Int. J. Pharm. Investigation, 2024; 14(4):1079-1084.
https://www.jpionline.org

Review Article

Assessment of Medication Adherence and Common Non-Adherence: A Routinely Overlooked Hurdle

Sindoora Dabbe Seetharama, Akalu Srinivas Kamakshi Shriya, Vaishnavi Bharat Pawar, Balaji Sathyanarayana Gupta, Shilpa Palaksha*

Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Mysuru, Karnataka, INDIA.

ABSTRACT

Medication adherence has always been an integral aspect to achieve any healthcare benefit of pharmacological treatment. Although health care has evolved remarkably, the need for conducting studies on medication adherence has its own noteworthiness, for instance, in clinical settings, the incapability to accurately identify medication non-adherence can lead to unwarranted intensification of the treatment. Hence assessment of medication adherence and common non-adherence plays a pivotal role in improving adherence in the future by promoting employment of techniques that may be beneficial in overcoming and preventing the global issue of non-adherence. The literature search was done using the keywords as mentioned below in EBSCO; further on the snowball method was employed. There are two types of measuring medication adherence: direct and indirect. Direct measurement for quantification is utilitarian in establishing a YES/NO result rather than elaborating upon the causes of non-adherence. Indirect measurements are the ones which cannot be quantified accurately. There are numerous types of direct and indirect measurements. Non-adherence can be classified as direct, indirect, intentional and nonintentional. Various factors contribute towards non-adherence such as patient knowledge, doctor-patient relationship and unintentional drivers. Approaches to overcome non-adherence can be from healthcare professionals, patients, pharmaceutical companies or system-based. Socio-economic factors, system, therapy, patient, condition-related factors constitute barriers of medication adherence.

Keywords: Medication adherence, Pharmacist, Non-adherence.

Correspondence:
Ms. Shilpa Palaksha
Associate Professor, Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education and Research, SS Nagar, Mysore, Karnataka, INDIA.
Email: shilpapalaksha@jssuni.edu.in
ORCID:0000-0001-5279-308X

Received: 24-01-2024;
Revised: 14-02-2024;
Accepted: 02-05-2024.

INTRODUCTION

Medication adherence has always been an integral aspect to achieve any healthcare benefit of pharmacological treatment. WHO defines medication adherence as "The extent to which a patient's behaviour in taking medication, following a diet and executing lifestyle changes, corresponds with agreed recommendations from a health-care provider."[1] Although health care has evolved remarkably through the years, the need for conducting studies on medication adherence has its own noteworthiness as there still exists scope for improvement, for instance, the incapability to accurately recognize medication non-adherence can lead to unwarranted intensification of the treatment causing ripple effect on health costs, adverse events and may reduce adherence rates due to the unreasonably high medication burden and treatment convolution.[2] Non-adherence prevails due to various factors ranging from 'trust' in healthcare professionals advice all the way to lack mobility or caregivers. At times, the disease condition themselves and numerous other factors contribute to medication non-adherence, for instance, failure to recall the time of administration, complex regimen, undesirable side effects and expensive medications can also be one of the factors paving a path to medication non-adherence. Studies have revealed that hardly 50% of the prescriptions are taken correctly. Among patients diagnosed with chronic conditions, such as hypertension, only 51% take medications continuously. Others may end up either taking fewer medications than prescribed or stop taking any at all.[3]

MATERIALS AND METHODS

The literature search for the review article was conducted on 30th July, 2023 using EBSCO wherein peer-reviewed and full-length articles were chosen. Later, on 5th August, 2023 the search was updated to include non-peer reviewed articles and textbook DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition authored by *DiPiro et al.* Further on, the snowball method was employed to include definitions, statistics and other relevant information based on the need. The study was confined to articles available in the english language and published in

DOI: 10.5530/ijpi.14.4.118

the period 2019 to 2023 to ensure relevance of the data to the current scenario. An array of search terms was used in context to adherence, medication adherence, medication non-adherence, clinical pharmacist, assessment of adherence, questionnaires and barriers of non-adherence.

RESULTS

Direct Measurement

Direct measurement for quantification is utilitarian in establishing a YES/NO result rather than elaborating upon the causes of non-adherence.

