

**MEDICATION ADHERENCE: AN OVERVIEW**

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**ABSTRACT**

Medication non-adherence is an unforeseen, emerging problem of the health care system. According to WHO any increasing the effectiveness of medication adherence have greater impact on clinical outcome than any other improvement made in medical treatment. Patient's medication behavior is hindered by various factors such as socioeconomic factors, patient related factors, physician related factors and health care system related factors. Poor medication adherence can lead to unforeseen medical complication, reduced quality of life, increased medical cost, frequent physician visit, medication changes etc. Various methods for measuring medication adherence are available such as subjective measures and objective measures like pill counting, electronic monitoring of medication adherence shown promising and validated measurement of any non-adherence. Barriers to medication adherence can be improved only by complete cooperation from patient, physician and other healthcare provider to follow some basic policies to improve adherence rate in patient. Using latest technologies such as e-health, reminders set in cell phone, watches, MEMS etc. can also improve rate of adherence. Soon, non-adherence would be a leading factor for decreased clinical outcome and can affect the growth of healthcare sector in a country.

**KEYWORDS:** Medication adherence, Clinical outcome, Measurement, Barriers, Healthcare providers.**INTRODUCTION**

WHO defines Medication adherence as "the extent to which the person's behavior (including medication-taking) corresponding to agreed recommendations from a healthcare provider".<sup>[1]</sup> It can also be explained as a combination of the term 'compliance' which means 'taking the right dose at the right time' and the term 'persistence' which means 'taking the treatment continuously during the period of time prescribed'.<sup>[2]</sup> The WHO, in its 2003 report on medication adherence, mentioned that increased effectiveness of adherence interventions may have a greater impact on the health of the population than any improvement made in specific medical treatment".<sup>[1]</sup> Adherence to medication is a crucial part of patient care and it is indispensable for reaching clinical outcome.<sup>[3]</sup> Increased adherence to medication regimens can improve clinical and economic outcomes of patients on long-term therapy.<sup>[4]</sup>

Adherence is a multifactorial phenomenon which can be influenced by various factors such as social and economic factors, therapy-related factors, disease-related factors, patient-related factors and health care system-related factors.<sup>[5,6]</sup> Factors associated with poor adherence especially in old patients are mainly due to multi-morbidity, cognitive impairment, complex regimens with multiple prescribing physicians, and problems with drug storage or formulation.<sup>[7]</sup> Poor

medication adherence can lead to changes such as unnecessary disease progression and complications, reduced functional abilities and quality of life, more medical costs and physician visits, increased use of expensive specialized medical resources and unneeded medication changes.<sup>[8]</sup>

Medication adherence can be somehow managed using non-technology and technology-based approaches such as Transplant Hero, Wiseapp, Smartassist, Medibox etc.<sup>[9]</sup> Measurement of medication adherence is a challenging process because adherence depends upon individual patient behavior.<sup>[10]</sup> There are various methods available for these measurements, but these need to prove to be valid, reliable, and sensitive to change.<sup>[11]</sup> Since no standard methods till now available, combination of methods such as direct and indirect methods used for measuring Medication Adherence.<sup>[12]</sup>

**FACTORS AFFECTING MEDICATION ADHERENCE**

According to WHO, there are multiple factors leading to poor medication adherence which is classified into some categories: socioeconomic factors, therapy-related factors, patients-related factors, physician related factors, condition-related factors, and health system/healthcare team- (HCT-) related factors.<sup>[13]</sup>

**SOCIOECONOMIC RELATED FACTORS**

Socioeconomic factors include age, sex, education, ethnicity, financial status and employment which has impact upon medication adherence of a patient. There was no significant relationship between sex and adherence.<sup>[14]</sup> Evidence for a positive impact of education on adherence was exclusively noted for cardiovascular conditions.<sup>[15,16]</sup> The impact of employment was mostly uncertain.<sup>[17]</sup> Among patients with chronic diseases and patients taking oral anticancer agents, there was some evidence that a better financial status having a better impact on patients medication adherence.<sup>[18,19]</sup> But the impact of financial status was uncertain in Parkinson disease, hepatitis C and cardiovascular conditions.<sup>[20]</sup>

