Mobile Applications to Improve Medication Adherence: Existing Apps, Quality of Life and Future Directions

Ashley Choi*, Annesha White Lovett, Jinhyang Kang, KyungMi Lee, Lydia Choi

College of Pharmacy, Mercer University, United States

Abstract   The aims of the study were to review the literature within the last decade with regard to existing applications to improve non-adherence, quality of life, and to discuss the pros and cons of currently marketed mobile applications. Based on review of a total of 33 articles and reports, hundreds of medication-related applications were shown to be currently available on the market. The findings were categorized based on the pros and cons of the applications. Results revealed that various applications are helpful to facilitate patient adherence, yet the majority of them have similar functions. These functions consist of manual reminder alerts and access to sources for drug information. Limited studies were found related to quality of life. Observational studies that were retrieved focused on physiological factors, such as a decrease in hemoglobin A1c. The target populations for mobile applications included caregivers, the elderly, low literacy patients, low income individuals, and other patients. Current mobile applications have a beneficial impact on patients, caregivers, and health-care providers including pharmacists. Although there were some concerns regarding methods for using mobile applications, such as privacy issues, the majority of previous studies showed positive perspectives on mobile applications. Future research on compatible features is encouraged for improved mobile application use in healthcare.

Keywords   Adherence, Compliance, Mobile Application, Smartphone, Quality of Life, mHealth

1. Introduction

Compliance is a complex behavioral process that involves maintaining or enhancing patients' health status and improving their disease state. Compliance is also referred to as adherence to a medicine regimen and more formally defined as "the extent to which a patient acts in accordance with the prescribed interval, and dose of a dosing regimen [1]." Koop et al 2010, noted that compliance plays a very important role in pharmacological therapy since medications will provide optimal benefit when patients adhere with their regimen [2]. Patients often do not achieve sufficient health outcomes due to non-compliance. Examples include taking medication incompletely, inconsistently or not at all [3].

For several decades, non-compliance with drug treatment has remained a common and major healthcare problem. About 50% of patients do not take their medication or do not take it as prescribed by their doctor [4]. Medication non-adherence can occur either intentionally or unintentionally. Intentional non-adherence refers to making a reasoned decision not to take a medication based on perceptions or feelings [5]. For instance, people often become discouraged and discontinue therapy when they do not receive an immediate response [4,6]. In contrast, unintentional non-adherence refers to intending to take a medication as prescribed but failing to do so for other reasons such as forgetfulness or carelessness. Studies show that non-adherence will affect patient health negatively most of the time whether it is intentional or unintentional [5].

Nonadherence has been researched and reviewed across the United States. A 2010 study by Smith and colleagues stated that the non-adherence rate of prescription medication over the past 30 years has remained as high as 40% [2]. Another study found that poor compliance causes approximately 33% to 69% of medication-related hospitalizations and accounts for $100 billion in annual health care costs [7]. The study indicated that roughly 125,000 Americans die every year because of poor medication compliance [2]. Other studies have searched for strategies and solutions to improve patient adherence, and a number of novel methods have been developed over the past years to diminish poor compliance problems [2,8].

Due to the convenient and effective features of information technology (IT) and its increased use, several studies have focused on the development of innovative IT for improving patient's health conditions [8,9]. Electronic Health Records (EHR), e-prescribing, and Electronic Drug Monitoring (EDM) for providers to monitor patients' medication adherence were commonly cited as beneficial methods [8]. In addition, more advanced health IT has been developed recently, playing an important role as a method to

improve healthcare quality and safety, as well as, to reduce medical and healthcare-related errors. Specifically, mobile applications are being used in healthcare settings not only by medical researchers, but also by diverse groups of patients who aim to improve their compliance [9].

According to the Pew Internet Research Center, 53% of US adults own a smartphone and 31% of them use it to search for health information. Furthermore, 19% of those smartphone users have downloaded and used an application to manage and monitor their health [10]. As the demand for applications has increased, the desire to utilize applications with more effective features, as well as easier-to-follow instructions has also increased. There is a need for more advanced applications and copious medication-related applications with discrete functions. The objectives of this study were to summarize the use of existing applications to improve adherence and quality of life, explore currently marketed health-related mobile applications noting pros and cons, and review security and privacy concerns associated with the use of mobile applications.

