue is the availability of medication histories to other parties participating in the system, such as pharmacists. According to [143], in their quantitative study of the differences between medication histories obtained by physicians and pharmacists by reviewing 200 medical records, pharmacists are better at identifying medication information from patients' medication histories. than physicians. In addition, several studies [144–147] found that all the medication histories information collected by pharmacists' interviews are complete when compared to the information collected by other caregivers. As a result, making the medication histories available to all parties involved in the system might enhance patient safety when prescribing or dispensing a new medication. Moreover, other study results showed that caregivers collect medication history information from patients at the initial interview during the admission process [122]. This process makes the information unreliable due to human errors, as it is dependent on the patient's memory, and it can lead to inaccurate information [143]. Thus, making electronic medication histories available and accessible to transfer when needed can improve the provided services' efficiency and quality.

3.4.3 Clinical decision support (CDS)

CDS systems are developed to help prescribers prescribe medications safely. The development of these systems aims to assist the prescribers and alert them of the various drug interactions that might occur while prescribing a medication to a patient [117]. Many studies [148–152] showed an improvement in avoiding medication errors when using e-Prescription with CDS alerts. However, other studies [153, 154] showed that prescribers tend to ignore and override less important alerts when overwhelmed by the number of alerts and the way they are displayed appearance. When the number of less important alerts increases, this might increase the risk of medication errors. Additionally, [154] found in their review of the studies reported prescribers overriding and ignoring of less important alerts, that between 49% to 96% of times the prescribers received drug interaction alerts were overridden or ignored. Therefore, incorporating CDS alerts to an e-Prescription system is necessary, and new visualization methods could reduce the ignoring and overriding of cases. A new algorithm based on the patient's medication information might reduce the number of less important alerts.

3.4.4 AI and Blockchain Technologies

Blockchain

is a technology deployed best for decentralized systems. It is a technology to store the data in a secure and distributed method. This technology intended to remove the need for a centralized authority to control and verify the data [51]. Therefore, we can see from Table 3.1 and 3.3 the US, Australia and Japan are candidates to implement the blockchain method because of their decentralized systems. However, those systems still lacking the connection between the other parties to facilitate such an approach. In the US, the e-Prescription system is operated by a middleman (i.e. Surescripts), which makes the system is semi-centralized when it comes to managing data sharing between the subscribers [51]. As mentioned in the Results section, Surescripts enables its subscribers to request patient records from other health centres. The other centres

Table 3.3: Comparison of the study aspects included in the studies between previous studies and this comparative study.

		System Architecture	**Medication History**	**CDs**	**Patient Privacy**	**System Security**	**AI and Blockchain capability**
Previous Studies (Samadbeik et al., 2017; Deetjen, 2016; Kierkegaard, 2013; Timonen et al., 2018)	Canada	CN	CN	CN	CN	CN	CN
	US	D [a]	No	No	AN	AN	AN
	UK	C	No	No	AN	AN	AN
	Spain	CN	CN	CN	CN	CN	CN
	Denmark	C	No	No	AN	AN	AN
	Sweden	C	No	No	AN	AN	AN
	Australia	CN	CN	CN	CN	CN	CN
	Japan	CN	CN	CN	CN	CN	CN
Current Study	Canada	C	Yes	No	Yes	Yes	Not Fully
	US	D	Yes	Yes	Yes	Yes	Semi [b]
	UK	C	No	No	Yes	Yes	Not Fully
	Spain	C	Yes	Yes	Yes	Yes	Semi
	Denmark	C	No	No	Yes	Yes	Not Fully
	Sweden	C	No	No	Yes	Yes	Not Fully
	Australia	D	Yes	No	Yes	Yes	Not Fully
	Japan	D	Yes	No	Yes	Yes	Not Fully

[a] C= Centralized System, D=Decentralized, CN= the country is not included in the study, AN= information about the aspect not included in the study, and = information about this aspect was included in the study.

[b] AI and Blockchain capability: Not Fully= system do not have the necessary requirements, and Semi= some infrastructure available for AI exist.

will then handle the request and share or hold that information (Surescripts, 2019). The subscription process limits the Blockchain network in making the data up to date and available to all the involved parties. Australian and Japan e-Prescription systems are not fully decentralized systems. Their approach is to provide peer-to-peer communication between the prescriber and the pharmacy. This approach allows the pharmacies to update the prescriber system about the status of their patients' e-Prescriptions. Therefore, the infrastructure of those systems lacks the capability at this time of adopting Blockchain technology.

For the other systems (i.e. the centralized systems), adopting the technology is more challenging since their approach has a central point to control the information. This approach is more costly to provide the needed security and privacy to protect patient data. Installing and managing the security of patient data might cost hundreds of millions of dollars [51, 155]. Thus, an approach that contains more of the benefits of the decentralized architecture, transparency, data integrity and immutability such as Blockchain will solve the security and privacy issues and address concerns about the patients' information in the ePrescription systems [156]. Moreover, this approach is more likely to help save valuable time wasted to look to the updated medication history for a patient [157, 158].

Artificial Intelligence (AI)

in healthcare is introduced to support medical decisions. AI is more likely to be adopted as the next logical step in healthcare technologies. It is more likely to provide better knowledge for patient care and keep updated information about patient status. Machine learning (ML) and Deep Learning (DL) are the leading technologies in AI. Both technologies are developed to learn patterns about a type of information to suggest accurate predictions. In order to predict efficiently and accurately, these technologies require learning patterns from a large amount of data. Thus, the type and amount of collected data about a patient are important factors. Therefore, developing the system infrastructure to collect the data about the patients' health is a necessary process [159].

Therefore, we can see from Tables 3.1 and 3.3 the leading country of collecting data process, is Spain. The type of collected data is an important factor and is more likely to help adopt ML and DL faster than other countries. However, the communication between parties in Spain might limit this process, as shown in Table 3.2. On the other hand, centralized systems are more likely to adopt these technologies faster than decentralized systems (e.g. US) due to the required data collection process.

3.5 Chapter Summary

According to our review, it may be worth considering a different e-Prescription model to overcome the discussed challenges in current systems. This model should include sharing prescription and medication history information between all participating parties in the system. This approach could benefit from the available centralized systems in the countries by incorporating a standalone service that securely transfers and stores medication history data and e-Prescriptions. This service should also preserve the patients' privacy by applying an authentication mechanism to the authorized parties to access the data. Moreover, medication histories should be available to patients to enhance patient safety regarding medication errors. Also, this process will grant the patient the ability to share accurate medication histories. Lastly, CDS systems should be incorporated in the e-Prescription service and redesigned to avoid ignoring and overriding alert issues when the less critical alerts overwhelm the caregiver. Furthermore, adopting the ePrescription systems would help avoid unnecessary contact, lowering the COVID-19 exposure rate. Moreover, it will emphasize the patient's safety and caregiver safety. Finally, we believe this review will provide a broader perspective on e-Prescription systems around the world. In addition, it will lead to a global e-Prescription system design available to patients when travelling outside of their home country.

Chapter 4

Preliminary Work on NFC System for Medication Dispensing

4.1 Introduction

Presented in detail in the research aptitude defence report, we proposed our first system design titled *"A System to lower the risk of dispensing medication errors at pharmacies using Near Field Communication (NFC)"* [160]. In this proposal, we developed an NFC-based system comprised of mobile applications for patients' smartphones to transfer verification information through NFC and a pharmacy management system connected to an NFC reader. Furthermore, the app uses biometric authentication to access the mobile application to ensure patients' sensitive information is secure. This authentication feature also restricts access to information to legitimate users and only during the medication dispensing process. In the next section, we will present our previously proposed design.

4.2 Proposed System

The proposed system components are: a smartphone (i.e. the patient's smartphone) with the application installed, the pharmacy management system, the web server, an NFC tag attached to the medication packaging, and an NFC reader for pharmacy management systems. Figure 4.1 shows the proposed system components. Figure 4.2 shows the sequence graph of the medication dispensing process.

In the first step, the user will need to authenticate his/her identity using the fingerprint scanner embedded in the phone. Then, the application will generate a timestamp the use it to generate the hash value. At the same time, the application will send the timestamp value to the webserver. Next, the application will request the active prescription IDs from the webserver. The prescription information will only be stored in the web server and only shared as needed with the user's phone. Then, the application will use the chosen prescription ID, user ID, and timestamp to generate the hash value and send it to the webserver. After, the user will tap their phone to send the hash value to the pharmacy management system to verify the identity with the webserver and obtain the necessary information (i.e. name, medication ID, prescription ID) to dispense the medication. If the verification is successful, the webserver will send back the necessary information. Then, the pharmacist will tap the medication, which has an NFC tag attached to the packaging. The NFC tag will contain the medication name and ID. After tapping, the pharmacy management system will verify the medication ID by matching it with the ID in the prescription information. If the matching is successful, the pharmacist will hand out the medication to the patient. Finally, fingerprinting has been set up for the first time using the app. The patient will not access the app without using their fingerprint, and transferring the information will not start. This authentication step will help validate the patient for the medication dispensing process and help secure the patient's sensitive information. Figure 4.3 shows the mobile application interfaces.

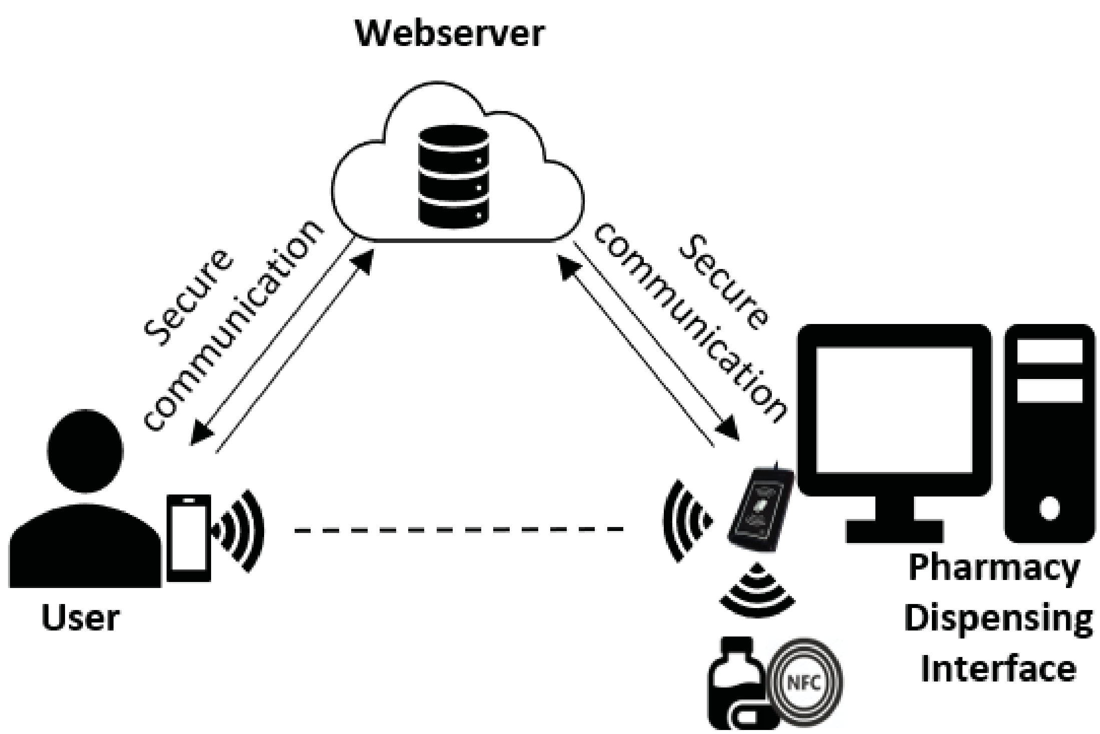


Figure 4.1: The components of the proposed System Architecture

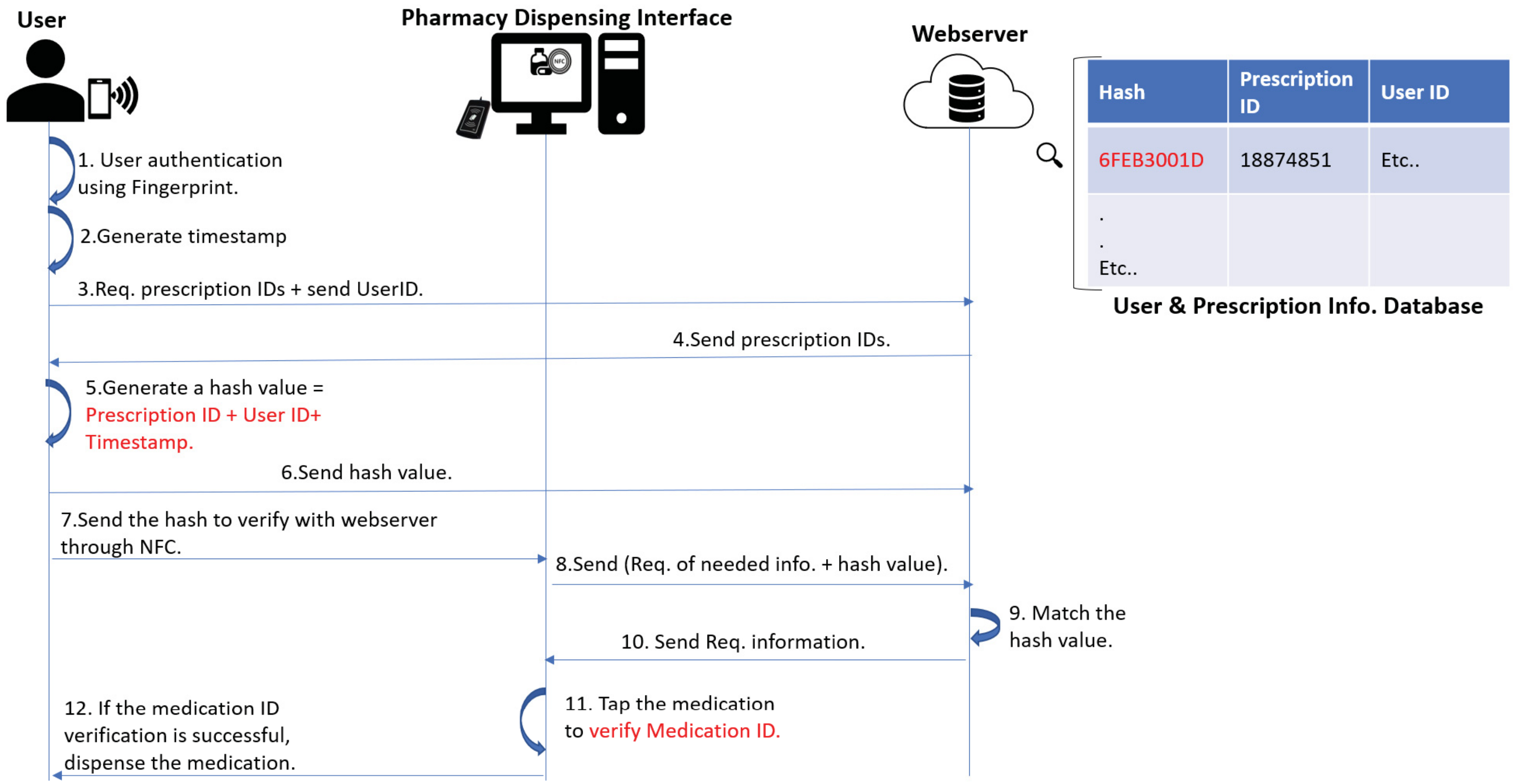


Figure 4.2: The sequence diagram of the dispensing medication process.

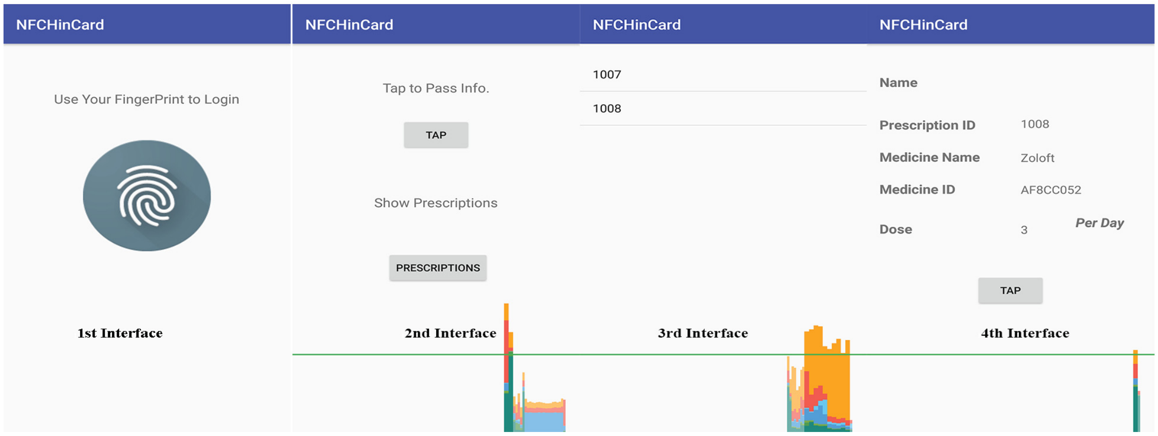


Figure 4.3: The mobile application interfaces.

Assumptions

Our proposed system introduced three components: the user smartphone, the pharmacy management system, and the webserver. These components in the medication dispensing process will communicate in order to transfer the information. However, these communications are essential toward achieving this research's objective, not the main focus of this chapter. Therefore, we assume that the communication between the smartphone and the webserver is secure, and the pharmacy management system is secure. Moreover, the prescriber will submit the prescriptions to the webserver through their management system. Such systems are presented in [71] and [10].

4.3 Proposed system compared to current systems

The authors in [1] proposed ten strategies to lower the risk of medication dispensing errors. The authors indicate that most dispensing errors are the result of error-prone systems and processes. Therefore, we aim to avoid most conditions and scenarios that might cause medication dispensing errors through the proposed system. In Table 4.1, we highlight the most relevant strategies and compare the current systems (mentioned in chapter 2) in the pharmacies and the proposed system. According to the authors in [1], the strategy of thoroughly checking the prescriptions will be the last step in the medication dispensing process. Thus, this step is encountered in the proposed system by validating the medication with NFC technology before dispensing.

The compared systems do not specify a checking process method, so the pharmacist deals with this manually. The proposed system will make the prescription and instruction always available in the application, while the compared systems offer only pharmacist counselling. Moreover, in designing the proposed system, we considered five goals for achieving quality service and minimizing the risk of medication errors. In Table 4.2, we mention the goals and discuss how we achieved these goals. First, we made the system highly available by making the prescription information available to the patient. Second, the system should be reliable and provide quality service by minimizing medication dispensing errors. Third, as discussed in the previous section, the system will provide security and privacy for the patient's sensitive information. Finally, the system will reduce the time needed to prepare the prescription in advance. This step will eliminate some unnecessary steps from the pharmacist's work rate.

4.4 Application and security analysis

4.4.1 Application performance analysis

This section will discuss the smartphone application performance regarding CPU, memory, and network connection. After analyzing the CPU performance, we found the highest usage of the CPU resources is 11.6% while creating the hash value. In the rest of the process, the average CPU usage was almost 6%. That including transferring information through NFC and connecting to the webserver to acquire the prescription information. In Figure 4.5, we show the smartphone application usage of the CPU.

Second memory usage The app starts by allocating 64 MB at the start of the app, and it uses only 33 MB in the idle stats (i.e., no activity in the app). The allocation will increase with the authentication process; then, it will reach 48.33 MB (i.e. the highest) while transferring the information through the NFC and the webserver. Finally, the app uses almost 50 MB from the allocated memory (i.e., 64 MB). It uses a considerably low allocation since the total memory in the smartphone we used is 3 GB. Figure 4.5 shows the memory allocation by the smartphone application.

Third network connection, we developed the app to use the minimum connection needed to send and receive the necessary information for the app. In Figure 4.5, we can see that it took almost a second to complete the connection session for both

Table 4.1: The comparison between the current e-prescription systems and the proposed System to encounter medication dispensing errors using the most relevant six strategies to prescription filling and medication dispensing [1].

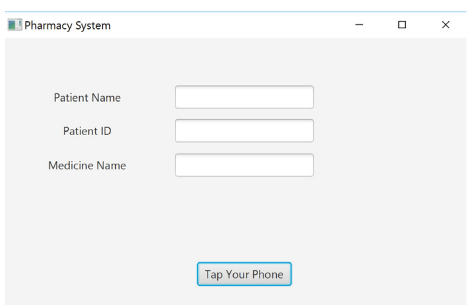
Strategies	**Surescripts & PrescribeIT**	**The Proposed System**
Ensure correct entry of the prescription	Yes	Yes
Confirm that the prescription is accurate	Yes	Yes
Beware of look-alike, sound alike drugs	No	Yes
Reducing stress and balancing heavy workloads	Yes	Yes
Thoroughly check all prescriptions	Manually	Electronically using NFC
Always provide thorough patient counselling	Pharmacist only	Pharmacist & patient mobile app

Table 4.2: The achieved goals by the proposed System.

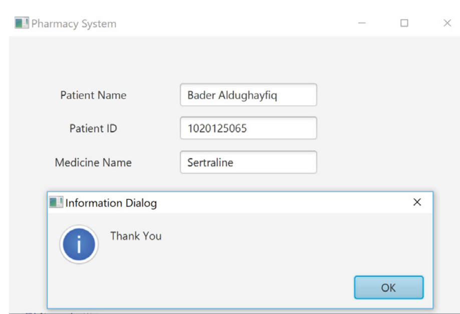
Goals of the proposed System	**How proposed System achieved goals**
Prescription information availability to the patient	∗Electronic prescriptions (i.e. present, and past). ∗Intake instructions available all times on the patient's mobile phone.
Reliability	∗Ensure to dispense the right medication and right dose to the right patient. ∗The electronic prescription from a prescriber prevents handwriting misinterpretation.
Security and privacy	∗The fingerprint authentication will control access to patient's sensitive information. ∗Only the needed information will be sent to requesting party.
Efficiency	∗Reducing the time needed to provide the service by sending prescriptions in advance.

connections. The first connection is to get the information on the list of prescriptions related to the patient. This connection had a data sent rate of 6.31 KB/S and a receiving rate of 5.04 KB/S. The second connection was to get the information for a single prescription, which the user chose in the previous connection. The connection rates were 14.76 KB/S for the sent data and 13.63 KB/S for the received data. We configured the app and web server connection to remain open only when needed. Therefore, this method intends to minimize the risk of threats due to open port attacks.

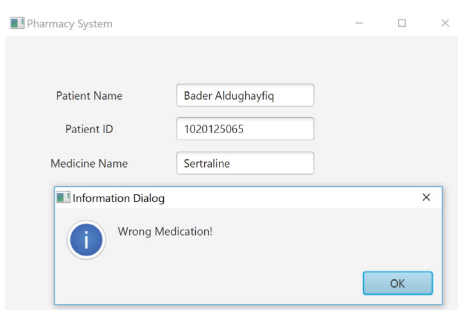
Finally, dispensing one medication to transfer the information and validate the user took almost 6 seconds. This time is optimal since the process includes the required verification steps.



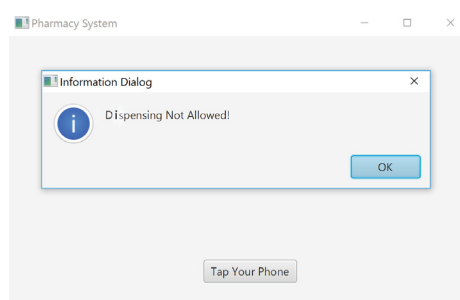
(a) The main interface.



(b) The dispensing successful interface.



(c) The medication verifying interface.



(d) The interface if prescription not valid.

Figure 4.4: The Pharmacy Management System Interfaces during the dispensing process.

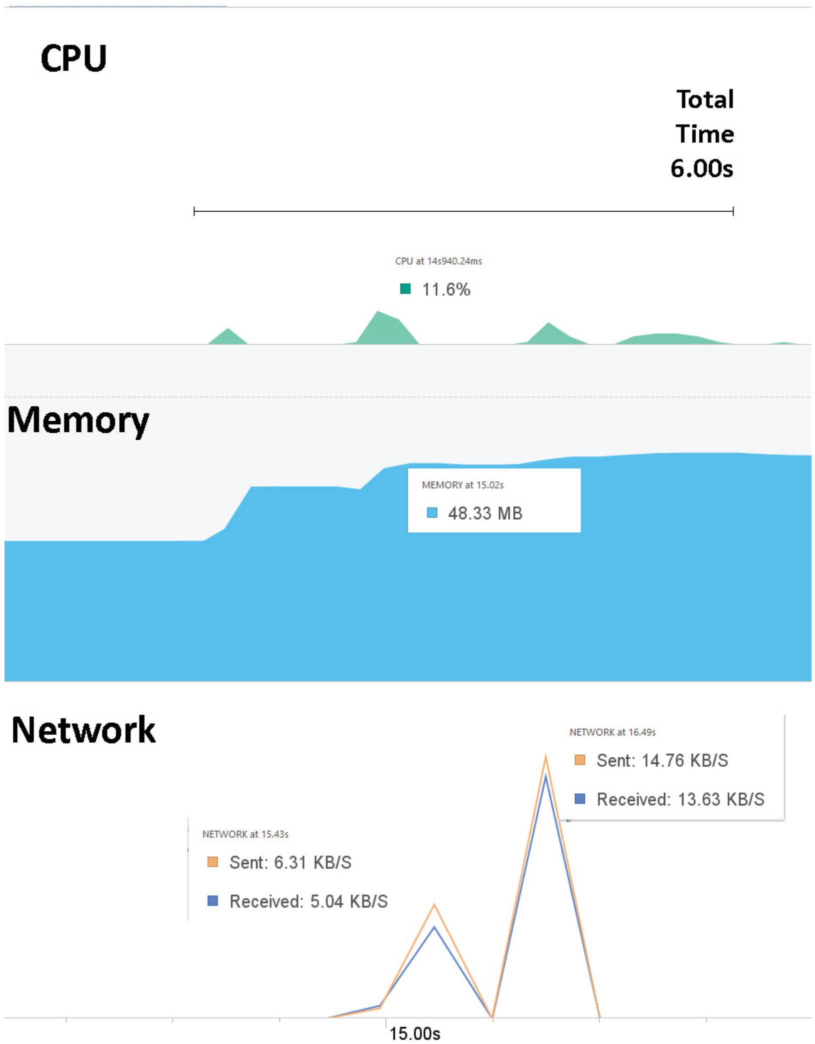


Figure 4.5: The mobile application CPU, memory, and network evaluation.

4.4.2 Security Analysis

Tempering the medication tag

Medicine information (i.e. the name and ID) entry process in the database will be during the manufacturing process. Therefore, the pharmacist management system will detect any attempt to tamper with the tag's content during the medication information matching process. Also, even in a scenario where the pharmacist will prepare the medication and change the packaging, the pharmacist will attach an NFC tag containing the same ID corresponding to the medicine name and ID in the database.

Hash confidentiality and integrity

The system uses the hash value to verify the user. It is only generated by the user's smartphone application using a timestamp (i.e. generated each session), user ID, and prescription ID. The User ID is stored in the smartphone application and the database. The phone will encrypt the User ID before transferring it through the NFC. As mentioned in the assumption section, it is only securely sent to the pharmacy management system from the webserver. Also, the prescription ID is sent securely to the smartphone application from the webserver. The prescription ID is not stored in the smartphone and is only requested when needed to lower the risk of any sniffing attack. Since the hash value is generated using three separately stored values, replicating the hash value will be difficult, and the attacker will need all three values. Thus, the proposed methods will protect the hash value's confidentiality and integrity in the system.

Fingerprint-based authentication

In our system, we require users to verify their identities using their fingerprints. This step ensures role access control of the application. The phone only permits the right user access to the application services, which will protect their sensitive information. After accessing the application, the patient will send their ID through NFC to allow the prescriber management system to send it to the webserver for the identity verification process. If the match is successful, the webserver will send the required information.

The biometrics information will be only used to log in to the mobile application and not stored in the framework servers. The Android os and Apple ios manage the storage of biometric information and the security and privacy. According to [161, 162] the user fingerprint will be stored into a secure memory in the phone separated from the main memory. In both operating systems, the developers will use biometric authentication as a feature to grant access to the application but not store any biometric information. The biometric information we use is a login mechanism to prevent any NFC conection without the user's knowledge. A PIN could replace this feature upon the user's preference.

NFC security and relay attack

The NFC is a close-range distance communication that requires the user to be in close range, 4 cm, from the NFC reader. This feature ensures users' physical presence, making obtaining the app ID difficult in any malicious activities. However, the relay-attack has proven it will be able to relay the information regardless of the range between the reader and the NFC device [163]. In the mentioned attack, the attacker will initiate an NFC communication channel with the victim's application using a rogue NFC reader simulating a legitimate reader (i.e. a pharmacy system's NFC reader). After obtaining the information (i.e. prescription ID), the attacker will submit the prescription using another NFC-enabled smartphone simulating the victim's device. Therefore, we require fingerprint authentication to prevent any rogue access to the information in the mobile application and to initiate any NFC connection. Therefore, establishing an NFC communication from the patient mobile application will not be possible unless the user accesses the application using their fingerprint and initiate the connection.

4.5 Chapter Summary

This chapter presented a system to provide an efficient, secure, and accurate medication dispensing process. Our work aims to minimize medication dispensing errors (i.e. wrong medication and/or wrong dose). We developed a mobile application for patient use. This application is used to authenticate the patient by using biometric authentication. Also, the patient will use NFC technology to transfer the necessary verification information to a pharmacy management system. Furthermore, medication validation is required at the last phase of the medication dispensing process to match the right medication with the right patient. Last, we evaluated the patient mobile application's efficiency and security. Also, we evaluated the efficiency of transferring information through NFC. Finally, even though the system will not prevent human errors, it will reduce the risk of dispensing the wrong medication or dosage.

Chapter 5

NFC-Based Mobile Application Usability Study

We conducted a user study to evaluate the usability of the proposed mobile application. We aimed to compare the current dispensing medications method with the proposed process using the NFC mobile application. The following are the research questions regarding the user study that we compiled to guide this study:

- What information is the patient willing to share to authenticate their identity before dispensing the medication? If yes, are they comfortable with sharing that information?
- How secure is the patient authentication process from the patient's point of view?
- Does the patient think it is reasonable to share this information?
- Verifying the patient's identity during the medication dispensing process will help mitigate medication errors by avoiding dispensing the wrong medication to the wrong patient.
- Transferring the prescription information securely using the NFC technology.
- What privacy precautions concern the patient while sharing confidential information during the medication dispensing process to avoid errors?
- What are the strengths and weaknesses of the proposed system from the patient's point of view?
- Will the proposed verification method help prevent medication dispensing errors?

We anticipate that the proposed system will enhance patients' privacy during the medication dispensing process from these questions. Moreover, we anticipate that the study will evaluate the current authentication process while dispensing medication to the patient. Also, we believe the study will explore what type of information the patient is willing to give to authenticate their identity. Also, we believe that the study will explore the methods of verifying the medication before and after a medication's intake times and give clear guidelines on the measurements needed to protect their privacy during the medication dispensing process from the patient's point of view. Finally, we anticipate that the usability study will help us understand the proposed system's effectiveness, ease of use, learnability, satisfaction, and usefulness.

5.1 Procedures

The usability study is a one-on-one session. We recruited 21 participants, all of whom had picked up medication from pharmacies in the past six months. Even though the sample size is small, research has indicated that five subjects are enough to detect errors in a usability test [164–166]. Hwang et al. proposed that using the rule 10 $\pm$ 2 is sufficient to discover 80% of usability problems [167]. Moreover, this number is recommended in thematic analysis approaches to provide reasonable quotes, codes and themes of the issue under study [168]. In addition, Jakob Nielsen [169] indicated that at least 20 users should participate in usability testing if it includes a quantitative method. Based on that information, we believe that 21 participants will be sufficient to evaluate the application's usability and expose most of the proposed application's weaknesses and strengths. Furthermore, we believe the study will provide thorough feedback for improving the overall framework in the following research phase.

We started with the pre-session questionnaire. The questionnaire is a set of general demographic questions that better understand an audience's background characteristics. These characteristics will measure the participant's comfort with using the smartphone application and sharing private information with a drugstore to verify their identity. Table 5.2 and 5.1 show the complete demographic statistical information about the participants.

The pre-session questionnaire is shown in Appendix E. Next, we ask the participants to perform the prepared tasks. We have four tasks divided into two sets, and each set has two conditions (i.e., the right medication and the wrong medication.) We are using the Latin Square design mod 5 to control the order of performing the tasks. Before the participant begins performing the tasks, they will be assigned to one of the tasks-order groups to draw a number from the hat method. After this, the participant will apply the tasks using the assigned order.

Moreover, the task will allow the participants to expose the application weaknesses and strengths as much as possible. The applications used in the tasks aim to give the participant a feeling of realism when performing the tasks. After each set of conditions, a post-condition questionnaire will be given to the participant to evaluate the method. The post-questionnaire for the conditions is shown in Appendix E. It includes general questions and adjusted TAM (Technology Acceptance Model) questions. TAM is an information systems theory. We used it to measure the usefulness and ease of the use of a technology we proposed. This model consists of two parts of a series of questions. These questions are intended to measure the degree to which the participant believes the proposed system will enhance the service quality they will receive. The questionnaire will mainly evaluate the ease of use and the usefulness of the proposed system available in Appendix E. Finally, a short, semi-structured interview was conducted after the session to identify the system's weaknesses and strengths and gather detailed recommendations for improvement (Appendix E).

Table 5.1: Participants' Demographic Information (Descriptive statistics).

	Gender	Age	Education	# Times of Picking Up Prescription	# Hours Using Smartphone	Using Tap-to-Pay Method
Mean	1.1429	1.8095	3.3810	1.6667	2.1905	1.3810
Median	1.0000	2.0000	3.0000	2.0000	2.0000	1.0000
Mode	1.00	1.00a	3.00a	2.00	2.00	1.00
Std. Deviation	0.35857	0.98077	1.32198	0.48305	0.60159	0.49761
Variance	0.129	0.962	1.748	0.233	0.362	0.248
Range	1.00	4.00	5.00	1.00	2.00	1.00
Minimum	1.00	1.00	1.00	1.00	1.00	1.00
Maximum	2.00	5.00	6.00	2.00	3.00	2.00

5.2 Data Collection Process

We designed the study to collect data at multiple levels. First, we will ask the participant to complete a background questionnaire to gather demographic data and measure their comfort level using the smartphone application in general and the NFC-enabled smartphone application tap specifically. Second, we will review the tasks' instructions to help the participant get familiarized with the nature of the tasks. This step will equalize the participant's experiences with using the application and the paper prescription. Third, we will ask the participant to perform two sets of tasks (i.e. four tasks in total). The first set of tasks will use the traditional method of picking up medication. In the traditional processing method, the patient will go to the pharmacy,

Table 5.2: Participants' Demographic Information (Percentage).

Participants (N=21)		
Gender	Male	85.7%
	Female	14.3%
Age	18-24 years old	42.9%
	25-34 years old	42.9%
	35-44 years old	9.5%
	55 years or older	4.8%
Education	High school	14.3%
	Undergraduate Diploma Degree	38.1%
	Masters Degree	38.1%
	Other	9.5%
Occupation	Academic Adviser	4.8%
	Industrial Engineering	4.8%
	Retired	4.8%
	Student	85.7%
# Times of Picking Up Prescription	Less than one	33.3%
	1-5 times	66.7%
Time Spent Using Smartphone/Daily	Less than one hour	9.5%
	1-5 hours	61.9%
	5-10 hours	28.6%
Using NFC	Yes	61.9%
	No	38.1%

submit the paper prescription, identify themselves to the pharmacist, and pick up the medication. In the second set of tasks, the investigator will ask the participant to use the application to pass the identification information to a pharmacist after choosing the prescription they wish to pick up. In all tasks, the participant will present the prescription to the pharmacist (i.e. the investigator) to pick up the medication. After each task in both sets, the investigator will ask the participant to verify whether they got the correct medication. In each set of tasks, the participant will get the right medication in one task and the wrong medication in the other task. The participants will not know which one they got until after the tasks session is over. After each set, the investigator will ask the participants to complete a post-condition questionnaire (Likert scale) to measure their experience with the task conditions and understand their opinions and feelings about the method used. After the tasks session, we will ask the participant to fill out a questionnaire (Likert scale) to measure their thoughts about the NFC application's usefulness and ease of use. We adopted the Technology Acceptance Model (TAM) as a guideline to develop our questionnaire [170, 171]. Finally, we conducted a semi-structured interview to gather qualitative data to (1) support the post-task questionnaire answers, (2) identify the weaknesses and strengths and (3) collect descriptive recommendations for improvements. We analyzed the data collected using general descriptive statistics and a one-way between-subject ANOVA. We used the test statistic (i.e. one-way ANOVA) to measure if the means of tasks' times and the successful completion of tasks in both methods (i.e. the traditional method and NFC application method) are significantly different [172]. Moreover, we used tools such as SPSS and Microsoft Excel to analyze and code the collected data.

5.3 User Study Results

5.3.1 Tasks Analysis

In Figure 5.1, the red dotted line is the mean of the tasks' times. Table 5.3 displays the descriptive statistics across the conditions in the two methods we used. As can be seen, both tasks 1 and 3 have a much lower mean value, and this is due to the tasks' nature, as we ask the participants to check the dispensed medication, and in these tasks, we gave the participants the right medication. In the first task using the traditional method, we noticed that participants would complete the task successfully (i.e. verifying the medication successfully) with a rate of 100% due to their assumption that it is the right medication. It is worth mentioning that in tasks 1 and 2, the participants will usually rely on their memory to verify the medication.

Tasks Time to Complete Mean Results

Right Medication Condition

The descriptive statistics show that participants in the *Traditional method* group scored a higher mean of time to complete the task of right medication Task 1 (M=41.00, SD=12.29, Min=26, Max=70). In comparison, the participants in the *NFC application method* group scored a lower mean of time to complete the task of right medication Task 3 (M=37.14, SD=4.40, Min=30, Max=46). The two tasks' distribution was normal since all the tasks' skew, and kurtosis scores were less than $|2.0|$ and $|9.0|$ respectively [173]. Moreover, a Shapiro-Wilk's test ($p>.05$) [174, 175] and a visual inspection of their histogram showed that the tasks time was approximately normally distributed for both methods. Task 1 had a skewness of 0.814 (Standard Errors SE= 0.501) and kurtosis of -0.159 (SE= 0.972) for the traditional method, and Task 3 had a skewness of 0.639 (Standard Errors SE= 0.501) and kurtosis of -0.345 (SE= 0.972) for the NFC application method [176–178].

To test the hypothesis that the two methods are associated with significantly different means of time to complete the tasks for the dependent variable (i.e. right medication), we performed a one-way between-groups ANOVA. The independent variables (i.e. two groups) show that there is no significant difference between the tasks' completing time mean between the two methods at (F(1,40)=1.833, P=.183, η^2= 0.044). Thus, we do not reject the null hypothesis that there is no difference between the mean times of completing the tasks, and 4.4% of the variance in time (effect size) was accounted for by the groups. We can observe that the participants who used the NFC application method completed the task in less time than the participants using the traditional method. However, the difference between the two groups' time means is not attributable to a factor other than random chance. Figure 5.1 shows the mean times plots.

Wrong Medication Condition The descriptive statistics show that participants in the *Traditional method* group scored a higher mean of time on completing the task of wrong medication Task 2 (M=54.29, SD=12.47, Min=37, Max=81). In comparison, the participants in the *NFC application method* group scored a lower mean of time to complete the task of wrong medication Task 4 (M=43.90, SD=6.33, Min=35, Max=58). The two tasks' distribution was normal since all the tasks' skew, and kurtosis scores were less than |2.0| and |9.0| respectively [173]. Moreover, a Shapiro-Wilk's test (p>.05) [174, 175] and a visual inspection of their histogram showed that the tasks' time was approximately normally distributed for both methods. Task 2 had a skewness of 0.604 (SE=0.501) and kurtosis of -0.222 (SE= 0.972) for the traditional method, and Task 4 had a skewness of 0.683 (SE=0.501) and kurtosis of -0.444 (SE= 0.972) for the NFC application method [176–178]. To test the hypothesis that the two methods are associated with significantly different means of time to complete the tasks for the dependent variable (i.e. wrong medication), we performed a one-way between-groups ANOVA. The independent variables (i.e. two groups) show that there is a significant difference between the tasks' completing time mean between the two methods at (F(1,40)=17.042, P<.000, η^2= 0.299). Thus, we reject the null hypothesis that there is no difference between the mean times of completing the tasks and 29.9% of the variance in time (effect size). We can observe that the participants who used

Table 5.3: Descriptive statistics for the four tasks between the two methods (Time of tasks completion)

	Conditions	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	Kurtosis
Traditional Method	Right Medication (Task 1)	21	26	70	41.00	12.29	0.814	-0.159
	Wrong Medication (Task 2)	21	37	81	54.29	12.47	0.604	-0.222
NFC Application	Right Medication (Task 3)	21	30	46	37.14	4.40	0.639	-0.345
	Wrong Medication (Task 4)	21	35	58	43.90	6.33	0.683	-0.444

the NFC application method completed the task less than the participants using the traditional method. Figure 5.1 shows the mean times plots.

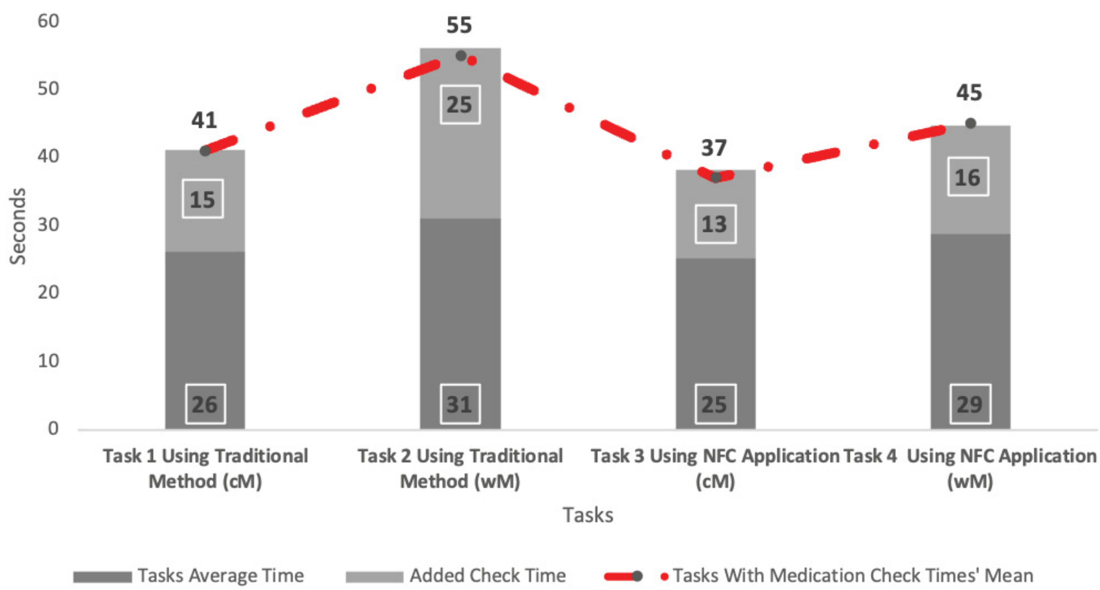


Figure 5.1: The overall mean percentage value for usefulness, ease of use, availability and reliability, and security and privacy based on the participants' response to the questionnaire.

Tasks of verifying The Medication Successfully Results

We analyzed the successful completion of tasks using IBM SPSS 22 with only two values: Complete represented as (1), and Incomplete represented as (2). Since our test values are binary, we are using the chi-squared test to evaluate the significant difference between the groups' results [179]. The following shows the results of our findings:

Right Medication Condition We performed a chi-squared test to determine whether there is a significant difference between the two groups in successfully completing the right medication tasks. In the traditional method group, 100% successfully completed the right medication task. In the NFC application method group, 90.5% completed the right medication task, while only 9.5% did not successfully complete the task. Figure 5.2 shows the percentage of participants that completed the task successfully. These differences were not statistically significant compared with the chi-squared test finding (Value= 2.100, df=1, P<.147). Thus, we do not reject the null hypothesis. There is no substantial evidence of a relationship between completing the right medication task and the independent variable (i.e. the two methods).

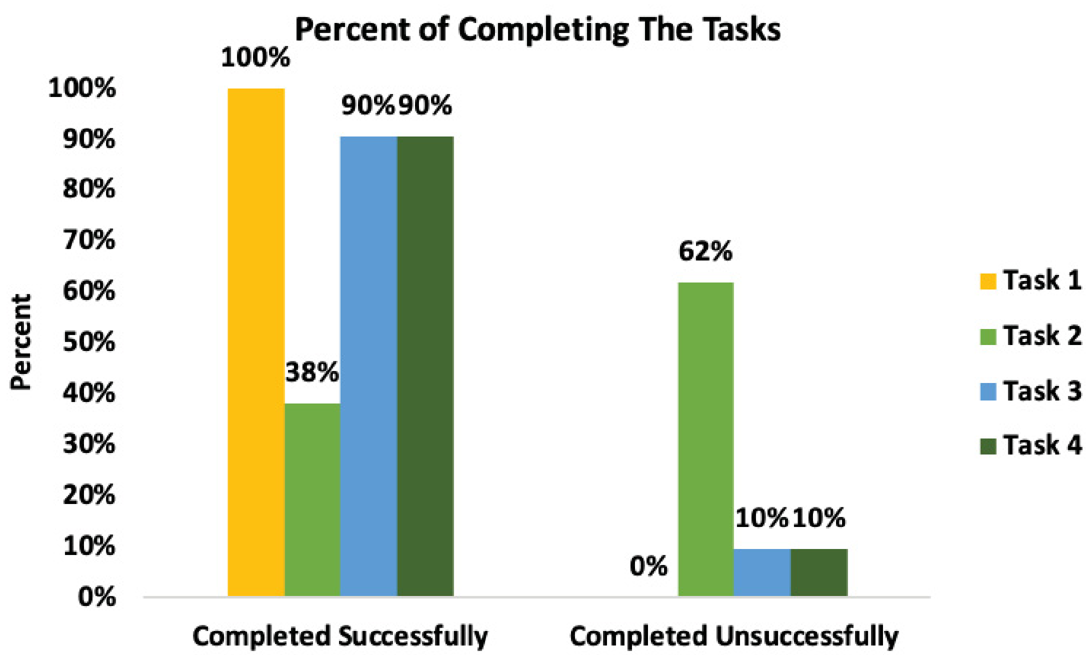


Figure 5.2: The overall percentage value of completing the tasks successfully for both methods across the two conditions.

Wrong Medication Condition We performed a chi-squared test to determine whether there is a significant difference between the two groups in successfully completing the wrong medication tasks. In the traditional method group, 61.9% did not successfully complete the wrong medication task, while 38.1% successfully completed the task. In the NFC application method group, 90.5% successfully completed the right medication task, while only 9.5% did not successfully complete the task. Figure 5.2 shows the percentage of participants that completed the task successfully.

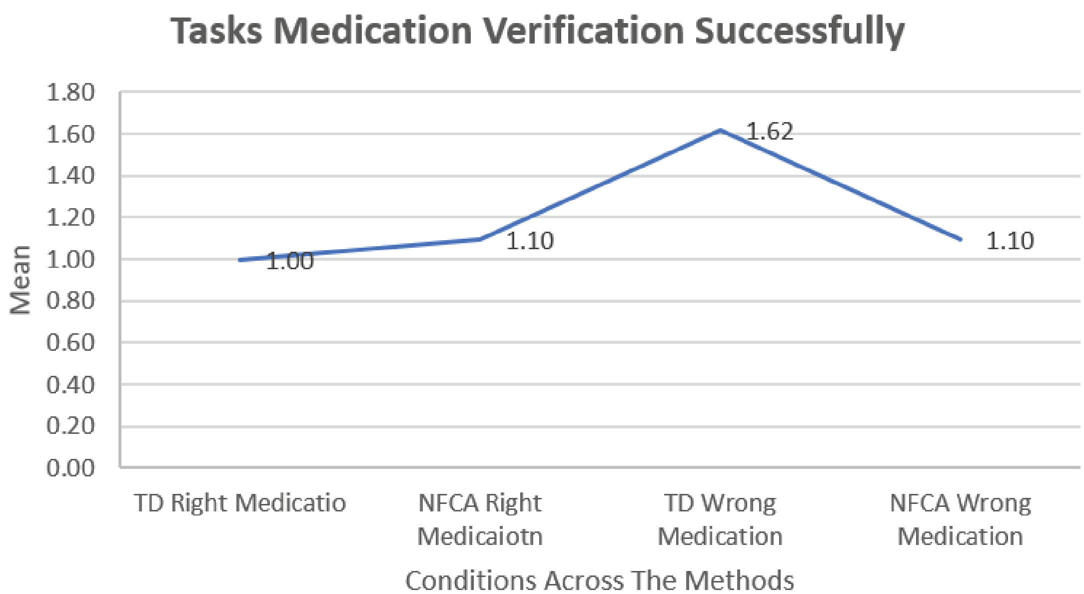


Figure 5.3: Mean plots of the medication verification successfully for all the condition across the two methods.

These differences were statistically significant from the finding of the chi-squared test (Value= 12.548, df=1, P<.000). Thus, we reject the null hypothesis, and there is strong evidence of a relationship between successfully completing the wrong medication task and the independent variable (i.e. the two methods).

Further, Cohen [180] demonstrated the effect size of Phi and Carmer's V as follows: (0.1) is a small effect, (0.3) is a medium effect, and (0.5) is a large effect. The Phi and Carmer's value is (Φc = 0.547, P<.000), which indicates that the strength of association between the variables is a very large effect.

5.3.2 Post Condition Questionnaires

The participants were asked in the questionnaires to compare their experience with both methods. The comparison was based on critical factors used to measure the participants' confidence in the method used in terms of their information security and privacy. Also, we asked them what they think about the availability of intake instruction in both methods and which method will help them avoid medication errors at their end. All questions used a 7-point Likert scale coded as follows: 1 (Strongly

Agree), 2 (Agree), 3 (Somewhat Agree), 4 (Neutral), 5 (Somewhat Disagree), 6 (Disagree), and 7 (Strongly Disagree).

In the following, we will discuss these factors in detail. As mentioned before, we have two sets of tasks, and each set consists of two tasks. After completing the tasks, we ask the participant to fill out a questionnaire for each method.

Security and privacy: The questionnaire shows that approximately 86% of the participants found that the NFC application can transfer their sensitive information to the pharmacy securely (M=2.2, SD= 1.3). In comparison, only 43% found that the traditional method can provide a secure and private way of transferring sensitive information (M=3.8, SD= 1.9). Furthermore, approximately 95% of the participants thought the NFC application is sufficient to verify their identity during the medication dispensing process (M=1.7, SD= .889). Meanwhile, only approximately 48% thought the traditional method could verify their identity (M=4.04, SD=2.17). Finally, all participants believed NFC technology is a secure and fast method to transfer information to pick up prescribed medications (M=1.6, SD= .658). In Figures 5.4, 5.5, and 5.6, we can see that the participants agree with the presented statements based on their experience with both methods in the study.

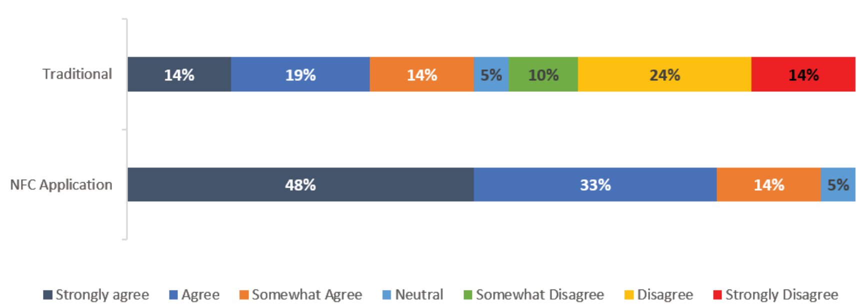


Figure 5.4: Q: I think this method will help me to verify my identity to the drugstore, which helps the drugstore to dispense the correct medication for me.

In the interview, when asked about their opinion on the fingerprint, the majority of participants thought it is a secure way to protect their sensitive information in the application from any unauthorized access. On the other hand, a few participants did not feel positive about the application's fingerprint login. One of the participants preferred not to use their fingerprints during the study and stated, "fingerprint is too

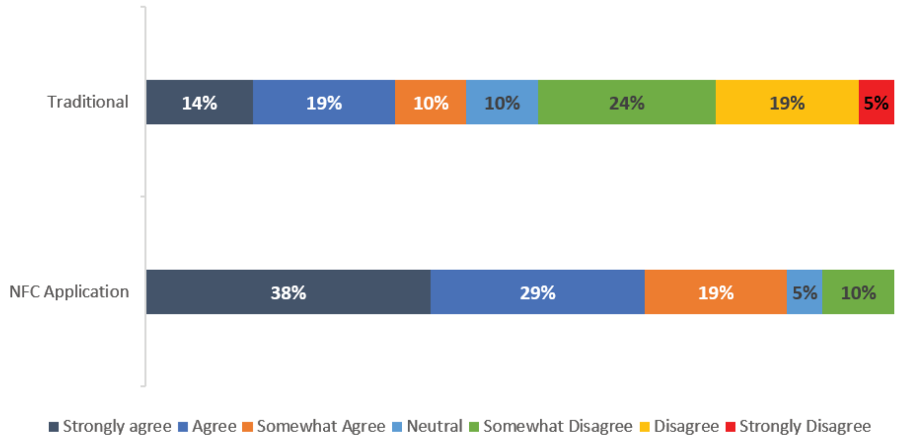


Figure 5.5: Q: I think this method will help me to keep my sensitive information private and secure.

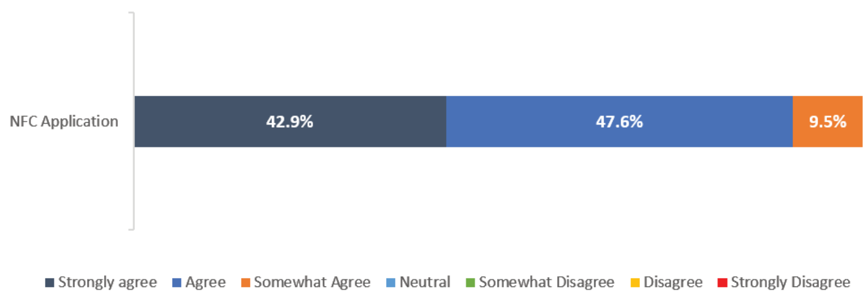


Figure 5.6: I think using NFC technology to transfer information is a secure and fast method in the picking up medication process.

private. This information should not ever be recorded of anybody, in my opinion" (P4). Moreover, the other participants did use the fingerprint login but suggested adding more options like a PIN code or facial recognition to access the application.

Availability and reliability: Almost 57% of the participants believed that the traditional method does not provide a way of tracking the current prescriptions and making them available for future use (M=4.6, SD=1.98) (i.e. Question PCTQ5 Figure 5.8). Meanwhile, only 39% of the participants thought the availability of intake instructions all the time is not provided by the traditional method, and almost 10% of the answers were neutral (M=3.7, SD=1.9) (i.e. Question PCTQ2 in Figure 5.8). This means that the traditional method of making the intake instructions available is insufficient for the patients. In comparison, almost 86% of the participants believed that the application would help them remember their medication intake instructions (i.e. by making them available to the patient when selecting the desired prescription (M=1.9, SD=1.04) (i.e. Question PCQA4 in Figure 5.7). All the participants thought the NFC application method would provide a way of tracking the current prescriptions and making them available for future use (M=1.7619, SD=.70034) (i.e. Question PCQA6 in Figure 5.7).

Moreover, almost 43% of the participants believed the traditional method would not provide a safe method to use to verify the medication. The verification process helps the pharmacy dispense the correct medication, avoid dispensing to the wrong patient with the same medication or name, and avoid dispensing look-alike or sound- and look-alike medication without the need to rely on human intervention. The rest of the answers on the ability to avoid dispensing the wrong medication using the information provided by the traditional method were 19% agreed (i.e. calculating all the agreement levels described by the 7-point Likert scale), and almost 38% were neutral (M=4.5, SD=1.8) (i.e. Question PCTQ6 Figure 5.8). This means the patients were not certain that the traditional method will provide enough information about a patient and a prescription to dispense the right medication. All participants thought the NFC technology (i.e. when the pharmacy management system reads the NFC tag attached to the medication packaging) would help the pharmacy verify the medication. Thus avoiding dispensing the wrong medication (M=1.8, SD= .792) (i.e. Question PCQA7 in Figure 5.7). Furthermore, almost 86% of the participants thought the NFC Application will provide the pharmacy management system with enough information to avoid dispensing the wrong medication to patients (M=1.9, SD=1.09) (i.e. Question PCQA8 in Figure 5.7), while only 61% of participants thought the traditional method will do so (M=3.42,SD=1.9) (i.e. Question PCTQ4 Figure 5.8).

In Figure 5.2, the percentage of tasks completed by verifying the medication successfully is affected by the availability of the prescription information. We can see in task 2 that only 38% of participants completed the tasks successfully, while 62% of participants failed to verify the medication. When we asked the participants, who failed to verify the medication, about why they think they failed to do so, the majority referred to the lack of information on hand as the reason. It is worth mentioning that all the participants in task 1, in which we gave them the right medication without their knowledge, believed that it is because the participants answered while thinking this is the right medication without any proof. Moreover, when we asked the participants about the difference in their performance between tasks 1 and 2 regarding the medication verification, they answered that they assumed it was the right medication. Moreover, they thought the pharmacy would not make a mistake and dispense the wrong medication.

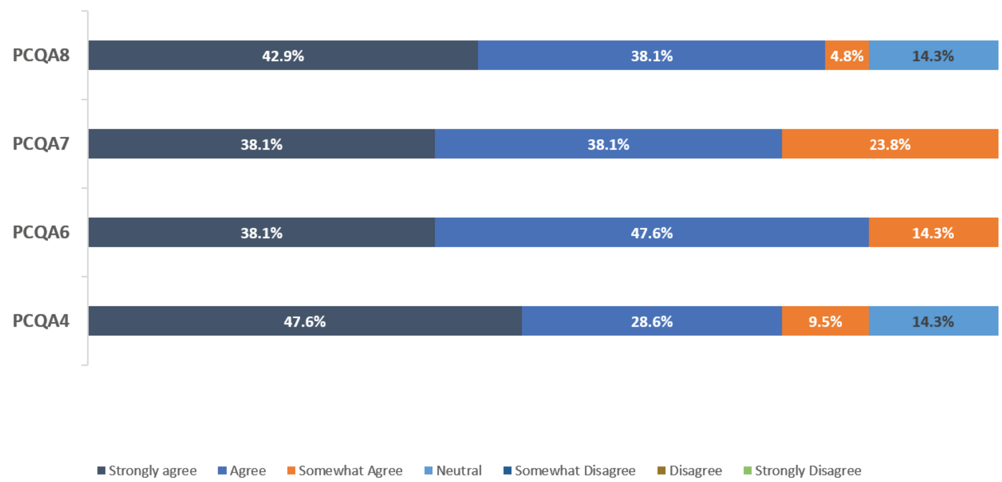


Figure 5.7: The percent of participants' answers on the availability and reliability of information questions for the NFC Application method

Usefulness The questionnaire shows that 91% of participants found the proposed NFC application useful (M=1.912, SD=1.017) (Figure 5.9). In the post-session interview, participants stated that they believe the application will help ease providing information to the pharmacy. They also thought the application would help pharmacies avoid dispensing the wrong medication to the wrong patient by verifying the patient and the medication regarding the provided prescription using NFC technology. Moreover, they strongly agree that NFC will help them transfer the needed information (i.e. patients' sensitive information) more securely and privately. Lastly, most believed that the application would help them keep past prescription information available if needed. The application will help by making the intake instructions

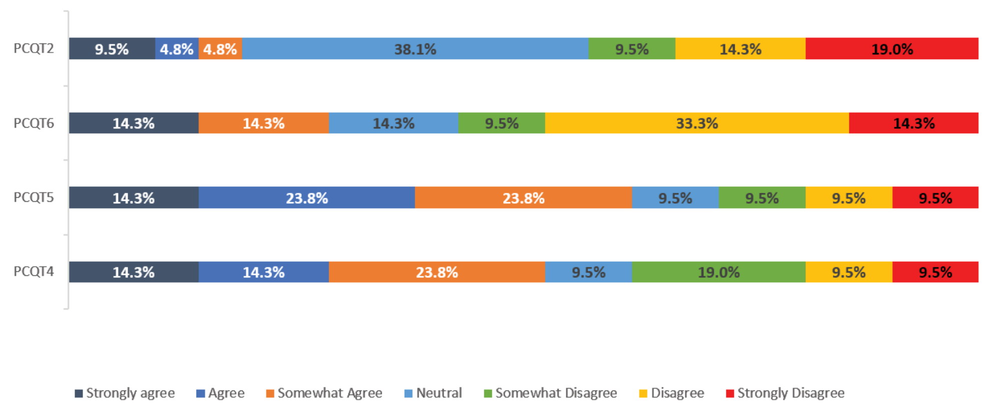


Figure 5.8: The percent of participants' answers on the availability and reliability of information questions for the Traditional method

available at all times. In Figure 5.2, we can see that the application affected the percentage positively, as 90% of participants in both tasks 3 and 4 verified the medication correctly. This shows how the application was useful regarding making the prescription available all the time. The type of information in the verification task was different across the participants; as some participants, we would only change the dosage information in the wrong medication condition to test if it will affect a participant's decision to fail to verify the medication. We found that 10% of participants in task 4 (i.e. the task in which we gave the wrong medication or wrong medication instruction) failed to verify the medication from the first attempt successfully or failed to notice the change in the intake instructions. We considered an attempt successful in the study when a participant successfully verified the medication the first time.

Easy to Use Based on the questionnaire about the ease of use, 97% of participants believed the application and NFC technology are easy to learn and use (M=1.52, SD=.724) (Figure 5.9). Also, participants found that browsing the list of prescriptions was easy and understandable. However, many suggested changing how the prescriptions are displayed by grouping the prescriptions issued by one doctor. Others suggested using the prescriber's name or the prescribing date for more clarity. On the other hand, participants found that the use of NFC to transfer information was easy. As we can notice from the tasks, participants spent less time using the proposed NFC application compared to the traditional method when at the dispensing process (Figure 5.1). In addition, according to the NFC application questionnaire, almost 81% of participants believed the application is suitable for novice and expert users (M=2.523, SD=1.123).

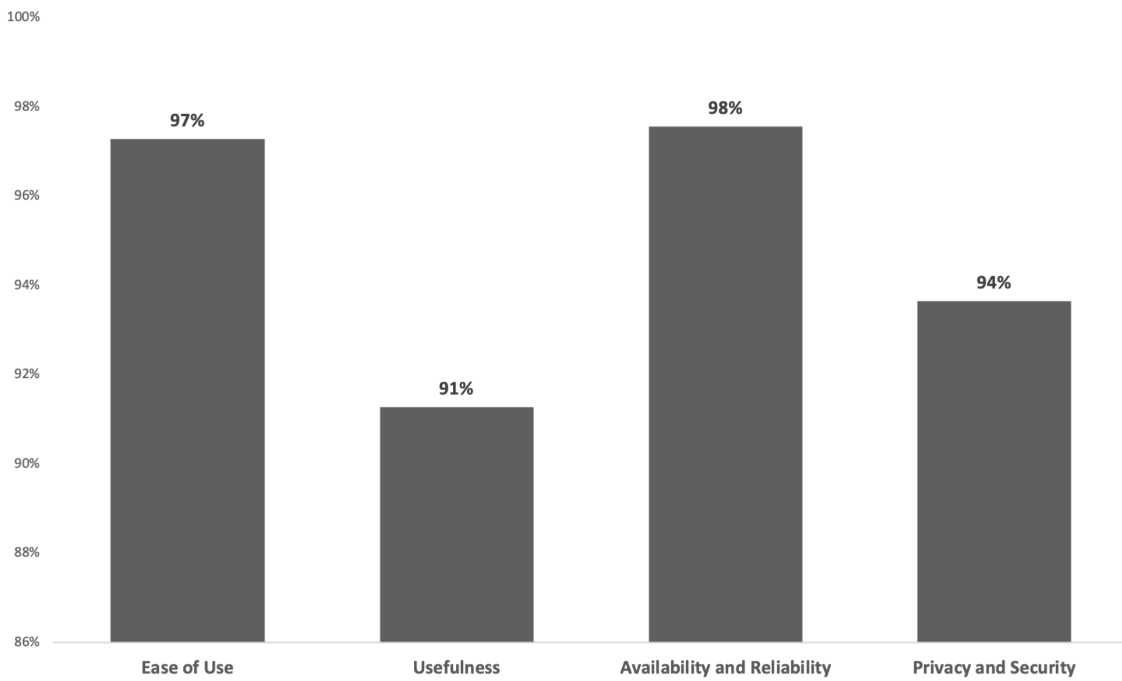


Figure 5.9: The overall percentage value of the positive answers (i.e. Strongly Agree $\longleftrightarrow$ Somewhat Agree) for usefulness, ease of use, availability and reliability, and security and privacy based on the participants' response to the NFC application questionnaire.

Weakness and Limitations of The Study With the positive findings of the proposed NFC application's usability study, some weaknesses and limitations should be considered in future research. One limitation is the number of participants in each age range, especially in the age range of 55+ years old. This age range is highly important to this research because they might take more medication than other age ranges due to their health condition. Another weakness is that the application lacks other options for logging into the application. Moreover, the current state's application does not share the prescription with other persons related to the patient to pick up the prescription on their behalf. The current state's application provides only an online mode to get the prescription information from the servers. Finally, some of the weaknesses of the study were there is no pharmacist's or prescriber's perspective in the study, security and application evaluation by the lay-persons, not expert participants of applications development and security.

5.4 Chapter Summary

The study findings show that an NFC application to manage prescriptions and pick up medications is acceptable in the participants' opinion. The results show that the participants believe the NFC application will mitigate dispensing medication errors, at least from their end. The patient can verify the medication and prescription information before leaving the pharmacy with the prescriber's information. Moreover, the application will help the patient remember their current prescription when they need to browse it, which helps them remember the medication intake instructions. We will overcome the limitations and weaknesses of the application from this study's results in future work. Moreover, our next phase is to expand on the system to overcome other e-prescription system issues to mitigate errors in the prescribing and dispensing of medication.

Chapter 6

Proposed Refined Framework

6.1 Motivation

We propose a secure system for optimizing the medication prescribing and dispensing process. The system introduces a more robust and secure method to confirm the patient's identity and minimize dispensing errors. We use NFC technology in smartphones to securely transfer information between the patient's smartphone app and the pharmacy. We also use biometric information (i.e., fingerprints) to grant the patient access to the application services. Then, the patient will be able to transfer the information needed using NFC technology.

Moreover, we propose to use blockchain technology to securely transfer and privately share patient information between the involved parties. Furthermore, we propose the use of the ML model to detect any serious outcome by anomalies in the submitted prescription that could potentially harm the patient. Finally, a combination of the Blockchain and ML will likely enhance the e-prescription system and improve patients' safety upon prescribing a medication.

6.2 Objectives

Based on the findings in both the user study and survey study, we propose a framework to use to overcome the limitations discussed in 5 and 3. We propose a framework for managing the patients' medication histories and facilitating the sharing of that information by giving the system a decentralized architecture. Moreover, we will use an NFC-enabled smartphone at the patient end. The following are the framework objectives:

- Making medication and prescription information available to the involved parties from all the available resources.
- To limit access to medication history data only to authorized parties by using

Blockchain.

- Making the prescription information and medication information always available to the patient through their mobile application.
- Enhancing patient safety by using ML to predict if the prescribed medication will harm the patient.
- Verifying a patient's identity during the medication dispensing process will likely help mitigate medication errors at that phase.
- Transferring prescription information securely to the pharmacies using the Blockchain.
- Ensuring patient safety at the end process by using NFC technology to dispense the medication.

Building upon these objectives, we will detail our new and improved proposed system in the next section.

6.3 Proposed Framework Overview

As discussed in 3 in the discussion section, the current systems are still being developed, but due to current systems' architecture and countries' regulations, these systems are limited in the number of services they can provide. Therefore, we propose our framework to overcome those limitations. The user study's findings show promising results for overcoming information privacy issues at the user end. Therefore, minor refinements will be implemented in the application's new design to achieve the intended goals. Those refinements are thoroughly discussed in 5. The following are the weaknesses of the application pointed out by the participants.

- There should be more options for logging in to the application; maintaining patient information privacy is the main goal.
- Offer an option for sharing prescription information with other users (e.g. family members, friends, partners, etc.) so they can pick up the prescription on their behalf.
- Provide an offline mode for the application to access the necessary information such as intake instructions and prescription information.

The framework should integrate most of the solutions suggested in the survey study mentioned in 3. Overcoming those challenges and limitations will serve to achieve the goals set in the objectives. The following sections will discuss how our approach will overcome the limitations and implement the proposed solutions.

6.3.1 Distributed System

As established in 3, most e-Prescription systems are centralized. The main reason for using a centralized system in most countries is to protect the patients' health information privacy. Despite the benefits of centralized systems, several medical studies have argued that this type of architecture does not protect the privacy and security of patient information [107]. Moreover, centralized systems are more vulnerable to security threats such as DDoS attacks and social engineering attacks [107–110]. Centralized systems limit patients' data privacy, as health records can be shared anywhere across the system [107, 111].

Although decentralized systems provide more protection from the security threats mentioned above, these systems do not have the same quality of service provided by centralized systems. One of the benefits of a centralized system is the availability of the patient's medication history, which helps minimize medication interaction errors and ADR. As shown in the US case study, decentralized systems also allow medication history to be shared with other parties. However, the service is only available to subscribers, and the other party's approval is required to share information.

Moreover, many countries' regulations require a central physical location to control access to medical data. Therefore, an adaptable approach is likely to solve most of the architecture issues, such as a system that is designed to store, transfer, and share needed data (e.g. the prescription history or medication history of a patient) from the patient while meeting the regulations and rules of different countries. Such a system can use any authentication protocol through a token that is handed to the patient, a key stored in a barcode, or a mobile application that can only be accessed by the patient. Therefore, a hybrid approach would be better suited to overcoming the limitations and challenges. A system should meet countries' regulations on patient privacy and security and have the ability to implement new technologies such as Blockchain and ML. Using these technologies will enhance the quality of the service and increase patient safety while prescribing medications [51, 155, 157, 158].

6.4 Medication History

According to the findings of our review, medication histories are a vital factor in advancing AI technologies in e-prescription systems. Moreover, making medication histories available to all parties involved in the system might enhance patient safety when prescribing or dispensing a new medication [144–147]. Therefore, we propose this feature be incorporated into the system and controlled by the patient. Giving control to the patient will facilitate making those history records available to all the parties. The patient will have a token ID that can be shared with the party of choice by the patient. This party will use the token ID to request the ML server to process the data. Also, they will use the token ID to encrypt the prescription block and update the Blockchain. Using the blockchain network will likely save time on requesting the medication history between parties compared to the slow process of sharing medication histories between parties in Surescripts (US e-Prescription network). As mentioned in 3, Surescripts provide a service for requesting patient records between network subscribers. However, the process of sharing the records is subject to the other party's approval [11]. Not only is the service a slow process for sharing records and limited only to subscribers of the network, but it also might cost valuable patient time. Thus, making electronic medication histories available and accessible to transfer in the blockchain network can improve the efficiency and quality of the services provided.

Furthermore, we will update the mobile app to help collect more information about the patient's intake process to help improve the ML model [159]. The app will send an alert to the patient based on the medication intake time for the e-prescription. Moreover, suppose the treatment requires the patient to monitor their health condition and record it during the treatment. In that case, the app will have the option to enter that information to be collected and stored in the patient's Blockchain. The monitoring process will help evaluate the treatment process and update the ML model to suggest better treatment options for future cases.

6.5 System Architecture Design

6.5.1 Overall Architecture

We propose an adaptable approach that will store the prescription and medication information about any patient in blocks as part of the patient's Blockchain. These blocks will be stored by distributing them among the blockchain network. The involved parties (i.e. healthcare centres, pharmacies, medical government authorities, and insurance companies) will be a part of the network to make the information more accessible. Figure 6.1 shows the overall architecture of the system framework. One of the framework's components is the enabled NFC mobile application and the main server to manage the information from the distributed e-prescription network. The mobile application is a continuation of the previous preliminary work 4. The mobile application is a key component of the system due to system authentication, which requires the patient's approval to share information. The results of the user study will drive the improvement in the mobile application we conducted in 5 and the new architecture of the system framework.

The ML server will have three modules for collecting, managing and processing the data required. The patient's information blocks will be aggregated based on the patient ID, which is shared upon the healthcare center or pharmacy visit. Then, the server will send messages to the network to collect the blocks. The blocks will contain information about the patient's medication and health condition. Then, the server will process the new e-prescription for any anomalies to avoid any interactions or anticipated harm from the prescribed medication. After this, the server will send this process to the Blockchain updater module in the prescriber's system. The result is only a suggestion based on the information available about the patient. The prescriber will make the final decision and submit the e-prescription to be added to the Blockchain. Finally, the updated Blockchain will be sent to the local healthcare centres to keep the information as updated as possible. Figure 6.2 shows the proposed process of the ML server.

The system will create two blocks to be added to the Blockchain. The first is the prescription authentication block, which contains the information needed to create the key to encrypt the second block. This information includes the time stamp for issuing the prescription, the prescription ID, and the prescriber's digital signature. The data on this block will be encrypted using the token ID provided only by the patient. The decryption process for this block will verify the patient's identity since only the patient can provide the key. The second block is the prescription data block, which contains information about the prescription, ML server validation for the prescription, and the prescriber's signature. This block is hashed using the authentication block (i.e. timestamp, prescription ID, and prescriber sign) and the token ID. This encryption using this hash will ensure that the prescription has not been modified and will prevent any fraudulent submission of an e-prescription from any rogue party to the patient blockchain. Moreover, the blocks are read-only; therefore, any tampering with prescription data will not be possible. Figure 6.3 shows the blocks' architecture in the patient's Blockchain.

Finally, we believe that using blockchain and ML technologies will achieve our objectives for the framework. By using these technologies, the framework will provide a private and secure method of sharing prescription data among the parties and making the information available all the time. Moreover, we believe the framework will provide a better method to verify the parties' identities involved in the system (i.e. patient, healthcare center, pharmacies, insurance companies, and medical government authorities) using the blockchain encryption and decryption mechanism. Lastly, we believe this framework will be the seed of a global approach to enabling patients to share their medication information with any health care provider.

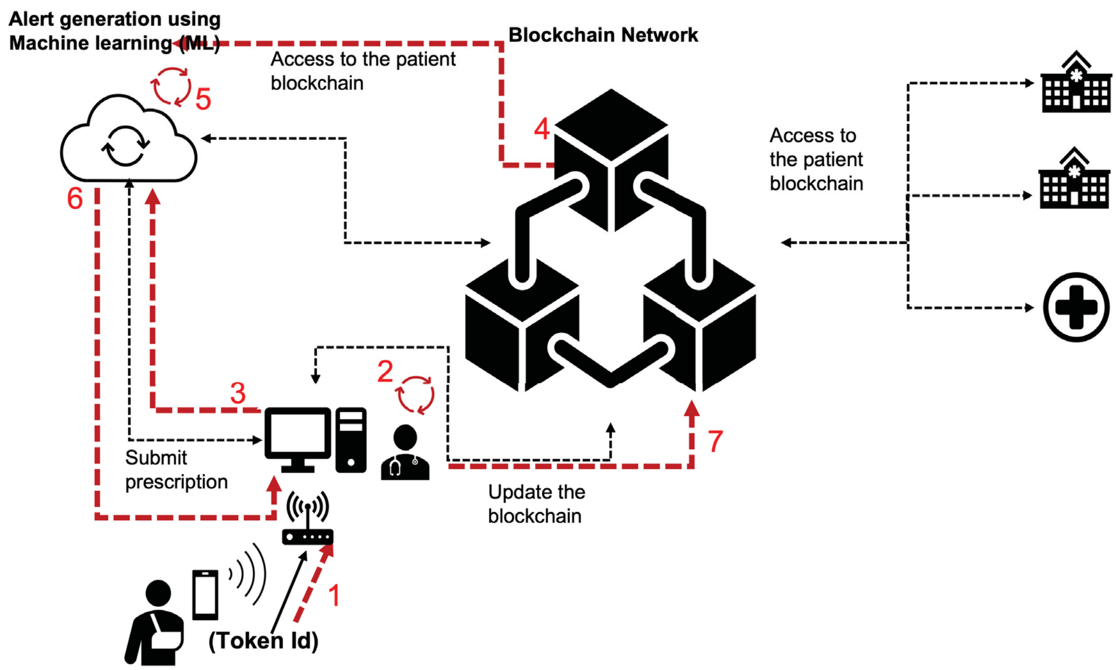


Figure 6.1: The proposed framework architecture

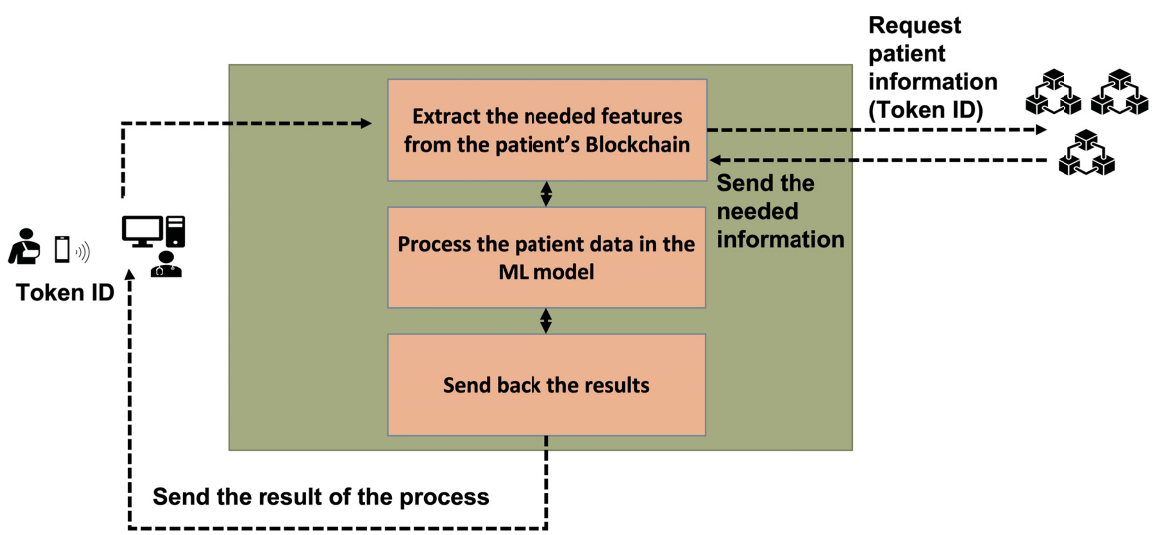


Figure 6.2: The proposed ML model architecture

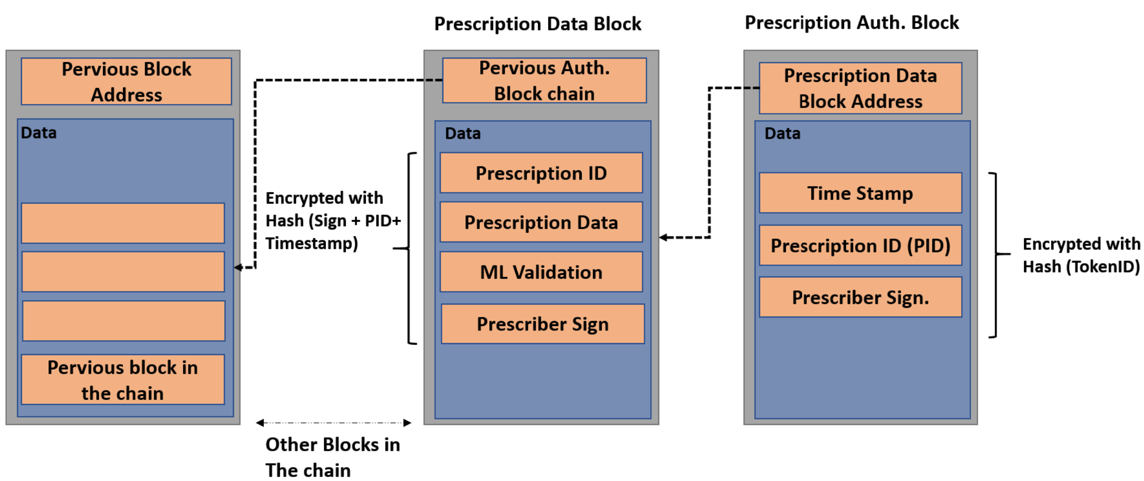


Figure 6.3: The proposed two blocks in the blockchain architecture

Chapter 7

Evaluation Methodology

7.1 Overview

To meet our research goals listed in 6, we need to evaluate the proposed framework in terms of the following aspects:

- Processing time of submitting the e-Prescription evaluation.
- The server resources performance.
- Evaluating the security features proposed in the framework.
- Conducting an online survey to evaluate such a system from the point of view of prescribers and pharmacists (Chapter 8).

