



IMPACT OF MEDICATION ADHERENCE ON TREATMENT OF CHRONIC AILMENTS

¹M.RangaPriya*, M.Elamparuthi, C.Elavarasan, S.Kaavya, K.Priyanka, ²R.Manivannan

¹Department of Pharmacy Practice, Excel College of Pharmacy, Namakkal – 637303

²Principal, Excel College of Pharmacy, Namakkal – 637303

***Author for Correspondance**

Dr.M.RangaPriya, M.Pharm., Ph.D.,
Professor & Head,
Department of Pharmacy Practice,
Excel College of Pharmacy, Namakkal – 637303
Tamilnadu

ABSTRACT

Medication adherence is an essential component of patient treatment and is required to meet clinical objectives. Medication adherence is an essential component of managing chronic diseases. The Global Initiative for Chronic Obstructive Lung illness (GOLD) states that airway restriction and persistent respiratory symptoms are the hallmarks of COPD, a prevalent, curable, and preventable illness. On the other hand, inadequate compliance wastes resources and has a detrimental impact on health, leading to increased healthcare expenses. When patients follow the instructions for the timing, dosage, and frequency of all of their medications, it is thought that they are compliant. When a patient follows the recommended pharmaceutical regimen and takes their prescription(s) as directed, the cost of sickness is decreased. In the end, it would lower the total cost of treatment by assisting patients in feeling better and recovering more rapidly. This would lessen the patient's direct and indirect drug costs. Additionally, the negative effects are decreased by drug adherence. The patients' demographics, as well as their knowledge, attitudes, and perceptions regarding the nature, severity, origin, and prevention of sickness, as well as the various forms of treatment regimens, are among the determinants of medication adherence. An increase in urgent care visits, hospitalizations, and treatment costs, have all been linked to therapeutic non-compliance. The patient's quality of life is negatively impacted by noncompliance. New systems will likely be created in the future, and they will likely offer a fascinating supplementary strategy to behavioral and motivational interventions that support the cornerstone of good adherence.

Key Words: Medication Adherence, Quality of life, Patient Compliance, Non-compliance, Drug adherence

INTRODUCTION

Patient compliance, also known as adherence, refers to the accurate application of medical recommendations by patients. Typically, medication compliance refers to the patient taking their medication on their own. However, adherence can also include using surgical appliances, such as compression stockings, self-directed physiotherapy exercises, chronic wound care, or attending counseling or other therapy sessions¹. "The degree to which an individual's behavior corresponds with the agreement to any advice or recommendations from a health care professional who provides health care," is how the World Health Organization (WHO) defines medication adherence³. Patients suffering from long-term medical diseases such as asthma, diabetes, cardiovascular disease, and chronic obstructive pulmonary disease frequently need emergency care and may need to be hospitalized because they are not adhering to their prescribed treatment plans, which can lead to negative outcomes and increased treatment expenses. Approximately half of patients with chronic illnesses do not take their medications as prescribed, according to estimates from the WHO. Two primary ideas adherence and persistence are used to describe medication adherence. Although both ideas are essentially identical, adherence refers to using the medicine as directed throughout therapy, whereas persistence relates to the course of the pharmacological therapy¹. The evidence makes it clear that poor drug adherence prevents patients from experiencing the anticipated therapeutic benefit, which in turn raises their risk of hospitalization and other unfavorable health outcomes that eventually put more financial strain on them. As a result, it is acknowledged that improving medication adherence strategies and employing medication education programs may contribute to reduced healthcare expenses by improving population health overall¹.

An aging population is contributing to an increased prevalence of long-term health issues. As pharmaceuticals are necessary treatments for the majority of chronic diseases, prescribing them is one of the most prevalent interventions in industrialized health economies². But even in cases of chronic diseases, non-adherence continues to be a major obstacle to getting the best results possible from medications that are given correctly. A major obstacle to society and the economy is the enormous expenses associated with non-adherence, which are both health-related and financially detrimental².

