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Smart pills: the future of adherence monitoring

Yosef Houmid Al Shammari
KSA, National Guard Health Affairs
Email: zx5zx6@hotmail.com

Homoud Awade Al Shammari
KSA, National Guard Health Affairs
Email: Abomlk022@gmail.com

Talal Muhammad bin Barak
KSA, National Guard Health Affairs
Email: gdmol2014@gmail.com

Bandar Said Alharbi
KSA, National Guard Health Affairs
Email: aa4605a@gmail.com

Saud Tawfiq Alshammari
KSA, National Guard Health Affairs
Email: Tobksa79@gmail.com

Saleh Abdullah Alnais
KSA, National Guard Health Affairs
Email: Salehalnais22@gmail.com

Saeed Awad Aljohani
KSA, National Guard Health Affairs
Email: 4uvideoclip@gmail.com

Abdulrahman Abdullah Alorf
KSA, National Guard Health Affairs
Email: abdulrahmanab7557@gmail.com

Meshari Abdulmajeed Alnawmasi
KSA, National Guard Health Affairs
Email: Alnomasime@gmail.com

Mohammed Awad Alshammari
KSA, National Guard Health Affairs
Email: alshammarimo15@ngha.med.sa

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Majed Farhan Alharbi
KSA, National Guard Health Affairs
Email: Alharbima2@ngha.med.sa

Abdulrahman Gobile Al Enazi
KSA, National Guard Health Affairs
Email: Alenazia13@ngha.med.sa

Abdulelah Mohammed Mubashir Alamri
KSA, National Guard Health Affairs
Email: Deloo.hellcat@gmail.com

***Abstract*---**Background: The precise assessment and monitoring of patient medication adherence is a worldwide concern due to the lack of universally accepted methodologies for accurately measuring adherence. There has been recent focus on using technology to monitor medication adherence, since they allow for continuous surveillance of an individual's behavior in taking their prescription. Nevertheless, the existing technologies for monitoring medication adherence range in terms of their technological characteristics and techniques of data collection, resulting in variations in their individual benefits and constraints. There is a dearth of suitable criteria to guide the evaluation of medication adherence monitoring devices for optimum uptake and utilization. Aim of Work: The objective of this research is to conduct a narrative evaluation of existing technologies for monitoring medication adherence and to suggest a set of criteria for assessing these technologies, which will aid in the development and implementation of such technologies. Methods: Using the terms medication adherence, measuring technology, and monitoring technology, a literature search was carried out on PubMed, Scopus, CINAHL, and ProQuest Technology Collection (2010-present). The selection concentrated on research concerning the technology used to monitor medication adherence, as well as its development and use. The technical characteristics, methods of data collection, and possible benefits and drawbacks of the identified technology applications were extracted. Additional techniques for using data for adherence monitoring were also found. Recurring aspects that were often seen were combined to provide prospective criteria for assessing technology. Results: The technical aspects of different technology types differed, but they all aimed to reliably monitor medication adherence and encourage adoption in patients' everyday lives. This was achieved via their unobtrusiveness and comfort of use. The majority of technologies were capable of offering real-time monitoring of medication-taking behaviors, but, they depended on indirect indicators of medication adherence. There have been few reports of successful deployment of these technologies in clinical settings. A total of 28 criteria for evaluating technology were defined and grouped into five categories: development information, technical characteristics, adherence to data collection and management,

feasibility and implementation, and acceptability and usability. Conclusion: This study provides an overview of the technical characteristics, methods of data collection, and the pros and cons of medication adherence monitoring technology discussed in existing literature. It also presents the suggested criteria for evaluating medication adherence monitoring technologies. This set of evaluation criteria may serve as a valuable instrument to direct the advancement and choice of pertinent technologies, enabling the ideal adoption and efficient use of technology to enhance medication adherence results. Additional research is required to evaluate the criteria used to assess medication adherence monitoring technologies and develop a suitable framework for technology evaluation.

