



Emerging Trends in Medication Adherence Technologies: A Comprehensive Review of Smart Pills and Reminder Systems

¹-Nazek Safug Nazal Alenazi,²-Saud Sanad Awad Alrashidy,³-Abdullah Shaya Hamad Aldossari,⁴-Al Anoud Abdullah Raheel Al Anzi,⁵-Fayez Nuwaysir Alruwaili,⁶- Watin Hutayl H Al-Shammari,⁷-Abdulaziz Ali Ibrahim Bussanah,⁸-Ali Ibrahim Abdullah Faqiri,⁹- Mahasen Fawaza Alharbi,¹⁰-Saud Nasser Salem Alotaibi,¹¹-Abdullah Mudshir Mansour Alanazi,¹²- Ahmed Nasser Alqahtani,¹³- Waleed Hassan Zaylaee,¹⁴-Hussain Habib Al Abdullah,¹⁵-Mohammed Muqbil Alqahtani

1. Ksa, Ministry Of Health, King Khaled General Hospital
2. Ksa, Ministry Of Health, Hospital Alhaia General
3. Ksa, Ministry Of Health, Dentalclunc South Riyadh
4. Ksa, Ministry Of Health, King Khalid General Hospital In Hafar Al-Batin
5. Ksa, Ministry Of Health, Shoabat Nusab General Hospital
6. Ksa, Ministry Of Health, King Khalid General Hospital In Hafar Al-Batin
7. Ksa, Ministry Of Health, Maternity And Children's Hospital Al Hassa
8. Ksa, Ministry Of Health, Al-Faqrah PHC
9. Ksa, Ministry Of Health, King Khalid General Hospital In Hafar Al-Batin
10. Ksa, Ministry Of Health, Rawidat Al-Ared General Hospital
11. Ksa, Ministry Of Health, Al-Sahdawi Primary Health Care Center
12. Ksa, Ministry Of Health, Alrain General Hospital
13. Ksa, Ministry Of Health, Prince Mohammed Bin Nasser Hospital.
14. Ksa, Ministry Of Health, King Fahad Specialist Hospital -Dammam
15. Ksa, Ministry Of Health, Rawidat Al-Ared General Hospital

Abstract

Background: As the global population of older adults rises, medication adherence has become a critical factor in managing chronic diseases and enhancing health outcomes. Despite the importance of adhering to prescribed medication regimens, non-adherence remains a persistent challenge, particularly among the elderly.

Methods: This review synthesizes current literature on medication adherence technologies, focusing on innovative monitoring solutions such as smart pills and reminder systems. A systematic search was conducted using databases like Google Scholar and IEEE Xplore, covering studies from 2004 to 2023. Articles that discussed technological interventions for medication adherence were included, while editorials and non-research articles were excluded.

Results: The findings illustrate a variety of technology-based solutions designed to improve medication adherence. These include smart pill bottles, wearable sensors, and mobile applications that provide reminders and monitor intake. The review highlights the advantages of these technologies, such as enhanced monitoring capabilities and user engagement, while also acknowledging challenges like user comfort, battery life, and data accuracy. Notably, technologies that integrate with the Internet of Things (IoT) show promise for real-time data transmission and user feedback.

Conclusion: The advancement of medication adherence technologies presents significant potential for improving health outcomes among patients, particularly in the geriatric population. However, further research is needed to address existing limitations and enhance the efficacy of these systems. Future studies

should focus on clinical trials to validate the impact of these technologies on adherence rates and health outcomes.

Keywords: Medication adherence, technology, smart pills, wearable sensors, elderly health.

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1. Introduction

As the average quality of life improves, human lifespans will continue to increase. Recent reports that emphasize the substantial rise in the geriatric population, particularly in developed nations, provide evidence of this [1-3]. As anticipated, the global population of individuals aged 60 years and elderly will increase by 250% in 2050 compared to 2013 [4]. Similarly, it is anticipated that long-term healthcare expenditures will rise as society matures [5]. The utilization of Assistive Health Technology (AHT) is on the rise in order to preserve a healthy geriatric population [4]. Subsequently, substantial endeavors are being undertaken to elevate healthcare systems' quality expectations [3]. It is undeniable that the 21st century will witness a revolution in research in a variety of fields, including human health, as a result of accelerated technological advancements. Innovative methods for monitoring human health, behavior, and activity will be implemented. Medication adherence is a critical aspect of health and well-being, as evidenced by a plethora of studies [6-10].

