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A Review of an Emerging Modern Technology for Monitoring Medication Adherence

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ABSTRACT:
The First and most challenging Problem is obtaining medication adherence for the maintenance of the healthcare system, even though this was most essential and widespread.Medication adherence is measured by how closely a patient adheres to their prescribed treatment plan advised by the healthcare provider when taking their medications whereas, Medication Non-adherence is the inability to take medication. Also in developed nations, the problem with medication non-adherence increases the intensity of the medical condition. It is essential to monitor drug consumption to improve the quality of every patient`s life. From the pharmaceutical manufacturer to the caregiver level, numerous techniques and technologies have been introduced to track and evaluate drug adherence by using electronic monitoring devices (EMDs).
Every technique has its pros and cons. In our study, we describe the technology employed to track adherence via sensor, vision, and proximity systems including ingestible and wearable sensors. The fusion-based systems are also discussed followed by the overall limitations of the techniques. We conclude our study that more research is still required to alleviate these limitations, especially those relating to reliability and user comfort, and the future direction of clinical trials need to be conducted with a large sample size for the evaluation of accuracy and user comfort.

Keywords: Medication Adherence, Medication Utilization, Monitoring, Tracking Technology, Sensor, Pill Bottle, RFID.

I. INTRODUCTION

Medication adherence is a widespread but difficult issue in healthcare.[1]Previous studies have demonstrated that patients may experience negative effects if they don't take their drugs as directed.[2]Around the world, up to 50% of people do not take their prescribed drugs for chronic diseases as directed. Based on the World Health Organization (WHO), increasing patient adherence to their drug regimens may have a greater impact on health than any other change in therapy.[3] To assess medication adherence, questionnaires, patient counselling, and pill counting are all frequently used as monitoring techniques. Dose counting, which compares the frequency of doses taken by the patient to the frequency of doses they have received after the study period, is another simple and affordable technique that may be used with various pharmaceutical forms, such as pills or inhalers. It does not, however, provide data on daily adherence or other patterns of drug use; it simply evaluates average adherence. A more objective way to track adherence is with electronic monitoring devices (EMDs). The use of EMDs is restricted in large populations despite being demonstrated to be extremely accurate because of their expensive costs and potential practical problems, such as challenges with medicine refills at a nearby pharmacy.[4]

Along with the potential for individuals to experience unfavorable health outcomes, poor adherence can result in excessive medical costs and a burden on the healthcare system. Researchers in medicine are particularly concerned about this problem since it makes it much harder to determine whether a treatment is beneficial when a patient chooses not to take the recommended dosage of their prescription. Thus, numerous approaches have been put out in recent years to deal with these challenges, including pill counts, self-reporting, interviews, and questionnaires to raise adherence rates. The accuracy of these approaches, however, is often low.[2]We have included three sections in this review based on the sensing technology utilized to describe how the most recent technology on medication adherence monitoring might enhance healthcare systems. In section 1, Background information including medication

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adherence, non-adherence, and assessing methods,s are described; Section 2 describes technology-based approaches to monitor medication compliance; Section 3 describes the difficulties in utilizing technologies followed by the conclusion of the study as the final part.

II. BACKGROUND:

MEDICATION ADHERENCE:

Medication adherence is defined by the level to which a patient follows the medication regimen advised by the healthcare provider when taking their medications. However, medication-taking behavior should not view as a single decision-making process but rather as a three-phase process, with the initiation phase (in which patients must begin treatment), the implementation phase (in which patients must implement the adequate dosing regimen), and the continuation phase (in which patients must continue the treatment)[5]

MEDICATION NON-ADHERENCE:

Medication Non-adherence is the inability to take medication as directed, which includes irregular drug usage, missed doses, and neglected prescription refills. However, research has shown that failure to adhere to the medication-intake schedule might lead to the development of drug resistance, an accelerated course of the disease, several permanent health issues, and higher mortality rates.[6] Figure 1 illustrates how the World Health Organization (WHO) categorized several non-adherence variables into five categories: social/economic, condition-related, therapy-related, patient-related, and health care team and system-related. [7]

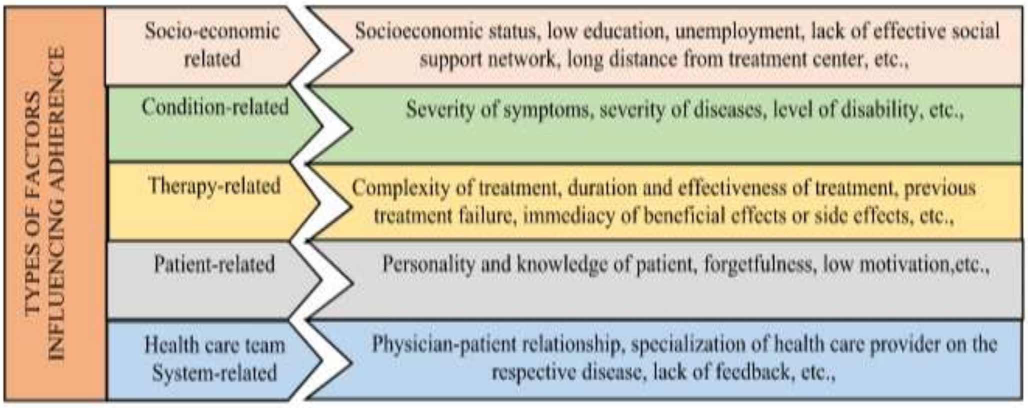

Fig 1: Factors Influencing Medication Adherence

CLASSIFICATION OF NON-ADHERENCE:

- Primary Medication Non-Adherence - Initiation
- Secondary Medication Non-Adherence - Non-persistence
- Intentional - active
- Unintentional – passive[8]

The advantages of therapy are limited for the patient, which causes under-treatment of their disease and makes it difficult for the practitioner to determine dose and efficacy. Non-adherence causes prescription waste, higher healthcare expenses, and drug resistance in the event of infectious illnesses that aren't completely treated.[9]