2. Materials and Methods

A search of literature databases PubMed, Google Scholar, and Web of Science was conducted to identify articles published between January 2004 and December 2014. This timeframe was selected because most currently used mobile phones have been actively developed in the early 2000's to present [11]. Both medical subject headings and free text search terms were used to identify relevant literature. Key terms were "adherence," "compliance," "prescriptions," "medication," "smartphone," "application," "security," "privacy," and "HIPAA." Where possible, the search was filtered to exclude incomplete or unoriginal works. All citations identified were screened for inclusion by reviewing titles and abstracts (See Appendix A).

2.1. Study Criteria

Those articles for which abstracts were not available from the electronic databases or that did not have abstracts were collected manually and screened for inclusion. Inclusion criteria were English language, original evaluation, publication date between January 2004 and December 2014, and reporting on a medication adherence application. Exclusion criteria consisted of non-health related studies, non-US based, commentaries, and studies that were not directly related to study objectives. Studies published in only abstract form were also not included. After reviewing titles and abstracts, a hard copy of each article that met the inclusion criteria was obtained for full review. In addition to the articles identified by the literature database search, several other methods were used to find pertinent literature. First, the authors examined medication-related applications in Apple's App Store and Android's Play Store, two of the leading application markets. Secondly, the authors examined

the bibliographies of included articles and studies on specific disease states relevant to application use.

2.2. Review Process

Articles identified through these methods again were collected and screened for inclusion, and added to the set of articles subjected to full review. In the full review process, each paper was randomly assigned to at least two of five reviewers who were to confirm inclusion criteria, abstract key information, and assess the quality of each article. Reviews were recorded on a standard report form and entered into a database for analysis. Discrepancies between reviewers were arbitrated by group consensus. Table 1 summarizes the number of articles retrieved from each key search term and the number of articles that were analyzed (See Appendix A). Major categories of data abstracted were title, year published, author, and key findings. Articles were classified by adherence, quality of life, existing health-related applications, and privacy concerns.

3. Results

A total of 14 articles and 4 application related reports were retrieved from the literature. Table 2 provides a summary of key findings (See Appendix B).

3.1. Adherence and Quality of Life

The number and use of apps in the area of health and wellness, not only for patients, but also for healthy people, is increasing. Several studies showed beneficial effects of mobile application use in terms of patient compliance and quality of life in various disease states. Some studies have shown that medication reminder systems are helpful for patient's adherence, especially when non-adherence is unintentional. Smartphone use is constantly growing in the United States, and apps that are helpful for adherence can be downloaded for little to no cost. The accessibility of these apps has been noted as a benefit for patients with complex medication regimens, as well as, caregivers of others or family members. Literature on the clinical application of smartphone with health-monitoring apps is growing, but analyses of improvement for quality of life are lacking [12].

The FOCUS system created by Ben-Zeev D and his colleagues was recently utilized to aid schizophrenic patients in self-management. Following current technology, a mobile application was invented called FOCUS, a mobile health (mHealth) intervention. The application was intended to allow schizophrenic patients to rehabilitate easily by using the mHealth intervention. In creating FOCUS, the main goal was to create a problem free mobile application to be used with ease since schizophrenia represents a complex and often difficult to manage disease state. Examination of application use revealed the need for several modifications. For example, all of the participants mentioned having difficulty in

understanding application abbreviations and terminology such as, transition and environment. Participants also complained about small font size, the space between buttons (menus) and high sensitivity when touching the screen. However, participants also commented on the helpfulness of mobile application visual aids. Out of a total of 12 participants, 8 participants felt strongly confident in using FOCUS, while 4 participants felt confident in its use. The authors concluded that the FOCUS mobile application should be further modified based on testing with medications. In doing so, they suggest that it will facilitate the rehabilitation of patients as well as quality of life [13].

Similarly, a study by Patel et al, 2013 revealed that the mobile healthcare application is a promising system not only to improve medication adherence, but also to enhance patients' quality of life. The study was completed with 48 high-risk urban patients with hypertension. The primary outcome measures were medication adherence assessed by pharmacy refill rate and Morisky self-reported medication scale, while the secondary outcome measures involved the use of a mobile automated medication reminder (Pill Phone) application and level of blood pressure. A limitation in this study related to use of the Pill Phone as approximately 40% of the "taken" responses were unanswered due to lack of accurate participant responses. However, findings revealed the overall medication adherence was improved as well as a decrease in blood pressure level (from average blood pressure level of 144/89 to 136/84), resulting in enhanced quality of life [14, 15].