Healthy aging is a difficult endeavor that necessitates the implementation of numerous critical strategies. Correct medication is undoubtedly one of these strategies that are primarily associated with the individual's behavior. Furthermore, it is widely recognized that medications are the primary method for treating the majority of maladies [11]. Therefore, it is necessary for the individual to adhere to the healthcare professional's instructions regarding medication administration [12]. Nevertheless, medication adherence continues to be a prevalent concern in the healthcare industry, particularly among senior individuals. In reality, over 50% of the elderly population is currently afflicted with multiple chronic ailments. Therefore, it is imperative to conduct consistent surveillance and evaluations of the individual's adherence in order to enhance their health outcomes [13]. Accurate assessment methodologies must be implemented in order to achieve success. There are both advantages and limitations to the current methods of evaluating medication adherence. The primary goal of this article is to offer a comprehensive understanding of the current state of medication adherence monitoring technologies and to identify unresolved research challenges that can be addressed to enhance their effectiveness.

This review paper comprises conference papers and proceedings, as well as articles from journals. Articles that were classified as editorials, book reviews, white papers, or newspaper reports were excluded. Electronic databases, such as Google Scholar, IEEE Xplore, ACM Digital Library, Springer Link, MDPI, and Science Direct, were employed during the paper search. The descriptors we employed were "medication adherence," "medication intake," "medication monitoring," or "medication compliance" in conjunction with at least one of the following: "technology," "sensor," "smartwatch," "wearable," "smart bottle," "pill bottle," "pillbox," "vision system," "Radio Frequency Identification (RFID)," and "Near Field Communication (NFC)." The inquiry encompassed all years from 2004 to 2023.

We selected articles that discussed medication adherence monitoring technologies and excluded papers that discussed intervention applications, primarily using the full text and abstracts. The literature review methodology employed in this paper is iterative and incremental [14], which resulted in the identification and incorporation of novel studies regarding medication adherence monitoring technologies and methodologies in the surveyed studies. It is important to note that there have been commercial endeavors to develop medication adherence monitors in the past few years, such as those described in [15-19]. Nevertheless, we have omitted these commercially available systems from this assessment, as they are akin to black boxes, and the information pertaining to their design is either not publicly available or is restricted.

The present paper is divided into several sections based on the primary monitoring or sensing technology used, with the objective of illustrating how the most advanced technology for medication

adherence monitoring can enhance healthcare systems. We also compare the various medication adherence monitoring techniques and approaches in terms of user convenience, energy efficiency, and accuracy. This paper addresses the requirements of healthcare monitoring researchers and investigators in both the engineering and medical communities, given the significance of technology embodiment in medication adherence systems.

2. Adherence to Medication

The degree to which an individual who is taking medication adheres to a self-administered protocol is referred to as medication adherence [8,20,21]. In other words, medication adherence is the act of adhering to a medication regimen that has been established by the healthcare provider, including the schedule, dosage, and frequency of medication consumption [22,23]. Non-adherence, from another perspective, is the failure to adhere to the prescribed medication regimen, which may include inconsistency, missed dosage, and the failure to reorder the medication. However, research has demonstrated that neglecting the medication-intake regimen can lead to the emergence of drug resistance, the acceleration of disease progression, numerous irrevocable health complications, and an increase in mortality [23-25].

There are numerous advantages to adhering to medication regimens. Nevertheless, patients who adhere to their prescribed medications experience fewer health complications, a greater number of treatment benefits, and a potentially active drug effect in the event of a fully treated infectious disease [22]. An additional advantage is that medication adherence contributes to the reduction of healthcare costs and the reduction of drug wastage [26]. Conversely, patients who are chronically ailing have been shown to experience a decline in their health that could result in significant disability or mortality [8,27].