The persistently elevated blood vessel pressure that is associated with hypertension. Because it frequently has no symptoms, hypertension is known as the silent killer³. To avoid complications that might result in death, they must manage their hypertension. Because it is so common to have vascular disease, stroke, renal disease, early mortality, and retinopathy, hypertension is a major global public health concern. It is the most important risk factor for cardiovascular disease, the leading cause of death globally each year, killing around 12 million people. As to the World Health Organization (WHO), the prevalence of hypertension is predicted to be 26.4% and affect 1 billion

people globally in 2018. According to the Ministry of Health's 2018 Basic Health Research, Indonesia has a 34.1% greater prevalence of hypertension than it had in 2013 (25.8%)⁵. In Central Java, 37.57% of people above 18 years of age have hypertension. Many factors, including lack of knowledge about treatment, more expensive drug prices, cultural and societal beliefs, the emergence of negative drug effects, the use of complementary drugs, and access to health services, as well as factors like education level, duration of hypertension, family support, the role of health workers, and motivation, are all explained by various research findings as to why people do not take their antihypertensive medications as prescribed⁶. Many issues with the factors that influence the adherence to hypertension medication regimens include people who do not have the financial means to pay for their treatment and who believe that their condition is not severe enough to require frequent checkups. A literature review study of the variables impacting drinking adherence in patients with hypertension⁷ is something the researcher is interested in doing in light of the aforementioned findings.

Medication adherence is an essential component of patient treatment and is required to meet clinical objectives. "Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment," according to the WHO's 2003 study on medication adherence⁸. "The extent to which the person's behavior (including medication-taking) corresponds with agreed recommendations from a healthcare provider" is how the World Health Organization defines adherence. It covers the start of the treatment, carrying out the suggested schedule, and stopping the medication⁹.

The World Health Organization (WHO) defines medication adherence as "the extent to which the person's behavior corresponds with the agreed recommendations from a health care provider"¹⁰. Medication adherence is an essential component of managing chronic diseases. The Global Initiative for Chronic Obstructive Lung illness (GOLD) states that airway restriction and persistent respiratory symptoms are the hallmarks of COPD, a prevalent, curable, and preventable illness. Dyspnea, a persistent cough, and sputum production are common long-term symptoms. Patients with COPD who adhere to their drug regimens optimally benefit from improved disease control and lower healthcare costs¹¹. Patients who follow their treatment plan more closely than those who don't are less likely to make their illness worse. Adherence to medication is essential for the efficient management of COPD and for addressing the illness's rising burden. On the other hand, inadequate compliance wastes resources and has a detrimental impact on health, leading to increased healthcare expenses¹¹.

According to several decades' worth of study, up to 20% of patients never fill a new prescription, and over 50% of those who do so stop their treatment within the first six months. Just 63% of patients completed the survey in a study of 139 research on diabetes, dyslipidemia, hypertension, and other cardiovascular diseases. This showed that patient, drug, and physician characteristics all function as comparable obstacles to adherence. Fear of side effects, expense, and complicated drug regimens were the most prevalent patient reasons. The most significant obstacles to medication adherence for a year were determined by physicians to be a lack of time, a strained relationship with the patient, and inadequate communication with the patient¹².

BEHAVIOURAL COMPONENTS OF MEDICATION ADHERENCE

Vrijens created taxonomy to categorize the behavior of taking medications, breaking down adherence into three behavioral components¹³:

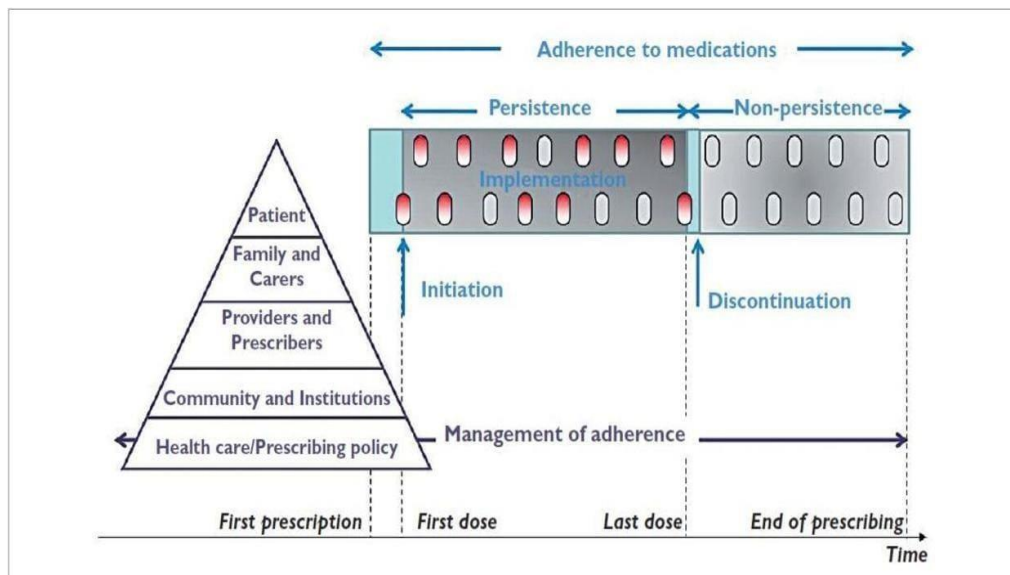
- ✓ Initiation
- ✓ Implementation
- ✓ Discontinuation