Moreover, we will implement a proof of concept of all the components of the framework. We will be using the Java programming language for the mobile application and the framework. Furthermore, we will conduct an online survey to evaluate the framework. The participants' sample for the online survey will include pharmacists, prescribers, and patients.

7.2 Framework Evaluation Methods

Parts of the proposed system's effectiveness and usability were evaluated by conducting the user study discussed in 5. The results of the study showed the effectiveness and usability of the mobile application. Furthermore, we will evaluate the mobile application's refinements by calculating the performance of mobile resources. Moreover, we will evaluate the system's efficiency for the framework blockchain network by calculating the processing time of issuing an e-Prescription, measured using timestamps. The total time will include the time for data processing on the server added to the time for requesting the information and reported in milliseconds. As for the

ML module, we will conduct a reliability and accuracy analysis to evaluate the accuracy of the algorithm in predicting the harm of medication. In the following, we will discuss in detail the evaluation methodology for the ML and the blockchain network.

7.2.1 Developing a Proof of Concept

To evaluate our system, a testbed consisting of four virtual servers is the main server, and the other three servers will act as care center local servers. The servers will be set up using a PC with Windows 10 with a 500-GB Hard Drive, Core i7 CPU, and 16 GB of memory. The main server will be set up on a laptop with Windows 10, a Core i7 CPU and 16 GB of memory. The laptop to be used in the testbed was reported in the previous work [160]. To evaluate the framework, we will be conducting three main analyses:

- Analysis of the framework resources using the proposed features and the processing time for issuing a prescription.
- Analysis of the framework's security features.
- Analysis of the reliability and accuracy of the ML.

7.2.2 ML Reliability and Accuracy Analysis

We will be using the confusion matrix to evaluate the data set classifier's accuracy and reliability as well as the framework data processing module's performance [181]. Table 7.1 represents the confusion matrix we will be using.

	Classified positive	**Classified negative**
Positive	true positive (TP)	false negative (FN)
Negative	false positive (FP)	true negative (TN)

Table 7.1: Confusion matrix

- Accuracy (AC) is the percentage of how often the classifier is correct overall in detecting serious outcomes or no serious outcomes in the submitted e-Prescriptions. AC is given by Equation 7.1:

$$AC = \frac{TP + TN}{TP + TN + FP + FN} \tag{7.1}$$

- Misclassification rate (MisCl) is the percentage of how often the classifier is incorrect overall in detecting serious outcomes or no serious outcomes in the submitted e-Prescriptions. MisCl is given by Equation 7.2:

$$MisCl = \frac{FP + FN}{TP + TN + FP + FN} \tag{7.2}$$

- Precision (P) is the number of times the classifier is correct when it identifies serious outcomes in e-Prescriptions. P is given by Equation 7.3:

$$P = \frac{TP}{TP + FP} \tag{7.3}$$

- Recall (R) is the percentage of how often the classifier identifies the serious outcomes in the submitted e-Prescriptions that have anomalies. R is given by Equation 7.4:

$$R = \frac{TP}{TP + FN} \tag{7.4}$$

- F score (F) is the balance between the precision (P) and the recall (R) values. A higher F value means the classifier has a good ratio of detecting serious outcomes in e-Prescriptions. F is given by Equation 7.5:

$$F = 2 * \frac{P * R}{P + R} \tag{7.5}$$

- False negative rate (FNR) is the percentage of how often the classifier identifies no serious outcome when there is a serious outcome. This evaluation parameter is important because if it is high, it means the server has a higher ratio of not sending an alert, even though the e-Prescription might cause a serious outcome. false negative rate (FNR) is given by Equation 7.6:

$$FNR = \frac{FN}{TP + FN} \tag{7.6}$$

- False positive rate (FPR) is the percentage of how often the classifier identifies the serious outcome when there is no serious outcome. This evaluation parameter is important because if it is high, then it means the server has a higher ratio of sending an alert even though the e-Prescription might not cause a serious outcome. false positive rate (FPR) is given by Equation 7.7:

$$FPR = \frac{FP}{FP + TN} \tag{7.7}$$

7.2.3 Blockchain Network Evaluation Metrics

We will be using the metrics execution time and throughput to evaluate the blockchain.

- **Execution Time** is defined as the total amount of time (number of seconds) during which the blockchain platform took to execute and confirm all ePrescription transactions in the data set Execution Time (ExT) is calculated by subtracting Execution Time when a transaction was confirmed in the blockchain (Ext1) from Submitting Time of an ePrescription transaction to the blockchain (SubT) [182]. The Equation is represented by the following 7.8:

$$ExT = Ext1 - SubT \tag{7.8}$$

- **Throughput** refers to the number of successful ePrescription transactions per second in the Blockchain. Starting from the first ePrescription transaction submitting time [182]. The evaluation will be executed using Apache JMeter, an open-source tool for testing the performance of an application [183–185].

7.2.4 Security Analysis

The system security and privacy of the patient's information rely on four main aspects:

- We will use Blockchain to manage and store the patient's information securely.
- The token ID to manage the access control to the information.
- Mobile application biometric login.
- Using blockchain technology will provide better privacy for patient information.

Chapter 8

Online Survey

8.1 Introduction

Electronic prescribing is becoming one of the most important emerging information technologies among health care organizations. Nowadays, many health care centers and organizations around the world are adopting ePrescription services. The reason for this massive increase in interest is because ePrescription services have the potential to improve the safety, quality, and efficiency of the medication prescribing process [61, 105, 148, 186–200]. While the focus of ePrescription services is on enhancing the safety of prescribing medications, it can improve other aspects of the process of prescribing, dispensing and purchasing medication [197, 201]. Even though ePrescription will help overcome many issues, it may create new problems in different stages [105, 186, 202]. Its implementation will affect prescribers' and pharmacists' workload and thus will affect health care services' quality and safety. Moreover, the transition to using ePrescription will affect patient medication safety from their end, and it will also affect the privacy and security of their prescription information. With the patient being more involved in the medical information process, they should be more involved in evaluating health care systems, specifically those they might deal with more often such as ePrescription systems. Many studies have found that patients that are satisfied with certain healthcare services are more likely to continue using those services [203, 204]. Therefore, it is important to evaluate the ePrescription system from the point of view of all the parties involved when considering potential improvements. In the literature, many of the studies evaluating ePrescription systems examined their benefits and problems [189, 205, 206], the facilitators and limitations of implementing ePrescription systems [66, 186, 207], and the effects of ePrescription systems on workflow and medication safety [187, 206, 208, 209]. These studies evaluated ePrescription systems from the point of view of healthcare experts and professionals. However, studies on patients' experiences that evaluated their role in the ePrescription system are limited [197]. Studies such as [210–214] evaluated ePrescription systems from the perspective of patients in the United States and Sweden [105]. In Australia [215] and Scotland [216], the studies included patients' attitudes toward ePrescription before implementation. These studies reported that the patients' attitudes toward ePrescription were mostly positive. However, these studies had limitations[197] due to being locally focused, having small samples, and involving patients from only one clinic [211, 212, 215], or one state [213, 214].

Therefore, we conducted this study to evaluate the system's involved parties' attitude towards the new features and to measure the potential benefits of introducing the use of blockchain and machine learning to strengthen the methods in place for safely prescribing medication. Our study is part of the research on developing a new ePrescription system that gives the patients an important role in the system by allowing them to control the access to their medication history and ePrescription information, how it is transferred, and whom it is shared with. The system aims to enhance the security and privacy and improve the availability of ePrescription information and reliability of the system. We mainly focus on utilizing blockchain technology to improve the privacy and security of the ePrescription information by designing a blockchain network for the proposed ePrescription system to facilitate the sharing of ePrescription information while maintaining the security and privacy of the patients' ePrescription information in the network. Moreover, we introduce a new feature to detect any drug interactions in ePrescriptions using machine learning algorithms and check ePrescriptions for anomalies before submitting them to the pharmacy. Such anomalies are the missing prescription values, wrong dosage, wrong medication strength the might harm the patient. All of these anomalies could be detected using the history of similar treatment cases.

Through this study, we aim to answer the following research question:

- What benefits and drawbacks exist when using the proposed ePrescription system compared to existing ePrescribing methods (specifically, generating medication prescribing error alerts, medication histories, and prescription information sharing)?

8.2 Previous Studies

In [105] the authors conducted a study to evaluate Swedish patients' attitudes towards e-prescribing, including the transfer of ePrescriptions, electronic storing of prescriptions and mail-order prescriptions. The study targeted Swedish patients nationwide to evaluate their attitudes using a postal questionnaire. The questionnaire was developed for the purpose of this study and aimed to evaluate respondents' views concerning e-prescribing, the electronic storing of ePrescriptions and mail-order prescriptions from multiple aspects, including safety, personal benefits and effectiveness. The study population is 1500 individuals who met the inclusion criteria and were randomly selected from a database of individuals in Sweden who store prescriptions electronically (n = 5 840 599). The response rate was 52% (739/1429). The authors found that the majority of the respondents (85%, 628/739) had a positive attitude towards ePrescriptions and the electronic storing of prescriptions (86%, 633/739) and considered ePrescriptions to be secure (79%, 584/739), beneficial (78%, 576/ 739), and an improvement to the medication dispensing process (69%, 512/739).

Another study conducted by [197] aimed to investigate Finnish pharmacy customers' experiences with purchasing medicine with ePrescriptions, renewing ePrescriptions, and acting on behalf of someone else at a pharmacy, ways in which they keep up to date with their ePrescriptions, and their overall satisfaction with ePrescriptions.

The study included 2913 pharmacy customers (older than 18 years) in 18 community pharmacies across Finland in 2015. The authors found that most respondents, 90.85% (1161/1278), did not face any issues during pharmacy visits. Almost 79.44% of the respondents were notified about the current status of their ePrescriptions after dispensing their medication(1013/1276).

8.3 Methodology

8.3.1 Overview of the Study

This study is a survey that evaluates the proposed ePrescription system based on the feedback of the involved parties (i.e. patients, pharmacists, and prescribers). The survey focuses on the computer science aspects of the ePrescription system. It involves questions about the features introduced in the proposed ePrescription system to evaluate the security, privacy, reliability, and availability of the ePrescription information in the system [186]. Moreover, the survey includes questions that generally evaluate the features provided by the current ePrescription systems (e.g. PrescribeIT in Canada, Surescripts in the US). Finally, the participants in the patient group were from several countries, including Canada, the US, the UK, India, Brazil, and different countries in Europe. In contrast, the pharmacist and the prescriber groups involved participants mainly from Canada, the US, and the UK.

8.3.2 Recruitment Procedure

We aimed to use Dalhousie University's email announcement for the patients' group to recruit the wider Dalhousie University community. Also, we posted the recruitment notice on social media (e.g. Facebook, Twitter, and LinkedIn) and the local classified website Kijiji Research Study [217].

In addition, we used Amazon Mechanical Turk (Mturk) as another method for recruiting people to broaden the recruiting process and gather data faster. Mturk is an online tool that helps recruit participants to perform tasks or fill out online surveys. Mturk uses a Human Intelligence Task (HIT) to represent a single virtual task or, in our case, a survey for one participant. A Human Intelligence Task, or HIT, is a question that needs an answer. A HIT represents a single, self-contained, virtual task that a Worker can work on, submit an answer, and collect a reward. HITs are created by Requester customers (i.e. the lead researcher) to be completed by Worker customers [218, 219]. Mturk allows researchers to control the kind of participants to see and respond to a recruitment notice and provides a reputation measure to ensure those participants recruited from the available frame are likely to participate in good faith and provide data of acceptable quality. Hit Approval Rate is one of the qualification criteria for Mturk users only. That represents the proportion of completed tasks that Requesters approve. Setting the "HIT Approval Rate" to greater than 95% will direct the survey to users who have consistently produced high-quality tasks by completing other tasks from other requesters on the website [220].

For the prescribers and pharmacists groups, I emailed pharmacies and clinics in Canada, the US, the UK directly using their provided email from the official websites. Also, we emailed various legal authorities representing the pharmacists and prescribers (i.e. pharmacists and physicians associations and a number of the pharmacy and medical universes' faculties in the three mentioned countries) to ask for participation in the survey. I provided the link to the survey in the dal Opinio server in the email text. I sent the emails using the primary researcher (Bader Aldughayfiq) dal email (bd256851@dal.ca). Also, I intend to post the study recruitment notice on the website LinkedIn [221]. This website is a social network for professional workers to communicate with each other [221]. We can find groups specific to prescribers and pharmacists on the website. Using LinkedIn will help us target our recruitment notice to an audience related to the prescribers and pharmacists groups.

Our targeted samples were at least 150 participants in the patient group and 25 participants in the pharmacist and prescriber groups. We set a low number for the pharmacist and prescriber group samples due to the pandemic's effects on these participants' time. Also, when trying to publish the online survey, we received some rejection emails from some health authorities to distribute the survey link due to both groups' limited time and high workload during the pandemic. Once we published the online survey, we had 365 respondents in the patient group, 62 respondents in the pharmacist group, and 69 respondents in the prescriber group. After excluding participants who did not meet our requirements, we had 284 respondents in the patient group, 39 respondents in the pharmacist group, and 27 respondents in the prescriber group.

Inclusion criteria

In the survey, there were three groups of participants: patients, pharmacists, and prescribers. All participants in the three groups had to be older than 18 years old. The patient group must have experience using ePrescription systems or paper prescriptions to pick up prescribed medication in the past year. For the prescriber and pharmacist group participants, we required the prescribers (i.e., all prescribers except pharmacists) to have experience using any electronic health record system and any ePrescribing method (e.g., email or an ePrescription system such as PrescribeIT) in

Table 8.1: Demographics of **the patients' group**(n=226)

	Frequency	Percent
Age (years)		
18-24	22	9.7%
25-34	130	57.5%
35-44	37	16.4%
45-54	18	8.0%
Over 55	19	8.4%
Gender		
Male	142	62.8%
Female	82	36.3%
Other	2	0.9%
Education		
High school	16	7.1%
College diploma	15	6.6%
Bachelor's degree	130	57.5%
Master's degree	57	25.2%
Doctoral degree	5	2.2%
Other	3	1.3%
Used ePrescription		
No	58	25.7%
Yes	168	74.3%

the past year. Pharmacists were required to have experience using any pharmacy management system and experience with any ePrescribing method (e.g., email or an ePrescription system such as PrescribeIT) in the past year.

8.3.3 The questionnaires

As was previously mentioned, each group received a different questionnaire based on their role in the proposed system. Each group was presented with two sections: the first section evaluated the current ePrescription system in general and its related features. The second section evaluated the proposed ePrescription system's new features from their perspective concerning their role in the system. For example, the alert generation feature that uses machine learning questions to evaluate the efficiency and efficacy of the generated alerts will not only be presented to the patient group. In each of the question sections, we provided a brief explanation of the ePrescription service features. All the questions used a 7-point Likert scale in which the participants

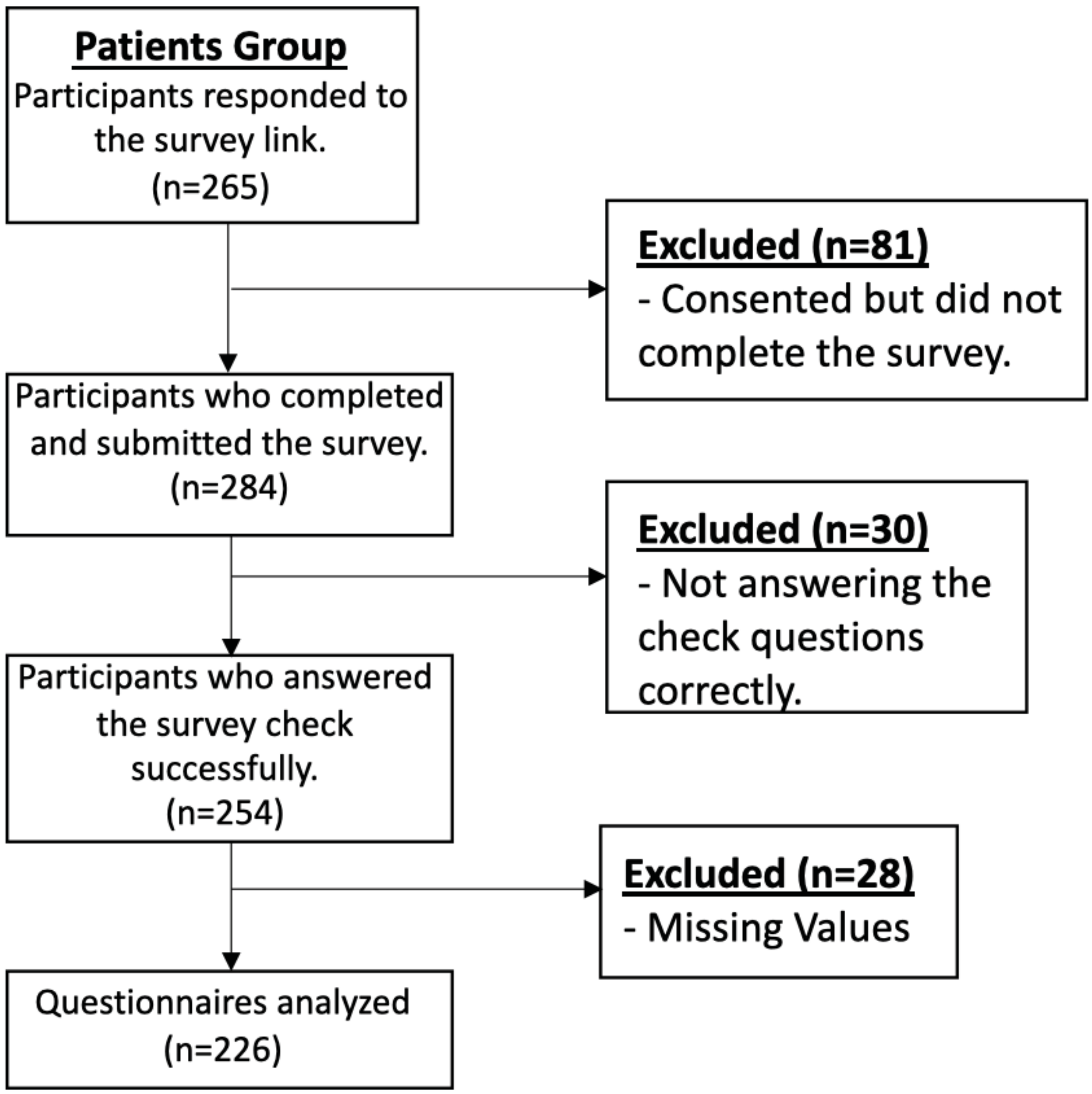


Figure 8.1: The process of selecting participants in the patient group.

responded on how much they agree with the presented statement from 1 - strongly agree to 7 - strongly disagree. Also, a final, open-ended question was asked so the participant could provide suggestions on how to improve the proposed ePrescription system and ePrescription systems in general.

8.3.4 Analysis of results

Collected answers were analyzed using SPSS (version 26 for macOS; SPSS). Differences between the respondents' answers and their demographic information, or their experience using the ePrescription system, were tested for significance using a chi-square test. The statistical significance was determined as $P < 0.01$. All results from the Likert-scale questions were regarded as nominal-level data, and statistical methods were chosen based on the information from [222].

The answers from the open-ended question were categorized into the most commonly mentioned opinions. Categories were not decided in advance but emerged during the analysis of the answer's context. The respondents' answers could belong to several categories if they contained more than one comment or suggestion.

8.4 Results

8.4.1 Patient Group

After the initial exclusion process (n=284), we excluded 30 more participants because they did not answer the check questions. The check questions were introduced to ensure no bots answered the survey since it is an online survey and made sure the participants fully read the questions and understood them. We asked the participants in these questions to choose a specific answer. The resulting number of participants after this was 254 participants. Finally, 28 participants' responses were removed because they did not answer more than two questions. Thus, the number of analyzed responses was from 226 respondents, and there was a response rate of 80% (226/284). The exclusion process is described in Figure 8.1, and a detailed statistical description about the patient group participants' demographic information is shown in Table 8.1.

Using ePrescription

Of the 226 respondents, almost 74% stated that they had used an ePrescription system before, while 26% had not used one. There was no significant difference (P>0.01) in answering this question between respondents of different ages. However, there was a significant difference (P<0.01) in answering this question between respondents of different education levels.

Patients Feedback on the Current ePrescription

The majority of respondents, or 88.1% (199/226), agreed that the current ePrescription system transfers ePrescriptions securely and keeps their information private. Almost 47.6% of the respondents agreed that the reliability of ePrescriptions and the availability of ePrescription information through the system is what motivates them to use ePrescriptions. Figure 8.3 shows the respondents' answer percentages. There was a significant difference (P<0.01) in the answers to the questions (i.e. about the reliability and the availability of ePrescription information) between respondents of different education levels (Figure 8.2). There was no significant difference (P>0.01) in the security and privacy question answers between respondents of different ages or depending on whether they had used an ePrescription system before or not.

On the other hand, almost 48% disagreed with the statement that the ePrescription system will improve the process of picking up prescriptions at the pharmacies (Figure 8.3). There was a significant difference (P<0.01) in the answers to the question (i.e. will the ePrescription system improve the process of picking up medication at the pharmacies) between the respondents of the group who had or had not used an ePrescription before and different ages (Figures 8.4 and 8.5).

Patients' feedback on the new proposed features

When we asked the respondents about the new features of the system, we found the following. Almost 81.4% of the respondents agreed that making the ePrescription in a read-only mode for the other parties after submission would help prevent any alterations, and nearly 83% agreed that the read-only mode would help prevent any fraud attempts. When we asked about introducing a unique ID to control access

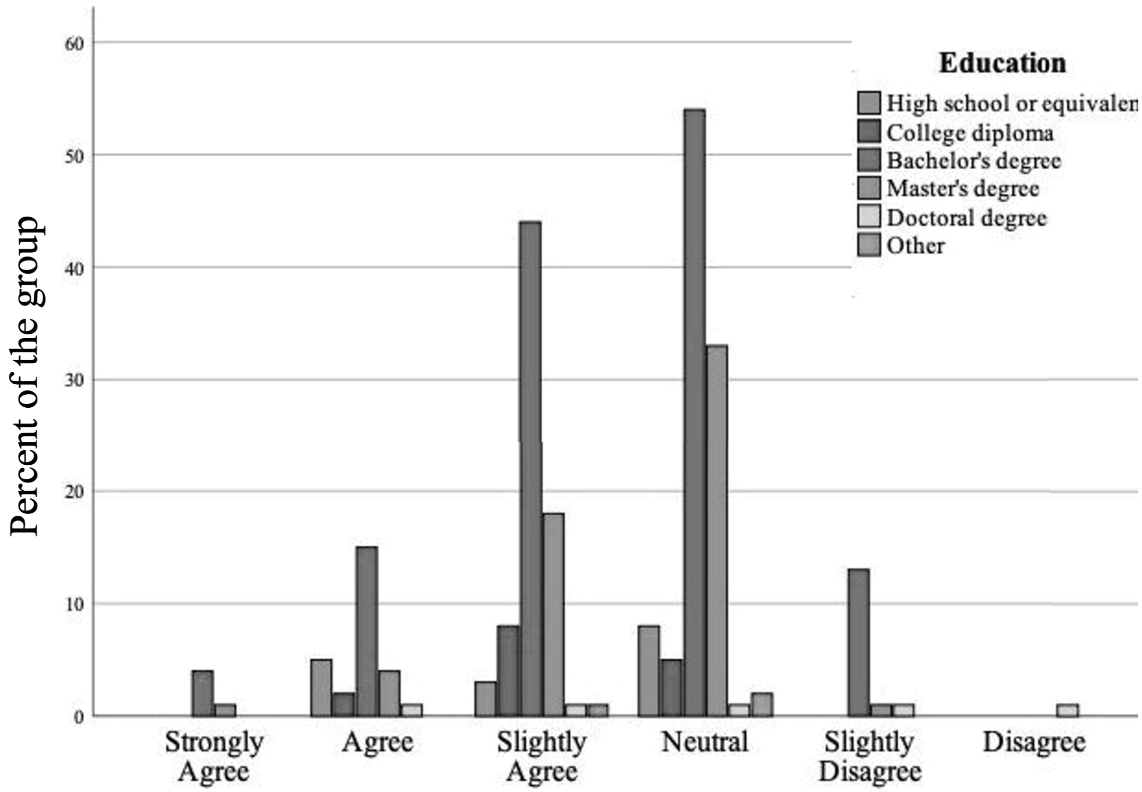


Figure 8.2: How the respondents in the patient group from different age groups regarding if using ePrescription will improve their experience during pickup medication in the pharmacies, on a seven-point Likert-type rating scale.

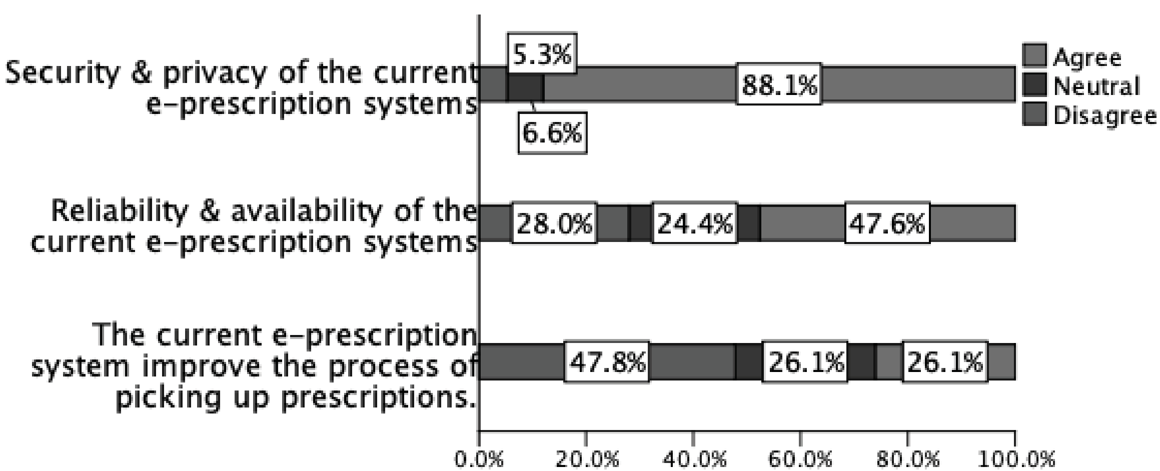


Figure 8.3: The percentages of the respondents' (in the patient group) answers about if the security, privacy, reliability, and availability of the ePrescription system will motivate them to use it.

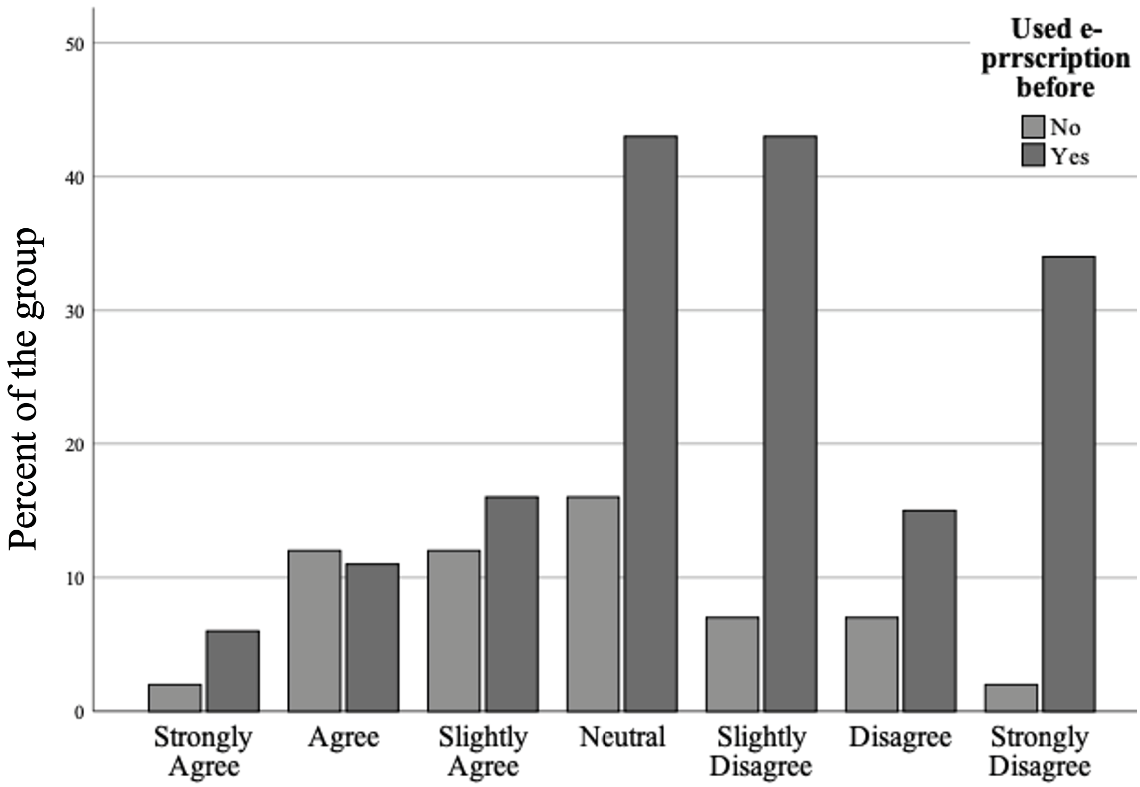


Figure 8.4: How the respondents in the patient group who used or not ePrescription before regarding if using ePrescription will improve their experience during pickup medication in the pharmacies, on a seven-point Likert-type rating scale.

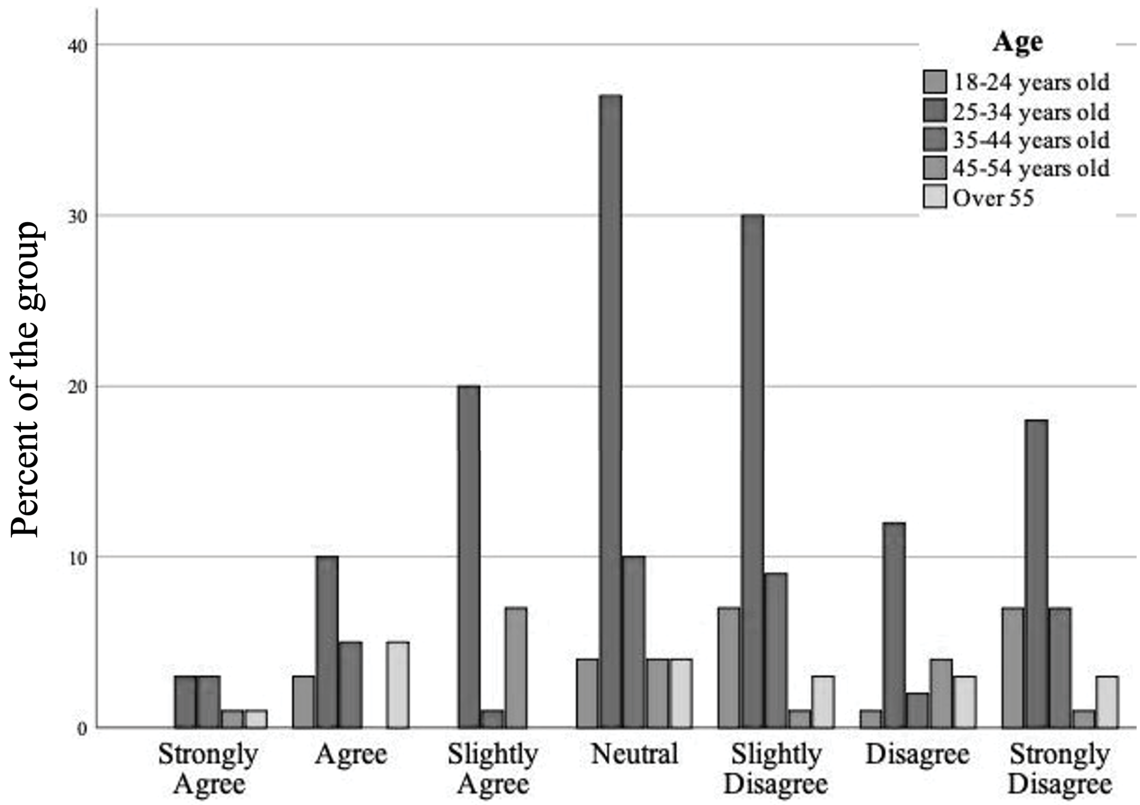


Figure 8.5: How the respondents in the patient group from different age groups regarding if using ePrescription will improve their experience during pickup medication in the pharmacies, on a seven-point Likert-type rating scale.

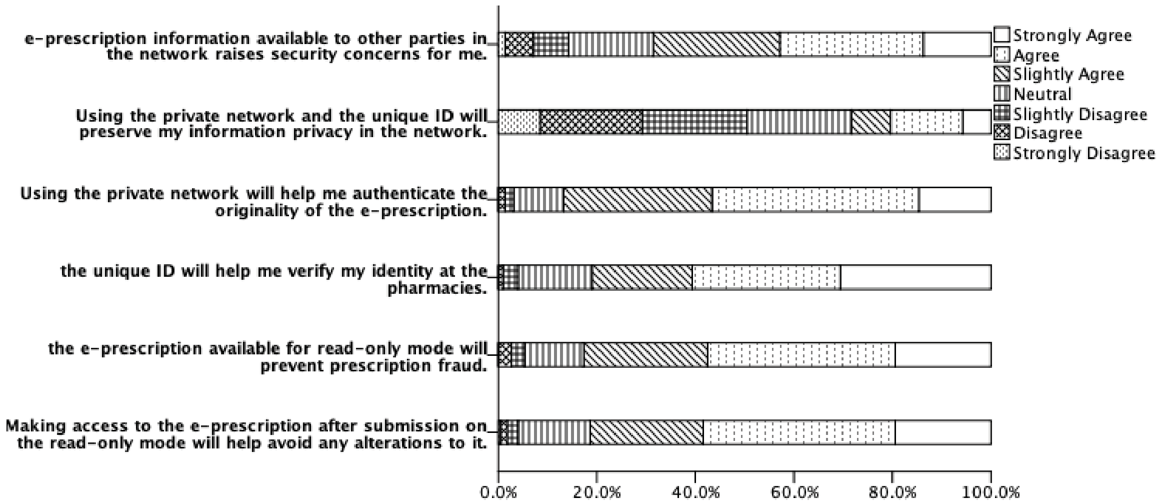


Figure 8.6: How the respondents in the patient group answered the different questions about the new proposed ePrescription system features on a seven-point Likert-type rating scale.

to the ePrescription information, the respondents agreed that the unique ID would help the pharmacists validate the patients' identity before dispensing the medication. However, only approximately 50% agreed that the unique ID would help keep their information private and only accessed by the authorized parties (i.e. authorization is granted by the patient when sharing their unique ID only). Regarding using the blockchain technology and the unique ID to ensure the originality of the ePrescription, almost 87% of respondents agreed with that statement. However, 67% of respondents believed using blockchain technology to share the ePrescription information would raise security concerns. Figure 8.6 shows the answer percentages for the above-discussed questions.

We performed the Chi-square test to find any significant differences between the question answers across demographic groups. For the question about whether the read-only mode will prevent any alterations (i.e. from all parties) to the submitted ePrescription, there was a significant difference ($P<0.01$) in the answers to the questions between participants of different education levels (Figure 8.7.)

There was a significant difference ($P<0.01$) in the answers to the question of whether the read-only mode will prevent fraud between the different education-level groups (Figure 8.8). For the question about whether using the unique ID will help verify the patient's identity at the pharmacy, there was a significant difference ($P<0.01$)

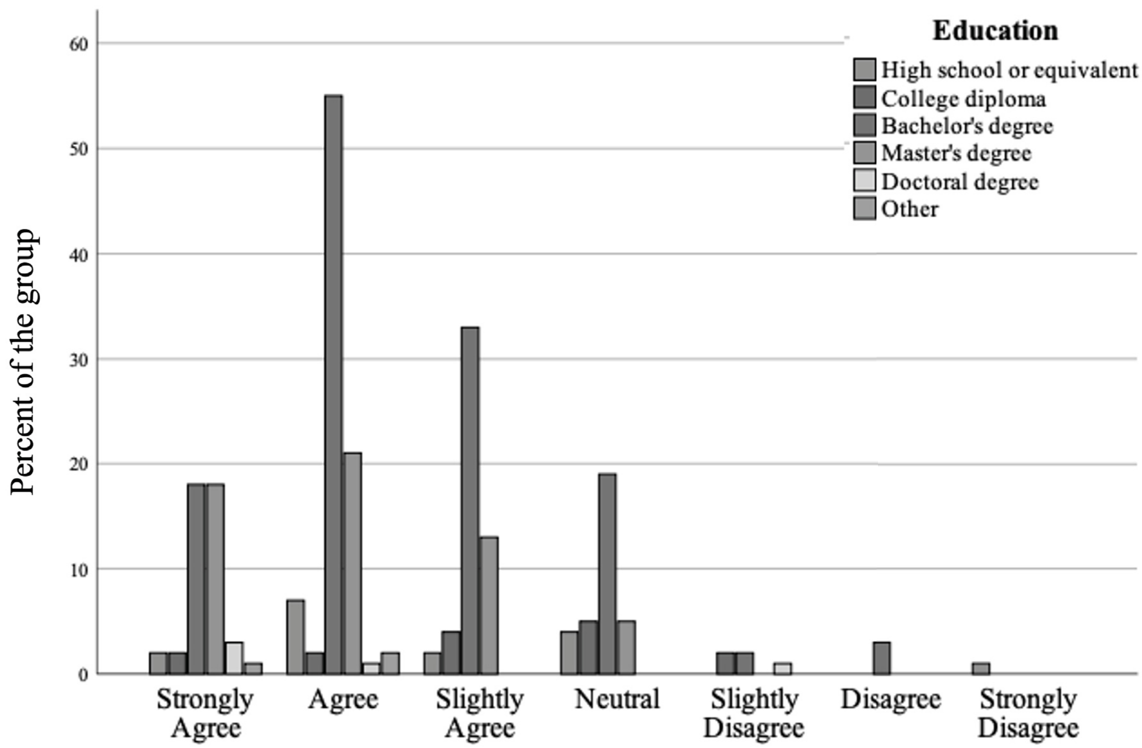


Figure 8.7: How the respondents in the patient group from different education levels regarding if using the read only mode for browsing the ePrescription will prevent any alteration, on a seven-point Likert-type rating scale.

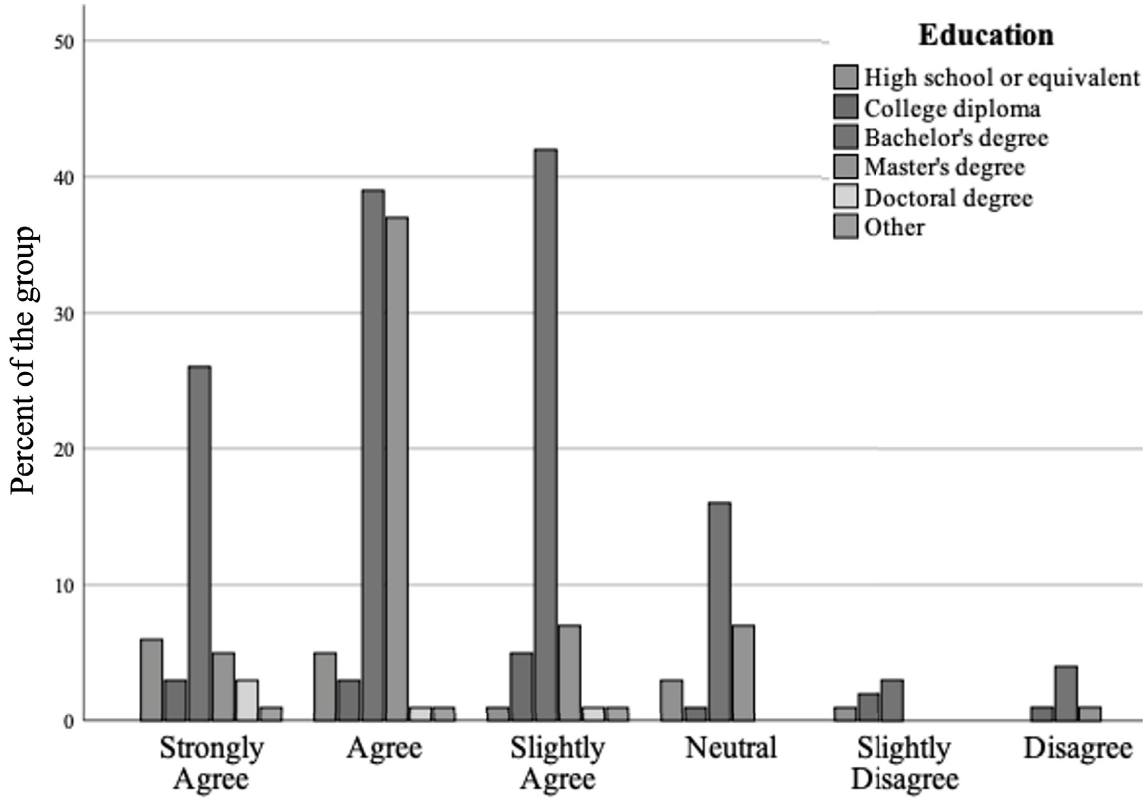


Figure 8.8: How the respondents from different education level groups regarding if using the read only mode will prevent fraud, on a seven-point Likert-type rating scale.

in the answers from the different education-level groups (Figure 8.9). On the other hand, there was a significant difference (P<0.01) in the different age groups' answers to the question about whether using the unique ID will preserve the ePrescription information in the network (Figure 8.10).

Finally, we found a significant difference (P<0.01) in the answers of respondents from different education-level and age groups regarding using blockchain to build a private network for sharing ePrescription information will raise security concerns (Figure 8.11 and 8.12).

8.4.2 Pharmacists Group

We excluded five more participants after the initial exclusion process (n=39) because they did not answer the check questions or missing values in their submitted survey. Thus, the number of analyzed responses was 34, with a response rate of 87% (34/39). The exclusion process is described in Figure 8.13, and Table 8.2 shows an overview

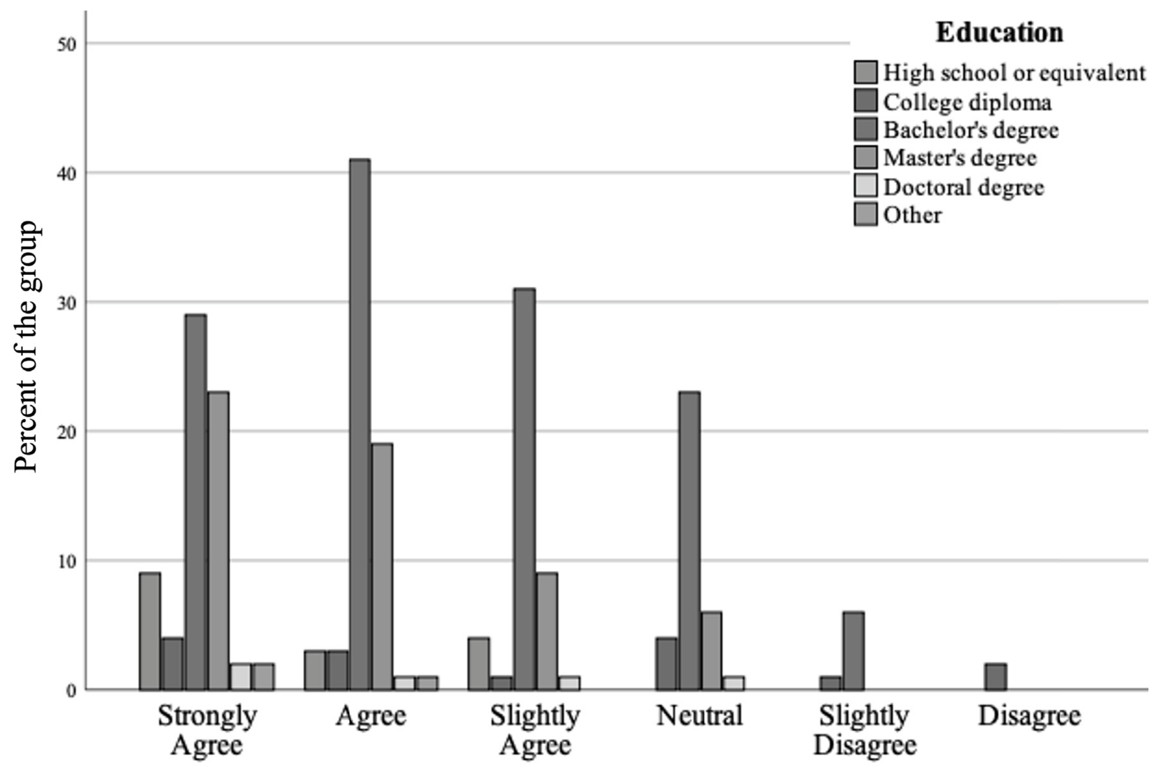


Figure 8.9: How the respondents from different education level groups regarding if using the unique Id will prevent fraud, on a seven-point Likert-type rating scale.

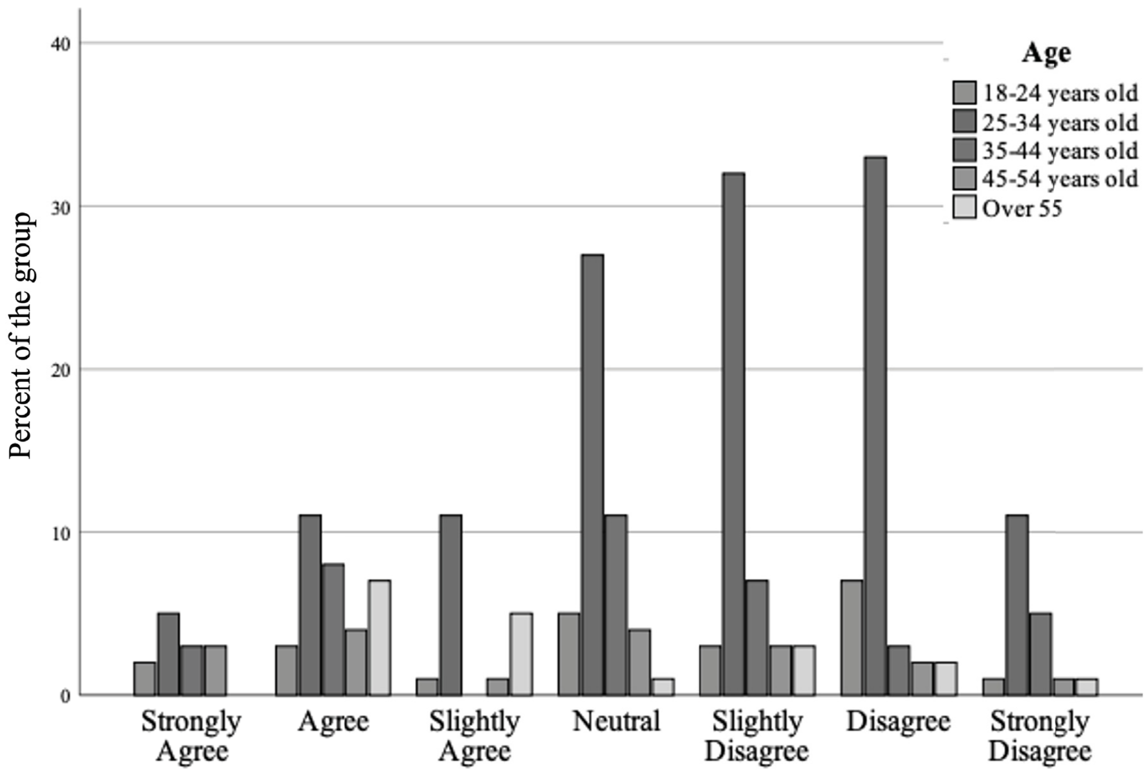


Figure 8.10: How the respondents from different age groups regarding if using the unique Id will preserve their ePrescriptions information in the network, on a seven-point Likert-type rating scale.

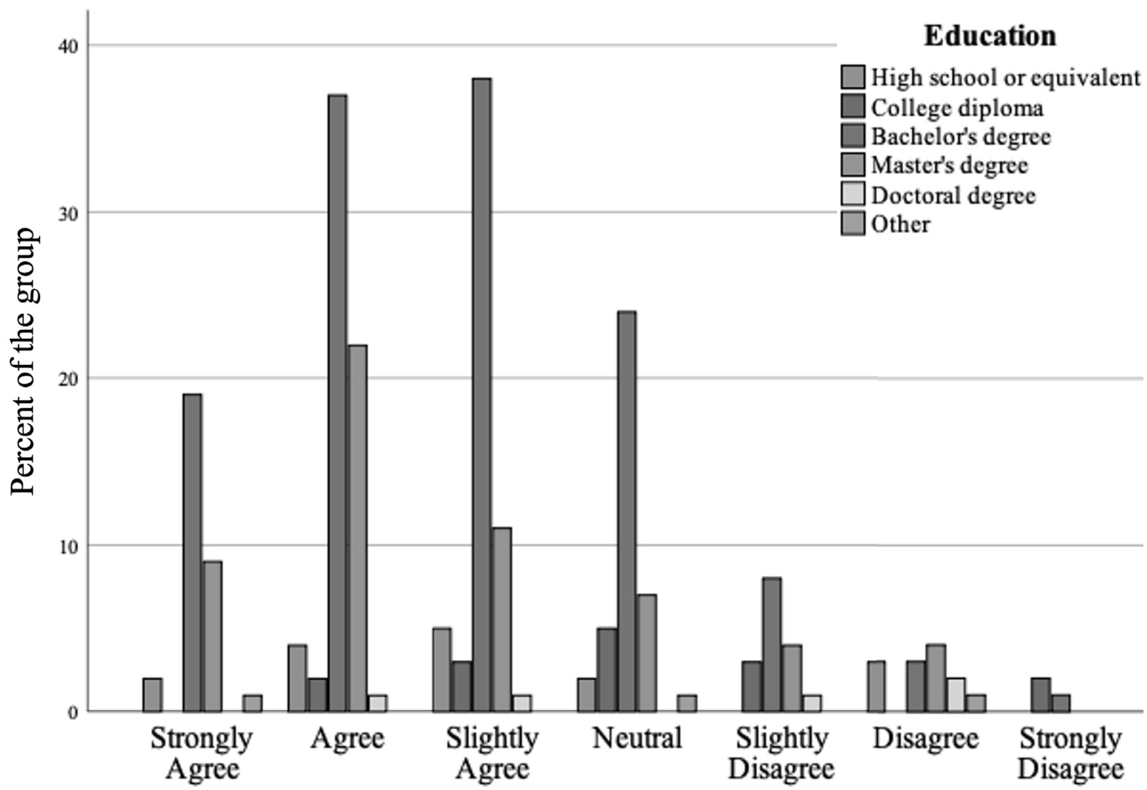


Figure 8.11: How the respondents from different education levels regarding if using a Blockchain-based network to share the ePrescription information will raises security concerns, on a seven-point Likert-type rating scale.

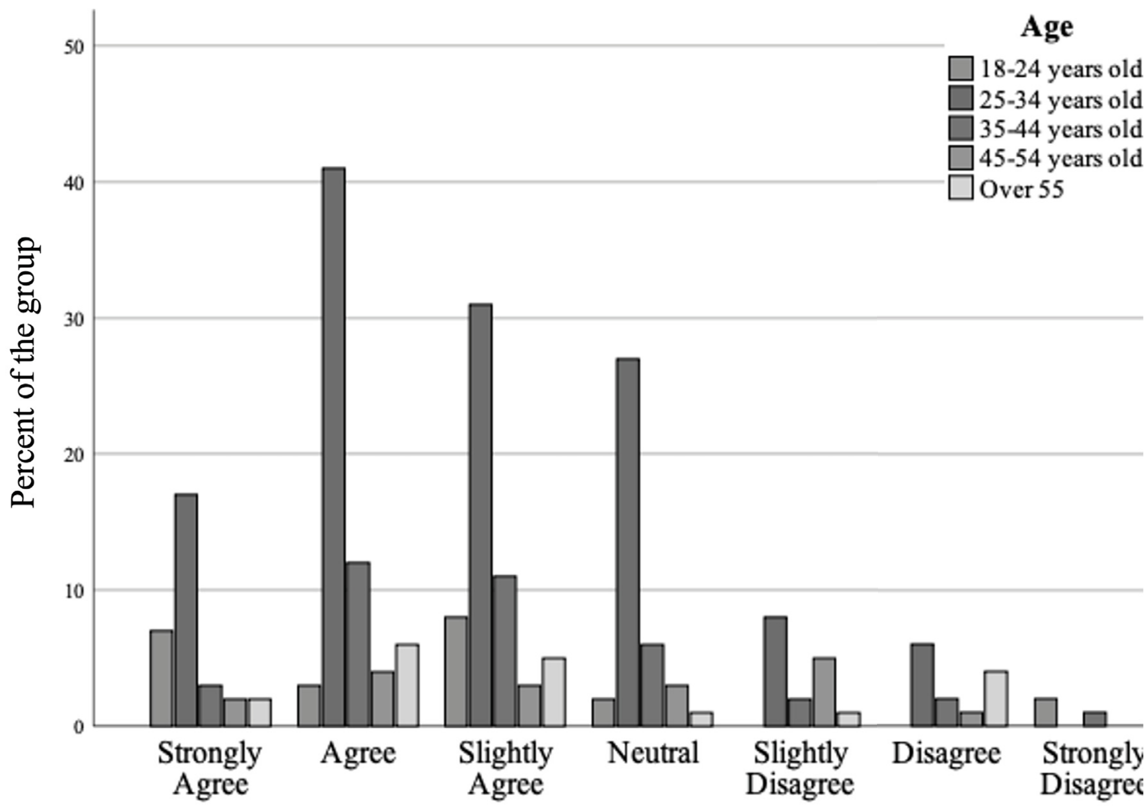


Figure 8.12: How the respondents from different Ages regarding if using a Blockchain-based network to share the ePrescription information will raises security concerns, on a seven-point Likert-type rating scale.

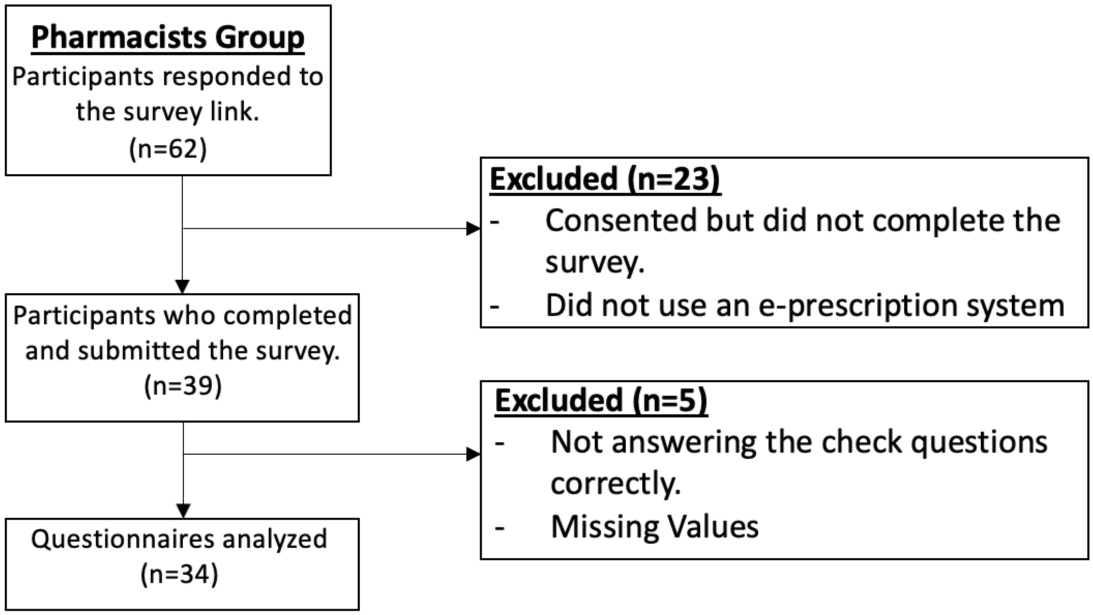


Figure 8.13: The process of selecting participants in the pharmacists group.

of the demographic data percentages distribution of the pharmacist group.

Pharmacists' attitudes toward ePrescription systems in general

We asked the pharmacists a series of questions about what motivates them to use ePrescription systems in general. Almost 95% of the pharmacists stated that they would use the ePrescription system because it will help transfer ePrescription information securely. Additionally, approximately 91% of the pharmacists stated that they would use the ePrescription system because it will keep a record of patients' ePrescription information easier, and 88.2% of the pharmacists think that, the ePrescription system will help prevent the misinterpretation of paper prescriptions. The majority of pharmacists, 73%, believe that the ePrescription system will improve communication with the prescribers, and 82% believe it will reduce the time spent on communicating with prescribers. Nearly 65% of the pharmacists think using the ePrescription system will help verify the originality of the received ePrescription. However, only 29% think the ePrescription system will help verify the prescriber's identity using a digital signature. Figure 8.14 shows the percentage of pharmacists' answers to the questions about the ePrescription system in general.

Table 8.2: Demographics of **the pharmacists' group**(n=34)

	Frequency	Percent
Age (years)		
18-24 years old	1	2.9%
25-34 years old	10	29.4%
35-44 years old	13	38.2%
45-54 years old	7	20.6%
Over 55	3	8.8%
Gender		
Male	15	44.1%
Female	19	55.9%
Other	0	0.0%
Education		
Bachelor's degree	23	67.6%
Master's degree	5	14.7%
Doctoral degree	4	11.8%
Other	2	5.9%

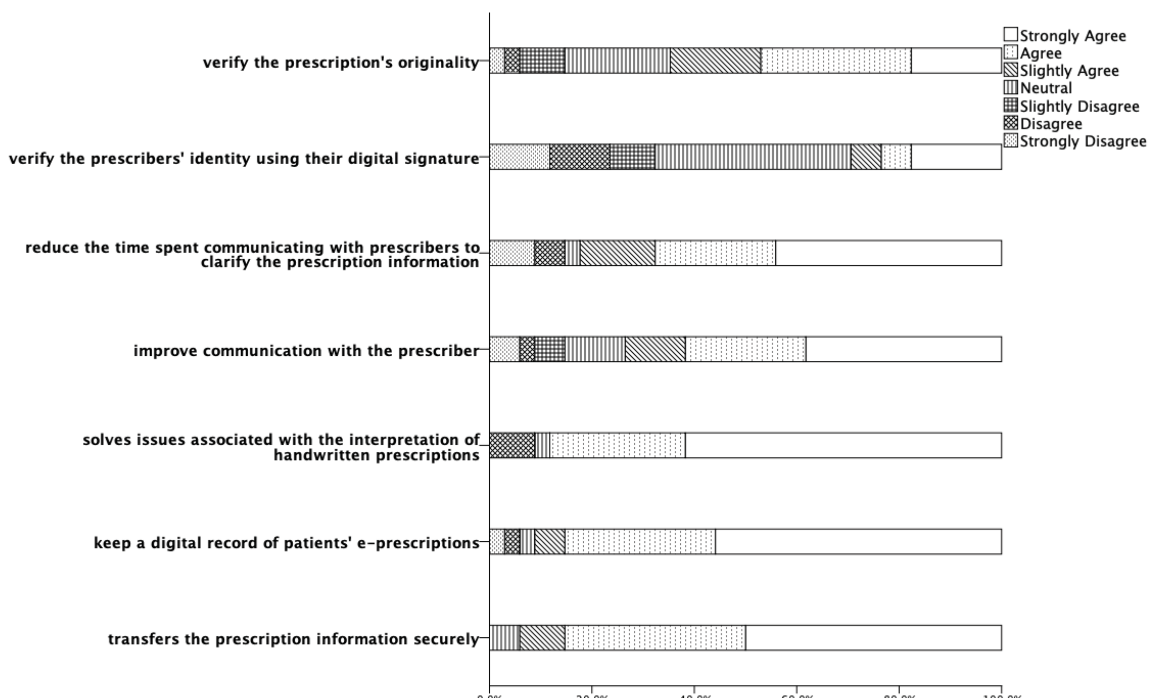


Figure 8.14: How the pharmacists answered the different questions about the ePrescription system in general on a seven-point Likert-type rating scale.

Pharmacists' feedback on the new proposed ePrescription alert generation feature

Only 47% of the pharmacists think checking the ePrescription system for any drug interactions in the patient will help reduce their workload. However, 82.4% of the pharmacists think checking the ePrescription system for anomalies (e.g. missing fields, misplaced information, or wrong dosage proportions) will help reduce their workload regarding communicating with the prescriber. Nearly 91% of the pharmacists agree that generating alerts for the prescribers to prescribe medication safely to the patient based on their past medication history will help the pharmacists dispense medications safely. Around 62% of them believe that the system checking for drug-to-drug interactions will improve the work efficiency in the pharmacy. Further, 68% of the pharmacists think checking alerts about the patient's drug allergies will improve the work efficiency in the pharmacy. Almost 68% of the pharmacists think checking for prescription anomalies will reduce any dispensing errors. Finally, 65% of the pharmacists believe that the proposed features for detecting anomalies will help to dispense medication safely. Figure 8.15 shows the percentage of the pharmacists' answers to the questions about the new proposed feature of generating alerts for the prescribers about ePrescription anomalies and drug interactions.

Pharmacists' feedback on the new proposed ePrescription sharing ePrescription feature

The majority of the pharmacists (94%) think that making the ePrescription in a read-only mode will help prevent alterations, and 52% believe this will help avoid prescription fraud. Almost 56% of the pharmacists think that controlling access to the ePrescription by patients using a unique ID will help verify the patient's identity during the dispensing process. Last, almost 80% of pharmacists, who responded to the survey, think the new proposed ePrescription system will help authenticate the submitted ePrescriptions. Figure 8.16 shows the percentage of the pharmacists' answers to the questions about using blockchain technology in the new proposed ePrescription system.

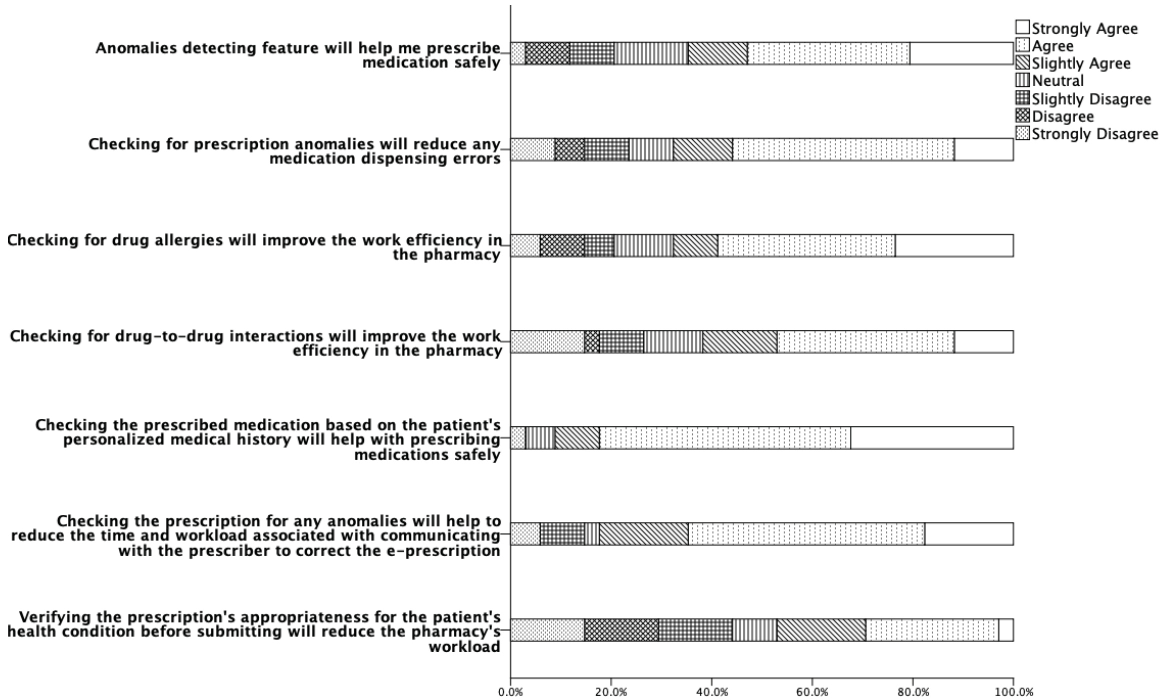


Figure 8.15: How the pharmacists answered the different questions about the new proposed feature of generating alerts to the prescribers about the ePrescription anomalies and drug interactions on a seven-point Likert-type rating scale.

8.4.3 Prescribers Group

After the initial exclusion process (n=27), we excluded one more participant because they did not answer the check questions or there were missing values in their submitted survey. Thus, the number of analyzed responses was 26, with a response rate of 96% (26/27). The exclusion process is described in Figure 8.17, and Table 8.3 shows an overview of the demographic data percentages distribution of the prescriber group.

Prescribers' attitudes toward ePrescription systems in general

We asked the respondent prescribers several questions about the ePrescription system in general and to what extent they agree with the presented statement that they are motivated to use or not to use the ePrescription system in general. Almost 92% of the prescribers believe they will use the ePrescription system because they will use it to securely transfer ePrescriptions. Nearly 88% of the prescribers think the system will allow them to keep a digital record of the patients' prescriptions, and 92% of them will use it because the system will solve most of the issues associated

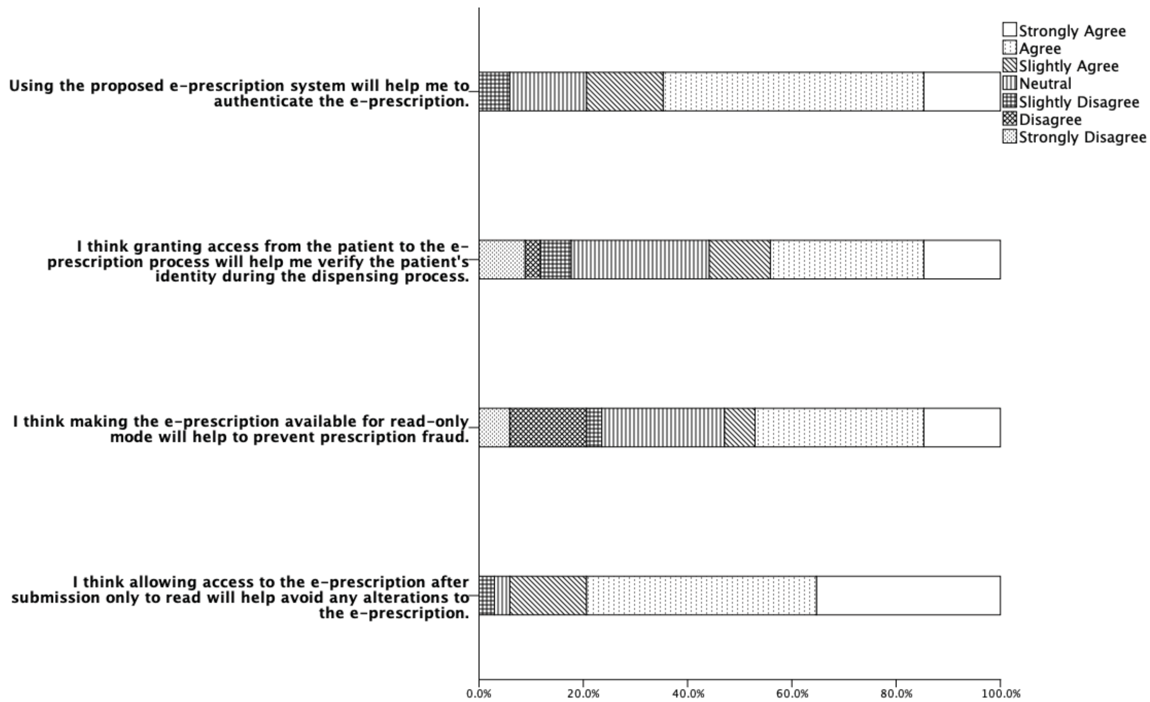


Figure 8.16: How the pharmacists answered the different questions about the new proposed feature of using Blockchain to securely sharing and preserving the prescription information on a seven-point Likert-type rating scale.

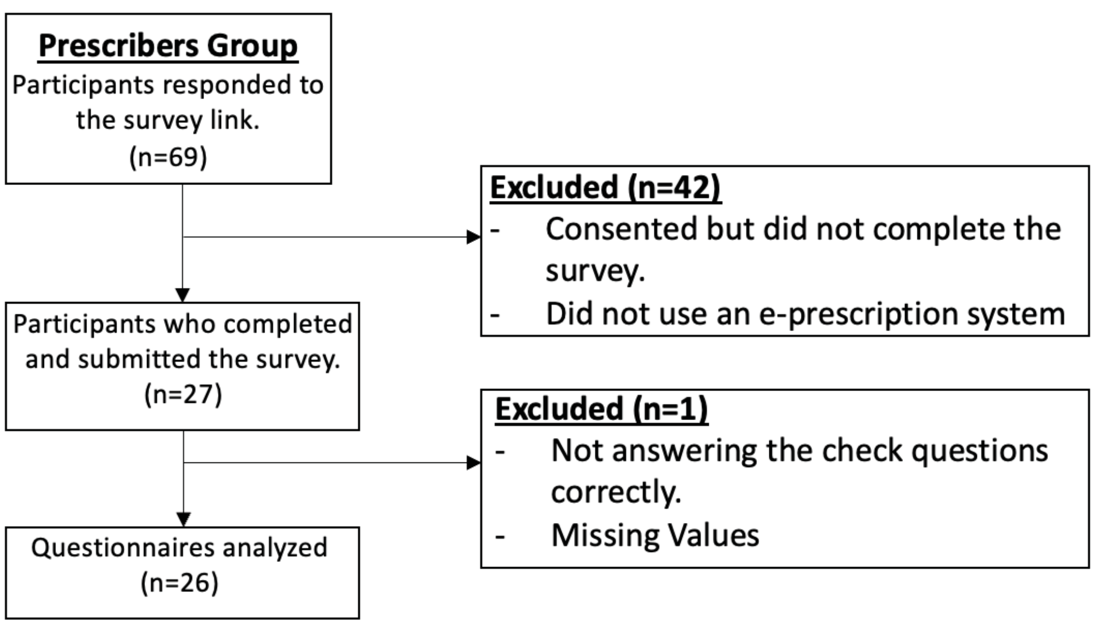


Figure 8.17: The process of selecting participants in the prescribers group.

Table 8.3: Demographics of **the prescribers' group**(n=26)

	Frequency	Percent
Age (years)		
18-24 years old	1	3.8%
25-34 years old	7	26.9%
35-44 years old	8	30.8%
45-54 years old	7	26.9%
Over 55	3	11.5%
Gender		
Male	18	69.2%
Female	8	30.8%
Other	0	0.0%
Education		
Bachelor's degree	6	23.1%
Master's degree	5	19.2%
Doctoral degree	12	46.2%
Other	3	11.5%

with paper prescriptions. Approximately 81% of the prescribers agreed that they will use the system because it will improve communication with pharmacists, and 85% would like to use the system because it will help track the fulfillment of prescriptions. However, 15% will not use the ePrescription system because it will take more time to type in and submit the prescription, and 23% will not use the system because of the possible security threats associated with the system being online and connected to the internet. Figure 8.18 shows the percentages of the prescribers' answers to the overview questions about ePrescription systems in general.

Prescribers' feedback on new proposed ePrescription alert generation feature

We asked the prescribers to answer if they agree with the provided statements regarding the feature of generating alerts using the machine learning algorithm (described in detail in chapter 6). The majority of prescribers (91%) believe generating alerts about the prescribed medication using one or a combination of previous patient medication history, current health condition, and previous similar cases of drug interactions will help safely prescribe the medication. However, 77% of the prescribers think using the

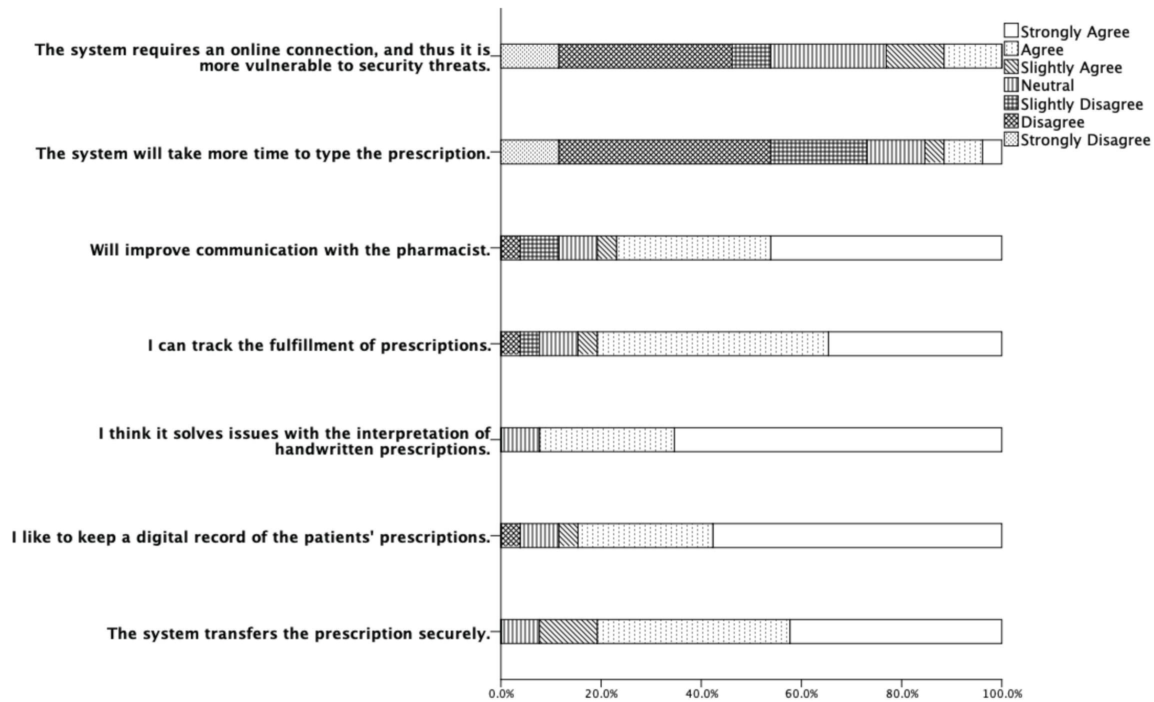


Figure 8.18: How the prescribers answered the different questions about the ePrescription system in general on a seven-point Likert-type rating scale.

previous health condition of the patient will help prescribe medication safely. Moreover, 81% of the prescribers think checking for any prescription anomalies will help reduce the time spent to correct the prescription by communicating with the pharmacists. Finally, 77% of the prescribers think integrating the alert-generating feature using machine learning will help prevent medication errors and enhance the safety of medication prescribing. Figure 8.19 shows the percentages of the prescribers' agreement with statements about the proposed ePrescription system's alert-generating feature.