**THERAPY RELATED FACTORS**

Therapy related factors such as duration of therapy, number of tablets, intake frequency, intake at meals was uncertain in almost all disease conditions.<sup>[21,22]</sup>

**DISEASE RELATED FACTORS**

Duration of disease was the major disease related factors. In most of the studies the impact of disease on adherence shown an uncertain or probably no impact at all.<sup>[21,22,23]</sup>

**PATIENT RELATED FACTORS**

Demographic factors which are negatively associated with adherence are older age and being male although there associations were weak.<sup>[24,25]</sup> Some other factors negatively associated with adherence included the neurotic personality trait (other personality traits did not have a significant impact), recent hospitalization, and lack of contact with a general practitioner.<sup>[25]</sup> Higher levels of comorbidity have positive association for poor patient adherence.<sup>[24]</sup>

**PHYSICIAN RELATED FACTORS**

Physician should respect patient perspective of illness and treatment. Most physicians responded to patients complaints about the effects of the medication by listening to the patients and educating them, and changing the medication; however, in some of the studies 33% of patients who report an adherence problem were ignored by the physician.<sup>[4]</sup>

**HEALTH-CARE SYSTEM RELATED FACTORS**

Fragmented health care systems has a negative impact on medication adherence by limiting the health care coordination and the patient's access to care.<sup>[26]</sup> Prohibitive drug costs or copayments also one of the factor leading to poor medication adherence.<sup>[27]</sup>

**Table 1: Factors affecting medication adherence.<sup>[9]</sup>**

| S.NO | FACTORS  | POSSIBLE SOLUTION   |
|------|--|---|
| 1.   | Forgetfulness on the dose and time to take medication  | Use of automated reminders and smart package  |
| 2.   | High pocket medication cost  | Health insurance plans;<br>Higher priority to low-income areas.   |
| 3.   | No follow-up by health physicians and family   | Directly observed therapy and therapeutic drug monitoring; More supportive patient-provider relationships and frequent follow-ups.  |
| 4.   | Number of pill doses   | Minimizing pill dose  |
| 5.   | Complexities (in drug dose)  | Minimizing the number of pills; Reducing the frequency of drug administration   |
| 6.   | Harmful side effects   | Enlightening patients through education on common side effects and ways to prevent them can help to attenuate the trepidation and concerns about adverse drug reactions; Emphasis on the need for treatment by physicians |
| 7.   | Lack of awareness of available reminder technologies   | Counselling and patient education   |
| 8.   | Changes in treatment schedule or drug dosage   | Fixed-dose combination therapies; Minimizing changes in treatment schedule and follow-ups.  |
| 9.   | Difficulty in transportation or pickup of medication from a pharmacy   | E-prescribing   |
| 10.  | Lack of income or health care insurance  | Health insurance plans; Prescription of cost-saving generic medication.   |
| 11.  | Ambiguous medication technologies  | Introduction of simplified, easy to use technologies  |
| 12.  | Depression   | Counselling and Providing physiological support.  |
| 13.  | Fear that reminders would become annoying over time Admitting to relatives that their memory is poor causes them to refuse medication reminders. | Pillboxes; Assistance from caregivers; Self-management technologies   |
| 14.  | Impaired cognition   | Use of technologies with diverse sensors (e.g. text to speech)  |

## MEASUREMENT OF MEDICATION ADHERENCE

Measurements of medication adherence are divided by the WHO as Subjective and Objective measurements.<sup>[1]</sup> Subjective measurements are those measurement requiring provider's or patient's evaluation of their medication-taking behavior. Self-report and healthcare professional assessments are the common methods used to rate adherence to medication.<sup>[28]</sup>

Objective measures includes methods such as pill counting, electronic monitoring, secondary database analysis and biochemical measures.<sup>[28,29]</sup>