***Keywords*---**Medication Adherence, Technology Evaluation, Remote Sensing Technology, Telemedicine, Smart Pills.

Introduction

Precisely assessing and tracking patient medication adherence is of utmost importance in both clinical practice and research contexts, although it remains a difficult undertaking worldwide. Multiple techniques are used to assess medication adherence, including patient self-reports, pill counts, pharmacy refill records, drug metabolites or biomarker tests, and directly observed treatment (DOT) [1]. Nevertheless, none of these approaches have been universally recognized as a standardized means of assessing medication adherence in various contexts [2]. In recent times, there has been a growing use of sensor technologies to monitor the medication adherence of patients. An example of this is the Medication Event Monitoring System (MEMS), which is capable of documenting each instance when the patient accesses the pill container by use of a sensor that is integrated into the top of the pill bottle [3,4]. These technologies provide a distinct opportunity to assess and track the extent to which patients adhere to their treatment regimen over a period of time. Some studies [3-9] have claimed that medication adherence monitoring technology is the most accurate method for measuring patient medication adherence. However, other researchers [10-15] have chosen to ignore this assumption. The absence of adequate technology evaluation criteria in the area of medication adherence monitoring has led to insufficient agreement on how to decide or pick the suitable technology for application.

The literature has provided descriptions of the benefits and drawbacks of the often used techniques for monitoring drug adherence. For instance, Directly Observed Therapy (DOT) enables the direct monitoring of patients' medication-taking behavior [16-18]. However, it is costly to maintain and imposes a restrictive time burden on both healthcare practitioners (HCPs) and patients' daily routines [1,12,18,19]. Patient self-reporting is a commonly used method to evaluate medication adherence. It allows patients to have control over reporting their own adherence. However, there is a danger that patients may either overestimate or underestimate their ability to stick to their prescription regimen [20-22]. Ongoing advancements are being made in the development and

enhancement of medication adherence monitoring devices, which come in different varieties and provide diverse functionalities [1]. Users may be unfamiliar with distinctive aspects of freshly emerging technology [23]. However, there is currently no comprehensive description or synthesis that accurately captures the distinct qualities and benefits of various drug adherence monitoring devices. There is an increasing need for technology evaluation criteria that may provide guidance in the development and selection of suitable technologies for monitoring medication adherence, with the goal of enhancing patient outcomes [24].

Stakeholders have different expectations when it comes to using health information technology for monitoring drug adherence. When choosing monitoring technology, clinicians prioritize a user-friendly interface and precise adherence monitoring [1]. From a technological standpoint, although maintaining high system accuracy and data integrity is important, developers must also take into account the viability of technical engineering aspects of the system, such as energy consumption and battery lifespan [25]. Advanced medication adherence monitoring systems provide the ability to obtain patient medication adherence information via several methods, rather than being restricted to just one approach. Furthermore, the use of these technologies might be complex due to the extensive medical and pharmacological aspects, as well as the multifaceted behaviors of patients when it comes to following their drug regimen [22]. An exhaustive compilation and evaluation of the existing applications of medication adherence monitoring technologies is crucial for gaining a comprehensive knowledge of their capabilities and effectiveness. This information is essential for making informed choices on their acceptance and use.

Aim of Work

The aim of this narrative review is to provide a concise summary of existing literature on the current uses of medication adherence monitoring technologies and to offer possible evaluation criteria that might assist in making choices on the development and use of such technologies.

Methods

The PubMed, Scopus, CINAHL, and ProQuest Technology Collection databases were selected for their extensive range of literature pertaining to health, healthcare, and technology. The search query consisted of the phrases "medication adherence" combined with "measurement technology" or "monitoring technology". The document contains a comprehensive compilation of search techniques used for each database.

Types and Characteristics of Technology

Out of the 98 papers that were evaluated, 81% of them documented the use of medication adherence monitoring technologies. The technology types that were identified have been classified into eight major groups according to their technical designs and functions for monitoring adherence. These groups include electronic pillboxes or bags, electronic pill bottles, ingestible sensors, blister pack

technology, electronic medication management systems, patient self-report–based technology, video-based technology, and motion sensor technology.

Smart Pill Bottles

This technology comprises a conventional-sized pill bottle and an electronic cap equipped with a microchip. It captures a date and time stamp when the cap is removed during an opening event. The transmission of adherence data is contingent upon the specific version of the electronic pill bottle device. Certain outdated iterations of the MEMS (Microelectromechanical Systems) often need the manual retrieval of patient medication adherence data from the MEMS cap. This data is then transferred into the MEMS software using a compact reader device [8-10,27,28]. Advanced electronic pill bottle technologies like the GlowCap and AdhereTech devices have the capability to communicate patient medication adherence data wirelessly. This allows for real-time assessment and monitoring of patient medication adherence [1,15,18,29-31].