3. Monitoring Medication Adherence

Adherence to the medication is essential, as its efficacy is contingent upon its taking [22]. However, it is imperative to adhere to strict medication adherence, which includes the maintenance of administration schedule, dosage quantity, and frequency [28]. In a multitude of reports, it was discovered that up to 50% of patients either fail to fulfill their medication prescriptions or do not adhere to the prescribed dosages in their medication regimens [8,27,29-32]. Regrettably, hospital admission is a frequent consequence of poor adherence among populations with chronic disorders [18,33,34]. In the United States alone, poor medication adherence leads to over 100,000 fatalities annually and hundreds of billions of dollars in healthcare expenditures each year [35-38]. A variety of methods have been employed to monitor medication adherence, as it has been demonstrated that enhancing adherence to medical therapy would result in significant health and economic advantages [8].

When discussing medication adherence, it is important to take into account two primary factors. Monitoring, which is also known as assessment, quantification, measurement, or evaluation, is the initial factor. Medication surveillance involves employing specific techniques to determine whether the patient has consumed the medication. Therefore, the surveillance method's efficacy is of paramount importance. Intervention is the second factor. Interventions are the methods that can be employed to enhance medication adherence or remedy it when erroneous or drifting behavior is identified. Nevertheless, the latter is more akin to the psychological and social sciences, as it necessitates a comprehension of the cultural, psychological, and social factors that influence the patient's behavior [39-41].

So far, medication adherence measurement methods have been broadly classified into two categories: direct and indirect [8,42]. Direct methods of adherence measurement, such as direct observation of the patient while taking the medication, laboratory detection of the drug in the patient's biologic fluid (e.g., blood or urine), laboratory detection of the presence of nontoxic markers added to the medication in the patient's biologic fluid, and laboratory detection of biomarkers in the dried blood spots [43], are used. In the interim, indirect methods of adherence measurement include the patient's self-reporting, pill-counting, pharmacy refill rate assessment, and utilization of electronic medication event monitoring systems. There is currently no gold standard measurement system that meets the requirements for optimal medication adherence surveillance. At the same time, each category possesses both advantages and disadvantages.

Direct measures are precise; however, they are typically costly and may necessitate invasiveness. In contrast, indirect methods are more cost-effective and offer a reliable assessment of medication adherence. Nevertheless, these techniques are contingent upon the user's reliability [44]. Therefore, it is imperative to consider these factors when selecting the adherence measurement methodology.

4. Technology-Based Solutions

The resolution of non-adherence necessitates the involvement of numerous factors. However, the surveillance method's effectiveness and reliability are essential for obtaining substantial improvements in adherence [9,45]. The patient's attention and effort are necessary for manual approaches. Direct biochemical methods necessitate that the patient attend a clinic for fluid testing. Furthermore, the interventions associated with biochemical measurements, particularly the collection of blood samples, are a significant burden on patients.

Continuous monitoring and evaluation of medication adherence is essential. Afterward, deviations can be identified, and improvements can be implemented. Numerous review studies have been conducted in the past to address the issue of medication adherence. Nevertheless, the majority of reviews examined medication adherence from a clinical perspective, in addition to interventions [6-9,20,21,27,34,35,38]. Moreover, the electronic-based interventions have been presented in a limited number of studies [29,43-45]. The utilization of technology in the surveillance and improvement of medication adherence has received relatively little attention in comparison to conventional methods. These reviews have clarified the potential benefits and limitations of technology-based solutions for medication adherence assessment. However, there was no comprehensive discussion of the cyber-physical system, which includes system design, hardware development, and data analytics.

Technology-based interventions for adherence monitoring and enhancement are described in a few rare studies. For instance, Park et al. [46] provided an overview of numerous electronic systems and medication measurement methodologies. Other review articles have examined the technology of tablet [44] and smartphone [47] applications for medication adherence, which are in the form of automated reminder systems. The authors presented a summary of several medication adherence measurement methodologies for older individuals who utilize alert and reminder systems, as well as their potential benefits, in [45]. Some technological medication reminder approaches have been briefly described in [48]. It is important to note that certain commercially available technology-based solutions have only been reported in a recent study by Rokni et al. [49]. Additionally, they briefly reviewed several clinical studies that employed electronic medication monitoring. It also addressed the obstacles associated with medication monitoring technologies in terms of scalability, reliability, and data analytics. It is evident that these survey studies are restricted in their ability to offer a comprehensive examination of the technical aspects of the various technology-based sensing or monitoring approaches for medication adherence.