### SUBJECTIVE MEASURES

Direct measures is the measurement of the drug or its metabolite concentration in body fluids, such as blood or urine or evaluation of the presence of a biological marker given with the drug and direct observation of patient's medication-taking behavior.<sup>[30]</sup>

### OBJECTIVE MEASURES

**i. Measures Involving Secondary Database Analysis**  
Secondary database analysis includes the sequences and patterns derived from the curated primary data in systems such as electronic prescription service or pharmacy insurance claim and this data allows quantification of medication adherence to various refill adherence measures. Refill adherence is the prescription-refilling patterns corresponded to the patient medication-taking behavior.<sup>[31]</sup> There are various equations available for measuring medication adherence using secondary database analysis like.<sup>[32,33,34]</sup>

- *Medication Possession Ratio (MPR)*- Days' supply obtained / refill interval or fixed interval
- *Dichotomous variable*- cutoff value or arbitrary value
- *Continuous, Multiple Interval Measure of Medication Acquisition (CMA)*- Cumulative day's supply obtained over a series of intervals / total days from the beginning to the end of the time period
- *Continuous, Multiple Interval Measure of Medication Gaps (CMG)*- Cumulative days without any medication over a series of intervals / total days from the beginning to the end of the time period
- *Continuous, Single Interval Measure of Medication Acquisition (CSA)*- Days' supply obtained in each interval / total days in the interval
- *Continuous, Single Interval Measure of Medication Gaps (CSG)*-Number of days without any medication / total days in the interval

### ii. Measures Involving Electronic Medication Packaging Devices

EMP devices are the "adherence-monitoring devices incorporated into the packaging of a prescription medication" before dispensing. They share some common features in general: (i) recorded dosing events and stored records of adherence; (ii) audiovisual

reminders to signal time for the next dose; (iii) digital displays; (iv) real-time monitoring; and (v) feedback on adherence performance. The Medication Events Monitoring System (MEMS) is the most commonly used EMP device in medication adherence studies.<sup>[35]</sup> The basic principle of this system is that whenever the medication is removed from the container, a microprocessor embedded inside it and it would record the time and date, assuming that the patient has taken that specific dose at that particular time.<sup>[30]</sup>

### iii. Pill Count

This is an indirect or objective measure of medication adherence in which the number of dosage units that have been taken between two scheduled appointments or clinic visits are counted. Then this number would then be compared with the total number of units received by the patient to calculate the adherence ratio.<sup>[32,33]</sup>

Measurement adherence ratio calculated with pill counts is given by the formula:

Medication possession ratio =

No. of pills absent in time A ÷ No. of pills prescribed for time A x 100

### iv. Measures Involving Clinical Assessment and Self-report

There are some commonly used methods for measuring clinical assessment;<sup>[32]</sup>

*Patient-Kept Diaries*- It is the only self-report tool that is continuously documented with how the patient follows their prescribed regimen.

*Patient Interviews*- Patient interviewing by clinicians is generally an easy-to-use, low-cost subjective method to assess patient's medication adherence.

*Questionnaires and Scales*- These are the methods which were first designed to minimize the limitations of other self-report methods by standardizing the measurement of adherence to a specific medication regimen.

A number of questionnaires have been used by researchers in this regard including:<sup>[8]</sup>

- Morisky Medication Adherence Scale
- Self-efficacy for Appropriate Medication Use (SEAMS)
- Brief Medication Questionnaire (BMQ)
- The Hill-Bone Compliance Scale
- Medication Adherence Report Scale (MARS)
- Adherence to Refills and Medications Scale (ARMS)
- Eight-Item Morisky Medication Adherence Scale (MMAS-8).