Understanding the significance of medication adherence, especially in elderly patients, Dr. Helmut Brath et al, designed a randomized cross over single blinded, controlled study. The objective was to examine the feasibility of a mHealth based adherence measurement system (mAMS). The study included elderly patients with two out of three defined cardiovascular risks: type 2 diabetes, hypertension, or hypercholesterolemia. The participants were randomly assigned to group 1 or group 2 with a control phase (CON) and monitoring phase (MON) in specific time flows for 52 weeks. A patient specific user card and a study mobile phone were provided to individual participants, and electronic medication blister and dedicated software applications were set up to monitor timing and medication intake automatically and immediately. When the system detected missing data from the patient due to not transmitting their scheduled events as directed, it automatically sent a text message to the patients' study phone on the following day as a reminder. Only one participant discontinued the study due to difficulties in operation. Results showed that there were no statistically significant differences in baseline demographics.

The study findings were in favor of the MON phase with significant adherence differences shown in the use of one medication, metformin ($p < .05$). There was no significant difference related to the other three medications, simvastatin, rosuvastatin, and Ramipril ($p > .05$). Although the study revealed no statistically significant differences between CON and MON, there were some limitations, small sample size, short duration of therapy, and outdated technology [16].

3.2. Existing Health-related Applications with Pros and Cons

Regarding existing health care applications, there are similar applications out in the market, yet most of them require a fee for use so that patients may keep their own medical records within one application based on category. Furthermore, there are several applications available on reminding patients when to take pills and these applications have been shown to be popular in the market. The majority of them are available for under $10 USD. Specifically, My Medical by Hyrax Inc. and MedHelper are the top two applications. Both applications have a similar concept: providing a tool to organize medical information in one place for app users. These applications are designed to help patients and/or caregivers keep track and schedule prescriptions, medications, refills, doctors, and pharmacies along with personal medication-related information [Hyrax, MedHelper].

Application users can place different kinds of medical information into an application such as a personal profile (e.g. weight, height, blood pressure level, cholesterol level), medical charts (e.g. X-rays, MRIs), and/or medication information (e.g. a picture of a pill). Each application has different categories, which enables users to accordingly place relevant information into each category. The goal is to help users to easily have access when they need to find specific information such as X-ray results or prescription refills. The main point of having an application is to facilitate users in viewing and/or managing their medical records in one place. These features in applications may help increase patient health care outcomes as well as medication safety.

Although users find it helpful to use these applications, a critical requirement is that users have to place all their medical records into the application themselves. This may be very time consuming and inconvenient if application users do not have necessary skills to enter the information. Furthermore, the process may become more difficult as patients take more medications/prescriptions and accumulate more chart data. The more health information the application users have, the higher the chance of them making errors in entering the medications' names, chart values, etc.

Another remarkable application reviewed was called 'M-prescription' developed by SK Telecom HC Biz Office. This free of charge application included unique functions to store and manage prescriptions in smart phones. It also allowed patients to access necessary information regarding their prescription medications, such as indications, directions, and common adverse drug reactions. The most significant function was the automated system. Unlike My Medical by Hyrax Inc. and MedHelper, in which patients need to manually place all the medical information into the application, M-prescription does not have this requirement. Information is automatically populated based on patient's medical records that are submitted by physician.

Based on several articles discussing the pros and cons of medical-related mobile applications results are summarized in Table 3 [12,17,18,19]. The medication applications were identified based on features claimed by manufacturers and ranked based on the relative desirability or usefulness of the features. The apps with basic medication reminder features coupled with enhanced levels of functionality tended to be rated the highest among all applications [12].

In searching for appropriate applications, users will have a difficult time finding the right application for them. For example, Apple lists the popular applications first and so on. Applications targeted for small audiences will not likely be visible and it will be hard for users to find and use them [18]. Additionally, many of the applications listed consist of beneficial features, yet significant controversy still remains regarding privacy in the use of applications. Users question whether their personal health information (PHI) will be protected during use.

3.3. Privacy Concerns

While the mHealth system provides benefits to healthcare with improved adherence and quality of life, it also precipitates other issues, such as privacy and security [20]. Many studies have been identified related to privacy and security being a primary concern within healthcare. For example, in utilizing mHealth patients realized that numerous mHealth related applications contain various functions that require security and privacy. Patient health information and personal health records are stored frequently. However, the majority of currently available mobile applications, including medical applications, impart little or no security. Furthermore, some of the popular applications, which retain personal health records, do not even provide a password for security [21]. As the adoption of the mHealth application by patients and health care providers has increased, several studies have investigated state/regulation and concerns/challenges related to privacy and security [21,22,23].