Despite the fact that we have previously discussed some recent applications for medication adherence monitoring [50] that rely on modalities such as proximity sensing and sensor networks, there is still a lack of comprehensive state-of-the-art survey studies concerning the recent medication adherence monitoring solutions. The primary objective of this paper is to further investigate this subject by extending the discussion on monitoring systems, expanding the list of surveyed papers, considering other medication monitoring systems, such as ingestible biosensors, and discussing the trade-offs of each technology in multiple dimensions. This is the first review that, to the best of our knowledge, examines medication adherence monitoring methods that employ a diverse array of emerging technologies. This is the first study to examine medication adherence monitoring approaches from a technical perspective, with the objective of advancing future systems that will assist in addressing the deficiencies that currently exist.

5. Medication adherence monitoring systems

Medication non-adherence is a complex issue that has been extensively researched. Several interventions are necessary to enhance medication adherence, as the unanimous conclusion of these studies indicates [29]. However, technological interventions are considered to be supportive instruments

that can be used to enhance adherence. This is a result of the fact that they enable the healthcare provider to obtain valuable information about the patient's conduct and that they enable timely surveillance [18]. A significant number of systems have been proposed and developed to date that employ monitoring and tracking techniques in a variety of health-related initiatives, such as medication adherence monitoring. In this section, we examine the current methods for designing monitoring systems for medication adherence applications using emerging technologies.

6. Sensor-Based Systems

The size, cost, and energy consumption of compact wireless sensors have decreased by several orders of magnitude in recent years [51]. In fact, low-power wireless sensors are now available at an affordable price. The visionary concept of the IoT has been achieved by the ability to connect commonplace objects to the Internet as a consequence of these advancements [52]. Although the Internet of Things (IoT) has a plethora of potential applications in the fields of security, industry, and the environment, the measurement of daily activities to enhance and monitor the health and well-being of individuals is becoming an increasingly active area of research [53]. In addition, the integration of CPS and the primary components of the Internet of Things (IoT), Wireless Sensor Networks (WSNs), into healthcare is significantly contributing to the development of new IoT-enabled CPS-based healthcare solutions [54].

Sensor networks and their subsets have been demonstrated to be exceptional instruments for bridging the divide between the physical world and computers by perpetually facilitating new applications in a variety of fields [55]. Sensor systems enable the seamless collection of data on daily activities in a free-living environment and potentially over extended periods of time in the context of human health [56]. The surveillance and evaluation of medication intake in subjects is a prospective application in that field [57]. Currently, sensor-based approaches are the most frequently employed among other methods for adherence monitoring. The integration of sensor networks into medicine intake and adherence monitoring systems offers a variety of advantages and features. A few examples are the regularity of measurements, the ability to monitor remotely, and context awareness [57]. In general, wireless sensors in this surveillance area can be classified into two primary categories based on the form of deployment: fixed and wearable.

Fixed sensors are connected to domestic apparatuses and minimally mobile objects, such as pillboxes or pill bottles. In contrast, wearable sensors are mobile devices that are affixed to the user's body, possess high data fidelity, and are lightweight. Consequently, wearable technology is increasingly prevalent in the development of a variety of healthcare applications, such as medication adherence assessment [58]. Another emerging sensor-based communication and network technology within the IoT family is in vivo or intra body communication and networking [102], which is facilitating a new set of healthcare applications. Wireless and real-time retrieval of medicine ingestion events is feasible through the integration of in vivo biosensors with ingestible dose forms [59].

7. Pill Container with Intelligent Technology

Sensor-equipped pill receptacles and pillboxes have been created to monitor medication consumption. MedTracker was developed by Hayes et al. [12] in this context. It is one of the earliest methods that employs a 7-day multi-compartment pillbox that embeds plungers in each compartment. The microcontroller was intended to be triggered by the plungers, which would actuate a switch within the pillbox, thereby detecting the opening of box lids. The data is wirelessly transmitted to a nearby computer using Bluetooth technology. The purpose of transmitting data over the Bluetooth link every two hours was to extend the lifespan of the system, which was powered by a 9 V battery. When there is no connection to the base station, the system incorporates RAM to store medication taking events. Nevertheless, it is evident that the system is straightforward and prone to errors, as it regards any cover opening as a medication intake. The system's lifespan was limited to eight weeks, despite its simplicity, as it was propelled by a battery that was significantly larger than average.