### v. Biochemical Measures

Biochemical process is performed by adding non-toxic markers to patient medication. Detecting the presence of the marker in blood and urine and measuring the serum drug level.<sup>[33]</sup>

**Table 2: Methods of measuring Medication Adherence.**<sup>[36]</sup>

| METHODS   | ADVANTAGE  | DISADVANTAGE  |
|---|--|---|
| <b>Direct methods</b><br>Directly observed therapy                      | Most accurate  | Patients can hide pills in the mouth and then discard them; impractical for routine use   |
| Measurement of the level of medicine or metabolite in blood             | Objective  | Variations in metabolism and “whitecoat adherence” can give a false impression of adherence; expensive; many technician or professional required to carry out the process |
| Measurement of the biologic marker in blood                             | Objective; in clinical trials, can also be used to measure placebo           | Requires expensive quantitative assays and collection of bodily fluids  |
| <b>Indirect methods</b><br>Patient questionnaires, patient self-reports | Simple; inexpensive; the most useful method in the clinical setting          | Susceptible to error with increases in time between visits; results are easily distorted by the patient   |
| Pill counts   | Objective, quantifiable, and easy to perform                                 | Data easily altered by the patient (e.g., pill dumping)   |
| Rates of prescription refills   | Objective; easy to obtain data   | A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system   |
| Assessment of the patient’s clinical response                           | Simple; generally easy to perform  | Factors other than medication adherence can affect clinical response  |
| Electronic medication monitors  | Precise; results are easily quantified; tracks patterns of taking medication | Expensive; requires return visits and downloading data from medication vials  |
| Patient diaries   | Help to correct for poor recall  | Easily altered by the patient   |

## INTERVENTIONS FOR IMPROVING MEDICATION ADHERENCE

### Theory Based Interventions

Theory-based interventions are developed to improve the knowledge, skill, and information that is required by patients need to improve their medication adherence.<sup>[37]</sup> It is performed through counselling, pictorial representation, audio clips etc.

### Patient Based Interventions

- Providing a “shame-free” environment to the patient.
- Pictorial and audio visual educational material to patients instead of written instructions for better understanding of the patient.
- Recognizing and treating mental illness must be the first priority on comparing treatment of patients with other chronic conditions
- Recognizing any patient’s economic constraints limiting their ability to adherence
- Programs providing financial assistance to patients recommended by the physician
- Self care assistance training to patients.
- Using reminders.<sup>[8]</sup>

### Physician Based Interventions

- Patients-Physician communication
- Provide patients with a rationale for the diagnosis and treatment.
- Negotiate a plan with each patient and expect problems.
- Using Morisky medication adherence scale to asses adherence rate.
- Motivational Interviewing

- Respecting patient’s perspective of the illness and its treatment.<sup>[4,8]</sup>

### Health Care Based Interventions

- Team-based approach
- Training non-physician staff to perform duties traditionally completed by physicians like an assessment of non-adherence by the patient which allows the physician more time to discuss the patient’s medication adherence patterns.
- Pharmacist monitoring has a positive influence on patient satisfaction and adherence ate.
- Practice of written information with prescriptions before dispensing by the pharmacist.
- Practice of counseling to patient by the pharmacist on dispensing.
- Phone call reminders by any healthcare staff.<sup>[4,8]</sup>

### Socioeconomic Based Interventions

- Establishing social support by family members, friends.
- Providing new health-care policies to improve adherence
- Employment of resources and workforce for improving individual medication adherence.
- Employment assistance.<sup>[8]</sup>

## TECHNOLOGIES USED FOR IMPROVING MEDICATION ADHERENCE

- 1) **Transplant Hero:** A mobile application with a smart watch for improving medication adherence. It is used to remind patients and provide helpful contents regarding their medication. From various studies conducted it was concluded that the use of

the mobile application or smart watch did not increase medication adherence levels to much better level as compared to users who did not use either of them.<sup>[38]</sup>