Prescribers' feedback on the proposed ePrescription sharing feature

We presented the prescribers with three questions about the use of a private ePrescription network using blockchain technology (details described in chapter 6). Approximately 77% of the prescribers think providing the ePrescription in a read-only mode after submission will help avoid any alterations to the initially submitted prescription, and 73% think the read-only mode will help prevent fraud. Finally, almost 65% of the prescribers agree that using a private network to make the ePrescription available to

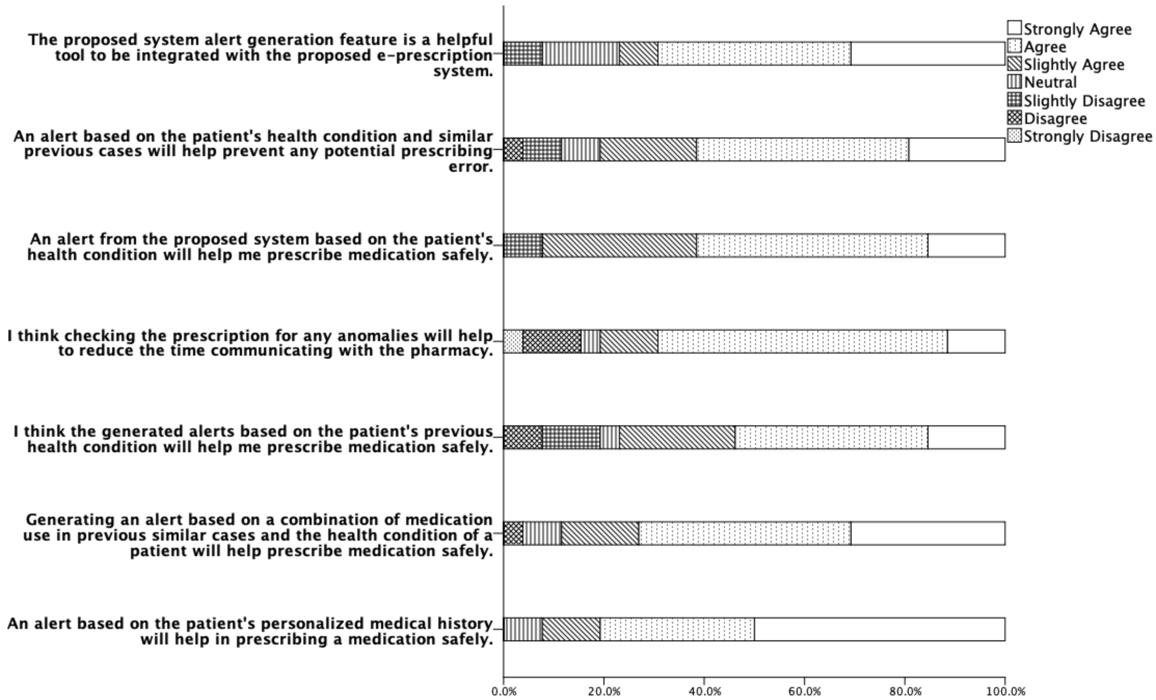


Figure 8.19: How the prescribers answered the different questions regarding the proposed ePrescription system's alerts generating feature on a seven-point Likert-type rating scale.

all parties (i.e. prescribers, pharmacists, and patients) will enhance the medication's safety. At the same time, 23% stated their opinion as neutral, and only 12% disagreed with the statement. Figure 8.20 shows the percentage of the prescribers' answers to the questions about using blockchain technology in the new proposed ePrescription system.

8.4.4 Suggested improvements

We asked the three groups if they have any suggestions on improvements or any comments in general about the proposed ePrescription system. Starting with the patient group, almost 39% (89/226) provided answers in free text. We excluded 51 answers unrelated to the question or answers that stated that they do not have any suggestions. The most common comment (n=35) was that the proposed system is sufficient and does not need any further improvements. However, the second most common comment (n=18) was about different security concerns the respondents had towards using the prescription information and sharing it with all parties in the blockchain

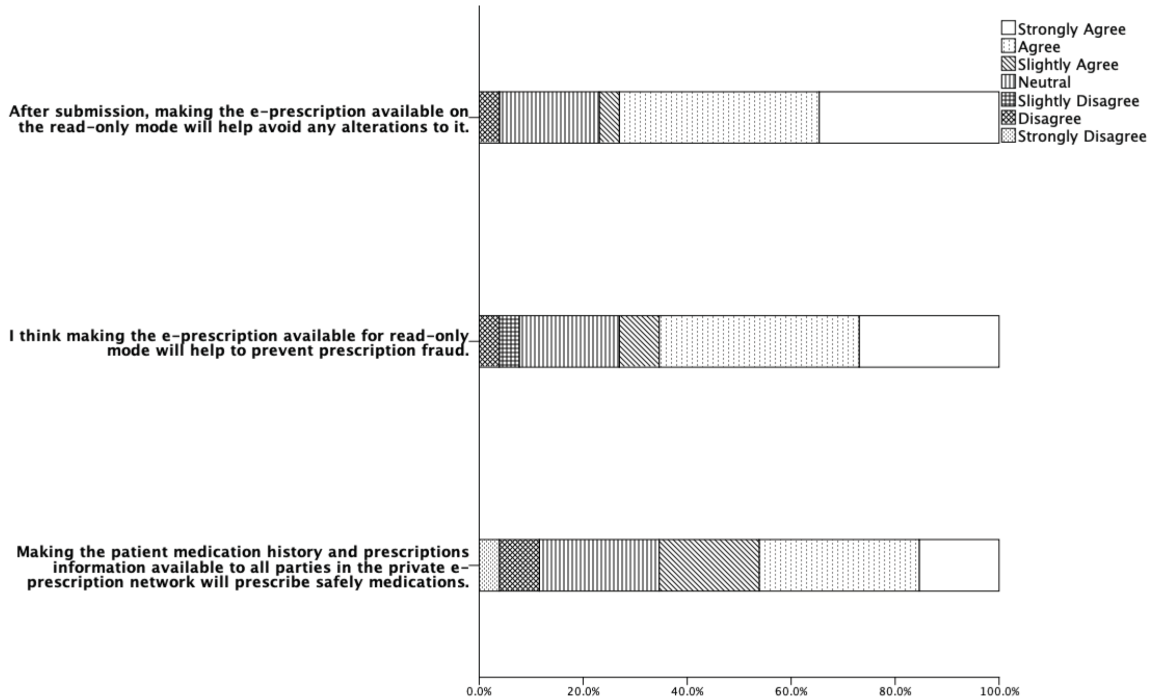


Figure 8.20: How the prescribers answered the different questions regarding the proposed ePrescription system provide the ePrescription information to all parties in the private network on a seven-point Likert-type rating scale.

network. Another common comment (n=17) was on using a more straightforward design for the mobile application to make it easier to read and navigate for the patient when they browse their ePrescriptions. It was also suggested that the mobile application use push notifications for any changes made to their ePrescription. Another exciting suggestion (n=6) is to use a two-factor authentication scheme to verify the identity of the patient and the originality of the ePrescription. Last, other respondents (n=4) suggested using a one-time password (OTP) authentication scheme [223] to grant access to the ePrescription blockchain. See Table 8.4 for the most common free-text answers and the improvements and comments provided by the patients.

In the pharmacist group, almost 44% (15/34) of the respondents answered in free text. The answers included 26 comments and suggestions with a rate of 1.62 comments or suggestions per answer. The most common suggestion (n=5) is to include the indication of the prescribed medication with the prescription to reduce the time spent communicating with the prescriber. Another common suggestion (n=3) is to provide an option for the patient to grant access to the ePrescription online

Table 8.4: The suggestions of the **patient group** for improvements and comments about the proposed ePrescriptions.

	n	**Percentage**
Suggestions		
The proposed system is sufficient	33	37%
Security concerns and improve information privacy	26	29%
Simpler design for the mobile application	11	12%
Two-factor authentication scheme	6	7%
Push notifications using the mobile application regarding the ePrescription	5	6%
Using a password to log in to the mobile application	4	4%
Use One-Time-Password (OTP)	4	4%
Total	89	100%

in order to reduce the waiting time for the patient. Sharing the drug interaction alerts sent to the prescriber with pharmacists was another suggestion provided (n=2). It was also suggested (n=2) to provide a digital signature for the prescriber with the ePrescription in order to prevent fraud when prescribing narcotics. Table 8.5 shows the entire suggestions and comments provided by the pharmacists regarding improving the proposed ePrescription system.

For the prescriber group, almost 50% (13/26) of the respondents answered in free text. The answers included 16 comments and suggestions with a rate of 1.23 comments or suggestions per answer. The most common suggestion i(n=5) is to design the visual alerts in a way that is easy to understand and overcome. Another common suggestion (n=4) was that the proposed system should be easily integrated or utilized by enhancing the currently used Electronic Health Record (EHR) systems. Other comments and suggestions are listed with all the comments in Table 8.6.

8.5 Discussion

8.5.1 ePrescription in general

We found from the study that the perceptions of the three groups towards the ePrescription system are mostly positive. In the patient group, we found that the respondents felt that the security and privacy of their prescription would improve if they use the ePrescription system. Most patients believe that the ePrescription system can reliably handle prescription information and make their information available to pick

Table 8.5: Suggestions from the **pharmacists group** for improvements and comments about the proposed ePrescriptions.

	n	**Percentage**
Suggestions		
Provide the indication of the medication	5	19%
The proposed system is sufficient	3	12%
Granting access to the prescription in advance	3	12%
Checking for allergies, adherence, and interactions	2	8%
Option to share the drug interaction alerts	2	8%
Multiple built-in alerts for all parties	2	8%
Digital signature for prescribers	2	8%
Better integration with the pharmacy system	1	4%
Web-based platform of the system to all parties	1	4%
Using fingerprint authentication to control access	1	4%
Built-in dosage forms for prescribers to select from	1	4%
Notification for a new prescription coming in	1	4%
Provide an offline mode of the system	1	4%
A print option for the prescription	1	4%
Total	26	100%

Table 8.6: Suggestions from the **prescribers group** for improvements and comments about the proposed ePrescriptions.

	n	**Percentage**
Suggestions		
Visually easy to understand alerts and simple	5	31%
Integrated with the current Electronic Health Record (EHR) systems	4	25%
List of drugs built-in and available to select from	1	6%
Two-factor authentication	1	6%
Cross-reference the interactions with official resources	1	6%
Option to override dosage restrictions	1	6%
The system should not override clinical judgment	1	6%
Easy to connect to and access it	1	6%
Registration of the patient's preferred pharmacy	1	6%
Total	26	100%

up medication when they are at pharmacies. However, they were not entirely sure that the ePrescription system will improve their experience with picking up medication in its current form. The patient group most likely to state that their experience will not be changed are 25–34 years old, had a bachelor's degree, or used an ePrescription system before. This might be because in the ePrescription system's current form, their role is still limited, and most of the features are directed to benefit the pharmacists and prescribers. They have limited control or might be limited to the individual's experiences with different ePrescription systems. Thus, more in-depth studies should be conducted to overcome this negative perception. In addition, an explanation of the indirect benefits affecting the safety of the medication dispensed to the patients. the patients' skepticism about the technological advancements in terms of prescription might lead to the patients opposing any new technologies that could be used in the future. The health service providers might think of providing more information to the public to close this knowledge gap.

In the other two groups (i.e. pharmacists and prescribers), we found more enthusiasm about using ePrescription systems since most of the systems were developed to solve most of the issues related to paper prescriptions. In the pharmacist group, we mainly found positive responses about how the ePrescription system will improve security and privacy while transferring prescriptions electronically. However, there is some hesitation about whether the system will verify the originality of the ePrescription by only using the prescriber's digital signature. We also found that the pharmacists' perceptions were positive about whether the ePrescription system will improve communication with prescribers. They positively responded that the system would help them keep a digital record of the prescriptions. In general, we found that the pharmacists reacted positively towards most of the presented statements, and they were motivated to use the ePrescription system. Similarly, in the prescriber group, we found positive responses towards using the ePrescription system for the reasons mentioned in the questionnaire. We also found that the prescribers are more likely to agree that tracking the fulfillment of the prescription is information they want to be knowledgeable about it.

8.5.2 Using a Blockchain Network

In the patient group, we found that they are more positive towards the read-only mode proposed, where the prescription can not be altered once submitted to the blockchain. Most of the patient group respondents who reacted positively to the read-only mode had at least a bachelor's degree for their education level. We also found that the patient group in the age range of 25–34 years old does not think using a unique ID to access the ePrescription information in the network will preserve their privacy. Analyzing the text responses on the question about suggesting any improvements, this age group might be more likely to prefer to add another security layer or use other methods to preserve their information privacy (e.g. two-factor authentication or a one-time password). Despite the patient group feeling negative about using the blockchain network because of privacy and security concerns, they responded positively to their access to their information. Thus, the patients would like to have a more significant role in managing and sharing their information. The patients' security and privacy concerns might be raised because their information is on the blockchain, where any node in the network can view the information. The design description presented to them specifically explained that their information would be encrypted when stored in the blockchain, but they still have concerns. It would be better for future research is to explore these concerns and provide a more unambiguous explanation. Finally, the patients think a more secure method is needed than using a unique ID only.

In the pharmacist group, we found that they responded positively, regarding that using the blockchain feature will help verify the originality of the ePrescription and authenticate it. Additionally, we found that the respondents feel positive about using the read-only mode, and they think it will help prevent any alterations to the original ePrescription. In contrast, we found that they think the read-only mode might prevent fraud. In short, the pharmacists think using blockchain will help prevent fraud and alterations to the prescription, will be used to authenticate the ePrescription, and will verify the patient's identity due to controlling access to ePrescriptions. Similarly, the prescriber group showed a positive attitude towards the blockchain feature. We found that the prescribers think using blockchain to make the medication history available to all parties will help prescribe medications safely. The blockchain provides a decentralized network connecting all the parties, making the patient's medication history blocks available to be accessed by authorized parties in the network.

8.5.3 Utilizing the machine learning algorithms to generate alerts

We asked both the pharmacist and prescriber groups about the new methods for generating alerts. We found that both groups think the new method will help prescribe and dispense medication safely. The pharmacists think detecting any anomalies in a prescription to be solved or changed by the prescriber before submitting it will help reduce the time spent clarifying the prescription. This will also help increase patient satisfaction with the service when their prescription is ready in advance. Correspondingly, a prescription checked for any allergies regarding the patient's prescribed medication and for any drug-on-drug interaction will help increase the efficiency in the pharmacy by reducing the workload. One of the most common suggestions is to indicate that including the medication prescribing resaons will help reduce the workload and time spent communicating with prescribers to clarify the prescriptions and the reasons for prescribing the medication. One pharmacist commented that the indication of the prescribed medication would help correct and verify the prescribed dosages. The pharmacist group answered slightly positively towards generating alerts about suggesting the appropriate dosages for the prescribed medication to the prescribers before submitting. However, they would like to receive the generated alerts to verify the prescribed dosages as part of the prescription.

Comparatively, the prescriber group also responded positively towards using the new generating alerts method. They think using the patient's current and previous health condition to check for any drug interactions or allergies towards the prescribed medication/s will help prescribe medications safely. In addition, utilizing information from previous similar cases that used the prescribed medication for the same indication will help prevent prescribing medication errors. Similarly, the prescribers think that using a combination of the previously mentioned information regarding checking the prescribed medication will help prescribe the medications safely to patients. However, the prescribers stated in a common comment that fewer alerts should be sent to prevent pop-up fatigue because of the high number of alerts [224]. Therefore, we designed the machine algorithm to check for all drug interactions and present the prescribers with only the most important ones. We also made them visually easy to understand and deal with. The generated alerts are intended to be suggestions only and should not be used by the prescribers to make decisions. Similarly, one of the suggestions is to provide two-factor authentication to grant access to ePrescription information.

Finally, all the groups responded to both features with positive attitudes and a few suggestions to be incorporated in the features. Most of the suggestions were about security and privacy concerns related to using blockchain to create a private network for the proposed ePrescription system. We believe the concerns are due to the lack of knowledge regarding how blockchain technology will manage the ePrescription information. While we provided a short but detailed description of the technology and how it will be used to manage the information, we still think more education for all the parties is needed before incorporating this technology. As for using the machine learning algorithms, we only surveyed the prescriber and pharmacist groups since they are the only groups that will be dealing with the alerts. Both groups have positive perceptions of the proposed features. However, minor suggestions such as sharing the alerts with the pharmacists and displaying the alerts in a simple and visually easy to understand method were given.

8.6 Limitations of the Survey

Besides the positive and promising results of this survey, there are some limitations we will explore in this section. One of the limitations is the number of participants in the prescribers and pharmacists groups. Due to the COVID-19 pandemic, the workload has increased on the healthcare providers. As explained to us from the associations we reached out to, it is not easy to recruit many participants during these times. Another limitation is the gender basis of the survey. The majority of participants in all groups were males, which might affect the results since the issues we are exploring affect the lives of all genders of the public. Lastly, most patients' group participants had used ePrescription before, which might have altered the results to favour the ePrescription systems.

8.7 Chapter Summary

To summarize, many studies showed that the prescribers and pharmacists appreciate using the ePrescription system to reduce their workflow and solve most of the issues associated with paper prescriptions. Additionally, this study provided information about the prescribers', pharmacists', and patient's evaluation of the security and privacy of the ePrescription system. Moreover, our survey showed that the proposed features would help prevent medication errors and enhance the safe prescribing of medication. Blockchain technology is used to build a private network to enable all the parties to share information about the patient's medication history and ePrescriptions submitted in their blockchain. All healthcare providers can access this network (i.e. patients, prescribers, and pharmacists); however, only by authorization from the patient, the healthcare providers can access the patient's specific encrypted information blocks. Moreover, using machine learning algorithms helps generate personalized alerts about the patient's health condition. The alerts help prevent medication errors and prescribe medication safely. In conclusion, we found from the study that our proposed ePrescription system would prevent medication errors and enhance the safe prescribing of medication.

Chapter 9

Machine Learning Module

9.1 Introduction

Preventing prescription errors and adverse drug events (ADEs) is considered difficult due to multiple-complected interventions by humans on multiple levels. It is estimated that these errors were preventable, account for 1 in 985 outpatient and inpatient deaths in the US. In addition, these prescription errors lead to a cost of approximately 30 billion USD. Although these prescription errors are linked to human errors, there are also failures in the utilization of information systems to prevent these errors [60, 225, 226]. Nowadays, the main approach employed to overcome this issue is the use of CDS systems. Although these systems can identify prescription errors, they still misidentify the majority of errors and cause "alert fatigue" due to the high number of false alerts [60, 227, 228]. Therefore, systems using ML will detect prescription errors accurately and generate fewer false alerts [229–231].

ML has evolved in recent years as part of the artificial intelligence (AI) field. ML refers to the use of computer algorithms to improve decision making by utilizing large datasets [232–234]. ML algorithms are widely used in fields such as education, industry, transportation, and medicine. In recent years, machine learning has been introduced and proposed in multiple health care fields to help health care workers make medical decisions safely [234, 235]. The ML algorithms are fed with data collected in the training phase to classify the data. Later, the classifier will be used to give specific predictions [236]. Therefore, both preparing data for processing and the collected data quality have a significant role in driving high-quality results that help improve the decision-making process [237]. Nowadays, most of the collected data are processed in different healthcare applications to deliver good health care services. The following are some examples of the uses of machine learning in the healthcare sector in general and prescribing medication in particular.

The authors [56] proposed to find any non-medical uses of drugs by applying an unsupervised ML algorithm on Twitter data, and [58] proposed the use of ML to identify antibiotics that could be used to treat urinary tract infections. Another study [60] developed an outlier CDS system based on ML to predict any medication prescribing errors for inpatient settings.

9.2 Literature Review

In this section, we will explore different studies that used ML for identifying prescription errors and medication errors in the healthcare sector. However, to the best of our knowledge, these are the only studies we could find that are related to our research question.

MedAware [238] is a detection system developed to identify and prevent prescription errors using a machine learning algorithm. The MedAware website did not specify a machine learning classifier. Several studies were conducted to evaluate the MedAware system's accuracy in generating alerts [229–231]. The studies showed that the MedAware system has an accuracy range between 75% and 85%, correctly identifying prescription errors.

The authors in [239] developed a ML model to predict ADR. They used a dataset collected over 12 months between 2016 and 2017 for every inpatient episode that was flagged to be a possible case of ADR. The resulting dataset had 2917 records with 245 cases of ADR. The authors used the classifier RF for their ML model. The classifier was able to correctly classify ADR cases with an AUC of 0.803.

The authors in [240] developed a ML model using a RF classifier to detect ADEs in emergency departments EHR for older adult patients. They used the RF to predict the mortality in a dataset collected over six months for older adults with congestive heart failure. Their model correctly classified patients who lived 82.6% (AUC = 0.826) of the time.

9.3 Overview of the proposed scheme

As discussed in 6, the ML server will have three modules for collecting, managing and processing the data required. The patient's information will be aggregated based on the patient ID, shared upon the healthcare center or pharmacy visit. Then, the ML server will send messages to the network to collect the blocks containing the patient's information. The information includes the patient's medication and health condition. Then, the server will process the new e-prescription for any anomalies to avoid any interactions or anticipated harm from the prescribed medication. Such anomalies are the missing prescription values, wrong dosage, wrong medication strength the might harm the patient. All of these anomalies could be detected using the history of similar treatment cases. Therefore in our experiment, we are detecting any serious outcome caused by these anomalies.

After this, the server will send the result of this process to the prescriber's management system. The outcome of this process is based on the available information on a patient's health condition and the past use cases of a medication with the same prescribed dosage description. The prescriber will make the final decision and submit the e-prescription to be added to the Blockchain. Finally, the updated Blockchain ledger will be sent to the synced nodes in the blockchain private network to make the information available. Figure 9.1 shows the proposed process of the ML server.

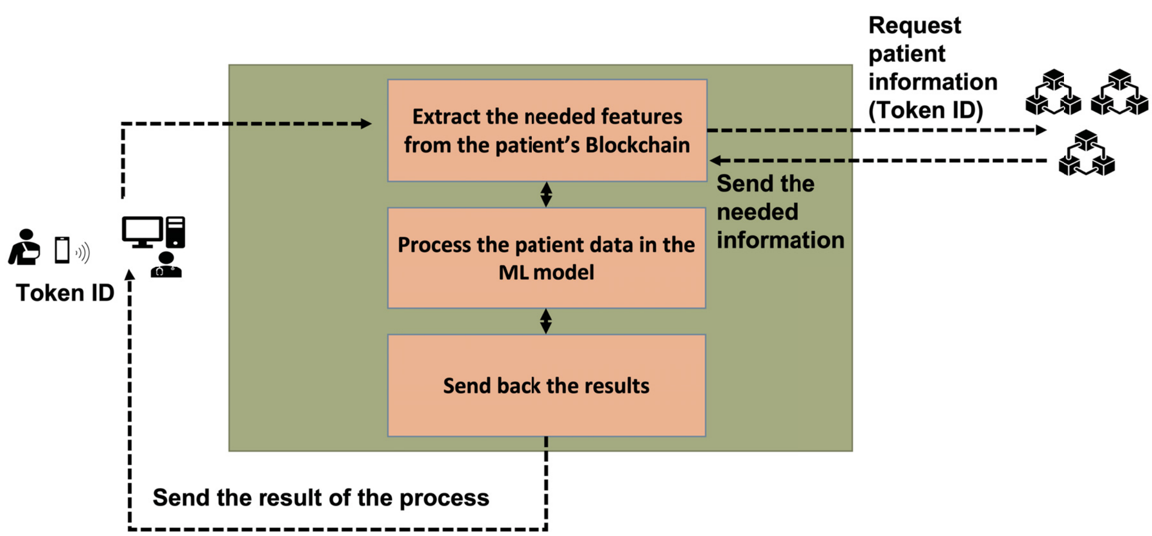


Figure 9.1: The proposed ML model architecture

9.4 Data Selection and Preprocessing

9.4.1 Data Selection

Our study used the publicly available Adverse Event Reporting System dataset extracted from the US Food and Drug Administration (FDA) website. The dataset is aggregated from the sub-dataset published from the year 2012 to 2020 [2]. The dataset is formatted as XML files with a total size of approximately three GB. We first converted the dataset to sub-CSV files using Python code, and then we aggregated the resulted CSV files to one dataset in a CSV file. The resulting dataset contained almost 10 million records and 85 features 9.2. The dataset fields included demographic and administrative information, drug information from the case reports, reaction information from the reports, patient reaction outcome information from the reports, and information on the source of the reports.

```
['Unnamed: 0', 'messagetype', 'messageformatversion', 'messageformatrelease', 'messagenumb',
'messagesenderidentifier', 'messagereceiveridentifier', 'messagedateformat', 'messagedate',
'safetyreportversion', 'safetyreportid', 'primarysourcecountry', 'occurcountry',
'transmissiondateformat', 'transmissiondate', 'reporttype', 'serious', 'receivedateformat',
'receivedate', 'receiptdateformat', 'receiptdate', 'fulfillexpeditecriteria', 'companynumb',
'duplicate', 'reportduplicate', 'duplicatesource', 'duplicatenumb', 'primarysource',
'reportercountry', 'qualification', 'sender', 'sendertype', 'senderorganization', 'receiver',
'receivertype', 'receiverorganization', 'patient', 'patientonsetage', 'patientonsetageunit',
'patientsex', 'reaction', 'reactionmeddraversionpt', 'reactionmeddrapt', 'reactionoutcome', 'drug',
'drugcharacterization', 'medicinalproduct', 'drugdosagetext', 'drugdosageform',
'drugadministrationroute', 'drugindication', 'activesubstance', 'activesubstancename',
'drugbatchnumb', 'drugauthorizationnumb', 'drugstructuredosagenumb', 'drugstructuredosageunit',
'drugstartdateformat', 'drugstartdate', 'actiondrug', 'drugenddateformat', 'drugenddate', 'summary',
'narrativeincludeclinical', 'seriousnessdisabling', 'seriousnessother', 'authoritynumb',
'drugrecurreadministration', 'seriousnesshospitalization', 'literaturereference', 'patientagegroup',
'patientweight', 'drugseparatedosagenumb', 'drugintervaldosageunitnumb',
'drugintervaldosagedefinition', 'seriousnesslifethreatening', 'seriousnessdeath',
'drugcumulativedosagenumb', 'drugcumulativedosageunit', 'drugadditional',
'seriousnesscongenitalanomali', 'drugrecurrence', 'drugrecuraction', 'drugtreatmentduration',
'drugtreatmentdurationunit']
```

Figure 9.2: The used dataset features (n=85).

9.4.2 Data Pre-Processing

The dataset had many missing values and misfiled values that needed to be removed before processing. We removed all of the records that had missing values, and this resulted in 839,548 thousand records. According to multiple resources, the prescription should have at least the patient name, patient sex, patient age, drug name, drug strength, dosage form, medication indication (i.e. the reason why the medication was prescribed), and the quantity of the prescribed medication [60, 241, 242]. Thus, we removed the features that were not relevant to the drug, patient, indication, dosage, and outcome reaction, and we removed any redundant features that had the same value but in a different form. As a result of the exclusion process, we had ten features to process with the ML algorithms as shown in Figure 9.3. The dataset had a reaction outcome field related to the patient's reaction toward the prescribed medication. The seriousness of the patient reaction was classified into one of six categories: the seriousness of disabling, the seriousness of other, the seriousness of hospitalization, the seriousness of life-threatening, the seriousness of death, and the seriousness of congenital anomaly. Not all the cases met the seriousness of any of the categories. To simplify, we aggregated all the seriousness categories into one serious feature, where if the reaction was severe, we gave a value of 1 and 0 if not. Since our goal was to use machine learning to develop a model to predict if a medication will harm a patient or not, we assigned this feature to be the ML algorithm target value.

Many ML algorithms require numerical values as input [243, 244]. Since the dataset we used included six features that were not numerical, we performed categorical variables encoding with a Python method *LabelEncoder* from the package *sklearn.preprocessing* [245, 246]. This method converts each value in a feature column to a numerical value. We converted the values of the features medication product, indication, dosage text form, and active substance for the dataset we used. Figure 9.4 shows the converted values compared to Figure 9.3.

9.4.3 Feature Selection

Further, we used three methods to learn more about the correlation between the features, the importance of the features to the target value (i.e. severe reaction), and explore irrelevant features. In the following, we explore the results of the three

Index	NewPatientAge	patientsex	patientweight	Indecation	drugindication	MedicationPrudect	medicinalproduct	drugdosagetext	Dosagetext	drugstructuredosageunit	drugadministrationroute	ctivesubstancenam	Activesubstance	reactionmeddrapt	Reaction	serious
0	53	0	81	5193	premedication	10835	cyclophosphamid	unk unk unknown freq	181627	7	65	cyclophospham…	1729	acute graft versus host disease	165	1
1	68	1	85	5671	routine health maint…	26855	multivitamins	1 df daily	13315	32	48	vitamins	5273	type 2 diabetes mellitus	9945	1
2	61	0	75	3127	hypertension	27481	nedal	5 mg qd	98206	3	65	nilotinib	3860	acute myocardial infarction	192	1
3	20	1	85	1614	contraception	26007	mirena	20 mcg 24hr cont	60682	4	15	levonorgestrel	3339	uterine injury	10144	1
4	25	1	83	3194	hypothyroidi…	9166	claravis	40 mg bid	89613	3	48	isotretinoin	3164	injury	5201	1
5	51	1	86	1212	cardiovascul…	22865	lipitor	10 mg daily	26320	3	48	atorvastatin calcium	643	type 2 diabetes mellitus	9945	1
6	49	1	90	566	asthma	32659	pro air inhaler	unk	177639	32	48	albuterol sulfate iprat…	222	asthma	855	1
7	29	1	81	1614	contraception	42183	wellbutrin	20 mcg 24hr cont	60682	4	15	bupropion hydrochloride	1018	complication of device removal	2315	1
8	70	0	76	1423	chronic lymphocytic …	24942	metformin	100 mg bid	29828	3	48	metformin hydrochloride	3575	febrile neutropenia	3656	1
9	73	1	87	3562	lacrimation increased	9239	claritin reditabs	10 mg once	26788	3	48	loratadine	3406	drug ineffective	3017	0
10	58	1	94	385	ankylosing spondylitis	13952	enbrel	50 mg weekly	102401	3	58	etanercept	2348	weight increased	10495	1
11	79	0	74	94	actinic keratosis	35926	simvastatin	qd	164354	3	48	simvastatin	4704	nephrolithiasis	6639	1
12	37	1	86	5363	pulmonary arterial hyp…	39087	tracleer	192 96 ug kg 0 134 ug kg 1 in …	50322	8	58	bosentan bosentan mono…	953	sinusitis	8967	1
13	13	1	53	5253	product used for unknown …	42829	zithromax	unk	177639	3	65	azithromycin dihydrate	701	condition aggravated	2336	1
14	62	1	82	1031	breast cancer female	25406	metoprolol	100 milligram daily	31504	3	42	metoprolol	3642	dehydration	2706	0
15	35	1	84	1799	depression	43143	zyrtec	unk	177639	4	15	cetirizine hydrochloride	1361	injury	5201	1
16	54	1	89	5671	routine health maint…	41678	vitamin b12	1 df daily	13315	32	48	cyanocobalamin	1705	type 2 diabetes mellitus	9945	1
17	58	1	94	3720	low density lipoprotein …	22865	lipitor	20 mg daily	61494	3	48	atorvastatin calcium	643	type 2 diabetes mellitus	9945	1
18	61	0	79	5253	product used for unknown …	17860	glyburide	unk	177639	7	65	glyburide	2762	dyspnoea	3109	1
19	33	1	82	1614	contraception	26007	mirena	20 mcg 24hr cont	60682	4	15	levonorgestrel	3339	uterine perforation	10151	1
20	44	1	84	1212	cardiovascul…	22865	lipitor	100 mg 2x day	29342	3	48	atorvastatin calcium	643	type 2 diabetes mellitus	9945	1

Figure 9.3: The best 10 features after removing the extra features.

Index	NewPatientAge	patientsex	patientweight	Indecation	MedicationPrudect	Dosagetext	drugstructuredosageunit	drugadministrationroute	Activesubstance	serious
0	53	0	81	5193	10835	181627	7	65	1729	1
1	68	1	85	5671	26855	13315	32	48	5273	1
2	61	0	75	3127	27481	98206	3	65	3860	1
3	20	1	85	1614	26007	60682	4	15	3339	1
4	25	1	83	3194	9166	89613	3	48	3164	1
5	51	1	86	1212	22865	26320	3	48	643	1
6	49	1	90	566	32659	177639	32	48	222	1
7	29	1	81	1614	42183	60682	4	15	1018	1
8	70	0	76	1423	24942	29828	3	48	3575	1
9	58	1	94	385	13952	102401	3	58	2348	1
10	79	0	74	94	35926	164354	3	48	4704	1
11	37	1	86	5363	39087	50322	8	58	953	1
12	13	1	53	5253	42829	177639	3	65	701	1
13	35	1	84	1799	43143	177639	4	15	1361	1
14	54	1	89	5671	41678	13315	32	48	1705	1
15	58	1	94	3720	22865	61494	3	48	643	1
16	61	0	79	5253	17860	177639	7	65	2762	1
17	33	1	82	1614	26007	60682	4	15	3339	1
18	44	1	84	1212	22865	29342	3	48	643	1
19	86	0	75	5253	25406	31384	3	48	3642	1
20	79	0	75	5000	41022	9320	3	42	950	1

Figure 9.4: The best 10 features after encoding the categorical variables.

feature selection methods we used.

Univariate Selection

This method uses statistical tests to select the best ten features that have the strongest impact on the target value (i.e. serious reaction) prediction. We ran the chi-squared (chi^2) test using the class *SelectKBest* from the sci-kit-learn library [246] in Python. Figure 9.5 shows the 10 best features using this method.

Feature Importance

We used the features importance method to learn the features importance scores. A higher score means a strong relationship with the target variable (i.e. serious reaction) [247]. We used the inbuilt class from the Tree-Based Classifier to calculate the importance of the features. Figure 9.6 shows the importance of the features towards the target value.

	Fetaures	Score
5	drugdosagetext	1693661044.24620
4	MedicationPrudect	465857856.58768
3	Indecation	38150922.99833
10	activesubstancename	34325133.42006
6	DrugdoasgStructer	19986761.71083
11	Reaction	15551624.40529
7	drugstructuredosageunit	392944.16711
8	drugadministrationroute	94959.58239
2	patientweight	36871.53856
0	NewPatientAge	28494.54949

Figure 9.5: The best 10 features selected using Chi^2 statistical test.

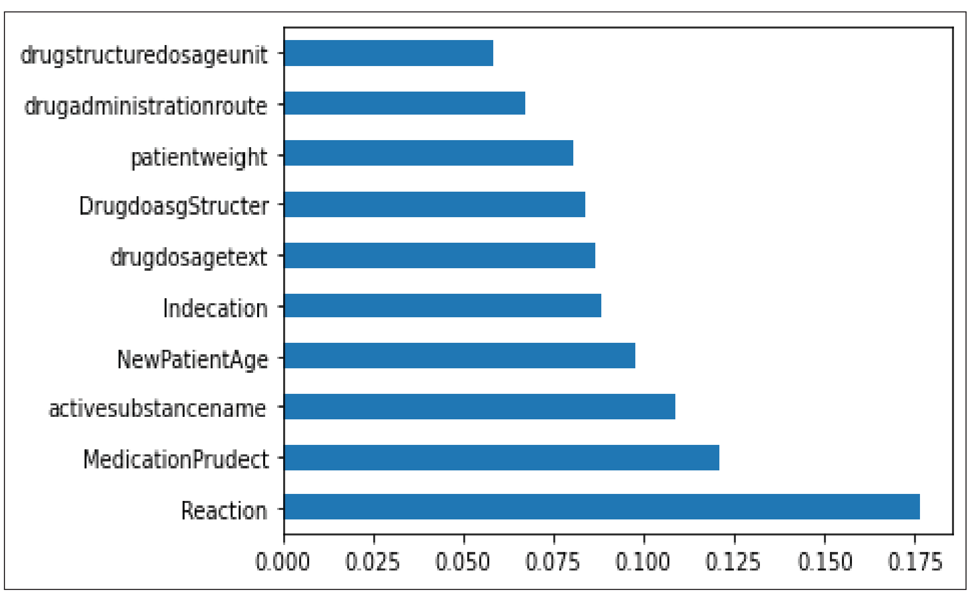


Figure 9.6: The importance of the features chart relative to their impact on predicting the target value.

Correlation Matrix with Heatmap

The correlation shows how the features are associated with each other or related to the target variable. The correlation can be easily identified using a heatmap of the correlation of the features. With this method, we can select the features most related to the target variable [247]. The closer the value to 1, the stronger the relationship is. We used the Seaborn library in Python to generate the heatmap of correlated features. Figure 9.7 shows the correlation heatmap of the features between each other and between each feature with the target value.

As a result of all the methods, we found that there are nine features that have the most impact towards predicting the target value. Table 9.1 shows the nine most relevant features and their description.

Table 9.1: The nine most relevant features and their description from the FDA [2]

Feature	**Description**
NewPatientAge	Value for patient age in the years unit.
patientsex	Gender indicator Possible codes are: 0= male 1= female.
patientweight	Weight in kilograms.
Indecation	A text string is used to characterize the indication for medication use (based on Medical Dictionary for Regulatory Activities preferred term) [248].
medicinalproduct	Medication trade name publicly.
drugdosagetext	Text describing drug dosage and frequency.
drugstructuredosageunit	Dose (unit) Possible codes are: 001=kg kilogram(s) 002=G gram(s) 003=Mg milligram(s) 004=µg microgram(s).
drugadministrationroute	Route of administration code. For example: 048=Oral 061=Topical.
Activesubstance	The medication product active ingredient.

9.5 Machine Learning Classifiers

In this section, we will discuss the chosen classifier and our selection of hyper-parameters. Further, we show the other ML classifiers and their hyper-parameters that we experiment with. It should be mentioned that we split the data into 70% for training and 30% for testing. This ratio was applied to all the used ML classifiers. The

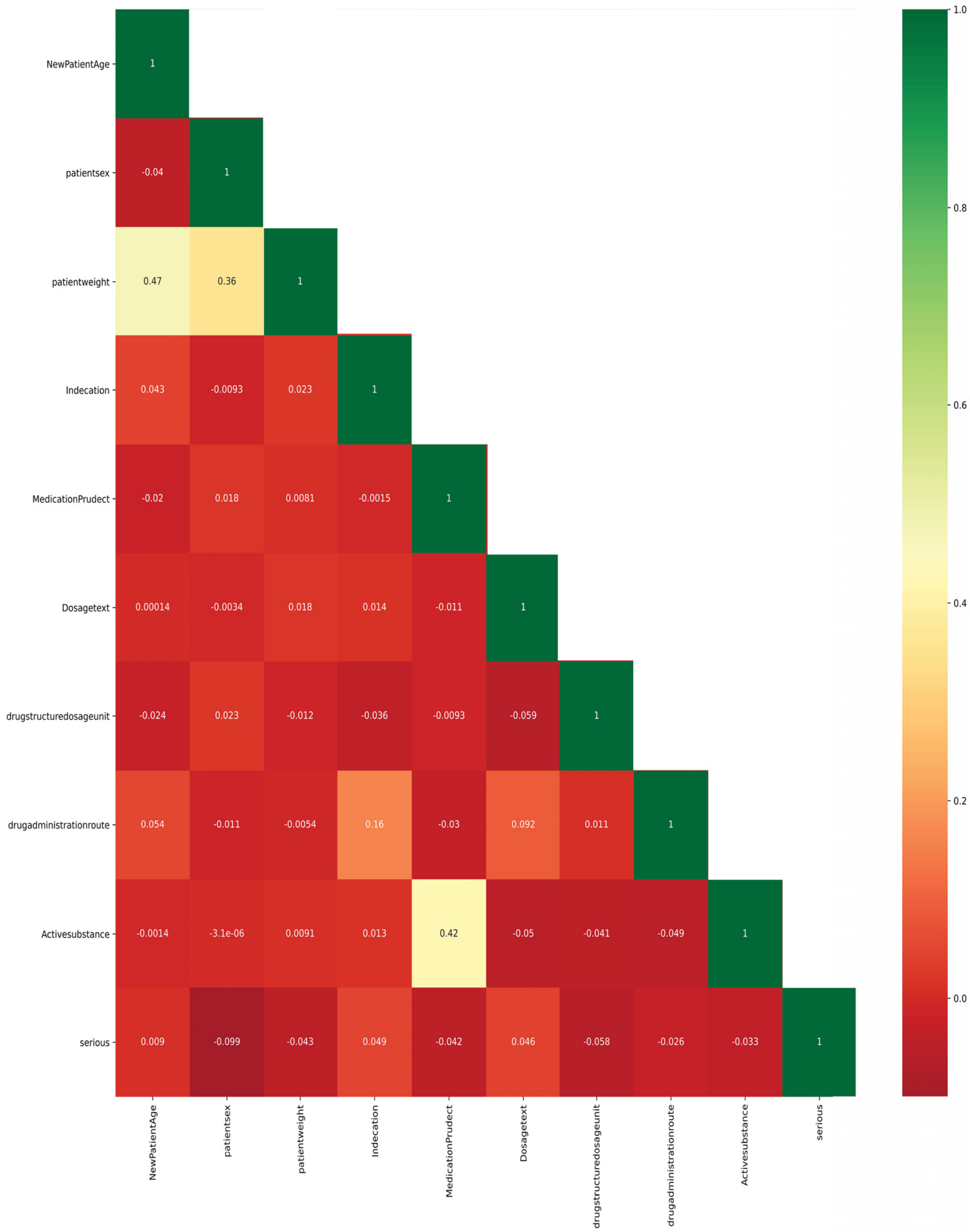


Figure 9.7: The heat-map of the features correlation with each other and with the target value.

implementation of the classifiers was done using the classification methods in Scikit-Learn Python 3.7 [246] and with a Windows PC that has an Intel(R) Core(TM) i5-7600K CPU at 3.80 GHz and 16 GB of memory.

9.5.1 Decision Tree (DT)

DT is one of the most widely used machine learning algorithms. The DT starts by placing the target feature as the root then forms a node for each of the features in the dataset. Then, the algorithm starts sorting down the tree based on the condition set at the root. This process continues until reaching the leaf node [249].

Selection of Hyper-parameters

The following are the parameters that were the best to use based on our dataset for the DT:

```
n_estimators = 100, criterion ='entropy', random_state= 0
```

9.5.2 Naive Bayes (NB)

NB is another well-known supervised ML algorithm for classification problems that need a fast and straightforward learning and testing process. The NB classifier is based on the Bayes' theorem, which is part of the Bayesian and probability theory and statistics [250–252].

Selection of Hyper-parameters

The following are the parameters that were the best to use based on our dataset for the NB:

```
GaussianNB()
```

9.5.3 K-Nearest Neighbors (K-NN)

K-NN algorithm is one of the supervised ML algorithms. K-NN is a lazy learning algorithm, which means the algorithm does not require a standalone training phase. K-NN will train by using all the data to train the classifier while running the classifying phase. K-NN is used for most real-world data classification applications because the K-NN does not make any initial assumption about the distribution of the input data, and it performs well in predictive analysis [253, 254].

Selection of Hyper-parameters

The following are the parameters that were the best to use based on our dataset for the K-NN:

```
n_neighbors = 5, metric ='minkowski', p = 2
```

9.5.4 Random Forest (RF)

RF is another supervised machine learning classifier proposed by Breiman in 2001 [255]. RF is many DTs combined in one algorithm. This classifier is based on the Ensemble learning type, in which the same or different algorithms are combined multiple times. This process made the RF powerful in terms of generating accurate predictions [255, 256].

Selection of Hyper-parameters

The following are the parameters that were the best to use based on our dataset for the RF:

```
max_features='sqrt', n_estimators= 1000
```

9.5.5 Extreme Gradient Boosting (XGBoost)

XGBoost is a supervised machine learning classification algorithm that uses decision trees as its estimator [256, 257]. XGBoost was introduced by [225, 258] based on the gradient boosting framework and designed to benefit from the machine's computational resources to provide more accurate results [255].

Selection of Hyper-parameters

The following are the parameters that were the best to use based on our dataset for the XGBoost:

```
use_label_encoder=False, booster='gbtree', n_estimators=1000, eta=0.3,
max_depth=6, gamma = 1, reg_lambda = 1
```

9.6 Evaluation Methodology

To achieve our mentioned research goals 6.2, we need to evaluate the ML module's reliability and accuracy to predict if the prescribed medication has the potential to harm the patient.

9.6.1 Reliability and Accuracy Analysis

In this section, we will explore the evaluation results of the classifiers mentioned in the above section. We will be using the evaluation methodology described in Chapter 7.2.2. The metrics we will use are the confusion matrix (Table 7.1), AC (Equation 7.1), MisCl (Equation 7.2), R (Equation 7.4), P (Equation 7.3), F (Equation 7.5), FNR (Equation 7.6), and FPR (Equation7.7).

Additionally, we will be using the following two criteria in the evaluation:

- Receiver operating characteristic (ROC) is a graph used to visualize a selected classifier based on its performance. The evaluation is done by plotting the true positive rate true positive rate (TPR) ($\boldsymbol{Y}$ axis) against the false positive rate (FPR) ($\boldsymbol{X}$ axis) at different thresholds in the graph [259].

- AUC is the area plotted based on the probability of a classifier ranking randomly chosen positive instances higher than randomly chosen negative instances [259]. The AUC measures the ability of a classifier to differentiate between the classes and is used as a summary of the ROC curve. The closer the curve to the Y-axis, the higher the chance of the classifier of detecting more numbers of TPs and TNs. Where the closest the curve to the X-axis, the higher the chance the classifier detecting more number of FPs and FNs. Therefore, the AUC value indicates the better performance of the classifier. AUC is given by the following Equation 9.1:

$$AUC = \int_0^1 f\left(\frac{TP}{P}\right) d\left(\frac{FP}{N}\right) \tag{9.1}$$

9.7 Results

9.7.1 Reliability and Accuracy Analysis

In this section, we will explore and discuss the results of the classifiers' performance evaluation. In all the classifiers' runs, we balanced the data split at the target feature value to be 50% for both the value of 1 (i.e. serious) and the target feature and 0 (i.e. not serious). This split was fed to the classifier only in the training phase. The balancing is done to ensure the classifier is equally trained for both values in the target feature and eliminate any data processing bias.

Decision Tree (DT)

In Table 9.2 we present the DT classifier's confusion matrix, and in Table 9.3 we show the reliability and accuracy analysis evaluation results. Figure 9.8 shows the AUROC graph for the DT classifier.

	Classified positive	**Classified negative**
Serious outcome (1)	85669	19415
No Serious outcome (0)	20916	83887

Table 9.2: DT classifier confusion matrix.

Measure	**Score**
AC	0.81
MisCl	0.19
R	0.82
P	0.80
F	0.81
FNR	0.18
FPR	0.20
AUC	0.81

Table 9.3: Reliability and accuracy analysis evaluation results for the DT classifier.

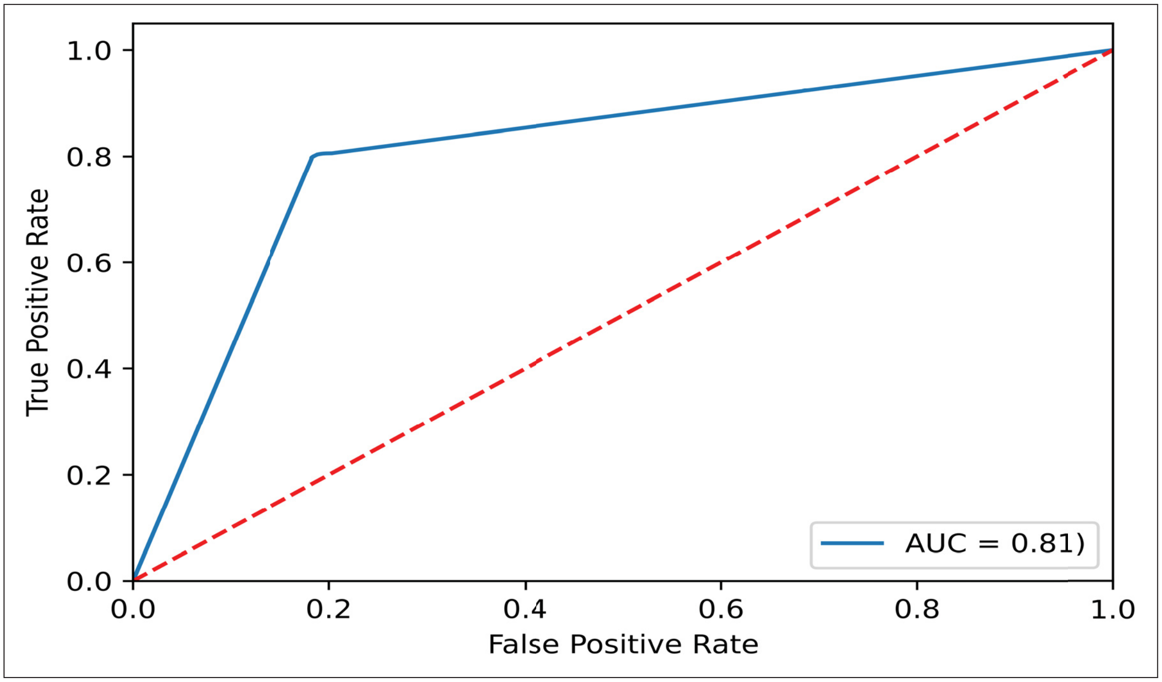


Figure 9.8: DT AUROC graph.

Naive Bayes (NB)

In Table 9.4 we present the NB classifier's confusion matrix, and in Table 9.5 we show the reliability and accuracy analysis evaluation results. Figure 9.9 shows the AUROC graph for the NB classifier.

	Classified positive	**Classified negative**
Serious outcome (1)	77807	27277
No Serious outcome (0)	63266	41537

Table 9.4: NB classifier confusion matrix.

Measure	**Score**
AC	0.57
MisCl	0.43
R	0.74
P	0.55
F	0.63
FNR	0.26
FPR	0.60
AUC	0.57

Table 9.5: Reliability and accuracy analysis evaluation results for the NB classifier.

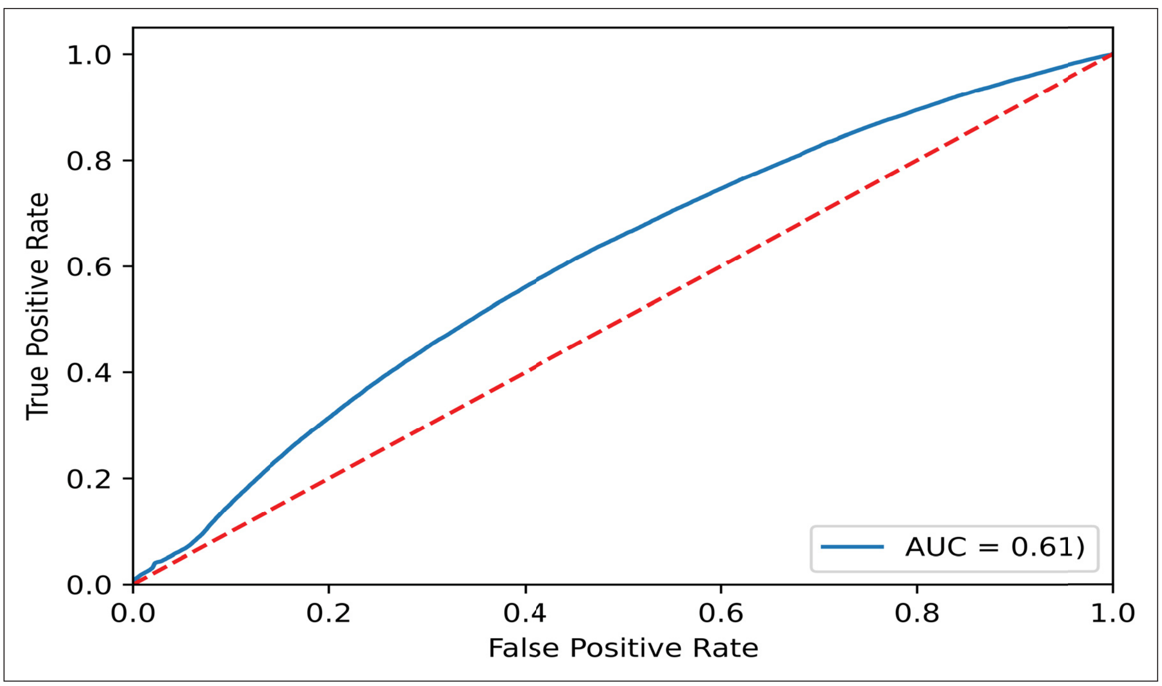


Figure 9.9: NB AUROC graph.

K-Nearest Neighbors (K-NN)

In Table 9.6 we present the K-NN classifier's confusion matrix, and in Table 9.7 we show the reliability and accuracy analysis evaluation results. Figure 9.10 shows the AUROC graph for the K-NN classifier.

	Classified positive	Classified negative
Serious outcome (1)	79194	25890
No Serious outcome (0)	27416	77387

Table 9.6: K-NN classifier confusion matrix.

Measure	Score
AC	0.75
MisCl	0.25
R	0.75
P	0.74
F	0.75
FNR	0.25
FPR	0.26
AUC	0.82

Table 9.7: Reliability and accuracy analysis evaluation results for the K-NN classifier.

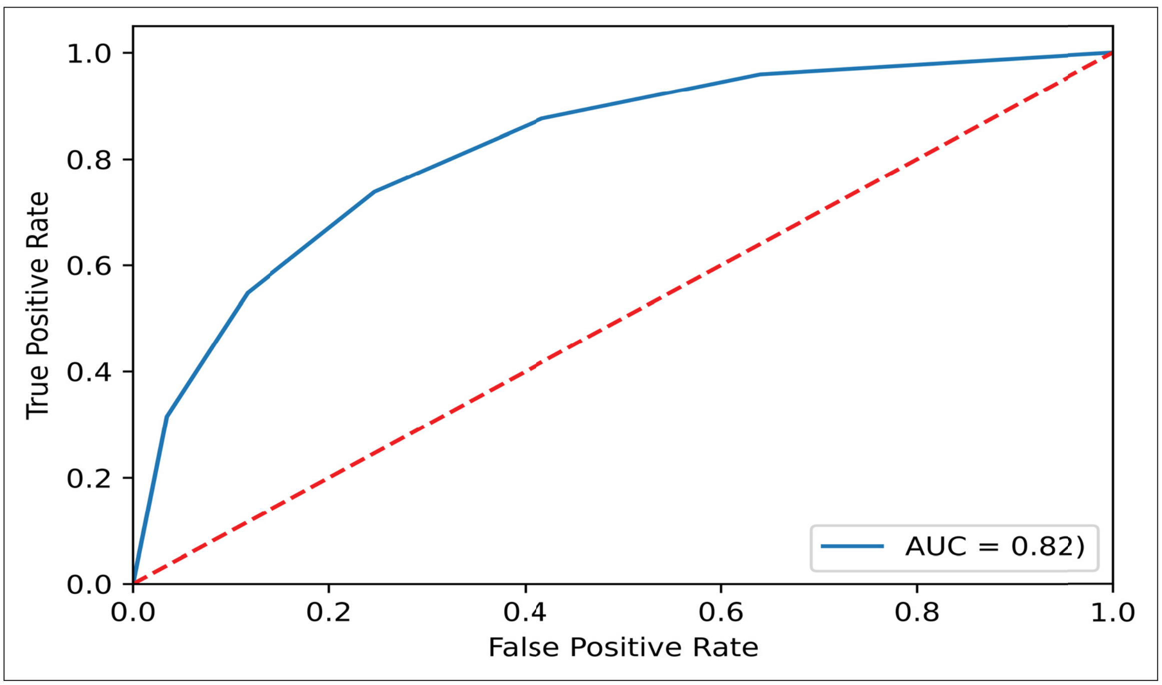


Figure 9.10: K-NN AUROC graph.

Random Forest (RF)

In Table 9.8 we present the RF classifier's confusion matrix, and in Table 9.9 we show the reliability and accuracy analysis evaluation results. Figure 9.11 shows the

AUROC graph for the RF classifier.

	Classified positive	Classified negative
Serious outcome (1)	87254	17830
No Serious outcome (0)	9591	95212

Table 9.8: RF classifier confusion matrix.

Measure	Score
AC	0.87
MisCl	0.13
R	0.83
P	0.90
F	0.86
FNR	0.17
FPR	0.09
AUC	0.94

Table 9.9: Reliability and accuracy analysis evaluation results for the RF classifier.

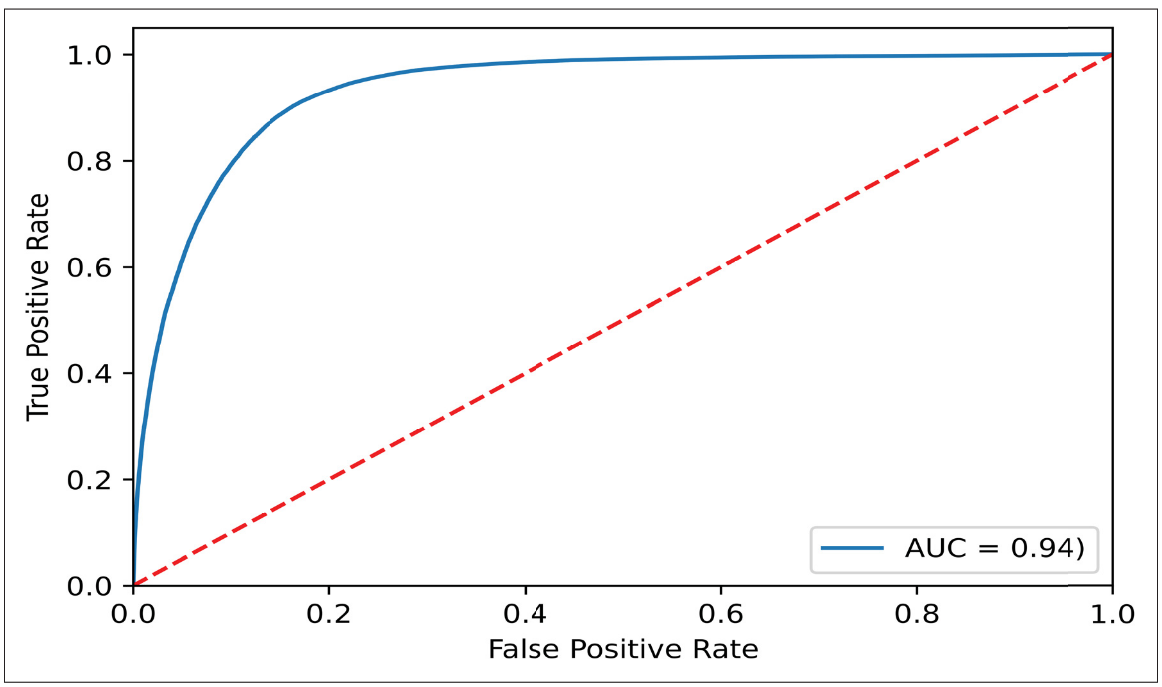


Figure 9.11: RF AUROC graph.

Extreme Gradient Boosting (XGBoost)

In Table 9.10 we present the XGBoost classifier's confusion matrix, and in Table 9.11 we show the reliability and accuracy analysis evaluation results. Figure 9.12 shows the AUROC graph for the XGBoost classifier.

	Classified positive	**Classified negative**
Serious outcome (1)	87449	17635
No Serious outcome (0)	7708	97095

Table 9.10: XGBoost classifier confusion matrix.

Measure	**Score**
AC	0.88
MisCl	0.12
R	0.83
P	0.92
F	0.87
FNR	0.17
FPR	0.07
AUC	0.95

Table 9.11: Reliability and accuracy analysis evaluation results for the XGBoost classifier.

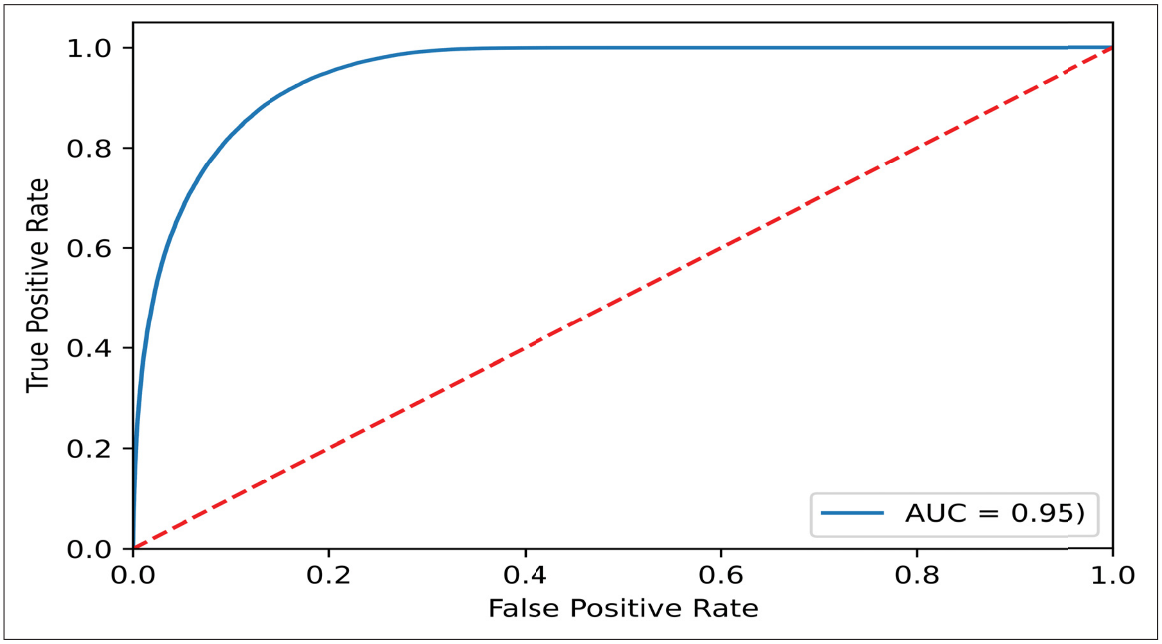


Figure 9.12: XGBoost AUROC graph.

9.8 Discussion

In this section, we will discuss the results of ML classifiers and how the ML classifier will contribute towards the goals mentioned in Chapter 6.2. We will compare the classifiers to each other based on the metrics mentioned in Section 7.2.2. We will also compare our classifier's results with the results from different studies discussed in the literature review (Section 9.2).

9.8.1 Comparison of the classifiers' results

To compare the tested classifiers and determine which is the best, we need to compare the top significant rates for our proposed framework: higher AC, lower FPR and lower FNR. Based on our goals, the classifier results should yield better accuracy when detecting a prescription error. However, from our literature review and the online survey results in Chapter 8 we found that the users of the framework would like to lower the number of false or less important alerts. Therefore, the decision will be based on the user's preferences and whether they need higher accuracy or reduce the chance of encountering a false alert and increasing the number of less important alerts. Table 9.12 shows the comparison between the classifiers in terms of the metrics percentage.

The XGBoost performed the best in terms of the AC rate, lower FPR, and lower FNR among all the machine learning classifiers we tested. The second best was RF by a small margin across all the metrics compared to XGBoost. Furthermore, the XGBoost classifier performed better in term of the MisCl rate with 0.12, R rate with 0.83, P rate with 0.92, F rate with 0.87 and AUC rate with 0.95. The chart in Figure 9.13 shows the classifiers' performance evaluation results.

Moreover, Figure 9.14 shows the AUROC plot for all the classifiers. We can see that the XGBoost classifier has the best AUC curve. Therefore, for our framework, our choice will be the XGBoost due to the excellent results we obtained through the testing phase.

Classifier	AC	MisCl	R	P	F	FNR	FPR	AUC
DT	0.81	0.19	0.82	0.80	0.81	0.18	0.20	0.81
NB	0.57	0.43	0.74	0.55	0.63	0.26	0.60	0.61
K-NN	0.75	0.25	0.75	0.74	0.75	0.25	0.26	0.82
RF	0.87	0.13	0.83	0.90	0.86	0.17	0.09	0.94
XGBOOST	0.88	0.12	0.83	0.92	0.87	0.17	0.07	0.95

Table 9.12: The comparison table of all the used classifiers measures.

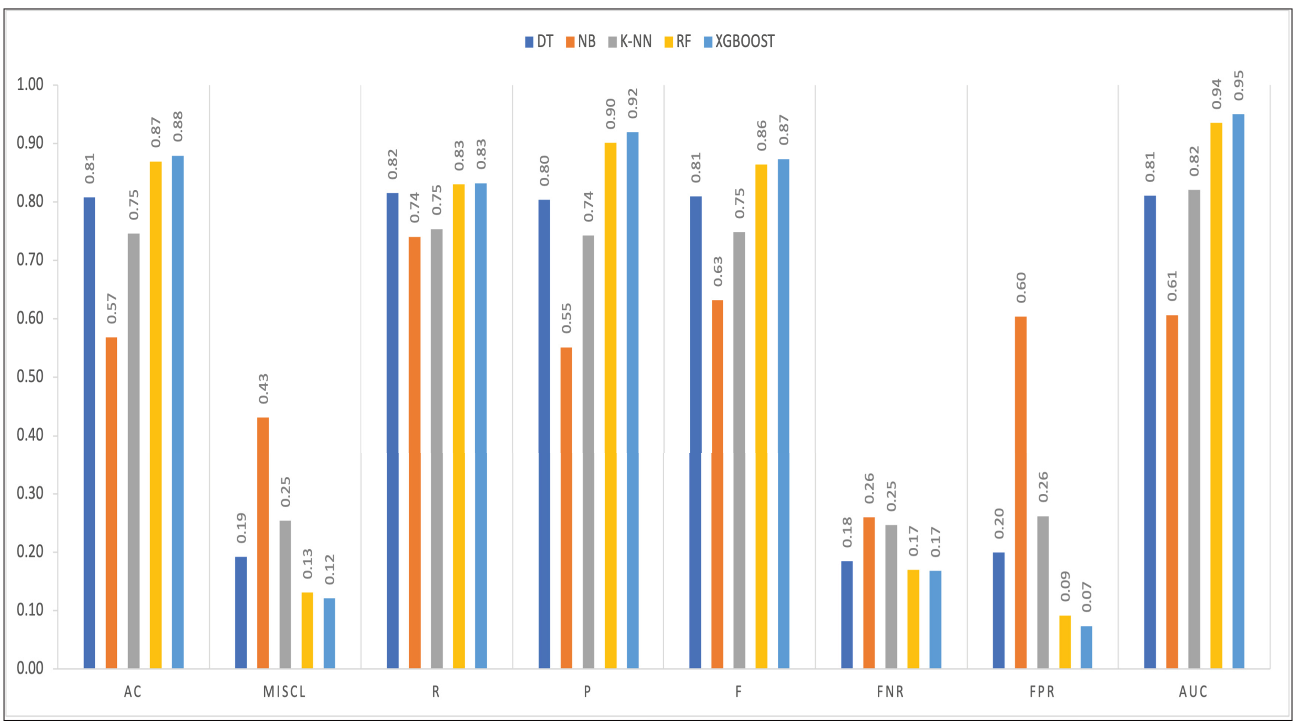


Figure 9.13: The comparison chart of all the used classifiers measures.

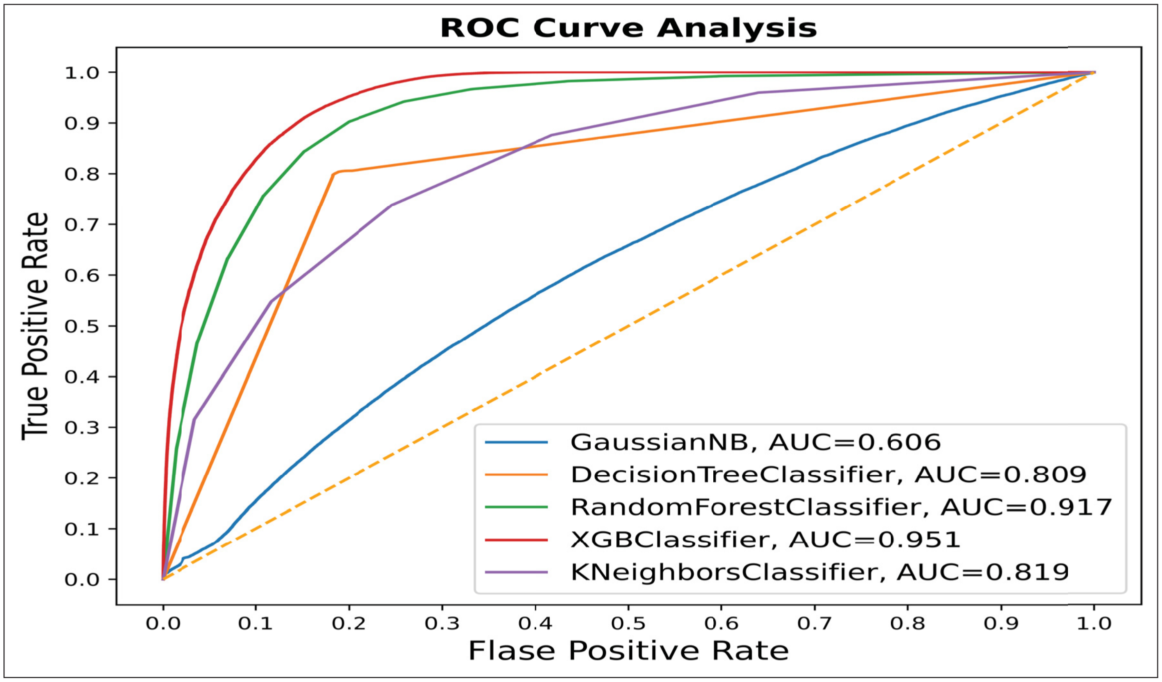


Figure 9.14: The AUROC graph of all the used classifiers AUC.

9.8.2 Comparison with the Literature Review Studies

In this section, we will compare our chosen classifier XGBoost with the studies from section 9.2. For the comparison with other studies, we will be using only the AUC metric. The AUC is the appropriate performance evaluation method for classifiers that use imbalanced datasets [259–262], and this metric is the only one provided by the studies. We will also use the accuracy metric to compare our results with the studies evaluated using the MedAware system.

In Table 9.13 we show the results of our classifier XGBoost along with the results from the other studies. As can be seen, not all the metrics were provided from the other studies, whereas we show our classifier results for all the metrics used. However, we will only compare our classifier with the other studies using the available metrics from the literature review.

In terms of the AC rate, only three studies provided this metric, but none of them have better results when detecting a prescription error and generating an alert based on the error. In the AUC metric, we can see from Table 9.13 that our proposed system has the highest score compared with the other studies. Finally, our proposed framework proved that it could detect prescription errors accurately and has a better classification percentage of harm medication with 95%.

Proposed systems	AC	MisCl	R	P	F	FNR	FPR	AUC
Proposed XGBoost	0.88	0.12	0.83	0.92	0.87	0.17	0.07	0.95
MedAware [229]	0.80	X	X	X	X	X	X	X
MedAware [230]	0.75	X	X	X	X	X	X	X
Segal et al. [231]	0.85	X	X	X	X	X	X	X
McMaster et al. [239]	X	X	X	X	X	X	X	0.80
Ouchi et al. [240]	X	X	X	X	X	X	X	0.83

Table 9.13: The comparison table of framework classifier with the other related studies.

9.9 Chapter Summary

In this chapter, we presented the machine learning algorithm model in detail. We discussed the model implementation, the process of feature selection, and the tested machine learning classifiers. We reported and discussed the evaluation results and concluded that the XGBoost classifier performed the best in terms of all metrics. Furthermore, we compared our results with the reviewed studies from the literature, and our proposed framework has the highest score in terms of AC and AUC.

Chapter 10

The Blockchain Private Network

10.1 Introduction

Blockchain is a decentralized network that includes a distributed chain of blocks. The blockchain network is a peer-2-peer network. Each block in the chain includes information about a transaction in the chain. All transactions are recorded in the blocks. These blocks are linked to each other by storing a hash value to the previous block data. The user verifies the block by calculating the hash value and matching it with other blocks' hash in the network. If the verification process is successful, then the new block will be added. One of the well-known examples of Blockchain is the Bitcoin network. Bitcoin is a finance network used to organize and monitor the participating peers' financial transactions [9]. Figure 2.5 shows the blockchain architecture. The blockchain network in its distributed architecture ensures the privacy of transaction information and the ability to share the blocks in the network securely [49–51].

The issues we found in the current systems of e-prescription reliability, availability, privacy, and security as illustrated in Chapter 3 Section 3.3. Those issues are slowing the advancements in improving healthcare services. As mentioned before in 3 The implementation of the blockchain approach provides a decentralized architecture, data transparency, data integrity, and immutability [156]. Compared to other approaches such as relational databases, the blockchain approach will address most of the issues related to the security and privacy of patient's information in the ePrescription system. Therefore, Blockchain was the most subtle technology to our framework. Blockchain technology provides the ability to share information with all the parties by posting the Blockchain. The Blockchain provides transparency regarding the posted information and by whom, which helps track the e-prescriptions process. The system will be reliable since the Blockchain provides a decentralized platform, where the information will be shared, and a copy will be stored in the local devices of the parties involved in the network. Moreover, the Blockchain will enhance the privacy and security of patient information. Lastly, an added bounce blockchain will enhance the efficiency of the process by eliminating the security checking of the process and identifying the prescriber and the patient [263, 264].

10.2 Literature Review

Many researchers have proposed the use of a blockchain network in the healthcare sector. We will explore some of the proposals in this section.

The authors in [50] proposed the use of Blockchain to manage and secure a patient's health data gathered from wearable devices. They proposed a framework with two blockchain networks: personal health care (PHC) and external record management (EMR). The patient will control the PHC blockchain network, and it will manage and maintain the health data generated by wearable devices. Moreover, the PHC network will store data in an external cloud database to facilitate sharing of a patient's health data with the doctor. Meanwhile, the EMR blockchain network will manage patients' health data while visiting a healthcare centre. The EMR network is controlled and managed by the healthcare centres. Insurance companies will be given access to the patient data on the EMR network. Lastly, the authors proposed using a machine learning module to detect any serious outcome in the patient health data generated by the patient.

In [49], the authors develop a cryptocurrency called RxCoin to be used to prescribe a medication using the principles of Blockchain electronically. The authors developed a proof of concept of their system to demonstrate the blockchain principles using the proposed RxCoin. Furthermore, they used the smart contract concept to create the prescription and store it to trace back the Blockchain's medication transaction histories. In their paper, they explain the process of creating RxCoin during the prescribing process. The prescriber will issue a new prescription, thus creating a new RxCoin. This coin will later be transferred to the pharmacist once the process of filling the prescription is started. Then, the pharmacist will create a new transaction with that RxCoin, informing the system that the prescription has been filled. When creating and transferring, RxCoin will issue a transaction for each process. The transactions will be stored in the Blockchain, and after each process (i.e. creating and transferring the RxCoin), the system will announce the new stored transaction.

The authors believe the use of Blockchain could help deal with the opioid crisis in the US [49, 52, 53].

Another proposed system was introduced by [51]. It is called the decentralized medication management system. This system aims to improve patient medication histories' security and privacy while sharing and transferring data between healthcare centres. The system utilizes a blockchain network to achieve the mentioned goals. The prescription is encrypted with the patient's public key in this system after the prescriber issues it. The patient will have full access to the medication history across the health care centres and will be able to decrypt it using their private key. Moreover, with the patient's approval, the prescriber can view the medication history from other healthcare centres.

MedRec is an MIT research project that aims to utilize the Ethereum blockchain as a solution for managing EHR and giving the patient agency over their medical record. The authors believe that MedRec will address fragmented medical data, slow access to medical data, system interoperability, and patient agency over their data. They believe it will improve the quality and quantity of data for medical research. MedRec will handle authentication, confidentiality, and accountability when sharing sensitive medical information. To achieve the system's goals, MedRec uses a smart contract to trace the patient's health record shared in the network. Finally, MedRec gives the patient full access to their health record history. Furthermore, MedRec allows the patient to store their medical record at their local database (e.g. local PC or mobile phone) [49, 54]. Relying heavily on the patient to manage their health record might make data vulnerable to privacy breaches at the patient end.

Similarly, Health Nexus is developing a blockchain network based on Ethereum. They aim to solve the same issues faced by MedRec except for the patient agency. Health Nexus focuses on providing a secure method for sharing health information between health care providers [49, 55].

As can be seen, most of the proposed blockchain networks focus on transferring patient information securely and preserving their data privacy. Moreover, only one proposal suggests giving the patient control over their medical information. As mentioned above, the patient agency might lead to privacy breaches at the patient end since they will store their private key used to decrypt the block on their local device.

Moreover, the other proposals will allow pharmacists to create a new transaction stating that the prescription-filling process has finished. Thus, this process might create the opportunity to misuse the prescribed medication. Furthermore, this system does not confirm that the patient has received the medication. Therefore, the blockchain network must have a confirmation stage that can be issued from the patient end. Moreover, confirmation of the validity of that prescription can be done by other participants in the network.

10.3 Proposed Blockchain in the Framework

10.3.1 Blockchain Approaches Background

The most and used popular blockchain approaches are Hyperledger and Ethereum platforms. These platforms are the most used in today's blockchain applications. They are both open-source platforms, and most of the developers of blockchain applications worldwide have been using one of these platforms and experimenting with them. Both approaches have their pros and cons in terms of the need for the developed blockchain application. Both approaches follow the general guidelines of a blockchain. The exact copy of the Blockchain is shared between the blockchain network participants and access to it.

Ethereum is a public, distributed, and decentralized approach. The Ethereum approach uses the concept of smart contracts. The contracts are programable to control the process of transferring the transactions among the blockchain application users. The Ethereum approach requires a cost for each transaction is transferred in the network. This cost is called gas, and it is paid with Ether cryptocurrency [265, 266].

Hyperledger is an open-source project to help developers can get the guidelines, tools, frameworks, and standards for building Blockchain for specified applications. The pros of the Hyperledger approach are suitable for a wide range of applications, has higher efficiency compared to other approaches, and can be set up with multiple features to suit applications' different needs [267, 268].

Another blockchain approach is BigchainDB. This approach is designed to merge the best of two worlds: the "traditional" distributed database world and the "traditional" blockchain world. With high throughput, low latency, powerful query functionality, decentralized control, immutable data storage and built-in asset support [269, 270]. Table 10.1 shows the comparison between the three blockchain approaches.

	Ethereum	**Hyperledger**	**BigchainDB**
Accessibility	Public	Private	permissions preferences
Confidentiality	More Transparent	Authorized Access	permissions preferences
Programming Language	Solidity	Node JS, Golang, or Java	MongoDB Query
Consensus Mechanism	Proof of Work	Developer Choice	proof-of-stake
Cryptocurrency	Ether (ETH)	None	None
Ledger Type	No Permission	Permissioned	User preferences

Table 10.1: The comparison between the three blockchain approaches.

For the framework blockchain approach, we would like to consider a hyper solution of an integrated blockchain approach using the Hyperledger with BigchainDB. The Hyperledger approach will be responsible for the blockchain private network, transferring transactions, and connecting the participants to the Blockchain. BigchainDB will be used to assist with managing, storing the Blockchain and query the blocks. Using these two integrated approaches will achieve the required goals of our framework blockchain security and privacy level.

Since our framework implementation is a proof-of-concept, we used the approach we could implement with the available resources and suit our application needs. Our implementation is similar to the Hyperledger approach since we require permission to access the blockchain network in general. Only the authorized parties can write blocks in the Blockchain (i.e. prescriber and pharmacies). Moreover, our implantation was programmed using Python and MySQL databases to store and access the information locally. Our implementation simulates Hyperledger and BigchainDB to provide the security and privacy of the patient information using the Blockchain.

10.3.2 Our Proposed Blockchain overview

We propose an adaptable approach that will store the prescription and medication information about any patient in blocks as part of the patient's Blockchain. These blocks will be stored by distributing them among the blockchain network. The involved parties (i.e. healthcare centers, pharmacies, medical government authorities, insurance companies, and patients) will be a part of the network as nodes to ease sharing the information. Not all the nodes will have the privilege to add a block and transfer transactions; only the prescriber and pharmacies will transfer blocks in the Blockchain. The other nodes (i.e. patients, medical government authorities, and insurance companies) can only view the Blockchain for their purposes related to their role in the healthcare services. The shared Blockchain will contain the prescription hash transactions block and the encrypted prescription information. Figure 6.1 shows the overall architecture of the system framework.