METHODS OF ASSESSING MEDICATION ADHERENCE

Method of assessment	Advantages	Disadvantages	Parameters measured
DIRECT: Monitoring drug/metabolite levels	-Effective -Objective, - Showing that the medication was consumed	-Expensive -Invasive -Interindividual variations	The drug's or metabolite's concentration

INDIRECT: **Pill count**	-Simple -Used mainly in clinical trials	No indication that medication was taken	Number of missed doses
Electronic databases	-Easy to use -Inexpensive -Non-invasive, -Patients not aware that they are being monitored -Especially specific to identifying non-adherent patients	Evidence of the drug being dispensed but not ingested	-Medication possession ratio (MPR) -Proportion of days covered (PDC)
Self-reported (questionnaires, visual analog scales)	-Easy to use -Inexpensive	-Overestimate adherence -Subjective, influenced by recall or reporting bias	A value that is interpreted regarding a pre-established cut-off point
Electronic monitoring systems	-Objective -Additional information on the degree of adherence -One of the most accurate methods	-The patient is aware of the evaluation -No actual evidence that the medication is being ingested	-Overall percentage of doses taken -Dosing regimen

TABLE 1: Anghl LA et al., Method of Medication Adherence[11]

The assessment of medication adherence in patients is done by two methods:

- Objective or Direct Method: - these are the methods by which the drugs can be identified in the patients
- Subjective or /indirect Method: - these methods include where there is an assessment either by the patient or some other individual to know whether the medication is taken or not.[10]

DEEDS OF TECHNOLOGY DEVELOPMENT:

Back in the days of Hippocrates, patients' noncompliance with medical treatment was one of the challenges to getting amazing healthcare results; this scenario still exists today. Several strategies have been created to prevent ineffective drug compliance and associated health hazards. The number of internet-based approaches concentrating on medication adherence has significantly increased during the past ten years.[12]

III. ADVANCED TECHNOLOGIES FOR MEDICATION ADHERENCE:

SENSOR-BASED SYSTEM:

Sensor systems can obtain information on daily tasks in a condition of free living for an extended length of time to measure human health. One of its applications is to monitor and evaluate patients' medication adherence. Rechargeable fixed and wearable sensors both seem to be effective for monitoring adherence. Smartphone items like pillboxes or pill bottles, along with home appliances, have set sensors attached. Wearable sensors are affixed to the user's body in the meanwhile. Wearables are therefore leading in several healthcare applications, including medication adherence.

SMART PILLS:

Pill bottles and pill boxes have embedded sensors to them designed to monitor medication adherence activity. Pill Sense was invented by Aldeer et al., in a pill container that has been 3D printed and is fitted with a load cell, an accelerometer, and a magnetic switch sensor. Additionally, it features a PIP-Tag mote that it uses to wirelessly communicate data to a nearby computer after gathering information from the sensors. Cap removal is tracked by a switch sensor, pill pickup is detected by an accelerometer, and

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bottle weight is tracked by a load cell. The accelerometer turns off during the re-closing of the cap. To find out if the weight varies every time that cap is removed, the validation process uses weight testing on pill bottles. On a coin-cell battery, this device can operate for over three weeks.

Figure 2 demonstrates a pillbox that was created by Lee and Dey, using a Microcontroller (MCU), a ZigBee wireless module, a battery, and an accelerometer. Afterward, the data was transferred to a patient's computer at home for subsequent processing. Two volunteers evaluated the system for 10 months, but no efficiency information was given. However, this system simply monitors the opening of the pill bottle and does not determine whether or not a user has swallowed a tablet.[13]

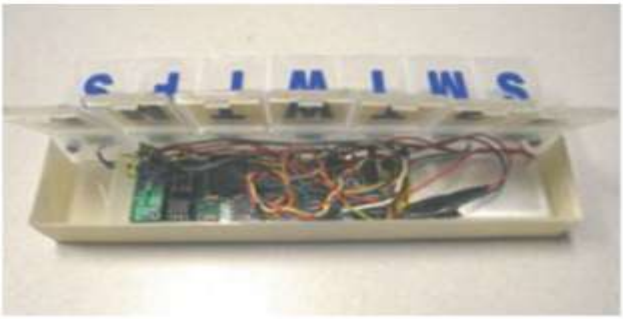

Fig 2: Med Tracker Designed by Lee and Dey [13.]

To evaluate patient compliance with continuous glaucoma ophthalmic medication tracking, Kazuaki Nishimura et al. designed an optic drop container sensor that monitors eye dropper action as shown in figure 3. The bottle sensor is an XYZ 3-axis acceleration sensor, which calculates the measure of gravity motion roughly every 0.08 seconds. Once the eye dropper bottle has been detected moving by the sensor, the data are sent across the IEEE802.15.4 wireless network to the processing terminal. The sensor continuously calculates the acceleration when in a stationary condition and records the information in its memory. As a result, information was gathered for a period that spanned usually less than 5 seconds before the motion was detected and 5 seconds after it had stopped. The sent data is then received through the case's integrated antenna (MW-AP4208) and forwarded to the TWE-Lite radio microprocessor. The data are processed by the radio microcomputer and then sent over a cable to the external data interface. Eventually, the information is stored on an SD memory card that is inserted into the SD socket. In this work, a method was devised and an eye dropper bottle sensor was used to precisely track instillation adherence.[14]