- 2) **Wise App:** A mobile self-management health application used for improving medication adherence especially for patients living with HIV. The application monitors patient's adherence in real-time and contains features like medtrackers, push notifications, testimonial videos from persons with the same condition, health surveys and a schedule of health-related tasks for each day. The health information technology usability evaluation scale assessed adherence level using Wiseapp showed that the application was useful.<sup>[39]</sup>
- 3) **MEDIBOX:** It is a portable device used for improving medication adherence. The device has sensors to track the temperature and humidity and helps to avoid deterioration of the medication stored in the box and also has a cooling system provided with power supply. It also stores patient's information such as discharge summary and other information on the cloud for further use by the patient.<sup>[40]</sup>
- 4) **Scan Med:** an application for tracking medication adherence. The system has a web interface for the healthcare professional and a mobile interface for patients use so that the health professional would be able to input all medication details on the interface and a QR code which contains the information, as printed on the medication container and can be shared with his patient. The mobile application with the patient acquires the information after it is scanned and displays the information on the patients mobile device. It reminds and notifies the patients when it's time to take the medication. Whenever patient take his medication patient had to scan his medication as an evidence of his adherence.<sup>[41]</sup>
- 5) **A drug checker system based on IOT** is to monitor drug adherence and to detect any adverse drug reactions. The application can be installed on smartphones and PDAs. The drugs to be taken can be verified using a pharmaceutical intelligent information system (PIIS) and patient's information obtained from a personal health record. After collecting the information required, an intelligent system which detects and reports any drug allergies, interactions, side-effects and give optimized times for drug consumption.<sup>[42]</sup>
- 6) **UbiMeds:** a mobile application used for improving medication adherence in the elderly and disabled with visual and cognitive impairment. It is easily accessible, provides details of medication to be taken. It also allows physician-patient monitoring, automated reminders, and text to speech features. It

shares patient's personal health record, tracks prescription intake, and notifies the patient's family and physician if the patient is not taking the medication. However, the application was designed to run only on Apple devices.<sup>[43]</sup>

## PHARMACIST ROLE IN MEDICATION ADHERENCE

Pharmacist plays a determining role in patient medication compliance. They are the persons who can have a direct contact with patient and has the ability detect patient compliance by collecting details about their medication. From various studies conducted showed positive impact for pharmacist-patient relationship mainly in community based pharmacies. They can note out any changes brought out by the drugs to patient and can be brought to the notice of physician. They can improve patient medication adherence by following ways:

- Written information about drug such as the name of drug, frequency etc on dispensing.
- Giving verbal counselling to the patient regarding the medication, any allergies, drug interactions, side effects etc.
- Preparing leaflet information regarding a disease and supplying to create awareness.
- Computerizing patient records for future reference.
- Filling the refill dates in prescription.
- In case of geriatric patient helping them in easy identification of their medication for different disease based on color, size, label etc.

## DISCUSSION

Our study shows that patient's adherence to a medication is intervened by various factors which can be controlled only by the collaborative cooperation of patient, physician and the healthcare team. Measurement of adherence rate is required for improving clinical outcome which can be carried out using direct and indirect methods. Implementation of electronic medical records and electronic prescribing has potentially increased adherence by identifying patients at risk of non-adherence and guiding them based on the interventions made. Pharmacies using automated reminders to alert patients on their prescriptions refill date and to remind physicians to contact their patients who do not refill their prescriptions have a positive impact on adherence. Therefore latest technological development has an impact upon improving poor adherence.

## CONCLUSION

As the former Surgeon General C. Everett Koop reminded us, "drugs don't work in patients who don't take them". Poor medication adherence is the key factor for decreased clinical outcome in both developed and developing countries. The barriers causing non adherence can be controlled only by the collaborative cooperation of patient, physician and other healthcare members. Even though several methods available for measuring medication adherence, the one which gives a

clear accurate result is still lacking. So development of new comprehensive approaches are required. Nowadays use of e-health by patients is gaining importance in the field of non adherence. Uses of newer technologies such as reminders through cell phones, watches, personal digital assistants and pillboxes with paging system can be source of help for patients who meets difficulty in maintaining proper adherence. The role of pharmacist as well as other healthcare members in the field of medication adherence should be given importance for future achievement in health care.

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#### CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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