Electronic pill bottle technologies are often cited for their discreet and compact form [10,16,32,33], capacity to objectively monitor medication adherence [1,8,11,14,34,35], and high acceptability among patients [1,30,31]. Nevertheless, due to the limitation of the pill bottle design to accommodate just one kind of medicine at a time, these devices are not appropriate for patients who have complicated multidrug regimens [1,4,8,9,18,30,32]. Furthermore, the act of opening a pill bottle is often used as a way to determine if a patient is taking their medication as prescribed. However, certain patient behaviors such as not actually consuming the removed medications, taking out multiple doses at once, or simply opening the bottle out of curiosity without taking any medication can result in inaccurate assessments of medication adherence [1,2,4,5,9-11,14-16,27,28,30,33,36,37].

Electronic pill dispensers or containers

Electronic pill boxes or bags, like the electronic pill bottle technology, register a date-and-time stamp each time they are opened. However, in contrast to electronic pill bottles, these technologies often include the capability to store many varieties or potencies of medicine in different compartments inside the device. The dimensions and storage capacity fluctuate among the many kinds of electronic pill boxes or bags that are now available. The majority of the electronic pill boxes or bags that were found had the capability to communicate data on patient medication adherence in real time. This data may be sent by current cellular networks [1,9,26-28,38-43], wireless Bluetooth, or general packet radio service [1,27,44,45,46]. One device required the manual downloading of patient adherence data during clinic visits [47]. The ability of these devices to hold several prescriptions makes them more suitable for complicated multidrug regimens. However, this benefit is contingent on the device, since they may vary significantly in size and pill storage capacity.

It was apparent when comparing the Wisepill device's storage capacity of 60 small-sized tablets with MedTracker's storage capacity of a week's worth of medicine [1,27,39,41,46,44]. Nevertheless, devices that are larger in size are

frequently characterized as conspicuous and pose greater threats to patient confidentiality, thereby restricting the device's suitability for patient populations, especially for individuals who prefer not to reveal their health condition (such as being HIV positive) to others. In addition, these devices are unable to directly verify the consumption of medications, which raises concerns about the accuracy of monitoring medication adherence. This is because certain patient behaviors, such as taking medication out of the container and curiosity-driven events, can affect the estimation of medication adherence rates. These concerns have been highlighted in various studies [1,10,15,16,26,27,30,38-40,44,48-50].

Blister Pack Technologies

Only 3 blister pack technology implementations were found without an attachable adhesive label that featured a microchip and conductive wire layout [4,36,51]. The act of extracting medicine from the blister pack caused a disruption in the label circuit, which was then detected and logged by the microchip along with a timestamp. Information on patient medication adherence is broadcast wirelessly to central servers and is often available to healthcare professionals (HCPs), enabling real-time monitoring of adherence [1,6,51-55]. The design of blister packs ensures that each dosage of medicine is stored in separate compartments. This allows for each removed dose to be recorded as a distinct event, which prevents patients from taking several doses at once or removing the packaging out of curiosity [56]. Currently, it has been discovered that removing a dose from these devices can sometimes and unintentionally damage the conductive tracks of the neighboring doses. This results in multiple removal events being registered, which reduces the accuracy of monitoring using these technologies [56,57]. Additionally, this approach of monitoring medication adherence is a surrogate measure and cannot definitively verify that patients have taken their medicine, which further decreases the precision of estimations about patient medication adherence [1,4,52,55].

Implantable Sensors

Ingestible sensors, often referred to as digital pills or digital ingestion monitoring, are composed of a technical system including microsensors, an adhesive external monitor worn on the belly, and a mobile application. The microingestible sensors are enclosed along with medicine and swallowed into the body, where the gastric secretions in the stomach breakdown the capsule that contains both the drug and the sensor. The sensor is activated when it comes into touch with stomach fluid, and it then sends a distinct signal to the external monitor. The identified ingestion event is sent to a mobile application that uploads the event's date and time stamp, along with other recorded physiological measurements (such as heartbeat), to a central server. These technological solutions have the benefit of directly seeing medicine consumption [3,13,15,16,30,37,58-65], as well as monitoring adherence in real-time [1,3,9,12,30,37,49,58,61-66]. By precisely recognizing specific instances of medicine consumption, these technologies may detect several instances of consumption simultaneously, thereby enhancing the precision of evaluating patient adherence rates to medication [60,61,65]. Furthermore, experimental observations have shown that ingestible sensors have a high accuracy in detecting ingesting events, with rates ranging from 95% to

99.1% [3,58,65]. Nevertheless, due to the direct consumption of technological sensors, there are significant issues about patient privacy and autonomy, primarily since these devices are intrusive in nature [9,13,20]. The significant drawbacks of these technologies include patient complaints of skin irritation produced by the external monitor and the likelihood of sensor retention inside the body [1,12,15,40,59,60, 61,63,64]. These limitations also pose potential concerns to patient health and safety.