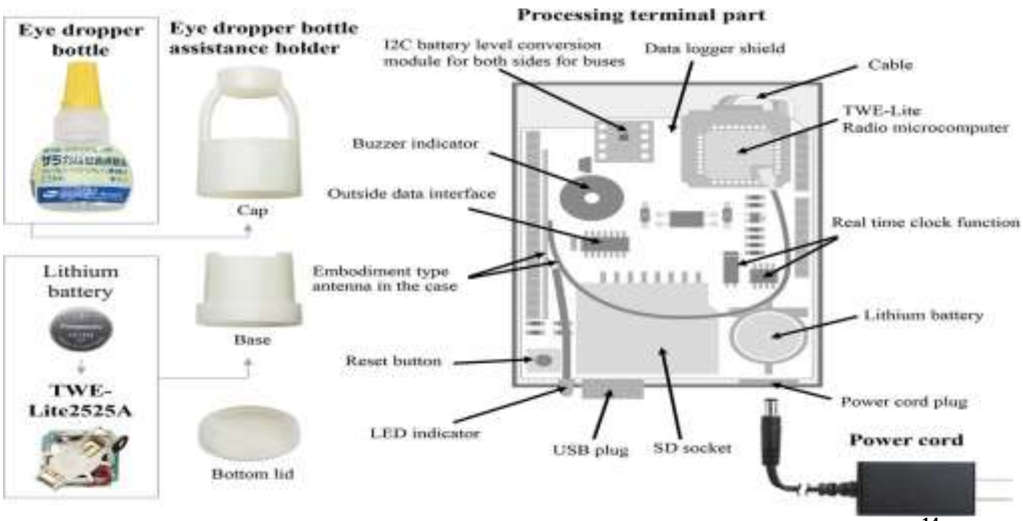

Fig 3: The Eye Dropper Bottle Sensor designed byKazuaki Nishimura et al[14]

WEARABLE SENSORS:

Devices made to be worn as accessories are commonly referred to as wearables.[15]Low inexpensive wearable sensor scan recall, monitor medication consumption to increase patient population medication adherence.[6]

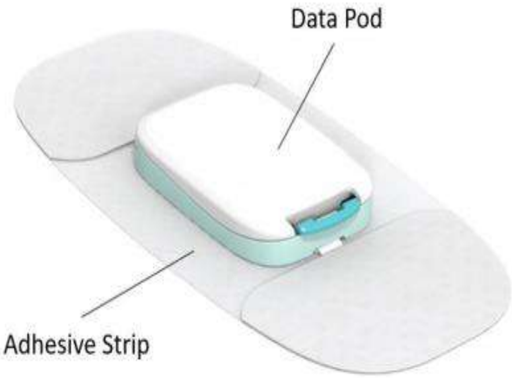

Fig 4: Design of Two-part Wearable Sensor[1]

Figure 4 represents the Two-Part Wearable Sensor with the data pod and a repositionable adhesive strip. For up to a year, the data pod may be utilized. Before switching to a new strip, the adhesive strip can be worn on the body for seven days. Information including heart rate, step counts, and body angle is measured and then transferred to the patient's linked mobile devices utilizing BLE radio.[1] Early uses of wearable sensing technology included the detection of illegal narcotics that alter the body's vital signals. This includes a wearable sensor used to track the heart rate decline induced by an opioid overdose and to start the supply of an antidote.[17]

In one of the trials, the authors suggested using wearable technology to gauge drug adherence. They created a pendant-style necklace out of a piezoelectric sensor, an RF circuit, and a battery. The mechanical tension generated by swallowing is applied to the piezoelectric sensor, which is positioned in the lower neck slightly above the clavicle bone. A piezoelectric sensor can be used to detect the mechanical stress brought on by skin movements during pill swallowing, and the sensor will produce a voltage as a result. To do further analysis, the Bluetooth transmission of the acquired data to a mobile phone is made. Using a Bayesian network, the data was classified. However, the patient must wear the necklace while taking the medication, which is uncomfortable.

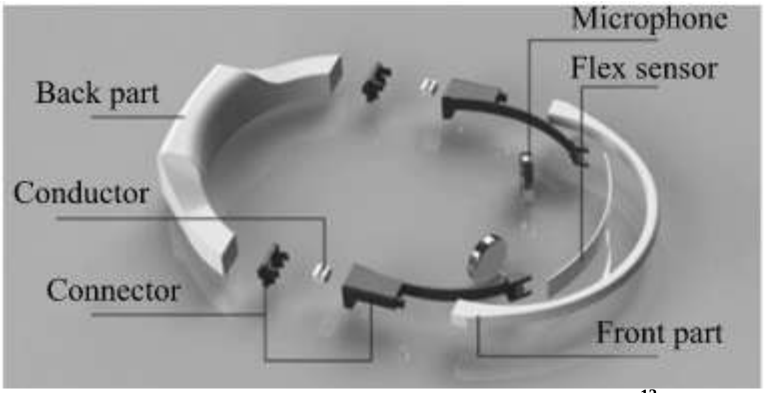

Fig 5: Neck Worn Sensor Designed by Wu et al.[13]

Wu et al. created another class of wearable which was represented in figure 5 consisting of an RFID reader, a flax sensor, and microphones. The microphones are used to detect neck movement when users are ingesting pills. A pill's passage through the throat is monitored by an RFID reader while it contains ingestible biosensors. The lack of validation trials in this study makes it challenging to assess how well the patient group performs and is accepted by society.[13]

Smartwatches provide effective activity-monitoring tools. They contain several embedded sensors, including a gyroscope, a three-axis accelerometer, a heart rate monitor, and Near-Field Communication (NFC). The information offered by the watch is also more accessible than that from other devices like a smartphone, tablets, or laptops. Using gyroscope and accelerometer sensors, FozoonMayeh et al. created a smartwatch for detecting medication ingestion. It is used to keep track of activities like taking pills, walking, writing, and drinking water. This is possible if the subject wears a smartwatch and takes medication. The number of tablets still present, however, was not determined by this study. To gather data, Chen's study created inertial sensors, an RGB-Depth camera, an accelerometer, and a gyroscope that were attached to the patient's wrist. [Dynamic time-wrapping was then used to assess the degree of similarity between time-series data of various lengths]. The simple storage service (S3) from Amazon Web Services (AWS) is intended to offer cost-effective storage based on requirements. Only authorized individuals can access the data because of the secure infrastructure it offers. Using an Android smartwatch, this study tracks patients' movements when they take their medication. The information is saved in the basic storage service (S3) of Amazon Web Services (AWS) and is subject to analysis using Apache Spark.[18] The data from a 3-axis accelerometer and gyroscope utilized to identify the opening of the pill bottle, picking the tablets out, placing the tablets into the other hands, and touching the water bottle activities were manufactured by Samsung Electronics Samsung Galaxy Gear wristwatch. When a smartwatch is worn on the wrist, the activity during lid opening and the wrist movement for the palm while tablets are placed into another hand have been detected by an application that has been created to assess medicines intake from the data gathered by the sensing devices. The authors identified the actions of opening the prescription container and raising the palm with 87.5% and 100% recall and precisions of 30% and 83.7%, respectively. To determine if taking a tablet with water is preferable to just drinking water without the pill, Wang et al. employed an accelerometer and a dynamic time-warping approach. Using hand gestures, they gathered information from 25 people. 84.17 percent of true positives were generated by this system. A triaxial accelerometer and gyroscope were used in the wearable sensor developed by Chen et al. to accurately detect the movements of "hand-to-mouth" and "cap twisting" with 95% and 97.5% accuracy, respectively.[13]