Drug/Metabolite Detection in the blood is the most accurate method of adherence detection. This method is invasive and expensive. Patients may take the medication consciously a few hours or days before testing which may manipulate the results.[2]

Smart Pills

AbilifyMyCite is an FDA-approved application with Ingestible Event Marker (IEM) incorporated with sensors which keeps track on ingestion and sends a signal to a wearable patch and the information is stored in the cloud data.[5,6] (3) *Direct observation*: Directly observing whether the patient is receiving the medication or not.[7]

Indirect

Patient Interviews

While interviewing patients about their medications, minimal and biased information may be available about their adherence to the dosing schedule. Thence, this method is sparsely adopted in research to evaluate adherence. A numerical value is estimated between 0 and 100 by calculation of ratio of no. of pills taken by the patient and the units of pills prescribed over a given time interval. This is called Drug Adherence Rates (DAR). However, the results might be subjected to recall bias, especially when the time period is prolonged. The cut off mark for patient adherence is individualised. It is of utmost importance to include questions like "have you skipped any medication in the previous week?" Patients may try to mislead the healthcare professional by refuting skipped doses. Whereas preceding with an empathetic statement such as, "Some patients may find it difficult to remember taking all their medications" may reassure patients allowing them to open up.[2]

Medication Measurement

Pill Count is the ratio of the units of medications ingested to the units of medications prescribed. Counting pills might give limited data regarding patterns of non-adherence after certain weeks or months after dispensing.[2]

Electronic Monitoring Devices

Electronic Medication Devices have numerous features including dosing events records, electronic displays, audio/visual reminders, monitoring and feedback of adherence performance based on which adherence is analysed. In many studies, the MEMS (Medication Event Monitoring System) are frequently used.

Prescription Record Review

Although this can be of great use for medications of chronic illness, patterns of over/under consumption for periods less than that between refills cannot be assessed.

Questionnaires

These are scales which are validated against various measures to assess the regimen for a wide range of diseased populations. A few Examples are Brief Medication Questionnaire (BMQ), Medication Adherence Rating Scale (MARS), Adherence to Refills and Medications Scale (ARMS), Morisky *et al.* developed an 8-scaled questionnaire to estimate adherence with antihypertensive therapy, The Hill Bone Compliance to High Blood Pressure Therapy Scale consists of 14 items, among which 8 assess the medication taking behaviour in patients with hypertension.[2] Patel *et al.* developed the Medication Adherence Assessment Scale which includes 09 YES/NO questions.[8]

Continuous, Multiple-Interval Measures of Medication Acquisition (CMA)

It is the proportion of the number of days the medication supply was procured to the total number of days indicating the number of days of medicine supply was procured but not the quantity consumed.[9]

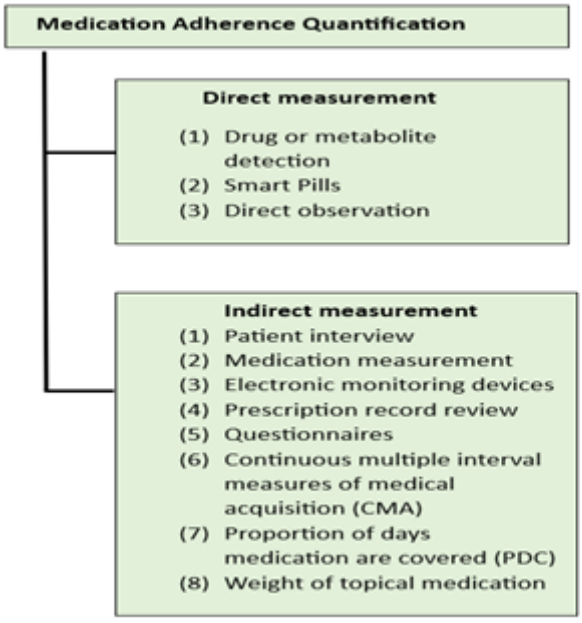

Figure 1: Factors Adherence Quantification.[2,4]

Proportion of Days Medications Covered (PDC)

It is a measurement of persistence wherein the total number of days of medication supply is divided by the number of days of study participation and is calculated in terms of percentage thereby yielding an approximate measure of medication adherence.[9]

Weight of Topical Medications

The weight of the remaining amount of the medication is compared with the log book of daily use. In clinical trials involving topical applications, the weights of the medication tubes were primary tools of measuring adherence.[10]

Repercussions of non-adherence usually include worsened therapeutic outcomes, aggravation of disease coupled with early onset of complications, increase in frequency and length of hospital stay. In order to achieve medication adherence, at least three steps must be abided by the patient- acceptance, persistence and execution of all the instructions by the Health Care Professional (HCP). Although undermedication occurs more frequently than over medication, it is a significant cause of concern especially with drugs which are extremely toxic and likely to cause adverse effects and in pathological states where the danger of overuse (addiction or abuse) of drugs exists.[2]

A concise flow chart regarding direct and indirect measurements is mentioned in Figure 1.