Providing complete privacy and security to patients, providers, organizations, and vendors is a challenging task. Currently, the Health Insurance Portability and Accountability Act (HIPAA) of 1996 mandates that a national baseline of privacy protection for health information be provided as a part of governmental regulation. Another legal policy called the Health Information Technology for Economic and Clinical Health Act (HITECH) addresses, as part of the American Recovery and Reinvestment Act of 2009 (ARRA), concerns regarding privacy and security [20,21]. In addition, several other governmental legislations, such as the Sarbanes-Oxiety Act, the Food and Drug Administration (FDA) regulations, the Office of Civil Rights (OCR) enforcements, and the Federal Communication Commission (FCC) imparts guidance regarding healthcare privacy and security [21,24]. Unfortunately, gaps and weaknesses found within the policies and regulations allow for leaking of privacy and security information [20].

For example, organizations such as the FDA provide regulations to address privacy concerns, but the regulations are specific for medical device mobile applications [21]. Another issue is that there is no unique age or skill requirement, knowledge set, credential, or legal documentation requirement to develop healthcare applications. As a result, Brandth and Durkin (2012) suggest that health IT staff may not have the appropriate knowledge or experiences in mobile privacy and security regarding application development and management. They also mention that many users are not aware of the lack of security regarding the release of their personal information [21].

As use of mHealth has increased, more concerns/challenges about medical privacy have increased. The primary concern is patients' misunderstanding the "outside of HIPAA protection" regarding individual medical data or sources that can be easily accessed to share patient's personal information.

For instance, patients assume that medical data collected by any healthcare provider will be under HIPAA regulation, while use of the mHealth application may not fall under HIPAA regulation. However, once the patient's data is collected by the healthcare provider, most of the collected data will be disclosed to the software vendor and/or third party sites for appropriate as well as inappropriate purposes (e.g. advertising without the patients' authority) [22]. In this situation, a spy, or also known as a data broker may be involved [20,22,25]. Data brokers do not adhere to HIPAA regulations.

Moreover, downloading and saving collected health data is another concern under HIPAA protection. The developers of mHealth have noted concerns and challenges related to privacy in terms of its quality and quantity of collected data. The mobile application collects an extensive amount of data over a period of time not only on health-related information, but also on the lifestyle of the patient. Once the data are collected, those data are shared with third parties, again, meaning patient personal information can be leaked [20]. Current studies suggest the development of more specific and suitable policies and regulation as well as further investigation seeking ways to improve [20-24].

4. Discussion

The objectives of this study were to review articles associated with existing applications to improve medication adherence and quality of life, to discuss currently marketed health-related mobile application with their pros and cons, and to explore security and privacy concerns with regard to mobile applications. This study provides beneficial information for patients and primary caregivers, as well as pharmacists and other health care providers. Specifically for patients and primary caregivers, current applications contribute to improve patient's adherence with medication by many different features including administration alarms,

drug information search, and medical records access. Various mobile applications allow pharmacists and other healthcare providers to back up and retrieve the patient's health information, such as patient's vitals, lab values, and medical charts, and to easily transmit and export medication regimens within the healthcare system [12,17,18,19]. The majority of reviewed studies showed a positive impact on the use of existing mobile applications for medication adherence and quality of life which eventually provided for an improvement in effectiveness and safety of medication therapy [12,13,14,15,17].

Even though the retrieved studies reflected positive perspectives, a few studies revealed negative aspects, especially related to privacy concerns [20-25].   For example, in order to access medical information, someone must place all medical records into an application, which is very time-consuming and inconvenient. As a patient takes more medication or receives more lab results, use of the app may become confusing and harder to manage after a certain point. This may also result in a greater chance of medication error [20,21,24].

In preparing for future development and use of mobile health related applications special features should be researched, with a few of them being patient medical record linking, pop-ups for automated medication administration alarms as well as contraindications. Use of signs and symptoms severity scales for pain, depression, blood pressure and glucose also can also be included to facilitate the conduct of clinical trials to improve patients' adherence and quality of life. In order to resolve the main concern regarding privacy, further research is warranted for the development of applications to include an enhanced Patient Health Information security feature with a unique code and passcode. In addition, an overall description of medications and other features should be included using a simplified format, such as icons or lay-terms, to improve patient's understanding.