The advantages of wearable sensors include they help monitor user behavior in a free-living environment and provide the accuracy of other sensor-based systems. However, the main disadvantage is that when considering elder patients it is causing discomfort and lesser acceptance with wearable-based systems. This is because wearable devices, which are often operated using tiny batteries, require wireless sensors to be connected to users for prolonged periods and to be frequently recharged.

INGESTIBLE SENSORS:

To measure medication adherence as part of the Digital Pill System, the ingestible sensor was first authorized in 2012 through the FDA's de novo method.[19] Using a unique formulation for tracking of the medicine inside the body, this method is used as it contains mobile technology, which is quite helpful for individuals who are not adhering.[20] Ingestible devices are tiny, capsule-like items that, when given orally like solid drugs, are broken down and absorbed. Data regarding particular physiological parameters are gathered by these devices as they pass through the digestive system and gastrointestinal tract. Using a capsule-filling machine at the pharmacy, pharmaceutical company, or contract manufacturing organization-level medications are over-encapsulated by the digital pill capsule.[21]

The Ingestible Event Marker is a mini sensor constructed from trace amounts of the edible minerals silicon, magnesium, and copper. The active layers, integrated circuit, and insulating skirt disc are the three primary parts of the sensor. A complementary metal-oxide semiconductor makes up the integrated circuit. The amount of minerals that enter the body is less than what is typically present in a normal diet. After ingestion, the sensor gets contact with the gastric fluid, and it improved the inventory of the medicine and dosage form, it transmits a special, highly secured number. Additionally, drug ingestion also measures health-related behaviors like physical activity, and other clinical metrics of physiological response, such as heart rate and sleep.[19]

A summary of the usage in a systematic review of an ingestible sensor that improves medication adherence was conducted by Peter R Chai et al. They have included a total of 21 manuscripts that describe the deployment of ingestible sensors and also involve qualitative investigations of digital pill systems with human subjects. Three of these clinical trials—which used ingestible sensors in human populations—included exploratory qualitative research. This study reveals the widespread of the Digital Pill System in a variety of disease situations, including HCV, organ transplantation, TB, schizophrenia, CVD and severe fractures. The Smart Pill System is used in the usage of medication therapy, even though they have ignored non-indexed articles, research papers, and other guidance notes that mention it.[22]

Eric S. Daar et al. conducted a pilot study on HIV-infected patients on treatment with ARV therapy and to assess the issues related to real-time data handling, co-encapsulation, patch use, and feedback about text messaging. They have included 15 HIV-infected individuals. acceptability of the individuals was examined by survey at weeks 4, 8, 12, and 16. At each visit, 75% of the patients responded that the patch was very or somewhat comfortable. Regarding text message reminders, only 10–15% of the patients felt that the text message reminders were not helpful. 55% of patients at week 4 and 83% at week 8 stated that they were somewhat or strongly satisfied with the sensor system.[23] DiCarlo et al. gathered data on the subjects' drug intake in hypertension people like daily steps, weight, and blood pressure. In the clinic, 98% of the accurate doses were given. 90% of the individuals adhering to their medication.[24]

PROXIMITY DETECTION SYSTEM:

The important invention of the Internet of Things (IoT) depends on a few technologies, one of which is proximity sensing Thus, by sensing an object's proximity to other items, we can keep track of how often we use it in our daily lives. RFID and NFC are two significant methodscurrently used. In general, RFID and NFC may be implemented from daily life to monitor activity.[13]

RFID:

RFID is employed in many areas of everyday culture, from logistics and inventory control to persistent technologies like mobile healthcare and personal security. The radio scanning unit, also known as a reader, and the remote transponders, usually known as tags, are the fundamental parts of an RFID system.[25] The tags use backscattering to connect with readers, where the tags intelligently reflect a portion of the reader signal, a technique that communicates the data kept in the tags.[26]The tags' design can beread-only, rewritable, read-many, or write-once, and they are made up of an antenna and a microchip transmitter with internal memory. Because of their lesser price, smaller size, and longer lifespan despite their restricted range, passive tags are increasingly often used.[9] RFID tags are added to regular plastic pill bottles; these tags are linked with particular prescription information and kept in a database of XML by a pharmacist including when people need to take these drugs, and there are specific cautions (like tablets) and the length of the prescription. The stand includes LEDs, a button, an RFID tag reader, and a network connection to a computer. When pill bottles are put on the stand, they display the RFID tag that requests routing information from a server's database. The stand utilizes the XML data to remind the user when to take their medications.As soon as a pill container is removed from the rack, it is assumed that the user is taking their medication; however, if the bottle is not replaced within a reasonable length of time, the stand will voice remind the user to "Please put back the pill bottle."A medicine monitor is the second element which is situated at a personal caregiver's house (e.g., a relative). It takes the form of a touch-sensitive picture frame with LEDs all around, which was inspired by LumiTouch.[27] The gadget is linked to the pill-taker via a photograph that is inserted. The stand notifies the medication monitor when a problem exists over missing medications, which causes the LEDs to flash. This may be done by the caregiver touching the image and leaving a voicemail. This message is sent to the pill bottle stand, which plays it again when the button is pressed and announces its presence.The RFID-based technology created by Agarawala et al. was depicted in figure 6.[28]