The term "initiation" describes when a patient takes a prescription drug for the first time. The degree to which a patient's conduct complies with the recommended dosage schedule once treatment has started is referred to as implementation. When a drug is discontinued, it means that it was last taken. Another name for the period of time between starting and stopping a medicine is persistence, while non-persistence is the act of a patient stopping a medication early on their own initiative without first speaking with their doctor¹³.

MEASUREMENT TECHNIQUES

The methods used to quantify non-adherence also vary widely, and each has its own set of restrictions. Direct observation or electronic adherence monitoring, for instance, has been proposed as the "gold standard" for measuring adherence¹⁴. These techniques can be expensive and intrusive, though, whereas more straightforward non-invasive techniques are typically more subjective. The variety of metrics employed in the literature increases the subject's complexity and makes it difficult to synthesize the non-adherence literature.

Figure 1 show the steps involved in managing adherence (dark blue) and adhering to medicine (light blue)



13.

Measures Involving Electronic Medication Packaging (EMP) Devices

"Adherence-monitoring devices integrated into the packaging of a prescription medication" is what EMP devices are called. They have a variety of options, but they all have these things in common:

- Digital displays;
- Audiovisual reminders to indicate when the next dosage is due;
- Recorded dosing events and saved records of adherence;
- Feedback on the performance of adherence in real-time¹⁵.

The characteristics listed above that are present in devices are arranged in decreasing order of popularity. While not all devices have these characteristics, it is crucial to record adherence performance in order to analyze data and customize treatments that are appropriate. Medication adherence studies are complicated because of the prevalence of the Medication Events Monitoring System (MEMS) EMP device, which makes it difficult to compile the non-adherence literature.

BENEFITS

Since medication adherence refers to the extent or coverage of patients who follow their provider's recommended prescription regimen, adherence is the most crucial factor. When patients follow the instructions for the timing, dosage, and frequency of all of their medications, it is thought that they are compliant. The crucial thing to remember is that once a patient leaves a clinic or doctor's office, it is up to them to continue managing their prescription regimen. Prescription adherence occurs throughout a patient's visit or upon hospital discharge¹⁶.

When a patient follows the recommended pharmaceutical regimen and takes their prescription(s) as directed, the cost of sickness is decreased. In the end, it would lower the total cost of treatment by assisting patients in feeling better and recovering more rapidly. This would lessen the patient's direct and indirect drug costs. Additionally, the negative effects are decreased by drug adherence. Medication adherence measures would be deciding factors for specific patients who are not compliant with the therapy for various reasons, and it increases the patient's quality of life while also being advantageous for the clinicians¹⁷. Occasionally, a variety of data sources are available. Adherence to medication is essential for achieving the intended results for patients, as medications do not exhibit their therapeutic effects in non-compliant individuals.

Role of Pharmacist in Medication Adherence

The following strategies can be used to strengthen the bond between patients and pharmacists¹⁸:

- ❖ Pharmacists ought to be amiable and readily available to patients.
- ❖ Their communication abilities have to be excellent.
- ❖ Pharmacists ought to take into account the patients' physiological requirements.
- ❖ They ought to provide patient counseling and enhance patients' education.