5. Limitations

Although this review provided a comprehensive overview of the landscape surrounding health care related mobile apps, several limitations exist. It should be noted that a large proportion of articles regarding health-related applications published between January 2004 and December 2014 were excluded because they were either non-health related studies, non-US based, commentaries or abstracts without full text access. Additionally, the articles that solely focused on patient adherence, quality of life, and privacy concerns were lacking. Instead, most articles focused on certain disease states and the effect of mobile applications on those disease states. The authors also caution readers as information on the commercial applications reviewed in this study was obtained solely from the existing literature and associated websites. Developers of the mobile apps were not contacted to obtain information for this study. Lastly, outdated mobile phones were used in some studies, which did not reflect contemporary technology and current trends. Those findings were not deemed to be useful and therefore excluded from the results as most patients currently utilize smartphones [15].

6. Conclusions

Future use of health related mobile applications is expected to increase in various healthcare settings. Mobile applications are considered to be a valuable tool for patients, caregivers, and healthcare professionals. For future innovative heath related mobile applications to be developed, they must focus on compatible features such as reinforced Patient Health Information security with unique code and passcode as well as automatic linking of prescriptions.

Appendix A

Table 1.   Summary of Key Search Terms for Retrieved Articles 2004-2014

Database Type	Key Search Terms	Number of Retrieved Articles	Number of Utilized Articles
PubMed	Smartphone and medication adherence and (application* or app*)	13	3
PubMed	(Mobile or smartphone) and (app* or application*) and (medical or medication) (adherence or compliance) and (pros or benefit*)	16	3
PubMed	(Mobile*) and (Medication*) and (automated) and (application*) and (Phones) and (medication adherence)	2	1
PubMed	mHealth and medication adherence and electronic	6	1
Google Scholar	"Evaluating" and "mobile health apps" and "healthcare" and pros and cons and e-health and technology and features	12	1
Google Scholar	"M-Health" and "Application" and Android Appliance* and features and portable and prescription	13	1
Google Scholar	"Privacy" and "Mobile Technology" and "Healthcare" and "application" and "mHealth" and "challenge*" and "medication" and (android or apple)	90	4
Web of Science	Medication* and (smartphone or mobile) and ("security" or HIPAA or privacy) and (application* or app*)	7	2
Android Play Store	Prescription	250+	0*
Android Play Store	Medication	250+	0*
Apple App Store	Medication	9	0*

*Information retrieved from the Android Play Store and the Apple App Store consisted of applications' descriptions of functions only

Appendix B

Table 2.   Summary of Articles 2004-2014: Quality of Life, Existing Health-Related Applications, and Privacy Concerns

Title	Year	Author	Measure	Method	Sample size	Key findings
Smartphone Medication Adherence Apps: Potential Benefits to Patients and Providers	2013	Dayer L, Heldenbrand S, Anderson P, Gubbins PO, Martin BC	Discussion of the potential for adherence apps; evaluation of features of adherence apps.	Identify adherence apps and rank by perceived importance to user desirability using a three-point rating system: 1, modest; 2, moderate; 3, high.	$N = 160$ adherence apps	Smartphone medication application use may be considered as a potential strategy for pharmacists to improve patients' nonadherence.
Development and usability testing of FOCUS: a smartphone system for self-management of schizophrenia	2013	Ben-Zeev D, Kaiser SM, Brenner CJ, Begale M, Duffecy J, Mohr DC	Use of mHealth for rehabilitation of individuals with psychiatric conditions.	Individuals with schizophrenia or schizoaffective disorder and practitioners complete a survey regarding their use of mHealth.	$N = 904$	Mobile health (mHealth) can be used by many people who have cell phones. Use of mHealth can provide rehabilitation to people who have psychiatric conditions. Many users expressed their interest in using mHealth and mHealth is under development to be used for other self-management illnesses as well.
Mobilizing Your Medications: An Automated Medication Reminder Application for Mobile Phones and Hypertension Medication Adherence in a High-Risk Urban Population	2013	Patel S, Jacobus-Kantor L, Marshall L et al.	Use of medication reminder software on a mobile phone provided to a high-risk urban population with relatively poor adherence to antihypertensive medications.	Assess medication adherence by review of pharmacy refill rates before, during, and after availability of the medication reminder software.	$N = 50$	This study was conducted with a high-risk urban population with relatively poor adherence to antihypertensive medications. By introducing an automated medication reminder application (Pill Phone), the pharmacy refill rate was improved, as well as the patients' blood pressure. In fact, the overall quality of life was enhanced. There were some limitations present, which were a small study population and a relatively short study period.
Adherence to Antidepressant Medications: A Randomized Controlled Trial of Medication Reminding in College Students	2014	Hammonds T, Rickert K, Goldstein C	Participants were divided into an antidepressant medication reminder via smartphone group and antidepressant medication non-reminder group to measure medication adherence to predict the potential benefit of medication reminder application usage.	Each participant required to complete the survey as well as a manual pill count on the first day and 30th day of the study.	$N = 57$	In order to determine whether the mobile health with medication reminding feature related to medication adherence, this study was conducted as a randomized placebo-controlled design with 57 college students who had a valid antidepressant prescription. As a result, the medication reminding via mobile phone was directly related to improved medication adherence.