The system will create two types of blocks to be added to the Blockchain. The first block is the prescription transactions, prescriptions submitted and dispensed transactions, containing the information needed to create the key to encrypt the second block and the prescription transaction hash. This hash will be used to fetch the prescription information by requesting the data from the node submitting the prescription transaction. The information in the transaction block is the time stamp for issuing the prescription, the sending node ID, the prescriber's digital signature, and the prescription transaction hash. The data on this block will be encrypted using the token Id provided only by the patient. The decryption process for this block will verify the patient's identity and the sender node's identity since only the prescriber node can submit a prescription transaction, and only the patient can provide the token Id.

A second block will be created and stored locally in the sender node server. This block contains the information about a submitted prescription transaction. The ML server will validate the submitted prescription; however, this implementation will not include the ML model process since it is a proof-of-concept implementation for a blockchain private network. We already discussed and presented the ML model in Chapter 9 and proved that it contributes toward the framework objectives. The block will contain prescription information that is encrypted using a key generated using the patient ID and the prescription transaction hash, where the patient ID will be provided to the patient mobile application (Chapter 4). This encryption using this prescription transaction hash and the patient ID will ensure that the prescription was not modified and prevent any fraudulent submission of an e-prescription from any rogue party to the patient blockchain. Moreover, the blocks are read-only after mining; therefore, tampering with prescription data will not be possible. Figure 10.1 shows the blocks' architecture in the patient's Blockchain.

After generating the key, the pharmacy node will request the encrypted block from the prescriber node to dispense the prescribed medication. Then, the pharmacy will create a transaction to indicate the prescription was processed and dispensed and will add the transaction to the block. Last, the pharmacy node will mine the block and add it to the patient's Blockchain. Finally, the Blockchain will be updated and synced among the nodes in the Blockchain after mining.

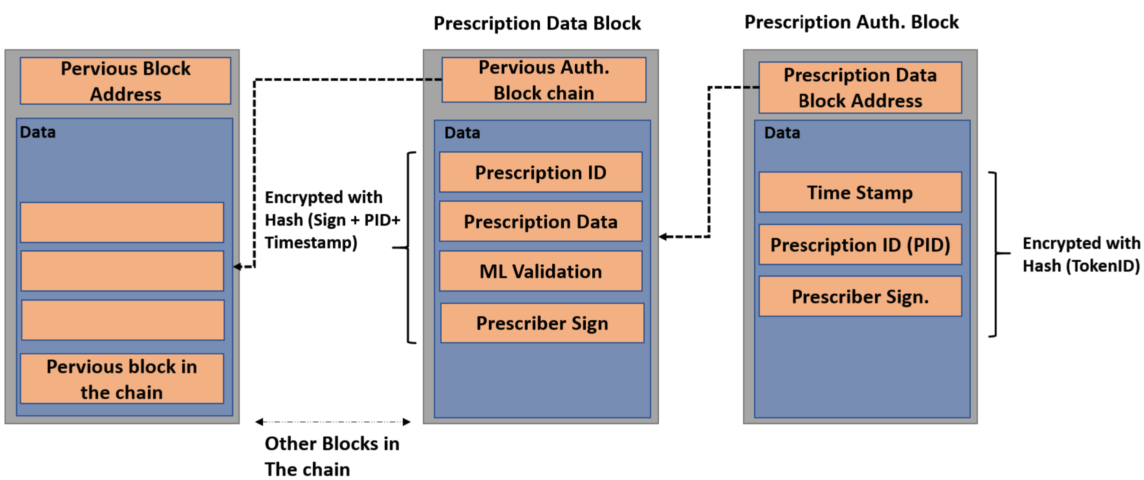


Figure 10.1: The proposed two blocks in the blockchain architecture

10.4 Proof-of-Concept Implementation

In our blockchain network, we developed two nodes to implement a proof of concept. For the node implementation, we used a Windows PC with an Intel(R) Core(TM) i5-7600K CPU at 3.80 GHz and 16 GB of memory for the prescriber node. We used a Windows laptop with an Intel(R) Core(TM) i7-7500U CPU at 2.70 GHz and 16 GB of memory for the pharmacy. Both devices had the same blockchain code to run and connect to the local network. We used the Python programming language to implement the Blockchain, and we used an open-source blockchain code from Github [271, 272] as a guideline to follow while building the private blockchain network. The Blockchain has the following features:

- Possibility of adding multiple nodes to the Blockchain.
- Transactions with RSA encryption.
- Generation of prescriptions and sending their transactions.
- Displaying the sent transactions and the requested prescription.
- Mining the blocks to be added in the Blockchain.
- Generating PKI for the nodes.

Finally, we implemented a dashboard to ease the interaction with the application using HTML/CSS/JS. We also used a local MySQL server for each node to store a copy of the Blockchain locally.

10.4.1 Blockchain User Interface

We developed three interfaces to interact with the Blockchain to send and receive transactions, mine the blocks in the Blockchain, and sync the nodes in the Blockchain.

Creating a Prescription UI

In this UI the prescriber will start by filling the prescription data. The public key and private key will be generated and filled to be ready to submit the transaction. Figure 10.2 shows the UI for creating the prescription transaction. Then, the prescriber will generate the transaction, and another transaction confirmation window will open. The prescriber will be presented with the transaction hash, patient ID, sender public key, transaction signature, transaction status, and receiver node URL in this window. The transaction signature will be used to validate the transaction at the receiver node by calculating the hash of the transaction signature. Then, the prescriber is requested to fill in the address of the pharmacy node to send the transaction to. Finally, the

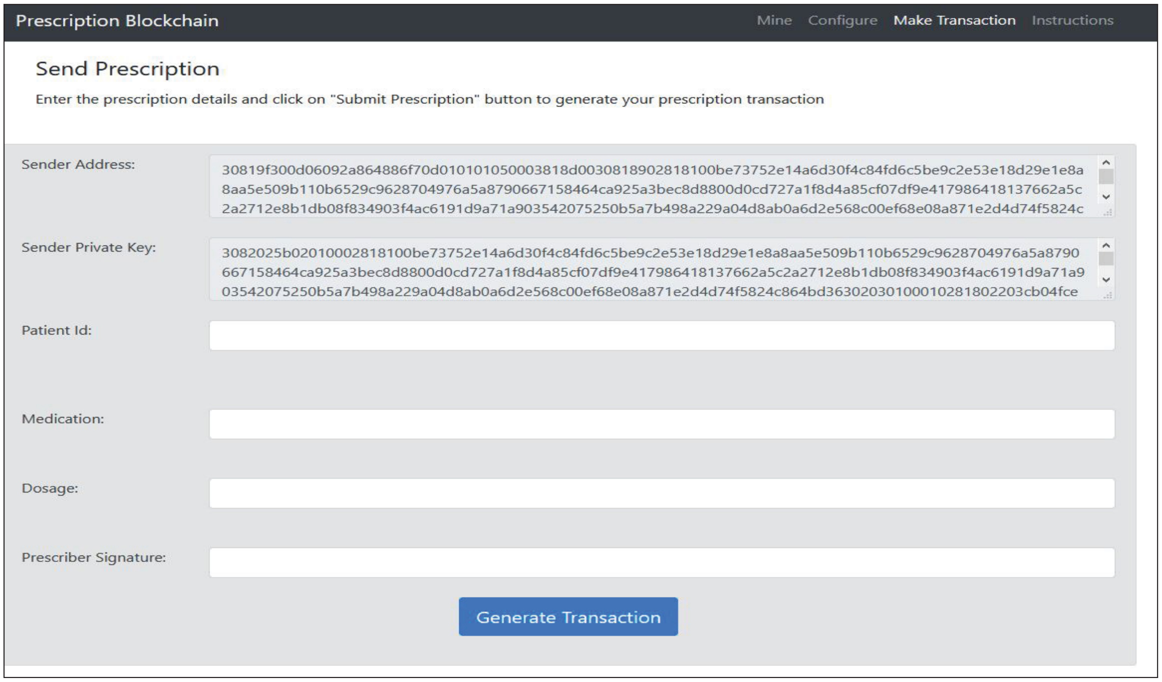


Figure 10.2: Syncing nodes in the blockchain UI.

transaction will be sent to the receiver (i.e. the pharmacy) node encrypted using the PKI scheme. Figures 10.3 and 10.4 show the UI of submitting the transaction and confirming the process. Once the prescriber confirms the sending of the transaction, the node will send the prescription information to the local MySQL database to be added in the Blockchain and to store it encrypted with the generated key from the patient ID and the hash as mentioned in Section 10.3. Figures 10.5 and 10.6 show the submitted transaction and prescription data encrypted stored in the local MySQL server.

Syncing the Blockchain Nodes UI

This interface is available at both nodes to sync the local node with other nodes in the Blockchain. The user is only required to enter the node URL to be synced. Then, the synced nodes only can share the Blockchain. In our proposed framework, every node should sync with the other Blockchain nodes to make the information updated and available to every participating node. Figure 10.7 shows the UI for syncing the blockchain nodes.

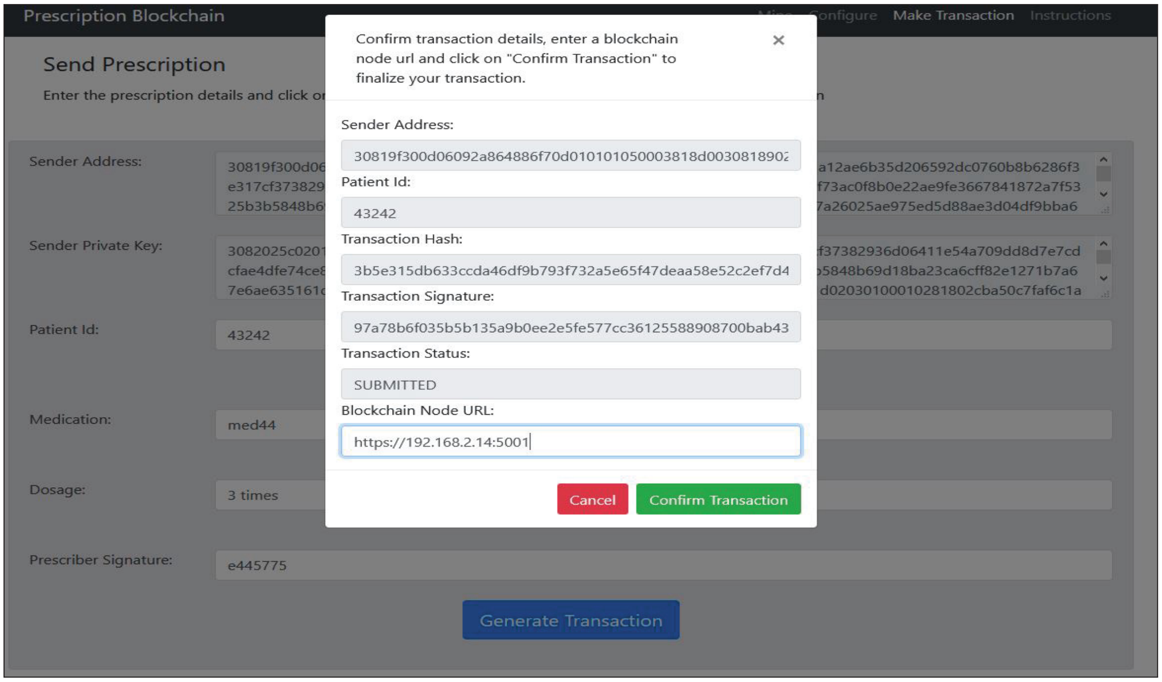


Figure 10.3: Syncing nodes in the blockchain UI.

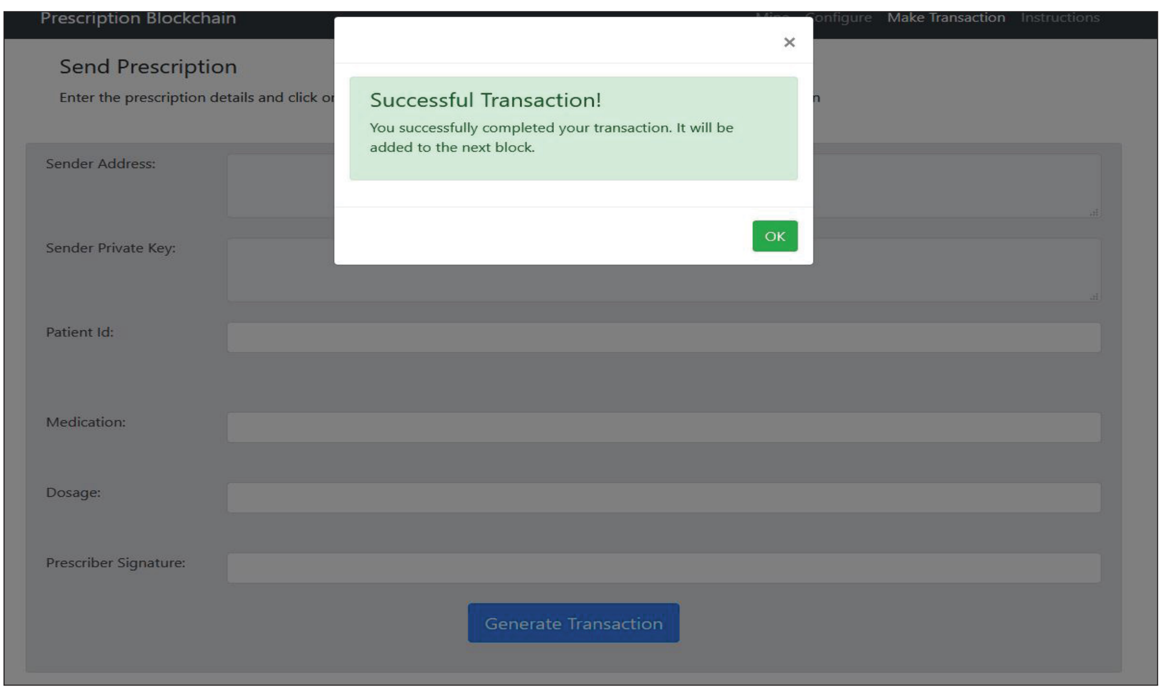


Figure 10.4: Syncing nodes in the blockchain UI.

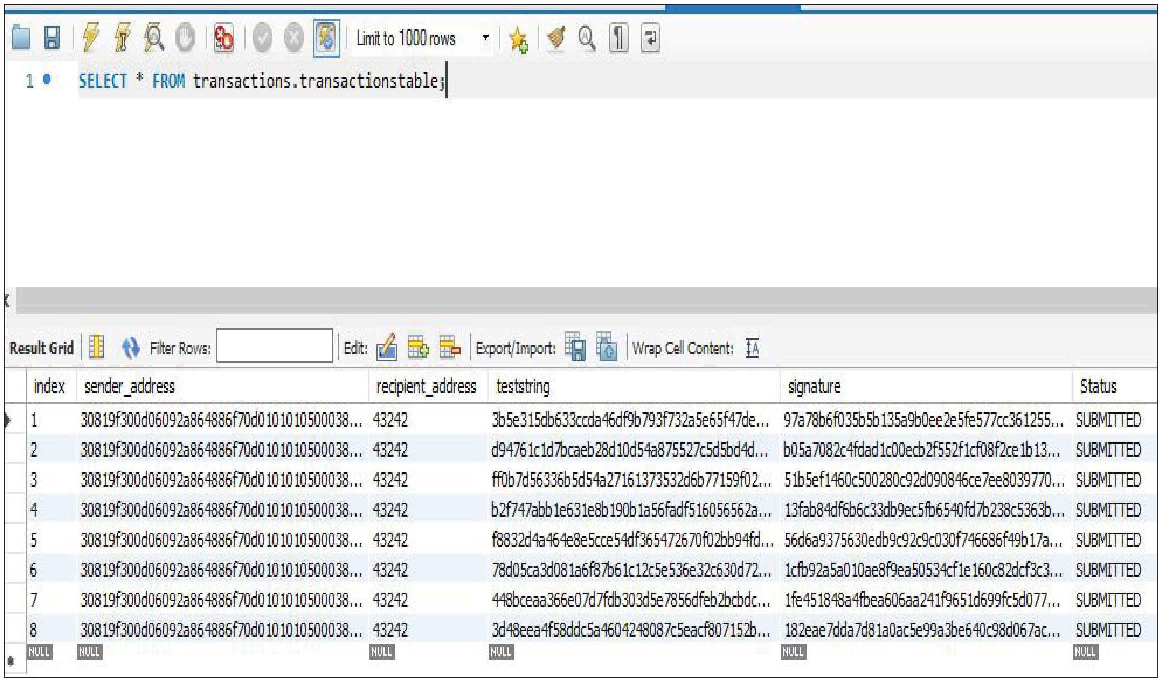


Figure 10.5: Syncing nodes in the blockchain UI.

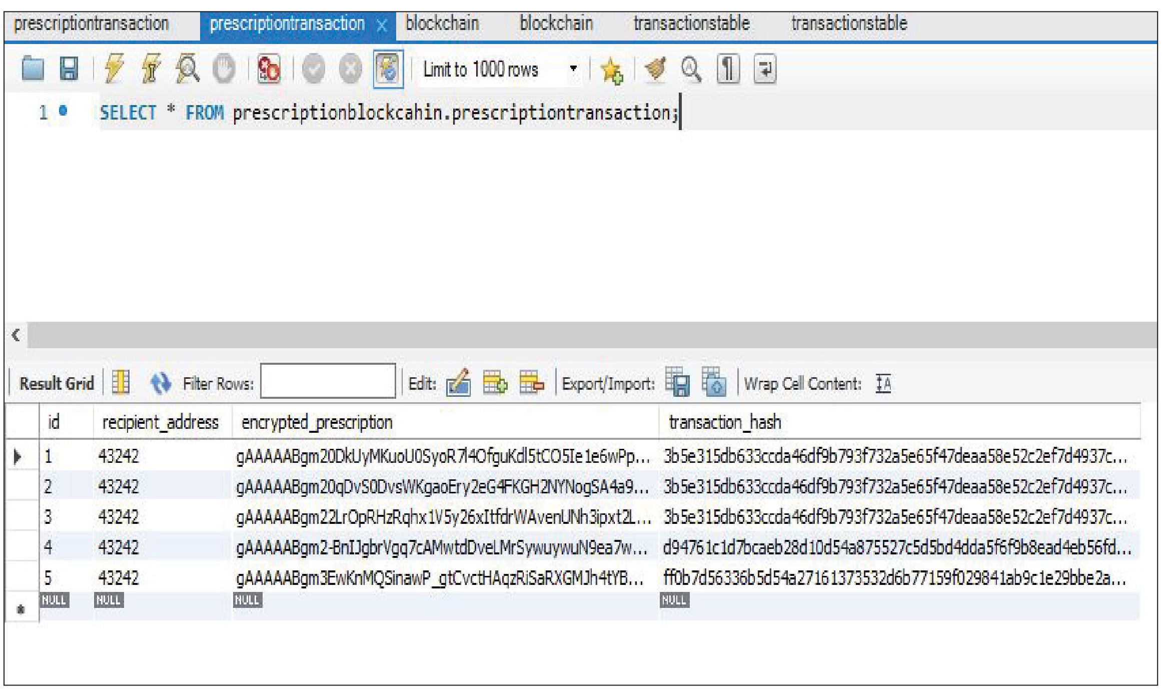


Figure 10.6: Syncing nodes in the blockchain UI.

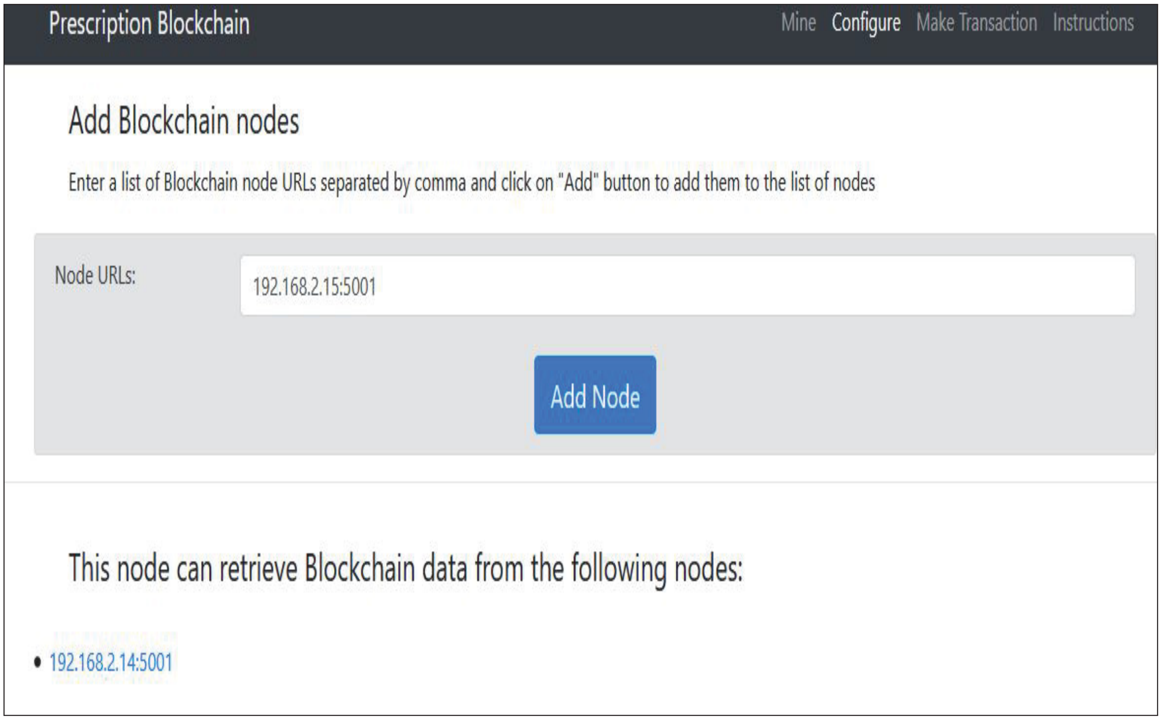


Figure 10.7: Syncing nodes in the blockchain UI.

Mining the Block UI

In this interface, the pharmacy node user will be able to display the prescription submission transaction information with the status "Submitted" to indicate the prescription is a pending process. The pharmacists will decrypt the authentication block (first block) using the node private key to start the dispensing process, then fetching the prescription data from the Blockchain using the prescription transaction hash. After, the prescription data block will be sent encrypted. The pharmacy node will decrypt the block by generating the key using the patient ID obtained from the patient and the information available in the authentication block (first block). After processing the prescription and dispensing it to the patient, the pharmacists will mine the block to the Blockchain by adding another transaction to update the prescription transaction status to "Dispensed." Figure 10.8 shows both the process of displaying the transaction and getting the prescription information. Figure 10.9 shows the updated Blockchain after adding the new block with the transaction data.

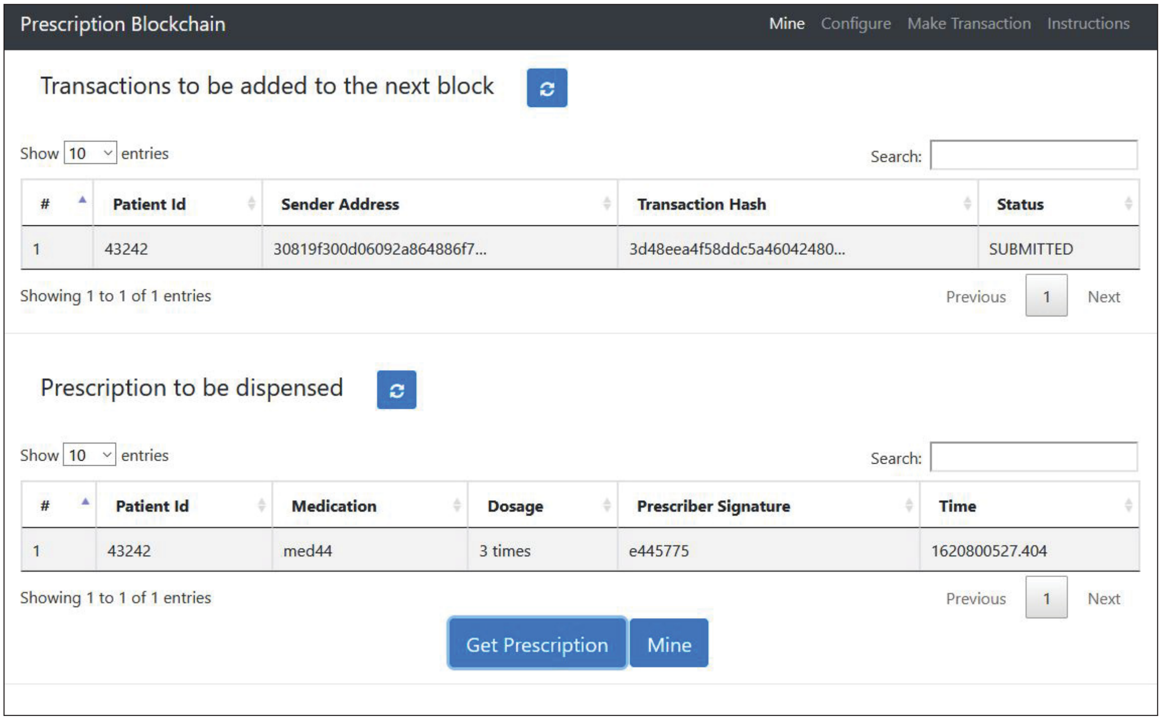


Figure 10.8: Displaying the received transaction and getting the prescription information UI.

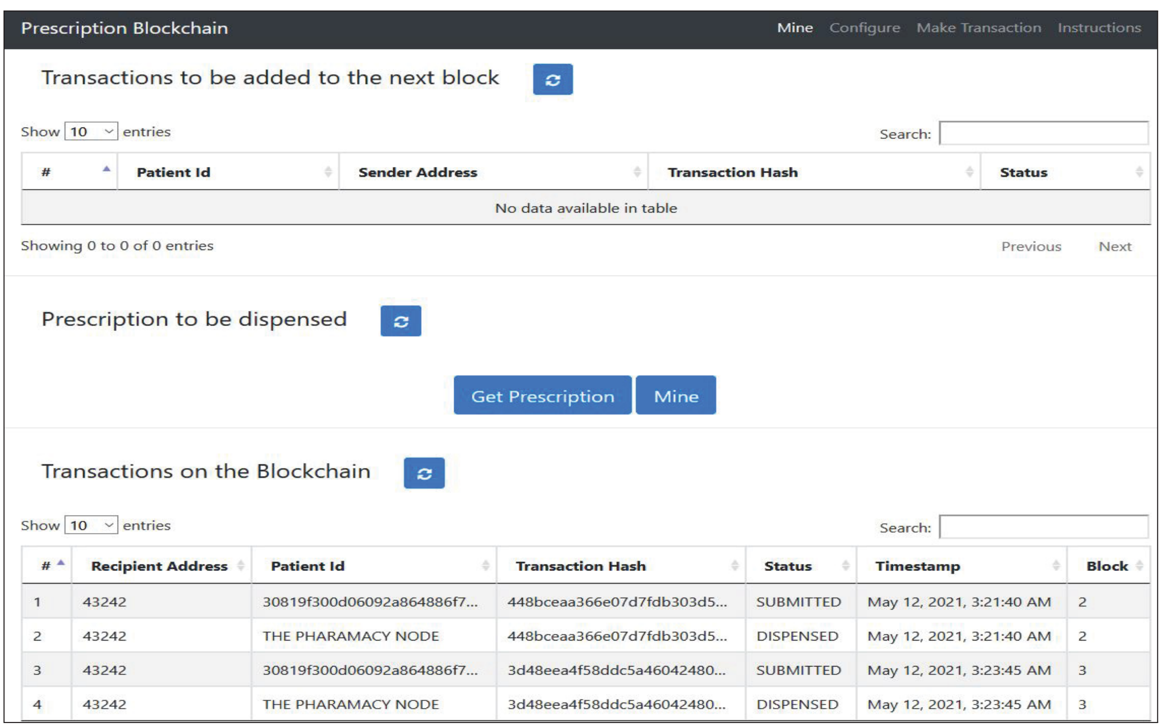


Figure 10.9: Mining the new block and displaying the updated blockchain UI.

10.5 Evaluation Methodology

To meet the research goals listed in Chapter 6.2, we need to evaluate the proposed Blockchain in terms of two aspects:

- The execution time of the transaction between submitting a new e-Prescription and its mining the block to the Blockchain.
- The performance of the blockchain network when executing the prescription transactions and sharing the Blockchain with the other nodes.

We will evaluate the Blockchain-based on the metrics stated in Chapter 7 ExT and throughput. Using JMeter, we will calculate the ExT and throughput of submitted and processed prescriptions' transactions in the blockchain network in four scenarios. The parameters in these scenarios differ in syncing the Blockchain or not and the number of users, with 1000 and 10,000 users. All the scenarios ran with a test ramp-up time equal to one hour and a delay time of 3 s after each request made to the blockchain server. In addition, we will evaluate the Blockchain with the metric Application Performance Index (APDEX) provided in the jMeter configuration. APDEX is an open standard developed to evaluate the performance of applications based on the satisfaction threshold of users for every transaction sent to the server [273]. The APDEX score is calculated between 0 and 1, where 0 is frustrated, 1 is satisfied, and 0.5 is a tolerating user. For the satisfaction threshold, we used the default values from jMeter, with a toleration threshold of 500 ms and frustration threshold of 1500 ms [185]. The APDEX is calculated using the following Equation 10.1 [273]:

$$APDEX_t = \frac{SatisfiedCount + (ToleratingCount * 500) + (FrustratedCount * 1500)}{TotalSamples} \tag{10.1}$$

10.6 Results

In this section, we will present the results of the blockchain performance evaluation based on the metrics mentioned in Chapter 7 ExT and the throughput for each request and in total. The evaluation of the Blockchain was done using four different scenarios, as mentioned in the previous section. Each scenario will be executing six requests: generating prescription data, creating a transaction, submitting a transaction, confirming a transaction, get at the node transaction, get the prescription data, and mine the block. Depending on the scenario, the requests count will be seven when adding syncing the Blockchain. The different scenarios in terms of parameters are presented as follows:

- scenario 1: 1000 users syncing the Blockchain with all nodes and dynamic prescription data generation.
- scenario 2: 10,000 users syncing the Blockchain with all nodes and dynamic prescription data generation.
- scenario 3: 1000 users without syncing the Blockchain with all nodes and dynamic prescription data generation.
- scenario 4: 10,000 users without syncing the Blockchain with all nodes and dynamic prescription data generation.

10.6.1 First Scenario

In this, we used the parameters of 1000 users with syncing the Blockchain with all nodes and dynamic prescription data generation. Table 10.2 shows the results metrics of response times, throughput, and sent and received data size. The total number of requests generated from 1000 users was 7000 with a fail request rate of 2.83% (198/7000 requests). Most of the errors 52.02% (103/198 errors) were responses to the request of confirming the transaction. The error code is 406, which means the server could not validate the transaction originality due to failing to generate the decryption key from the given transaction data. The other 47.98% (95/198 errors) were responses from the MySQL server with the error code 500. The error code illustrates an internal server error, which means the prescription data were not found based on the transaction hash provided. From Figure 10.10 we can see the blockchain throughput (i.e. number of transactions per second) for the transaction from creating until block mining has increased compared to the first scenario. In Figure 10.12 we can see that the number of failure codes is stable through the test duration, and all are a response to the request of getting the prescription information from the MySQL server.

We can see from the table that the server response time average for the scenario in total from creating the prescription transaction until mining the block in the Blockchain is almost 84.10 seconds. The APDEX score is 0.512 in total, which means the users were tolerating. Figure 10.13 shows the distribution of the number of responses over the satisfactory response time threshold. Figure 10.11 shows the average response latency. Figure 10.14 shows the response times percentiles for all the requests made using the different codes in the Blockchain.

	Executions	Resp. Times(ms)			Throughput
Request Label	**Error%**	**Average**	**Min**	**Max**	**Transactions/s**
ConfirmationTransaction	10.30%	2894.35	41	16291	0.18
CreateTransaction	0.00%	128570	56	656699	0.18
DecryptPrescription	9.50%	2639.89	29	21545	0.18
GenrateData	0.00%	215902.44	31	2407590	0.18
GetChain	0.00%	233126.07	21	1019997	0.17
GetTransactionAtNode	0.00%	602.71	8	4039	0.18
Total	2.83%	84102.93	8	2407590	1.22

Table 10.2: The jMeter metrics results for the first scenario.

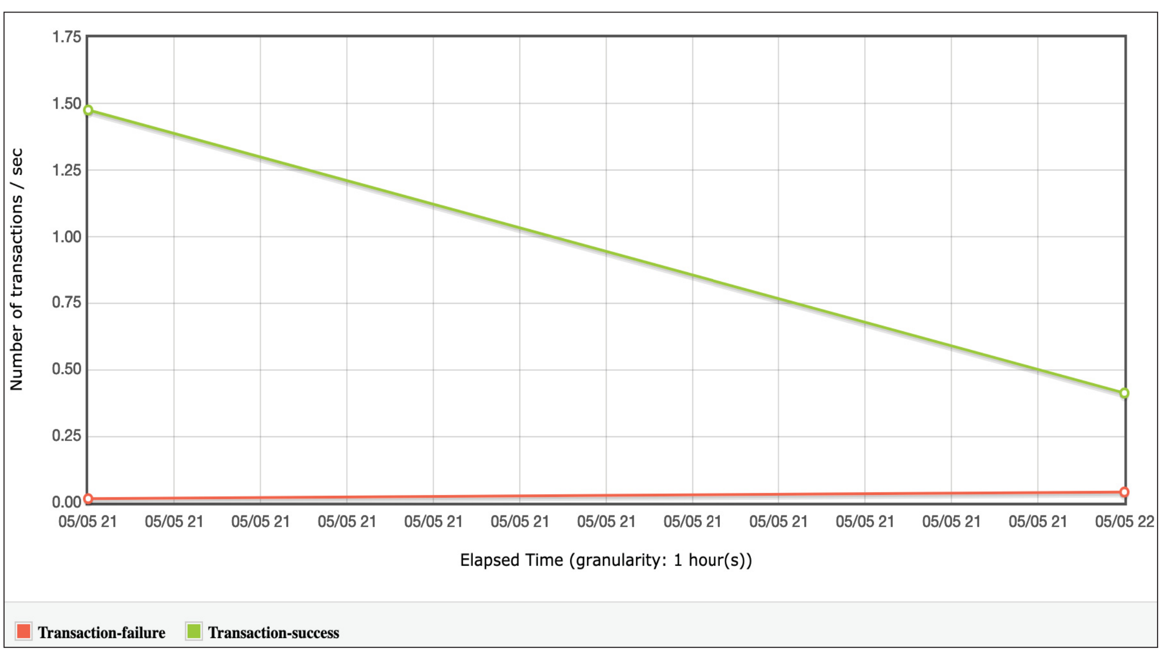


Figure 10.10: The number of transactions chart over the elapsed time (i.e. one hour).

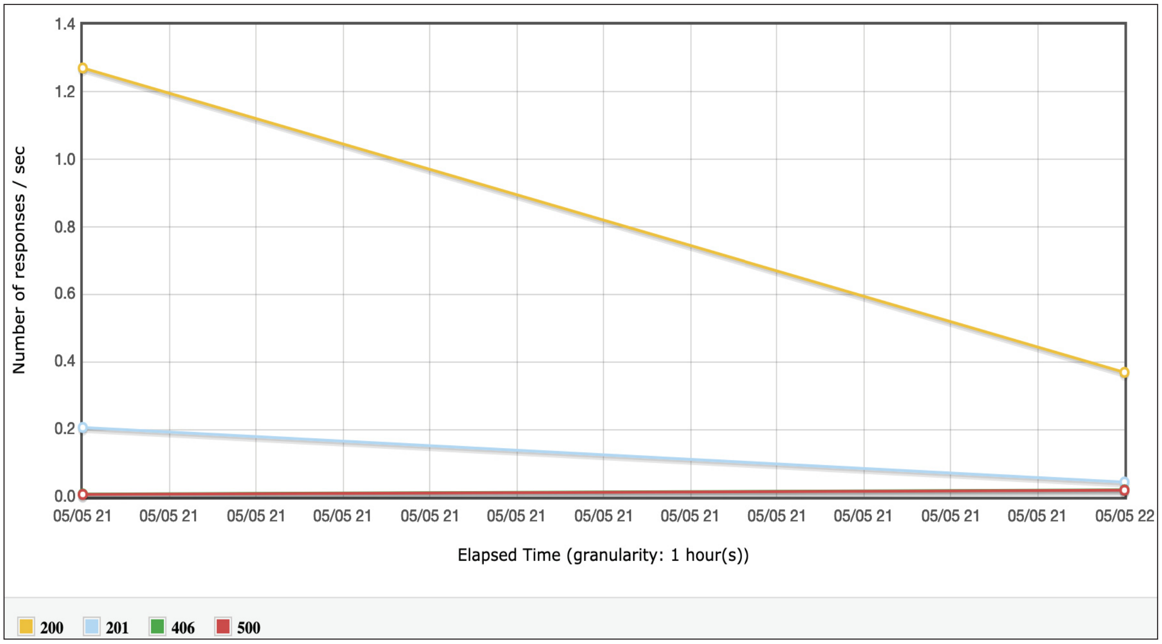


Figure 10.12: The response codes to the HTTP requests per seconds.

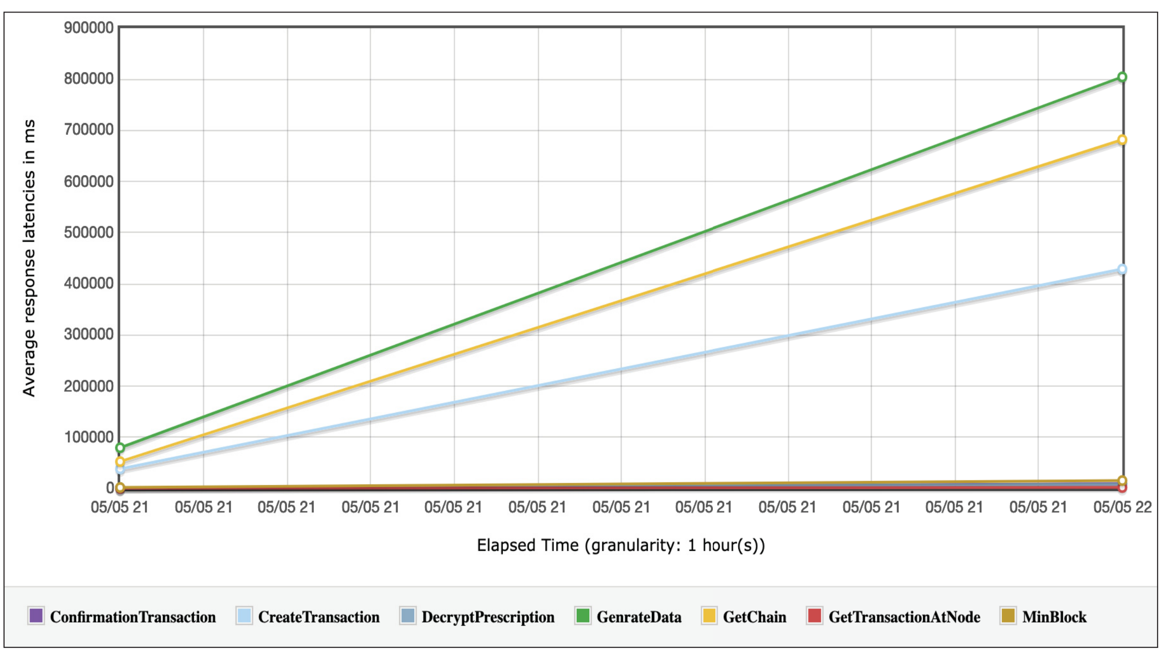


Figure 10.11: The average response latency in ms.

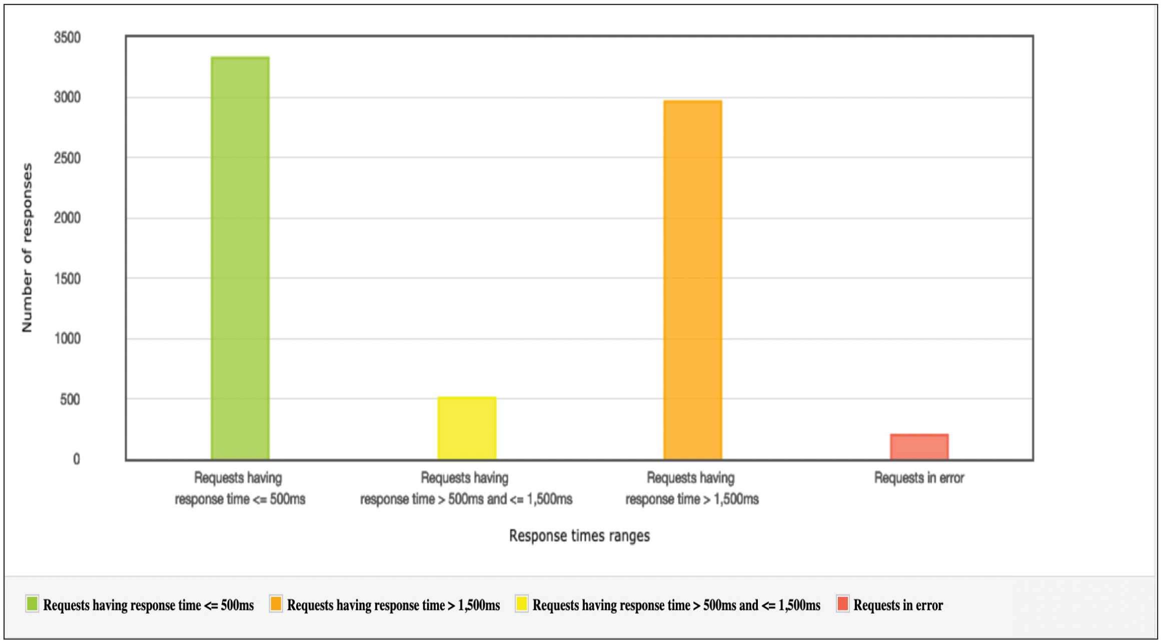


Figure 10.13: The number of responses over the response time ranged base of the satisfaction threshold.

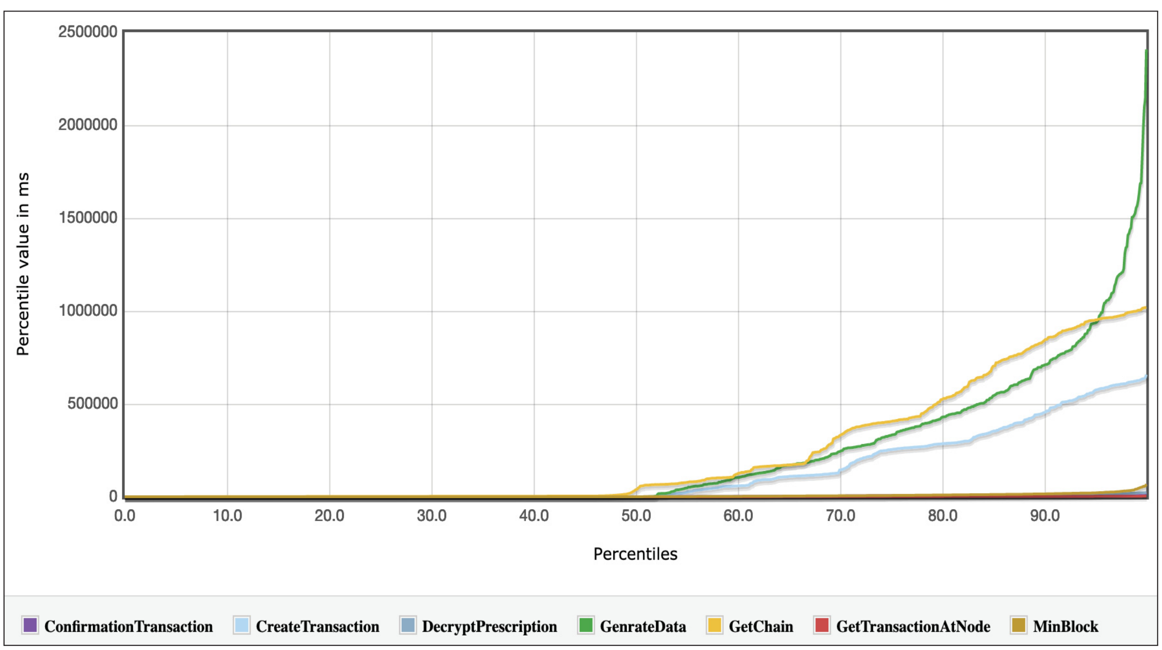


Figure 10.14: The response time percentiles for all the transactions.

10.6.2 Second Scenario

In this, we used the parameters of 10,000 users with syncing the Blockchain with all nodes and dynamic prescription data generation. Table 10.3 shows the results metrics of response times, throughput, and data sent and received size. The total number of requests generated from 10,000 users was 53,469, with a fail request rate of 85.20% (45,554/53,469 requests). Because of the limitation in the testbed device memory, the test could not be completed when the size of the synced Blockchain was too big to be sent using our simple testbed. Most of the errors, 95.36% (43,439/45,554 errors), were a connection failure from the server-side confirming the transaction, connection socket was closed, or no socket was found at the server-side. These error responses could happen for several reasons. However, the most relevant reason could be because of the windows firewall responding to a large number of requests (i.e. almost 58 KB/s) in a limited time. From Figure 10.15, we can see that the number of the failed requests sent to the server went up to 9 transactions (t)/second (s), then went down to 4 t/s. Figure 10.17 shows how unknown or refused connection error codes started after 50% of the sent requests. This might explain the reason behind a large number of failed requests and why the windows refused the connection after. The other 3.82% (1739/45,554 errors) were responses from the MySQL server with the error code 500. The error code illustrates an internal server error, which means the prescription data were not found based on the transaction hash provided. Other errors 0.83% (376/45,554) had the response code 406, which means the server could not validate the transaction originality due to failing to generate the decryption key from the given transaction data.

Further, we can see from the table that the server response time average for the scenario in total from creating the prescription transaction until mining the block in the Blockchain is 224.98 seconds. This sizeable average response time is due mainly to the waiting time until the transaction response failure and generating of a new prescription data request (Figure 10.16). The APDEX score is 0.021 in total, which means the users were frustrated. Figure 10.18 shows the distribution of the number of responses over the satisfactory response time threshold. Figure 10.19 shows the response times percentiles for all the requests made using the different codes in the Blockchain.

	Executions	Resp. Times(ms)			Throughput
Request Label	**Error%**	**Average**	**Min**	**Max**	**Transactions/s**
ConfirmationTransaction	94.71%	18738.43	42	357684	1
CreateTransaction	84.69%	136249.27	57	3481583	1.01
DecryptPrescription	94.06%	21445.71	31	362511	0.99
GenrateData	69.58%	985736.03	35	6785798	1.11
GetChain	90.20%	288118.88	64	4733972	0.98
GetTransactionAtNode	82.53%	14715.02	8	264926	0.99
Total	85.20%	224988.08	8	6785798	7.06

Table 10.3: The jMeter metrics results for the second scenario.

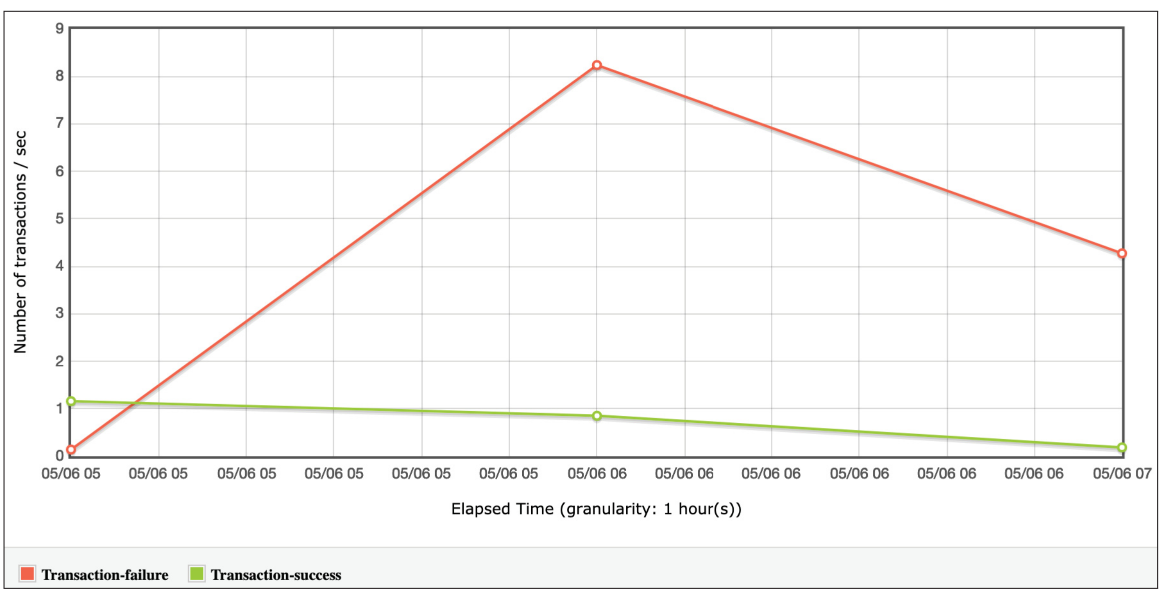


Figure 10.15: The number of transactions chart over the elapsed time (i.e. one hour).

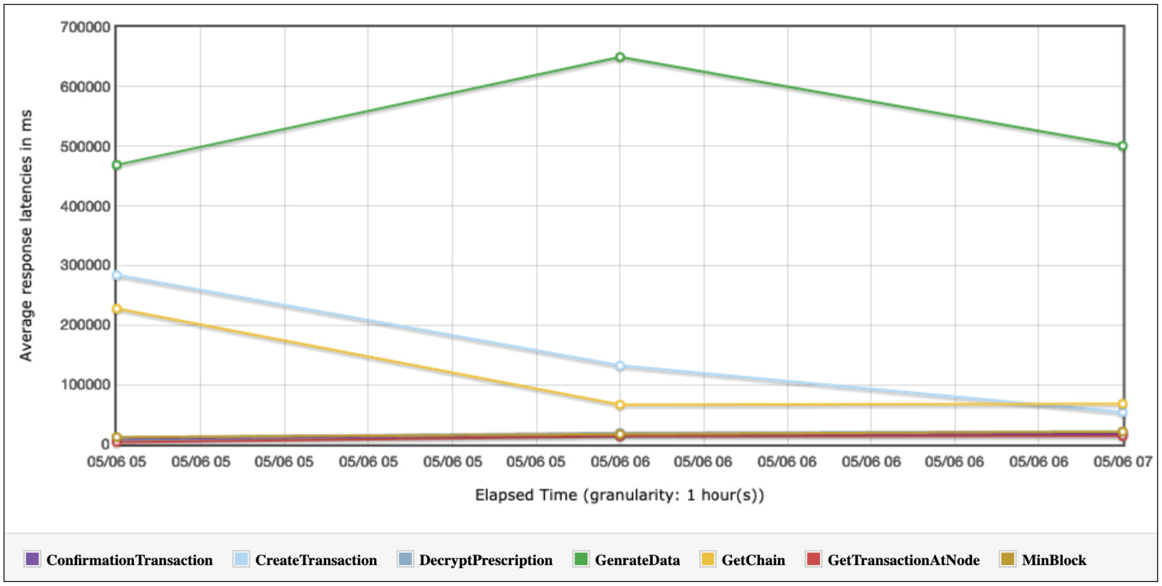


Figure 10.16: The average response latency in ms.

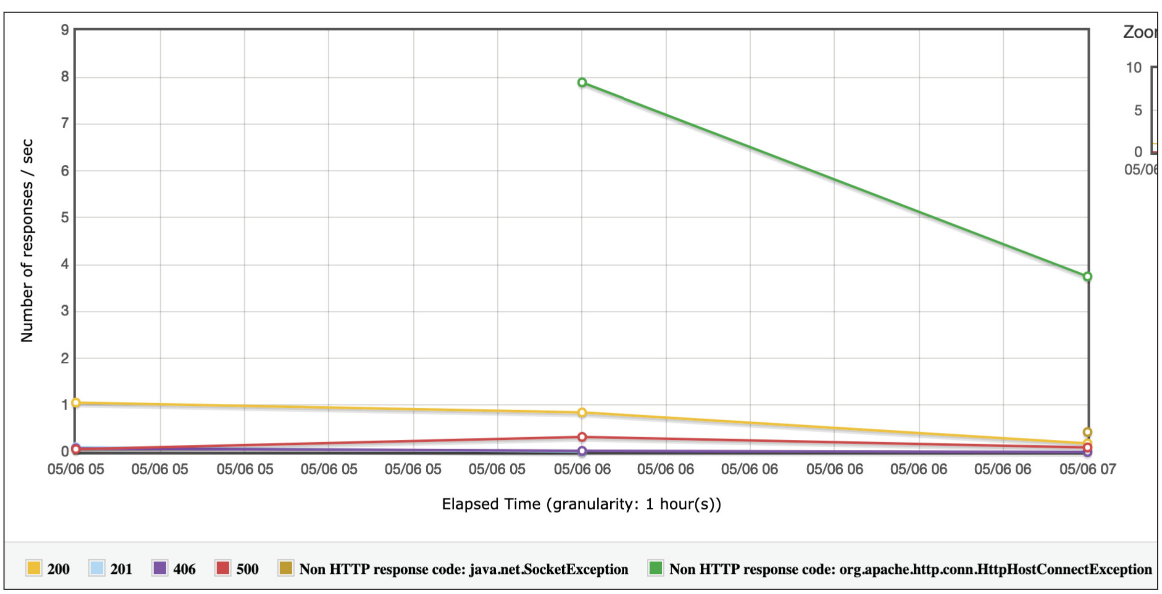


Figure 10.17: The response codes to the HTTP requests per seconds.

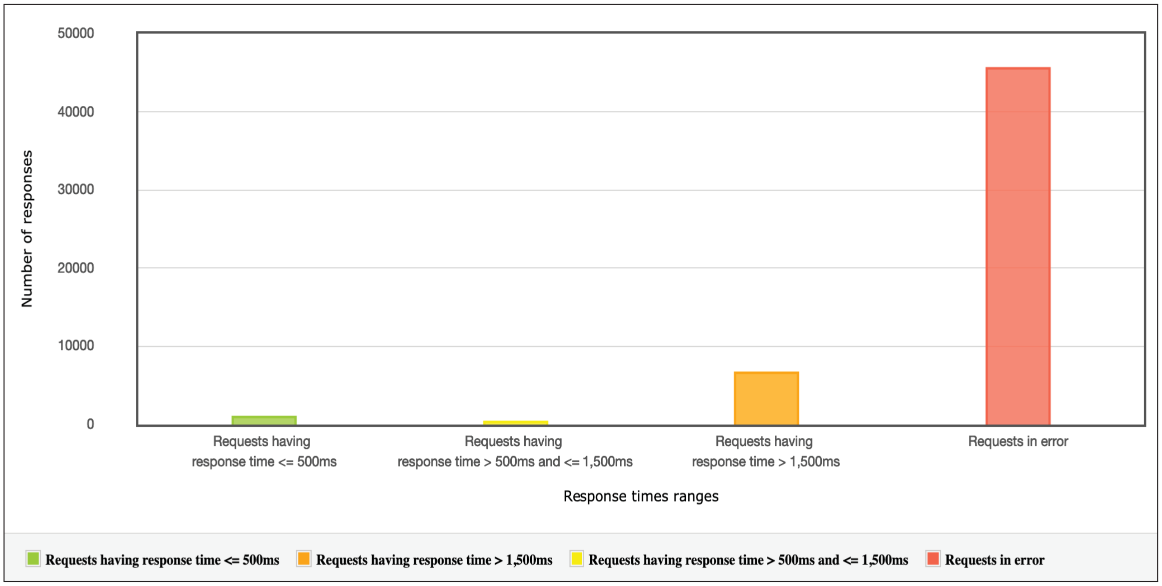


Figure 10.18: The number of responses over the response time ranged base of the satisfaction threshold.

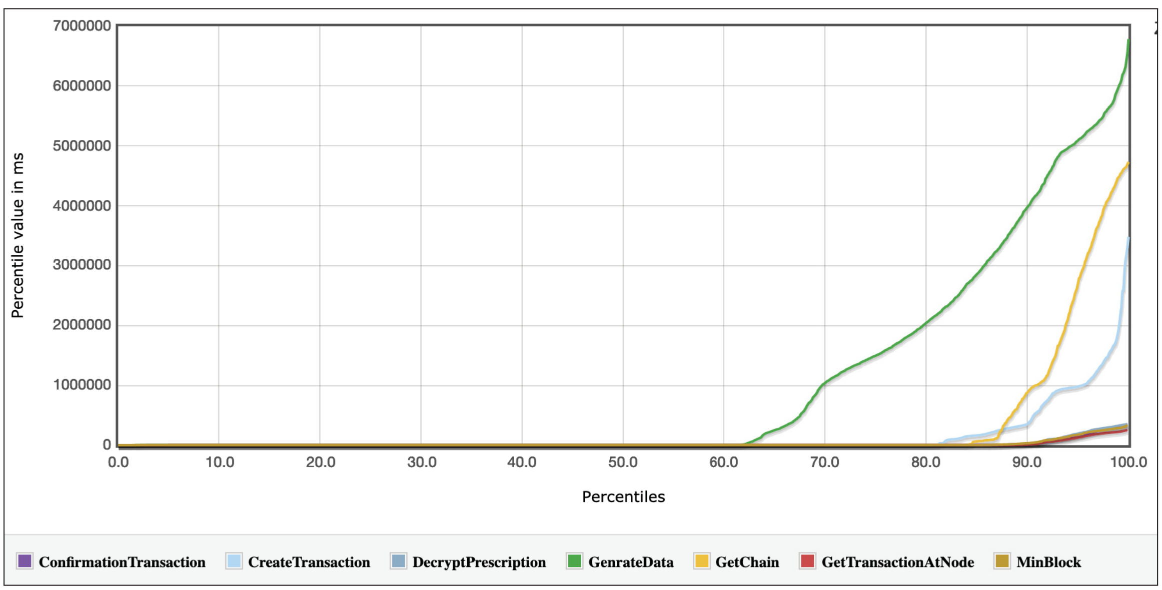


Figure 10.19: The response time percentiles for all the transactions.

10.6.3 Third Scenario

In this, we used the parameters of 1000 users with no syncing the Blockchain with all nodes and dynamic prescription data generation. Table 10.4 shows the results metrics of response times, throughput, and data sent and received size. The total number of requests generated from 1000 users was 6000 (i.e. without syncing the Blockchain) with a fail request rate of 0.27% (16/6000 requests). All the errors 100% (16/16 errors) were from the MySQL server with the error code 500. This error code illustrates an internal server error, which means the prescription data were not found based on the transaction hash provided. From Figure 10.20 we can see the blockchain throughput (i.e. number of transactions per second) for transactions from the creation until the block mining is increasing at the end of the test duration. This is due to not syncing the blockchain process as part of the e-prescription submitting and dispensing. In Figure 10.22 we can see that the number of failure codes has decreased due to the fewer error responses for transactions in the Blockchain.

Further, we can see from the table that the server response time average for the scenario in total from creating the prescription transaction until mining the block in the Blockchain is 0.109 seconds. The APDEX score is 0.974 in total, which means the users were very satisfied. Figure 10.23 shows the distribution of the number of responses over the satisfactory response time threshold. Figure 10.21 shows the average response latency. Figure 10.24 shows the response times percentiles for all the requests made using the different codes in the Blockchain.

	Executions	**Resp. Times(ms)**			**Throughput**
Request Label	**Error%**	**Average**	**Min**	**Max**	**Transactions/s**
ConfirmationTransaction	0.00%	52.85	40	170	0.28
CreateTransaction	0.00%	72.27	56	1070	0.28
DecryptPrescription	0.00%	33.72	29	203	0.28
GenrateData	0.00%	72.74	27	253	0.28
GetTransactionAtNode	0.00%	10.98	9	61	0.28
MinBlock	0.00%	99.73	77	210	0.28
Total	0.00%	57.05	9	1070	1.67

Table 10.4: The jMeter metrics results for the third scenario.

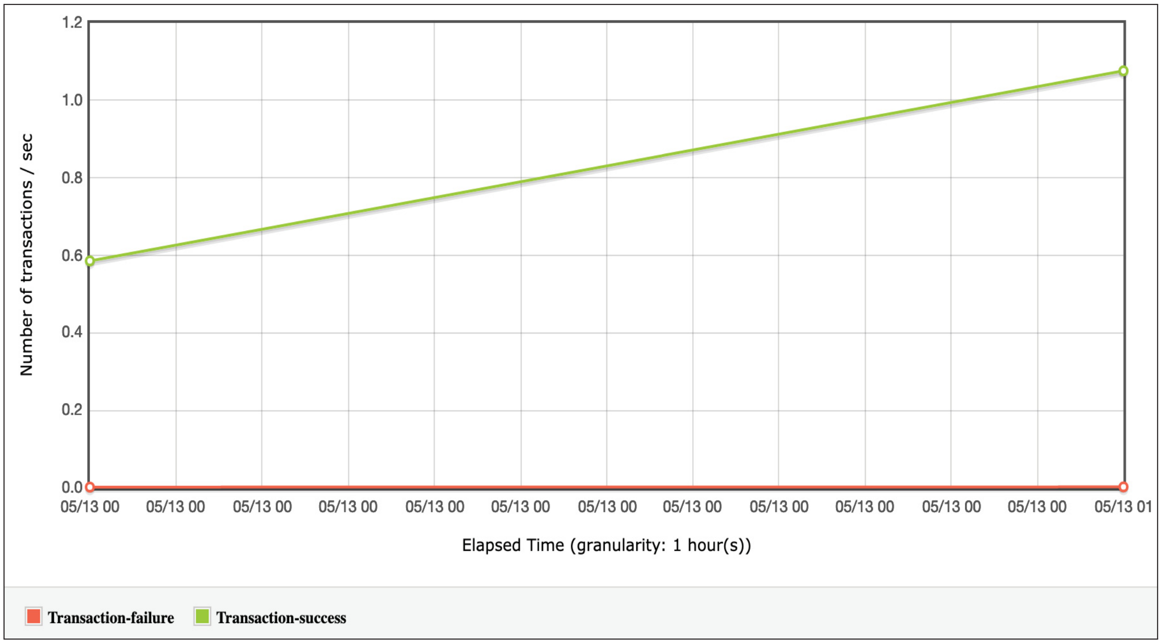


Figure 10.20: The number of transactions chart over the elapsed time (i.e. one hour).

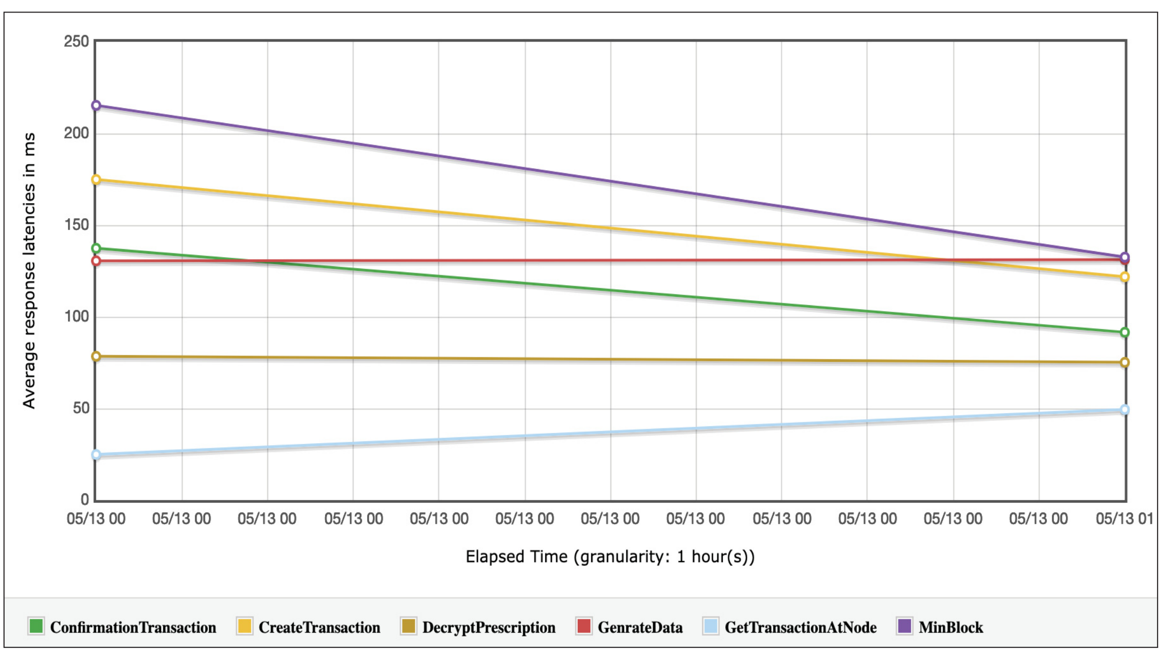


Figure 10.21: The average response latency in ms.

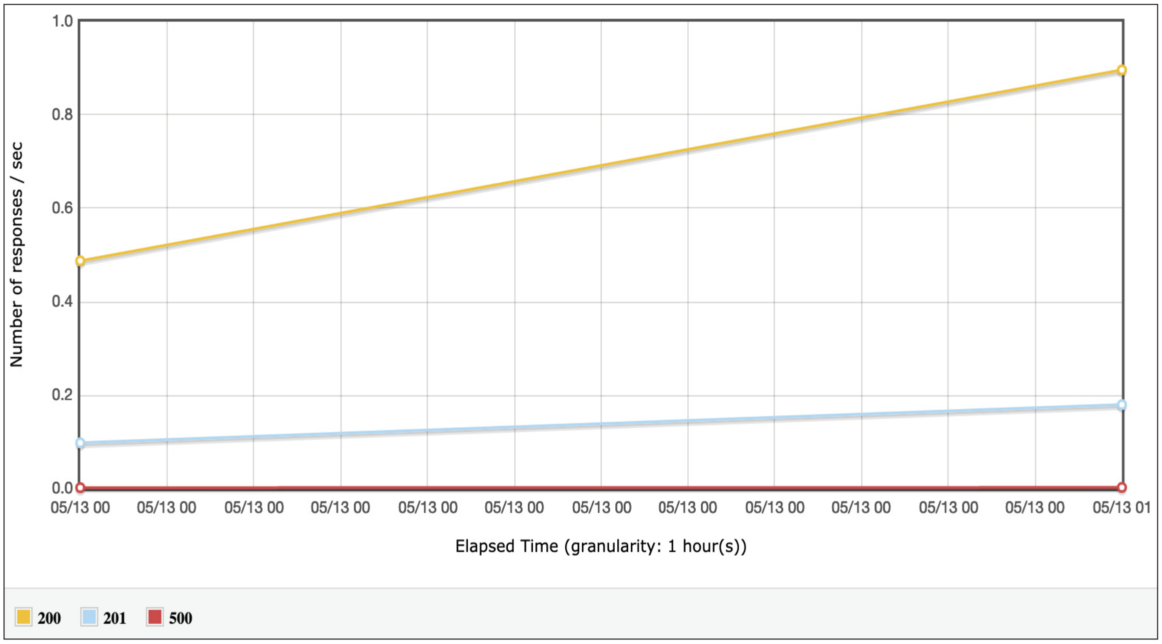


Figure 10.22: The response codes to the HTTP requests per seconds.

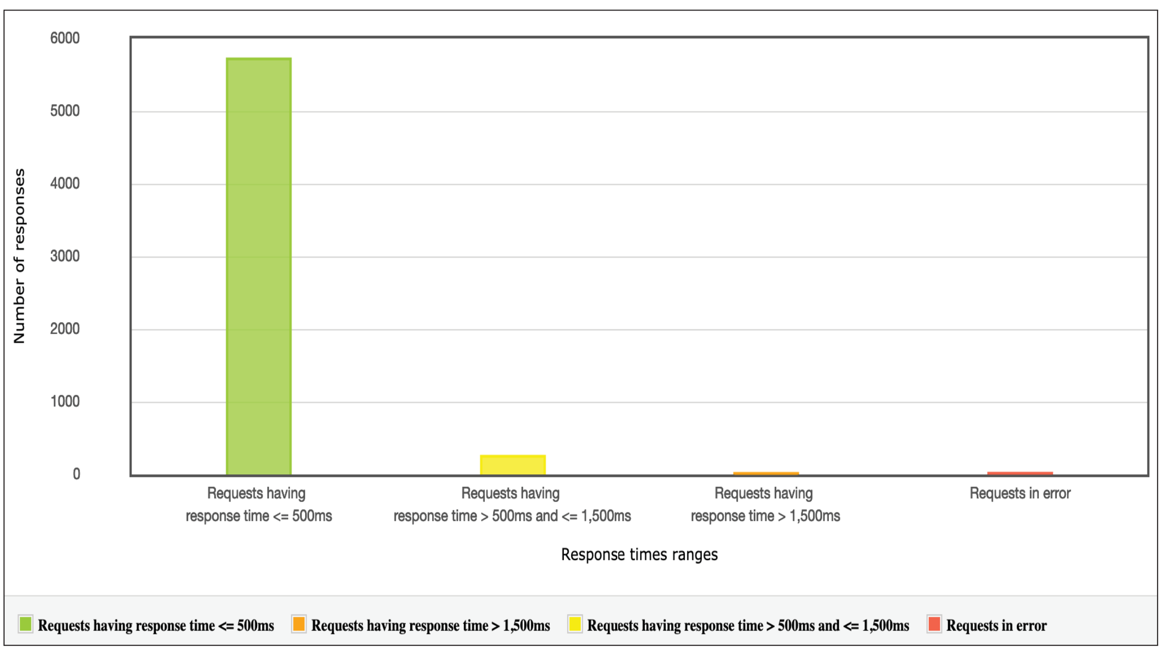


Figure 10.23: The number of responses over the response time ranged base of the satisfaction threshold.

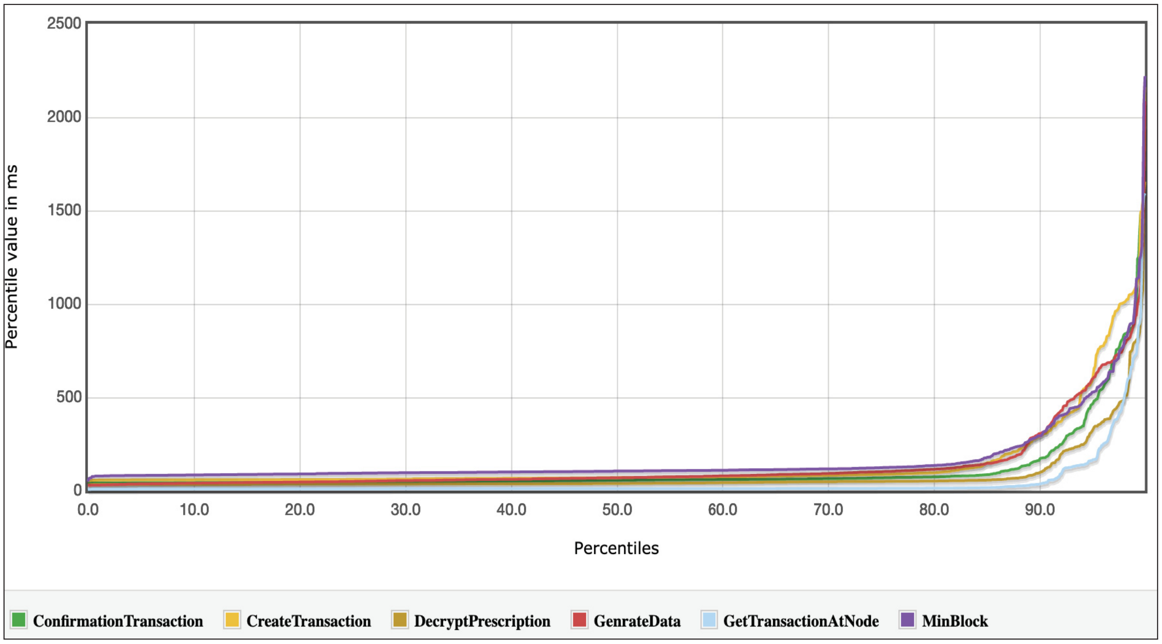


Figure 10.24: The response time percentiles for all the transactions.

10.6.4 Fourth Scenario

In this, we used the parameters of 10,000 users with no syncing the Blockchain with all nodes and dynamic prescription data generation. Table 10.5 shows the metrics of response times, throughput, and data sent and received size. The total number of requests generated from 10,000 users was 60,000 (i.e. without syncing the Blockchain) with a fail request rate of 3.19% (1916/60,000 requests). All the errors 99.79% (1912/1916 errors) were from the MySQL server with the error code 500. This error code illustrates an internal server error, which means the prescription data were not found based on the transaction hash provided. The other errors, 0.21% (4/1916 errors), were responses to the request of confirming the transaction. The error code is 406, which means the server could not validate the transaction's originality due to failing to generate the decryption key from the given transaction data.

From Figure 10.25 we can see the blockchain throughput (i.e. number of transactions per second) for transactions from the creation until the block mining increased compared to the first scenario. This is due to not syncing the blockchain process as part of the e-prescription submitting and dispensing. In Figure 10.27 we can see the number of failure codes is stable through the test duration, and all are a response to the request of getting the prescription information from the MySQL server.

Further, we can see from the table that the server response time average for the scenario in total from creating the prescription transaction until mining the block in the Blockchain is almost 0.084 seconds. The APDEX score is 0.966 in total, which means the users were very satisfied. Figure 10.28 shows the distribution of the number of responses over the satisfactory response time threshold. Figure 10.26 shows the average response latency. Figure 10.29 shows the response times percentiles for all the requests made using the different codes in the Blockchain.

	Executions	**Resp. Times(ms)**			**Throughput**
Request Label	**Error%**	**Average**	**Min**	**Max**	**Transactions/s**
ConfirmationTransaction	0.04%	67.12	40	596	1.39
CreateTransaction	0.00%	96.68	55	928	1.39
DecryptPrescription	19.12%	96.37	29	3021	1.39
GenrateData	0.00%	107.97	27	1136	1.39
GetTransactionAtNode	0.00%	14.97	6	479	1.39
MinBlock	0.00%	119.77	46	1314	1.39
Total	3.19%	83.81	6	3021	8.33

Table 10.5: The jMeter metrics results for the fourth scenario.

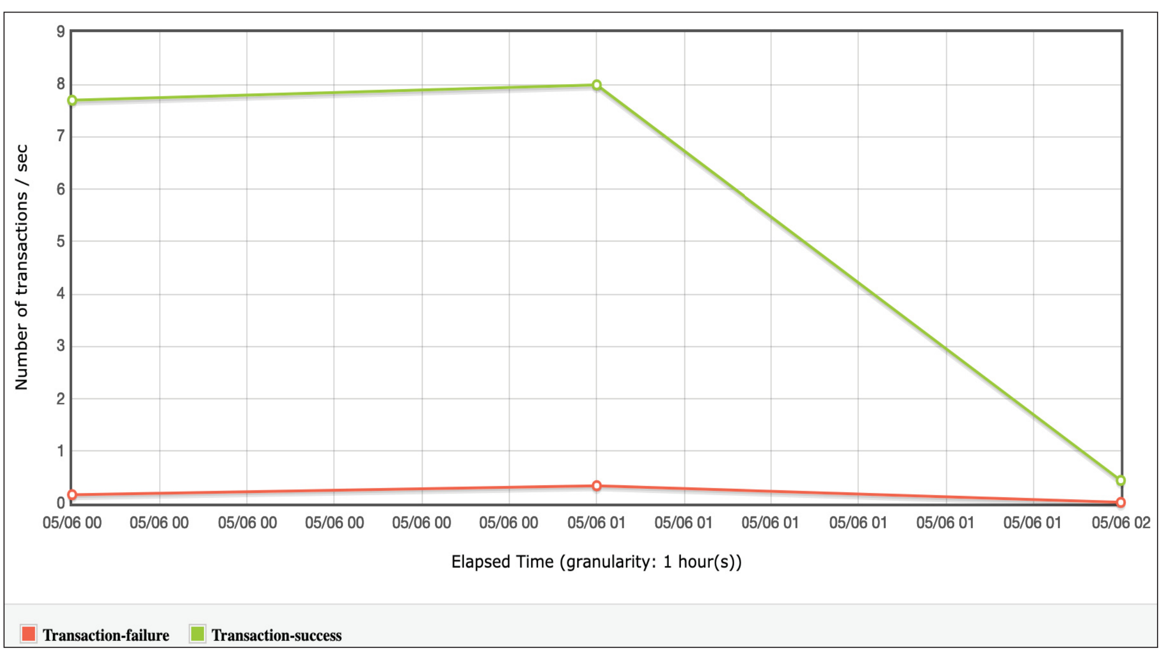


Figure 10.25: The number of transactions chart over the elapsed time (i.e. one hour).

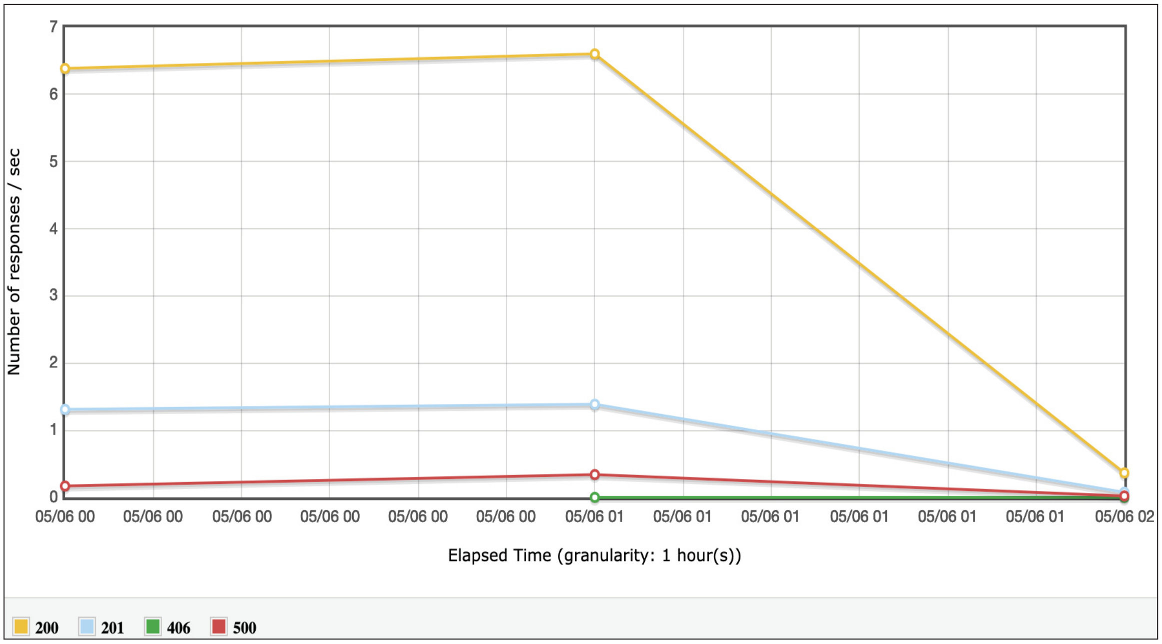


Figure 10.27: The response codes to the HTTP requests per seconds.