Aldeer et al. [60] have recently taken another approach, which involves the use of PillSense. It employs a 3D printed pill container that is equipped with a magnetic switch sensor, an accelerometer, and a load cell.

Furthermore, the system employs the PIP-Tag mote [61] as a platform for the collection of data from the employed sensors, which are subsequently transmitted wirelessly to a base station that is connected to a nearby computer. The system is based on the concept of collaborative sensing, which involves the use of the switch sensor to monitor cap removal, the accelerometer to monitor pill collection events, and the load cell to sense bottle weight. Therefore, in order to conserve energy, PillSense was developed to monitor cap removal via the magnetic switch sensor and only activate the accelerometer for motion sampling when cap removal is detected. The accelerometer is deactivated and the weight sensor is activated for a single-use bottle weight sensing upon cap re-closure. Pill container weight testing is an additional validation measure that determines whether there is a discrepancy in weight when the closure is removed. The system facilitates portability, is wireless, and is unobtrusive. More importantly, it is energy-efficient, as it can operate for over three weeks on a coin-cell battery.

Lee and Dey [62] created a pillbox that was comparable to the one described in [12] for a project that aimed to observe the daily activities of elderly individuals. A ZigBee wireless module, an accelerometer, a battery, and a Microcontroller (MCU) have been incorporated into a 7-day compartment. The data were transferred to a laptop situated in the patient's residence for additional processing. The system was clinically tested with two participants for a period of ten months; however, no performance results were reported. It is evident that the objective of this method is to eliminate the need for the intervention and attachment of sensors to the human body. This approach guarantees the user's comfort while maintaining accuracy through the use of the accelerometer sensor. Nevertheless, the system is unable to determine whether or not the user has ingested the medication.

8. Sensors that are worn on the body

Inertial Measurement Units (IMU) have made significant progress in recent years, both in terms of intelligence and cost [63]. Accelerometers, gyroscopes, and magnetometers, or a combination of these, are typically the components of IMUs [64]. Tracking individuals and sensing motion have been extensively employed in healthcare applications [65]. Ultimately, the utilization of motion sensors can assist in the disclosure of potential health information [61]. In this section, we introduce a variety of wearable sensing systems for medication adherence monitoring and categorize them into two groups: neck-worn and wrist-worn, based on the bodily location.

Neck-Worn Sensors: In one of the studies [66], the authors suggest a wearable system for detecting user adherence to medication, up to the point of determining whether the medication has been ingested. They constructed a pendant-style necklace that comprises a battery, a Radio Frequency (RF) board, and a piezoelectric sensor. The piezoelectric sensor is employed to detect the mechanical tension that arises from the movement of the epidermis during the ingestion of pills and to produce voltage as a response. The data that has been collected is transmitted via Bluetooth to a mobile device that implements classification algorithms, where it is subjected to additional analysis. We employed a Bayesian-Network classifier to classify the data received from the smart necklace, and we trained and tested the proposed system using data collected from a population of 20 subjects. The capsule's precision and recall were 87.09% and 90%, respectively. It is important to note that this system also employs a commercial smart capsule [67]. The primary obstacles associated with this method are user convenience and social acceptability [68]. This is due to the fact that the necklace must be worn by the patient and affixed to come into contact with the skin during the ingestion of the dosage.

Acoustic sensors in the form of neck accessories are an additional method for evaluating medication administration. This method has been implemented for the purpose of monitoring food intake [69]. Despite the fact that this method necessitates additional research, it exhibits potential for application in medication monitoring [70]. In general, acoustic-based approaches concentrate on the collection of acoustic data from ingesting or ingestion activity using a microphone inserted by the pharynx. The data is then analyzed and classified using a specific data analytics methodology. Wu et al. [71] developed only one prototype of this category of devices. The neckwear device is equipped with an RFID reader, microphones, and a flex sensor. The transducers and the flex sensor are to be used to detect the movement of the pharynx and the sound of

chomping that is associated with the act of ingesting medication. Therefore, the authors incorporated an RFID reader to enhance medication adherence verification by monitoring tablets that are endowed with ingestible biosensors as they travel through the pharynx. Nevertheless, the absence of any validation trials in the current iteration of the study renders it challenging to conclude the performance, social acceptability, and comfort of this approach.