Mobile Health (mHealth) based medication adherence measurement - a pilot trial using electronic blisters in diabetes patients	2013	Brath H, Morak J, Kastenbauer T, et al	The participants were elderly patients with increased risk of cardiovascular disease, such as diabetes, hypertension, and hypercholesterolemia. Each participant used mAMS to measure medication adherence.	Measures drug adherence by controlled randomized doctor and medication adherence measurement system (mAMS) using blinded study with crossover design.	$N = 53$	Findings from this study revealed that a mobile health (mHealth) based remote medication adherence measurement system (mAMS) is practicable and well accepted by elderly patients with increased cardiovascular risk. An increase patient adherence was also shown.
Evaluating user perceptions of mobile medication management applications with older adults: a usability study	2014	Grindrod KA, Li M, Gates A	Investigated the usability of medication management applications that are currently available.	All participants provided with an iPad with four different medication management applications included: MyMedRec, DrugHub, Pillboxie, and PocketPharmacist. The qualitative data was analyzed by using grounded theory.	$N = 35$	The authors concluded that older adults can be capable and interested in using mobile health applications for their medication management. The lack of perceived usefulness of a mobile medication management application appears to be the greatest barrier to adopt such technology. For older adults, reminder systems may be considered of little use, whereas drug interaction features may be more desirable.
Evaluating and selecting mobile health apps: strategies for healthcare providers and healthcare organizations	2014	Boudreaux ED, Waring ME, Hayes RB, Sadasivam RS, Mullen S, Pagoto S	Summarized seven strategies for evaluating and selecting health-related apps.	Seven strategies as follows: (1) Review the scientific literature, (2) Search the app clearinghouse websites, (3) Search the app stores, (4) Review app descriptions, (5) Conduct a social media query within the profession and, if available, patient networks, (6) Pilot the apps, and (7) Elicit feedback from patients	N/A	The authors stated that since there is variation in the quality among applications, strategies for evaluating and selecting them would be necessary. The study addressed seven strategies that help healthcare providers and organizations to evaluate and select health-related apps. The seven strategies that were summarized could also be appropriately used to patients and caregivers.
A Ubiquitous "M-Health" Application Using Android Appliances	2014	Potdar MS, Pawar IB	Presented an ubiquitous M-Health android application that could be shared in between doctor-pharmacist-patient, patient-insurance agents.	Development of architecture and an initial model that could be used for quick notification between a client terminal and a server system	N/A	The main objective of this study was to decrease the gap between physicians and patients by using m-Health in android devices. This application provided remote access that allowed for the viewing of medical records, doctor's prescriptions, database and insurance policies of patients.
Privacy in Mobile Technology for Personal Healthcare	2012	Avancha S, Baxi A, Kotz D	Observed the required privacy technologies that could be potentially transformed to healthcare.	Development of a conceptual privacy framework for mHealth as well as itemizing the required privacy properties, in which, the privacy challenges were identified in mHealth systems.	N/A	Author discussions supported the idea that for any personal monitoring device/technology, privacy is the most important factor. It was concluded that mHealth allows physicians to remotely access patients' data and doctor's prescriptions, but a well-developed privacy plan is required. This article discussed the technologies and privacy framework that could be applied to mHealth supporting privacy-sensitive mHealth systems.