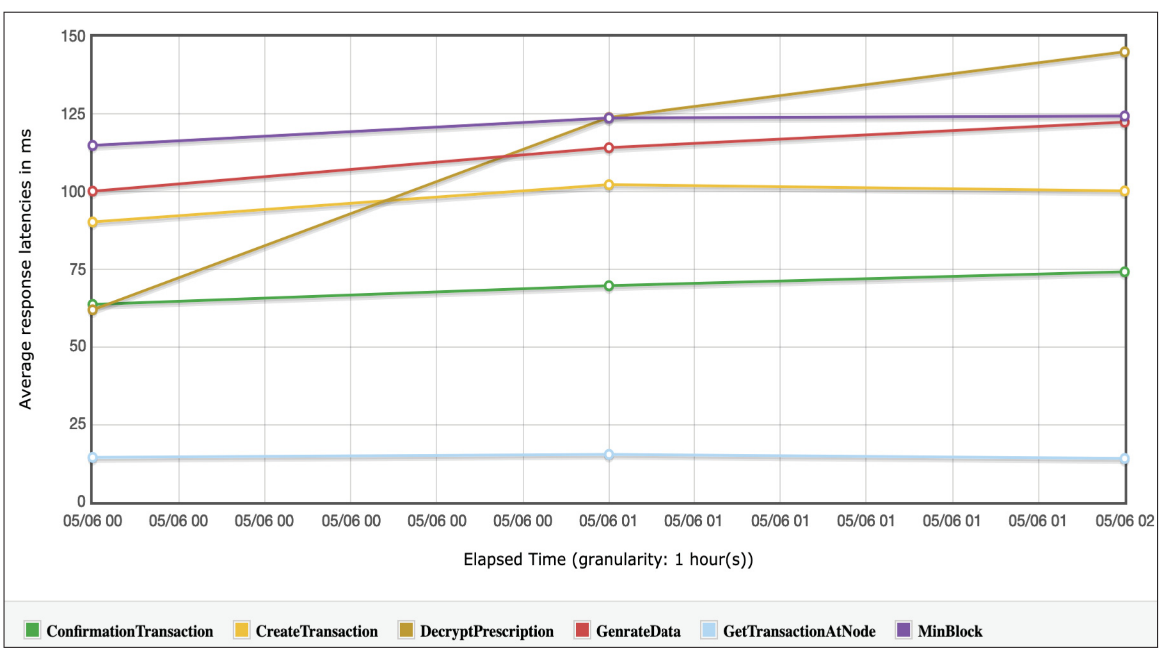


Figure 10.26: The average response latency in ms.

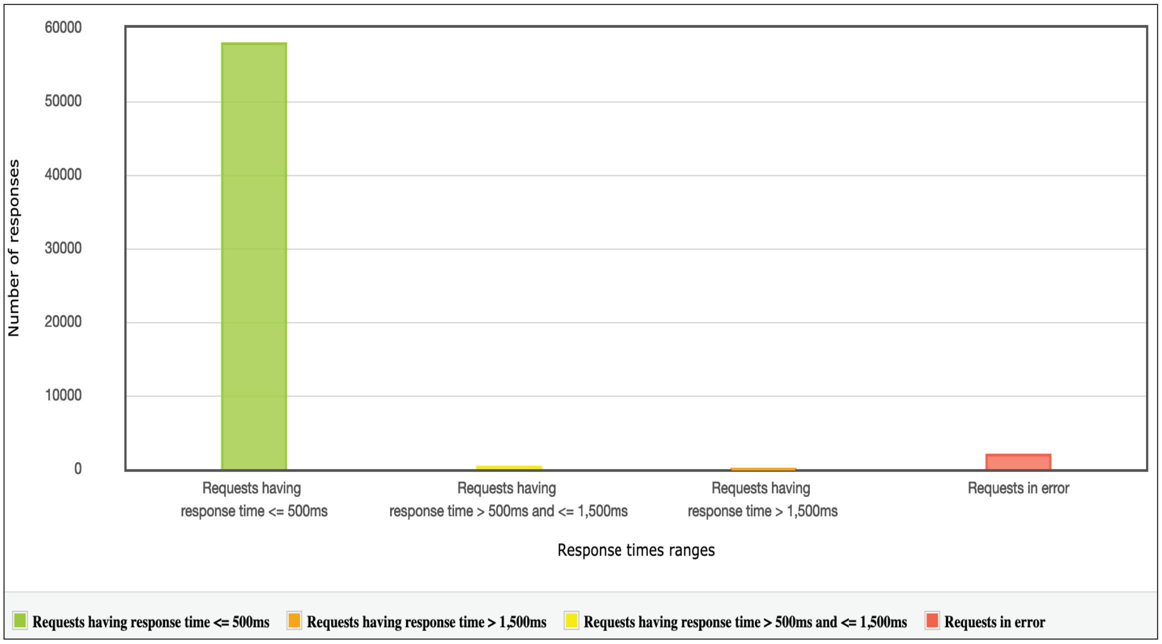


Figure 10.28: The number of responses over the response time ranged base of the satisfaction threshold.

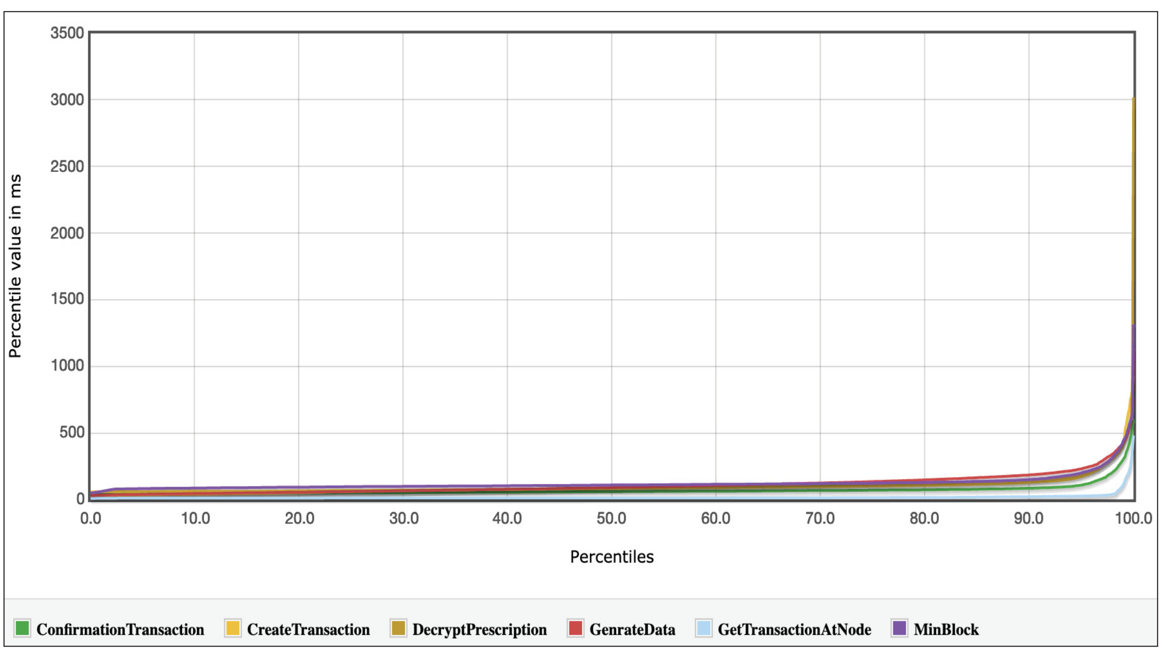


Figure 10.29: The response time percentiles for all the transactions.

10.7 Discussion

In this section, we will discuss and compare the results of the blockchain performance experiments. Further, we will compare our results with other blockchain systems. The comparison will be based on the evaluation metrics we mentioned in Chapter 7 on the ExT of the transactions, latency, and throughput of the Blockchain.

We will be comparing our results to the following analysis studies. The authors in [182] conducted a performance analysis on private blockchain platforms. They used the same evaluation metrics used in this thesis for the execution time of transactions, throughput, and latency. In their analysis, they investigated two platforms: Ethereum and Hyperledger Fabric. Their experiment was conducted using Amazon AWS EC2 with an Intel e5-1650 8 core CPU and 15 GB RAM. In this study, the authors only deployed one blockchain node. They developed a money transfer application to utilize the Blockchain. The number of requests ranged from 1 to 10,000 requests. Further, we will compare our results with the performance evaluation results summarized in the systemic survey [274]. The authors in their review compiled a list of experimental analysis studies on the distributed ledger technologies. From their systemic review, they found that the most used metrics to evaluate blockchain applications are the same as we are using in this evaluation methodology.

10.7.1 Transaction Execution Time (ExT)

From the results of the scenarios, we can see that the transaction execution time has increased when using the get chain request. This request allows the Blockchain of the stored patient's e-prescriptions to be updated. Scenarios one and two show larger execution times in total than scenarios three and four. This is due to generating dynamic data for the e-prescriptions and syncing the Blockchain with the pharmacy node. On the other hand, we noticed that when we removed the syncing the blockchain request, the average execution times of the transactions from creating until mining the Blockchain in both scenarios three and four were lower. The average execution time in scenario three was almost 57.05 s, and in scenario four was 83.81 s. This indicates that syncing the e-prescriptions blockchain request should be a back-end process executed after sharing the transactions with the pharmacy to expedite the dispensing process. The e-prescriptions blockchain containing all the patient's e-prescriptions data can be shared after, as an update process could be processed once a day. The pharmacy should receive the e-prescription to be dispensed at the time of submission. Table 10.6 shows the comparison of our results of the execution time of transactions with the results from the studies mentioned above [182] and [274]. From the table, we can see that only [182] reported the ExT for their experiment. Compared to our results, we find that our experiment reported better ExT than their results.

10.7.2 Throughput

From the results of the scenarios, we can see that the number of transactions per second (i.e. throughput) is lower when using the get chain request. This request allows the Blockchain of the stored patient's e-prescriptions to be updated. Scenarios one and two show a lower throughput in total than scenarios three and four. This is due to generating dynamic data for the e-prescriptions and syncing the Blockchain with the pharmacy node. On the other hand, when we removed the syncing the blockchain request, the average throughput from creating the transaction until mining the block in scenarios three and four was higher. The average throughput was 1.67 tx/s, and in scenario four was 8.33 tx/s. This indicates that the larger the number of requests, the higher the throughput.

Table 10.7 shows a comparison of our results of the throughput with the results from other studies mentioned above [182] and [274]. We can see our results from the table, and we found that our experiment reported lower throughput than the other results. We believe that if we increase the number of transactions, the throughput will improve. Also, none of the other studies reported the ramp-up time for the transactions; therefore, we believe the comparison will be difficult.

10.7.3 Latency

From the results of the scenarios, we can see that the transaction execution time increased when using the get chain request. This request allows the Blockchain of the stored patient's e-prescriptions to be updated. Scenarios one and two show larger execution times in total than scenarios three and four. This is due to the request to generate dynamic data for the e-prescriptions and syncing the Blockchain with the

Table 10.6: The execution time of transactions results comparison with other popular blockchain platforms performance analysis table.

Studies	**ExT(s)**	**Workload**	**Network (Size)**
HLF v0.6 [275]	-	YCSB	8 nodes
HLF v0.6 [275]	-	Smallbank	8 nodes
Ethereum [275]	-	YCSB	8 nodes
Ethereum [275]	-	Smallbank	8 nodes
Parity [275]	-	YCSB	8 nodes
Parity [275]	-	Smallbank	8 nodes
Quorum [276]	-	write-only/null	3 nodes
Quorum [276]	-	null	4 nodes
Quorum [276]	-	write-only	4 nodes
HL Sawtooth [277]	-	Smallbank	6 nodes
EOS [277]	-	Smallbank	6 nodes
Ethereum [277]	-	Smallbank	6 nodes
HLF v1.0 [278]	-	Payment transaction	16 nodes
HLF v0.6 [278]	-	Invoking chaincode	16 nodes
Ripple v0.6 [278]	-	Payment transaction	16 nodes
hline Tendermint v0.22.4 [279]	-	Invoke Payment transaction	16 nodes
Tendermint v0.22.4 [279]	-	Query Payment transaction	16 nodes
R3 Corda v3.2 [279]	-	Query Payment transaction	4 nodes
Ethereum [280]	-	YCSB(N=10,000)	4 nodes
Ethereum [280]	-	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	-	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	-	YCSB(N=10,000)	4 nodes
Ethereum [281]	-	Payment transaction	1 node
Parity [281]	-	Payment transaction	1 node
Ethereum [182]	936.12	TransferMoney (N=10,000)	1 node
HLF v0.6 [182]	103.75	TransferMoney (N=10,000)	1 node
proposed system (scenario 3)	57.05	e-prescription (N=1000)	2 nodes
proposed system (scenario 4)	83.81	e-prescription (N=10,000)	2 nodes

Table 10.7: The throughput results comparison with other popular blockchain platforms performance analysis table.

Studies	Throughput (TPS)	Workload	Network (Size)
HLF v0.6 [275]	1273	YCSB	8 nodes
HLF v0.6 [275]	1122	Smallbank	8 nodes
Ethereum [275]	284	YCSB	8 nodes
Ethereum [275]	255	Smallbank	8 nodes
Parity [275]	45	YCSB	8 nodes
Parity [275]	46	Smallbank	8 nodes
Quorum [276]	2000+	write-only/null	3 nodes
Quorum [276]	1900	null	4 nodes
Quorum [276]	1800	write-only	4 nodes
HL Sawtooth [277]	3	Smallbank	6 nodes
EOS [277]	21	Smallbank	6 nodes
Ethereum [277]	10	Smallbank	6 nodes
HLF v1.0 [278]	1700	Payment transaction	16 nodes
HLF v0.6 [278]	2600	Invoking chaincode	16 nodes
Ripple v0.60.0 [278]	1450	Payment transaction	16 nodes
Tendermint v0.22.4 [279]	6000	Invoke Payment transaction	16 nodes
Tendermint v0.22.4 [279]	5600	Query Payment transaction	16 nodes
R3 Corda v3.2 [279]	50	Query Payment transaction	4 nodes
Ethereum [280]	130	YCSB(N=10,000)	4 nodes
Ethereum [280]	235	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	535	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	1033	YCSB(N=10,000)	4 nodes
Ethereum [281]	-	Payment transaction	1 node
Parity [281]	-	Payment transaction	1 node
Ethereum [182]	21	TransferMoney (N=10,000)	1 node
HLF v0.6 [182]	160	TransferMoney (N=10,000)	1 node
proposed system (scenario three)	1.67	e-prescription application (N=1000)	2 nodes
proposed system (scenario four)	8.33	e-prescription application (N=10000)	2 nodes

pharmacy node. On the other hand, we noticed that when we removed the syncing the blockchain request, the average execution times of the transactions from creating until mining the Blockchain in both scenarios three and four were lower. In scenario three, the average execution time was almost 0.109 s, and in scenario four, it was 0.084 s. This indicates that syncing the e-prescriptions blockchain request should be a back-end process executed after sharing the transactions with the pharmacy to expedite the dispensing process. The e-prescriptions blockchain containing all the patient's e-prescriptions data can be shared as an update process that can be processed once a day. The pharmacy should receive the e-prescription to be dispensed at the time of submission.

Table 10.6 shows the comparison of our results of the latency with the results from the studies mentioned above [182] and [274]. From the table, we can see our results, and we found that our experiment had better results than most of the other results.

Even though the comparison showed that our proposed blockchain model has good results in terms of ExT and latency as well as an acceptable result for the throughput evaluation, it is difficult to compare different blockchain applications due to the lack of standards for blockchain interface evaluation. Since each application has its own different goals, the evaluation metrics differ. For example, our application goals are to make the information available and updated using reliable technology. We found that utilizing the Blockchain will help achieve the goals named in 6.2.

Lastly, the blockchain approach will help improve the efficiency of the dispensing process by eliminating the need to verify the originality of the prescription by contacting the prescriber. On the Blockchain, only a prescriber is allowed to submit the e-prescription. Moreover, the Blockchain provides a way to track the previous e-prescriptions, which will help to provide the information for the prescribers while prescribing medication to avoid any medication interactions using the ML model. The blockchain approach will be ensuring the security and privacy of the patient's information by preventing any alteration to it. Once it is mined in the Blockchain, it is only accessible in the read-only mode. In addition, access to the Blockchain is restricted to parties involved in the network (i.e. prescribers, pharmacies, patients). Although anyone in the blockchain network can read the information in the Blockchain, it can not be processed because it is encrypted. The block information can be decrypted

Table 10.8: The latency results comparison with other popular blockchain platforms performance analysis table.

Studies	**Latency (s)**	**Workload**	**Network (Size)**
HLF v0.6 [275]	38	YCSB	8 nodes
HLF v0.6 [275]	51	Smallbank	8 nodes
Ethereum [275]	92	YCSB	8 nodes
Ethereum [275]	114	Smallbank	8 nodes
Parity [275]	3	YCSB	8 nodes
Parity [275]	4	Smallbank	8 nodes
Quorum [276]	1.5	write-only/null	3 nodes
Quorum [276]	3.2	null	4 nodes
Quorum [276]	3.5	write-only	4 nodes
HL Sawtooth [277]	-	Smallbank	6 nodes
EOS [277]	-	Smallbank	6 nodes
Ethereum [277]	-	Smallbank	6 nodes
HLF v1.0 [278]	-	Payment transaction	16 nodes
HLF v0.6 [278]	1.8	Invoking chaincode	16 nodes
Ripple v0.60.0 [278]	6	Payment transaction	16 nodes
Tendermint v0.22.4 [279]	0.15	Invoke Payment transaction	16 nodes
Tendermint v0.22.4 [279]	0.05	Query Payment transaction	16 nodes
R3 Corda v3.2 [279]	8	Query Payment transaction	4 nodes
Ethereum [280]	1297	YCSB(N=10,000)	4 nodes
Ethereum [280]	569	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	78	YCSB(N=10,000)	4 nodes
HLF v1.0 [280]	40	YCSB(N=10,000)	4 nodes
Ethereum [281]	0.199	Payment transaction	1 node
Parity [281]	0.105	Payment transaction	1 node
Ethereum [182]	361	TransferMoney (N=10,000)	1 node
HLF v0.6 [182]	4	TransferMoney (N=10,000)	1 node
proposed system (scenario three)	0.109	e-prescription application (N=1000)	2 nodes
proposed system (scenario four)	0.084	e-prescription application (N=10000)	2 nodes

only by a key generated using the patient token id, granted only by the patient's consent through the mobile application using NFC. Finally, we discussed the blockchain results in this section, and we compared our results to popular blockchain platforms. We showed how the Blockchain would improve efficiency, security and make the information available to the parties.

10.8 Chapter Summary

In this chapter, we presented the blockchain model architecture in detail. We reported and discussed the result of our proof-of-concept experiment of proposing the use of Blockchain. We also compared our reported results with the results of several papers about the performance analysis of blockchain implementations studies that experimented with popular blockchain platforms. Finally, we showed that our blockchain performance results have acceptable scores in terms of ExT, latency, and throughput metrics.

Chapter 11

Conclusion and Future Work

Medication errors are a global issue and can lead to death if the errors are fatal. The cause of medication errors can vary from the misinterpretation of the prescriber's handwriting to dispensing the wrong medication. Moreover, developing an e-Prescription system is only a part of the solution, and more in-depth solutions are needed. Patient safety should be enhanced by providing new approaches to avoid any implications from prescribing a wrong medication or an incorrect dose to the patient. Such solutions need to ensure the availability of patient information regarding their current or past health status. Moreover, accurate verification of the patient's identity during the dispensing process is more likely to mitigate the wrong medication being dispensed.

Therefore, we propose a new framework for mitigating medication errors by ensuring the availability, security, and privacy of patient e-prescription information. Further, the framework aims to increase medication prescribing safety and reduce any human errors involved in dispensing medication to the patient.

The framework aims to use an NFC-enabled mobile application to verify the patient's identity. Moreover, the NFC mobile application will share the patient's token ID to make the information available to the other models. The framework will also utilize blockchain technology to securely and privately provide the ability to share the patient's e-prescription information with the pharmacy and record the e-prescription dispensing process. Finally, we propose the use of the ML model to detect serious outcomes caused by any anomalies in the submitted e-prescription and avoid any potential harm that might affect the patient's health. Such anomalies are the missing prescription values, wrong dosage, wrong medication strength the might harm the patient. All of these anomalies could be detected using the history of similar treatment cases. Therefore in our experiment, we are detecting any serious outcome caused by these anomalies.

We have implemented a proof of concept of the NFC mobile application and ran a user study to test the usability. Our study included 21 participants from different age groups ranging from 18 years old to 55 years old. The study showed that the participants have a positive attitude towards the NFC mobile application. We also implemented the ML model using the Python programming language. We used the ADEs reports dataset with 800,0000 records from [2]. Our evaluation was aiming for higher accuracy and a reliable ML classifier. We found from all the tested classifiers that XGBoost had higher accuracy (i.e. 0.88) and a better AUC score (i.e. 0.95) compared to the tested classifier and compared to the other mentioned studies. Finally, we implemented a proof-of-concept private blockchain model to test the transfer of e-prescription information between the two nodes: the prescriber and the pharmacy. We evaluated the blockchain model using jMeter with the metrics throughput, latency, and transaction execution time. We found that our blockchain model scored acceptable results compared to popular blockchain platforms. In the next section, we will list the framework for future work.

11.1 Future Work

We will conduct a usability study for the framework to test a real-world workload on it in future work. We are also planning to test the ML classifier using a more organized, larger, and more complete dataset of submitted prescriptions. Last, we will deploy the Blockchain in a usability study with an expanded number of nodes and evaluate the blockchain performance with a real-world workload. Our blockchain implementation for the real-world demo will be an integration of Hyperledger and BigchainDB.

References

[1] R. P. Nair, D. Kappil, and T. M. Woods, "Pharmacist to pharmacist-10 strategies for minimizing dispensing errors-dispensing errors can be costly for the pharmacist as well as potentially dangerous for the patient. pharmacists can take simple steps to help eliminate this problem." *Pharmacy Times*, vol. 76, no. 1, p. 92, 2010.

[2] U.S. Food and Drug Administration and others, "FDA Adverse Event Reporting System (FAERS) quarterly data extract files," 2020. [Online]. Available: https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-latest-quarterly-data-files

[3] J. Webb, "Pharmacy dispensing errors: Claims study emphasizes need for systematic vigilance," *Drug Topics, Modern Medicine Network*, 2015.

[4] HPSO, "A ten-year analysis 2013 pharmacist liability," Healthcare Providers Service Organization (HPSO), Tech. Rep., 2013.

[5] S. Fan, M. Wen, C. Hsu, C. Hung, S. Hsu, M. Chuang, J. K. Zao, and C. Lin, "Health pal: a pda phone that will take care of your health," in *IEEE International Conference on Systems, Man and Cybernetics*, Oct 2007, pp. 3703–3708.

[6] C. J. Wang, M. H. Patel, A. J. Schueth, M. Bradley, S. Wu, J. C. Crosson, P. A. Glassman, and D. S. Bell, "Perceptions of standards-based electronic prescribing systems as implemented in outpatient primary care: a physician survey," *Journal of the American Medical Informatics Association*, vol. 16, no. 4, pp. 493–502, 2009.

[7] J. K. Zao, M. Y. Wang, P. Tsai, and J. W. S. Liu, "Smart phone based medicine in-take scheduler, reminder and monitor," *12th IEEE International Conference on e-Health Networking, Application and Services, Healthcom*, 2010.

[8] B. M. Silva, I. M. Lopes, M. B. Marques, J. J. P. C. Rodrigues, and M. L. Proença, "A mobile health application for outpatients medication management," in *2013 IEEE International Conference on Communications (ICC)*, June 2013, pp. 4389–4393.

[9] S. Nakamoto, "Bitcoin: A peer-to-peer electronic cash system," Manubot, Tech. Rep., 2019.

[10] Canada Health Infoway, *Prescribers: See How PrescribeIT™ Works in an Electronic Medical Record System and Pharmacy Management System*. Canada Health Infoway, 2018, accessed August, 2019. [Online]. Available: https://www.infoway-inforoute.ca/en/what-we-do/news-events/webinars/

[11] Surescripts, "Protecting patient privacy," *Surescripts.com*, 2019. [Online]. Available: https://surescripts.com/our-story/privacy

[12] eRx, "https://www.erx.com.au/for-pharmacists/how-erx-works/," website, 2018. [Online]. Available: https://www.erx.com.au/for-pharmacists/how-erx-works/

[13] National Health Service NHS, "Start using electronic prescriptions," Apr. 2019. [Online]. Available: https://www.nhs.uk/using-the-nhs/nhs-services/pharmacies/electronic-prescription-service/

[14] Ministry of Health, Social Services and Equality, *ePrescription in Spain Patient safety*. Ministry of Health, Social Services and Equality, 2014. [Online]. Available: http://www.ehealth2014.org/wp-content/uploads/2014/05/ePrescription-in-Spain.pdf

[15] L. Ministry of Health and Welfare, "Complete demonstration project for full-scale operation of electronic prescriptions [translated from japanese]," Ministry of Health, Labor and Welfare, Tech. Rep., 2019. [Online]. Available: https://www.mhlw.go.jp/content/11120000/000496837.pdf

[16] ——, "Operation guidelines for electronic prescriptions [translated from japanese]," Ministry of Health, Labor and Welfare, Tech. Rep., 2016. [Online]. Available: https://www.mhlw.go.jp/file/05-Shingikai-12601000-Seisakutoukatsukan-Sanjikanshitsu_Shakaihoshoutantou/0000119545_2.pdf

[17] M. Hassel, "E-prescriptions in Sweden," Swedish eHealth Agency, Tech. Rep., 2019, accessed August, 2019. [Online]. Available: https://ehealthresearch.no/files/documents/Undersider/WHO-Symposium-2019/3-1-Hassel-ENG.pdf

[18] R. Marchitelli, "Go public parents find son's lifeless body after pharmacy switches sleep medication for toxic dose of another drug," CBC News, 2016. [Online]. Available: http://www.cbc.ca/news/canada/toronto/go-public-sleep-medication-accidentally-switched-1.3811972

[19] A. Boucher, C. Ho, N. MacKinnon, T. A. Boyle, A. Bishop, P. Gonzalez, C. Hartt, and J. R. Barker, "Quality-related events reported by community pharmacies in nova scotia over a 7-year period: a descriptive analysis," *cmajo*, vol. 6, no. 4, pp. E651–E656, 2018. [Online]. Available: http://cmajopen.ca/lookup/doi/10.9778/cmajo.20180090

[20] L. T. Kohn, J. Corrigan, M. S. Donaldson *et al.*, *To err is human: building a safer health system*. National academy press Washington, DC, 2000, vol. 6.

[21] M. A. Makary and M. Daniel, "Medical error—the third leading cause of death in the us," *Bmj*, vol. 353, 2016.

[22] Canadian Institute for Health Information, *Health Care in Canada 2009: A Decade in Review*. Canadian Institute for Health Information (CIHI), 2009. [Online]. Available: https://secure.cihi.ca/free_products/HCIC_2009_Web_e.pdf

[23] G. R. Baker, P. G. Norton, V. Flintoft, R. Blais, A. Brown, J. Cox, E. Etchells, W. A. Ghali, P. Hébert, S. R. Majumdar *et al.*, "The canadian adverse events study: the incidence of adverse events among hospital patients in canada," *Cmaj*, vol. 170, no. 11, pp. 1678–1686, 2004.

[24] N. Harder, J. Plouffe, D. Cepanec, K. Mann, M.-L. Lê, P. Gregory, P. Griffith, and K. Doerksen, "Use of mobile devices and medication errors in acute care: a systematic review protocol," *JBI database of systematic reviews and implementation reports*, vol. 14, no. 9, pp. 47–56, 2016.

[25] Canadian Institute for Health Information, *Patient Safety in Canada: An Update*. Canadian Institute for Health Information, 2007. [Online]. Available: https://secure.cihi.ca/free_products/Patient_Safety_AIB_EN_070814.pdf

[26] P. J. Lewis, T. Dornan, D. Taylor, M. P. Tully, V. Wass, and D. M. Ashcroft, "Prevalence, incidence and nature of prescribing errors in hospital inpatients," *Drug safety*, vol. 32, no. 5, pp. 379–389, 2009.

[27] C. Schoen, R. Osborn, P. T. Huynh, M. Doty, K. Zapert, J. Peugh, and K. Davis, "Taking the pulse of health care systems: Experiences of patients with health problems in six countries: Patients' voices can provide policy leaders with a window onto what is happening at the front lines of care." *Health affairs*, vol. 24, no. Suppl1, pp. W5–509, 2005.

[28] J. G. Anderson, "Information technology for detecting medication errors and adverse drug events," *Expert opinion on drug safety*, vol. 3, no. 5, pp. 449–455, 2004.

[29] Pharmacy Association Of Nova Scotia, "Filling a prescription (dispensing)," 2018. [Online]. Available: https://pans.ns.ca/public/pharmacy-services/filling-prescription-dispensing

[30] International Organization for Standardization (ISO), *ISO/IEC18092:2013-Information technology – Telecommunications and information exchange between systems – Near Field Communication – Interface and Protocol (NFCIP-1)*, International Organization for Standardization Std., 2013. [Online]. Available: https://www.iso.org/standard/38578.html

[31] European Computer Manufacturers Association (ECMA), *ECMA-340-Near Field Communication Interface and Protocol (NFCIP-1)*, European Computer Manufacturers Association (ECMA) Std., 2004. [Online]. Available: https://www.ecma-international.org/publications/files/ECMA-ST/ECMA-340.pdf

[32] International Organization for Standardization (ISO), *ISO/IEC14443-4:2018-Cards and security devices for personal identification – Contactless proximity objects – Part 4: Transmission protocol*, International Organization for Standardization (ISO) Std., 2018. [Online]. Available: https://www.iso.org/standard/73599.html

[33] Trusted Connectivity Alliance (TCA), "Secure Element Deployment and Host Card Emulation V10," website, 2018, accessed December, 2019. [Online]. Available: http://simalliance.org/wp-content/uploads/2015/03/Secure-Element-Deployment-Host-Card-Emulation-v1.0.pdf

[34] M. Roland and J. Langer and J. Scharinger, "Practical attack scenarios on secure element-enabled mobile devices," in *2012 4th International Workshop on Near Field Communication*, March 2012, pp. 19–24.

[35] M. Roland, J. Langer, and J. Scharinger, "Applying relay attacks to Google Wallet," in *2013 5th International Workshop on Near Field Communication (NFC)*. IEEE, 2013, pp. 1–6.

[36] C. H. Chen, I. C. Lin, and C. C. Yang, "Nfc attacks analysis and survey," in *2014 Eighth International Conference on Innovative Mobile and Internet Services in Ubiquitous Computing*, July 2014, pp. 458–462.

[37] T. Engel, M. Koennings, N. von Heydebrand, S. Goswami, and H. Krcmar, "A nfc-based concept for medication related patient services," in *Smart SysTech 2013; European Conference on Smart Objects, Systems and Technologies*, June 2013, pp. 1–10.

[38] L. Mertz, "Ultrasound? fetal monitoring? spectrometer? there's an app for that!: Biomedical smart phone apps are taking healthcare by storm," *IEEE Pulse*, vol. 3, no. 2, pp. 16–21, March 2012.

[39] Mobisante, "Smartphone Ultrasound: The MobiUS SP1 System," 2019. [Online]. Available: http://www.mobisante.com/products/product-overview/

[40] AirStrip, "AirStrip Accelerator Services," 2019. [Online]. Available: https://www.airstrip.com/airstrip

[41] P. Gupta, D. Agrawal, J. Chhabra, and P. K. Dhir, "Iot based smart healthcare kit," in *2016 International Conference on Computational Techniques in Information and Communication Technologies (ICCTICT)*, March 2016, pp. 237–242.

[42] J. Bravo, R. Hervas, C. Fuentes, G. Chavira, and S. W. Nava, "Tagging for nursing care," in *2008 Second International Conference on Pervasive Computing Technologies for Healthcare*, Jan 2008, pp. 305–307.

[43] A. Alzahrani, A. Alqhtani, H. Elmiligi, F. Gebali, and M. S. Yasein, “Nfc security analysis and vulnerabilities in healthcare applications,” in *2013 IEEE Pacific Rim Conference on Communications, Computers and Signal Processing (PACRIM)*, Aug 2013, pp. 302–305.

[44] M. Isomursu, M. Ervasti, and V. Törmänen, “Medication management support for vision impaired elderly: Scenarios and technological possibilities,” in *2nd International Symposium on Applied Sciences in Biomedical and Communication Technologies*, Nov 2009, pp. 1–6.

[45] R. Iglesias, J. Parra, C. Cruces, and N. G. de Segura, “Experiencing nfc-based touch for home healthcare,” in *Proceedings of the 2Nd International Conference on PErvasive Technologies Related to Assistive Environments*, ser. PETRA ’09. New York, NY, USA: ACM, 2009, pp. 27:1–27:4. [Online]. Available: http://doi.acm.org/10.1145/1579114.1579141

[46] S. Dunnebeil, F. Kobler, P. Koene, J. M. Leimeister, and H. Krcmar, “Encrypted nfc emergency tags based on the german telematics infrastructure,” in *2011 Third International Workshop on Near Field Communication*, Feb 2011, pp. 50–55.

[47] A. J. Jara, F. J. Belchi, A. F. Alcolea, J. Santa, M. A. Zamora-Izquierdo, and A. F. Gómez-Skarmeta, “A pharmaceutical intelligent information system to detect allergies and adverse drugs reactions based on internet of things,” in *2010 8th IEEE International Conference on Pervasive Computing and Communications Workshops (PERCOM Workshops)*, March 2010, pp. 809–812.

[48] A. J. Jara, A. F. Alcolea, M. A. Zamora, A. F. G. Skarmeta, and M. Alsaedy, “Drugs interaction checker based on IoT,” in *2010 Internet of Things (IOT)*. Tokyo, Japan: IEEE, Nov. 2010, pp. 1–8. [Online]. Available: http://ieeexplore.ieee.org/document/5678458/

[49] C. Thatcher and S. Acharya, “Pharmaceutical uses of blockchain technology,” in *2018 IEEE International Conference on Advanced Networks and Telecommunications Systems (ANTS)*. IEEE, 2018, pp. 1–6.

[50] S. Chakraborty, S. Aich, and H.-C. Kim, “A secure healthcare system design framework using blockchain technology,” in *2019 21st International Conference on Advanced Communication Technology (ICACT)*. IEEE, 2019, pp. 260–264.

[51] P. Li, S. D. Nelson, B. A. Malin, and Y. Chen, “Dmms: A decentralized blockchain ledger for the management of medication histories,” *Blockchain in Healthcare Today*, 2019.

[52] E. Hargan, “Determination that a public health emergency exists,” *Department of Health and Human Services*, 2017.

[53] C. for Disease Control, Prevention *et al.*, "Prescription opioid overdose data," *Injury prevention and control. Available at: https://www. cdc. gov/drugoverdose/data/overdose. html. Accessed January*, vol. 24, 2017.

[54] A. Ekblaw, A. Azaria, J. D. Halamka, and A. Lippman, "A case study for blockchain in healthcare:"medrec" prototype for electronic health records and medical research data," in *Proceedings of IEEE open & big data conference*, vol. 13, 2016, p. 13.

[55] L. Hendren and K. Kuzmeskas, "Health Nexus," CrushCrypto, Tech. Rep., 2017. [Online]. Available: https://crushcrypto.com/wp-content/uploads/2018/03/HLTH-Whitepaper.pdf

[56] J. Kalyanam, T. Katsuki, G. R. Lanckriet, and T. K. Mackey, "Exploring trends of nonmedical use of prescription drugs and polydrug abuse in the twittersphere using unsupervised machine learning," *Addictive behaviors*, vol. 65, pp. 289–295, 2017.

[57] X. Yan, J. Guo, Y. Lan, and X. Cheng, "A biterm topic model for short texts," in *Proceedings of the 22nd international conference on World Wide Web*, 2013, pp. 1445–1456.

[58] I. Yelin, O. Snitser, G. Novich, R. Katz, O. Tal, M. Parizade, G. Chodick, G. Koren, V. Shalev, and R. Kishony, "Personal clinical history predicts antibiotic resistance of urinary tract infections," *Nature medicine*, vol. 25, no. 7, pp. 1143–1152, 2019.

[59] X. Didelot and K. B. Pouwels, "Machine-learning-assisted selection of antibiotic prescription," *Nature medicine*, vol. 25, no. 7, pp. 1033–1034, 2019.

[60] G. Segal, A. Segev, A. Brom, Y. Lifshitz, Y. Wasserstrum, and E. Zimlichman, "Reducing drug prescription errors and adverse drug events by application of a probabilistic, machine-learning based clinical decision support system in an inpatient setting," *Journal of the American Medical Informatics Association*, vol. 26, no. 12, pp. 1560–1565, 2019.

[61] A. E. P. I. eHealth Initiative *et al.*, "Electronic prescribing: toward maximum value and rapid adoption," *Washington, DC*, 2004. [Online]. Available: http://www.providersedge.com/ehdocs/ehr_articles/Electronic_Prescribing-Toward_Maximum_Value_and_Rapid_Adoption.pdf

[62] D. Johnston, E. Pan, J. Walker, D. W. Bates, and B. Middleton, "The value of computerized provider order entry in ambulatory settings," *Boston, MA: Center for Information Technology Leadership*, 2003.

[63] eHealth Initiative *et al.*, "A clinician's guide to electronic prescribing," *Washington DC: serial online*, 2008.

[64] eHealth Observatory, *eHealth Observatory ePrescribing WorkflowHandbook v3.0*, 2011. [Online]. Available: http://www.ehealth.uvic.ca/resources/tools/WorkflowModeling/2011.02.18-ePrescribing_Workflow_Handbook-v3.0.pdf

[65] T. C. for Improving Medication Management, *A Cinician'sGuide to Electronic Prescribing*, 2011.

[66] M. Samadbeik, M. Ahmadi, F. Sadoughi, and A. Garavand, "A copmarative review of electronic prescription systems: Lessons learned from developed countries," *Journal of research in pharmacy practice*, vol. 6, no. 1, p. 3, 2017. [Online]. Available: http://www.jrpp.net/text.asp?2017/6/1/3/200993

[67] S. Nayani, *Report: 2017 Current Prescribing and Dispensing Landscape in Canada*. Canada Health Infoway, 2017. [Online]. Available: https://infocentral.infoway-inforoute.ca/en/resources/docs/1778-report-2017-current-prescribing-and-dispensing-landscape-in-canada/view-document

[68] B. R. Michael Green, *Improving Medication Management and Patient Safety through e-Prescribing*. Canada Health Infoway, 2017.

[69] PrescribeIT, *PrescribeIT Information Security Policy*. PrescribeIT, 2018. [Online]. Available: https://prescribeit.ca/component/edocman/169-prescribeit-information-security-policy/view-document?Itemid=106

[70] Canada Health Infoway, "Our approach to privacy," Website, 2019. [Online]. Available: https://www.prescribeit.ca/about-us/privacy

[71] Surescripts, "E-prescribing," 2018. [Online]. Available: http://surescripts.com/products-and-services/e-prescribing

[72] M. G. Joy, R. B. Ellyn, A. C. Dori, and R. C. Genna, "Physician practices e-prescribing and accessing information to improve prescribing decisions," *Health System Change (HSC) Research Brief No. 20*, 2011. [Online]. Available: http://www.hschange.org/CONTENT/1202/

[73] D. Castro, "Explaining international it application leadership: Health it," *Available at SSRN 1477486*, 2009.

[74] King, Christie, and Alami, "Process implications of e-prescribing information integration models: United states versus a middle east approach," *e-Service Journal*, vol. 5, no. 3, p. 15, 2007. [Online]. Available: https://www.jstor.org/stable/10.2979/esj.2007.5.3.15

[75] R. Gasbarro, "My pharmacist says he needs "prior authorization" – what's that all about?" *ConsumerAffairs*, 2015. [Online]. Available: https://www.consumeraffairs.com/news/my-pharmacist-says-he-needs-prior-authorization-whats-that-all-about-040615.html

[76] Surescripts, *Demystifying Electronic Prior Authorization (ePA)*. Surescripts, 2015. [Online]. Available: https://surescripts.com/docs/default-source/products-and-services/surescripts-white-paper---demystifying-electronic-prior-authorization_final.pdf

[77] The Australian Digital Health Agency, *Set up Electronic Transfer of Prescriptions (ETP) in your Organisation*. The Australian Digital Health Agency, 2019. [Online]. Available: https://www.digitalhealth.gov.au/get-started-with-digital-health/set-up/set-up-electronic-transfer-of-prescriptions

[78] ——, *Viewing and Uploading Prescription and Dispense Records*. The Australian Digital Health Agency, 2019, accessed August, 2019. [Online]. Available: https://www.digitalhealth.gov.au/using-the-my-health-record-system/digital-health-training-resources/software-demonstrations/viewing-and-uploading-prescription-and-dispense-records

[79] AustralianGovernment, *National e-Authentication Framework*. Australian Government, 2009, accessed August, 2019. [Online]. Available: https://www.finance.gov.au/sites/default/files/NeAFFramework.pdf

[80] eRx, "Privacy policy," 2018. [Online]. Available: https://www.erx.com.au/support/privacy-policy/

[81] MediSecure, "Medisecure how it works," 2019. [Online]. Available: http://www.medisecure.com.au/products-and-platforms/#etp

[82] ——, "Medisecure privacy policy," 2019. [Online]. Available: http://www.medisecure.com.au/privacy-policy/

[83] ——, "Medisecure patient consent," 2019. [Online]. Available: http://www.medisecure.com.au/patient-consent/

[84] N. B. S. Authority, *Requirements and Guidance for Endorsementin the Electronic Prescription Service(EPS)*. National Health Service, 2018. [Online]. Available: https://www.nhsbsa.nhs.uk/sites/default/files/2019-02/NHSBSAGuidanceforEndorsement_v7%200_August_2018_Final%20%28PDF%20396kb%29.pdf

[85] NHS Digital, "Spine," Aug. 2019, accessed August, 2019. [Online]. Available: https://digital.nhs.uk/services/spine

[86] P. S. N. C. PSNC, *Spine (NHS IT)*. Pharmaceutical Services Negotiating Committee PSNC, 2019, accessed August, 2019. [Online]. Available: https://psnc.org.uk/contract-it/pharmacy-it/spine-nhs-it/

[87] NHS Digital, *Electronic Prescription Service overview for developers*. NHS Digital, 2019. [Online]. Available: https://digital.nhs.uk/services/electronic-prescription-service/guidance-for-developers/guidance-for-developers-electronic-prescription-service-overview

[88] Pharmaceutical Services Negotiating Committee PSNC, *PSNC Briefing 005/18: Dealing with Smartcards – Quick reference guide*. Pharmaceutical Services Negotiating Committee PSNC, 2018. [Online]. Available: https://psnc.org.uk/wp-content/uploads/2018/01/PSNC-Briefing-005.18-Dealing-with-Smartcards-Quick-reference-guide.pdf

[89] NHS Digital, *Registration authorities and smartcards*. NHS Digital, 2019.

[90] Pharmaceutical Services Negotiating Committee PSNC, *The guiding principles of patient nomination*. Pharmaceutical Services Negotiating Committee PSNC, 2016, accessed August, 2019. [Online]. Available: https://psnc.org.uk/wp-content/uploads/2013/04/PSNC-Briefing-034.16-EPS-nomination-%E2%80%93-core-principles.pdf

[91] R. Hibberd, T. Cornford, V. Lichtner, W. Venters, and N. Barber, "England's electronic prescription service," in *Information Infrastructures within European Health Care*. Springer, Cham, 2017, pp. 109–128.

[92] HL7UK, "Hl7 delivers healthcare interoperability standards," Website, 2019. [Online]. Available: https://www.hl7.org.uk/

[93] HL7, "Introduction to hl7 standards," official website, 2019. [Online]. Available: http://www.hl7.org/implement/standards/index.cfm

[94] NHS Digital, *Electronic Prescription Service identifiers and what they mean*. National Health Service Digital, 2019. [Online]. Available: https://digital.nhs.uk

[95] ——, *Controlled drugs in the Electronic Prescription Service*. National Health Service Digital, 2019, accessed August, 2019. [Online]. Available: https://digital.nhs.uk/services/electronic-prescription-service/controlled-drugs

[96] P. Kierkegaard, "E-prescription across europe," *Health and Technology*, vol. 3, no. 3, pp. 205–219, Sep 2013. [Online]. Available: https://doi.org/10.1007/s12553-012-0037-0

[97] Japan Government, "Ministry of health, labor and welfare / conducting demonstration tests for full-scale operation of electronic prescriptions [translated from japanese]," Distribution news, 2019. [Online]. Available: https://www.ryutsuu.biz/government/l040343.html

[98] S. Nakagawa and N. Kume, “Pharmacy practice in japan,” *The Canadian Journal of Hospital Pharmacy*, vol. 70, no. 3, pp. 232–242, 2017. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491200/

[99] K. Masuda, “The electronic prescriptions that have been lifted and the actual operation (page 2) [translated from japanese],” *Digital Health*, 2016. [Online]. Available: https://tech.nikkeibp.co.jp/dm/atcl/feature/15/327441/051000066/?ST=health&P=2

[100] M. Akiyama and R. Nagai, “Information technology in health care: E-health for japanese health services,” *A Report of the CSIS global health policy center, The Center for Strategic and International Studies and the Health and Global Policy Institute*, 2012.

[101] HL7-FHIR-Release-4, “FHIR Overview,” website, Nov. 2019. [Online]. Available: https://www.hl7.org/fhir/overview.html

[102] S.-E. Öhlund, B. Åstrand, and G. Petersson, “Improving interoperability in eprescribing,” *Interact J Med Res*, vol. 1, no. 2, p. e17, Nov 2012. [Online]. Available: http://www.i-jmr.org/2012/2/e17/

[103] M. Grepstad and P. Kanavos, “A comparative analysis of coverage decisions for outpatient pharmaceuticals: Evidence from denmark, norway and sweden,” *Health Policy*, vol. 119, no. 2, pp. 203–211, 2015.

[104] G. O. Klein, “History of electronic prescriptions in sweden: From time-sharing systems via smartcards to edi,” in *IFIP Conference on History of Nordic Computing*. Springer, 2010, pp. 65–73.

[105] T. Hammar, S. Nyström, G. Petersson, B. Astrand, and T. Rydberg, “Patients satisfied with e-prescribing in sweden: A survey of a nationwide implementation,” *Journal of Pharmaceutical Health Services Research*, vol. 2, pp. 97–105, 06 2011.

[106] A. Krag, B. Hansen, and E. Nielsen, “eHealth in Denmark. eHealth as a part of a coherent Danish health care system,” technical report, Danish Ministry of Health, Copenhagen, Tech. Rep., 2012, accessed August, 2019. [Online]. Available: https://www.medcom.dk/media/1211/ehealth-in-denmark-ehealth-as-a-part-of-a-coherent-danish-health-care-system.pdf

[107] E. Zaghloul, T. Li, and J. Ren, “Security and privacy of electronic health records: Decentralized and hierarchical data sharing using smart contracts,” in *2019 International Conference on Computing, Networking and Communications (ICNC)*, Feb 2019, pp. 375–379.

[108] F. Lau, S. H. Rubin, M. H. Smith, and L. Trajkovic, "Distributed denial of service attacks," in *Smc 2000 conference proceedings. 2000 ieee international conference on systems, man and cybernetics. 'cybernetics evolving to systems, humans, organizations, and their complex interactions' (cat. no.0*, vol. 3, Oct 2000, pp. 2275–2280 vol.3.

[109] R. Anderson, *Security engineering: a guide to building dependable distributed systems*. John Wiley & Sons, 2020.

[110] H. K. Patil and R. Seshadri, "Big data security and privacy issues in healthcare," in *2014 IEEE international congress on big data*. IEEE, 2014, pp. 762–765.

[111] L. PONEMON, "Cost of a data breach study: Global overview," *Benchmark research sponsored by IBM Security Independently conducted by Ponemon Institute LLC*, 2018.

[112] T. B. Jensen and A. A. Thorseng, "Building national healthcare infrastructure: The case of the danish e-health portal," in *Information Infrastructures within European Health Care*. Springer, 2017, pp. 209–224.

[113] N. Sellberg and J. Eltes, "The swedish patient portal and its relation to the national reference architecture and the overall ehealth infrastructure," in *Information Infrastructures within European Health Care*. Springer, 2017, pp. 225–244.

[114] P. Kruus, "Developing an evaluation framework for the country-wide electronic prescribing system in estonia," *Tallinna Tehnikaülikool*, 2013.

[115] L. Patrao, R. Deveza, and H. Martins, "Pem-a new patient centred electronic prescription platform," *Procedia Technology*, vol. 9, pp. 1313–1319, 2013.

[116] J. Pereira, M. Beir, J. Teixeira, and R. J. Machado, "Patient-centric e-prescription services - an integrated system architecture proposal," in *2018 International Conference on Intelligent Systems (IS)*, Sep. 2018, pp. 576–583.

[117] H. Bell, S. Garfield, S. Khosla, C. Patel, and B. D. Franklin, "Mixed methods study of medication-related decision support alerts experienced during electronic prescribing for inpatients at an english hospital," *European Journal of Hospital Pharmacy*, vol. 26, no. 6, pp. 318–322, 2019.

[118] K. Kawamoto, C. A. Houlihan, E. A. Balas, and D. F. Lobach, "Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success," *Bmj*, vol. 330, no. 7494, p. 765, 2005.

[119] O. Ojeleye, A. Avery, V. Gupta, and M. Boyd, "The evidence for the effectiveness of safety alerts in electronic patient medication record systems at the point of pharmacy order entry: a systematic review," *BMC medical informatics and decision making*, vol. 13, no. 1, p. 69, 2013.

[120] Health and Social Care Information Centre (Great Britain), *Health and Social Care Information Centre (HSCIC) Annual Report and Accounts 2018-19*. NHS Digital, 2019, accessed August, 2019. [Online]. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/815360/NHS_Digital_annual_accounts_and_report_2018-19.pdf

[121] A. J. Grizzle, J. Horn, C. Collins, J. Schneider, D. C. Malone, B. Stottlemyer, and R. D. Boyce, "Identifying common methods used by drug interaction experts for finding evidence about potential drug-drug interactions: Web-based survey," *Journal of medical Internet research*, vol. 21, no. 1, p. e11182, 2019.

[122] T. M. Nester and L. S. Hale, "Effectiveness of a pharmacist-acquired medication history in promoting patient safety," *American Journal of Health-System Pharmacy*, vol. 59, no. 22, pp. 2221–2225, 2002.

[123] R. A. Blouin and M. L. Adams, "The role of the pharmacist in health care expanding and evolving," *North Carolina medical journal*, vol. 78, no. 3, pp. 165–167, 2017.

[124] P. W. Bush and R. Daniels, "Health care systems and transitions of care implication on interdisciplinary pharmacy services," *North Carolina medical journal*, vol. 78, no. 3, pp. 177–180, 2017.

[125] J. L. Belden, P. Wegier, J. Patel, A. Hutson, C. Plaisant, J. L. Moore, N. J. Lowrance, S. A. Boren, and R. J. Koopman, "Designing a medication timeline for patients and physicians," *Journal of the American Medical Informatics Association*, vol. 26, no. 2, pp. 95–105, 2018.

[126] Surescripts, "Electronic prescribing for controlled substances," Surescripts Website, 2018. [Online]. Available: https://surescripts.com/enhance-prescribing/e-prescribing/e-prescribing-for-controlled-substances/#

[127] D. E. Administration, *Electronic Prescriptions for Controlled Substances Final Rule*. US Federal Register, 2010, no. 2013-06918. [Online]. Available: https://bit.ly/3vQnf2q

[128] Drug Enforcement Administration, *Electronic Prescriptions for Controlled Substances Notice of Approved Certification Process*. US Federal Register, 2013, no. 2010-6687. [Online]. Available: https://www.federalregister.gov/documents/2010/03/31/2010-6687/electronic-prescriptions-for-controlled-substances

[129] D. Bender and K. Sartipi, "Hl7 fhir: An agile and restful approach to healthcare information exchange," in *Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems*, June 2013, pp. 326–331.

[130] R. Saripalle, C. Runyan, and M. Russell, "Using hl7 fhir to achieve interoperability in patient health record," *Journal of biomedical informatics*, vol. 94, p. 103188, 2019.

[131] M. Mäkinen, P. Rautava, J. Forsström, and M. Äärimaa, “Electronic prescriptions are slowly spreading in the european union,” *Telemedicine and e-Health*, vol. 17, no. 3, pp. 217–222, 2011.

[132] P. Doupi, E. Renko, S. Giest, J. Heywood, and J. Dumortier, “Country brief: Sweden,” *European Commission, Bonn/Brussels*, 2010.

[133] S. Goundrey-Smith, *Information technology in pharmacy: an integrated approach*, ser. Health informatics. Springer, 2013, OCLC: ocn773666076.

[134] J. Eichwald, “Impact of electronic health records implementation on the early detection hearing and intervention programs,” website presentation "Discretionary Advisory Committee on Heritable Disorders in Newborns and Children", p. 54, May 2014.

[135] I. Chouvarda and N. Maglaveras, “Medical informatics education & research in greece,” *Yearbook of medical informatics*, vol. 24, no. 01, pp. 220–226, 2015.

[136] Q. Chen, J. Lambright, and S. Abdelwahed, “Towards autonomic security management of healthcare information systems,” in *2016 IEEE First International Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE)*, June 2016, pp. 113–118.

[137] J. Henderson, A. Pollack, J. Gordon, and G. Miller, “Technology in practice-gp computer use by age (vol 43, pg 831, 2014),” *AUSTRALIAN FAMILY PHYSICIAN*, vol. 44, no. 1-2, pp. 8–8, 2015.

[138] C. P. Association, “Recommendations for the implementation of electronic prescriptions in canada,” pharmacists.ca, 2009. [Online]. Available: https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/PPRecommendationsElectronicPrescriptions.pdf

[139] E. Ball, D. W. Chadwick, and D. Mundy, “Patient privacy in electronic prescription transfer,” *IEEE Security & Privacy*, vol. 1, no. 2, pp. 77–80, 2003.

[140] M. A. Azad, J. Arshad, S. Mahmoud, K. Salah, and M. Imran, “A privacy-preserving framework for smart context-aware healthcare applications,” *Transactions on Emerging Telecommunications Technologies*, vol. n/a, no. n/a, p. e3634, 2019, e3634 ett.3634. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/ett.3634

[141] S. Park and J. Moon, “Strategic approach towards clinical information security,” in *Improving health management through clinical decision support systems*. IGI Global, 2016, pp. 329–359.

[142] F. Al-Nayadi and J. H. Abawajy, “An authorization policy management framework for dynamic medical data sharing,” in *The 2007 International Conference on Intelligent Pervasive Computing (IPC 2007)*, Oct 2007, pp. 313–318.

[143] J. Hatch, T. Becker, and J. T. Fish, "Difference between pharmacist-obtained and physician-obtained medication histories in the intensive care unit," *Hospital Pharmacy*, vol. 46, no. 4, pp. 262–268, 2011.

[144] N. M. A. LaPointe and J. G. Jollis, "Medication errors in hospitalized cardiovascular patients," *Archives of Internal Medicine*, vol. 163, no. 12, pp. 1461–1466, 2003.

[145] V. C. Tam, S. R. Knowles, P. L. Cornish, N. Fine, R. Marchesano, and E. E. Etchells, "Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review," *Cmaj*, vol. 173, no. 5, pp. 510–515, 2005.

[146] M. K. Carter, D. M. Allin, L. A. Scott, and D. Grauer, "Pharmacist-acquired medication histories in a university hospital emergency department," *American journal of health-system pharmacy*, vol. 63, no. 24, pp. 2500–2503, 2006.

[147] T. Vira, M. Colquhoun, and E. Etchells, "Reconcilable differences: correcting medication errors at hospital admission and discharge," *BMJ Quality & Safety*, vol. 15, no. 2, pp. 122–126, 2006.

[148] E. Ammenwerth, P. Schnell-Inderst, C. Machan, and U. Siebert, "The effect of electronic prescribing on medication errors and adverse drug events: a systematic review," *Journal of the American Medical Informatics Association*, vol. 15, no. 5, pp. 585–600, 2008.

[149] S. Eslami, A. Abu-Hanna, and N. F. De Keizer, "Evaluation of outpatient computerized physician medication order entry systems: a systematic review," *Journal of the American Medical Informatics Association*, vol. 14, no. 4, pp. 400–406, 2007.

[150] R. Kaushal, K. G. Shojania, and D. W. Bates, "Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review," *Archives of internal medicine*, vol. 163, no. 12, pp. 1409–1416, 2003.

[151] M. Prgomet, L. Li, Z. Niazkhani, A. Georgiou, and J. I. Westbrook, "Impact of commercial computerized provider order entry (cpoe) and clinical decision support systems (cdsss) on medication errors, length of stay, and mortality in intensive care units: a systematic review and meta-analysis," *Journal of the American Medical Informatics Association*, vol. 24, no. 2, pp. 413–422, 2016.

[152] K. M. Cresswell, D. W. Bates, R. Williams, Z. Morrison, A. Slee, J. Coleman, A. Robertson, and A. Sheikh, "Evaluation of medium-term consequences of implementing commercial computerized physician order entry and clinical decision support prescribing systems in two 'early adopter'hospitals," *Journal of the American Medical Informatics Association*, vol. 21, no. e2, pp. e194–e202, 2014.

[153] P. J. Embi and A. C. Leonard, "Evaluating alert fatigue over time to ehr-based clinical trial alerts: findings from a randomized controlled study," *Journal of the American Medical Informatics Association*, vol. 19, no. e1, pp. e145–e148, 2012.

[154] H. Van Der Sijs, J. Aarts, A. Vulto, and M. Berg, "Overriding of drug safety alerts in computerized physician order entry," *Journal of the American Medical Informatics Association*, vol. 13, no. 2, pp. 138–147, 2006.

[155] B. Healthcare, "5 epic contracts and their costs so far in 2016," 2016. [Online]. Available: https://www.beckershospitalreview.com/healthcare-information-technology/5-epic-contracts-and-their-costs-so-far-in-2016.html

[156] C. Esposito, A. De Santis, G. Tortora, H. Chang, and K.-K. R. Choo, "Blockchain: A panacea for healthcare cloud-based data security and privacy?" *IEEE Cloud Computing*, vol. 5, no. 1, pp. 31–37, 2018.

[157] S. Schmiedl, M. Rottenkolber, J. Hasford, D. Rottenkolber, K. Farker, B. Drewelow, M. Hippius, K. Saljé, and P. Thürmann, "Self-medication with over-the-counter and prescribed drugs causing adverse-drug-reaction-related hospital admissions: results of a prospective, long-term multi-centre study," *Drug safety*, vol. 37, no. 4, pp. 225–235, 2014.

[158] G. N. Norén, R. Sundberg, A. Bate, and I. R. Edwards, "A statistical methodology for drug–drug interaction surveillance," *Statistics in medicine*, vol. 27, no. 16, pp. 3057–3070, 2008.

[159] A. Flynn, "Using artificial intelligence in health-system pharmacy practice: Finding new patterns that matter," *American Journal of Health-System Pharmacy*, vol. 76, no. 9, pp. 622–627, 04 2019. [Online]. Available: https://doi.org/10.1093/ajhp/zxz018

[160] B. Aldughayfiq and S. Sampalli, "A system to lower the risk of dispensing medication errors at pharmacies using nfc," in *2018 IEEE International Conference on Internet of Things (iThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData)*, July 2018, pp. 196–202.

[161] Google Support, "Fingerprint data is stored securely," Google inc website, 2021. [Online]. Available: https://support.google.com/pixelphone/answer/6300638?hl=en#zippy=%2Cfingerprint-hardware-security-requirements

[162] Apple Support, "About Touch ID advanced security technology," Apple inc website, 2021. [Online]. Available: https://support.apple.com/en-ca/HT204587

[163] Z. Wang, Z. Xu, W. Xin, and Z. Chen, "Implementation and analysis of a practical nfc relay attack example," in *2012 Second International Conference on Instrumentation, Measurement, Computer, Communication and Control*, Dec 2012, pp. 143–146.

[164] C. W. Turner, J. R. Lewis, and J. Nielsen, "Determining usability test sample size," *International encyclopedia of ergonomics and human factors*, vol. 3, no. 2, pp. 3084–3088, 2006.

[165] J. Rubin and D. Chisnell, "How to plan, design, and conduct effective tests," *Handbook of usability testing*, p. 348, 2008.

[166] R. A. Virzi, "Refining the test phase of usability evaluation: How many subjects is enough?" *Human factors*, vol. 34, no. 4, pp. 457–468, 1992.

[167] W. Hwang and G. Salvendy, "Number of people required for usability evaluation: the 10±2 rule," *Communications of the ACM*, vol. 53, no. 5, pp. 130–133, 2010.

[168] J. W. Creswell and C. N. Poth, *Qualitative inquiry and research design: Choosing among five approaches*. Sage publications, 2016.

[169] J. Nielsen, "How many test users in a usability study," *Nielsen Norman Group*, vol. 4, no. 06, 2012.

[170] F. D. Davis, "Perceived usefulness, perceived ease of use, and user acceptance of information technology," *MIS quarterly*, pp. 319–340, 1989.

[171] F. D. Davis, R. P. Bagozzi, and P. R. Warshaw, "User acceptance of computer technology: a comparison of two theoretical models," *Management science*, vol. 35, no. 8, pp. 982–1003, 1989.

[172] Statistics.laerd, "One-way anova in spss statistics," Website, 2018. [Online]. Available: https://statistics.laerd.com/spss-tutorials/one-way-anova-using-spss-statistics.php

[173] E. Schmider, M. Ziegler, E. Danay, L. Beyer, and M. Bühner, "Is it really robust?" *Methodology*, 2010.

[174] S. S. Shapiro and M. B. Wilk, "An analysis of variance test for normality (complete samples)," *Biometrika*, vol. 52, no. 3/4, pp. 591–611, 1965.

[175] N. M. Razali, Y. B. Wah *et al.*, "Power comparisons of shapiro-wilk, kolmogorov-smirnov, lilliefors and anderson-darling tests," *Journal of statistical modeling and analytics*, vol. 2, no. 1, pp. 21–33, 2011.

[176] D. Cramer, *Fundamental statistics for social research: step-by-step calculations and computer techniques using SPSS for Windows*. Psychology Press, 1998.

[177] D. Cramer and D. L. Howitt, *The Sage dictionary of statistics: a practical resource for students in the social sciences*. Sage, 2004.

[178] D. P. Doane and L. E. Seward, "Measuring skewness: a forgotten statistic?" *Journal of statistics education*, vol. 19, no. 2, 2011.

[179] M. L. McHugh, "The chi-square test of independence," *Biochemia medica*, vol. 23, no. 2, pp. 143–149, 2013.

[180] J. Cohen, "A power primer." *Psychological bulletin*, vol. 112, no. 1, p. 155, 1992.

[181] C. Sammut and G. I. Webb, *Encyclopedia of machine learning*. Springer Science & Business Media, 2011.

[182] S. Pongnumkul, C. Siripanpornchana, and S. Thajchayapong, "Performance analysis of private blockchain platforms in varying workloads," in *2017 26th International Conference on Computer Communication and Networks (ICCCN)*. IEEE, 2017, pp. 1–6.

[183] M. Niranjanamurthy, M. Kiran, S. Anupama, and C. Dharmendra, "Comparative study on performance testing with JMeter," *Int. J. Adv. Res. Comput. Commun. Eng.*, vol. 5, no. 2, pp. 70–76, 2016.

[184] E. H. Halili, *Apache JMeter: A practical beginner's guide to automated testing and performance measurement for your websites*. Packt Publishing Ltd, 2008.

[185] JMeter, Apache, "Apache JMeter," *Online.(2016). http://jmeter. apache. org/-Visited*, pp. 04–25, 2017.

[186] B. Aldughayfiq and S. Sampalli, "Digital health in physicians' and pharmacists' office: A comparative study of e-prescription systems' architecture and digital security in eight countries," *OMICS: A Journal of Integrative Biology*, vol. 25, no. 2, pp. 102–122, 2021.

[187] K. L. Lapane, M. E. Waring, C. Dubé, and K. L. Schneider, "E-prescribing and patient safety: results from a mixed method study," *The American journal of pharmacy benefits*, vol. 3, no. 2, p. e24, 2011.

[188] B. Åstrand, E. Montelius, G. Petersson, and A. Ekedahl, "Assessment of eprescription quality: an observational study at three mail-order pharmacies," *BMC medical informatics and decision making*, vol. 9, no. 1, pp. 1–8, 2009.

[189] L. Hellström, K. Waern, E. Montelius, B. Åstrand, T. Rydberg, and G. Petersson, "Physicians' attitudes towards eprescribing–evaluation of a swedish full-scale implementation," *BMC medical informatics and decision making*, vol. 9, no. 1, pp. 1–10, 2009.

[190] W. S. Tan, J. S. Phang, and L. K. Tan, "Evaluating user satisfaction with an electronic prescription system in a primary care group," *Annals Academy of Medicine Singapore*, vol. 38, no. 6, p. 494, 2009.

[191] P. Donyai, K. O'Grady, A. Jacklin, N. Barber, and B. D. Franklin, "The effects of electronic prescribing on the quality of prescribing," *British journal of clinical pharmacology*, vol. 65, no. 2, pp. 230–237, 2008.

[192] C. P. Schade, F. M. Sullivan, S. De Lusignan, and J. Madeley, "e-prescribing, efficiency, quality: lessons from the computerization of uk family practice," *Journal of the American Medical Informatics Association*, vol. 13, no. 5, pp. 470–475, 2006.

[193] D. Papshev and A. Peterson, "Electronic prescribing in ambulatory practice: promises, pitfalls, and potential solutions." *The American journal of managed care*, vol. 7, no. 7, pp. 725–736, 2001.

[194] S. T. McMullin, T. P. Lonergan, and C. S. Rynearson, "Twelve-month drug cost savings related to use of an electronic prescribing system with integrated decision support in primary care," *Journal of Managed Care Pharmacy*, vol. 11, no. 4, pp. 322–332, 2005.

[195] J. M. Teich, P. R. Merchia, J. L. Schmiz, G. J. Kuperman, C. D. Spurr, and D. W. Bates, "Effects of computerized physician order entry on prescribing practices," *Archives of internal medicine*, vol. 160, no. 18, pp. 2741–2747, 2000.

[196] R. Kaushal, L. M. Kern, Y. Barrón, J. Quaresimo, and E. L. Abramson, "Electronic prescribing improves medication safety in community-based office practices," *J Gen Intern Med*, vol. 25, no. 6, pp. 530–536, Jun. 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2869410/

[197] E. Lämsä, J. Timonen, and R. Ahonen, "Pharmacy customers' experiences with electronic prescriptions: cross-sectional survey on nationwide implementation in finland," *Journal of medical Internet research*, vol. 20, no. 2, p. e68, 2018.

[198] G. Eysenbach, "What is e-health?" *Journal of medical Internet research*, vol. 3, no. 2, p. e20, 2001.

[199] M. Gabriel and M. Swain, "ONC Data Brief No. 18. Washington (DC): US Office of the National Coordinator for Health Information Technology; 2014. E-prescribing trends in the United States." [Online]. Available: https://www.healthit.gov/sites/default/files/oncdatabriefe-prescribingincreases2014.pdf

[200] J. Brennan, A. McElligott, and N. Power, "National health models and the adoption of e-health and e-prescribing in primary care–new evidence from Europe," *Journal of Innovation in Health Informatics*, vol. 22, no. 4, pp. 399–408, 2015.

[201] Health Information and Quality Authority (HIQA), “Eprescribing and electronic transfer of prescriptions: an international review,” Health Information and Quality Authority (HIQA), The Irish Health Repository, 2012.

[202] T. Steinschaden, G. Petersson, and B. Åstrand, “Physicians’ attitudes towards eprescribing: a comparative web survey in austria and sweden,” *Journal of Innovation in Health Informatics*, vol. 17, no. 4, pp. 241–247, 2009.

[203] P. N. Panvelkar, B. Saini, and C. Armour, “Measurement of patient satisfaction with community pharmacy services: a review,” *Pharmacy world & science*, vol. 31, no. 5, pp. 525–537, 2009.

[204] M. Asadi-Lari, M. Tamburini, and D. Gray, “Patients’ needs, satisfaction, and health related quality of life: towards a comprehensive model,” *Health and quality of life outcomes*, vol. 2, no. 1, pp. 1–15, 2004.

[205] K. L. Lapane, R. K. Rosen, and C. Dubé, “Perceptions of e-prescribing efficiencies and inefficiencies in ambulatory care,” *International journal of medical informatics*, vol. 80, no. 1, pp. 39–46, 2011.

[206] O. K. Odukoya and M. A. Chui, “Relationship between e-prescriptions and community pharmacy workflow,” *Journal of the American Pharmacists Association*, vol. 52, no. 6, pp. e168–e174, 2012.

[207] M.-P. Gagnon, É.-R. Nsangou, J. Payne-Gagnon, S. Grenier, and C. Sicotte, “Barriers and facilitators to implementing electronic prescription: a systematic review of user groups’ perceptions,” *Journal of the American Medical Informatics Association*, vol. 21, no. 3, pp. 535–541, 2014.

[208] H. Kauppinen, R. Ahonen, and J. Timonen, “The impact of electronic prescriptions on medication safety in Finnish community pharmacies: a survey of pharmacists,” *International journal of medical informatics*, vol. 100, pp. 56–62, 2017.

[209] H. Kauppinen, R. Ahonen, P. Mäntyselkä, and J. Timonen, “Medication safety and the usability of electronic prescribing as perceived by physicians—a semistructured interview among primary health care physicians in finland,” *Journal of evaluation in clinical practice*, vol. 23, no. 6, pp. 1187–1194, 2017.

[210] K. L. Lapane, C. Dubé, K. L. Schneider, and B. J. Quilliam, “Patient perceptions regarding electronic prescriptions: is the geriatric patient ready?” *Journal of the American Geriatrics Society*, vol. 55, no. 8, pp. 1254–1259, 2007.

[211] R. L. Duffy, S. Yiu, E. Molokhia, R. Walker, and R. A. Perkins, “Effects of electronic prescribing on the clinical practice of a family medicine residency,” *Fam Med*, vol. 42, no. 5, pp. 358–63, 2010.

[212] A. R. Bergeron, J. R. Webb, M. Serper, A. D. Federman, W. H. Shrank, A. L. Russell, and M. S. Wolf, "Impact of electronic prescribing on medication use in ambulatory care." *The American journal of managed care*, vol. 19, no. 12, pp. 1012–1017, 2013.

[213] G. L. Cochran, L. Lander, M. Morien, D. E. Lomelin, J. Brittin, C. Reker, and D. G. Klepser, "Consumer opinions of health information exchange, e-prescribing, and personal health records," *Perspectives in health information management*, vol. 12, no. Fall, 2015.

[214] L. J. Schleiden, O. K. Odukoya, and M. A. Chui, "Older adults' perceptions of e-prescribing: impact on patient care," *Perspectives in health information management*, vol. 12, no. Winter, 2015.

[215] G. Lau, J. Ho, S. Lin, K. Yeoh, T. Wan, and M. Hodgkinson, "Patient and clinician perspectives of an integrated electronic medication prescribing and dispensing system: A qualitative study at a multisite australian hospital network," *Health Information Management Journal*, vol. 48, no. 1, pp. 12–23, 2019.

[216] T. Porteous, C. Bond, R. Robertson, P. Hannaford, and E. Reiter, "Electronic transfer of prescription-related information: comparing views of patients, general practitioners, and pharmacists." *British Journal of General Practice*, vol. 53, no. 488, pp. 204–209, 2003. [Online]. Available: https://bjgp.org/content/53/488/204

[217] Kijiji, "Kijiji Research Study," Dec. 2020. [Online]. Available: https://www.kijiji.ca/b-gta-greater-toronto-area/research-study/k0l1700272

[218] Amazon Mechanical Turk, "About Amazon Mechanical Turk (FAQs)," website, December 2020. [Online]. Available: https://www.mturk.com/

[219] ——, "Access a global, on-demand, 24x7 workforce," website, December 2020. [Online]. Available: https://www.mturk.com/worker/help

[220] ——, "Qualifications and worker task quality," website, December 2020. [Online]. Available: https://blog.mturk.com/qualifications-and-worker-task-quality-best-practices-886f1f4e03fc

[221] Linkedin, "About linkedin," website, December 2020. [Online]. Available: https://about.linkedin.com/?trk=homepage-basic_directory_aboutUrl

[222] S. Jamieson, "Likert scales: how to (ab)use them," *Medical Education*, vol. 38, no. 12, pp. 1217–1218, 2004.

[223] N. Haller, C. Metz, P. Nesser, and M. Straw, "A one-time password system," *Network Working Group Request for Comments*, vol. 2289, 1998.

[224] J. Cash, "Alert fatigue," *American Journal of Health-System Pharmacy*, vol. 66, no. 23, pp. 2098–2101, 2009.

[225] J. H. Friedman, "Greedy function approximation: a gradient boosting machine," *Annals of statistics*, pp. 1189–1232, 2001.

[226] G. P. Velo and P. Minuz, "Medication errors: prescribing faults and prescription errors," *British journal of clinical pharmacology*, vol. 67, no. 6, pp. 624–628, 2009.

[227] S. Hoffman and A. Podgurski, "Drug-drug interaction alerts: emphasizing the evidence," *. Louis UJ Health L. & Pol'y*, vol. 5, p. 297, 2011.

[228] A. B. McCoy, E. J. Thomas, M. Krousel-Wood, and D. F. Sittig, "Clinical decision support alert appropriateness: a review and proposal for improvement," *Ochsner Journal*, vol. 14, no. 2, pp. 195–202, 2014.

[229] R. Rozenblum, R. Rodriguez-Monguio, L. A. Volk, K. J. Forsythe, S. Myers, M. McGurrin, D. H. Williams, D. W. Bates, G. Schiff, and E. Seoane-Vazquez, "Using a machine learning system to identify and prevent medication prescribing errors: a clinical and cost analysis evaluation," *The Joint Commission Journal on Quality and Patient Safety*, vol. 46, no. 1, pp. 3–10, 2020.

[230] G. D. Schiff, L. A. Volk, M. Volodarskaya, D. H. Williams, L. Walsh, S. G. Myers, D. W. Bates, and R. Rozenblum, "Screening for medication errors using an outlier detection system," *Journal of the American Medical Informatics Association*, vol. 24, no. 2, pp. 281–287, 2017.

[231] G. Segal, A. Segev, A. Brom, Y. Lifshitz, Y. Wasserstrum, and E. Zimlichman, "Reducing drug prescription errors and adverse drug events by application of a probabilistic, machine-learning based clinical decision support system in an inpatient setting," *Journal of the American Medical Informatics Association*, vol. 26, no. 12, pp. 1560–1565, 2019.

[232] K. Sharma and R. Nandal, "A literature study on machine learning fusion with iot," in *2019 3rd International Conference on Trends in Electronics and Informatics (ICOEI)*. IEEE, 2019, pp. 1440–1445.

[233] O. Simeone, "A very brief introduction to machine learning with applications to communication systems," *IEEE Transactions on Cognitive Communications and Networking*, vol. 4, no. 4, pp. 648–664, 2018.

[234] C. Malhotra, V. Kotwal, and S. Dalal, "Ethical framework for machine learning," in *2018 ITU Kaleidoscope: Machine Learning for a 5G Future (ITU K)*. IEEE, 2018, pp. 1–8.

[235] P. Singh, S. Singh, and D. Singh, "An introduction and review on machine learning applications in medicine and healthcare," in *2019 IEEE Conference on Information and Communication Technology*. IEEE, 2019, pp. 1–6.

[236] G. Seni and J. F. Elder, "Ensemble methods in data mining: improving accuracy through combining predictions," *Synthesis lectures on data mining and knowledge discovery*, vol. 2, no. 1, pp. 1–126, 2010.

[237] A. Dey, "Machine learning algorithms: a review," *International Journal of Computer Science and Information Technologies*, vol. 7, no. 3, pp. 1174–1179, 2016.

[238] M. LEPE, "Our products | medaware alerting system." 2021, accessed January 24, 2021. [Online]. Available: http://www.medaware.com/our-products/

[239] C. McMaster, D. Liew, C. Keith, P. Aminian, and A. Frauman, "A machine-learning algorithm to optimise automated adverse drug reaction detection from clinical coding," *Drug safety*, vol. 42, no. 6, pp. 721–725, 2019.

[240] K. Ouchi, C. Lindvall, P. R. Chai, and E. W. Boyer, "Machine learning to predict, detect, and intervene older adults vulnerable for adverse drug events in the emergency department," *Journal of Medical Toxicology*, vol. 14, no. 3, pp. 248–252, 2018.

[241] P. A. of Nova Scotia (PANS), "Filling a prescription (dispensing)," 2020. [Online]. Available: https://pans.ns.ca/public/pharmacy-services/filling-prescription-dispensing

[242] B. J. Kenny and C. V. Preuss, "Pharmacy prescription requirements," *StatPearls [Internet]*, 2020.

[243] P. Cerda, G. Varoquaux, and B. Kégl, "Similarity encoding for learning with dirty categorical variables," *Machine Learning*, vol. 107, no. 8, pp. 1477–1494, 2018.

[244] K. Potdar, T. S. Pardawala, and C. D. Pai, "A comparative study of categorical variable encoding techniques for neural network classifiers," *International journal of computer applications*, vol. 175, no. 4, pp. 7–9, 2017.

[245] W. D. McGinnis, C. Siu, S. Andre, and H. Huang, "Category encoders: a scikit-learn-contrib package of transformers for encoding categorical data," *Journal of Open Source Software*, vol. 3, no. 21, p. 501, 2018.

[246] E. Bisong, "Introduction to scikit-learn," in *Building Machine Learning and Deep Learning Models on Google Cloud Platform*. Springer, 2019, pp. 215–229.