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Fig 6: The RFID-Based Technology Created byAgarawala et al [28]

Smart Drawer, another RFID-based prototype system was illustrated in figure 7. It uses a drawer equipped with an RFID reader that can both inventory the pill bottles kept inside and keep track of drug usage. The system keeps track of the kind of bottle and the time it is taken out of the drawer. In other words, when the medication bottle is taken out of the drawer and out of the range of the RFID reader, the medication has previously been used, which is why it has only been used occasionally.[40]

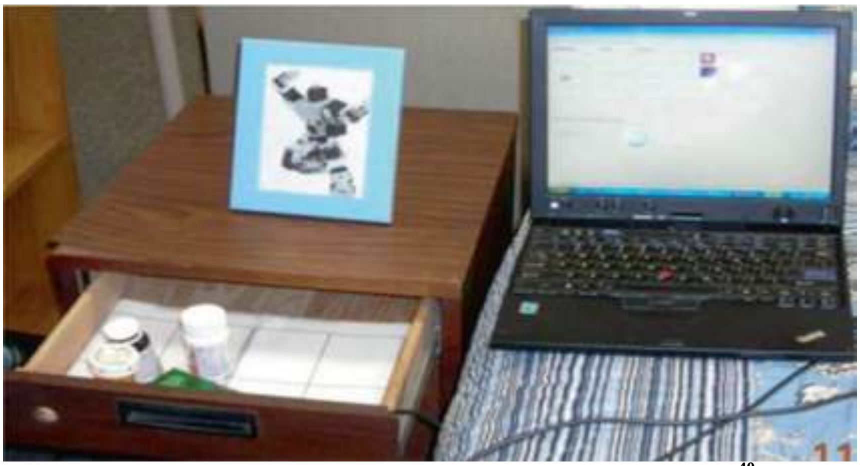

Fig 7: Smart drawer System Developed by Becker et al [40]

NFC:

Future mobile phones and smartphones will have Near Field Communication (NFC), a new wireless interface. NFC is a wireless technology with a limited range (10 cm) that developed from radio frequency identification (RFID).[29] NFC is particularly suited to enable any user action that can be translated to a "tap and go" concept, for example, where users must "touch" an object in their surroundings to begin and carry out a fleeting communication with this object, for example, to read out sensor data. It has previously been suggested that NFC-enabled electronic blisters function as a part of mobile health-based prescription management solutions. However, further research is needed on how to handle packaging (many smart blisters in one blister pack) and give them to patients in a real pharmacy setting.[30]

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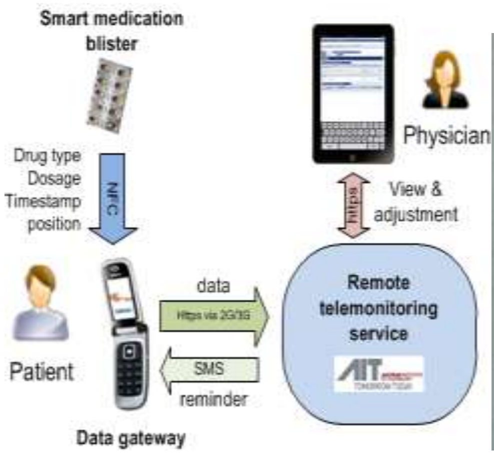

Fig 8: NFC-capable smart pill blister **Fig 9: Data port based on mobile phone**

Morak J et al., in figure 8 and 9 represent an outline of the system for tracking treatment adherence, which consists of remote telemonitoring services, NFC-enabled medicine blisters, and a mobile phone-based data gateway.

ADVANTAGE:

- The ability to access data such as medication recommendations, which may include details on timing, duration, and amount
- Elder patients are more benefited
- Non-invasive method [31]

DISADVANTAGE:

- Presence of pill bottle at a closer distance (a few millimeters) from the reader
- Wrong consideration as if the bottle gets slightly moved from the reader even when the patient is not taking the drug

• A baby's exposure to Ultra-High Frequency (UHF) RFID scanners, while the mother is pregnant, might be harmful.[31]

VISION-BASED SYSTEM:

Nowadays, there has been a significant amount of interest in image processing and machine vision research, which has resulted in the creation of several algorithms for the representation and categorization of human activities.[32] Batz D et al. developed a computer vision technique for tracking the medicine usage patterns. In the pharmaceutical section, which could consist of several medication bottles, the system employs one camera that has been mounted. Only one user must be visible near the camera during the medicine-taking session for the device to function. To differentiate between shades of skin, algorithms for skin color discrimination have been developed. The systems begin by removing every skin area from the subject standing before the cam. Following that, this data is employed to identify hand/hand (bottle-twisting) occlusions and hand/face (hand over mouth). Six of the eight instances of taking pills were correctly identified. Therefore, they view the actions of opening the container, taking a tablet, and shutting it as a pill-taking experience.[33]

In their research, Dauphin G et al. developed a method for background-suppressing videos taken by low-resolution cameras and used it to the tracking of drug consumption. The method was only tested on one subject, and there were no reported accuracy results. Additionally, because the studies were done with adark-colored subject in the background, the system's accuracy may be impacted by people wearing other colored clothing.[34]

LIMITATIONS:

- Although vision-based technologies will be vital in AAL settings, their usage is restricted and their reliability isn't always accurate.
- Vision-based methods may also require several resources, which is costly.
- The significant computational cost involved with system training is still another drawback, particularly with surveillance-video techniques.[35]

FUSION-BASED SYSTEM:

The research we discussed shows that each technique has shortcomings. As a result, fusion-based systems have been created to combine advancements from several methodologies to improve one or more technological shortcomings.[13]

PROXIMITY-SENSOR SYSTEM:

Li et al. developed a system for tracking medication adherence that consists of a computer, a wireless wristband, and a 7-compartment pillbox illustrated in figure 10. It consists of a ZigBee transceiver, an Arduino microcontroller, a battery, a motor, and an RFID reader in the pillbox. A diode and a photodiode are also included in each compartment to find pill removal. When it is necessary to take pills and when the RFID-based wristbands are recognized close to the pillbox, the MCU functions to guide the motor to twist the container in the direction of the user. IMU, RFID, and an LED are all included within the wristband. As a result, it is applied for recording motion data related to selecting and consuming pills. Additionally, RFID proximity monitoring inside the pillbox and reminder purposes is supplied by the RFID tag and LED, respectively. Once the wristband is located near the pillbox, the IMU is activated to collect the motion data in search of any relevant pill-taking-related hand motions.Finally, based on the light absorbed from the LED, the photodetector creates a voltage that is recognized by MCU at a certain level. This voltage is applied to validate the pill removal.[36]

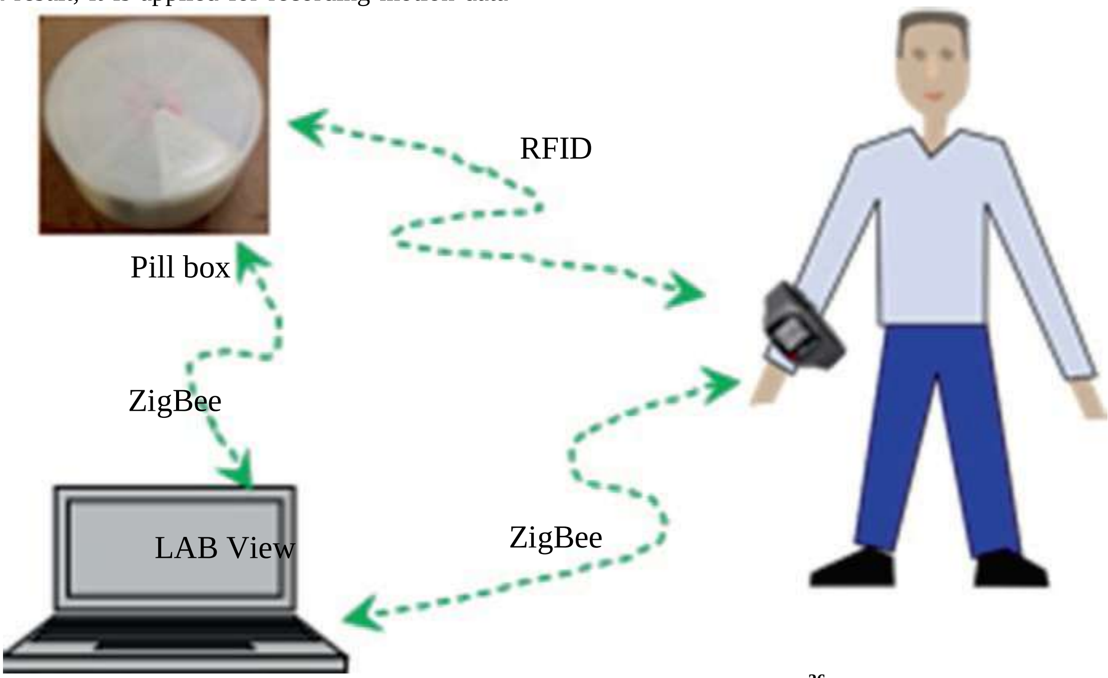

Fig 10: The Fusion-Based System by Li J et al[36]

In a recent study, Boonnuddar and Wuttidittachotti presented a pillbox-based framework utilizing an Arduino UNO Wi - fi access and a weight sensor. Drug frequency alterations were uploaded to a database through the Web. A smartphone application was also developed to remind patients to take their pills if there have been no variations in weight measures. The system underwent 160 rounds of medication administration testing, and the functional accuracy of the mobile application notification was 96.88%.[37]

PROXIMITY-VISUAL SYSTEM:

The activity of taking medications in a home environment has been described by Hasanuzzaman et al., using a combination of RFID sensors and video cameras. Here, RFID-tagged medication bottles were placed in a medicine cabinet equipped with an RFID reader. For the goal of identifying the medication bottles kept in the cabinet, RFID technology is used. But if a bottle is taken out of the medicine cabinet and outside the reader's antenna's range, it is no longer possible to identify it using RFID technology. As a result, the vision system is set up such that it begins to work as soon as the drug container leaves the reader's line of sight. Depending on recognizing moving objects and the color of the bottle, the camera is used to monitor and confirm when medication is taken.[38]

VISION-SENSOR SYSTEM:

Based on the patient's activity, assistive living strategies have been employed to monitor medicine intake. One such is iMEC, which Suzuki and Nakauchi developed for medication scheduling and pill-taking detection. Some household items including chairs, microwaves, refrigerators, and beds, have been fitted with ubiquitous sensors to predict the behavior of the patient. To detect pill removal, a medication case with a camera has been employed. In the end, the combined data from various devices were applied to verify drug adherence.[39]

IV. LIMITATIONS:

SYSTEM ACCURACY AND DATA FIDELITY:

Accurate technologies that record user activities are necessary to improve healthcare. Systems for tracking medication adherence fall under this category as well. The gadget is used to record the drug-taking action generally determines accuracy. Additionally, the environment in which medications are taken might impact and constrain technological advancements. As a compromise for reducing energy usage, the system can, for instance, run at low sampling rates. Lower data quality is a trade-off for this, though. Data fidelity, precision, and quality are all components of accuracy.[41] Data fidelity can be expressed in terms of sample rate, sensor operating mode, duty switching, and other factors if the device supports them. The system must be operating at high fidelity to obtain data with high accuracy. High-fidelity systems, on the other hand, are powered by a battery that quickly depletes since their central processing unit must run often to properly record the event being observed. Therefore, it is important to carefully regulate energy consumption when designing a drug tracking system.[13]

ENERGY CONSUMPTION AND LIFETIME:

For instance, battery-powered sensor networks and mobile device-based systems, including tablets, smartphones, and smartwatches can be utilized to assess medication adherence.[13] Due to the battery's constrained energy budget, this presents a problem.[42] From a system perspective, it is expected that the system is receiving enough electric current to ensure its functionality. In addition, since the designers of the applications have either constantly removed batteries or employed rechargeable batteries, users expect the system's lifetime to endure as long as possible. This would probably be expensive and insufficient for user acceptability.[43]

ACCEPTABILITY AND USERS' COMFORT:

The acceptance and success of a monitoring system are significantly influenced by the user's impression of it. First, there are substantial technical obstacles that prevent the widespread usage of technology-based methods for tracking patient compliance.
These obstacles include mobility support, battery energy consumption, and others. Second, there are ethical issues like confidentiality and privacy. Users are concerned about the possibility of unintended users accessing the information obtained as well as the monitoring of actions other than medicine use.[44]

By "active sensing," researchers recommend that the sensor should be in place and function while the patient is taking their medication. The sensing device should be near the patient's body. A smartwatch is an illustration of such a system. Passive sensing, on the other hand, utilizes a technology that is not connected to the body of the patient. However, to retain comfort for the user while earning their perception, medication adherence solutions should include portability as a major criterion. Most of the wireless systems, such as sensor devices, however, as we pointed out, demand the consumer's attention which would need regular battery change or recharge.[45]

V. CONCLUSION:

Medication adherence is a widespread but difficult issue in healthcare. The patients may experience negative effects if they don't take their drugs as directed**.** Developing medication adherence monitoring technologies have become an interesting area for many researchers which can detect the correct medication-taking regimens. Smart adherence technology is changing how individuals and health professionals administer drugs. These technologies provide information regarding medication-taking adherence to healthcare professionals. In our study, we presented methods using advanced technologies to improve drug compliance. Additionally, we have included the advantages, disadvantages, and limitations associated with these techniques. We conclude our study that more research is still required to address these issues, particularly the precision and convenience; and future direction of clinical trials need to be conducted with a large sample size for the evaluation of accuracy and user comfort.

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REFERENCES:

[1]. Weeks WA, Dua A, Hutchison J, Joshi R, Li R, Szejer J, Azevedo RG. A low-power, low-cost ingestible, and wearable sensing platform to measure medication adherence and physiological signals. 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2018 Jul; 18;5549-5553.

[2]. Kalantarian H, Motamed B, Alshurafa N, Sarrafzadeh M. A wearable sensor system for medication adherence prediction. Artificial intelligence in medicine. 2016 May 1;69:43-52.

[3]. Zijp TR, Touw DJ, van Boven JF. User acceptability and technical robustness evaluation of a novel smart pill bottle prototype designed to support medication adherence. Patient preference and adherence. 2020 March 20;14:625.

[4]. Holtkötter J, Amaral R, Almeida R, Jácome C, Cardoso R, Pereira A, Pereira M, Chon KH, Fonseca JA. Development and Validation of a Digital Image Processing-Based Pill Detection Tool for an Oral Medication Self-Monitoring System. Sensors. 2022 Apr 12;22(8):2958.

[5]. Van Heuckelum M, van den Ende CH, Houterman AE, Heemskerk CP, van Dulmen S, van den Bemt BJ. The effect of electronic monitoring feedback on medication adherence and clinical outcomes: a systematic review. PloS one. 2017 Oct 9;12(10):0185453.

[6]. Stankovic JA. Research directions for cyber-physical systems in wireless and mobile healthcare. ACM Transactions on Cyber-Physical Systems. 2016 Nov 3;1(1):1-2.

[7]. Sabaté E, Sabaté E. Adherence to long-term therapies: evidence for action. World Health Organization; Geneva, 2003.

[8]. Piña IL, Di Palo KE, Brown MT, Choudhry NK, Cvengros J et al., Medication adherence: importance, issues, and policy. American Heart Association. Progress in cardiovascular diseases. 2021 Jan; 1;64:111-20.

[9]. Connor J, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. Bulletin of the World Health Organization. 2004 Dec; 82;12:935-9.

[10]. Breckenridge A. Compliance of hypertensive patients with pharmacological treatment. AHA Journal-Hypertension. 2018 Sep; 1;5(5)pt 2):III85.

[11]. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Medicine and pharmacy reports. 2019 Apr; 22;92(2):117-22.

[12]. Mrosek R, Dehling T, Sunyaev A. Taxonomy of health IT and medication adherence. Health Policy and Technology. 2015 Sep 1;4(3):215-24.

[13]. Aldeer M, Javanmard M, Martin RP. A review of medication adherence monitoring technologies. Applied System Innovation. 2018 May 6;1(2):14.

[14]. Nishimura K, Tabuchi H, Nakakura S, Nakatani Y, Yorihiro A, Hasegawa S, Tanabe H, Noguchi A, Aoki R, Kiuchi Y. Evaluation of automatic monitoring of instillation adherence using eye Dropper bottle sensor and deep learning in patients with glaucoma. Translational Vision Science & Technology. 2019 May 1;8(3):55.

[15]. Johansson D, Malmgren K, Alt Murphy M. Wearable sensors for clinical applications in epilepsy, Parkinson's disease, and stroke: a mixed-methods systematic review. Journal of neurology. 2018 Feb; 9; 265(8):1740-52.

[16]. Ma J, Ovalle A, Woodbridge DM. Medhere: A smartwatch-based medication adherence monitoring system using machine learning and distributed computing. 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2018 Jul; 18;4945-4948.

[17]. Teymourian H, Parrilla M, Sempionatto JR, Montiel NF, Barfidokht A et al., Wearable electrochemical sensors for the monitoring and screening of drugs. ACS sensors. 2020 Aug; 21;5(9):2679-700.