Privacy and Security	2012	Brandt J, Durkin S	This article discussed the impact of medical device regulations, concerns, potential goals, and patient reported data regarding privacy and security in mobile healthcare.	NA	NA	Authors concluded that privacy and security are critical in healthcare. However, the current status of privacy and security shows a lack of compliance with HIPAA mandates, the Food and Drug Administration (FDA) regulations, the Office of Civil Rights (OCR) enforcements, and requirements from other governing agencies and health sectors, in terms of mobile health. Furthermore, a vast amount of data leakage is common.. In order to lessen those complications, the authors suggest a mHIMSS Roadmap for healthcare organizations and vendors to facilitate patients' privacy and security.
Privacy in the Digital World: Medical and Health Data Outside of HIPAA Protections	2014	Glenn T, Monteith S	Discussed medical and health data created outside of HIPAA protection, including the use of credit cards for physician visits and medication co-pays, internet searches, email content, social media, support groups, and mobile health apps.	Data controlled by third party data brokers and internet companies discussed.	NA	The data are used for predictive profiling of individual health status, and often sold for other purposes such as advertising. This was noted as an issue that causes encroaching on privacy and the doctor-patient relationship. The authors concluded that it is necessary to discuss in detail regarding the appropriate handling of medical and health data between individuals and a wide variety of healthcare professionals.
Security Concerns in Android mHealth Apps	2014	He D, Naveed M, Gunter C, Nahrstedt K	Investigated security and privacy risks in Android mHealth apps.	Identify potential attack surfaces, learning size of attacked surfaces, and severity of the threat.	$N = 160$ Android mHealth apps	The authors stated that Mobile Health (mHealth) applications carry an increasingly large amount of sensitive information for both professionals and patients, yet the data shall be secured based on regulatory protection including Health Insurance Portability and Accountability Act of 1996 (HIPAA). This study highlighted privacy and security concerns and suggested areas for improvement in mHealth by presenting three studies. Findings revealed extensive use of unsecured internet communication and open access to third party servers.
Wireless Technology Poised to Transform Health Care	2010	Jackson Andrea	Discussed the positive impact and concerns of existing applications on health care delivery.	NA	NA	Article noted that wireless health enhances the quality, efficacy, and compliance of healthcare by extending access at relatively low costs. Furthermore, it was stated that wireless health also encourages patient's involvement in monitoring and managing of their health condition. Authors suggest that users should carefully choose the correct technology since the design of wireless health can be based on the technology system. In addition, there is a large issue regarding regulatory and privacy concerns, although, most parts of the wireless health solution are regulated by the Food and Drug Administration (FDA) and the Federal Communications Commission (FCC).
Telemetric monitoring in the behavior sciences	2008	Goodwin MS, Velicer WF, Intille SS	Reviewed current information regarding telemetric monitoring.	NA	NA	The authors concluded that although telemetric (i.e. wearable computers) may be useful in a scientific approach to behavioral assessment, issues with privacy and confidentiality, practical considerations, and statistical and measurement challenges exist.

Table 3. Pros and Cons of existing applications 2004-2014 [12,17,18,19]

Pros	Cons
Having a companion website that allows medication regimen entry from a computer	Not available in various languages
Being able to schedule medication instructions	Not having a HIPAA compliance statement
Being able to back up and retrieve data from a storage system	Being unable to generate medication reminders for multiple individuals on different medications
Allowing the user to enter, search, and select medications	Being unable to generate medication reminders without use of cellular or wireless connectivity
Being able to remind patients to take their medication and to record taken and missed doses	Lack of provision of drug interactions information
Being able to transmit, print, or export medication regimens and/or medication-taking behaviors	Difficult to choose an appropriate medical mobile application from a proliferative number of applications available in markets
Allowing providers to input and maintain the patient's medication regimen	Not available on every platforms, limited to a single platform (e.g. iOS)

REFERENCES

[1]   Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. Value Health. 2008; 11(1): 44-7. doi: 10.1111/j.1524-4733.2007.00213.x.

[2]   Bexley D, Heil AM, Lalonde J, Easter J, Fox MB, Buchanan S, Oliver W. The 21st Century Intelligent Pharmacy Project: The Importance of Medication Adherence. The Center for Health Transformation. Available at: http://www.mirixa.com/uploads/pdfs/2010_-_CHTMedAdhr Wp.pdf. Accessed September 11, 2014.

[3]   Miller N, Hill M, Kottke T, Ockene I. The multilevel Compliance Challenge: Recommendation s for a Call to Action. Circulation. 1997; 95: 1085-1090

[4]   Evans L, Spelman M. The problem of non-compliance with drug therapy. Drugs. 1983;25(1):63-76.