Electronic Medication Management Systems

The Electronic Medication Management System (EMMS) encompasses a range of devices that differ in functionality, but share common features aimed at assisting patients in managing their medication and documenting their adherence patterns. Three innovative EMMS devices with intriguing functional features are the radio frequency identification (RFID)-based medication adherence intelligence system, ReX (DosentRx Ltd), and the Medication Behavior Monitoring System (MBMS) [44,67,68,69]. The RFID-based medication adherence intelligence system (RMAIS) consists of an RFID reader, scale, microprocessor, liquid crystal display screen, and a motorized rotating platform [44,67]. The patient's pill bottles are equipped with an RFID tag that contains the drug's details, including the name of the medication and the correct dosage [67]. During a designated time for administering medicine, the RMAIS system produces auditory reminders for taking medication and spins the appropriate pill container in front of the patient. The pill container is weighed by the scale located underneath the rotating platform, and the medicine information is shown using an RFID reader. Once the patient has taken out the medicine from the pill bottle, the scale assesses the weight of the bottle and utilizes the disparity in weight to calculate the quantity of doses that have been eliminated. When the system identifies instances of nonadherence, it notifies a healthcare professional (HCP) [44,67]. One benefit of this method is that it offers assistance to patients who have to manage complicated multidrug regimens by removing the requirement for patient decision-making on which medicine to take, the dosage, and the timing [67]. However, the accuracy of this approach is restricted since it serves as a proxy monitor of medication adherence and cannot verify the actual consumption of medicine [44].

ReX is a newly created device consisting of a medicine dispensing unit that may be used several times, a disposable cassette, a mobile application, and a cloud system called Dose-E Analytics [68]. The medicine of the patient is kept inside the device and can only be dispensed at the proper time, in the precise dosage, and directly into the patient's oral cavity. The mobile application uploads data on patient medication adherence from the drug dispensing unit to the Dose-E Analytics cloud system. This system can be accessed by healthcare professionals, enabling them to monitor medication adherence in real-time. An essential benefit of the device is its dispenser mechanism, which effectively prevents patients from taking excessive amounts of medicine and ensures that medication is administered at the precise time intervals [68]. Although the gadget can track the drug until it reaches the patient's lips, it is unable to verify if the medication has really been consumed, which limits the accuracy of its estimations about medication adherence.

MBMS devices use cutting-edge technology such as the Internet of Things, deep learning, and artificial intelligence. The MBMS stands out due to its integration of three distinct kinds of medication adherence monitoring technologies: electronic pillboxes, motion sensor technology, and video-based monitoring technology. The gadget employs a predetermined alert to encourage patients to adhere to their prescription regimen. When the patient gets close to the device, motion sensors installed around the patient's house detect the movement and send a signal to the MBMS device to start capturing a video of the patient's behavior with their medicine. After detecting the patient's action of lifting their arm to drink water, the gadget triggers the release of the correct medicine and amount from the inside pillbox onto a platform equipped with a scale. The Medication Adherence Behavioral Monitoring System (MBMS) assesses the patient's medication intake by analyzing the convergence of the scale to zero [67]. Healthcare professionals (HCPs) get weekly updates on adherence from the Medication-Based Monitoring System (MBMS). Roh et al [69] discovered that the use of an MBMS device resulted in improved medication adherence compared to those who did not utilize the device. Nevertheless, like RMAIS and ReX, the system's failure to identify real medicine use hinders its capacity to accurately monitor patient adherence to medication.

Collection and Use of Medication Adherence Data

Current medication monitoring systems vary not just in their technological aspects, but also in how they acquire data and utilize that data to evaluate patients' adherence to medicine. The capacity of the majority of medication adherence monitoring technologies to provide immediate observations of patient medication adherence behaviors is advantageous to healthcare professionals (HCPs) and researchers in order to avoid nonadherence and enable suitable treatments [1,15,36,37,70]. However, the majority of these technologies depend on indirect indicators of medicine adherence, such as occurrences of device opening. This, in turn, restricts the accuracy of the data they provide [2,9,11,14,16,27,30,33,37,41,48-50]. Moreover, there is a scarcity of reports on the effective incorporation of these technologies in clinical settings or the assimilation of patient medication adherence monitoring data into clinical practice.