[247] A. K. Verma and S. Pal, "Prediction of skin disease with three different feature selection techniques using stacking ensemble method," *Applied biochemistry and biotechnology*, pp. 1–20, 2019.

[248] E. G. Brown, L. Wood, and S. Wood, "The medical dictionary for regulatory activities (meddra)," *Drug safety*, vol. 20, no. 2, pp. 109–117, 1999.

[249] P. H. Swain and H. Hauska, “The decision tree classifier: Design and potential,” *IEEE Transactions on Geoscience Electronics*, vol. 15, no. 3, pp. 142–147, 1977.

[250] A. H. Jahromi and M. Taheri, “A non-parametric mixture of gaussian naive bayes classifiers based on local independent features,” in *2017 Artificial Intelligence and Signal Processing Conference (AISP)*. IEEE, 2017, pp. 209–212.

[251] D. Berrar, “Bayes’ theorem and naive bayes classifier,” *Encyclopedia of Bioinformatics and Computational Biology: ABC of Bioinformatics; Elsevier Science Publisher: Amsterdam, The Netherlands*, pp. 403–412, 2018.

[252] T. M. Ma, K. YAMAMORI, and A. Thida, “A comparative approach to naïve bayes classifier and support vector machine for email spam classification,” in *2020 IEEE 9th Global Conference on Consumer Electronics (GCCE)*. IEEE, 2020, pp. 324–326.

[253] M. M. Islam, H. Iqbal, M. R. Haque, and M. K. Hasan, “Prediction of breast cancer using support vector machine and k-nearest neighbors,” in *2017 IEEE Region 10 Humanitarian Technology Conference (R10-HTC)*. IEEE, 2017, pp. 226–229.

[254] N. E. M. Isa, A. Amir, M. Z. Ilyas, and M. S. Razalli, “The performance analysis of k-nearest neighbors (k-nn) algorithm for motor imagery classification based on eeg signal,” in *MATEC web of conferences*, vol. 140. EDP Sciences, 2017, p. 01024.

[255] S. Kabiraj, M. Raihan, N. Alvi, M. Afrin, L. Akter, S. A. Sohagi, and E. Podder, “Breast cancer risk prediction using xgboost and random forest algorithm,” in *2020 11th International Conference on Computing, Communication and Networking Technologies (ICCCNT)*, 2020, pp. 1–4.

[256] S. Ghosh and C. Banerjee, “A predictive analysis model of customer purchase behavior using modified random forest algorithm in cloud environment,” in *2020 IEEE 1st International Conference for Convergence in Engineering (ICCE)*. IEEE, 2020, pp. 239–244.

[257] T. Chen and C. Guestrin, “Xgboost: A scalable tree boosting system,” in *Proceedings of the 22nd acm sigkdd international conference on knowledge discovery and data mining*, 2016, pp. 785–794.

[258] J. Friedman, T. Hastie, R. Tibshirani *et al.*, “Additive logistic regression: a statistical view of boosting (with discussion and a rejoinder by the authors),” *Annals of statistics*, vol. 28, no. 2, pp. 337–407, 2000.

[259] T. Fawcett, “An introduction to roc analysis,” *Pattern recognition letters*, vol. 27, no. 8, pp. 861–874, 2006.

[260] F. Bagattini, I. Karlsson, J. Rebane, and P. Papapetrou, "A classification framework for exploiting sparse multi-variate temporal features with application to adverse drug event detection in medical records," *BMC medical informatics and decision making*, vol. 19, no. 1, pp. 1–20, 2019.

[261] A. P. Bradley, "The use of the area under the roc curve in the evaluation of machine learning algorithms," *Pattern recognition*, vol. 30, no. 7, pp. 1145–1159, 1997.

[262] J. A. Hanley and B. J. McNeil, "The meaning and use of the area under a receiver operating characteristic (roc) curve." *Radiology*, vol. 143, no. 1, pp. 29–36, 1982.

[263] M. Mettler, "Blockchain technology in healthcare: The revolution starts here," in *2016 IEEE 18th international conference on e-health networking, applications and services (Healthcom)*. IEEE, 2016, pp. 1–3.

[264] G. Zyskind, O. Nathan *et al.*, "Decentralizing privacy: Using blockchain to protect personal data," in *2015 IEEE Security and Privacy Workshops*. IEEE, 2015, pp. 180–184.

[265] C. Dannen, *Introducing Ethereum and solidity*. Springer, 2017, vol. 318.

[266] G. Wood *et al.*, "Ethereum: A secure decentralised generalised transaction ledger," *Ethereum project yellow paper*, vol. 151, no. 2014, pp. 1–32, 2014.

[267] C. Cachin *et al.*, "Architecture of the hyperledger blockchain fabric," in *Workshop on distributed cryptocurrencies and consensus ledgers*, vol. 310, no. 4. Chicago, IL, 2016.

[268] E. Androulaki, A. Barger, V. Bortnikov, C. Cachin, K. Christidis, A. De Caro, D. Enyeart, C. Ferris, G. Laventman, Y. Manevich *et al.*, "Hyperledger fabric: a distributed operating system for permissioned blockchains," in *Proceedings of the thirteenth EuroSys conference*, 2018, pp. 1–15.

[269] T. McConaghy, R. Marques, A. Müller, D. De Jonghe, T. McConaghy, G. McMullen, R. Henderson, S. Bellemare, and A. Granzotto, "Bigchaindb: a scalable blockchain database," *white paper, BigChainDB*, 2016.

[270] F. Tian, "A supply chain traceability system for food safety based on HACCP, blockchain & Internet of things," in *2017 International conference on service systems and service management*. IEEE, 2017, pp. 1–6.

[271] L. Dabbish, C. Stuart, J. Tsay, and J. Herbsleb, "Social coding in github: transparency and collaboration in an open software repository," in *Proceedings of the ACM 2012 conference on computer supported cooperative work*, 2012, pp. 1277–1286.

[272] M. Adil, "Blockchain python tutorial," https://github.com/adilmoujahid/blockchain-python-tutorial, 2018.

[273] P. Sevcik, "Defining the application performance index," *Business Communications Review*, vol. 20, 2005.

[274] C. Fan, S. Ghaemi, H. Khazaei, and P. Musilek, "Performance evaluation of blockchain systems: A systematic survey," *IEEE Access*, vol. 8, pp. 126 927–126 950, 2020.

[275] T. T. A. Dinh, J. Wang, G. Chen, R. Liu, B. C. Ooi, and K.-L. Tan, "Blockbench: A framework for analyzing private blockchains," in *Proceedings of the 2017 ACM International Conference on Management of Data*, 2017, pp. 1085–1100.

[276] A. Baliga, N. Solanki, S. Verekar, A. Pednekar, P. Kamat, and S. Chatterjee, "Performance characterization of hyperledger fabric," in *2018 Crypto Valley conference on blockchain technology (CVCBT)*. IEEE, 2018, pp. 65–74.

[277] S. Benahmed, I. Pidikseev, R. Hussain, J. Lee, S. A. Kazmi, A. Oracevic, and F. Hussain, "A comparative analysis of distributed ledger technologies for smart contract development," in *2019 IEEE 30th Annual International Symposium on Personal, Indoor and Mobile Radio Communications (PIMRC)*. IEEE, 2019, pp. 1–6.

[278] R. Han, V. Gramoli, and X. Xu, "Evaluating blockchains for IoT," in *2018 9Th IFIP international conference on new technologies, mobility and security (NTMS)*. IEEE, 2018, pp. 1–5.

[279] R. Han, G. Shapiro, V. Gramoli, and X. Xu, "On the performance of distributed ledgers for internet of things," *Internet of Things*, vol. 10, p. 100087, 2020.

[280] Y. Hao, Y. Li, X. Dong, L. Fang, and P. Chen, "Performance analysis of consensus algorithm in private blockchain," in *2018 IEEE Intelligent Vehicles Symposium (IV)*. IEEE, 2018, pp. 280–285.

[281] S. Rouhani and R. Deters, "Performance analysis of ethereum transactions in private blockchain," in *2017 8th IEEE International Conference on Software Engineering and Service Science (ICSESS)*. IEEE, 2017, pp. 70–74.

Appendix A

Publications

These paper has been published as part of this PhD thesis.

A.1 Published

A.1.1 Journals

- Aldughayfiq B, Sampalli S. Digital Health in Physicians' and Pharmacists' Office: A Comparative Study of e-Prescription Systems' Architecture and Digital Security in Eight Countries. OMICS. 2020 Sep 15. doi: 10.1089/omi.2020.0085. Epub ahead of print. PMID: 32931378.

- B. Aldughayfiq and S. Sampalli, "A framework to lower the risk of medication prescribing and dispensing errors: A usability study of an nfc-based mobile application," International Journal of Medical Informatics, p. 104509, 2021.

A.1.2 Conferences

- Aldughayfiq, B., Sampalli, S. (2018, July). A system to lower the risk of dispensing medication errors at pharmacies using NFC. In 2018 IEEE International Conference on Internet of Things (iThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData) (pp. 196-202). IEEE.

A.2 Under Review

A.2.1 Journals

- Aldughayfiq B, Sampalli S. Patients', Pharmacists', and Prescribers' Attitudes Towards Using Blockchain and Machine Learning in a Proposed ePrescription System: Online Survey. JAMIA Open 2021.

Appendix B

Copes of the publications

The following are copes of the publications.

OMICS A Journal of Integrative Biology
Volume 25, Number 2, 2021
Mary Ann Liebert, Inc.
DOI: 10.1089/omi.2020.0085

Digital Health in Physicians' and Pharmacists' Office: A Comparative Study of e-Prescription Systems' Architecture and Digital Security in Eight Countries

Bader Aldughayfiq and Srinivas Sampalli

Abstract

e-Prescription systems are key components and drivers of digital health. They can enhance the safety of the patients, and are gaining popularity in health care systems around the world. Yet, there is little knowledge on comparative international analysis of e-Prescription systems' architecture and digital security. We report, in this study, original findings from a comparative analysis of the e-Prescription systems in eight different countries, namely, Canada, United States, United Kingdom, Australia, Spain, Japan, Sweden, and Denmark. We surveyed the databases related to pharmacies, eHealth, e-Prescriptions, and related digital health websites for each country, and their system architectures. We also compared the digital security and privacy protocols in place within and across these digital systems. We evaluated the systems' authentication protocols used by pharmacies to verify patients' identities during the medication dispensing process. Furthermore, we examined the supporting systems/ services used to manage patients' medication histories and enhance patients' medication safety. Taken together, we report, in this study, original comparative findings on the limitations and challenges of the surveyed systems as well as in adopting e-Prescription systems. While the present study was conducted before the onset of COVID-19, e-Prescription systems have become highly relevant during the current pandemic and hence, a deeper understanding of the country systems' architecture and digital security that can help design effective strategies against the pandemic. e-Prescription systems can help reduce physical contact and the risk of exposure to the virus, as well as the wait times in pharmacies, thus enhancing patient safety and improving planetary health.

Keywords: e-prescription, digital security, privacy, system architecture, digital authentication, digital health, Blockchain

Introduction

Ensuring the safety of patients is one of the primary goals of all health care services. Most of these services rely on health information technologies related to the patient. Unfortunately, the availability of information about patients is often not adequate. Therefore, developing technologies that support medical decisions to provide quality care for patients is a necessity. Researchers proposed new approaches and technologies for managing patients' medical data and benefit from the medical history of patients to provide better medical care. The technologies were motivated by the lower efficiency of traditional methods in collecting and providing this information.

The interest of digital health and related technologies such as machine learning (ML) increased rapidly in clinical medicine as well as biomedical research and drug discovery (Koromina et al., 2019; Swan et al., 2013). Electronic Health Records (EHRs) are another and critical component of digital health, which help enhance patients' health care by transforming medicine from analog to digital age (Birkhead et al., 2015; Motulsky et al., 2015; Ploner and Prokosch, 2020; Shickel et al., 2018). Although the technology for creating patients' EHRs is advancing, records are still not available for caregivers and visiting patients from other health centers (Motulsky et al., 2015).

Medication errors can be a cause of significant concern to patient health. These errors can occur at any stage of the medication prescribing or dispensing process. They can occur when a prescription created for a medication that interacts with another medication the patient is taking or causes an allergic reaction. Moreover, errors can occur at the pharmacy due to the misinterpretation of paper prescriptions because of

Faculty of Computer Science, Dalhousie University, Halifax, Canada.

handwriting or missing information (Aldughayfiq and Sampalli, 2018; Nair et al., 2010; Samadbeik et al., 2017; Velo and Minuz, 2009).

Hence, e-Prescription systems can ensure patient safety while prescribing medication and are gaining popularity (Agrawal, 2009; Porteous et al., 2003). One of the benefits of e-Prescription is to improve the quality-of-care service and patient safety by reducing medication-prescribing errors (Agrawal, 2009). Moreover, a study about transferring prescriptions electronically was conducted in the United Kingdom with focus groups, and interviews with participants from all the involved parties, that is, patients, general practitioners, and pharmacies, after UK's National Health Service (NHS) revealed their intention to use the e-Prescription system. The study found that using e-Prescription will enhance patients' convenience, especially for patients who have repeated prescriptions (Agrawal, 2009; Deetjen, 2016; Porteous et al., 2003).

E-Prescription is defined as using an electronic device to submit and exchange the prescription information among the involved parties, namely, the patient, prescriber, pharmacy, and health insurance company. It is worth mentioning that the patient involvement in the majority of the e-Prescription systems we reviewed is only to consent to use an e-Prescription by the prescriber and the pharmacy. The use of e-Prescription will allow the involved parties to provide a safe, quality, and efficient care service. Moreover, e-Prescription systems will provide the communication medium between a prescriber and a pharmacist upon reviewing a prescription before dispensing (AMA et al., 2011; Bell et al., 2004; Mon, 2009; Odukoya and Chui, 2013; Samadbeik et al., 2017; Van Dijk et al., 2011).

E-Prescription will likely reduce medication errors caused by paper prescriptions. In addition, e-Prescription will improve the low service quality associated with paper prescriptions by decreasing the amount of work needed to sort the related paperwork. More importantly, providing a medication history for each patient will enhance the patient safety while prescribing medication (Aldughayfiq and Sampalli, 2018; Byrne et al., 2010; Devine et al., 2010; Kohn, 2011; Odukoya and Chui, 2013; Samadbeik et al., 2013; Taylor et al., 2008; Timonen et al., 2018; Van Dijk et al., 2011; Wang et al., 2009). However, not all medication errors are entirely preventable by e-Prescriptions. Moreover, there are risks related to the prescriber's adaptation of the e-Prescription system, since they need to familiarize themselves with the e-Prescription software (Odukoya and Chui, 2013; Timonen et al., 2018).

In addition, according to one study, nearly 5% of e-Prescriptions introduced errors related to the prescriber's information entry or due to a lack of information about the appropriate treatment procedure (Odukoya et al., 2014). Discovering these risks is more likely to eliminate them if found by the pharmacist or by including more features in the system. These features will support the prescriber's decision to the benefit of patients' safety (Odukoya et al., 2014; Reed-Kane et al., 2014; Salmon and Jiang, 2012; Yang et al., 2018).

The COVID-19 pandemic has made e-Prescription systems especially relevant. Physical distancing, limiting unnecessary trips out of home, and minimizing social contacts have become necessary worldwide (WHO, 2020). E-Prescription systems is likely to help in reducing visits to the clinics for picking up prescriptions and reduce the wait times in pharmacies when prescriptions are sent electronically in advance for medications to be prepared. Moreover, implementing ePrescription will minimize the risk of getting exposed to the virus due to handling paper prescriptions.

We report here original findings from a comparative analysis of the e-Prescription systems in eight different countries, namely, Canada, United States, United Kingdom, Australia, Spain, Japan, Sweden, and Denmark.

We explore recent studies conducted in the domain of digital health and e-Prescription systems. Wherever available, an overview of the digital security and privacy protocols in place for each e-Prescription system is highlighted. Furthermore, we discuss the protocols and policies for verifying patient identity. We identify the challenges in the current systems drawing from the comparative analysis and solutions are suggested as well.

This study critically compares the currently implemented e-Prescription systems in the selected countries and evaluates the security and privacy protocols of those systems and the capability of those systems to integrate new technologies such as Artificial intelligence (AI) and Blockchain.

Materials and Methods

We have reviewed and explored e-Prescription systems using a jurisdiction comparison method. Countries with e-Prescription system were selected from each content.

The selection process was as follows:

(1) We chose the leading countries that have deployed e-Prescription systems from each continent. In Europe, many countries have adopted digital health initiatives in the past decade. However, we considered a few leading countries that have fully implemented e-Prescription systems. This approach is part of the national electronic-health strategy in the European Union (EU) countries (AEPI eHealth Initiative, 2004; Johnston et al., 2003).
(2) In the second stage, we considered the availability of the e-Prescription systems in community pharmacies and whether the system is nationwide or state/province-wide in the selection process. We excluded e-Prescription implemented only within hospitals or health centers.
(3) A key factor in our selection process is the security and privacy protocols, which we used to compare and assess the e-Prescription systems from a technical and security aspect.

Finally, the countries resulted from the selection process were four EU countries (United Kingdom, Spain, Sweden, and Denmark), two North American countries (United States and Canada), Australia, and Japan.

The data collection process was based on the main components of the e-Prescription system model (eHealth Initiative and Center for Improving Medication Management, 2008; eHealth Observatory, 2011; Samadbeik et al., 2017; The Center for Improving Medication Management, 2011). The publicly available data collected from the countries included the following:

- The e-Prescription system architecture components: Such components are the architecture type (i.e., centralized or

decentralized system), prescription database, medication database, medication history database, clinical decision support (CDS) features, issuing a paper prescription, electronic prescribing types, medical records, and e-Prescription for controlled medicine.
- The system security and privacy protocols (use of Health Level Seven International [HL7] protocol, patient consent, and patient's identity verification) and the system components identifiers (Pharmacy ID, Prescriber ID, Medication ID, Prescription ID, and Patient ID).
- The e-Prescription system process (the e-Prescription information availability to the involved parties, the availability of Drug-Drug Interactions [DDI] information based on the patient health record, storing the e-Prescription information for future uses, and the electronic transfer of the prescription to a pharmacy).

Data for this survey were retrieved by searching for keywords and/or a combination of keywords from the search engines Google, Google Scholar, PubMed, IEEE, ACM, Dalhousie University Libraries, and the official digital health websites of the selected countries.

The keywords used for the search were ''Eprescription,'' ''e-prescription,'' ''electronic prescription,'' ''e-Rx,'' ''eDispensing,'' or ''electronic dispensing'' with the name of each of the selected countries. Then, all the retrieved papers and related documents were examined. In addition, we compared all the retrieved data with the official website of the systems used in this survey to remove any outdated or false information. Finally, we compared the systems' countries, and the data are shown in comparative tables.

Results

e-Prescription systems

PrescribeIT: Canada's e-prescription system. PrescribeIT is a government-founded system for e-Prescriptions. The system has been partially implemented in some of the provinces and entirely in others. The system's aim is to be used across the nation in all the provinces in the near future. Infoway conducted a workshop in 2016 with a number of prescribers and pharmacists to explore issues in the paper prescription system (Canada Health Infoway, 2018). Therefore, the system's main purpose is to act as a medium to transfer and exchange prescription information between a prescriber and a pharmacist. The following are the main requirements that resulted from the study for PrescribeIT (Nayani, 2017):

- Secure communication between the pharmacy and the prescriber.
- Effective Drug Information System (DIS) to detect drug interactions for both the pharmacy and prescriber.
- Integration with an Electronic Medical Record (EMR) management system.
- e-Prescription status and alert to the prescriber.
- Security and privacy in accessing patient information.

PrescribeIT defines e-Prescription as the process of transmitting a prescription between a prescriber and a pharmacy with the condition of not affecting the clinical workflow (Canada Health Infoway, 2018). Therefore, PrescribeIT's primary focus is to enable transmitting an e-Prescription securely between the involved parties. In addition, PrecribeIT met the requirements by integrating the system with existing health care systems (e.g., DISs, and EMR) available in care provider software (Green and Reinholdt, 2017).

The prescription information is sent encrypted from a prescriber to a patient's pharmacy of choice. Moreover, in terms of security, the system provides access control. Figure 1 illustrates the architecture of the system. PrescribeIT aims to connect the involved parties by enabling them to exchange prescription information. The system intends not to replace the current management system in the pharmacies or the prescriber's office. Instead, the system helps monitor the prescription by storing the prescription information of a patient in the system. Figure 2 shows the complete architecture and features that will be deployed in the future.

Patients' data security and privacy. The prescription information is sent encrypted from a prescriber to a patient's pharmacy of choice. Moreover, the user of PrescribeIT

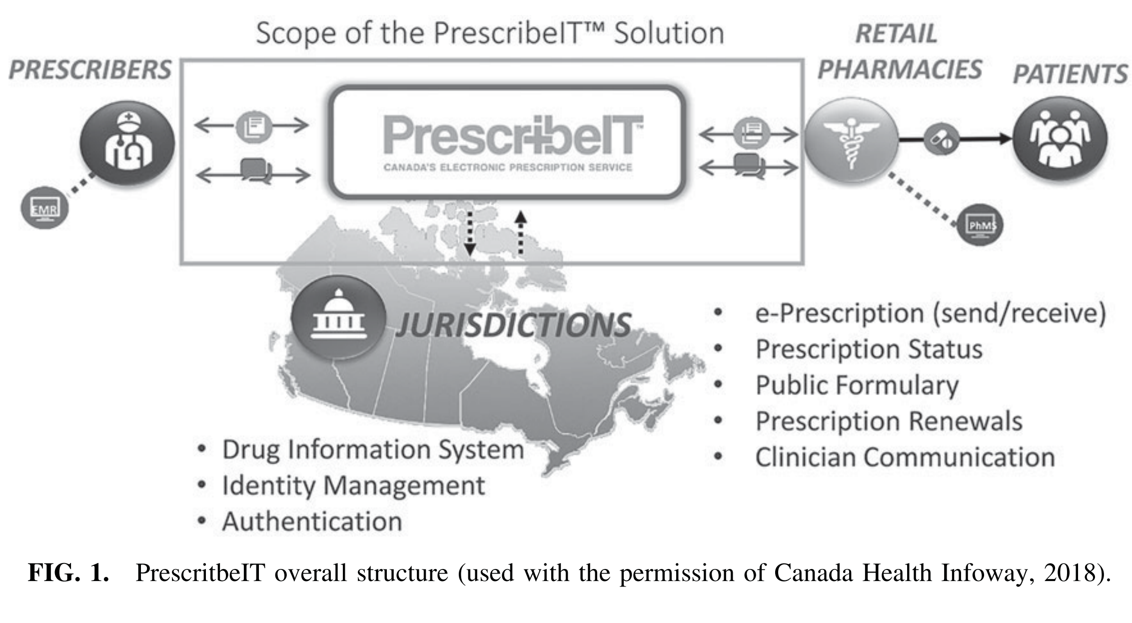


FIG. 1. PrescritbeIT overall structure (used with the permission of Canada Health Infoway, 2018).

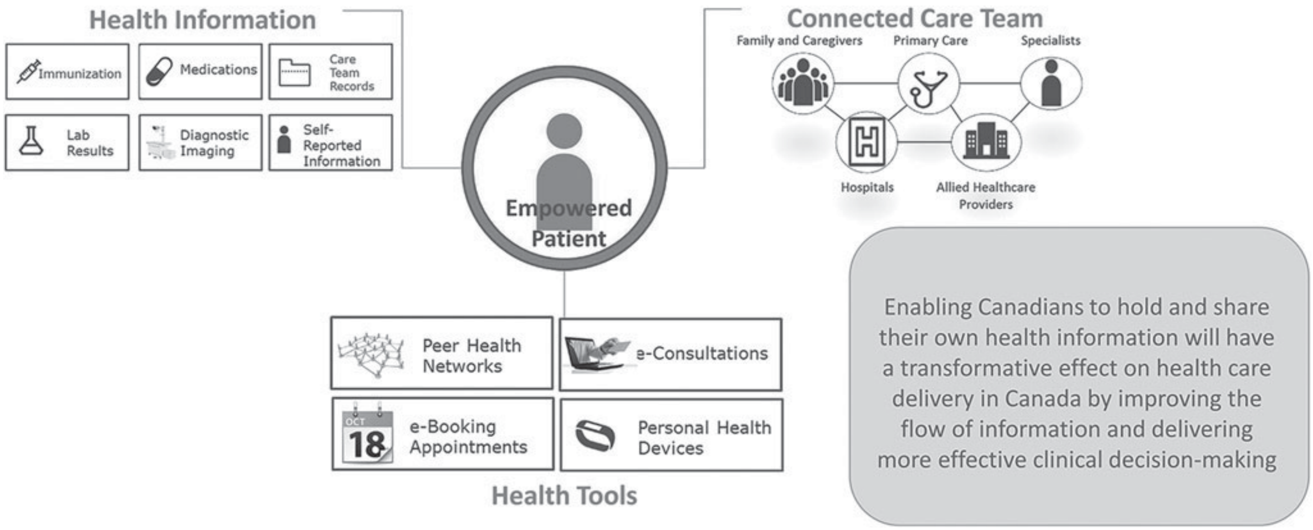


FIG. 2. PrescribeIT future features (used with the permission of Canada Health Infoway, 2018).

(i.e., a prescriber or a pharmacist) must use multifactor authentication to access the patient's prescription information. An access control process is used to grant and revoke accounts on the system. The user is required to use password authentication to access the assigned levels in the system. Moreover, for security, all transactions in the system are logged and audited (Canada Health Infoway, 2019; PrescribeIT, 2018).

Surescripts: United States e-prescription system. Surescripts is an e-Prescription network where the stakeholders in the system can communicate and exchange data. Surescripts is a decentralized e-Prescription network. The parties in the network can communicate with each other using peer-to-peer communication (Surescripts, 2018a). Surescripts provides the prescriber with the patient's medication history and formulary and benefits information from participating insurers and pharmacy benefit managers (PBMs) (Castro, 2009; Joy et al., 2011; King et al., 2007). Figure 3 illustrates the key features of the Surescripts system.

Patients' data security and privacy. Surescripts manages the security and privacy of the patient data based on the provided service. Benefit optimization is one of the services that Surescripts provides to caregivers. This service ensures that the patient's drug information is updated and accessible in real-time during patient visits. Surescripts works with the PBMs and the health care payers to acquire this information. Another service Surescripts provides is the medication history.

This service provides the caregivers with medication-related information about the patient from the participating patient's community pharmacies and health insurance companies. This service requires the patient's consent to give the caregivers access to the patient's medication history information. Clinical history is another service provided by Surescripts. In this service, the caregivers will request the previous care location the patient has attended. The service will cover the location of the past health record and the past prescribed and dispensed prescriptions. Surescripts handles the caregiver request for the medical record from the discovered location about the patient. Most importantly, the e-Prescription service allows the exchange of the prescription electronically. The network allows the prescriber and the pharmacy to exchange prescription information (Surescripts, 2019).

Electronic prior authorization. A prescriber asks for prior authorization (PA) from a patient's health insurance before prescribing any medication. This requirement is the health insurance technique used for minimizing the cost of covered medications. In addition, the insurance will not pay any benefits for any medical care without preapproval. However, this is mostly the case for more expensive medication. Several drugs are subject to PA. The following is a list of the most frequent reasons why PA is required (Gasbarro, 2015):

- Brand medications that are available in a generic form
- Expensive medications
- Cosmetic medications
- Medications not usually covered by insurance companies.

Obtaining PA used to be a challenging process. In the past, prescribers needed to send the prescription to the pharmacy choice of the patient. Then, the pharmacist would start to process the prescription and find out if the prescription needed a PA, usually through a phone call or by faxing a form. The patient would then be informed using the available channels, usually by phone. Following that, the pharmacist would start the PA approval process using phone calls or fax. This process would take days or weeks to finish.

Finally, after getting approval, the patient would be notified through a phone call that the prescription is ready to be picked up. In addition, the increased use of expensive drugs that require PA approval made the process more complicated and time consuming. The process of obtaining PA eventually affected the quality of service at the prescriber's office. Finally, the prescriber's office had to meet all the different requirements from the insurance, based on the plan and the patient (Surescripts, 2015). The PA approval process

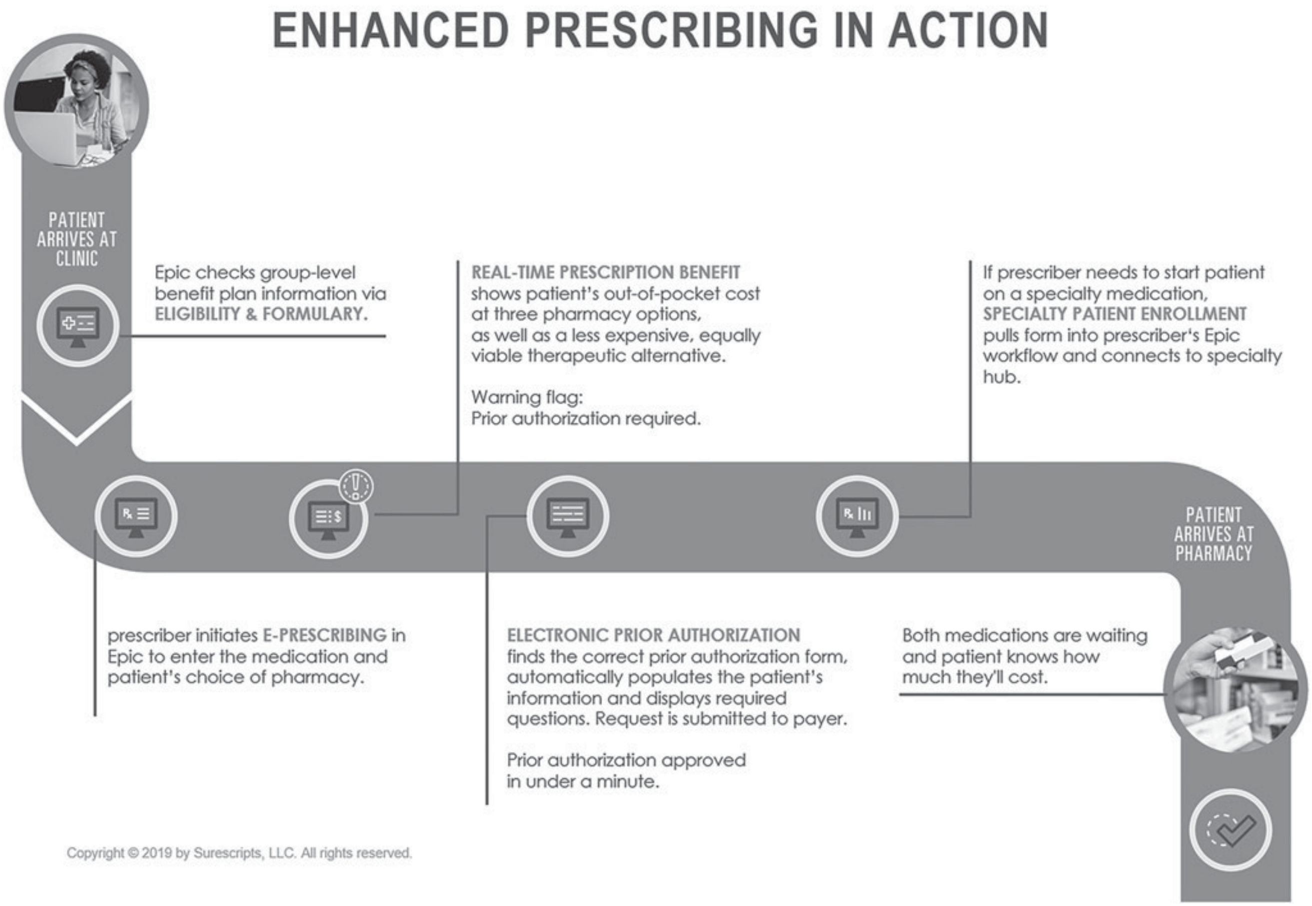


FIG. 3. Key features of the Surescripts system (used with the permission of Surescripts, 2019).

sometimes would take several days. According to Surescripts, 69% of the patients had to wait several days to get their medications approved by the insurance company (Surescripts, 2015). Figure 4 illustrates the traditional process of PA.

Surescripts provides an ePA process. This process simplifies the process and increases the efficiency of getting the prescription from the pharmacy without any delay. The prescriber will request the PA approval during the e-Prescribing process. The system will notify the prescriber if there is a PA requirement or not. Then, the prescriber has the option of selecting another medication option or sending PA electronically using the EHR system. Following this, the prescription will be sent to the pharmacy, where it will be ready to be picked up (Surescripts, 2015). Figure 5 illustrates the electronic PA process.

Australia's e-prescription system. The Australian Digital Health Agency defines electronic prescription as an Electronic Transfer Prescription (ETP) service. ETP is defined as transferring a prescription securely between a prescriber and pharmacy. The pharmacies and prescribers must use a

FIG. 4. Traditional PA (used with the permission of Surescripts, 2019). PA, prior authorization.

FIG. 5. Electronic PA in Surescripts (used with the permission of Surescripts, 2019).

Prescription Exchange Service (PES) system to communicate and exchange the prescription information securely. The PES system must be approved by the Commonwealth and meet specified security and privacy standards. In Australia, there are currently two PES systems: electronic medical prescription (eRx) Script Exchange and MediSecure. The involved parties (i.e., the pharmacy or the prescriber) may be connected to one or more PES systems.

According to the Australian Digital Health Agency, the prescriber is responsible for registering their clinical practice with a PES. Also, the prescriber must have software with the ability to send e-Prescriptions. Moreover, the prescriber is responsible for encryption key management. The e-Prescription must be encrypted when transferred to the pharmacy's PES. Moreover, both ETP and PES services are essential components for keeping records of the prescriptions and dispensing history.

The records are stored in the patient's health record in the My Health Record system. Then the prescription and dispensing information can be viewed through the system. For that, the provider and the pharmacy must have the patient's consent to upload the information to the My Health Record system, and the patient must have an active My Health Record account. The authorized health care providers can view prescription and dispensing history through My Health Record system (The Australian Digital Health Agency, 2019a, 2019b). Figure 6 illustrates the Australian eRx architecture.

eRx meets all the legal privacy requirements described in the Privacy Act 1988 in Australia and the eAuthentication framework of the Australian Government (2009; eRx, 2018a). According to eRx, all the prescription information is encrypted when transferred through the system. eRx acts as an electronic mail carrier, and only the prescriber and the pharmacist can access the prescription information (eRx, 2018a). eRx can only unlock the first layer of the three-layer encryption. The first layer has just the header information of the data package. This information is needed to send the right prescription corresponding with a scanned barcode in the paper prescription. The header information does not include any personal or medical information about the patient (eRx, 2018b).

MediSecure offers the same service as eRx in terms of being an electronic medium used to transfer prescription information between the involved parties. In addition, MediSecure offers the DrShop service, which is a real-time prescription monitoring service. This service will provide the prescriber alerts, if the prescribed medication could lead to addiction (MediSecure, 2019a). In terms of privacy, MediSecure (2019c) follows the same privacy methods as

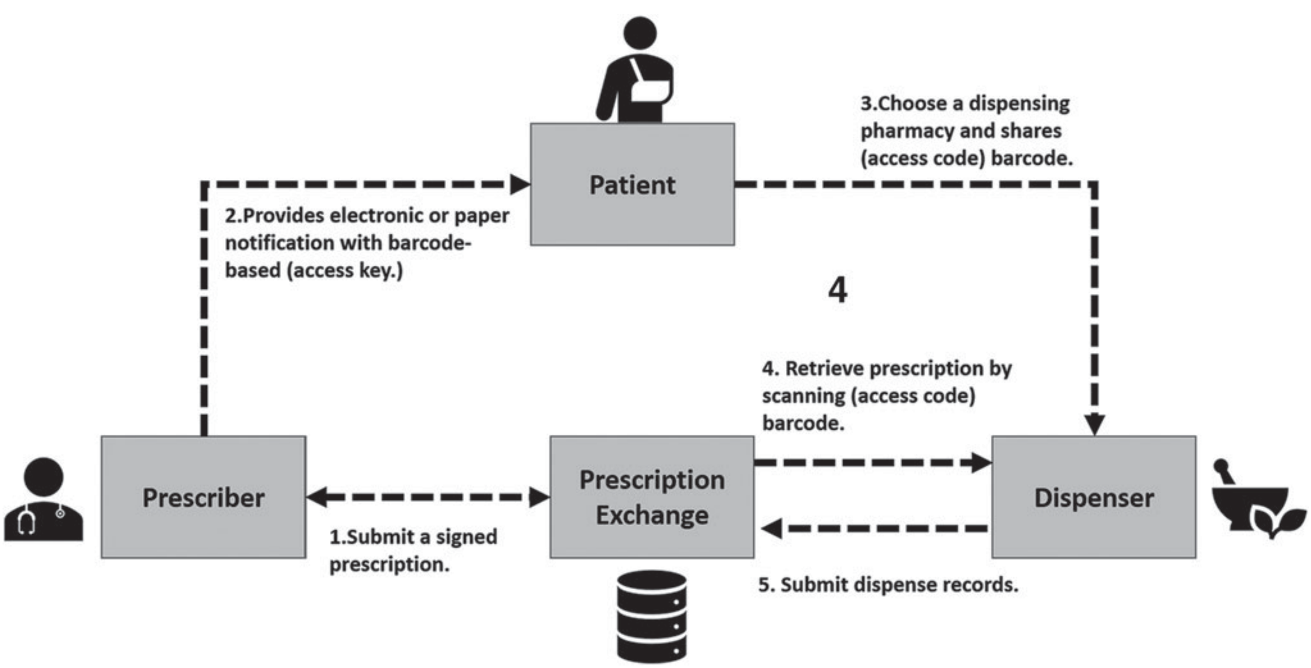


FIG. 6. Australia eRx Architecture (adapted from eRx, 2018a). eRx, electronic medical prescription.

eRx. However, MediSecure (2019c) has a secure Script Vault, where they will keep the encrypted prescription until it is retrieved by the pharmacy. Moreover, patient consent is required to send the prescription electronically through MediSecure (2019b).

United Kingdom's e-prescription system. According to the United Kingdom NHS, almost 1.5 million prescriptions are processed every day, and this rate is expected to increase by 5% every year. Seventy percent of those prescriptions are repeat prescriptions. Therefore, to provide more efficient and accurate service, electronic prescriptions are necessary (NHS BSA, 2018). The NHS identifies that the most common users of the Electronic Prescription Service (EPS) are patients who get repeat prescriptions and patients who use one pharmacy to dispense all their prescriptions (NHS, 2019).

Furthermore, EPS is a more efficient method to send prescriptions securely to pharmacies. The EPS is sent through the NHS Spine system. Spine is a central system that allows the secure exchange of patients' health and care information between care provider organizations when needed (National Health Service Digital, 2019e; PSNC, 2019). Patient consent is needed for participation in the EPS. Figure 7 shows the EPS overview system (National Health Service Digital, 2019c).

The system uses smartcard authentication for the health care provider to access NHS Spine services, such as EPS and the patient's Summary Care Record (National Health Service Digital, 2019d, 2019e; PSNC, 2019). Spine has more than 800,000 Smartcard users. The service is used to identify the health care provider and their access levels for patient information (National Health Service Digital, 2019d; PSNC, 2018). The system also provides the ability to choose the preferred pharmacy for the patient through the prescriber. This step is called nomination, and a patient's consent is required to participate in the EPS service. Moreover, the patient has the right to request a paper prescription at any time from the prescriber (Hibberd et al., 2017; NHS, 2019; PSNC, 2016).

Moreover, The system uses unique identifiers for the prescription form, and when the prescriber issues a prescription, the system creates three identifiers: (1) the prescription form, (2) the short prescription form ID, and (3) the prescription line item Unique User Identifier (UUID). Identifiers 1 and 3 will not be visible for the end users and only used by the messaging protocol HL7 (HL7, 2019; HL7UK, 2019). Identifier number 3 will be visible to the end users and printed and barcoded in the paper prescription (Hibberd et al., 2017; National Health Service Digital, 2019b). NHS has allowed the use of EPS to prescribe a selected list of controlled drugs as of March 25, 2019. For the controlled drugs not on the selected list, the prescriber will need to use paper prescriptions (National Health Service Digital, 2019a).

Spain's e-prescription system. In Spain, the e-Prescription system's primary goal is to ensure the patient's safety and improve the patient's treatment care. According to the health authorities in Spain, the system must include a list of possible medications that allowed to be prescribed. The medication list has a coding system for all the information about every medication approved on the list. The list is likely to help detect drug interactions.

Moreover, the system is connected to the patient's EHR to help identify any additional other interactions or allergies to the prescribed medicine. In addition, the prescription will be shared with any other prescriber treating the patient. Furthermore, the active prescription will be accessible by all pharmacies in the country. The patients will be able to pick up their medications at any pharmacy in the country or in the

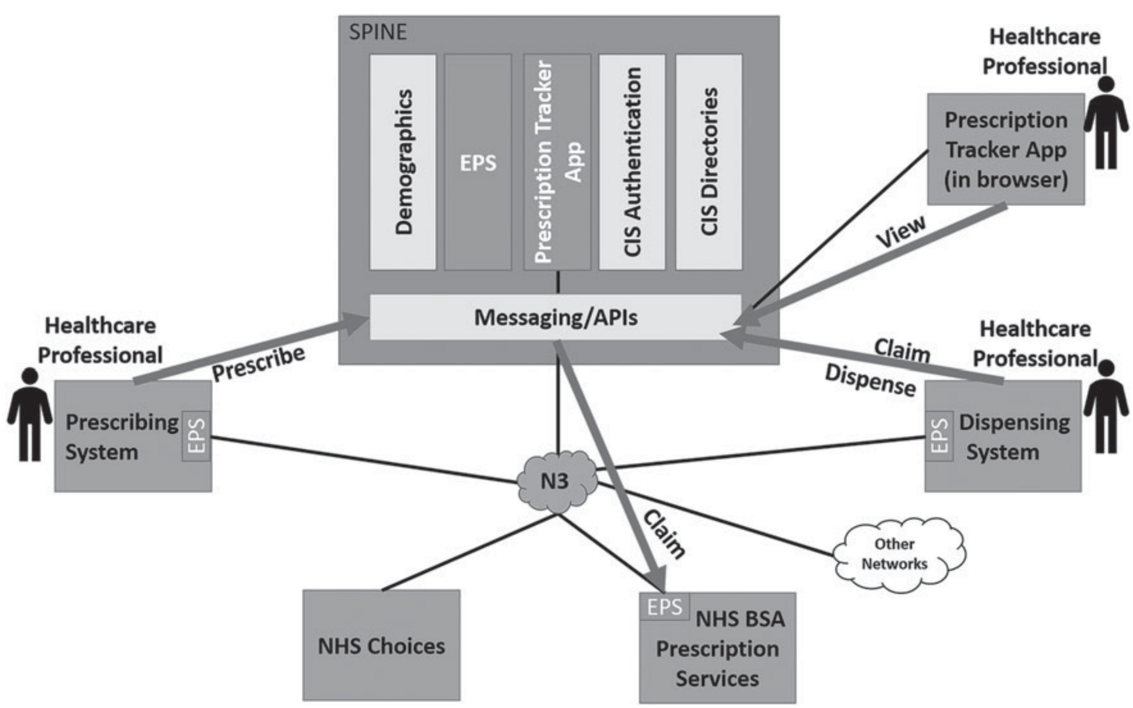


FIG. 7. UK e-Prescription service architecture (adapted from NHS, 2019).

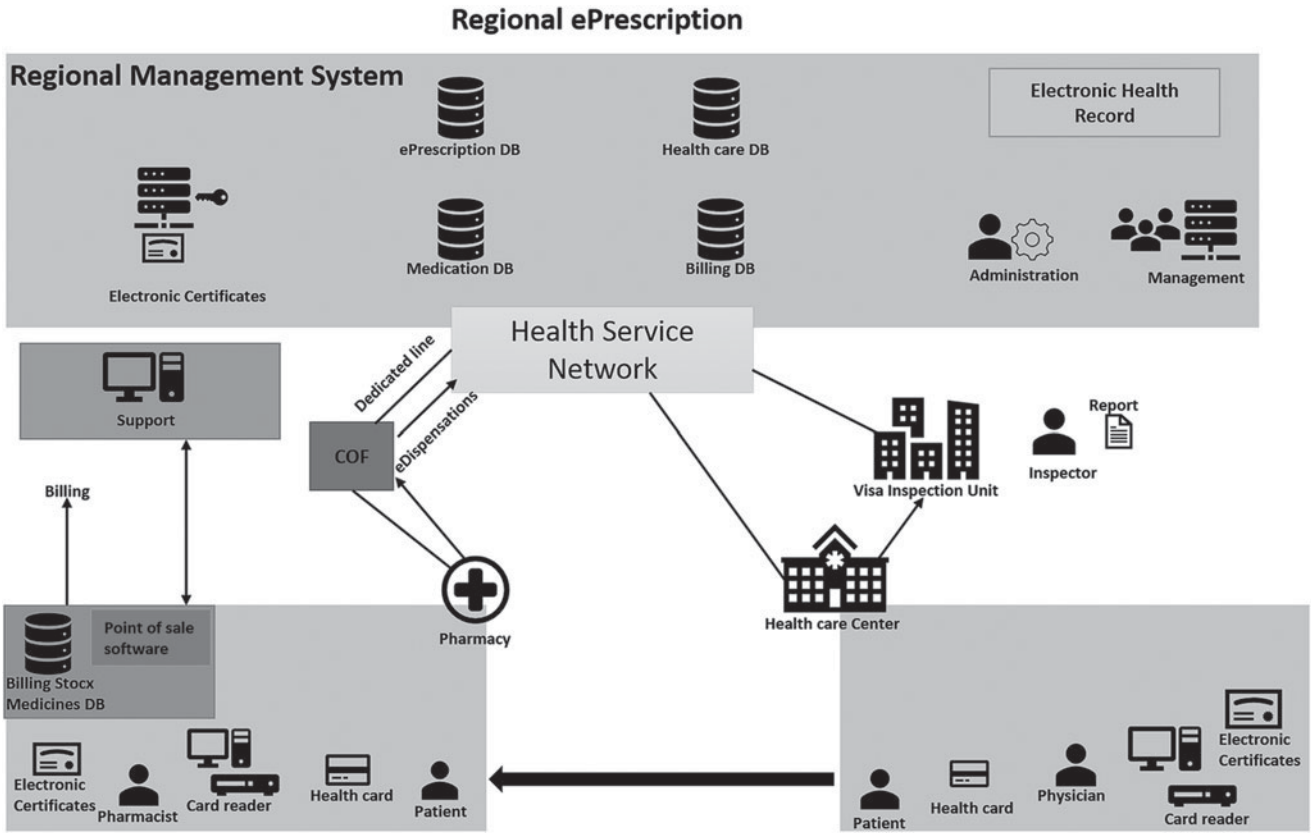


FIG. 8. Spain e-Prescription system architecture (adapted from Ministry of Health, Social Services, and Equality, 2014).

surrounding countries using the eDispensation service, which is part of the e-Prescription system. Finally, the system uses Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT) to code all the information in the system (Kierkegaard, 2013; Ministry of Health, Social Services and Equality, 2014). Figure 8 illustrates the Spanish ePrescribing system architecture.

Japan's e-prescription system. The current prescription dispensing process in Japan is still in paper form. Figure 9

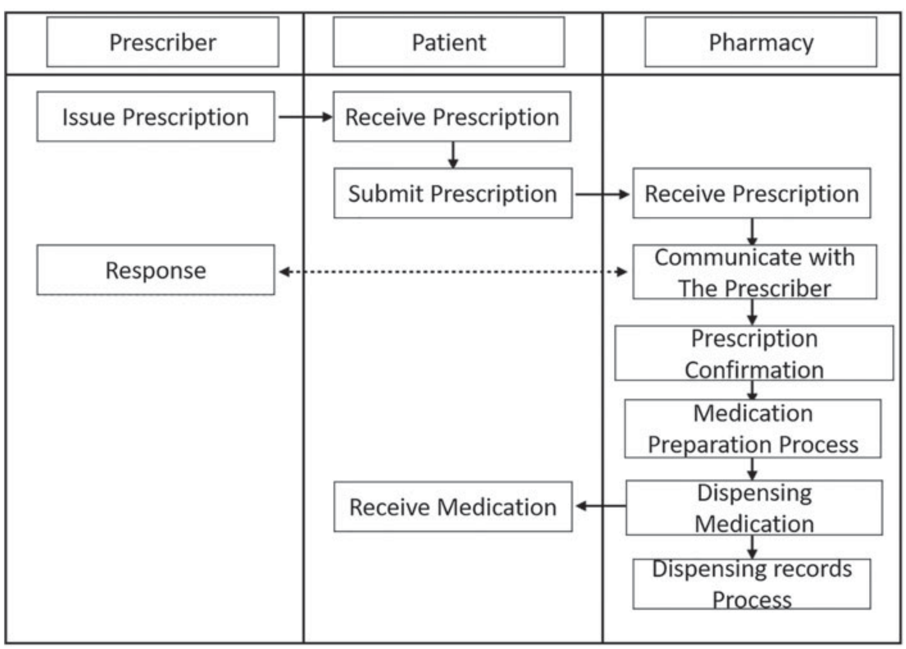


FIG. 9. Japan current prescription process steps translated from Ministry of Health, Labor, and Welfare (2019).

shows the flow of the dispensing process. The prescriber prints the paper prescription and delivers it to the patient. Then, the patient submits the prescription to the pharmacy of their choice. Next, the pharmacy starts the process of dispensing the medication and dispenses it to the patient. Finally, the pharmacy prepares the medication-dispensing records.

In addition, patients in Japan have a notebook where they keep a sticker for each dispensed medication. The pharmacy provides the stickers after dispensing. Some of the pharmacies provide an app that acts as the medication history notebook. This notebook acts as a medication database for each patient (Japan Government, 2019; Ministry of Health, Labor and Welfare, 2019; Nakagawa and Kume, 2017). Even though Japan is using a paper prescription format, the government has proposed electronic prescription system guidelines in 2016 (Akiyama and Nagai, 2012; Masuda, 2016; Ministry of Health, Labor and Welfare, 2016).

Figure 10 shows the flow as described in the guidelines published in 2016. The system proposes the use of a copy of the electronic prescription in a paper form. The electronic prescription paper contains the prescription ID with the prescription contents. This version of the electronic prescription is carried by the patient and submitted by hand to the pharmacy. There are two types of participating pharmacies in this system. A pharmacy equipped with a management system that can handle electronic prescriptions. The second type is pharmacies, where only the paper version of the prescriptions is acceptable (Japan Government, 2019; Ministry of Health, Labor and Welfare, 2016).

The Health Ministry in Japan later conducted interviews with the involved parties, namely, prescribers and pharmacies. The result of the interviews is that the proposed system is more complex and requires the added cost of hiring more staff to manage different system components. Therefore, as a result, they proposed more simplified system guidelines, which were supposed to be ready for use in late 2019 or early 2020 (Ministry of Health, Labor and Welfare, 2019).

Figure 11 illustrates the newly proposed system where the patient gets an access code from the prescriber. The prescription system issues this access code after the prescriber submits prescription data. The patient can choose to get the access code in a paper form or an electronic form sent to their Personal Health Record (PHR) application. The system generates the access code using QR code technology. After the patient goes to the pharmacy to pick up the medication, the pharmacy scans the QR code to get the prescription information from the prescription system in the cloud. The pharmacy then starts the dispensing process. Finally, the pharmacy updates the prescription system with the prescription dispensing data. Furthermore, the patient's PHR application will be updated with the dispensing information to keep it in the electronic medication notebook (Japan Government, 2019; Ministry of Health, Labor and Welfare, 2019).

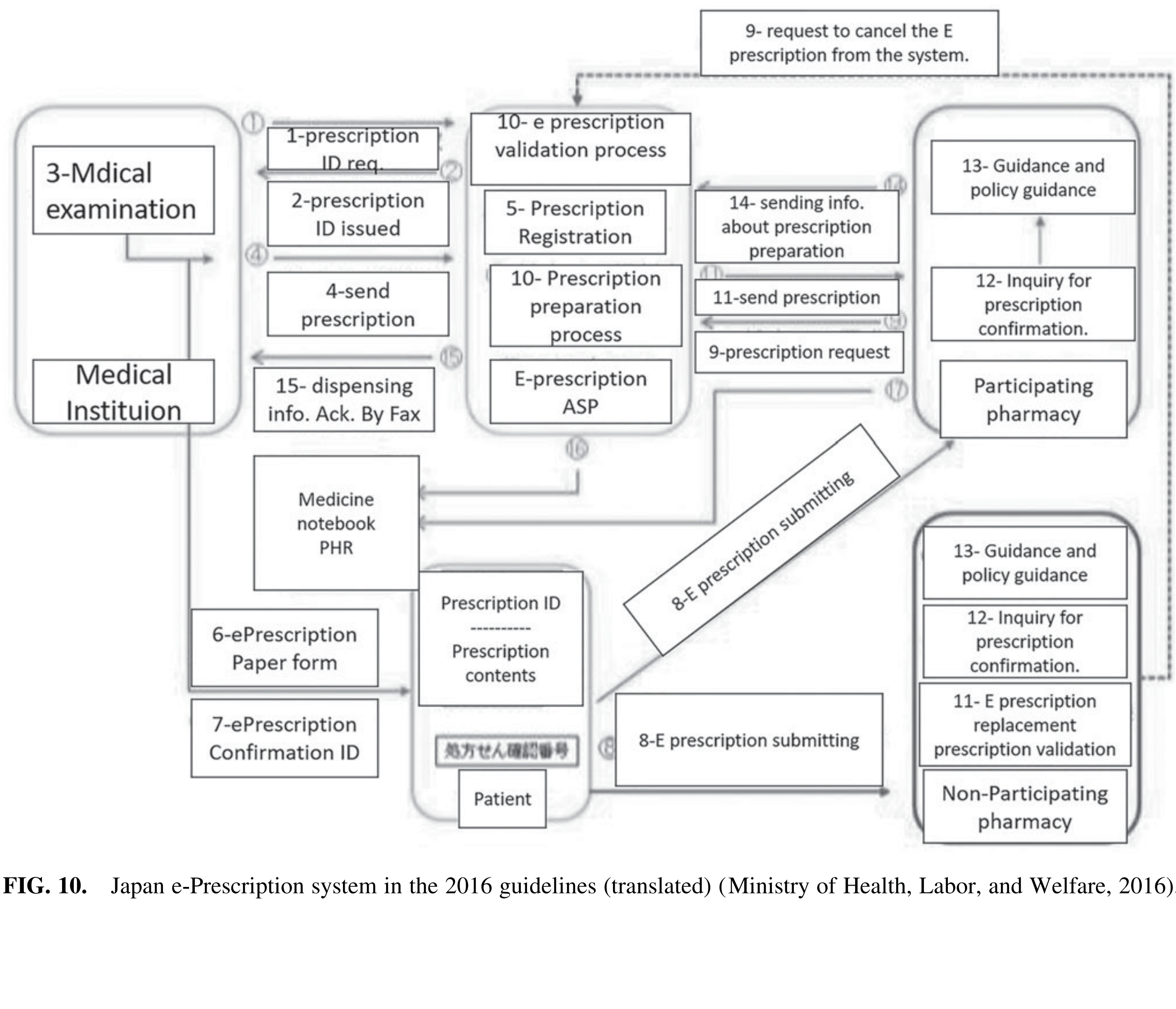


FIG. 10. Japan e-Prescription system in the 2016 guidelines (translated) (Ministry of Health, Labor, and Welfare, 2016).

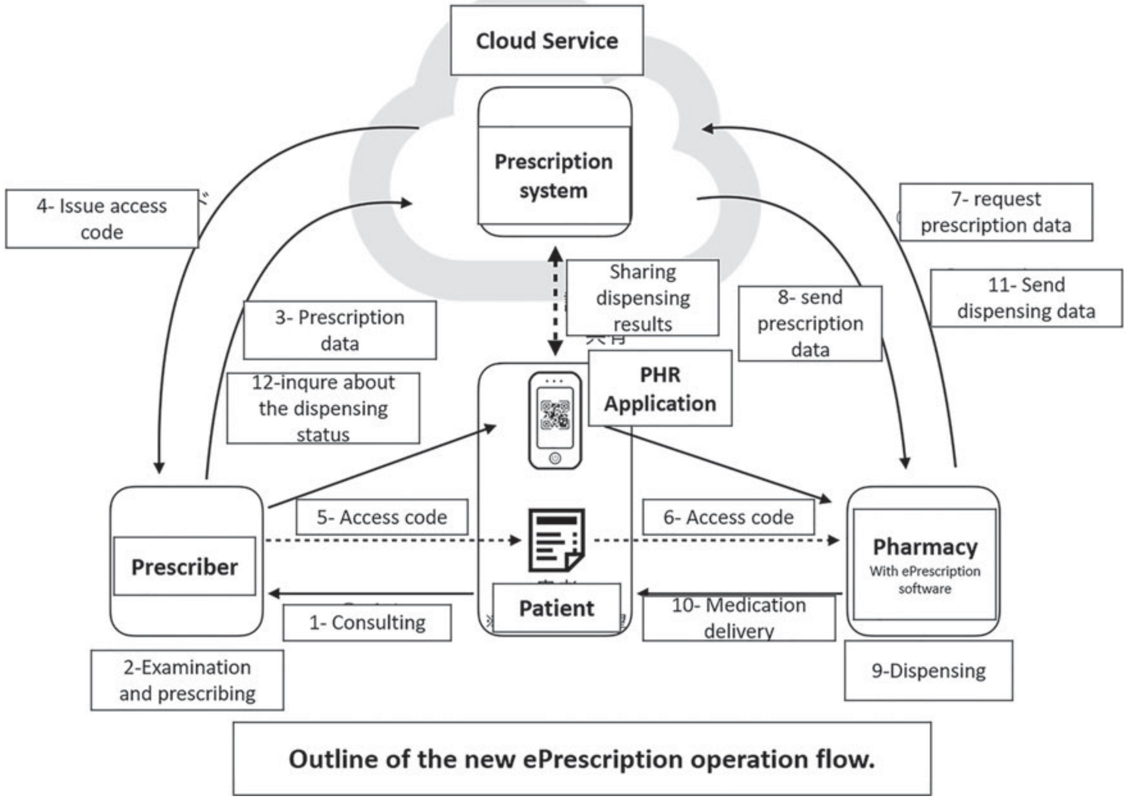


FIG. 11. Japan new e-Prescription system expected in 2020 (translated) (Ministry of Health, Labor, and Welfare, 2019).

According to the Distribution news (a Japanese news website), the Ministry of Health in Japan published an official statement about its final report on the e-Prescription system design study results in March 2019 (Japan Government, 2019). The system will connect the EMR system with the pharmacies' databases using the HL7 standard Fast Healthcare Interoperability Resources (FHIR) (HL7, 2019; HL7-FHIR-Release-4, 2019; Japan Government, 2019; Ministry of Health, Labor and Welfare, 2019).

e-Prescription overview in Sweden. The computerization of Sweden's health care started in the 1970s when the National Corporation of Swedish Pharmacies was the only pharmacy retailer in Sweden. They distributed minicomputers to all the offices in Sweden with built-in software from the Swedish branch of Data General. These minicomputers printed medication labels to simplify safety checks in the pharmacies and at the patient's home. In addition, the minicomputers played an essential role in developing the national prescription database in the early years of e-health compared with other countries.

In the 1980s, patient smart cards were introduced to replace paper prescriptions. The patient's smart cards contain information about recently prescribed medications. After the prescriber writes the information on the card, the patient takes it to a pharmacy. Then, the pharmacist can access the information in the card with the help of the supporting system. Furthermore, the patient can take the card, which holds their recent medication history, to any other prescriber. In the prescription writing process, the prescriber uses the support system to access all the information about medication from a national database generated from three sources:

- The product database created and updated by the pharmacies.
- The medication information about each medication, the recommended dose, and the side effects.
- The drug book is containing information about diseases and which medications are used to treat certain diseases.

For access control, the smart card developers made the patient's information only accessible by using the keys stored in the authorized caregiver card keys. In the late 1990s, the use of EHR systems in outpatient clinics increased by 90%. Therefore, interest in the electronic transfer of prescriptions has greatly increased in recent decades. Sweden and Denmark were the world leaders in the adoption of electronically transferring prescriptions using the Electronic Data Interchange For Administration Commerce and Transport (EDIFACT) message format. In 2001, the message format was replaced by the XML message format based on the European pre-standard ENV 13607.

In 2000, the National Corporation of Swedish Pharmacies replaced the process of transferring prescriptions between the prescriber and pharmacies. They requested the prescribers to electronically transfer prescriptions to an e-Prescription repository instead of using the patient's smart card. This was feasible because the National Corporation of Swedish Pharmacies was the only pharmaceutical company in Sweden. In 2019, the Swedish eHealth Agency changed the system framework by managing the e-Prescription repository. This was due to the increased number of pharmacy chains, which has led to an increased number of different systems at pharmacies (Grepstad and Kanavos, 2015; Hammar et al., 2011;

Hassel, 2019; Klein, 2010; Öhlund et al., 2012). Figure 12 illustrates Sweden's e-Prescription system components.

Denmark's e-prescription system. Similar to Sweden, Denmark is one of the world leaders in the deployment of eHealth for the better care of patients (Hammar et al., 2011; Kierkegaard, 2013; Samadbeik et al., 2017). In the 2000s, Denmark used an ongoing EHR system accessible by all caregivers in public hospitals. Moreover, nearly 85% of Denmark's population had health records in the EHR system by the year 2011 (Krag et al., 2012). The centralized EHR system provided a robust infrastructure for establishing an e-Prescription system.

Therefore, in 2002, Denmark introduced its e-Prescription system nationwide. The Danish Medicines Agency manages the system, and the system is responsible for managing and storing the electronic prescriptions issued by a prescriber. The e-Prescriptions can then be accessed by the patient as well as by prescribers and pharmacies. The e-Prescription records, when accessed by any of the above parties, will provide an overview of all the prescribed medications (Kierkegaard, 2013; Krag et al., 2012; Samadbeik et al., 2017).

Overall system architecture

As we can see from Table 1, the systems are divided into two types, namely, centralized and distributed. First, in centralized systems, all the medical records are stored in centralized servers that are controlled by a federal regulatory body. The centralized systems help make all the medical records for a patient in all health care centers available for the caregiver at any of the health centers. Moreover, centralized systems offer better services for future research and studies. However, many researchers and medical institutions will argue that there is a loss of patient privacy and security when using centralized systems (Zaghloul et al., 2019). Many studies showed that centralized systems are vulnerable to Distributed Denial of Service (DDoS) cyber-attacks (Zaghloul et al., 2019; Lau et al., 2000) and social engineering attacks (Zaghloul et al., 2019; Anderson, 2008; Patil and Seshadri, 2014).

Moreover, the centralized systems will limit the data privacy of the patient, as health records can be shared anywhere across the system (Zaghloul et al., 2019; Ponemon, 2018). In the US, Surescripts (Surescripts, 2015) is an e-Prescription network that helps transfer e-prescriptions between a prescriber and a pharmacist. This means the e-Prescription system is not centralized, and each part of the patient information is stored in their local system. A recent update to Surescripts provides the ability to request any health information through the network; however, both parties who want to exchange it need to subscribe to Surescripts. This means each healthcare center stores its EMR in their systems, and it is not accessible from other healthcare centers unless requested.

The decentralized systems offer more information privacy and more protection. However, the centralized approach improves the quality of the offered service and helps minimize the errors in that service. In terms of e-Prescription, one of the benefits of a centralized system is the availability of the patient's medication history to all parties. This helps minimize medication interaction errors and Adverse Drug Reactions (ADR). As shown in the US case study, decentralized systems are also able to share medication history with other parties.

However, this process is subject to in-place conditions such as a health center agreeing to share information with

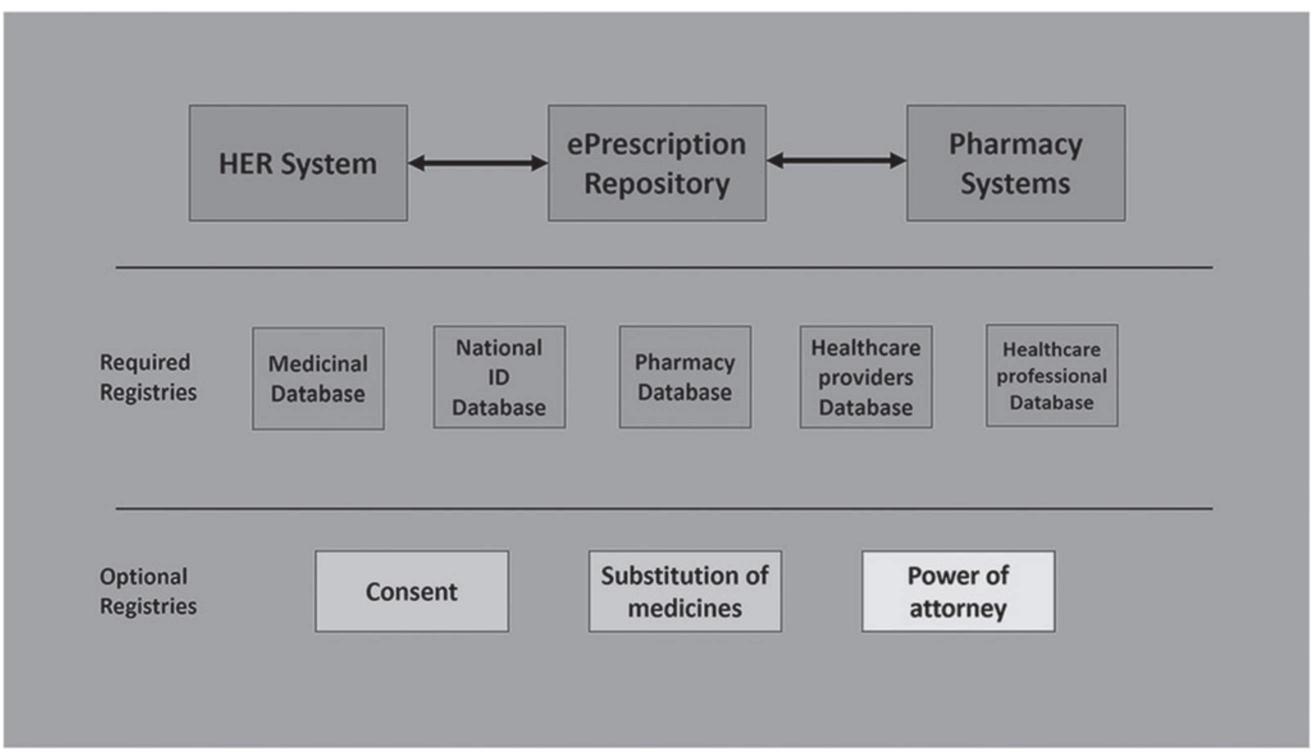


FIG. 12. Sweden e-Prescription system components (adapted from Hassel (2019).

other parties or subscribing to the same e-Prescribing service. Other approaches, such as the Japanese, they propose that the medication history should be controlled by the patient and sent to the requesting parties (Japan Government, 2019). Moreover, other approaches provide access to the patient using web portals to display relevant information about an e-Prescription to request medication delivery to the home (Jensen and Thorseng, 2017; Kruus, 2013; Patrao et al., 2013; Sellberg and Eltes, 2017). Other researcher proposes an e-Prescription system in which the patient has the central role. This approach aims to give the patients priority in making decisions regarding their health (Pereira et al., 2018).

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Moreover, other approaches suggested providing access to the patient using web portals to display relevant information about an e-Prescription to request medication delivery to the home (Jensen and Thorseng, 2017; Kruus, 2013; Patrao et al., 2013; Sellberg and Eltes, 2017). Other researchers propose an e-Prescription system in which the patient has the central role. This approach aims to give the patients priority in making decisions regarding their health (Pereira et al., 2018).

One central aspect of the e-Prescribing systems is that they support prescriber decisions regarding prescribing medications to patients. These systems aim to help prescribers safely prescribe medications to patients. Such features are DDI alerts, drug–allergy alerts, recommended doses, and drug information when prescribing any medication to a patient (Bell et al., 2019; Kawamoto et al., 2005).

From Table 1, only the Surescripts (i.e., the US e-Prescription network) and Spain's e-Prescription systems have DDI alerts integrated in their systems (Ministry of Health, Social Services and Equality, 2014; Surescripts, 2018a). For other countries, to the best of our knowledge, there is no mention on the systems' websites about the description of their system, or the system architecture does not have the required CDS features.

However, other survey studies suggested that most systems are likely to incorporate the CDS. For example, in the United Kingdom, CDS systems are not a part of hospitals' systems or part of the e-Prescription system, but there is interoperability between the CDS systems and other systems to help with prescribing medications to patients safely [Bell et al., 2019; Health and Social Care Information Centre (Great Britain), 2019; Ojeleye et al., 2013]. Moreover, a survey on the most common methods used to identify any case of Potential of Drug–Drug Interactions (PDDI) found that more than half of the participants tend to search for the drug name and use facts and comparisons to identify PDDI. They used various keyword strategies to search for multiple databases and web resources (Grizzle et al., 2019).

The patient's medication history is an essential part of improving the safe prescription of medication to a patient. This feature is likely to help avoid any DDI and enhance the treatment process to lead to personalized care (Blouin and Adams, 2017; Bush and Daniels, 2017; Nester and Hale, 2002).

In Table 1, we see that not all the systems have this feature available to the prescriber. However, most of the systems incorporate this feature in EHR systems. For example, the UK system has this information in the patient record rather than in the e-Prescription service. The incorporation of medication history is different in some countries because of their definition of the e-Prescription system. In the United Kingdom, e-Prescription is defined as a service for transferring electronic prescriptions from a prescriber to a pharmacy. While in Japan, the medication history information is included in a patient's e-Prescription service application (Ministry of Health, Labor and Welfare, 2016).

Moreover, to save doctors' time, a new approach was proposed for displaying patients' medication history in a timeline model. In their timeline, the medications will be displayed relevant to the time a patient took them. Their

TABLE 1. COMPARISON OF THE SYSTEMS' OVERALL ARCHITECTURE

System	*Surescripts*	*Prescritbe IT*	*United Kingdom*	*Sweden*	*Denmark*	*Spain*	*Australia*	*Japan*
Benefit Optimization	✓	×	—	—	—	✓	×	×
Electronic Prescribing	✓	✓	—	—	—	✓	✓	✓
Prior Authorization	✓	×	—	—	—	—	—	×
Clinical History	✓	×	✓	—	—	✓	—	×
DDI Alerts[a]	✓	×	—	—	—	✓	—	×
Centralized System	×	✓	✓	✓	✓	✓	×	×
Prescription Database	×	—	✓	✓	✓	✓	✓	✓
Medication History	✓	✓	—	—	—	✓	Consent required	✓
Medication Database	×	—	✓	✓	✓	✓	✓	✓
Issuing Prescription	×	✓	✓	✓	×	—	✓	✓
e-Prescription for controlled Medicine	✓	—	×	×	×	—	—	×

[a]DDI alerts incorporated as part of the system.
DDI, Drug–Drug Interaction.

Table 2. Comparison of Security and Privacy Features Across the Systems

System	*Surescripts*	*PrescritbeIT*	*United Kingdom*	*Sweden*	*Denmark*	*Spain*	*Australia*	*Japan*
Pharmacy ID	✓	—	✓	×	×	—	✓	×
Prescriber ID	✓	—	✓	✓	✓	—	✓	×
Medication ID	✓	—	✓	✓	✓	✓	✓	✓
Prescription ID	×	✓	✓	×	×	✓	✓	✓
Patient ID	Master index	✓	✓	✓	✓	✓	✓	✓
Patient ID verification	—	—	—	—	—	Health card	—	×
Participate consent	×	×	Choosing pharmacy	×	×	—	✓	×
Using HL7[a]	✓	—	✓	×[b]	×[c]	—	✓	×

[a]HL7 is communication protocol to transfer the medical information from ehealth service system to another. HL7 is used to encode the information to be readable to all the ehealth service systems (Bender and Sartipi, 2013; HL7, 2019; Saripalle et al., 2019).

[b]Sweden eHealth systems uses a service-oriented communication endpoint for the technical protocol, They use ENV 13607 standard (Doupi et al., 2010; Mäkinen et al., 2011; Sellberg and Eltes, 2017).

[c]Denmark e-Prescription uses the MedCom communication standard nationwide. MedCom was established in 1994 to develop the communication standards for transferring the medical records and information between health centers nationwide (Krag et al., 2012; Öhlund et al., 2012).

HL7, Health Level Seven International.

design aims to provide a better understanding of a patient's complex medication history, which is likely to help a prescriber reduce the work rate load of looking up the medication history and when those medications are taken.

Issuing an e-Prescription for controlled medication is a significant limitation in all the systems mentioned above, except Surescripts (2018b). In the United States, the e-Prescribing of controlled medication was permitted in 2010, and the certification process was approved in 2013 (Drug Enforcement Administration, 2010, 2013). In other systems, to the best of our knowledge, there is no available information about how to use e-Prescriptions to dispense controlled medication or the e-Prescription service does not offer the prescription of controlled medication.

Patient identity verification and e-prescription encryption

The need for a unique ID for all the involved parties in e-Prescription systems is crucial to make the systems fully automated. We can see in Table 2 that most of the systems have assigned unique IDs for the involved parties in the system, that is, patient ID, prescriber ID, and pharmacy ID. Assigning unique IDs for the abovementioned parties is likely to help manage to transfer e-Prescriptions efficiently and help avoid transferring or storing errors. Moreover, assigning unique IDs to each prescription and medication is likely to help manage each patient's prescription and all the prescribed medications in that prescription. As a standard practice, prescription IDs and medication IDs were used to keep a medication record for each patient at the pharmacy. Furthermore, prescriptions and medication records help manage the vast number of prescriptions a pharmacy had to manage.

Despite all the unique IDs used in the e-Prescription systems mentioned in Table 2, to the best of our knowledge, there is no evidence from their websites that they are using them in their e-Prescription system to verify patients' identities in the medication dispensing process. In Spain's e-Prescription system, the patient is required to show their health card to pick up their medication. However, other verification methods might be in place (e.g., asking for the patient's name, birthday, address).

In terms of the communication protocol, most of the systems are using the HL7 protocol to encode and decode e-Prescription information between the involved parties (Chen et al., 2016; Chouvarda and Maglaveras, 2015; Eichwald, 2014; Goundrey-Smith, 2013; Pereira et al., 2018; Saripalle et al., 2019). For encryption, most systems use standard encryption methods such as public key infrastructure such as in Australia and Canada (Canadian Pharmacists Association, 2009; Henderson et al., 2015), or other standard authentication algorithms.

Discussion

Overarching context and related work

A comparative study between five countries (United States, United Kingdom, Sweden, Denmark, and Finland) has compared the e-Prescription systems in those countries (Samadbeik et al., 2017). The latter study aimed to evaluate and compare the available e-Prescription systems in the selected countries. The review period of the study was 2013–2015. The authors had three phases of selecting the participating countries in the study. First, they selected all the countries with a fully implemented e-Prescription system such as the EU and United States. In the second phase, they eliminated the countries that did not fit their specified criteria regarding their proposed system's preferred features.

The authors chose three features that must be in the definition of e-Prescription. The features were, namely, electronically creating e-Prescriptions, electronically sending the e-Prescriptions to the pharmacy from the prescriber, and two-way communication between the pharmacy and the prescriber. This study limited the selection to eight countries (Denmark, Finland, Germany, New Zealand, the Netherlands, Sweden, United Kingdom, and the United States), which have the potential to have the specified features mentioned above. The final stage of selecting the participating countries was to review the national prescription system in each country. The authors aimed to select only the systems capable of electronically sending prescriptions to the pharmacies and providing a two-way communication channel between the prescriber and the pharmacist.

As a result, only five of the initially selected countries were eligible for the review study. Later, they created a data collection form from the main components of the prescription system model. They collected the data using the search engines and related websites of the selected countries' e-Prescription service. Moreover, they sent emails to the organizations that provide the e-Prescription service to clarify any ambiguity regarding the information collected about the service (Samadbeik et al., 2017). They categorized the results regarding the main components of the e-Prescription service model.

First, they found in all the selected countries that the prescriber's electronic signature was required and legal. Also, the consent of the patient is necessary to access the required information from the involved parties. However, none of the countries accept or process e-Prescriptions from other countries.

Second, in the comparison results about the e-Prescription systems' architecture, they found that all the European countries use a centralized system and have a national database of e-Prescriptions. However, in the United States, the system is decentralized and not controlled or managed by a national organization, which results in the absence of an e-Prescription national database. The rest of the countries use governmental resources to provide e-Prescription services.

Third, in terms of setting identification information for prescriptions and patients, the United States, Sweden, and Denmark do not have a Prescription Unique ID (PUID) at the time of creating the prescription. The PUID is used to link the prescriptions to the patients and help to keep records of past ones. In addition, only the US system does not have patient identification information, used to identify patients in the database. Finally, only the US e-Prescription system provides pharmacies' ability to request the patient's historical information from the prescriber. To implement a fully functioning e-Prescription system, the authors concluded that a country needs to have the base infrastructure for the e-health and national e-Prescription database (Samadbeik et al., 2017).

Another study focused on examining the economic, health, and social benefits gained from e-Prescription systems across Europe. Their findings confirmed that e-Prescriptions would benefit the involved parties in the e-Prescription systems economically. Such benefits are cost savings from the level of transparency provided by the system, reducing the fraud related to the systems and minimizing the cost of printing prescriptions. In terms of health benefits, the system reduced medication errors, provided a better level of medicine accessibility, and improved the monitoring of patient medication intake. Furthermore, the system's leading social benefit is the increased confidence of the patient toward the prescribing system (Deetjen, 2016). However, those benefits will depend on the country's e-Prescription system architecture and its implementation process.

A review was conducted on the literature and government reports relevant to implementing e-Prescribing systems at a national level in several European countries (Kierkegaard, 2013). They aimed to examine the issues that will limit providing eHealth services across EU countries' borders. The study found that the EU countries have different health care policies, different levels of medical data privacy laws, communication networks and methods between the involved parties in e-Prescription systems, and various implementations of the prescriber's digital signature for e-Prescriptions. From the findings, the authors stated that the interoperability of different eHealth systems across the EU countries is part of the solution. More importantly, the authors opined that medical data's privacy and security should be enforced equally among the EU countries (Kierkegaard, 2013).