[5]   Dayer L, Heldenbrand S, Anderson P, Gubbins PO, Martin BC. Smartphone Medication Adherence Apps: Potential Benefits to Patients and Providers. J Am Pharm Assoc. 2013;53(2): 172-181.

[6]   Lin R, Ramakrishnan S, Chang H, Spraragen S, Zhu X. Designing a Web-based Behavior Motivation Tool for Healthcare Compliance. IBM Watson Research. 2013; 23(1): 58-67.

[7]   Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353:487-497.

[8]   Williams A, Kenyon K. Issue Brief: Medication Adherence and Health IT. Available at: http://www.healthit.gov/sites/default/files/medicationadhere nce_and_hit_issue_brief.pdf. Accessed September 11, 2014.

[9]   Seabrook HJ, Stromer JN, Shevkenek C, Bharwani A, Grood J, Ghali WA. Medical applications: a database and characterization of apps in Apple iOS and Android platforms. BMC Research Notes. 2014; 7:573. doi:10.1186/1756-0500-7-573.

[10] Fox S, Duggan M. Mobile Health 2012. Available at: http://www.pewinternet.org/2012/11/08/mobile-health-2012/. Accessed September 17, 2014.

[11] Cromar S. Smartphones in the U.S.: Market Analysis. 2010: 1-41.

[12] Dayer L, Heldenbrand S, Anderson P, Gubbins PO, Martin BC. Smartphone Medication Adherence Apps: Potential Benefits to Patients and Providers. *J Am Pham Assoc.* 2013;53(2):172-181.

[13] Ben-Zeev D, Kaiser SM, Brenner CJ, Begale M, Duffecy J, Mohr DC. Development and usability testing of FOCUS: a smartphone system for self-management of schizophrenia. *Psychiatr Rehabil J.* 2013;36(4):289-96. doi: 10.1037/prj0000019.

[14] Patel S, Jacobus-Kantor L, Marshall L et al. Mobilizing Your Medications: An Automated Medication Reminder Application for Mobile Phones and Hypertension Medication Adherence in a High-Risk Urban Population. *J Diabetes Sci Technol.* 2013;7:630. doi:10.1177/193229681300700307

[15] Hammonds T, Rickert K, Goldstein C. Adherence to Antidepressant Medications: A Randomized Controlled Trial of Medication Reminding in College Students. *J Am Coll Health.* 2014.

[16] Brath H, Morak J, Kastenbauer T, et al. Mobile Health (mHealth) based medication adherence measurement - a pilot trial using electronic blisters in diabetes patients. *Br J Clin Phamacol.* 2013;76:47-55. doi: 10.1111/bcp.12184.

[17] Grindrod KA, Li M, Gates A. Evaluating user perceptions of mobile medication management applications with older adults: a usability study. *JMIR Mhealth Uhealth.* 2014;2(1):e11. doi: 10.2196/mhealth.3048.

[18] Boudreaux ED, Waring ME, Hayes RB, Sadasivam RS, Mullen S, Pagoto S. Evaluating and selecting mobile health apps: strategies for healthcare providers and healthcare organizations. *TBM.* 2014. doi: 10.1007/s13142-014-0293-9.

[19] Potdar MS, Pawar IB. A Ubiquitous "M-Health" Application Using Android Appliances. *International Journal of Science and Research (IJSR)*. 2014;3:10.

[20] Avancha S, Baxi A, Kotz D. Privacy in Mobile Technology for Personal Healthcare. *CSUR*. 2012; 45(1): 3:1-3:45. doi: 10.1145/2379776.2379779

[21] Brandt J, Durkin S. Privacy and Security. *mHIMSS Roadmap*. 2012: 6-01-6-16

[22] Glenn T, Monteith S. Privacy in the Digital World: Medical and Health Data Outside of HIPAA Protections. *Curr Pschiatry Rep*. 2014;16:494. doi: 10.1007/s11920-014-0494-4

[23] He D, Naveed M, Gunter C, Nahrstedt K. Security Concerns in Android mHealth Apps. *AMIA Symposium*. 2014

[24] Jackson Andrea. Wireless Technology Poised to Transform Health Care. *Rady Business Journal*. 2010; 3(1): 24-26

[25] Goodwin MS, Velicer WF, Intille SS. *Telemetric monitoring in the behavior sciences*. Behavior Research Methods. 2008. 40(1):328-341. doi:10.3758/BRM.40.1.328