- ❖ It is recommended that they support each patient in talking about their concerns without cutting the session short or interrupting it.
- ❖ It is important to extract the patient's expectations, feelings, and perspective of the condition.
- ❖ Active listening should be employed, and they ought to be kind toward the sufferers.
- ❖ They clearly explain everything to the patients.
- ❖ They must to assess the patients' comprehension of the illness and the prescribed medications.
- ❖ Together with the patients, they should go over therapy options.

FACTORS INFLUENCING OF MEDICATION ADHERENCE

Even though the group in go adherence measurements described themselves as calm and collected, they were classified as direct and indirect in several other studies. Because every patient's circumstances are unique, it is challenging to anticipate drug adherence. Three categories may be used to describe the elements impacting adherence or other health-related behaviors, based on scientific research¹:

Predisposing factor

The patients' demographics, as well as their knowledge, attitudes, and perceptions regarding the nature, severity, origin, and prevention of sickness, as well as the various forms of treatment regimens, are among these determinants. According to certain thought patterns, the health belief model, which was created in 1974, predicted changes in behavior linked to health, including adherence. According to this model, the patients must adhere to the following sequence of belief events in order for them to be considered adherents:

- ❖ The patients must believe that their health is in danger.
- ❖ The patients must recognize the potential consequences of the condition, such as symptoms, missed work, financial hardship, etc.
- ❖ After assessing their circumstances, patients should feel that the advantages of therapy outweigh the drawbacks.
- ❖ They should be motivated to take their medications as prescribed.

Enabling Factors

These are the resources and abilities needed for compliance. The capacity of the patient to adopt behaviors that support medication adherence and, consequently, schedule a visit with the doctor to acquire a prescription order is referred to as skill. The ability and accessibility of healthcare facilities, including physicians, pharmacies, clinics, and hospitals, is referred to as resources.

Reinforcing Factors

Patients would have sufficient support from peers, members of the local community, healthcare practitioners, and society at large, who would urge them to take their medications as prescribed. Whether the

patient's family supports medication adherence depends on these criteria. Depending on each person's attitude or conduct, this support might be either beneficial or bad. Some people may have greater influence than others.

Choosing a Suitable Medication Adherence

A medicine adherence measure that meets all of these criteria would be inexpensive, practical, user-friendly, simple to implement, extremely reliable, and flexible¹⁹. Nevertheless, as each of these gold standards has the aforementioned disadvantages, no one metric can satisfy them all. Cost-effectiveness ratios play a major role in the general preference for subjective and objective metrics in clinical and research contexts, respectively. In a busy clinical setting with limited resources and a population with moderate to high literacy, self-report questionnaires are more beneficial due to their decent predictive value. Interviews with patients by doctors are favored in populations with poor literacy rates, or they serve as a supplement in cases where patients are already anticipated to be low medication adherers. While pill count is an objective metric, its primary application in ordinary clinical practice is due to staffing requirements and time constraints. Pharmacy refill measures are preferable to employing EMPs for a sizable study population where accuracy and cost are balanced. In the meanwhile, patients and researchers alike find direct methods to be excessively costly and invasive, thus they are rarely employed²⁰.

PROBLEMS WITH NON-ADHERENCE

From the many views of healthcare providers, therapeutic compliance is the most significant clinical concern. There are primarily two reasons: first, non-compliance may have a significant impact on the patient's care results and have direct medical repercussions²¹. Furthermore, in a number of illnesses and ailments, non-compliance is closely linked to subpar treatment results. In the health practice, non-compliance takes many different forms. Non-compliance is a regular occurrence in clinical practice or medicine on a daily basis. Regarding treatment methods such as exercise or nutrition, the term "compliance" is either not well defined across studies done under different circumstances or it doesn't seem to fit any common standards for what constitutes acceptable or good compliance¹.

In addition to direct consequences, noncompliance with illness management guidelines might lead to indirect consequences as well. Moreover, the bulk of patients who did not comply well with the recommended course of treatment eventually stopped taking all of the drugs, depriving them of the therapy's purported benefits. Non-adherence to the treatment led to a rise in the financial burden on society in addition to a reduction in the clinical outcome²². An increase in urgent care visits, hospitalizations, and treatment costs, for instance, have all been linked to therapeutic non-compliance. The patient's quality of life is negatively impacted by noncompliance.