9. Conclusion

In the healthcare sector, medication non-adherence is a significant issue. Healthcare resource wastage and suboptimal treatment outcomes are the consequences of poor medication adherence. Consequently, it has become a highly appealing research area for numerous researchers from a variety of disciplinary backgrounds, to create novel surveillance and intervention systems that can identify and rectify deviations in medication-taking regimens. The technology-based techniques and systems for medication adherence monitoring have been discussed in this paper. In addition, we emphasize the advantages, disadvantages, and challenges that are associated with these approaches. However, the extent to which these factors are translated into altered operational and clinical outcomes necessitates additional feedback and observations from both patients and clinical practitioners. Based on the findings of this review, it is evident that additional effort is necessary to improve technology-based systems that can surmount these obstacles, particularly in terms of battery consumption, user comfort, and accuracy. Ultimately, the paper indicates that in order to assess the accuracy and efficacy of medication adherence systems, it is necessary to conduct numerous additional clinical trials with large sample sizes and over extended periods of time.

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الاتجاهات الناشئة في تقنيات الالتزام الدوائي: مراجعة شاملة للأقراص الذكية وأنظمة التذكير

الملخص

الخلفية: مع تزايد عدد كبار السن على مستوى العالم، أصبح الالتزام الدوائي عاملاً حاسماً في إدارة الأمراض المزمنة وتحسين النتائج الصحية. على الرغم من أهمية الالتزام بالجرعات الدوائية الموصوفة، لا يزال عدم الالتزام يمثل تحدياً مستمراً، خاصة بين كبار السن.

الطرق: تجمع هذه المراجعة بين الأدبيات الحالية المتعلقة بتقنيات الالتزام الدوائي، مع التركيز على حلول المراقبة المبتكرة مثل الأقراص الذكية وأنظمة التذكير. تم إجراء بحث منهجي باستخدام قواعد بيانات مثل Google Scholar و IEEE Xplore، شمل الدراسات المنشورة بين عامي 2004 و 2023. تضمنت المراجعة المقالات التي ناقشت التدخلات التكنولوجية لتحسين الالتزام الدوائي، بينما تم استبعاد المقالات التحريرية وغير البحثية.

النتائج: أظهرت النتائج مجموعة متنوعة من الحلول التكنولوجية المصممة لتحسين الالتزام الدوائي، بما في ذلك زجاجات الأدوية الذكية، وأجهزة الاستشعار القابلة للارتداء، والتطبيقات المحمولة التي تقدم تذكيرات وتراقب تناول الأدوية. سلطت المراجعة الضوء على مزايا هذه التقنيات، مثل تحسين قدرات المراقبة وزيادة تفاعل المستخدمين، مع الإشارة أيضاً إلى التحديات مثل راحة المستخدم، وعمر البطارية، ودقة البيانات. من الجدير بالذكر أن التقنيات التي تدمج مع إنترنت الأشياء (IoT) تُظهر وعوداً كبيرة في نقل البيانات في الوقت الفعلي وتقديم ملاحظات للمستخدمين.

الاستنتاج: يمثل تقدم تقنيات الالتزام الدوائي إمكانيات كبيرة لتحسين النتائج الصحية للمرضى، لا سيما في فئة كبار السن. ومع ذلك، هناك حاجة إلى المزيد من الأبحاث لمعالجة القيود الحالية وتعزيز فعالية هذه الأنظمة. يجب أن تركز الدراسات المستقبلية على التجارب السريرية للتحقق من تأثير هذه التقنيات على معدلات الالتزام والنتائج الصحية.

الكلمات المفتاحية: الالتزام الدوائي، التكنولوجيا، الأقراص الذكية، أجهزة الاستشعار القابلة للارتداء، صحة كبار السن.