[18]. Cheon A, Jung SY, Prather C, Sarmiento M, Wong K, Woodbridge DM. A machine learning approach to detecting low medication state with wearable technologies. 42nd Annual International Conference of the IEEE Engineering in

Medicine & Biology Society (EMBC) 2020 Jul; 20;4252-4255.
[19]. Plowman RS, Peters-Strickland T, Savage GM. Digital medicines: clinical review on the safety of tablets with sensors. Expert opinion on drug safety. 2018 Sep 2;17(9):849-52.
[20]. Dukes CK, Sheaffer EA. Biosensing Technology to Track Adherence: A Literature Review. InHealthcare 2021 Oct; 9; 9(10);1339.
[21]. Chai PR, Goodman G, Bustamante MJ, Mohamed Y, Castillo-Mancilla J et al., Long-term stability of the electronic sensor component of a digital pill system in real-world storage settings. Journal of Pharmacy Technology. 2021 jan; 6;37;(3):135-9.
[22]. Chai PR, Vaz C, Goodman GR, Albrechta H, Huang H, et al., Ingestible electronic sensors to measure instantaneous medication adherence: A narrative review. Digital Health. 2022 Feb;8:20552076221083119.
[23]. Daar ES, Rosen MI, Wang Y, Siqueiros L, Shen J, et al., Real-time and wireless assessment of adherence to antiretroviral therapy with co-encapsulated ingestion sensor in HIV-infected patients: A pilot study. Clinical and translational science. 2020 Jan;13(1):189-94.
[24]. Alipour A, Gabrielson S, Patel PB. Ingestible sensors and medication adherence: focus on use in serious mental illness. Pharmacy. 2020 Jun; 16;8(2):103.
[25]. Marrocco G. The art of UHF RFID antenna design: Impedance-matching and size-reduction techniques. IEEE antennas and propagation magazine. 2008 Apr; 25;50(1):66-79
[26]. Bolić M, Rostamian M, Djurić PM. Proximity Detection with RFID in the Internet of Things. IEEE. 2014 Nov; 2;711-714.
[27]. Chang A, Resner B, Koerner B, Wang X, Ishii H. LumiTouch: an emotional communication device. Extended abstracts on Human factors in computing systems 2001 Mar; 31; 313-314.
[28]. Agarawala A, Anand A, Greenberg S, Ho G. The context-aware pill bottle and medication monitor. ACM UBICOMP2004. 2004;25:50-75.
[29]. Strommer E, Kaartinen J, Parkka J, Ylisaukko-Oja A, Korhonen I. Application of near field communication for health monitoring in daily life. International Conference of the IEEE Engineering in Medicine and Biology Society 2006 Aug; 30;3246-3249.
[30]. Morak J, Schwarz M, Hayn D, Schreier G. Feasibility of mHealth and Near Field Communication technology-based medication adherence monitoring. Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2012 Aug; 28; 272-275.
[31]. Fiocchi S, Parazzini M, Liorni I, Samaras T, Ravazzani P. Temperature increase in the fetus exposed to UHF RFID readers. IEEE Transactions on Biomedical Engineering. 2014 Mar; 14;61(7):2011-19.
[32]. Zhang S, Wei Z, Nie J, Huang L, Wang S, et al., A review on human activity recognition using the vision-based method. Journal of healthcare engineering. 2017 Jul 20;2017.
[33]. Batz D, Batz M, da Vitoria Lobo N, Shah M. A computer vision system for monitoring medication intake. The 2nd Canadian Conference on Computer and Robot Vision (CRV'05), IEEE Xplore. 2005 May 9;362-369.
[34]. Dauphin G, Khanfir S. Background suppression with low-resolution camera in the context of medication intake monitoring. In3rd European Workshop on Visual Information Processing 2011 Jul; 4;128-133.
[35]. Alexander SM, Nerminathan A, Harrison A, Phelps M, Scott KM. Prejudices and perceptions: patient acceptance of mobile technology use in health care. Internal Medicine Journal. 2015 Nov;45(11):1179-81.
[36]. Li J, Peplinski SJ, Nia SM, Farajidavar A. An interoperable pillbox system for smart medication adherence. In 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2014 Aug; 26;1386-1389. IEEE.
[37]. Boonnuddar N, Wuttidittachotti P. Mobile Application: Patients' Adherence to Medicine In-take Schedules. In Proceedings of the International Conference on Big Data and Internet of Thing. 2017 Dec; 20;237-241.
[38]. Hasanuzzaman FM, Yang X, Tian Y, Liu Q, Capezuti E. Monitoring activity of

taking medicine by incorporating RFID and video analysis. Network Modeling Analysis in Health Informatics and Bioinformatics. 2013 Jul;2(2):61-70.

[39]. Suzuki T, Nakauchi Y. Intelligent medicine case for dosing monitoring and support. In 2010 IEEE/RSJ International Conference on Intelligent Robots and Systems 2010 Oct; 18;3471-3476. IEEE.

[40]. Becker E, Metsis V, Arora R, Vinjumur J, Xu Y et al., SmartDrawer: RFID-based smart medicine drawer for assistive environments. In Proceedings of The 2nd international Conference on Pervasive Technologies Related to Assistive Environments 2009 Jun; 9;1-8.

[41]. Aldeer MM, Martin RP, Howard RE. Tackling the fidelity-energy trade-off in wireless body sensor networks. In 2017 IEEE/ACM International Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE) 2017 Jul; 17;7-12. IEEE.

[42]. Rukpakavong W, Guan L, Phillips I. Dynamic node lifetime estimation for wireless sensor networks. IEEE Sensors Journal. 2013 Dec; 18;14(5):1370-9.

[43]. Jovanov E, Milenkovic A, Otto C, De Groen PC. A wireless body area network of intelligent motion sensors for computer-assisted physical rehabilitation. Journal of Neuro Engineering and rehabilitation. 2005 Dec;2(1):1-0.

[44]. Campbell JI, Eyal N, Musiimenta A, Haberer JE. Ethical questions in medical electronic adherence monitoring. Journal of general internal medicine. 2016 Mar;31(3):338-42.

[45]. Saleem K, Shahzad B, Orgun MA, Al-Muhtadi J, Rodrigues JJ, et al., Design and deployment challenges in immersive and wearable technologies. Behaviour & Information Technology. 2017 Jul 3;36(7):687-98.