Patients' deliberate and inadvertent behaviors are reflected in their non-compliance with the therapy. Various causes, such as medication costs, lack of knowledge, side effects, forgetfulness, or just forgetting to take medication, can lead to major safety problems when it comes to non-adherence. Moreover, the cost of prescription drugs is the component of health care costs that is increasing the fastest. For this reason, it is important to prioritize

addressing the negative effects of therapeutic non-compliance in order to achieve desired clinical and economic outcomes²².

HEALTH IMPACTS OF NON-ADHERENCE

Adherence strategies are predicated on the implicit belief that adherence enhances patient outcomes. They examined 63 studies examining the correlation between outcomes (such as survival, reported pain, blood pressure control, visual acuity, cholesterol levels, and organ rejection) and adherence to medical advice (including prescribed medication, diet modification, physical activity, and eye patching)²³. In general, high adherers had a three times better chance of having a positive treatment outcome than poor adherers. Furthermore, there is a 2-3 fold higher chance of death for those with "poor" adherence than for those with "good" adherence². Improvements in any one medical therapy may not have as much of an impact on population health as enhancing drug adherence²⁴.

The impact of non-adherence may be more problematic for some health conditions than for others, depending on the role and outcome of a particular medicine. The health conditions in which non-adherence and non-initiation have been shown to affect clinical outcomes (e.g., increase in severity of symptoms, morbidity and mortality) include HIV, cancer, diabetes, asthma, cardiovascular disease (CVD), mental illness, organ transplant, etc²⁵. Among these conditions, non-adherence and non-initiation are arguably most important.

The fact that non-adherence could not necessarily be detrimental to the patient must be understood. Should the prescription be unsuitable and maybe harmful, it might be protective, or if it's not the best, it could have no impact at all²⁵. Choosing the right diagnosis and course of therapy for a patient is a "therapeutic experiment" that the prescriber conducts, and the patient's adherence to the plan determines the outcome.

FUTURE DIRECTIONS

Even though the above-mentioned correlates of non-adherence have been the subject of much research, traditional methods of mapping these correlates (such as the WHO framework) have significant drawbacks. Extensive research has previously been conducted to discover correlates of non-adherence, which may be utilized to determine risk variables associated with non-adherence. However, we must go beyond risk factors for non-adherence to gain a deeper comprehension of the effects that certain correlations have on patients across time and across different therapies.

Focus on the interaction between an individual and a particular disease/treatment

A significant drawback of conventional methods for mapping correlates of non-adherence is that the degree to which a particular correlation will have an impact may differ from person to person and even over time within the same person²⁵. More research is required to determine how possible adherence variables affect people's motivation and capacity to follow suggestions consistently throughout time and across various treatment modalities.

Focus on modifiable factors relating to non-adherence

The fact that sociodemographic and trait characteristic approaches to investigating the correlates of non-adherence frequently concentrate on finding unchangeable elements associated with non-adherence is another drawback.

Apply theoretical frameworks to understand correlates of non-adherence that can be used to guide intervention design

These study methodologies are frequently lacking in theoretical foundation, even in cases when changeable elements are examined. Future research should focus on creating and utilizing theoretical frameworks that attempt to combine various correlates into a logical and practical model that may direct the creation of treatments, as this will be most helpful in supporting the development of interventions to encourage adherence.

Triangulate measurements of non-adherence

Therefore, it is recommended that future research look into a combined approach to measuring non-adherence²⁶, in which objective forms of adherence measures, like prescription refill rates or electronic monitoring, are combined with self-report measures to produce combined, all-encompassing assessments of adherence.

COMMUNICATING WITH THE PATIENT

The perceptions of the efficacy of care and treatment adherence are closely linked to a healthy, trustworthy connection between the doctor and the patient. Furthermore, it has been linked to a higher probability of patients disclosing details about how they utilize medications, including problems and obstacles that prevent appropriate use²⁷. Conversely, the best indicator of patients' trust in their doctors is the doctor's communication style (e.g., active listening, offering emotional support, giving clear and comprehensive information, involving the patient in the decision-making process regarding treatment, and allocating sufficient time for patient questions). This communication style also has a direct correlation with improved medication adherence²⁷. Asking the patient directly about adherence is one method of assessing medication adherence. Other methods include keeping an eye on the patient's drug level, lack of therapeutic response, and appointment skipping. Electronic monitoring methods include pill counting, medication event monitoring systems, and pharmacy fill rates²⁸.