A recent study was conducted in Finland to explore the e-Prescription anomalies (i.e., errors, ambiguities, and other shortcomings) frequency occurrence, what methods to clarify the e-Prescription, and how those anomalies affect the patient safety in the community pharmacies. Of the surveyed nearly 41,000 e-Prescriptions during the study period (i.e., 3 days),

Table 3. Comparison of Previous Studies and the Current Study

		System architecture	*Medication history*	*CDS*	*Patient privacy*	*System security*	*AI and Blockchain capability*
Previous studies	Canada	XC	XC	XC	XC	XC	XC
(Deetjen, 2016;	United States	D	✓	✓	XA	XA	XA
Kierkegaard, 2013;	United Kingdom	C	✓	✓	XA	XA	XA
Samadbeik et al., 2017;	Spain	XC	XC	XC	XC	XC	XC
Timonen et al., 2018)	Denmark	C	✓	✓	XA	XA	XA
	Sweden	C	✓	✓	XA	XA	XA
	Australia	XC	XC	XC	XC	XC	XC
	Japan	XC	XC	XC	XC	XC	XC
Current study	Canada	C	✓	✓	✓	✓	AI
	United States	D	✓	✓	✓	✓	X
	United Kingdom	C	✓	✓	✓	✓	AI
	Spain	C	✓	✓	✓	✓	AI
	Denmark	C	✓	✓	✓	✓	X
	Sweden	C	✓	✓	✓	✓	X
	Australia	D	✓	✓	✓	✓	AI
	Japan	D	✓	✓	✓	✓	X

AI and Blockchain capability: AI, the infrastructure for AI exist; X, not ready.

AI, artificial intelligence; C, centralized system; CDS, clinical decision support; D, decentralized; XA, information about the aspect not included in the study; XC, the country is not included in the study; ✓, information about this aspect was included in the study.

only 7% of the dispensed e-Prescription had anomalies. A total of 54 community pharmacies, who participated in the study, reported those anomalies. Almost 63% of the e-Prescriptions contained errors in the dosage intake instruction (i.e., the most common anomalies), and 28% of the e-Prescriptions were missing the reason for using the prescribed medication. In most of the 69% anomalies cases, the pharmacist clarified them by writing the dosage instructions, and nearly 23% of them, the patient corrected the dosage instructions.

Accordingly, the pharmacy's workload will increase from interpreting the pharmacist's e-Prescriptions' anomalies, which will affect the overall quality of service. In the above anomalies cases, the pharmacy's workload increased by 39%, which led to an increase in the wait time for the patient (Timonen et al., 2018).

Table 3 shows the scope of the current study results compared with the previous studies. In this study, we expanded the scope of studied countries to get a global overview of a number of the leading countries in e-Prescription. Moreover, we believe that expanding the scope and exploring the implemented systems is more likely to help adopt new approaches to implement more efficient digital health systems, specifically e-Prescription systems in the future. Furthermore, our study aims to compare the security and privacy protocols in place for the selected countries and the system architecture. Moreover, we evaluate the capabilities of the surveyed countries to adopt new technologies, specifically Blockchain and AI. Finally, the study proposes solutions from a technical view to overcoming the resultant challenges and limitations.

Limitations and challenges

After exploring the current e-Prescription systems, it is clear that they are different in applying this service. The difference is due to several reasons; some related to the countries' regulations and rules or the existing infrastructure (Samadbeik et al., 2017). However, several limitations might hinder the progress of improving the quality of the service provided to the patient.

Centralized or decentralized systems are progressing toward applying the Internet of Things (IoT) solutions in health care services to enhance the quality of service and efficiency regarding the provided service. Moreover, an essential factor when handling a patient's medical information is the privacy and security of their medical data. E-Prescription and medication history are part of the patient's medical data. This part of medical data requires a critical level of privacy, and it should be stored securely due to the severe risks associated with it.

One type of risk is tampering with a patient's medication intake instructions, which could cause the patient's death. Therefore, many researchers emphasize the need for security and privacy policies and protocols to use IoT solutions in health care (Al-Nayadi and Abawajy, 2007; Azad et al., 2019; Ball et al., 2003; Park and Moon, 2016). One crucial challenge of e-Prescription systems is whether the system's overall architecture should be centralized or decentralized. As shown in Table 1, many e-Prescription services are centralized and connect to the patients' EHR system. Moreover, some countries have adopted the decentralized approach because of the existing infrastructure. For example, in the United States, EHR systems are available at most hospitals and health care centers.

Although the US system is a decentralized system for e-Prescription, it is still a network that facilitates communication between the involved parties. Surescript is heavily dependent on the local centralized system in the health care center or the pharmacies to store their patient data. Therefore, the network will more likely be vulnerable to the security threats caused by the centralized system connected to it. Moreover, from Table 1, we can see that most of the decentralized systems are dependent on centralized local systems and that it is to facilitate the process of collecting medical data. In Australia, their e-Prescription service is connected to the main EHR system, which is centralized. However, Japan's e-Prescription service uses the patient's mobile application to store the patient's medication history. Therefore, Japan is the most decentralized e-Prescription service compared with the United States and Australia.

Because of the issues related to centralized systems, several novice approaches proposed decentralized systems for health records, medication histories, and e-Prescription to preserve patients' privacy and prevent any pointed attacks on medical information (Li et al., 2019).

However, many countries' regulations require a central physical location to control access to medical data. Therefore, an adaptable approach is likely to help solve most of the architecture issues, such as a system designed to store, transfer, and share needed data (e.g., the prescription history or medication history of a patient) from the patient. Such a system can use any authentication protocol through a token handed to the patient, a key stored in a barcode, or a mobile application accessed by only the patient. From Table 2, we can see that the United States and Australia have most of the needed identifiers to facilitate the management of the required data about medications and e-Prescriptions. These systems are more likely to adopt a new approach toward using Blockchain, which will be more likely to protect against the security threats related to centralized systems.

Medication history. Another challenging issue is the availability of medication histories to other parties participating in the system, such as pharmacists. A quantitative study about the differences between medication histories obtained by physicians and pharmacists was conducted by reviewing 200 medical records. The authors found that pharmacists are better at identifying medication information from patients' medication histories than physicians (Hatch et al., 2011). In addition, several studies found that information of medication histories collected by pharmacists' interviews are complete when compared with the information collected by other caregivers (Carter et al., 2006; LaPointe and Jollis, 2003; Tam et al., 2005; Vira et al., 2006).

As a result, making the medication histories available to all parties involved in the system might enhance patient safety when prescribing or dispensing a new medication. Moreover, other study results showed that caregivers collect medication history information from patients at the initial interview during the admission process (Nester and Hale, 2002). This process makes the information unreliable due to human errors, as it is dependent on the patient's memory, and it can lead to inaccurate information (Hatch et al., 2011).

Thus, having electronic medication histories available and accessible to transfer when needed can improve the efficiency and quality of the provided services. Canada, the United States, Spain, Australia, and Japan are progressing well by making the medication history available to all participating parties. However, only Spain looks like it is ready for adopting future technologies. Despite the United States having the ability to share the medication history, it is still a slow process that needs to be accelerated to make the medication history available in case of emergency. Moreover, the United States, Canada, Australia, and Japan make the medication history available as a service depending on the data stored in the health care centers and pharmacies. This is more likely to slow the progress to adopting AI technologies. A dedicated server to collect and process the data is more likely to help toward that.

Clinical decision support. CDS systems are developed to help prescribers prescribe medications safely and alert them of the various drug interactions that might occur while prescribing a medication to a patient (Bell et al., 2019). Many studies showed an improvement in avoiding medication errors when using e-Prescription with CDS alerts (Ammenwerth et al., 2008; Cresswell et al., 2014; Eslami et al., 2007; Kaushal et al., 2003; Prgomet et al., 2016). However, other studies showed that prescribers tend to ignore and override less important alerts when overwhelmed by a number of alerts and how the system is displaying them (Embi and Leonard, 2012; Van Der Sijs et al., 2006).

When the number of less important alerts increases, this might increase the risk of medication errors. Additionally, the authors found in their systemic review that between 49% and 96% of drug interaction alerts were overridden or ignored (Van Der Sijs et al., 2006). Therefore, incorporating CDS alerts to an e-Prescription system is a necessity, and new visualization methods could reduce the ignoring and overriding of cases.

In addition, a new algorithm based on the patient's medication information might reduce the number of less important alerts. The United States and Spain are the only systems that provide this service as part of the e-Prescription system. However, the CDS systems are progressing toward using AI technologies to enhance the patient's quality of care. Therefore, a large amount of data collection is needed for this progress, which from Table 1 shows Spain is leading the score. US system needs to progress toward data collection and processing to meet the new demands of a better quality of care.

Proposed solutions

Blockchain. Blockchain is a technology deployed best for decentralized systems. It is a technology to store the data in a secure and distributed method. This technology intended to remove the need for a centralized authority to control and verify the data (Li et al., 2019). Therefore, we can see from Tables 1 and 3 that the United States, Australia, and Japan are candidates to implement the Blockchain method because of their decentralized systems. However, those systems still lack the connection between the other parties to facilitate such an approach.

In the United States, e-Prescription systems are handled by a middleman (i.e., Surescripts), making the system semicentered when it comes to managing data sharing between the subscribers (Li et al., 2019). As mentioned previously, the Surescripts enables subscribers to request patient records from other health centers. Other centers will then handle the request, and they have the option to share or hold that information (Surescripts, 2019). This process is more likely to limit the progress toward integrating Blockchain technology. The Blockchain aims to store the data securely and make the data available to all the involved parties.

Australia and Japan's e-Prescription systems are not a fully decentralized system, and their approach is to provide peer-to-peer communication between the prescriber and the pharmacy. This approach allows the pharmacies to send an update to the prescriber system about their patients' e-Prescriptions. Therefore, the infrastructure of those systems lacks the capability at this time of adopting Blockchain technology.

Regarding the centralized systems, adopting the technology is more challenging since their approach is to have a central point to control the information. This approach is more costly to provide the needed security and privacy to protect patient data. Installing and managing patient data security might cost hundreds of millions of dollars (Becker's Healthcare, 2016; Li et al., 2019). Thus, an approach containing more of the benefits of the decentralized architecture integrated with Blockchain will save costs to manage the patients' security and privacy data. Moreover, this approach more likely helps save valuable time wasted to look up the updated medication history of a patient (Norén et al., 2008; Schmiedl et al., 2014).

Artificial intelligence. AI in health care is introduced to support the medical decision. AI is more likely to be adopted as the next logical step in health care technologies. It is more likely to provide better patient care knowledge and keep updated information about patient status. ML and Deep Learning (DL) are the leading technologies in AI. Both technologies are developed to learn patterns about a type of information to suggest accurate predictions. For the system to predict efficiently and accurately, these technologies require learning patterns from large amounts of data. Thus, the type and size of collected data about a patient are important factors. The infrastructure to collect the data is key to assessing the capability of the surveyed systems (Flynn, 2019).

Therefore, we can see from Table 1, the leading country of collecting data is Spain. The type of collected data in Spain's system is an essential factor and more likely to help adopt the ML and DL faster than other countries. However, the communication between parties in Spain might limit this process, as shown in Table 2. On the other hand, the centralized systems are more likely to adopt these technologies faster than the decentralized systems (e.g., United States) due to the required data collection process.

To summarize, it may be worthwhile to consider a different e-Prescription model to overcome the discussed challenges in the current systems. This model should include the ability to share prescription and medication history information between all participating parties in the system. This approach could benefit from the available centralized systems in the countries by incorporating a standalone service that transfers and stores medication history data and e-Prescriptions securely. This service should also preserve the patients' privacy by applying an authentication mechanism to the authorized parties so they can access the data such as Blockchain. Moreover, medication histories should be kept available to patients to enhance patient safety regarding medication errors. Also, this process will grant the patient the ability to share accurate medication histories.

Lastly, CDS systems should be incorporated in the e-Prescription service and also redesigned to avoid ignoring and overriding alert issues when the less important alerts overwhelm the caregiver. In addition, redesigning the system to incorporate future technologies such as AI technologies will more likely enhance the care quality of the patient. Furthermore, in the current COVID-19 climate, e-Prescription systems have become highly relevant in preventing unnecessary contact and ensuring patient and caregivers' safety.

Conclusions

In this study, we compared the selected e-Prescription systems. The comparison process is based on the systems' security and privacy protocols and the systems' architecture. Furthermore, we evaluated the systems' capabilities to progress toward using future technologies such as Blockchain and AI. Finally, we believe this survey provides broad and timely insights on e-Prescription systems around the world. We suggest conducting future studies about the capabilities of the e-Prescription systems to cooperate and communicate on a global scale. This research might contribute toward designing a universal e-Prescription system design that is available to patients when traveling outside of their home country.

Author Disclosure Statement

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References

AEPI eHealth Initiative. (2004). Electronic prescribing: toward maximum value and rapid adoption. Washington, DC: AEPI eHealth Initiative.

Agrawal A. (2009). Medication errors: prevention using information technology systems. Br J Clin Pharmacol 67, 681–686.

Akiyama M, and Nagai R. (2012). Information technology in health care: e-health for Japanese health services. A Report of the CSIS Global Health Policy Center, The Center for Strategic and International Studies and the Health and Global Policy Institute, Washington, DC.

Al-Nayadi F, and Abawajy JH. (2007). An authorization policy management framework for dynamic medical data sharing. Presented at the 2007 International Conference on Intelligent Pervasive Computing (IPC 2007), Jeju City, Korea, 313–318.

Aldughayfiq B, and Sampalli S. (2018). A system to lower the risk of dispensing medication errors at pharmacies using NFC. Presented at the 2018 IEEE International Conference on Internet of Things (iThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData), Halifax, NS, Canada, 196–202.

American Medical Association (AMA), American Academy of Family Physicians (AAFP), American College of Physicians (ACP), Medical Group Management Association (MGMA), eHealth Initiative, and the Center for Improving Medication Management—a colloborative of the Surescripts, AAFP, MGMA, BlueCross BlueShield Association, Humana, and Intel. (2011). Clinician's guide to e-prescribing. http://www.americanehr.com/Upload/Clinicians-Guide-to-E-Prescribing.pdf (Last accessed September, 2019).

Ammenwerth E, Schnell-Inderst P, Machan C, and Siebert U. (2008). The effect of electronic prescribing on medication errors and adverse drug events: a systematic review. J Am Med Inform Assoc 15, 585–600.

Anderson R. (2008). *Security Engineering*. John Wiley & Sons. Hoboken, New Jersey.

Australian Government. (2009). National e-Authentication Framework. Canberra: Australian Government.

Azad MA, Arshad J, Mahmoud S, Salah K, and Imran M. (2019). A privacy-preserving framework for smart context-aware healthcare applications. Transact Emerg Telecommun Technol. 2019;e3634. DOI: 10.1002/ett.3634.

Ball E, Chadwick DW, and Mundy D. (2003). Patient privacy in electronic prescription transfer. IEEE Security Privacy 1, 77–80.

Becker's Healthcare. (2016). 5 Epic contracts | and their costs | so far in 2016. https://www.beckershospitalreview.com/healthcare-information-technology/5-epic-contracts-and-their-costs-so-far-in-2016.html Accessed July 12, 2020.

Belden JL, Wegier P, Patel J, et al. (2018). Designing a medication timeline for patients and physicians. J Am Med Inform Assoc 26, 95–105.

Bell DS, Cretin S, Marken RS, and Landman AB. (2004). A conceptual framework for evaluating outpatient electronic prescribing systems based on their functional capabilities. J Am Med Inform Assoc 11, 60–70.

Bell H, Garfield S, Khosla S, Patel C, and Franklin BD. (2019). Mixed methods study of medication-related decision support alerts experienced during electronic prescribing for inpatients at an English hospital. Eur J Hosp Pharm 26, 318–322.

Bender D, and Sartipi K. (2013). HL7 FHIR: an agile and restful approach to healthcare information exchange. Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems, Porto, Portugal, 326–331.

Birkhead GS, Klompas M, and Shah NR. (2015). Uses of electronic health records for public health surveillance to advance public health. Annu Rev Public Health 36, 345–359.

Blouin RA, and Adams ML. (2017). The role of the pharmacist in health care expanding and evolving. North Carolina Med J 78, 165–167.

Bush PW, and Daniels R. (2017). Health care systems and transitions of care implication on interdisciplinary pharmacy services. North Carolina Med J 78, 177–180.

Byrne CM, Mercincavage LM, Pan EC, Vincent AG, Johnston DS, and Middleton B. (2010). The value from investments

in health information technology at the US Department of Veterans Affairs. Health Affairs 29, 629–638.
Canada Health Infoway. (2018). Prescribers: see how PrescribeIT works in an electronic medical record system and pharmacy management system. Canada Health Infoway, Toronto, Canada.
Canada Health Infoway. (2019). Our approach to privacy. Canada Health Infoway, Toronto, Canada.
Canadian Pharmacists Association. (2009). Recommendations for the implementation of electronic prescriptions in Canada. Ottawa: Canadian Pharmacists Association.
Carter MK, Allin DM, Scott LA, and Grauer D. (2006). Pharmacist-acquired medication histories in a university hospital emergency department. Am J Health Syst Pharm 63, 2500–2503.
Castro D. (2009). Explaining international it application leadership: health it. Available at SSRN 1477486. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1477486 (Last accessed 2019).
Chen Q, Lambright J, and Abdelwahed S. (2016). Towards autonomic security management of healthcare information systems. Presented at the 2016 IEEE First International Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE), Washington, DC, 113–118.
Chouvarda I, and Maglaveras N. (2015). Medical informatics education & research in Greece. Yearb Med Inform 24, 220–226.
Cresswell KM, Bates DW, Williams R, et al. (2014). Evaluation of medium- term consequences of implementing commercial computerized physician order entry and clinical decision support prescribing systems in two ‘early adopter’hospitals. J Am Med Inform Assoc 21, e194–e202.
Deetjen U. (2016). European e-prescriptions: benefits and success factors. Working Paper Series-No. 5. University of Oxford, Oxford, United Kingdom.
Devine EB, Hansen RN, Wilson-Norton JL, et al. (2010). The impact of computerized provider order entry on medication errors in a multispecialty group practice. J Am Med Inform Assoc 17, 78–84.
Doupi P, Renko E, Giest S, Heywood J, and Dumortier J. (2010). Country brief: Sweden. Bonn/Brussels: European Commission.
Drug Enforcement Administration. (2010). Electronic prescriptions for controlled substances final rule. Number 2013-06918. US Federal Register.
Drug Enforcement Administration. (2013). Electronic prescriptions for controlled substances notice of approved certification process. Number 2010-6687. US Federal Register.
eHealth Initiative, and Center for Improving Medication Management. (2008). A clinician’s guide to electronic prescribing. Washington DC: serial online. https://www.thecimm.org/PDF/Clinician%27s_Guide_to-e-Prescribing_Final_100708.pdf (Last accessed 2019).
eHealth Observatory. (2011). *eHealth Observatory ePrescribing Workflow Handbook v3.0*. University of Victoria, Victoria, BC, Canada.
Eichwald J. (2014). Impact of electronic health records implementation on the early detection hearing and intervention programs. Website presentation ‘‘Discretionary Advisory Committee on Heritable Disorders in Newborns and Children.’’ https:www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/meetings/Heritable%20Disorders%202004-2015/2014/May%2029-30%202014/eichwaldpresentation.pdf (Last accessed 2019).
Embi PJ, and Leonard AC. (2012). Evaluating alert fatigue over time to EHR-based clinical trial alerts: findings from a randomized controlled study. J Am Med Inform Assoc 19, e145–e148.
eRx. (2018a). https://www.erx.com.au/forpharmacists/how-erx-works/ (Last accessed 2019).
eRx. (2018b). Privacy policy. https://www.erx.com.au/support/privacy-policy (Last accessed 2019).
Eslami S, Abu-Hanna A, and De Keizer NF. (2007). Evaluation of outpatient computerized physician medication order entry systems: a systematic review. J Am Med Inform Assoc 14, 400–406.
Flynn A. (2019). Using artificial intelligence in health-system pharmacy practice: finding new patterns that matter. Am J Health Syst Pharm 76, 622–627.
Gasbarro R. (2015). My pharmacist says he needs ‘‘prior authorization’’—what’s that all about? *ConsumerAffairs*. https://www.consumeraffairs.com/news/my-pharmacist-says-he-needs-prior-authorization-whats-that-all-about-040615.html (Last accessed 2020).
Goundrey-Smith S. (2013). *Information Technology in Pharmacy: An Integrated Approach*. Health informatics. Springer, Berlin/Heidelberg, Germany. OCLC: ocn773666076.
Green M, and Reinholdt B. (2017). Improving medication management and patient safety through e-prescribing. Canada Health Infoway, Toronto, Canada.
Grepstad M, and Kanavos P. (2015). A comparative analysis of coverage decisions for outpatient pharmaceuticals: evidence from Denmark, Norway and Sweden. Health Policy 119, 203–211.
Grizzle AJ, Horn J, Collins C, et al. (2019). Identifying common methods used by drug interaction experts for finding evidence about potential drug-drug interactions: web-based survey. J Med Internet Res 21, e11182.
Hammar T, Nyström S, Petersson G, Astrand B, and Rydberg T. (2011). Patients satisfied with e-prescribing in sweden: a survey of a nationwide implementation. J Pharm Health Serv Res 2, 97–105.
Hassel M. (2019). E-prescriptions in Sweden. Technical report, Swedish eHealth Agency, Sweden.
Hatch J, Becker T, and Fish JT. (2011). Difference between pharmacist- obtained and physician-obtained medication histories in the intensive care unit. Hosp Pharm 46, 262–268.
Health and Social Care Information Centre (Great Britain). (2019). Health and Social Care Information Centre (HSCIC) annual report and accounts 2018–19. NHS Digital, United Kingdom.
Henderson J, Pollack A, Gordon J, and Miller G. (2015). Technology in practice-GP computer use by age (vol 43, pg 831, 2014). Aust Fam Physician 44, 8.
Hibberd R, Cornford T, Lichtner V, Venters W, and Barber N. (2017). England’s Electronic Prescription Service: Infrastructure in an Institutional Setting. In: Aanestad M, Grisot M, Hanseth O, et al., eds. *Information Infrastructures within European Health Care: Working with the Installed Base* [Internet]. Cham (CH): Springer, 2017. Chapter 8. https://www.ncbi.nlm.nih.gov/books/NBK543695/ DOI: 10.1007/978-3-319-51020-0_8.
HL7. (2019). Introduction to HL7 standards. http://www.hl7.org/implement/standards/index.cfm (Last accessed 2019).
HL7-FHIR-Release-4. (2019). FHIR overview. https://www.hl7.org/fhir/overview.html (Last accessed 2019).
HL7UK. (2019). HL7 delivers healthcare interoperability standards. https://www.hl7.org.uk/ (Last accessed 2019).

Japan Government. (2019). Ministry of Health, Labor and Welfare/conducting demonstration tests for full-scale operation of electronic prescriptions [translated from Japanese]. Distribution news.

Jensen TB, and Thorseng AA. (2017). Building national healthcare infrastructure: the case of the Danish e-health portal. In: Aanestad M, Grisot M, Hanseth O, Vassilakopoulou, P, eds. *Information Infrastructures Within European Health Care*. Health Informatics. Springer, Cham. https://doi.org/10.1009/978-3-319-51020-0_13. pgs. 209–224.

Johnston D, Pan E, Walker J, Bates DW, and Middleton B. (2003). The value of computerized provider order entry in ambulatory settings. Boston, MA: Center for Information Technology Leadership.

Joy MG, Ellyn RB, Dori AC, and Genna RC. (2011). Physician practices e-prescribing and accessing information to improve prescribing decisions. Res Brief 1–10.

Kaushal R, Shojania KG, and Bates DW. (2003). Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. Arch Intern Med 163, 1409–1416.

Kawamoto K, Houlihan CA, Balas EA, and Lobach DF. (2005). Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ 330, 765.

Kierkegaard P. (2013). E-prescription across Europe. Health Technol 3, 205–219.

King N, Christie T, and Alami KM. (2007). Process implications of e-prescribing information integration models: United States versus a Middle East approach. e-Service J 5, 15.

Klein GO. (2010). History of electronic prescriptions in Sweden: from time-sharing systems via smartcards to EDI. In: Impagliazzo J, Lundin P, Wangler B, eds. History of Nordic Computing 3. HiNC 2010. IFIP *Advances in Information and Communication Technology*, vol. 350, pgs. 65–73. Springer, Berlin/Heidelberg. https://doi.org/10.1007/978-3-642-23315-9_8.

Kohn LT. (2011). *Electronic Prescribing: CMS Should Address Inconsistencies in Its Two Incentive Programs That Encourage the Use of Healthy Information Technology*. DIANE Publishing, Darby, Pennsylvania, USA.

Koromina M, Pandi MT, and Patrinos GP. (2019). Rethinking drug repositioning and development with artificial intelligence, machine learning, and OMICS. OMICS 23, 539–548.

Krag A, Hansen B, and Nielsen E. (2012). eHealth in Denmark. eHealth as a part of a coherent Danish health care system. Technical report. Copenhagen: Danish Ministry of Health.

Kruus P. (2013). Developing an evaluation framework for the country-wide electronic prescribing system in Estonia. Master's thesis. Tallinn: Tallinn University of Technology.

LaPointe NMA, and Jollis JG. (2003). Medication errors in hospitalized cardiovascular patients. Arch Intern Med 163, 1461–1466.

Lau F, Rubin SH, Smith MH, and Trajkovic L. (2000). Distributed denial of service attacks. Presented at the SMC 2000 Conference Proceedings. 2000 IEEE International Conference on Systems, Man and Cybernetics. ''Cybernetics Evolving to Systems, Humans, Organizations, and Their Complex Interactions.'' Nashville, Tennessee, USA. Cat. No. 0, Volume 3, 2275–2280.

Li P, Nelson SD, Malin BA, and Chen Y. (2019). DMMS: a decentralized blockchain ledger for the management of medication histories. Blockchain Healthc Today 2, 38.

Mäkinen M, Rautava P, Forsström J, and Aärimaa M. (2011). Electronic prescriptions are slowly spreading in the European Union. Telemed J E Health 17, 217–222.

Masuda K. (2016). The electronic prescriptions that have been lifted and the actual operation (page 2) [translated from Japanese]. Digital Health, Japan.

MediSecure. (2019a). Medisecure how it works. MediSecure, Australia. http://www.medisecure.com.au/products-and-platforms/\#etp (Last accessed 2019).

MediSecure. (2019b). Medisecure patient consent. MediSecure, Australia. http://www.medisecure.com.au/patient-consent/ (Last accessed 2019).

MediSecure. (2019c). Medisecure privacy policy. MediSecure, Australia. http://www.medisecure.com.au/privacy-policy/ (Last accessed 2019).

Ministry of Health, Labor and Welfare. (2016). Operation guidelines for electronic prescriptions [translated from Japanese]. Technical report. Ministry of Health, Labor and Welfare, Japan.

Ministry of Health, Labor and Welfare. (2019). Complete demonstration project for full-scale operation of electronic prescriptions [translated from Japanese]. Technical report. Ministry of Health, Labor and Welfare, Japan.

Ministry of Health, Social Services and Equality. (2014). ePrescription in Spain patient safety. Ministry of Health, Social Services and Equality, Spain.

Mon DT. (2009). American Health Information Management Association (AHIMA) written and oral testimony at the NCVHS privacy, confidentiality and security subcommittee hearing on personal health records. AHIM, May 20, 2009. www.ahima.org/downloads/pdfs/advocacy/AHIM Atestimony onPHRprivacy-final052009.pdf. Accessed December 1, 2010.

Motulsky A, Sicotte C, Gagnon M-P, et al. (2015). Challenges to the implementation of a nationwide electronic prescribing network in primary care: a qualitative study of users' perceptions. J Am Med Inform Assoc 22, 838–848.

Nair RP, Kappil D, and Woods TM. (2010). Pharmacist to pharmacist- 10 strategies for minimizing dispensing errors-dispensing errors can be costly for the pharmacist as well as potentially dangerous for the patient. Pharmacists can take simple steps to help eliminate this problem. Pharm Times 76, 92.

Nakagawa S, and Kume N. (2017). Pharmacy practice in Japan. Can J Hosp Pharm 70, 232–242.

National Health Service (NHS). (2019). Start using electronic prescriptions. National Health Service Digital, United Kingdom.

National Health Service Business Services Authority (NHS BSA). (2018). Requirements and guidance for endorsement in the electronic prescription service (EPS). Newcastle upon Tyne: National Health Service.

National Health Service Digital. (2019a). Controlled drugs in the Electronic Prescription Service. National Health Service Digital, United Kingdom.

National Health Service Digital. (2019b). Electronic Prescription Service identifiers and what they mean. National Health Service Digital, United Kingdom.

National Health Service Digital. (2019c). Electronic Prescription Service overview for developers. National Health Service Digital, United Kingdom.

National Health Service Digital. (2019d). Registration authorities and smartcards. National Health Service Digital, United Kingdom.

National Health Service Digital. (2019e). Spine. National Health Service Digital, United Kingdom.

Nayani S. (2017). Report: 2017 current prescribing and dispensing landscape in Canada. Canada Health Infoway, Toronto, Canada.

Nester TM, and Hale LS. (2002). Effectiveness of a pharmacist-acquired medication history in promoting patient safety. Am J Health Syst Pharm 59, 2221–2225.

Norén GN, Sundberg R, Bate A, and Edwards IR. (2008). A statistical methodology for drug–drug interaction surveillance. Stat Med 27, 3057–3070.

Odukoya OK, and Chui MA. (2013). E-prescribing: a focused review and new approach to addressing safety in pharmacies and primary care. Res Soc Admin Pharm 9, 996–1003.

Odukoya OK, Stone JA, and Chui MA. (2014). E-prescribing errors in community pharmacies: exploring consequences and contributing factors. Int J Med Inform 83, 427–437.

Öhlund S-E, Åstrand B, and Petersson G. (2012). Improving interoperability in eprescribing. Interact J Med Res 1, e17.

Ojeleye O, Avery A, Gupta V, and Boyd M. (2013). The evidence for the effectiveness of safety alerts in electronic patient medication record systems at the point of pharmacy order entry: a systematic review. BMC Med Inform Decis Mak 13, 69.

Park S, and Moon J. (2016). Strategic approach towards clinical information security. In: Moon JD and Galea MP, eds. *Improving Health Management Through Clinical Decision Support Systems.* IGI Global, 329–359. http://doi:10.4018/978-1-4666-9432-3.ch015.

Patil HK, and Seshadri R. (2014). Big data security and privacy issues in healthcare. In *2014 IEEE International Congress on Big Data.* IEEE, 762–765.

Patrao L, Deveza R, and Martins H. (2013). Pem-a new patient centred electronic prescription platform. Proc Technol 9, 1313–1319.

Pereira J, Beir M, Teixeira J, and Machado RJ. (2018). Patient-centric e-prescription services—an integrated system architecture proposal. Presented at the 2018 International Conference on Intelligent Systems (IS), 576–583. Madeira, Portugal.

Pharmaceutical Services Negotiating Committee (PSNC). (2016). The guiding principles of patient nomination. Pharmaceutical Services Negotiating Committee (PSNC), United Kingdom.

Pharmaceutical Services Negotiating Committee (PSNC). (2018). PSNC briefing 005/18: dealing with smartcards—quick reference guide. Pharmaceutical Services Negotiating Committee (PSNC), United Kingdom.

Pharmaceutical Services Negotiating Committee (PSNC). (2019). Spine (NHS IT). Pharmaceutical Services Negotiating Committee (PSNC), United Kingdom.

Ploner N, and Prokosch HU. (2020). Integrating a secure and generic mobile app for patient reported outcome acquisition into an EHR infrastructure based on FHIR resources. Stud Health Technol Inform 270, 991–995.

Ponemon L. (2018). Cost of a data breach study: global overview. Benchmark research sponsored by IBM Security independently conducted by Ponemon Institute LLC.

Porteous T, Bond C, Robertson R, Hannaford P, and Reiter E. (2003). Electronic transfer of prescription-related information: comparing views of patients, general practitioners, and pharmacists. Br J Gen Pract 53, 204–209.

PrescribeIT. (2018). PrescribeIT information security policy. PrescribeIT, Toronto, Canada.

Prgomet M, Li L, Niazkhani Z, Georgiou A, and Westbrook JI. (2016). Impact of commercial computerized provider order entry (CPOE) and clinical decision support systems (CDSSS) on medication errors, length of stay, and mortality in intensive care units: a systematic review and meta-analysis. J Am Med Inform Assoc 24, 413–422.

Reed-Kane D, Kittell K, Adkins J, Flocks S, and Nguyen T. (2014). E-prescribing errors identified in a compounding pharmacy: a quality-improvement project. Int J Pharm Compound 18, 83–86.

Salmon JW, and Jiang R. (2012). E-prescribing: history, issues, and potentials. Online J Public Health Inform (Vol. 4, No. 3).

Samadbeik M, Ahmadi M, and Asanjan SMH. (2013). A theoretical approach to electronic prescription system: lesson learned from literature review. Iran Red Crescent Med J 15, e8436.

Samadbeik M, Ahmadi M, Sadoughi F, and Garavand A. (2017). A comparative review of electronic prescription systems: lessons learned from developed countries. J Res Pharm Pract 6, 3.

Saripalle R, Runyan C, and Russell M. (2019). Using HL7 FHIR to achieve interoperability in patient health record. J Biomed Inform 94, 103188.

Schmiedl S, Rottenkolber M, Hasford J, et al. (2014). Self-medication with over the counter and prescribed drugs causing adversedrug-reaction-related hospital admissions: results of a prospective, longterm multi-centre study. Drug Saf 37, 225–235.

Sellberg N, and Eltes J. (2017). The Swedish patient portal and its relation to the national reference architecture and the overall ehealth infrastructure. In: Aanestad M, Grisot M, Hanseth O, and Vassilakopoulou P, eds. *Information Infrastructures within European Health Care.* Health Informatics, Springer, Cham, pgs. 225–244. https://doi.org/10.1007/978-3-319-51020-0_14.

Shickel B, Tighe PJ, Bihorac A, and Rashidi P. (2018). Deep EHR: a survey of recent advances in deep learning techniques for electronic health record (EHR) analysis. IEEE J Biomed Health Inform 22, 1589–1604.

Surescripts. (2015). Demystifying electronic prior authorization (ePA). Surescripts, USA.

Surescripts. (2018a). E-prescribing. Surescripts, USA.

Surescripts. (2018b). Electronic prescribing for controlled substances. Surescripts, USA. https://surescripts.com/enhance-prescribing/e-prescribing/e-prescribing-for-controlled-substances/# (Last accessed 2019).

Surescripts. (2019). Protecting patient privacy. Surescripts.com

Swan AL, Mobasheri A, Allaway D, Liddell S, and Bacardit J. (2013). Application of machine learning to proteomics data: classification and biomarker identification in postgenomics biology. OMICS 17, 595–610.

Tam VC, Knowles SR, Cornish PL, Fine N, Marchesano R, and Etchells EE. (2005). Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. CMAJ 173, 510–515.

Taylor JA, Loan LA, Kamara J, Blackburn S, and Whitney D. (2008). Medication administration variances before and after implementation of computerized physician order entry in a neonatal intensive care unit. Pediatrics 121, 123–128.

The Australian Digital Health Agency. (2019a). Set up electronic transfer of prescriptions (ETP) in your organisation. The Australian Digital Health Agency, Australia.

The Australian Digital Health Agency. (2019b). Viewing and uploading prescription and dispense records. The Australian Digital Health Agency, Australia.

The Center for Improving Medication Management. (2011). A clinician's guide to electronic prescribing.

Timonen J, Kangas S, Kauppinen H, and Ahonen R. (2018). Electronic prescription anomalies: a study of frequencies, clarification and effects in Finnish community pharmacies. J Pharm Health Serv Res 9, 183–189.

Van Der Sijs H, Aarts J, Vulto A, and Berg M. (2006). Overriding of drug safety alerts in computerized physician order entry. J Am Med Inform Assoc 13, 138–147.

Van Dijk L, De Vries H, and Bell D. (2011). Electronic prescribing in the United Kingdom and in the Netherlands. Prepared for: Agency for Healthcare Research and Quality US Department of Health and Human Services, Rockville, MD, 540.

Velo GP, and Minuz P. (2009). Medication errors: prescribing faults and prescription errors. Br J Clin Pharmacol 67, 624–628.

Vira T, Colquhoun M, and Etchells E. (2006). Reconcilable differences: correcting medication errors at hospital admission and discharge. BMJ Qual Saf 15, 122–126.

Wang CJ, Patel MH, Schueth AJ, et al. (2009). Perceptions of standards-based electronic prescribing systems as implemented in outpatient primary care: a physician survey. J Am Med Inform Assoc 16, 493–502.

World Health Organization (WHO). (2020). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports (Last accessed 2020).

Yang Y, Ward-Charlerie S, Kashyap N, DeMayo R, Agresta T, and Green J. (2018). Analysis of medication therapy discontinuation orders in new electronic prescriptions and opportunities for implementing CancelRx. J Am Med Inform Assoc 25, 1516–1523.

Zaghloul E, Li T, and Ren J. (2019). Security and privacy of electronic health records: decentralized and hierarchical data sharing using smart contracts. Presented at the 2019 International Conference on Computing, Networking and Communications (ICNC), Honolulu, HI, USA. pgs. 375–379.

Address correspondence to:
Srinivas Sampalli, PhD
Faculty of Computer Science
Dalhousie University
6050 University Avenue, Room No. 319
Halifax, Nova Scotia B3H 1W5
Canada

E-mail: srini@cs.dal.ca

Abbreviations Used

ADR = Adverse Drug Reactions
AI = Artificial intelligence
CDS = clinical decision support
DDI = Drug-Drug Interactions
DIS = Drug Information System
DL = deep learning
EHR = Electronic Health Record
EMR = Electronic Medical Record
EPS = Electronic Prescription Service
eRx = electronic medical prescription
ETP = Electronic Transfer Prescription
EU = European Union
FHIR = Fast Healthcare Interoperability Resources
HL7 = Health Level Seven International
IoT = Internet of Things
ML = machine learning
NHS = National Health Service
PA = prior authorization
PBM = pharmacy benefit manager
PDDI = Potential of Drug–Drug Interactions
PES = Prescription Exchange Service
PHR = Personal Health Record
PUID = Prescription Unique ID

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A framework to lower the risk of medication prescribing and dispensing errors: A usability study of an NFC-based mobile application

Bader Aldughayfiq *, Srinivas Sampalli [1]

Faculty of Computer Science, Dalhousie University, Halifax, Canada

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ABSTRACT

Background: Wrong medication and wrong dosage are major risks in the pharmaceutical industry, as many medication errors occur when dispensing medication. The dispensing process in its current form is limited in verifying the patient's identity before dispensing the medication. Furthermore, this process does not offer a robust method for providing accurate medication intake instructions. Therefore, we have developed a framework to accurately and securely overcome issues associated with transferring patient credentials and prescription information. The long-term goal of this research is to develop a framework to mitigate medication dispensing errors. One of the framework components is the mobile application that uses near-field communication (NFC) to transfer information. Therefore, in this paper, we designed a user study to assess the proposed NFC-based mobile application in terms of usefulness and ease of use compared with the traditional method of picking up a prescribed medication.

Methods: We conducted a usability study with 21 participants to perform four tasks to simulate the process of picking up a prescribed medication using the proposed *NFC application method* and the *traditional method* of picking up medication. Then, we asked the participants to complete two post-questionnaires after using each method to evaluate the participants' experience of the process. Next, we asked the participants to complete an additional questionnaire about the usefulness of the *NFC application method*. Finally, we conducted semi-structured interviews with the participants to get more evidence to back up the questionnaire answers.

Results: Our findings show that 91% of the participants believe using the *NFC application method* will improve patient safety during the medication pickup process. Nearly 97% of participants found the *NFC application method* easy to use. Our findings show that the participants scored lower when using the *NFC application method* compared with the *traditional method* when trying to identify the wrong medication after dispensing. In addition, 90% of the participants successfully identified the wrong medication when using the *NFC application method*, compared to only 38% when using the *traditional method*. Finally, the results show that the participants preferred using the *NFC application method* in terms of information availability, security, and privacy.

Conclusions: The study findings show that the proposed NFC application for managing patients' prescriptions and picking up medication might improve patient safety. The results show that the participants believe the NFC application will mitigate medication dispensing errors, at least from their end. The participants believe the application will provide a fast and accurate method of verifying dispensed medication from the patient end. Moreover, the application will help the patient to track their current prescription, which also helps them remember the medication intake instructions. Finally, the study indicates that the application will provide a secure, private, and accurate method to help verify the patient's identity, thus minimizing medication errors during the medication dispensing process.

* Corresponding author.
E-mail addresses: Baderaldu@dal.ca (B. Aldughayfiq), srini@cs.dal.ca (S. Sampalli).
[1] https://web.cs.dal.ca/~srini/

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1. Introduction

1.1. Background

In 1999, the Institute of Medicine (IOM) stated that medical errors were the primary cause of 45,000–98,000 deaths per year in the US alone [1]. Furthermore, more recent studies estimated that medical errors are the third leading cause of death in the US and the third leading cause of death in Canada [2–5]. Other analysis studies [6–8] found that among the critical causes of medication errors are wrong medication, wrong dose, or both. Additionally, the review studies [9,10] found that prescription errors have a major role in causing medication errors in hospital admissions cases and pharmacy alert events.

Consequently, many researchers have proposed solutions and new approaches to overcome medication errors. The authors in [11] introduced ten strategies for reducing stress in the work area. However, these strategies add more cost and affect the efficiency of the pharmacy's dispensing process, and they do not contribute to overcoming paper prescription issues. Therefore, e-prescriptions were introduced to improve patient safety while prescribing [12,13]. Many centuries around the world use a method of ePrescribing such as faxing or emailing prescriptions. However, several studies define an ePrescription service to submit, change, review, and send a prescription electronically to the pharmacies using a computer device. Also, ePrescribing service should provide a communication channel with the medication dispensers [12,14–16]. Therefore the number of countries implementing the ePrescribing service varies on the features provided with the service. In our survey [12] about the implementation of ePrescription systems around the world, we compared eight countries that fully implemented the ePrescription system based on their security and privacy protocols. The countries are the US, Canada, UK, Australia, Spain, Denmark, Sweden, and Japan. Other studies [16–22] reviewed nine other countries (i.e. Netherlands, Estonia, Austria, Croatia, Greece, Italy, Portugal, Finland, and India) in which the ePrescription system or service is fully implemented. The European Commission expects the eHealth digital service to be available and established in 25 European countries by 2025 [23]. However, e-prescription systems do not help avoid medication errors in the dispensing process, such as dispensing the wrong medication, dispensing to the wrong patient, or verifying the patient's identity before dispensing the medication [24].

1.2. Medication management mobile apps

In this section, we will review related work focusing on medication management apps. Medication management term refers to either organizing medications for patients or detecting medication interactions. Tabi et al. reviewed and analyzed 328 medication management mobile applications. They categorized the mobile application based on the provided features. They found most of the apps ($n = 282$) focus feature is medication reminder, 152 apps can track symptoms and side effects, 135 apps can share reports with others, and 63 have educational components. The authors found that the software companies developed most of the apps, and there is a lack of health care professionals and academia involved in developing the applications. They are of the opinion that this is a limitation and might affect the general purpose of the application and the privacy and security of the patient information [25–27]. Ahmed et al. conducted a review study for 420 apps related to medication adherence. Their analyses found the most used adherence strategies, reminders, behavioral, and educational. They also found most apps ($n = 250$ apps) adopted one feature only, 149 apps had two features, and only 22 apps adopted three features. The limitations they identified were the lack of health care professionals in app development and the limited use of multiple adherence strategies in the apps [28]. Other studies conducted systemic reviews on medication management apps (approximately 400) found most applications lacked useful features to improve medication adherence. There should be more regulations to help with quality control, including data security and privacy [29–31]. Most of these applications were limited to medication management from the patient end and did not provide features about protecting the patient data security and privacy. Further, most of these apps do not provide features for prescription management and sharing.

1.3. Objectives

Therefore, we have proposed a framework to optimize the prescribing process and the prescribed medication dispensing process. The system aims to introduce an improved robust and secure method of transferring e-prescriptions and preserving the patient's information privacy in the system using the near-field communication (NFC) technology [31]. This study intends to show the results of using NFC technology in the mobile application by the patients. Besides, the study collects the participants' feedback about using the mobile application to control sharing their information and making the e-prescription information available at all times.

An improved version of the framework from [31] is shown in Fig. 1. We introduce the use of blockchain and machine learning algorithms to improve prescribing the medication safely. This section of the framework is still under development and will be introduced in future publications. The other component is the NFC-mobile application offers three main features to securely transfer information, confirm the patient's identity, and track e-prescription and medication histories. Finally, the application uses biometric information authentication (i.e. fingerprints) to control access to the app. Although the proposed system will not prevent human errors, we believe it will mitigate medication dispensing errors. This paper focuses on the user study implemented using the NFC-enabled phone. Also, the scope of this paper discussing only the patient side of the system. Thus, we will not be discussing or show any result of the other framework components. In a future publication, we will be discussing the other components of the framework.

In this paper, we show and discuss the results of our usability study of the NFC mobile application. The paper is organized as follows. Section 2 discusses the proposed system architecture and the usability study we conducted. Section 3 discusses the preliminary findings of the user study we conducted. Finally, Section 4 provides concluding remarks and discusses future work.

2. Methodology

2.1. The proposed framework

As mentioned before, the framework consists of three essential parts: a blockchain network, a machine learning algorithm, and an NFC-enabled mobile application. The three parts are shown in the overall overview of the proposed framework Fig. 1. In this paper, we only discuss the results of the usability study of the NFC-enabled mobile application. Fig. 2 shows the process of dispensing medication to a patient.

2.2. Application usability study

We conducted one-on-one usability testing to evaluate the NFC-enabled smartphone application's use to pick up prescribed medication from the patient's prescriptive. In addition, the study evaluates the security and privacy of the shared patient information from the patient's perspective. We recruited 21 participants, all of whom have picked up medication from pharmacies in the past six months. Even though the sample size is small, research has indicated that five subjects are enough to detect errors in a usability test [32–34]. In addition, articles [9,35] mentioned at least 12 participants are enough to drive valid results for a System Usability Scale (SUS) test. Hwang et al. proposed that using the rule 10 ± 2 is sufficient to discover 80% of usability problems [36]. Moreover, this number is recommended in thematic analysis approaches

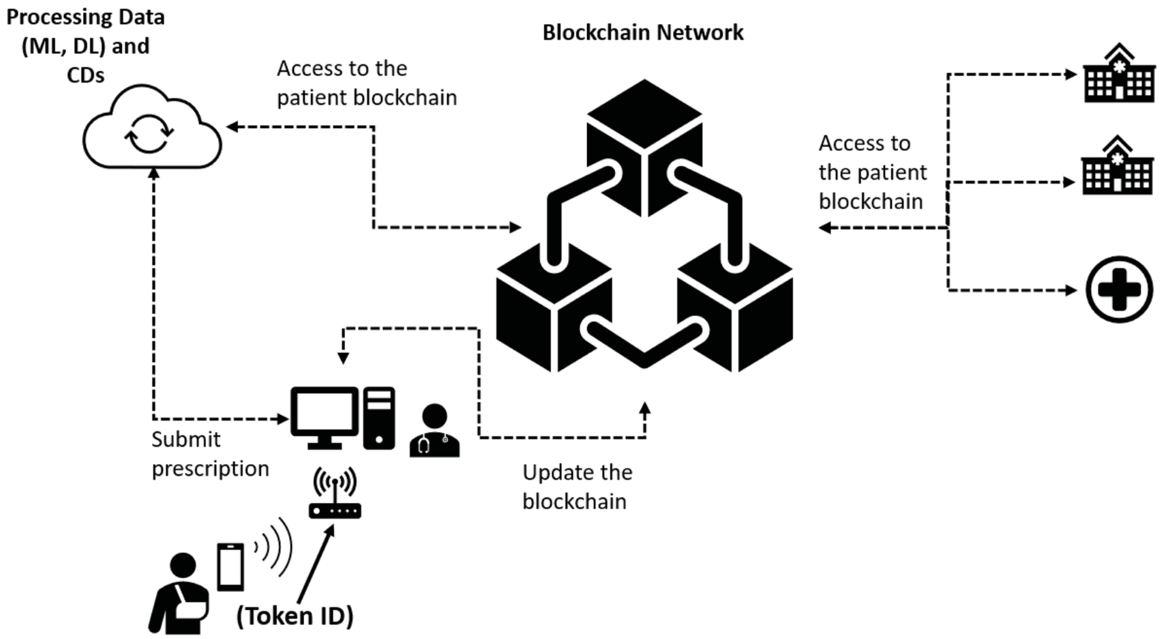


Fig. 1. The proposed framework architecture.

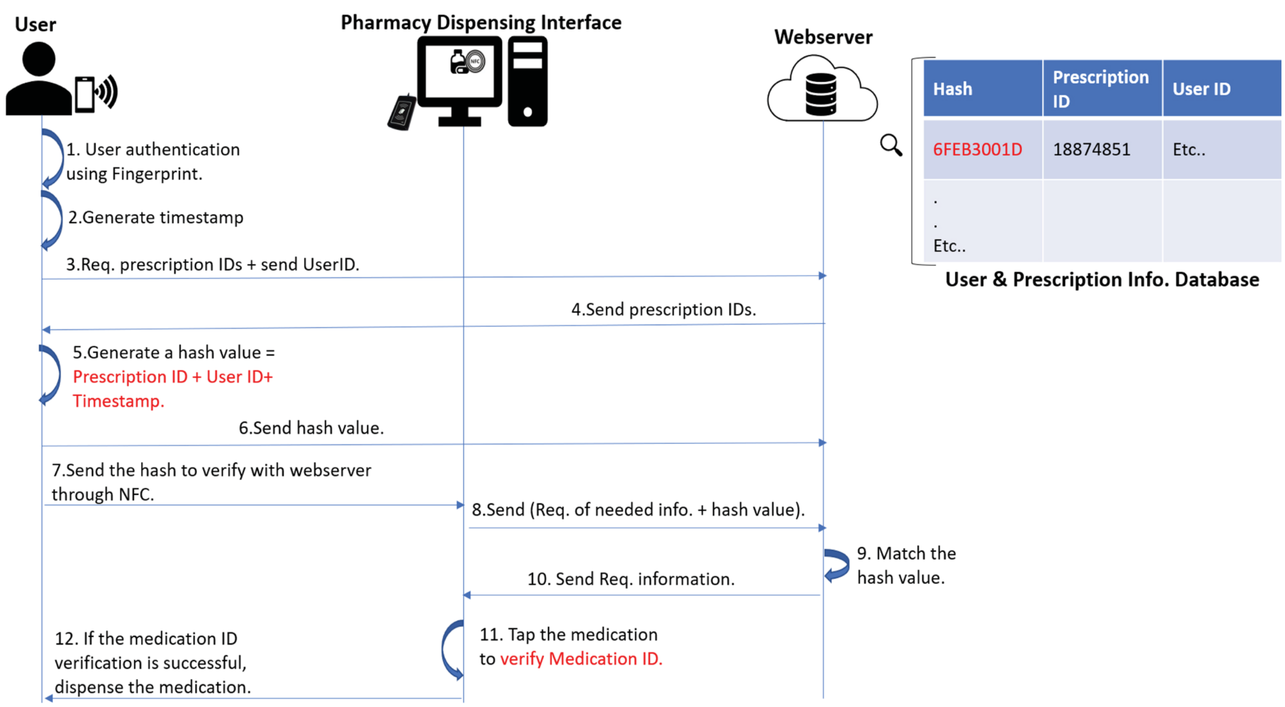


Fig. 2. The sequence diagram of the dispensing medication process.

to provide reasonable quotes, codes, and themes for the study [37]. In addition, the authors in [38] indicated that at least 20 users should should participate if the usability testing includes a quantitative method. Based on that information, we believe that 21 participants will be sufficient to evaluate the application's usability and expose most of the proposed application's weaknesses and strengths. Thus, we believe the study will provide thorough feedback to improve the overall framework's next phase. The study was held in the MyTech laboratory in the Faculty of Computer Science at Dalhousie University and the university libraries' study rooms. Once the participant responds to the notice, we will meet with them at an agreeable time in one of the mentioned places. All the sessions took an average time between 30 and 40 min.

2.2.1. Study design

We designed the study to collect data at multiple levels. First, we asked the participant to complete a background questionnaire to gather demographic data about the participant and measure their comfort level using the smartphone application in general, and the NFC-enabled smartphone application tap in particular (Table 1). Second, we asked the participant to perform two sets of tasks (i.e. four tasks in total). In the first set of tasks, the participants used the traditional method of picking up medication. In the traditional method of processing a paper prescription, the participant simulates picking up the pharmacy's prescribed medication using a paper prescription. At the pharmacy, the participant identifies themselves to the pharmacist and picks up the

Table 1
Participants' demographic information.

Participants ($N = 21$)		
Gender	Male	85.7%
	Female	14.3%
Age	18–24 years old	42.9%
	25–34 years old	42.9%
	35–44 years old	9.5%
	55 years or older	4.8%
Education	High school	14.3%
	Undergraduate diploma degree	38.1%
	Masters' degree	38.1%
	Other	9.5%
Occupation	Academic adviser	4.8%
	Industrial engineering	4.8%
	Retired	4.8%
	Student	85.7%
Times of picking up prescription	Less than one	33.3%
	1–5 times	66.7%
Time spent using smartphone/daily	Less than one hour	9.5%
	1–5 h	61.9%
	5–10 h	28.6%
Using NFC	Yes	61.9%
	No	38.1%

medication. In the second set of tasks, the investigator asked the participant to use the application to pass the identification information to a pharmacist after choosing the prescription they wish to pick up. In all tasks, the participant presents the prescription to the pharmacist (i.e. the investigator) to pick up the medication. After each task in both sets, the investigator asked the participant to verify whether they got the correct medication. In each set of tasks, the participant received the right medication in one of the tasks and the wrong medication in the other task for both groups (i.e., traditional and NFC application). The participants did not know which one they received until after the tasks session is over.

We adopted the Technology Acceptance Model (TAM) as a guideline to develop our questionnaire [39,40]. After each set of tasks, we asked the participants to complete a post-condition questionnaire (Likert scale) to measure their experience with the task conditions and to understand their opinions and feelings about the method used. After the tasks session, we asked the participant to fill out a questionnaire (Likert scale) to measure their thoughts about the usefulness and ease of use of the NFC application. Finally, we conducted a semi-structured interview to gather qualitative data to (1) support the post-task questionnaire answers, (2) identify the weaknesses and strengths and (3) collect descriptive recommendations for improvements.

2.2.2. *Statistical analysis*

According to [41] in their review study on the usability testing methods for eHealth applications, the majority of the articles used two quantitative methods questionnaires and task completion analyses. Therefore, after the collecting data process, we analyzed the data using general descriptive statistics. We also used the statistical tests one-way ANOVA for numerical variables and chi-square for categorical variables. We ran the tests to measure if the means of tasks' times and the successful completion of tasks in both methods (i.e. the traditional method and NFC application method) are significantly different [42]. A P of <0.05 was considered the threshold for the statistical significance difference. We performed the tests using SPSS version 26 (IBM Corporation, Armonk, NY, USA) and Microsoft Excel to analyze and code the collected data.

3. Preliminary findings

3.1. *Tasks analysis*

In Fig. 4, the red dotted line is the mean of the tasks' times. Table 2 displays the descriptive statistics across the conditions in the two methods we used. As can be seen, both tasks 1 and 3 have a much lower mean value, and this is due to the tasks' nature, as we asked the participants to check the dispensed medication, and in these tasks, we gave the participants the right medication. In the first task using the traditional method, we noticed that participants would complete the task successfully (i.e. verify the medication successfully) with a rate of 100% due to their assumption that it is the right medication. It is worth mentioning that in tasks 1 and 2, the participants will usually rely on their memory to verify the medication.

3.1.1. *Tasks time to complete mean*

Table 2 and Fig. 4 show the mean times plots. We can see that the participants using the *NFC application method* scored a lower mean time to complete the tasks for both conditions. After performing the one-way between-groups ANOVA test, we found a significant difference in completing the tasks between the two methods for the wrong medication condition. There was a 29.9% variance in time to complete the tasks (effect size) accounted for by the groups. We found the participants, when using the *traditional method* spent more time trying to remember and verify the prescription information relying on their memory only, which led to the time difference between the methods. Using the NFC application method, the participants did not need to remember the information since it is available on the screen.

On the other hand, there is no significant difference for the right medication condition, and only 4.4% of the variance in time (effect size) was accounted for by the groups [43–45]. We think this is due to the nature of the question we asked them (i.e. is this the medication the doctor prescribed to you?). All the participants in *traditional method* group, once they read the right medication name, answered directly. Table 3 shows the scores of the one-way between-groups ANOVA test scores for both conditions. Finally, all the tasks' distributions were normal since all the tasks' skew and kurtosis scores were less than $|2.0|$ and $|9.0|$ respectively [46], and the Shapiro–Wilk's test scores were ($p>.05$) (see Table 2) [47,48]. As shown in Fig. 3 the tasks' times were approximately normally distributed for both methods.

3.1.2. *Tasks for verifying the medication successfully*

We analyzed the successful completion of tasks using IBM SPSS 22

Table 3
A one-way between-groups ANOVA test scores for the tasks' time to complete.

	$F(1,40)$	Sig.	η^2
Right medication (both methods)	1.833	0.183	0.044
Wrong medication (both methods)	17.042	0.000	0.299

Table 2
Descriptive statistics of the tasks times to complete.

	Conditions	N	Min	Max	Mean	SD	Skewness	Kurtosis	Shapiro–Wilk's
Traditional method	Right medication (Task 1)	21	26	70	41.00	12.29	0.814	− 0.159	0.081
	Wrong medication (Task 2)	21	37	81	54.29	12.47	0.604	− 0.222	0.184
NFC application	Right medication (Task 3)	21	30	46	37.14	4.40	0.639	− 0.345	0.173
	Wrong medication (Task 4)	21	35	58	43.90	6.33	0.683	− 0.444	0.137

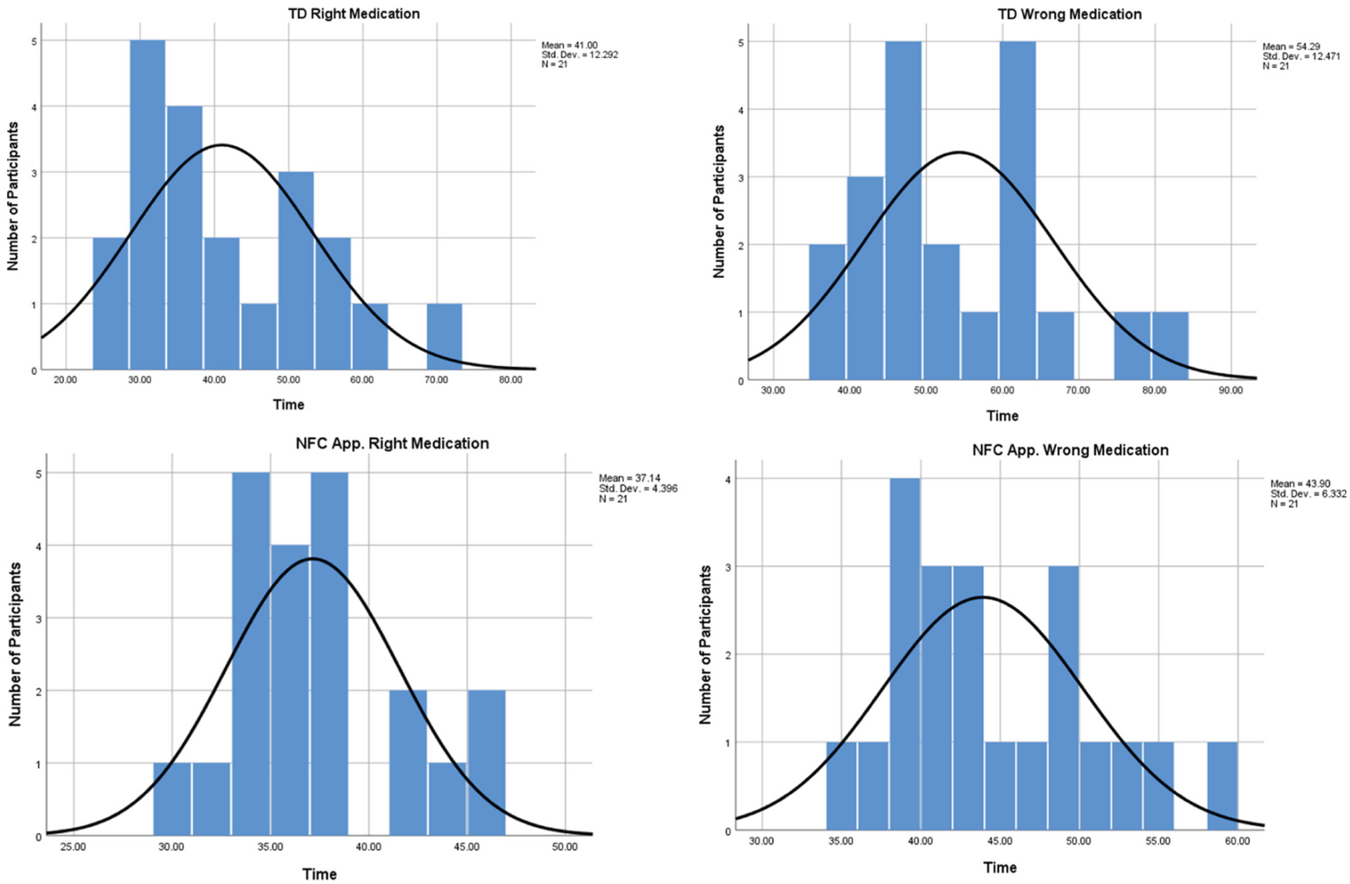


Fig. 3. Tasks' time normality distribution histograms. Where (NFC): *NFC application method*, (TD): *traditional method*.

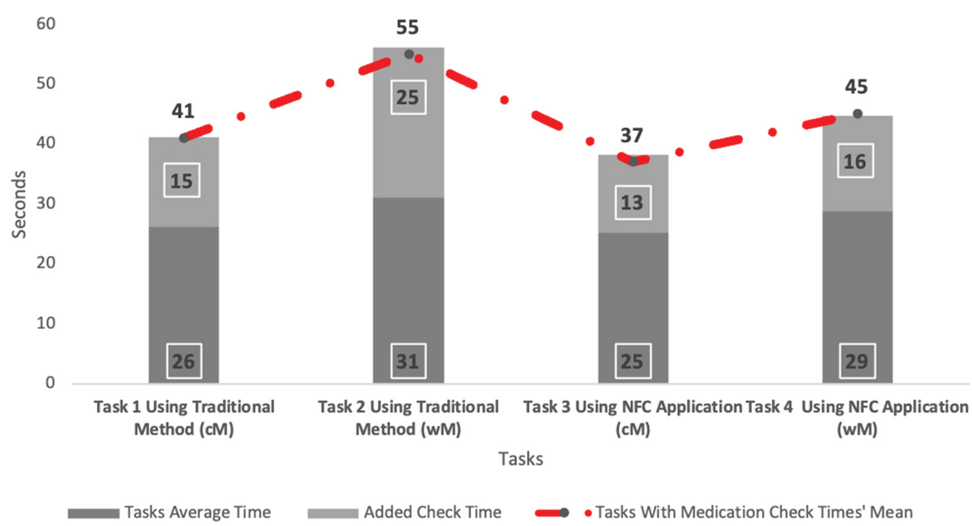


Fig. 4. The overall mean percentage value for usefulness, ease of use, availability and reliability, and security and privacy based on the participants' response to the questionnaire. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

with only two values: "Complete" represented as (1), and "Incomplete" represented as (2). We report the descriptive statistics across the two groups in Table 4. We found that all of the participants successfully verified the medication using the method *traditional method* for the right medication condition compared to 90% when using the *NFC application method*. However, only 62% of the participants successfully verified the medication using the *traditional method* for the wrong medication condition compared to 90% using the *NFC application method*.

We performed a chi-squared test for both conditions tasks, to determine if there is a significant difference between the two groups. We found no significant difference for the right medication condition between the two methods. Fig. 5 shows the percentage of participants who completed the task successfully. In the traditional method group, 100% of participants successfully completed the right medication task. In the NFC application method group, 90.5% of participants completed the right medication task, while only 9.5% of participants did not

Table 4
ANOVA and chi-square test scores for completing the tasks successfully (verifying the medication successfully).

	Conditions	Mean and Std. Dev.		Chi-square	
		Mean	SD	Value	*P*-Value
Right medication	Traditional method	1.0000	0.0000	2.100	<0.147
	NFC application	1.0952	0.3008		
Wrong medication	Traditional method	1.6190	0.4976	12.548	<0.000
	NFC Application	1.0952	0.3008		

successfully complete the task. Fig. 5 shows the percentage of participants that completed the task successfully. These differences were not statistically significant compared with the chi-squared test finding (Value = 2.100, df = 1, $P < 0.147$). Thus, we do not reject the null hypothesis. There is no substantial evidence of a relationship between completing the right medication task and the independent variable (i.e. the two methods). Table 4 shows the result of chi-squared test.

As for the wrong medication condition, 61.9% of the participants in the traditional method group did not successfully complete the wrong medication task, and only 38.1% successfully completed the task. In the NFC application method group, 90.5% successfully completed the right medication task, while only 9.5% did not successfully complete the task. Fig. 5 shows the percentage of participants that completed the task successfully. These differences were statistically significant from the chi-squared test finding (Value = 12.548, df = 1, $P < 0.000$). Thus, we reject the null hypothesis, and there is strong evidence of a relationship between successfully completing the wrong medication task and the independent variable (i.e. the two methods). Further, Cohen [49] demonstrated the effect size of Phi and Carmer's V as follows: (0.1) is a small effect, (0.3) is a medium effect, and (0.5) is a large effect. The Phi and Carmer's value is ($\Phi c = 0.547, P < 0.000$), which indicates that the strength of association between the variables is a very large effect.

3.2. Post-condition questionnaires

The participants were asked in the questionnaires to compare their experience using both methods in picking up the prescribed medication. All questions used a 7-point Likert scale coded as follows: 1 (Strongly Agree), 2 (Agree), 3 (Somewhat Agree), 4 (Neutral), 5 (Somewhat Disagree), 6 (Disagree), and 7 (Strongly Disagree).

3.2.1. Security and privacy

The questionnaire shows that approximately 86% of the participants found that the NFC application will keep their sensitive information secure and private while transferring it to the pharmacy, while only 43% of the participants preferred the traditional method to transfer their information securely. The application does not store any personal information other than the patient Id to be used in the server's authentication process. The fingerprint or any login information is required to keep the Id information from any misuse by the attacker. Although the application does not initiate any communication and does not transfer any information to verify the user first, we think of using two-factor authentication when the pharmacy or the prescriber communicates with the server. Two-factor authentication will be used in the improved version to avoid any privacy implications.

Furthermore, approximately 95% of the participants thought the NFC application is a good method to verify their identity in the medication dispensing process. Finally, all participants believed that NFC technology is a secure and fast method to transfer information to pick up prescribed medications. In Fig. 6a–c, we can see that the participants agree with the presented statements based on their experience with both methods in the study. Since NFC technology offers a proximate wireless method to transfer any data, it will offer the needed security layer for transferring the patient information. However, The NFC technology is vulnerable to a number of security threats such as eavesdropping, ticket cloning, phishing, and relay attack. These security threats could occur because of the NFC technology's physical nature, and its operation methodology [50,31,51,52]. Thus, to protect patient information privacy, the application requires fingerprint authentication to initiate the NFC communication, and the information is sent hashed to the reader.

In the interview, when asked about their opinion on using their fingerprint to control the application access, most participants thought it is a secure way to protect their sensitive information in the application from any unauthorized access. On the other hand, a few participants did not feel optimistic about the application's fingerprint login. One of the participants preferred not to use their fingerprint feature during the study and stated, "fingerprint is too private. This information should not ever be recorded of anybody, in my opinion" (P4). Other participants did use the fingerprint login but suggested adding more options like a PIN code or facial recognition to access the application.

3.2.2. Availability and reliability

Almost 57% of the participants believed that the traditional method does not provide a way of tracking the current prescriptions and making them available for future use (i.e. Question PCTQ5 Fig. 8). Meanwhile, approximately 19% of the participants thought the Availability of intake

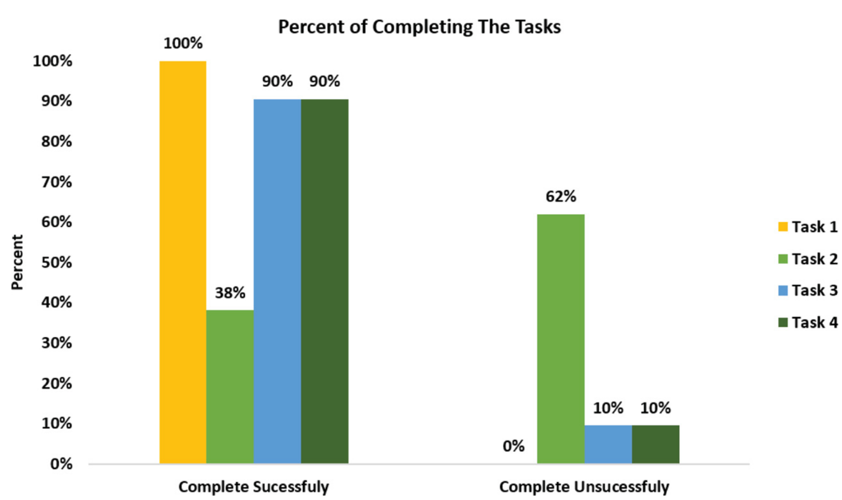
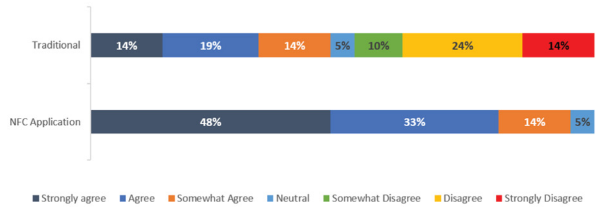
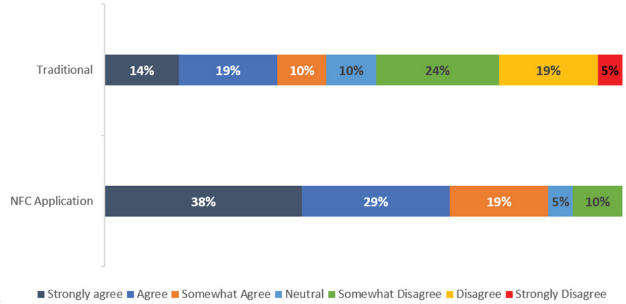


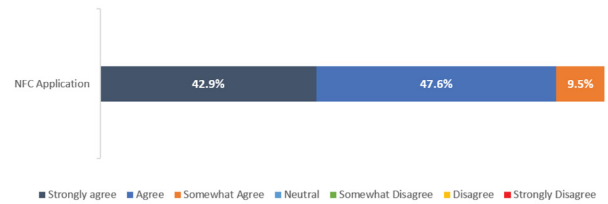
Fig. 5. The overall percentage value of completing the tasks successfully for both methods across the two conditions.



(a) Q: I think this method will help me to verify my identity to the drugstore, which helps the drugstore to dispense the correct medication for me.



(b) Q: I think this method will help me to keep my sensitive information private and secure.



(c) I think using NFC technology to transfer information is a secure and fast method in the picking up medication process.

Fig. 6. The percent of participants' answers on the security and privacy questions for both the traditional and NFC application method.

instructions should be provided all the time by the traditional method (i.e. Question PCTQ2 in Fig. 8). In comparison, almost 86% of the participants believed the application would help them remember their medication intake instructions (i.e. Question PCQA4 in Fig. 7). All the participants thought the NFC application method would provide a way of tracking the current prescriptions and making them available for future use (i.e. Question PCQA6 in Fig. 7).

Moreover, almost 43% of the participants believed the traditional method would not provide a safe method to verify the medication (i.e. Question PCTQ6 Fig. 8). However, all participants thought the NFC technology (i.e. when the pharmacy management system reads the NFC tag attached to the medication packaging) would help the pharmacy verify the medication, thus avoiding dispensing the wrong medication (i.e. Question PCQA7 in Fig. 7). Additionally, Almost 86% of the participants thought the NFC application would provide the pharmacy management system with enough information to avoid dispensing the wrong medication to patients (i.e. Question PCQA8 in Fig. 7). In contrast, only 61% of participants thought the traditional method would do so (i.e. Question PCTQ4 Fig. 8).

3.2.3. *Usefulness*

The questionnaire shows that 91% of participants found the proposed NFC practical application for the process of picking up medication (Fig. 9). In the post-session interview, participants stated that they believe the application will help facilitate providing information to the pharmacy. They also thought the application would help pharmacies avoid dispensing the wrong medication to the wrong patient by verifying both the patient and the medication regarding the provided prescription using NFC technology. Likewise, participants strongly agree that NFC will help them transfer the needed information (i.e. patients' sensitive information) more securely and privately. Lastly, most of them believed that the application would help them keep past prescription information readily available if needed. The application will help by making the intake instructions available at all times.

3.2.4. *Easy to use*

Based on the questionnaire about the ease of use, 97% of participants believed the application and NFC technology are easy to learn and use (Fig. 9). Also, participants found that browsing the list of prescriptions was easy and understandable. However, many suggested changing the

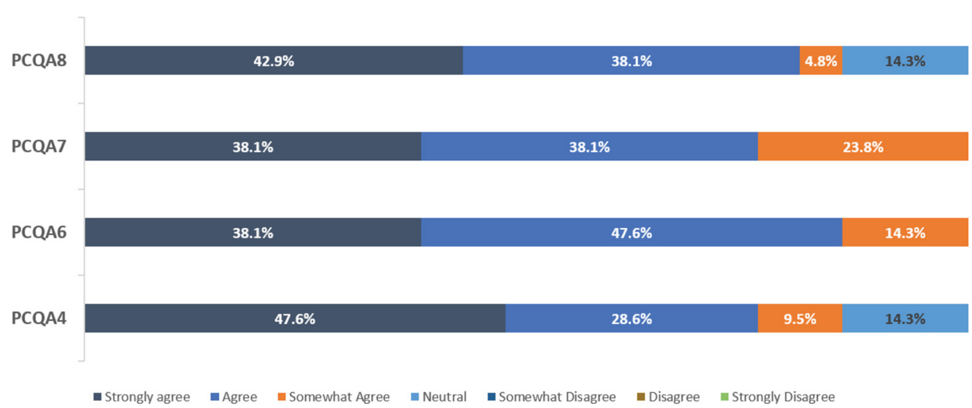


Fig. 7. The percent of participants' answers on the availability and reliability of information questions for the NFC application method.

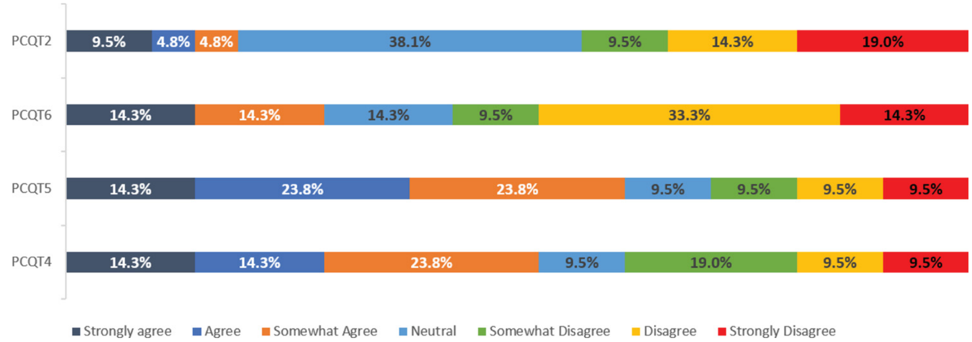


Fig. 8. The percent of participants' answers on the availability and reliability of information questions for the traditional method.

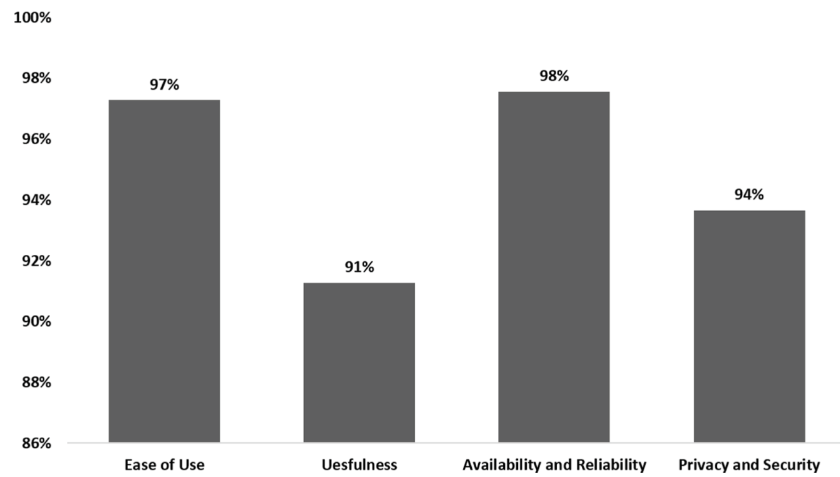


Fig. 9. The overall percentage value of the positive answers (i.e. Strongly Agree ⟷ Somewhat Agree) for usefulness, ease of use, availability and reliability, and security and privacy based on the participants' response to the NFC application questionnaire.

way the prescriptions are displayed, such as grouping the prescriptions issued by one prescriber. On the other hand, participants found that using NFC to transfer the information was easy. In addition, almost 81% of participants believed the application is suitable for novice and expert users.

3.2.5. Weaknesses and limitations of the study

Besides the positive findings related to the proposed NFC application's usability study, some weaknesses and limitations should be considered in future research. One of the limitations is the number of participants in each age range, especially in the age range of 55+ years old. This age range is highly important to this research because this population takes more medication than other age ranges due to the aging process. Other weaknesses are that the application lacks other options for logging into and does not currently offer the ability to share prescriptions with others to pick up the prescription on their behalf. Lastly, the application currently only provides an online mode to get prescription information from the servers.

4. Conclusion and future work

The study findings show that an NFC application to manage the patients' prescription and to pick up the medication is acceptable from the participants' opinion. The results show that the participants believe the NFC application will mitigate dispensing medication errors, at least from their end. The patient can verify the medication and prescription information before leaving the pharmacy with the prescriber's information. Further, the application will help the patient remember their current prescription when they need to browse it, which helps them remember the medication intake instruction. In future work, we will overcome the limitation and weaknesses of the application from this study's results. In addition, our next phase is to expand on the system to overcome other issues in the e-prescription system to mitigate the prescribing and dispensing of medication errors.

Finally, the mobile application was intended to be used by smartphones enabled with NFC technology; but some of the feature phones have the NFC technology and could be used to transfer the information only. We might expand the framework to include a web-based application to review the e-prescriptions information for browsing the prescription information. Further, the project might consider adding a one-time password system [53,54] using SMS text to authenticate the patient with the prescriber and pharmacy management system.