An important obstacle is the lack of compatibility between these monitoring technology systems and existing clinical information systems and workflow. In order to enhance patient care, it is necessary to make it easier for clinical systems to include medication adherence monitoring technology. This may be achieved by ensuring that the technique used to gather adherence data is practical for the intended patients and that the collected data can be seamlessly incorporated into standard electronic health record systems. The study provides insights into the techniques of capturing medication adherence data and its use, which may assist healthcare professionals and researchers in choosing the most suitable technology for monitoring medication adherence. Developers should also take into account the consequences of capturing medication adherence data in clinical and research environments to provide enhanced user-friendliness for both patients and providers.

Criteria for Evaluating Technology

As far as we know, this is the first compilation of evaluation standards specifically targeting devices designed to track and measure patient compliance with medicine. The evaluation criteria consist of five main categories: development information, technical characteristics, adherence to data collection and management, feasibility and execution, and acceptability and usability. The stated criteria emphasize crucial characteristics of medication adherence monitoring systems that must be taken into account throughout the development and deployment of the technology. One crucial factor in using medication adherence monitoring technology is the cost. However, a frequent drawback of these technologies is their high price tags [1,2,5,7,9,12,18,27,38,54]. The suggested criteria prioritize the cost effectiveness of technology used to monitor medication adherence, specifically within the feasibility and implementation area. The expensive nature of devices limits their use in clinical and research environments, since other approaches such patient self-reports are much more cost-effective [1].

This compilation of assessment criteria was developed by examining the current literature. It also takes into account other challenges related to technology acceptance and technology design features, such as the risks to patient privacy and the impact of large device size on user adoption due to daily life inconveniences [25]. The suggested evaluation criteria, because to their complex character, may serve as a guide for enhancing these technologies in order to enhance medication adherence measures and monitoring.

Furthermore, our suggested evaluation criteria exhibited a structure similar to those of existing recognized frameworks for evaluating mobile health. An instance of an app evaluation framework, known as the pyramid model, was initially suggested by Henson et al [71] and later modified by the American Psychiatric Association as the App Evaluation Model. This model introduces a 5-level structure for evaluating apps, which includes categories such as access and background, privacy and security, clinical foundation, usability, and data integration towards therapeutic objectives [71,72]. Each area has distinct evaluation criteria. For instance, the usability category includes an assessment of ease of use [72]. Usability, privacy and security, and data integration are common technology evaluation criteria that may be used to evaluate both mobile health applications and medication adherence monitoring systems. Adherence monitoring technology has technological capabilities that help in storing and managing medication. This leads to specific criteria for evaluating it, such as the device's ability to store medication or the presence of date-and-time stamps that show when medication is taken. The criteria for assessing medication adherence monitoring technologies were developed by a thorough study of existing literature and synthesis of information. This process has established a strong evidence base, but it also highlights the need for further empirical testing and validation.

Constraints

This narrative review is subject to some constraints. Initially, our database selection and search methodologies may not have been enough comprehensive to

include all published material. In addition, we restricted our analysis to studies published in English, which may have resulted in the exclusion of medication adherence monitoring devices from non-English sources. The suggested criteria for assessing medication adherence monitoring technologies are based on the aspects highlighted in our literature research and synthesis. These criteria will undergo additional validation and evaluation. We did not examine in-depth information provided by individual manufacturers. Considering that this research only examined medication adherence technologies used to monitor pill form pharmaceuticals, it is important to note that the evaluation criteria and our results may not apply to other forms of medication. Significantly, a substantial number of the retrieved publications were pilot or feasibility studies. Therefore, our evaluation scope for the criteria may likewise be restricted to the first phases of technological development.

Conclusion

This narrative review provides an overview of the existing technical characteristics and techniques for collecting data. It discusses the benefits and drawbacks of monitoring technologies for medication adherence in pill form, and suggests a set of criteria for evaluating these technologies. The establishment of our evaluation standards is vital for the development and acceptance of these technologies. More specifically, more technical advancements are necessary to enhance the compatibility of medication adherence monitoring technology systems in clinical environments. The growing use of technology that monitor patient medication adherence has shown promise in enhancing patient medication adherence habits. While this technology approach to monitoring patient medication adherence may not be considered the most reliable way, its features have the potential to enhance patient medication adherence and contribute to better patient health outcomes in the long run.

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