The pharmaceutical interest model is a prototype patient-centered approach that emphasizes patient choice. It offers a clarifying theory, known as the Choice triangle, to help explain how and why patients decide to begin or continue taking a medicine. According to the Choice Triad, patients decide whether to begin or continue taking a drug because

- They feel as though there is an issue with them;
- They are driven to test a medicine because they think it can assist alleviate their symptoms;

- They think the advantages of the medication exceed the drawbacks. With very few exceptions, this paradigm does not consider a patient's decision to stop taking or refuse to take a drug as resistance.

The pharmaceutical interest model offers targeted, behaviorally defined interviewing strategies for identifying patient concerns at every stage of the Choice Triad and then resolving those issues.

CONSEQUENCES OF POOR ADHERENCE IN CHRONIC DISEASES

Numerous investigations have verified that inadequate treatment compliance is linked to unfavorable health consequences that surpass inadequate management of clinical measures. A low level of adherence has been linked to a higher risk of cardiovascular events such as myocardial infarction, stroke, angina pectoris, or heart failure, as well as damage to target organs such as left ventricular hypertrophy and albuminuria, among patients with diabetes, hypertension, or dyslipidemia. Suboptimal adherence in nephrology is linked to a higher risk of declining kidney function³⁰. Nevertheless, a lack of adherence has a detrimental impact on several other areas of managing illnesses, such as heightened illness that may need acute hospitalizations, escalated medical expenses, and naturally, a decline in the quality of life for patients²⁹.

QUALITY OF LIFE

World Health Organization (WHO) defines quality of life (QOL) as an individual's assessment of their place in life in relation to their objectives, standards, and concerns as well as the culture in which they live³³. Due to the lengthy treatment periods required for patients with chronic illnesses, quality of life (QoL) and treatment adherence have emerged as critical metrics for evaluating the efficacy of the disease management strategy. Enhancing the quality of life of patients is crucial for the effective management of chronic illnesses, since a low quality of life can contribute to the emergence of problems linked to the disease³².

QOL, or quality of life, is a crucial metric for assessing the effects of chronic illness. It is a metric used to determine the general state of health in a population and encompasses social, emotional, and physical facets of health and well-being. Due to its limitations on physical, social, and leisure activities, COPD sufferers' quality of life is significantly impacted. Numerous characteristics, including sex, the severity of the condition, smoking status, the existence of co-morbidities, the frequency of exacerbations, and hospital admissions, are linked to a lower quality of life and COPD³⁴. Thus, research on QOL and non-adherence in COPD patients will benefit policy makers and healthcare professionals³⁴.

The World Health Organization (WHO) reported that 19.4 million people in Pakistan had diabetes in 2019, placing the country in fourth place. With an expected 26.2 million people living with diabetes in 2030, this figure is predicted to rise to 26.2 million by 2045, making it the third most populous country in the world. Ninety percent of instances of diabetes mellitus worldwide are type 2 diabetes mellitus (T2DM), which affects the majority of people.

Since type 2 diabetes is becoming more prevalent in Pakistan at an alarming pace, immediate action is required to treat the condition and increase medication adherence among diabetes³².

Heart failure, stroke, and coronary artery disease are among the major risk factors for cardiovascular disease associated with hypertension. In Poland and across the world, these illnesses are among the leading causes of death, morbidity, and disability. The quality of life (QOL) of individuals with hypertension is impacted by several factors, including the chronic nature of the condition, its diagnosis, the detrimental effects it has on the patient's physical, emotional, and social well-being, and features of pharmaceutical treatment³⁵. The adoption of strategies to improve the efficiency of antihypertensive medication and, consequently, lower mortality and morbidity, as well as non-adherence to treatment guidelines, are among the reasons of diminished quality of life and its effects that need to be identified. A suitable quality of life (QOL) may play a role in the positive outcomes of antihypertensive medication, according to the research that is currently available³⁵.