Summary table

- Medication errors can occur due to many reasons, but many studies have found that prescription errors are one of the main drivers.
- Taking the wrong medication or wrong dosage can be harmful, life-threatening or even fatal in many cases.
- e-prescription systems were introduced to eliminate prescription errors; however, many of them do not provide a patient identity verification method when dispensing the medications.
- Utilizing NFC technology and a mobile application to verify the patient while dispensing medication will minimize medication errors that occur due to a lack of identity confirmation.
- Using NFC technology provides a secure and private method for transferring patient information.

- The Availability of prescription information will enable the patient to ensure they have received the right medication after dispensing.

Ethics approval

Approval was obtained from the Dalhousie University Health Sciences Research Ethics Board.

Conflict of interest

The authors declare they have no conflict of interest for this study.

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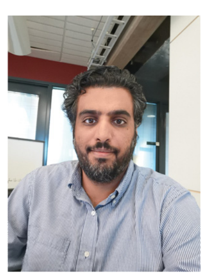
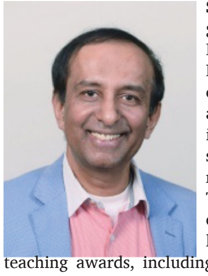
References

[1] L.T. Kohn, J. Corrigan, M.S. Donaldson, et al., To Err Is Human: Building A Safer Health System, vol. 6, National Academy Press, Washington, DC, 2000.
[2] Canadian Institute for Health Information, Health Care in Canada 2009: A Decade in Review, Canadian Institute for Health Information (CIHI), 2009.
[3] G.R. Baker, P.G. Norton, V. Flintoft, et al., The canadian adverse events study: the incidence of adverse events among hospital patients in Canada, CMAJ 170 (11) (2004) 1678–1686.
[4] N. Harder, J. Plouffe, D. Cepanec, et al., Use of mobile devices and medication errors in acute care: a systematic review protocol, JBI Database Syst. Rev. Implement. Rep. 14 (9) (2016) 47–56.
[5] M.A. Makary, M. Daniel, Medical error—the third leading cause of death in the us, BMJ 353 (2016).
[6] Canadian Institute for Health Information, Patient Safety in Canada: An Update, 2007.
[7] J. Webb, Pharmacy dispensing errors: Claims study emphasizes need for systematic vigilance, Drug Top. Mod. Med. Netw. (2015).
[8] HPSO, A Ten-Year Analysis 2013 Pharmacist Liability. Technical Report., Healthcare Providers Service Organization (HPSO), 2013.
[9] P.J. Lewis, T. Dornan, D. Taylor, et al., Prevalence, incidence and nature of prescribing errors in hospital inpatients, Drug Saf. 32 (5) (2009) 379–389.
[10] A. Boucher, C. Ho, N. MacKinnon, et al., Quality-related events reported by community pharmacies in nova scotia over a 7-year period: a descriptive analysis, CMAJ Open 6 (4) (2018) E651.
[11] R. Nair, D. Kappil, T. Woods, 10 strategies for minimizing dispensing errors, Pharmacy Times (2010).
[12] B. Aldughayfiq, S. Sampalli, Digital health in physicians' and pharmacists' office: A comparative study of e-prescription systems' architecture and digital security in eight countries, OMICS: J. Integr. Biol. (2020). Online.
[13] J.G. Anderson, Information technology for detecting medication errors and adverse drug events, Expert Opin. Drug Saf. 3 (5) (2004) 449–455.
[14] D.S. Bell, S. Cretin, R.S. Marken, et al., A conceptual framework for evaluating outpatient electronic prescribing systems based on their functional capabilities, J. Am. Med. Informatics Assoc. 11 (1) (2004) 60–70.
[15] A. M. A. (AMA), A. A. of Family Physicians (AAFP), A. C. of Physicians (ACP), et al., Clinician's Guide to e-Prescribing, 2011.
[16] P. Kierkegaard, E-prescription across europe, Health Technol. 3 (3) (2013) 205–219.
[17] J.E. Brennan, A. McElligott, N. Power, National Health Models and the Adoption of Ehealth and Eprescribing in Primary Care-New Evidence from Europe, 2015.
[18] K. Priya, N. Joy, A.V. Thottumkal, et al., Impact of electronic prescription audit process to reduce outpatient medication errors, Indian J. Pharmaceut. Sci. 79 (6) (2018) 1017–1022.
[19] A. Soni, S. Nagpal, A. Mittal, E-prescription-curbing the covid-19!, Indian J. Med. Sci. 72 (2) (2020) 119.
[20] M. Samadbeik, M. Ahmadi, F. Sadoughi, et al., A copmarative review of electronic prescription systems: lessons learned from developed countries, J. Res. Pharmacy Pract. 6 (1) (2017) 3.
[21] N. Hossain, M.B. Sampa, F. Yokota, et al., Factors affecting rural patients' primary compliance with e-prescription: a developing country perspective, Telemed. e-Health 25 (5) (2019) 391–398.
[22] M. Nalin, I. Baroni, G. Faiella, et al., The European cross-border health data exchange roadmap: case study in the Italian setting, J. Biomed. Informatics 94 (2019) 103183.
[23] MyHealth @ EU, Electronic Cross-Border Health Services, eHealth: Digital Health and Care, 2021 (Accessed March 2021).
[24] Pharmacy Association Of Nova Scotia, Filling a Prescription (Dispensing), 2018.
[25] K. Tabi, A.S. Randhawa, F. Choi, et al., Mobile apps for medication management: review and analysis, JMIR mHealth uHealth 7 (9) (2019) e13608.
[26] N. Pereira-Azevedo, L. Osório, V. Cavadas, et al., Expert involvement predicts mhealth app downloads: multivariate regression analysis of urology apps, JMIR mHealth uHealth 4 (3) (2016) e86.
[27] Y. Subhi, S.H. Bube, S.R. Bojsen, et al., Expert involvement and adherence to medical evidence in medical mobile phone apps: a systematic review, JMIR mHealth uHealth 3 (3) (2015) e79.
[28] I. Ahmed, N.S. Ahmad, S. Ali, et al., Medication adherence apps: review and content analysis, JMIR mHealth uHealth 6 (3) (2018) e62.
[29] K. Santo, S.S. Richtering, J. Chalmers, et al., Mobile phone apps to improve medication adherence: a systematic stepwise process to identify high-quality apps, JMIR mHealth uHealth 4 (4) (2016) e132.
[30] Z. Huang, E. Lum, G. Jimenez, et al., Medication management support in diabetes: a systematic assessment of diabetes self-management apps, BMC Med. 17 (1) (2019) 1–12.
[31] B. Aldughayfiq, S. Sampalli, A system to lower the risk of dispensing medication errors at pharmacies using nfc. 2018 IEEE International Conference on Internet of Things (iThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData), IEEE, Halifax, NS, Canada, 2018, pp. 196–202. IEEE.
[32] C.W. Turner, J.R. Lewis, J. Nielsen, Determining usability test sample size, Int. Encycl. Ergonom. Human Fact. 3 (2) (2006) 3084–3088.
[33] J. Rubin, D. Chisnell, How to plan, design, and conduct effective tests. Handbook of Usability Testing, 2008, p. 348.
[34] R.A. Virzi, Refining the test phase of usability evaluation: how many subjects is enough? Human Fact. 34 (4) (1992) 457–468.
[35] F.J. García-Peñalvo, A. García-Holgado, A. Vázquez-Ingelmo, et al., Usability test of wyred platform, in: P. Zaphiris, A. Ioannou (Eds.), Learning and Collaboration Technologies. Design, Development and Technological Innovation, Springer International Publishing, Cham, 2018, pp. 73–84.
[36] W. Hwang, G. Salvendy, Number of people required for usability evaluation: the 10±2 rule, Commun. ACM 53 (5) (2010) 130–133.
[37] J.W. Creswell, C.N. Poth, Qualitative Inquiry and Research Design: Choosing Among Five Approaches, Sage Publications, 2016.
[38] J. Nielsen, How many test users in a usability study, Nielsen Norman Group 4 (06) (2012).
[39] F.D. Davis, Perceived usefulness, perceived ease of use, and user acceptance of information technology, MIS Quart. (1989) 319–340.
[40] F.D. Davis, R.P. Bagozzi, P.R. Warshaw, User acceptance of computer technology: a comparison of two theoretical models, Manag. Sci. 35 (8) (1989) 982–1003.
[41] I. Maramba, A. Chatterjee, C. Newman, Methods of usability testing in the development of ehealth applications: a scoping review, Int. J. Med. Informatics 126 (2019) 95–104.
[42] Statistics.laerd, One-Way Anova in SPSS Statistics, Website, 2018.
[43] D. Cramer, Fundamental Statistics for Social Research: Step-By-Step Calculations and Computer Techniques Using SPSS FOR Windows, Psychology Press, 1998.
[44] D. Cramer, D.L. Howitt, The Sage Dictionary of Statistics: A Practical Resource for Students in the Social Sciences, Sage, 2004.
[45] D.P. Doane, L.E. Seward, Measuring skewness: a forgotten statistic? J. Stat. Educ. 19 (2) (2011).
[46] E. Schmider, M. Ziegler, E. Danay, et al., Is it really robust? Methodology (2010).
[47] S.S. Shapiro, M.B. Wilk, An analysis of variance test for normality (complete samples), Biometrika 52 (3/4) (1965) 591–611.
[48] N.M. Razali, Y.B. Wah, et al., Power comparisons of Shapiro-Wilk, Kolmogorov-Smirnov, Lilliefors and Anderson-darling tests, J. Stat. Model. Anal. 2 (1) (2011) 21–33.
[49] J. Cohen, A power primer, Psychol. Bull. 112 (1) (1992) 155.
[50] A. Albattah, Y. Alghofaili, S. Elkhediri, Nfc technology: assessment effective of security towards protecting nfc devices & services, 2020 International Conference on Computing and Information Technology (ICCIT-1441) (2020) 1–5.
[51] M.M. Singh, K. Adzman, R. Hassan, Near field communication (nfc) technology security vulnerabilities and countermeasures, Int. J. Eng. Technol. 7 (4.31) (2018) 298–305.
[52] N. Akinyokun, V. Teague, Security and privacy implications of nfc-enabled contactless payment systems, Proceedings of the 12th International Conference on Availability, Reliability and Security (2017) 1–10.
[53] N. Haller, C. Metz, P. Nesser, et al., A one-time password system. Network Working Group Request for Comments, 1998, p. 2289.
[54] J. Bonneau, C. Herley, P.C. Van Oorschot, et al., The quest to replace passwords: a framework for comparative evaluation of web authentication schemes, 2012 IEEE Symposium on Security and Privacy (2012) 553–567.



Bader Aldughayfiq is currently a Ph.D. candidate in the Faculty of Computer Science at Dalhousie University. He holds a master's degree in computer science from Dalhousie University, Halifax, Canada. He pursues his Ph.D. degree at the same university. Bader's primary research about the security and privacy of the healthcare application, specifically ePrescription systems.



Srinivas Sampalli received the Bachelor of Engineering degree from Bangalore University and the Ph.D. degree from the Indian Institute of Science, Bengaluru, India. He is currently a Professor and a 3M National Teaching Fellow with the Faculty of Computer Science, Dalhousie University, Halifax, NS, Canada. He currently supervises 5 Ph.D. and 10 master's students in his Emerging Wireless Technologies (MYTech) Lab and has supervised over 150 graduate students in his career. He has led numerous industry-driven research projects on Internet of Things, wireless security, vulnerability analysis, intrusion detection and prevention, and applications of emerging wireless technologies in healthcare. He was a recipient of numerous teaching awards, including the 3M National Teaching Fellowship, the Canada's most prestigious teaching acknowledgement. Since September 2016, he has been the Vice President (Canada) of the International Federation of National Teaching Fellows, a consortium of national teaching award winners from around the world.

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A System to lower the risk of dispensing medication errors at pharmacies using NFC

Bader Aldughayfiq
Faculty of Computer Science
Dalhousie University
Halifax, Canada
Email: bader@cs.dal.ca

Srinivas Sampalli
Faculty of Computer Science
Dalhousie University
Halifax, Canada
Email: srini@cs.dal.ca

***Abstract*—Medication dispensing errors are a great risk in pharmacies. These errors can be the result of issues such as heavy workload, misinterpretation of a prescriber's handwriting, or simply handing the wrong medication to the wrong patient. Hence, researchers have recently proposed the use of e-prescription to overcome these issues. Moreover, several mobile apps that use Near Field Communication (NFC) have been proposed for managing patients' medication intake instructions and reminding them about intake times. However, neither the e-prescription nor medication management apps solve dispensing errors. Therefore, we developed an NFC-based system comprised of mobile applications for patients' smartphones to transfer verification information through NFC and a pharmacy management system connected to an NFC reader. Furthermore, to ensure the security of the patient's sensitive information, we require biometric authentication to gain access to the mobile application. This authentication feature is also used to restrict access to the information to the legitimate user only during the medication dispensing process. Finally, we believe the proposed system will help to reduce medication dispensing errors.**

I. Introduction

In 2016, a tragic incident [1] led to the death of an eight-year-old boy. The parents of the boy gave him what they thought was his sleep medication; however, the medication was not what the doctor had prescribed. The pharmacist gave them Baclofen, a muscle relaxant. The coroner found that the high dosage of Baclofen administered was fatal for a boy of that age. Hence, ingesting the wrong medication and dosage errors are an elevated risk in the pharmaceutical industry [1]. Moreover, according to [2] the insurance group CAN and the Healthcare Providers Organization (HPSO) in their analysis of ten years of data reported that 75.3% of closed claims are because of either a wrong dose or wrong drug. Moreover, from the already-closed claims, injuries resulted from 13.6% of these overdoses and 11.7% of these led to death [2] [3]. Therefore, to address the above issues, the authors in [4] introduced ten strategies. These strategies mainly focused on minimizing medication dispensing errors but did not focus on reducing the time required to prepare a prescription, which will affect the quality of the service provided. Also, one of the strategies suggests adding more staff to reduce the increased work rate, which also will increase costs for the pharmacy.

According to [5], patient identity confirmation is needed to dispense the medication. However, they did not specify any methods of confirming the identity of the patient. To the best of our knowledge, the common practice is verifying the patient by home address and name. This practice will raise some security and privacy issues where any person (i.e. knows address and name) could pick up the medication. Also, sharing an address and a name publicly could implication on other matters.

A critical factor in improving the quality of the service provided by drugstores is to make the process of dispensing medication efficient, accurate, and effortless. Therefore, automating methods of getting prescriptions and dispensing medications will help to minimize the risk caused by receiving the wrong medication or wrong dose. The Internet of Things (IoT) offers the ability to exchange information securely and efficiently by using wireless and wired network technologies. Such technology is known as Near Field Communication (NFC) technology and is available on smartphones. This technology has been used to open several opportunities to optimize the quality of services such as tap-to-pay services. Also, a variety of fields (e.g. healthcare, access control) use NFC to gather and transmit information securely.

Thus, we propose a secure System to optimize the medication dispensing process. The system aims to introduce more robust and secure method to confirm patient identity and minimize dispensing errors. We are using NFC technology in smartphones to securely transfer information (e.g. insurance ID numbers, or prescription IDs) between the patient's smartphone app and the pharmacy. Also, we are using NFC technology by validating the medication and the patient at the final part of the dispensing process. Lastly, we are using biometric information (i.e. fingerprints) to grant the app access to the patient.

Although the proposed system will not prevent human errors, we believe it will mitigate medication dispensing errors. In this paper, we will discuss the use of NFC technology and biometric authentication.

Finally, the organization of the paper is as follow. In the second section, we explore and discusses the recent literature proposed regarding the use of NFC technology in health care systems, and the current systems for the e-prescribing technology. The third section will discuss the proposed system architecture and the comparison with the current systems. Last, the fourth section will discuss the proposed application

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analyses and the proposed security features in the system.

II. Background and Literature Review

In this section, we looked at the proposed systems in healthcare or medication-related services that use NFC technology or mobile apps. Some proposed systems also use both NFC and mobile apps. We also explored some of the current systems and services that use the e-prescription approach.

A. NFC technology

NFC is a technology that comes in several forms. The first, is an NFC reader or NFC chip (e.g. a card, or bracelet). The NFC chip can store a small amount of data, such as a unique ID (e.g. Social Insurance Number). Second, which is most commonly used these days, is the NFC-enabled smartphone, where the smartphone can act as an NFC reader and an NFC card. One advantage of using smartphones over chips is the larger amount of storage and resources available, which allow the NFC card to perform more complicated processes.

B. NFC systems and mobile apps systems for health care

In this section, we will review related work focusing on medication management apps. Medication management refers to either organizing medication for patients or detecting medication interactions.

S. Fan et al. proposed a mobile app called the Health Pal [6]. This app is designed to help elderly individuals by reminding them about and managing their health tasks, such as doctor appointments, exercise times, taking blood pressure, pulse rates, and medication intake times. The reminders use audio and visual alerts. The app will prevent patients from forgetting their medication time and type. Moreover, the visual alerts will help patients avoid mixing or taking the wrong medication.

In [7] [8], the authors presented Wedjat, a mobile app that helps patients remember medication intake instructions. Wedjat also keeps the intake records for the patient and updates a user database or a personal health records system [9]. In [10] the authors describe the possibilities of utilizing NFC technology in smartphones to help elderly individuals with vision impairment to manage their medication. The authors proposed two scenarios of medication management and organization. In the first scenario, a pharmacist will attach an NFC tag to the medication packaging, which contains information about that medication. Then, the user will have to touch the tag with their smartphone to enable the NFC reader mode in the application. An audio interface will convert the information so that the user can listen to information about that medication. In the second scenario, the application will be used to manage the medication intake instructions. A home care service provider operates a backend system to store the intake instructions. Also, the home care service provider will provide an NFC tag for the medication with the intake schedule information, such as required doses and medication intake times. The NFC tag will be attached to the medication packaging with all the required above information [9].

Silva et al. presented SapoMed, a mobile application for healthcare that is designed for medication management and monitoring. The focus of their work is to prevent medication intake errors by tracking and managing all prescribed medication. To input the medication and intake information, the user has two options: inputting the information manually or scanning the medication barcode. For the second choice, the application will obtain the required information from a web server. The web server will store all medication information and past intake information in a medication database [9].

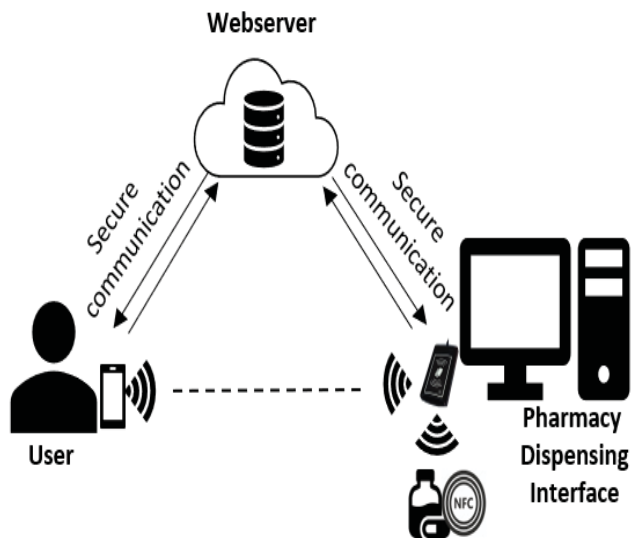


Fig. 1: Shows the components of the proposed System

C. Current electronic prescriptions system and framework

In this section, we will explore the current electronic prescription systems and frameworks and discuss their limitations. Surescripts [11] is a large company that has operated an e-prescribing service nationwide in the United States for more than 15 years. The company aims to replace paper prescriptions with digital prescriptions that can be transmitted from a prescriber to a pharmacy electronically. The e-prescription service will overcome most paper prescription issues. They claim that the service will increase first-fill medication adherence, which will lead to reductions in the costs of healthcare services. Also, the service will optimize the safety of patients by eliminating handwriting limitations and reducing the time spent on entering prescription information manually. Moreover, the service will reduce the communication between prescribers and pharmacies by making health information available to any future prescribers. However, since the service only aims to lower the risks of paper prescriptions, it does not contribute to preventing medication dispensing errors. Finally, the system only requires authentication for dispensing narcotic medications. Prescribe IT [12] is a project funded by the Canadian government to provide an e-prescribing service which will enable the prescriber to send a prescription

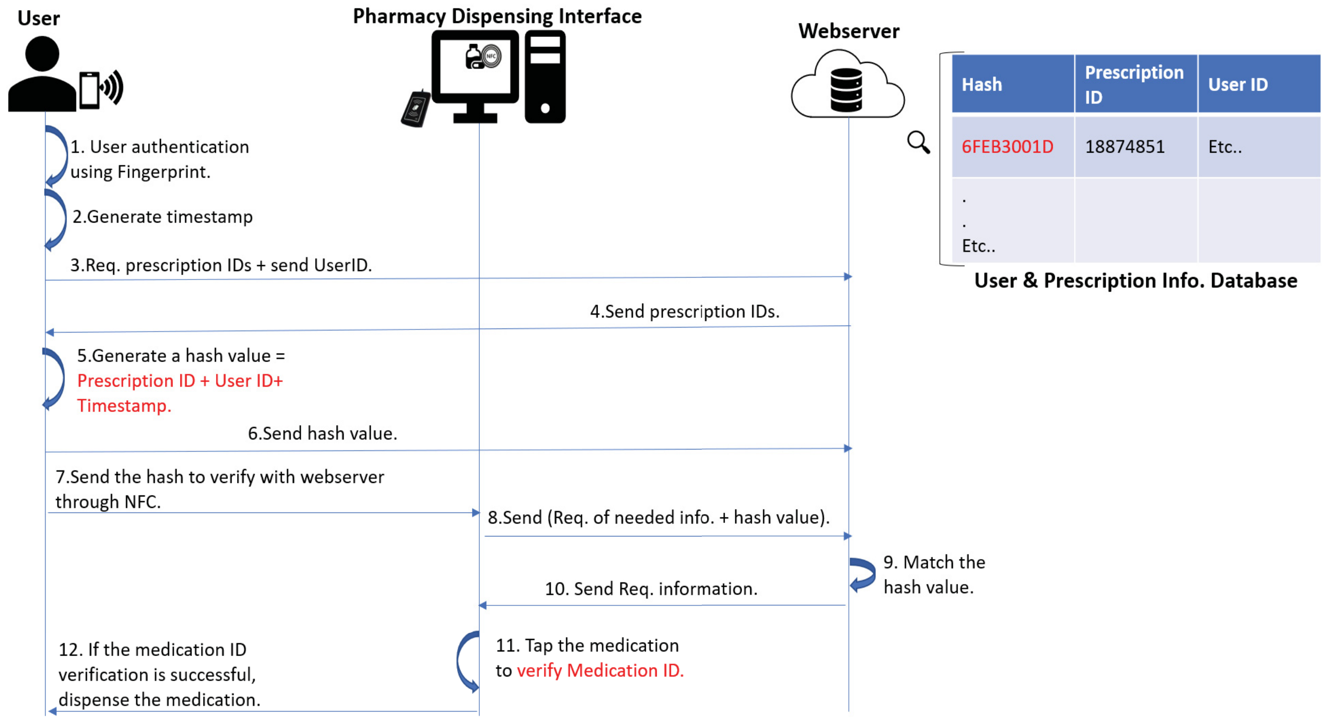


Fig. 2: The sequence diagram of the dispensing medication process.

electronically to a patient's pharmacy of choice. The service will replace the paper prescription process, securely transmit health data, and sustain a paper prescription-free environment. The features of the service provide improved efficiency and better communication between prescribers and pharmacies. The focus of the service is on lowering prescription errors such as losing prescriptions, avoiding privacy breaches due to fax machine transmission errors, and reducing prescription fraud and abuse. However, Prescribe IT does not solve medication dispensing issues. Although it does provide the secure and electronic transmission of prescriptions, the availability of the prescription is limited. Only the prescriber and the chosen pharmacy are allowed to request a prescription, while the patient can not have a copy unless it is in paper form. Moreover, with Prescribe IT, the process of medication dispensing has not changed. Therefore, these issues lead us back to the focus of this paper (i.e., medication dispensing issues): dispensing the wrong medication, lowering the cost of the process, and reducing the time taken to prepare the prescription.

III. System Architecture

A. The proposed system

The proposed system components are: a smartphone (i.e. the patient's smartphone) with the application installed, the pharmacy management system, the web server, an NFC tag attached to the medication packaging, and an NFC reader for pharmacy management systems. Figure 1 shows the proposed system components. Figure 2 shows the sequence graph of the medication dispensing process.

In the first step, the user will need to authenticate his/her identity using the fingerprint scanner embedded in the phone. Then, the application will generate a time-stamp, which will be used to generate the hash value. At the same time, the time-stamp value will be sent to the web server. Next, the application will request the active prescription IDs from the web server. These IDs are kept in the web server at all times and are not stored on the user's phone. After, the application will use the chosen prescription ID, user ID, and the time-stamp to generate the hash value and send it to the web server. After, the user will tap their phone to send the hash value to the pharmacy management system to verify the identity with the web server and obtain the necessary information (i.e. name, medication ID, prescription ID) to dispense the medication. If the verification is successful, the web server will send back the necessary information. Then, the pharmacist will tap the medication, which has an NFC tag attached to the packaging. The NFC tag will contain the medication name and ID. After tapping, the pharmacy management system will verify the medication ID by matching it with the ID in the prescription information. If the matching is successful, the pharmacist will dispense the medication. Finally, fingerprinting has been set up for the first time using the app. Without using their fingerprint, the patient will not be able to gain access to the app and no information will be transferred. This authentication step will help with validating the patient for the medication dispensing process and will help secure the privacy of the patient's sensitive information.

1) Assumptions: In our proposed system, we introduced three main components: the user smartphone, the pharmacy management system, and the web server. These components in the medication dispensing process will communicate in order to transfer the information. Although these communications are essential toward achieving the objective of this research, not all the main focus of this paper. Therefore, we assume that the communication between the smartphone and the web server is secure, and the communication between the pharmacy management system and the web server is secure. Moreover, prescriptions are submitted to the web server through the doctor management system. Such systems are presented in [11] and [12].

B. Proposed system compared to the current systems

The authors in [4] proposed ten strategies to lower the risk of medication dispensing errors. The authors indicate that most dispensing errors are the result of error-prone systems and processes. Therefore, through the proposed system we aim to avoid most of the conditions and scenarios that might cause medication dispensing errors. In Table I we highlight the most relevant strategies and compare the current systems (mentioned in section 2) in the pharmacies and the proposed system. According to the authors in [4], the strategy of thoroughly checking the prescriptions will be the last step in the medication dispensing process. Thus, in the proposed system, this step is encountered by validating the medication with NFC before dispensing. In comparison, the compared systems do not specify a method for the checking process, so the pharmacist deals with this manually. The proposed system will make the prescription and instruction always available in the application, while the compared systems offer only pharmacist counseling. Moreover, in designing the proposed system, we considered five goals for achieving quality service and minimizing the risk of medication errors. In Table II we mention the goals and discuss how we achieved these goals. First, we made the system highly available by making the prescription information available to the patient at all times . Second, the system should be reliable and provide quality service by minimizing medication dispensing errors. Third, as we discussed in the previous section, the system will provide security and privacy for the patient's sensitive information. Finally, the system will reduce the time needed to prepare the prescription in advance. This step will eliminate some unnecessary steps from the pharmacist's work rate.

C. Proposed system implementation

We developed the application for the user (i.e. the patient) end using Android Studio. We deployed the application on a Samsung Galaxy A8 smartphone running Android OS version 7.0. The smartphone has a fingerprint and proximity (i.e., NFC) sensors. Figure 3 shows the mobile interfaces. Also, we developed a Java application to simulate the doctor management system, which will mainly be used to submit patients' prescriptions to the web server. The second Java application we developed was for the pharmacy management system. Figure 4 shows the pharmacy management system interfaces of the dispensing process in different scenarios. This application has all the functions required by the proposed system. First, the application will receive the hash value from the smartphone through the NFC reader. Then, the system will send it to the web server for verification. Figure 4 (b), (c), and (d) show the system messages depends on the received information from the web server. In figure 4 (b) there are no issues, and the verification process was successful. However, in figure 4 (c) the system shows the wrong medication as we scan a wrong medication and the IDs did not match. Finally, figure 4 the system showed this message when we used a no refill prescription twice (i.e. the double spending problem.) The reader we used is the ACR122U NFC Reader developed by Advanced Card Systems (ACS) [13].

Finally, we used XAMPP (a PHP development environment) to install a local Apache web server and MySQL database [14]. We created three tables in the database: a patient information table, prescription table, and medication table. The patient table contained a hundred values. Each row has four attributes: first name, last name, age, and patient ID. For the names and ages, we used one hundred random names with ages. We developed a Java application to randomly generate a ten-digit number to represent the User ID. Moreover, the prescription table has six attributes: prescription ID, patient ID, medication ID, dispensing count, refill, and dose. The prescription table values are filled in the process of the doctor submitting a prescription. Last, the medication table contains six values with two attributes: medication ID and medication name. We used six medications from the top 100 medications list [15], and we used six NFC tags containing only the unique ID information that represents the medication ID.

IV. Application and security analysis

Moreover, we will discuss the proposed system security.

A. Application performance analysis

In this section, we will discuss the smartphone application performance regarding CPU, memory, and network connection. After analyzing the CPU performance, we found the highest usage of the CPU resources is 11.6% while creating the hash value. Where in the rest of the process the average CPU usage was almost 6%, and that includes transferring information through NFC and connecting to the web server to acquire the prescription information. In Figure 5 we show the smartphone application usage of the CPU.

Second memory usage The app starts by allocating 64 MB at the start of the app, and it uses only 33 MB in the idle stats (i.e., no activity in the app). The allocation will increase starting with the authentication process; then it will reach 48.33 MB (i.e. the highest) while transferring the information through the NFC and with the web server. Finally, the app uses a total of almost 50 MB from the allocated memory (i.e., 64 MB). It uses a considerably low allocation since the total

TABLE I: Medication errors causes, and the comparison between the current e-prescription systems and the proposed System.

Strategies	Surescripts & Prescribe IT	The Proposed System
Ensure correct entry of the prescription	Yes	Yes
Confirm that the prescription is accurte	Yes	Yes
Beware of look-alike, sound alike drugs	No	Yes
Reducing stress and balancing heavy workloads	Yes	Yes
Thoroughly check all prescriptions	Manually	Electronically using NFC
Always provide thorough patient counseling	Pharmacist only	Pharmacist & patient mobile app

TABLE II: The achieved goals by the proposed System.

Goals of the proposed System	How proposed System achieved goals
Availability	∗Electronic prescriptions (i.e. present, and past). ∗Intake instructions available all times on the patient's mobile phone.
Reliability	∗Ensure to dispense the right medication and right dose to the right patient. ∗The electronic prescription from a prescriber prevents handwriting misinterpretation.
Security and privacy	∗The fingerprint authentication will control access to patient's sensitive information. ∗Only the needed information will be sent to requesting party.
Efficiency	∗Reducing the time needed to provide the service by sending prescriptions in advance.

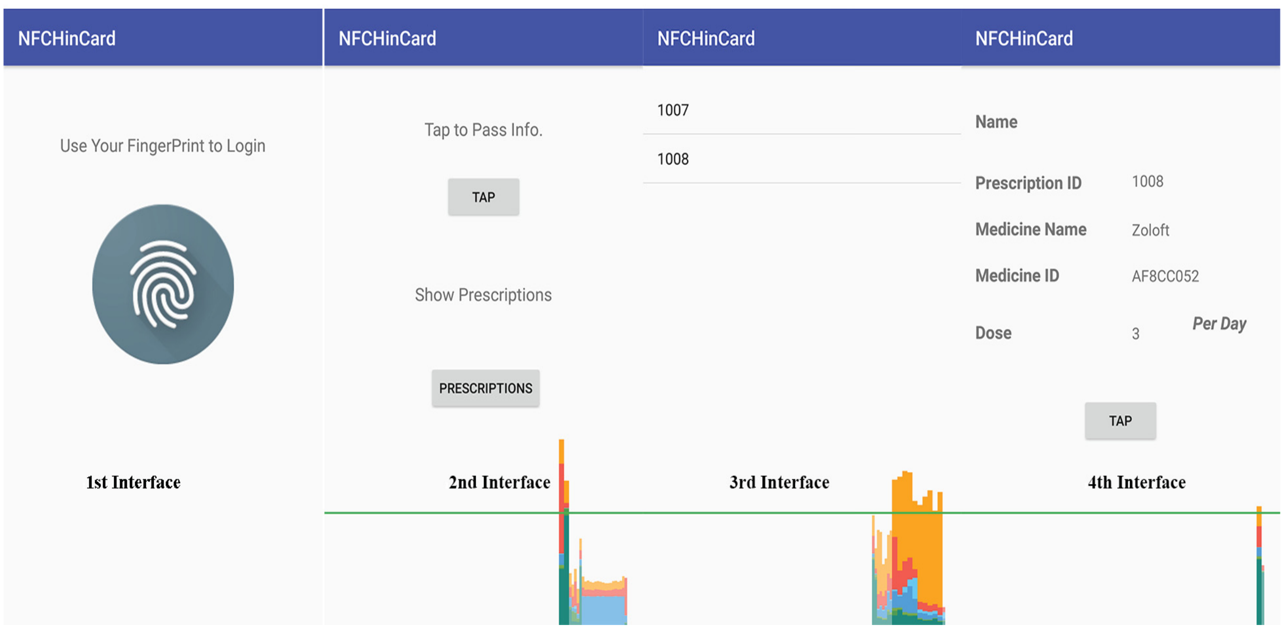


Fig. 3: The mobile application interfaces.

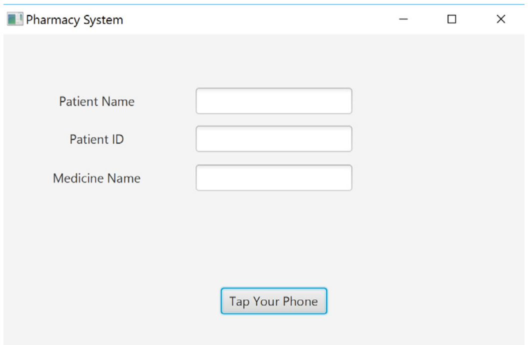
memory in the smartphone we used is 3 GB. Figure 5 shows the memory allocation by the smartphone application.

Third network connection, we developed the app to use the minimum connection needed to send and receive the necessary information for the app. In Figure 5 we can see that it took almost a second to complete the connection session for both connections. The first connection is to get the information on the list of prescriptions related to the patient. This connection had a data sent rate of 6.31 KB/S and data received rate of 5.04 KB/S. The second connection was for getting the information for a single prescription, which the user chose in the previous connection. The connection rates were 14.76 KB/S for the sent data and 13.63 KB/S for the received data. We configured the app and web server connection to remain open only when needed. Therefore, this method is intended to minimize the risk of threats due to open ports attacks.

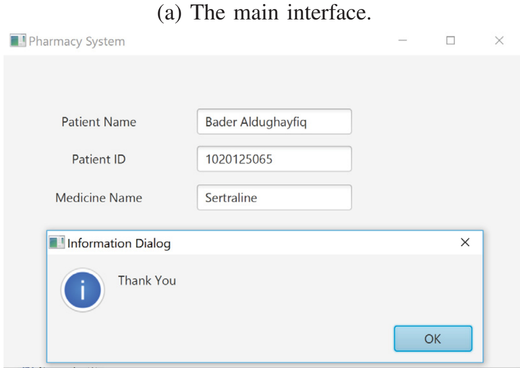
Finally, the process of dispensing one medication in term of transferring the information and validating the user took almost 6 seconds. The time is considered an optimal, since the process includes the required verification steps.

B. Security Analysis

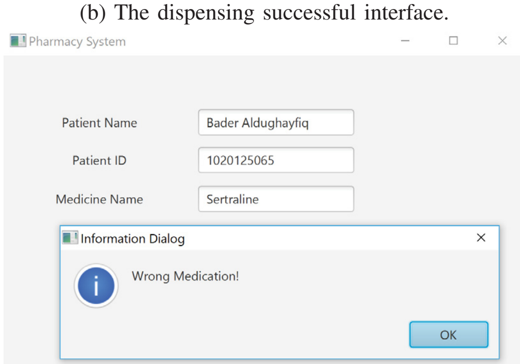
1) Tempering the medication tag: Every packaged medicine information (i.e. the name and ID) is entered in the



(a) The main interface.



(b) The dispensing successful interface.



(c) The medication verifying interface.

(d) The interface if prescription not valid.

Fig. 4: The Pharmacy Management System Interfaces during the dispensing process.

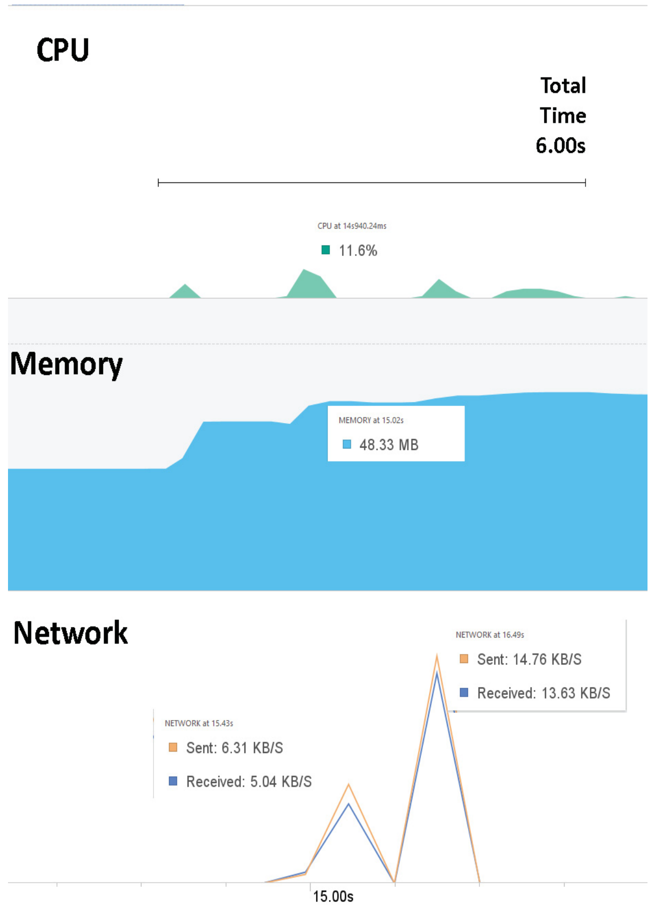


Fig. 5: The mobile application CPU, memory, and network evaluation.

database during the manufacturing process. Therefore, any attempt to tamper with content of the tag will be detected during the medication process. Also, even in a scenario where the pharmacist will prepare the medication and change the packaging, the pharmacist will attach an NFC tag containing the same ID that corresponds with the medicine name and ID in the database.

2) Hash confidentiality and integrity: The hash value is used mainly to verify the user and is only generated by the user's smart phone application using a time stamp (i.e. generated each session), user ID, and prescription ID. The User ID is stored in the smart phone application and database but is not transferred through the NFC in plain text. It is only sent to the pharmacy management system from the web server securely as mentioned in the assumption section. Also, the prescription ID is sent securely to the smart phone application from the web server. The prescription ID is not stored in the smart phone and is only requested when needed in order to lower the risk of any sniffing attack. Even if the attacker is able to obtain the prescription ID, they will not be able generate the same hash. Therefore, the confidentiality and integrity of the hash value will be protected in the system by the proposed methods.

3) Fingerprint-based authentication: In our system, we require the users to verify their identities using their fingerprint. This step ensures role access control of the application. Only the right user will be granted access to the application services, and this will protect their sensitive information. After accessing the application, the patient will send their ID through NFC to allow the prescriber management system to send it to the web server for the identity verification process. If the match is successful, the web server will send the required information.

4) NFC security and relay attack: The NFC is a close-range distance communication that requires the user to be in close range, 4 cm, from the NFC reader. This feature ensures the physical presence of users, which makes obtaining the app ID difficult in any malicious activities. However, the relay-attack has proven to be able to relay the information regardless of the range between the reader and the NFC device [16]. In the mentioned attack, the victim's application will be initiated by an NFC connection to the smartphone from a rogue NFC reader simulating a legitimate reader (i.e. a pharmacy system's NFC reader). After obtaining the information (i.e. prescription ID), the attacker will submit the prescription by using another NFC-enabled smartphone simulating the victim's device. Therefore, we require the fingerprint authentication to prevent any rogue access to the information. Basically, the NFC communication will not be initiated unless the user authenticates himself herself with their fingerprint.

V. Conclusion

In conclusion, we presented a system to provide an efficient, secure, and accurate medication dispensing process. Our work aims to minimize medication dispensing errors (i.e. wrong medication and/or wrong dose). We developed a mobile application for patient use. This application is used to authenticate the patient by using biometric authentication. Also, the patient will use NFC technology to transfer the necessary verification information to a pharmacy management system. Furthermore, medication validation is required at the last phase of the medication dispensing process to match the right medication with the right patient. Last, we evaluated the patient mobile application's efficiency and security. Also, we evaluated the efficiency of transferring information through NFC. Finally, even though the system will not prevent human errors, it will reduce the risk of dispensing a wrong medication or wrong dosage.

VI. Future Work

In future work, as this system is a work in progress, we will run a user study to evaluate the usability and accuracy of the system. Finally, we aim to develop a management tool for the prescriptions to ensure security and privacy.

Acknowledgment

The authors would like to thank Al Jouf University for supporting this research partially.

References

[1] R. Marchitelli, "Go public parents find son's lifeless body after pharmacy switches sleep medication for toxic dose of another drug," CBC News, 2016. [Online]. Available: http://www.cbc.ca/news/canada/toronto/go-public-sleep-medication-accidentally-switched-1.3811972

[2] J. Webb, "Pharmacy dispensing errors: Claims study emphasizes need for systematic vigilance," *Drug Topics, Modern Medicine Network*, 2015.

[3] HPSO, "A ten-year analysis 2013 pharmacist liability," Healthcare Providers Service Organization (HPSO), Tech. Rep., 2013.

[4] R. Nair, D. Kappil, and T. Woods, "10 strategies for minimizing dispensing errors," *Pharmacy Times*, 2010.

[5] P. A. O. N. Scotia, "Filling a prescription (dispensing)," 2018. [Online]. Available: https://pans.ns.ca/public/pharmacy-services/filling-prescription-dispensing

[6] S. Fan, M. Wen, C. Hsu, C. Hung, S. Hsu, M. Chuang, J. K. Zao, and C. Lin, "Health pal: a pda phone that will take care of your health," in *IEEE International Conference on Systems, Man and Cybernetics*, Oct 2007, pp. 3703–3708.

[7] M. Wang, J. K. Zao, P. H. Tsai, and J. W. S. Liu, "Wedjat: A mobile phone based medicine in-take reminder and monitor," *Proceedings of the 2009 9th IEEE International Conference on Bioinformatics and BioEngineering, BIBE*, pp. 423–430, 2009.

[8] J. K. Zao, M. Y. Wang, P. Tsai, and J. W. S. Liu, "Smart phone based medicine in-take scheduler, reminder and monitor," *12th IEEE International Conference on e-Health Networking, Application and Services, Healthcom*, 2010.

[9] B. M. Silva, I. M. Lopes, M. B. Marques, J. J. P. C. Rodrigues, and M. L. Proença, "A mobile health application for outpatients medication management," in *2013 IEEE International Conference on Communications (ICC)*, June 2013, pp. 4389–4393.

[10] M. Isomursu, M. Ervasti, and V. Törmänen, "Medication management support for vision impaired elderly: Scenarios and technological possibilities," in *2nd International Symposium on Applied Sciences in Biomedical and Communication Technologies*, Nov 2009, pp. 1–6.

[11] Surescripts, "E-prescribing," 2018. [Online]. Available: http://surescripts.com/products-and-services/e-prescribing

[12] PrescribeIT, "Prescribeit," 2018. [Online]. Available: https://www.prescribeit.ca/about-us

[13] A. C. S. ACS, "Acr122u usb nfc reader," http://www.acs.com.hk/en/products/3/acr122u-usb-nfc-reader/, 2017.

[14] XAMPP, "Xampp," https://www.apachefriends.org/index.html, 2017.

[15] T. Guerra, "The top 200 drugs of 2017?" *Pharmacy Times*, 2017. [Online]. Available: http://www.pharmacytimes.com/contributor/tony-guerra-pharmd/2017/03/the-top-200-drugs-of-2017

[16] Z. Wang, Z. Xu, W. Xin, and Z. Chen, "Implementation and analysis of a practical nfc relay attack example," in *2012 Second International Conference on Instrumentation, Measurement, Computer, Communication and Control*, Dec 2012, pp. 143–146.

Appendix C

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Digital Health in Physicians' and Pharmacists' Office: A Comparative Study of e-Prescription Systems' Architecture and Digital Security in Eight Countries

Author: Bader Aldughayfiq, Srinivas Sampalli

Publication: OMICS: A Journal of Integrative Biology

Publisher: Mary Ann Liebert, Inc.

Date: Feb 1, 2021

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A Framework To Lower The Risk of Medication Prescribing and Dispensing Errors: A Usability Study of An NFC-Based Mobile Application

Author: Bader Aldughayfiq,Srinivas Sampalli

Publication: International Journal of Medical Informatics

Publisher: Elsevier

Date: September 2021

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A System to Lower the Risk of Dispensing Medication Errors at Pharmacies Using NFC

Conference Proceedings:
2018 IEEE International Conference on Internet of Things (iThings) and IEEE Green Computing and Communications (GreenCom) and IEEE Cyber, Physical and Social Computing (CPSCom) and IEEE Smart Data (SmartData)

Author: Bader Aldughayfiq

Publisher: IEEE

Date: July 2018

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Appendix D

The Studies Ethics Approval Letters

The following are copes of the ethics approval letters for both the usability study and the online survey.

Subject: REB # 2019-4912 Letter of Approval
Date: Monday, December 23, 2019 at 11:34:36 AM Atlantic Standard Time
From: j.karle@dal.ca
To: Bader Aldughayfiq
CC: Srinivas Sampalli, James Karle

****This was sent from a no-reply address. To respond to this message, please reply directly to Jim Karle at j.karle@dal.ca.*

DALHOUSIE UNIVERSITY
Research Services

Social Sciences & Humanities Research Ethics Board
Letter of Approval

December 23, 2019
Bader Munif Aldughayfiq
Computer Science\Computer Science

Dear Bader Munif,

REB #: 2019-4912
Project Title: Testing the Usability of an NFC Based System to Transfer Credentials Securely to the Pharmacies and Lowering the Medication Dispensing Errors

Effective Date: December 23, 2019
Expiry Date: December 23, 2020
The Social Sciences & Humanities Research Ethics Board has reviewed your application for research involving humans and found the proposed research to be in accordance with the Tri-Council Policy Statement on *Ethical Conduct for Research Involving Humans.* This approval will be in effect for 12 months as indicated above. This approval is subject to the conditions listed below which constitute your on-going responsibilities with respect to the ethical conduct of this research.
Sincerely,

[redacted]

Dr. Karen Foster, Chair

Post REB Approval: On-going Responsibilities of Researchers
After receiving ethical approval for the conduct of research involving humans, there are several ongoing responsibilities that researchers must meet to remain in compliance with University and Tri-Council policies.
1. Additional Research Ethics approval
Prior to conducting any research, researchers must ensure that all required research ethics approvals are secured (in addition to this one). This includes, but is not limited to, securing appropriate research ethics approvals from: other institutions with whom the PI is affiliated; the research institutions of research team members; the institution at

which participants may be recruited or from which data may be collected; organizations or groups (e.g. school boards, Aboriginal communities, correctional services, long-term care facilities, service agencies and community groups) and from any other responsible review body or bodies at the research site

2. Reporting adverse events

Any significant adverse events experienced by research participants must be reported **in writing** to Research Ethics **within 24 hours** of their occurrence. Examples of what might be considered "significant" include: an emotional breakdown of a participant during an interview, a negative physical reaction by a participant (e.g. fainting, nausea, unexpected pain, allergic reaction), report by a participant of some sort of negative repercussion from their participation (e.g. reaction of spouse or employer) or complaint by a participant with respect to their participation. The above list is indicative but not all-inclusive. The written report must include details of the adverse event and actions taken by the researcher in response to the incident.

3. Seeking approval for protocol / consent form changes

Prior to implementing any changes to your research plan, whether to the protocol or consent form, researchers must submit a description of the proposed changes to the Research Ethics Board for review and approval. This is done by completing an Amendment Request (available on the website). Please note that no reviews are conducted in August.

4. Submitting annual reports

Ethics approvals are valid for up to 12 months. Prior to the end of the project's approval deadline, the researcher must complete an Annual Report (available on the website) and return it to Research Ethics for review and approval before the approval end date in order to prevent a lapse of ethics approval for the research. Researchers should note that no research involving humans may be conducted in the absence of a valid ethical approval and that allowing REB approval to lapse is a violation of University policy, inconsistent with the TCPS (article 6.14) and may result in suspension of research and research funding, as required by the funding agency.

5. Submitting final reports

When the researcher is confident that no further data collection or participant contact will be required, a Final Report (available on the website) must be submitted to Research Ethics. After review and approval of the Final Report, the Research Ethics file will be closed.

6. Retaining records in a secure manner

Researchers must ensure that both during and after the research project, data is securely retained and/or disposed of in such a manner as to comply with confidentiality provisions specified in the protocol and consent forms. This may involve destruction of the data, or continued arrangements for secure storage. Casual storage of old data is not acceptable.

It is the Principal Investigator's responsibility to keep a copy of the REB approval letters. This can be important to demonstrate that research was undertaken with Board approval, which can be a requirement to publish.

Please note that the University will securely store your REB project file for 5 years after the study closure date at which point the file records may be permanently destroyed.

7. Current contact information and university affiliation

The Principal Investigator must inform the Research Ethics office of any changes to contact information for the PI (and supervisor, if appropriate), especially the electronic mail address, for the duration of the REB approval. The PI must inform Research Ethics if there is a termination or interruption of his or her affiliation with Dalhousie University.

8. Legal Counsel

The Principal Investigator agrees to comply with all legislative and regulatory requirements that apply to the project. The Principal Investigator agrees to notify the University Legal Counsel office in the event that he or she receives a notice of non-compliance, complaint or other proceeding relating to such requirements.

9. Supervision of students

Faculty must ensure that students conducting research under their supervision are aware of their responsibilities as described above, and have adequate support to conduct their research in a safe and ethical manner.

Subject: REB # 2020-5367 Letter of Approval
Date: Friday, January 15, 2021 at 10:08:00 AM Atlantic Standard Time
From: ethics@dal.ca
To: Bader Aldughayfiq
CC: Srinivas Sampalli, Research Ethics

DALHOUSIE UNIVERSITY
Research Services

Health Sciences Research Ethics Board
Letter of Approval

January 15, 2021

Bader Munif Aldughayfiq
Computer Science\Computer Science

Dear Bader Munif,

REB #: 2020-5367
Project Title: Developing a framework for ePrescription system using Machine learning and blockchain to minimize medication errors

Effective Date: January 15, 2021
Expiry Date: January 15, 2022

The Health Sciences Research Ethics Board has reviewed your application for research involving humans and found the proposed research to be in accordance with the Tri-Council Policy Statement on *Ethical Conduct for Research Involving Humans.* This approval will be in effect for 12 months as indicated above. This approval is subject to the conditions listed below which constitute your on-going responsibilities with respect to the ethical conduct of this research.

Effective March 16, 2020: Notwithstanding this approval, any research conducted during the COVID-19 public health emergency must comply with federal and provincial public health advice as well as directives from Dalhousie University (and/or other facilities or jurisdictions where the research will occur) regarding preventing the spread of COVID-19.

Sincerely,

[redacted]

Dr. Lori Weeks, Chair

Post REB Approval: On-going Responsibilities of Researchers

After receiving ethical approval for the conduct of research involving humans, there are several ongoing responsibilities that researchers must meet to remain in compliance with University and Tri-Council policies.

1. Additional Research Ethics approval

Prior to conducting any research, researchers must ensure that all required research ethics approvals are secured (in addition to Dalhousie approval). This includes, but is not limited to, securing appropriate research ethics approvals from: other institutions with whom the PI is affiliated; the institutions of research team members; the institution at which participants may be recruited or from which data may be collected; organizations or groups (e.g. school boards, Indigenous communities, correctional services, long-term care facilities, service agencies and community groups) and from any other responsible review body or bodies at the research site.

2. Reporting adverse events

Any significant adverse events experienced by research participants must be reported **in writing** to Research Ethics **within 24 hours** of their occurrence. Examples of what might be considered "significant" include: a negative physical reaction by a participant (e.g. fainting, nausea, unexpected pain, allergic reaction), an emotional breakdown of a participant during an interview, report by a participant of some sort of negative repercussion from their participation (e.g. reaction of spouse or employer) or complaint by a participant with respect to their participation, report of neglect or abuse of a child or adult in need of protection, or a privacy breach. The above list is indicative but not all-inclusive. The written report must include details of the situation and actions taken (or proposed) by the researcher in response to the incident.

3. Seeking approval for changes to research

Prior to implementing any changes to your research plan, whether to the risk assessment, methods, analysis, study instruments or recruitment/consent material, researchers must submit them to the Research Ethics Board for review and approval. This is done by completing the amendment request process (described on the website) and submitting an updated ethics submission that includes and explains the proposed changes. Please note that reviews are not conducted in August.

4. Continuing ethical review - annual reports

Research involving humans is subject to continuing REB review and oversight. REB approvals are valid for up to 12 months at a time (per the Tri-Council Policy Statement (TCPS) article 6.14). Prior to the REB approval expiry date, researchers may apply to extend REB approval by completing an Annual Report (available on the website). The report should be submitted 3 weeks in advance of the REB approval expiry date to allow time for REB review and to prevent a lapse of ethics approval for the research. Researchers should note that no research involving humans may be conducted in the absence of a valid ethical approval and that allowing REB approval to lapse is a violation of the University Scholarly Misconduct Policy, inconsistent with the TCPS and may result in the suspension of research and research funding, as required by the funding agency.

5. Final review - final reports

When the researcher is confident that all research-related interventions or interactions with participants have been completed (for prospective research) and/or that all data acquisition is complete, there will be no further access to participant records or collection of biological materials (for secondary use of information research), a Final Report (available on the website) must be submitted to Research Ethics. After review and acknowledgement of the Final Report, the Research Ethics file will be closed.

6. Retaining records in a secure manner

Researchers must ensure that records and data associated with their research are managed consistent with their approved research plans both during and after the project. Research information must be confidentially and securely retained and/or disposed of in such a manner as to comply with confidentiality provisions specified in the protocol and consent forms. This may involve destruction of the records, or continued arrangements for secure storage.

It is the researcher's responsibility to keep a copy of the REB approval letters. This can be important to demonstrate that research was undertaken with Board approval. Please note that the University will securely store your REB project file for 5 years after the REB approval end date at which point the file records may be permanently destroyed.

7. Current contact information and university affiliation

The lead researchers must inform the Research Ethics office of any changes to contact information for the PI (and supervisor, if appropriate), especially the electronic mail address, for the duration of the REB approval. The PI must inform Research Ethics if there is a termination or interruption of his or her affiliation with Dalhousie University.

8. Legal Counsel

The Principal Investigator agrees to comply with all legislative and regulatory requirements that apply to the project. The Principal Investigator agrees to notify the University Legal Counsel office in the event that he or she receives a notice of non-compliance, complaint or other proceeding relating to such requirements.

9. Supervision of students

Faculty must ensure that students conducting research under their supervision are aware of their responsibilities as described above and have adequate support to conduct their research in a safe and ethical manner.

Appendix E

NFC-Based Mobile Application Usability Study

Following in the next page are the materials used in the user-study 5.

Tasks

Participant ID:…………

Please read the following scenarios and then perform the tasks using the proposed application, and the traditional method of processing a prescription. For all the following tasks please try to verify the correct medication.

Scenarios picking up a medication using the traditional method of processing a prescription:

Task 1

You have a prescription and you are in the drugstore to pick up the medication from the pharmacist.

- Please go through with the process of picking up a prescription from the pharmacy.
- Please try to identify if the medication you got is the correct medication using any methods available. The simulated paper prescription will not be returned to you.

Scenarios picking up a medication using the traditional method of processing a prescription:

Task 2

You have a prescription and you are in the drugstore to pick up the medication from the pharmacist.

- Please go through with the process of picking up a prescription from the pharmacy.
- Please try to identify if the medication you got is the correct medication using any methods available. The simulated paper prescription will not be returned to you.

Scenarios picking up a medication using the smartphone application with the NFC system:

Task 3

You have a prescription in the smartphone application, and you are in the drugstore to pick up the medication.

- Please go through with the process of picking up the medication using the proposed application.
- Please try to identify if the medication you got is the correct medication using any methods available.

Scenarios picking up a medication using the smartphone application with the NFC system:

Task 4

You have a prescription in the smartphone application, and you are in the drugstore to pick up the medication.

- Please go through with the process of picking up the medication using the proposed application.
- Please try to identify if the medication you got is the correct medication using any methods available.

Efficiency and Effectiveness Notes

Participant ID: .....

Scenarios	Tasks	Time to Complete (Efficiency)	Successful of Completion (Effectiveness)	
			Attempts to (Complete – incomplete)	Error Rates (Number of Attempts to verify the medication)
The Current System	Task 1			
	Task 2			
The Proposed System	Task 3			
	Task 4			

- Time to complete in minutes and seconds.
- Complete the task (Correctly) or incomplete the task (Incorrectly).
- Error rates: the number of errors occurred while doing the tasks (verifying the correct medication for them).

Pre-Session Questionnaire

Participant ID:…………

Demographic Questions

1. Gender
    Male Female Other
2. Age (in years):
    - 18-24 years old
    - 25-34 years old
    - 35-44 years old
    - 45-54 years old
    - 55 years or older
3. What is the highest degree or level of school you have completed?
    - High school.
    - Some college credit (no degree).
    - Undergraduate diploma Degree.
    - Master Degree.
    - Ph.D. Degree.
    - Other (Please Specify): ………………….
4. What is your occupation (If a student, what is your major?):

5. How often have you filled and picked-up one of your own prescriptions at a drug store in the last six months?
    - Less than one.
    - 1 – 5 times.
    - 5 – 10 times.
    - Other (Please Specify): ……………………
6. How much time do you spend using your smartphone applications daily?
    - Less than one hour.
    - 1 – 5 hours.
    - 5 – 10 hours.
    - Other (Please Specify): ……………………..
7. Do you use the tap to pay (e.g. Apple Pay, or Google Pay) application on your smartphone?
    - Yes
    - No
    - I did not know about this application.
8. If your answer is yes to the previous question, how often do you use the tap to pay application on a daily base?
    - Less than 5 times.
    - 5 – 10 times.
    - 10 – 20 times.
    - Other (Please Specify): …………………

Post-Condition Questionnaire

Participant ID:………….

1- Post Questionnaire Using the Traditional Method of Processing a Prescription

Picking up the medication from drugstore using the traditional method of processing a prescription of picking up the medication:	Strongly agree	Agree	Somewhat Agree	Neutral	Somewhat Disagree	Disagree	Strongly Disagree
I think this method will help me to keep my sensitive information private and secure.							
I expect this method will make intake instructions and times always available to me.							
I think this method will help me to verify my identity to the drugstore, which helps the drugstore to dispense the correct medication for me.							
I expect this method will provide enough information to the drugstore to dispense the correct medication to me.							
I think this method will help me to keep track of my current prescription/s to provide to prescribers if needed.							
I think this method will help the drugstore to avoid dispensing the incorrect medication to me such as misplacing the medication bag.							
I think this method will help to remember the medication intake instructions and times.							

Participant ID:…………

2- Post Questionnaire Using the Smartphone Application with NFC Technology

The smartphone with NFC application to pick up the medication:	Strongly agree	Agree	Somewhat Agree	Neutral	Somewhat Disagree	Disagree	Strongly Disagree
I think this method will help me to keep my sensitive information private and secure.							
I expect this method will make intake instructions and times always available to me.							
I think this method will help me to verify my identity to the drugstore, which helps the drugstore to dispense the correct medication for me.							
I expect this method will provide enough information to the drugstore to dispense the correct medication to me.							
I think this method is a shortcut process to transfer the information to the drugstore management system securely and accurately through NFC.							
I think this method will help me to keep track of my current prescription/s to provide to prescribers if needed.							
By reading the NFC tag on the prescription packaging, I think that this method both provides enough information and is a sufficiently powerful enough tool/method to verify the medication, thus avoiding dispensing errors.							
I think this method will help me to remember intake instructions and times.							
I think this method will be suitable for novices and expert users.							
I think using NFC technology to transfer information is a secure and fast method in the picking up medication process.							

Participant ID:………

Perceived usefulness and Ease of Use:

- I would like to ask you about your opinion regarding the usability of the proposed application.

Perceived usefulness

	Strongly	Agree	Somewhat Agree	Neutral	Somewhat Disagree	Disagree	Strongly Disagree
1) I think the smartphone application with NFC would improve my:							
a) dispensing medication process.							
b) intake instructions and times availability.							
c) finding active prescriptions.							
2) Using the smartphone application with NFC would make it easier to:							
a) detect medication dispensing errors from my end of the process.							
b) browses my active prescriptions.							
c) transfer sensitive information to the drugstore.							
3) Using the smartphone application with NFC would provide me with the accurate information that I need during:							
a) The process verifying my identity.							
b) The process verifying the correct medication.							
4) Using the smartphone application with NFC would serve to enhance my privacy by providing the pharmacy with only the needed authentication information.							
5) Using the smartphone application with NFC would give me greater control over the shared information.							
6) Using the smartphone application with NFC would save my time during picking up a prescription.							
7) Overall, I found the smartphone application with NFC to be helpful with having my prescription filled correctly and/or more quickly.							

Participant ID:………….

Perceived ease of use

	Strongly agree	Agree	Somewhat Agree	Neutral	Somewhat Disagree	Disagree	Strongly Disagree
Learning to use the smartphone application with NFC was easy for me.							
Browsing the active prescription using the smartphone application with NFC was easy.							
Finding the intake instructions and times using the smartphone application with NFC was easy.							
Transferring the needed information to the drugstore system via the smartphone application with NFC was easy.							
I found it easy to get the smartphone application with NFC to do what I want it to do.							
My interaction with the smartphone application with NFC was flexible in terms of finding all the needed information about my prescription.							
Overall, I found the smartphone application with NFC easy to use.							

Semi-Structured Interview Questions

Participant ID:…………

Simi-Structured Interview Questions

- **Post the usability study tasks:**
  1. What is your opinion in general about the smartphone application with NFC?
  2. Do you like this method (smartphone application with NFC) of transferring the information securely while preserving your privacy compared to your traditional method of processing a prescription? Why?
  3. What type of confidential information you welling to share to verify your identity?
  4. Would you want to use it in actual practice?
  5. What specific features or functionalities do you like about the smartphone application with NFC? Why?
  6. What specific features or functionalities do you dislike about the smartphone application with NFC? Why?
  7. What would you recommend for improving the smartphone application with NFC in terms of its content and functions?
  8. What would you recommend for improving the smartphone application with the NFC interface?
  9. What other comments do you have regarding the study in general and smartphone application with NFC in particular?

Performing the Tasks Instructions

- **Instructions on how to pick-up medication using the traditional method of processing a prescription. These instructions apply for both tasks of the traditional method of processing a prescription.**
    1. You will be presented with a paper prescription from the lead researcher, who will act for the role of the prescriber. The prescription will contain your name, health card number (i.e. the number is simulated for the purpose of the study), medicine name, and dosage.
    2. After, you will provide the prescription to the pharmacist, which is also a role played by the lead researcher, as if you in a real drugstore.
    3. The pharmacist (i.e. the lead researcher) will ask you a set of questions to verify your identity to dispense the medication.
    4. After, the prescriber will verify the dispensing of the correct medication by verifying the name with the patient.
    5. Upon the dispensing process, the pharmacist will explain any needed instructions (e.g. the medication intake instructions, and medication intake times) as if it is the first time to pick up a prescription.
    6. After picking up the medication, the researcher will ask you to verify the medication is filled correctly and correspond with your prescription with any available methods. Also, look for the medication intake instructions if available. The simulated paper prescription will not be returned to you.
- **Instructions on how to pick-up medication using the smartphone application with NFC. These set of instructions apply for both tasks of the smartphone application with NFC.**
    1. You will be asked to step your application login biometric (fingerprint) for the first time only. According to Google Android, which is the operating system we are using in the used smartphone, the fingerprint will be stored in the smartphone storage only to be used internally. After the end of the session, the fingerprint will be deleted in your present to keep your privacy and to prepare for the next session.
    2. Then, you will log in to the application using your fingerprint then press the tap button in order to transfer the personal information to the prescriber management system.
    3. After, the prescriber (i.e. lead researcher) will submit your prescription to the server. Then it will be available to you in the application.
    4. After, the pharmacist (i.e. lead researcher) will ask you to transfer the information needed to verify your identity and the prescription you want to pick up.
    5. In the application, you will select your prescription from the list of prescriptions interface. Then, click the tab button to transfer that information with your personal information to dispense the medication.
    6. After, the prescriber will verify dispensing the correct medication by taping the medication packaging to the NFC reader. The system will give the match message if the medication is correct.
    7. After, the prescriber will explain the needed instruction (e.g. the medication intake instructions, and medication intake times) as if it is the first time to pick up a prescription.
    8. After picking up the medication, the researcher will ask you to verify the medication is filled correctly and correspond with your prescription using any available method in the smartphone application and look for the medication intake instructions and times.

Appendix F

Online Survey Materials

The following are the materials (i.e. the background questionnaire, and the three surveys for all three groups) submitted to the Dalhousie ethics board committee to approve the online survey.

Background Questions (for all groups)

1. **What is your age?**

○ 18 – 24 years old

○ 25 – 34 years old

○ 35 – 44 years old

○ 45 – 54 years old

○ Over 55

2. **Please choose your gender:**

○ Male

○ Female

○ Other (please specify) ………….

3. **What is the highest level of education you have completed?**

○ Less than high school

○ High school or equivalent

○ College diploma

○ Bachelor's degree

○ Master’s degree

○ Doctoral degree

○ Other ……….

4. **Have you ever used any e-prescription system before? <u>(patient group only)</u>**

○ Yes

○ No

Prescriber Survey

Section A:

An example of an e-prescribing service is Prescribe IT. The service, according to the official website [1]” enables prescribers to electronically transmit a prescription directly from an electronic medical record to the pharmacy

To what extent do these reasons agree with your motivations for using or not using an e-prescription system (e.g. Prescribe IT in Canada)?	1 (Strongly disagree)	2 (Disagree)	3 Slightly disagree	4 Neutral	5 Slightly agree	6 Agree	7 Strongly agree
Because the system transfers the prescription securely.							
Because I like to keep a digital record of the patients’ prescriptions.							
Because I think it solves issues with the interpretation of handwritten prescriptions.							
Because I can track the fulfillment of prescriptions.							
Because it will improve the communication with the pharmacist.							
Because the system will take more time to type the prescription.							
Because the system requires an online connection, and thus it is more vulnerable to security threats.							

management system of a patient’s pharmacy of choice.”

[1] PrescribeIT. " About Us " Retrieved December 25th (2020) from: https://www.prescribeit.ca/about-us.

Section B:

- **The proposed e-prescription system's alerts:**

Before answering questions in this section, here is the explanation of the feature of generating alerts. Upon the patient visit, the patient will grant the prescriber access to the information. Then the prescriber will start the prescribing process. Once the prescription is ready to be submitted, the prescriber will submit the prescription to the proposed e-prescription system to be processed for any medication prescribing errors that might harm the patient. The system will check the prescribed medication against the patient medication history, current health condition, and drug-drug interaction with other prescribed medications the patient is taking. Then, the system will generate an alert that is specific to the patient only. Next, the system will notify the prescriber only if the prescribed medication has potential dangerous impacts on the patient's health. These impacts include any drug-on-drug interaction alerts. The proposed system will also check for any anomalies such as missing fields, misplaced information, or wrong dosage proportion in the prescription before submission to the e-prescription private network the patient.

	Strongly disagree	Disagree	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
An alert based on the patient's personalized medical history will help in prescribing a medication safely.							
Generating an alert based on a combination of medication use in previous similar cases and the health condition of a patient will help prescribe medication safely.							
I think the generated alerts based on the patient's previous health condition will not help me prescribe medication safely.							
I think checking the prescription for any anomalies will not help to reduce the time and workload associated with communicating with the pharmacy to correct the submitted e-prescription.							
An alert from the proposed system based on the patient's health condition will not help me prescribe medication safely.							
An alert from the proposed system based on the patient's health condition and similar previous cases will not help prevent any potential medication error (e.g. prescribing the wrong medication, wrong dosage, etc.).							
The proposed system alert generation feature is not a helpful tool to be integrated with the proposed e-prescription system.							

- **The security of the proposed e-prescription system:**

After submission, an e-prescription in the system is only accessible by the health center after granting access from the patient. This access only allows the user to read and not edit any information in the original e-prescription. Once the prescriber submits the e-prescription, it will be securely stored in the e-prescription private network (i.e., only accessible by health care providers and the patients). The e-prescription private network is developed to preserve the patients' information privacy and securely sharing the information. All the health care providers and patients can access the private network. Still, they can not read any information without the patients' authorization. Only the prescriber can generate the e-prescription after validating and checking for any medication errors (i.e., drug on drug interactions or any alerts that the medication might harm the patient). Making the e-prescription read-only mode will preserve the originality of the prescription. The prescription information will also be available to all parties (i.e. prescribers, pharmacists, and patients) in the network. However, only the authorized health care providers (i.e., prescriber or pharmacist) by the patient can access this information to read.

	Strongly disagree	Disagree	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
After submission, making the e-prescription available on the read-only mode will help avoid any alterations to it.							
I think making the e-prescription available for read-only mode will help to prevent prescription fraud.							
Making the patient medication history and prescription information available to all parties in the private e-prescription network will not provide a safe prescribing of medication to the patient.							

Section C:

Q: What improvements do you suggest to enhance the proposed e-prescription system?

A:

Pharmacist Survey

Section A:

An example of an e-prescribing service is Prescribe IT. The service, according to the official website [1]" enables prescribers to electronically transmit a prescription directly from an electronic medical record to the pharmacy management system of a patient's pharmacy of choice."

To what extent do these reasons agree with your motivations for using or not using an e-prescription system (e.g. Prescribe IT in Canada)?	1 (Strongly disagree)	2 (Disagree)	3 Slightly disagree	4 Neutral	5 Slightly agree	6 Agree	7 Strongly agree
Because the system transfers the prescription information securely between the prescriber and the pharmacist.							
Because I like to keep a digital record of patients' prescriptions.							
Because I think it solves issues associated with the interpretation of handwritten prescriptions.							
Because it will improve communication with the prescriber.							
Because it will reduce the time spent communicating with prescribers to clarify the prescription information.							
Because it will not help to verify the prescriber's identity automatically by using their digital signature.							
Because the system does not provide a method for verifying the prescription's originality.							

[1] PrescribeIT. " About Us " Retrieved December 25th (2020) from: https://www.prescribeit.ca/about-us.

Section B:

- **The proposed e-prescription system's alerts:**

Before answering questions in this section, here is the explanation of the feature of generating alerts.

Upon the patient's visit to the prescriber, the e-prescription issuing process is started. The process will involve checking the prescribed medication against the patient medication history, current health condition, and drug-drug interaction with other prescribed medications the patient is taking. Furthermore, the e-prescription will be checked for any anomalies, such as missing fields, misplaced information, or wrong dosage proportion in the e-prescription before submission to the proposed e-prescription system's private network. Then, the pharmacist will access the prescription information after the patient grants them access. The e-prescription will include a validation code to state the prescription already checked for any anomalies and any possible implication to the patient's health from the prescribed medication. Since only the patient can grant access to the e-prescription, this will validate the patient identity when the pharmacist retrieves the prescription information.

	Strongly disagree	Disagree	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
Verifying the prescription's appropriateness for the patient's health condition before submitting will not reduce the pharmacy's workload.							
I think checking the prescription for any anomalies will help to reduce the time and workload associated with communicating with the prescriber to correct the e-prescription.							
Checking the prescribed medication based on the patient's personalized medical history will help with prescribing medications safely.							
Reducing the workload associated with checking for drug-to-drug interactions will not improve the work efficiency in the pharmacy.							
Reducing the workload associated with checking for drug allergies will improve the work efficiency in the pharmacy.							
Checking for prescription anomalies will not reduce any medication dispensing errors.							
I think the proposed system alerts generating anomalies detecting feature will help me prescribe medication safely.							

- **The security of the proposed e-prescription system:**

After submission, an e-prescription in the system is only accessible by the health center after granting access from the patient. This access only allows the user to read and not edit any information in the original e-prescription. Once the prescriber submits the e-prescription, it will be securely stored in the e-prescription private network (i.e., only accessible by health care providers and the patients). The e-prescription private network is developed to preserve the patients' information privacy and securely sharing the information. All the health care providers and patients can access the private network. Still, they can not read any information without the patients' authorization. Only the prescriber can generate the e-prescription after validating and checking for any medication errors (i.e., drug on drug interactions or any alerts that the medication might harm the patient). Making the e-prescription read-only mode will preserve the originality of the prescription. The prescription information will also be available to all parties (i.e., prescribers, pharmacists, and patients) in the private e-prescription network. However, only the authorized health care providers (i.e., prescriber or pharmacist) by the patient can access this information to read.

	Strongly disagree	Disagree	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
I think allowing access to the e-prescription after submission only to read will help avoid any alterations to the e-prescription.							
I think making the e-prescription available for read-only mode will not help to prevent prescription fraud.							
I think granting access from the patient to the e-prescription process will help me verify the patient's identity during the dispensing process.							
Using the proposed e-prescription system will help me to authenticate the e-prescription.							

Section C:

Q: What improvements do you suggest enhancing the proposed e-prescription system?

A:

Patient Survey

Section A

- **Explanation of e-prescription systems:**

An example of an e-prescribing service is Prescribe IT. The service, according to the official website [1],” enables prescribers to electronically transmit a prescription directly from an electronic medical record to the pharmacy management system of a patient’s pharmacy of choice.” However, most of the e-prescription systems focus only on electronically transferring the prescription.

To what extent do these reasons agree with your motivations for using or not using an e-prescription system (e.g. Prescribe IT in Canada)?	(Strongly disagree)	(Disagree)	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
Because the system transfers my prescription securely.							
Because e-prescription prevents the loss of the prescription.							
Because I cannot keep track of all my past prescriptions.							
Because I can control the access to my prescription records.							
Because using this system will not improve nor change my process of picking up prescriptions.							

[1] PrescribeIT. " About Us " Retrieved December 25th (2020) from: https://www.prescribeit.ca/about-us.

Section B:

- **The security of the proposed e-prescription system**

We propose a secure system for optimizing the medication dispensing process. The system aims to introduce a more robust and secure method to confirm the patient's identity and minimize dispensing errors. We use a private network (i.e. only accessible prescribers, pharmacists, and patients) to securely manage the sharing of patient medication and e-prescription information and control access to it to preserve the confidentiality of patient information. The e-prescription private network is developed to protect the patients' information privacy and securely share the information. All the health care providers and patients can access the private network. Still, they can not read any information without the patients' authorization. Each patient can only access their stored data in the network, that securely stored using a unique ID provided from the patient's smartphone application. The smartphone application enables the patient to share the unique ID with the health care service providers to allow them to issue an e-prescription and view it and view the related information (i.e., medication history, current health condition, and past prescriptions information). Also, the application allows the patient to view the current prescription information. The application will be only accessible by the patient.

Upon the patient visit to the physician or the pharmacy, the patient will share the unique ID only to get the provided service (e.g., issuing e-prescription or pickup a prescribed medication)

Note: we are only seeking your response on the below survey based on the explanation we provided above. You are not requested to use your phone or perform any tasks.

	Strongly disagree	Disagree	Slightly disagree	Neutral	Slightly agree	Agree	Strongly agree
Making access to the e-prescription after submission on the read-only mode will help avoid any alterations to it.							
I think making the e-prescription available for read-only mode will help prevent prescription fraud.							
I think using the unique ID will help me verify my identity during the dispensing process.							
Using the private network will help me authenticate the originality of the e-prescription.							
Using the private network and the unique ID will not preserve my information privacy in the network.							
Making my medication and e-prescription information available to other parties in the network raises security concerns for me.							

Section C:

Q: What improvements do you suggest enhancing the proposed e-prescription system?

A:

Human Intelligence Task

Survey Task For Academic Research:

Developing an e-prescription system using machine learning and blockchain to minimize medication errors.

HIT Text

Please complete a short survey for academic research.

The study aims to evaluate the proposed e-prescription system we developed. The system aims to introduce a more robust and secure method for confirming the patient's identity and minimizing dispensing errors and prescribing errors. The system uses the blockchain network technology. Blockchain is technology used to securely manage the sharing of patient medication and with parties involved in the proposed e-prescription system (i.e., prescribers, pharmacists, and patients) prescription information. Also, the blockchain technology controls access to the information and preserve the confidentiality of patient information by giving the control of sharing the information to the patient. Also, the system uses machine learning algorithm to safely prescribe the medication by generating alerts specific past medication history, prescription information and current health condition. Machine learning algorithms are computer programed algorithms trained to analyze, understand, and identify patterns in the given data. The study will help to enhance ad improve the proposed e-prescription system by giving feedback on the use of the features (i.e., blockchain, machine learning) in the proposed e-prescription system. Thus, contribute to the research area of minimizing medication errors.

All responses and information collected for this study will remain private and secure. Data will be stored on a password-protected laptop that can only be accessed by the primary investigator. No identifiable information about the participants will be collected for the purposes of this study, and any other identifiable information such as IP addresses (i.e. will be used to ensure there are no multiple submissions) will be deleted before the data analyses, as they are not relevant to the purpose of this study. The user IDs on the Amazon Mechanical Turk website will not be collected nor linked to the participants since the survey will be conducted in the Opinio server (i.e. a secure and private server provided by Dalhousie University). Data will be stored in the Opinio server until the data collection process is finished. After, the researcher will assign a participation number (e.g. P1, P2, etc.) to all the survey responses data randomly to ensure the participants anonymity and help organizing the data before the analysis process. The survey response data and consent forms will be stored in sperate folders to help preventing any attempt to link the participants information in the consent forms with the survey response data. Both the survey response data and consent form will be stored in encrypted folders on the researcher laptop which is password protected. The data will be stored until the results are published, then they will be deleted.

This HIT has been allocated 30 minutes to complete, **but should take approximately 20-30 minutes total.** We do not want your HIT to expire, so have allocated significantly more time than you will require.

The survey will be conducted via another website. Here are the relevant instructions:

1. When you are ready to take the survey, please click this link: *The link appears here.*
2. Before taking the survey, please take the time to read and consider the consent document provided. The survey will begin when you click through an onscreen prompt.
3. Please choose the group of participants you belong to.

Please complete the survey give to you.