QOL SCALE

Mobility, self-care, regular activities, pain/discomfort, and anxiety/depression are the five (5) domains that make up the EQ-5D-5L21 quality of life scale. There are five severity levels for each domain: no problem, slight problem, moderate problem, severe problem, and extreme problem. The aim of the research was to evaluate the correlation between QOL and the degree of compliance with treatment guidelines in senior hypertension patients, as well as to investigate the influence of specific variables on the adherence level³⁶.

CHALLENGES

Recently, there has been a lot of interest in creating technology-based methods to increase adherence. These consist of social media, telemedicine, text messaging, and smart phone apps. Improvements in medication adherence and clinical endpoints, such as in patients with diabetes or hypertension and other chronic diseases²⁹, have been reported with the use of telemonitoring, mobile health tools (mHealth), and digital health. However, the impact on morbidity and mortality needs to be demonstrated using carefully conducted prospective randomized controlled trials in order to determine their true added value. A broader use of these technologies in clinical practice is still hampered by certain issues, despite the fact that some patients find them to be well received³¹. Among them is the general physician's capacity to oversee these methods in the clinical context. There are still unanswered concerns about data confidentiality and how easily elderly patients can use the techniques.

CONCLUSION

Medication Adherence is a major issue in the completion and effectiveness of treatment of chronic ailments. The patient's quality of life is negatively impacted by noncompliance. A broader use of the newer technologies in clinical practice is still hampered by certain issues, despite the fact that some patients find them to be well received. Still, new systems will likely be created in the future, and they will likely offer a fascinating supplementary strategy

to behavioral and motivational interventions that support the patient-physician relationship which is still the cornerstone of good adherence.

REFERENCE

1. Juhi Singh, Md Shamshir Alam, Anuj Malik, Shubham Singh Tyagi, et.al. Ways to Improve Medication Adherence in Chronic Disease Patients. *J Evolution Med Dent Sci*. 2021; Vol. 10 (36): 3172.
2. Sarah-Jane F. Stewart et.al. Medication non-adherence: health impact, prevalence, correlates and interventions. *Psychology & health*. 2023; Vol.38, (6):726–765.
3. Morrissey EC, Durand H, Nieuwlaat R, Navarro T, Haynes RB, Walsh JC, et al. Effectiveness and content analysis of interventions to enhance medication adherence and blood pressure control in hypertension: A systematic review and meta-analysis. *Psychol Health*. 2017; 32(10):1195–232.
4. Chinnakali P, Mohan B, Upadhyay RP, Singh AK, Srivastava R, Yadav K. Hypertension in the elderly: prevalence and health seeking behavior. *N Am J Med Sci*. 2012; 4(11):558–62.
5. Edy Soesant, Indra Ramadlan, et.al. Factors affecting medication adherence in hypertension patients. *Bali medical journal*. 2021, Vol. 10, (3): 1364-1370.
6. Indonesian Ministry of Health Research and Development Agency. National Health Indicator Survey Report. 2016. 1–245 p.
7. Ekarini D. Factors Associated with the Level of Hypertension Client Compliance in Undergoing Treatment at the Gondangrejo Karanganyar Community Health Center. *J Kesmadaska*. 2012; 3(1):1–13.
8. Wai Yin Lam and Paula Fresco. Medication adherence measures. *BioMed Research International* 2015.
9. B. Jimmy and J. Jose, “Patient medication adherence: measures in daily practice,” *Oman Medical Journal*. 2011; 26(3): 155– 159.
10. World Health Organization. Adherence to long-term therapies: evidence for action.
11. Bimbishar Bhattarai, Ramesh Walpola, et.al. Barriers and Strategies for Improving Medication Adherence among People Living With COPD. *Respiratory care*. 2020; vol 65 (11):1738-1739.
12. Helin-Salmivaara A, Lavikainen PT, Korhonen MJ, et al. Pattern of statin use among 10 cohorts of new users from 1995 to 2004: a register-based nationwide study. *Am J Manag Care*. 2010; 16:116-122.
13. Vrijens, B., De Geest, S., Hughes, D. A., et.al. A new taxonomy for describing and defining adherence to medications. *British Journal of Clinical Pharmacology*. 2012; 73(5):691–705.
14. Chan, A. H. Y., Reddel, H. K., Apter, A., Eakin, M., Riekert, K., & Foster, J. M. Adherence monitoring and e-health: How clinicians and researchers can use technology to promote inhaler adherence for asthma. *The Journal of Allergy and Clinical Immunology*. 2013; 1(5): 446–454.
15. K. D. Checchi, K. F. Huybrechts, J. Avorn, and A. S. Kesselheim. Electronic medication packaging devices and medication adherence: a systematic review. *The Journal of the American Medical Association*. 2014; vol. 312 (12):1237–1247.

16. Cramer JA, Scheyer RD, Mattson RH. Compliance declines between clinic visits. *Arch Intern Med.* 1990; 150(7):1509- 10.
17. Vrijens B, Antoniou S, Burnier M, et al. Current situation of medication adherence in hypertension. *Front Pharmacol.* 2017; 8:100.
18. Roter DL, Hall JA. Why physician gender matters in shaping the physician-patient relationship. *J Womens Health.* 1998; 7(9):1093-7.
19. E. Vermeire, H. Hearnshaw, P. Van Royen, and J. Denekens, "Patient adherence to treatment: three decades of research. A comprehensive review," *Journal of Clinical Pharmacy and Therapeutics.* 2001; vol. 26(5): 331–342.
20. K. C. Farmer, "Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice," *Clinical Therapeutics.* 1999; vol. 21(6):1074–1090
21. Bond WS, Hussar DA. Detection methods and strategies for improving medication compliance. *Am J Hosp Pharm.* 1991; 48(9):1978-88.
22. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther.* 2001; 23(8):1296-310.
23. DiMatteo, M. R., Giordani, P. J., Lepper, H. S., & Croghan, T. W. Patient adherence and medical treatment outcomes A meta-analysis. *Medical Care.* 2000; 40(9):794–811.
24. Haynes, R. B., McDonald, H. P., & Garg, A. X. Helping patients follow prescribed treatment clinical applications. *JAMA.* 2002; 288(22):2880–2883.
25. Horne, R., Weinman, J., Barber, N., Elliot, R., & Morgan, M. Concordance, adherence and compliance in medicine taking. National co-ordinating centre for NHS service delivery and organisation R and D. 2005:1–309.
26. Dobbels, F., Berben, L., De Geest, S., Drent, G., Lennerling, A., Whittaker, C., Kugler, C., Force. The psychometric properties and practicability of self-report instruments to identify medication non-adherence in adult transplant patients. *Transplantation.* 2010; 90(2): 205–219.
27. Stephen A. Brunton MD. Improving Medication Adherence in Chronic Disease Management. *The journal of pharmacy practice.* 2011; vol 60 (4).
28. Davis D, Galbraith R. Continuing medical education effect on practice performance: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest.* 2009; 135(3):42S-48S.
29. Michel Burnier. The role of adherence in patients with chronic diseases. *European Journal of Internal Medicine.* 2023.
30. Peacock E, Joyce C, Craig LS, Lenane Z, Holt EW, Muntner P, Krousel-Wood M. Low medication adherence is associated with decline in health-related quality of life: results of a longitudinal analysis among older women and men with hypertension. *J Hypertens.* 2021; 39:153–61.
31. Burnier M. Improving blood pressure control in the community: can new technologies help us? *Am J Hypertens.* 2007; 20: 949.

32. Abdul Majeed, Muhammad Rehman, Iltaf Hussain, et.al. The Impact of Treatment Adherence on Quality of Life among Type 2 Diabetes Mellitus Patients – Findings from a Cross-Sectional Study. *Patient Preference and Adherence*. 2021;15 475–481.
33. Christeena S Varghese, Harshita Krishna Naik, et.al. A Study on Medication Adherence and Quality of Life in Patients with Chronic Kidney Disease. *Journal of Drug Delivery and Therapeutics*. 2020; 10(3-s):52-60.
34. Shorouk Mohsen, Fadia Zaki Hanafy, et.al. Non-adherence to treatment and quality of life among patients with chronic obstructive pulmonary disease. *Lung India*. 2019; 36:193-8.
35. Bartosz Uchmanowicz, Anna Chudiak, et.al. The influence of quality of life on the level of adherence to therapeutic recommendations among elderly hypertensive patients. *Patient Preference and Adherence*. 2018; 12: 2593–2603.
36. Euqator Group. EQ-5D-5L; 2020.