Types of Non-adherence

Primary Non-adherence (Initiation Non-adherence) Occurs when prescribed medications are not filled at a pharmacy. Secondary Non-adherence occurs when patients miss doses, discontinue therapy prematurely or takes fewer doses than the prescribed quantity. This gradually develops over time. Unintentional Non-adherence Occurs when patients are unable to refill prescriptions inadvertently. This could be either due to lack of mobility or financial support. Intentional Non-adherence (Volitional Non-adherence/ Intelligence Non-adherence) Non-adherence in spite of availability of medications. This could be due to patient-related factors such as disbelief in the medication or prescriber, apprehensive of side effects or carelessness.[2]

Barriers to Medication Adherence

Socio-Economic Factors

Various socio-economic factors that may influence medication adherence include education, affordability, employment, transportation, caregiver and family support. Education plays a vital role in creating awareness regarding the benefits of medication and the consequences of non-adherence. Affordability encompasses economic status, employment status and insurance coverage. Therapies that demand more expenditure like chemotherapy, radiation therapy and medications for chronic diseases can impose a significant financial burden. Not all patients, especially from remote areas can have frequent access to pharmacies for refills and hospitals for follow-ups. Patients with mental illness, paediatric and geriatric populations, immobilised patients may need additional support for adhering to their prescribed regimen. Those suffering from stigmatised conditions require emotional support from society in general to overcome the bigotry.[7]

System Related Factors

Doctors may not be able to educate all the patients regarding the significance of medication adherence due to lack of time or the high patient count. Consequently, patient's medical history may be incomplete leading to misdiagnosis and prescription errors. Additionally, clinical pharmacists are not posted in all settings for counselling patients and community pharmacists may not be aware or qualified for educating patients regarding optimal use of medications. Occasionally, the HCPs may not be mindful of the latest policies of prescribing.[7]

Therapy Related Factors

Diseases that stipulate complex medication regimens and polypharmacy may notably cause medication non-adherence as

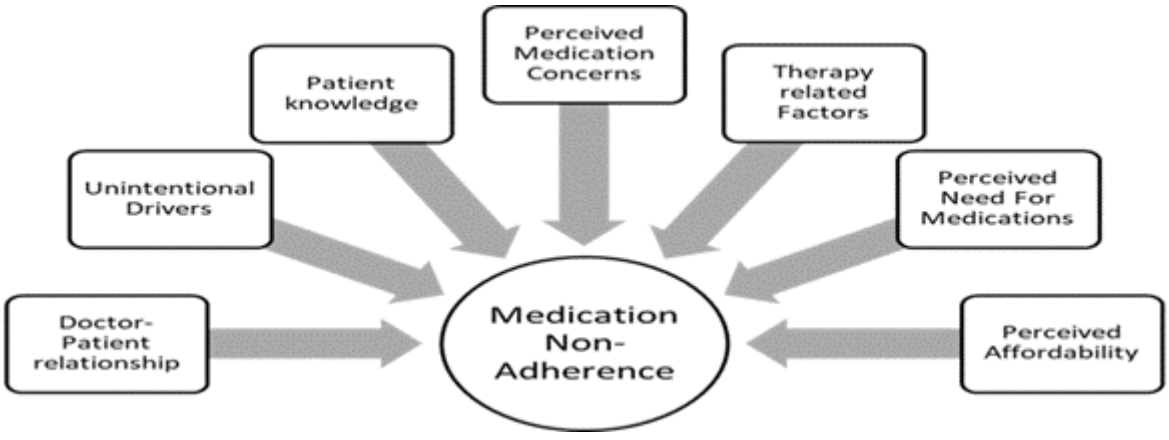

Figure 2: Barriers to Medication Adherence.

not all patients will understand the regimen thereby aggravating the burden of medication intake. Frequent alterations in treatment (tapering dose of steroids) can confuse the patients sometimes leading to discontinuation or overtaking of medicines. Therapies that include not only drugs that take longer to show effect (Anti-TB drugs) but also those that must be taken in spite of symptomatic improvement (Antibiotics) can easily result in non-adherence and set off early onset of complications (ARDS, Antimicrobial Resistance). Adverse effects of any given regimen are also an important cause of non-adherence.[7]

Patient-Related Factors

For any treatment to be effective, patients must first of all trust the instructions of the HCP, for lack of trust can make them heed to various sources, unprofessional or professional. This often precipitates discontinuation of current medicines or concomitant use of folk, herbal or vitamin supplements without informing the HCP. Therefore, health literacy of patients and good patient-professional relationships can not only refine the understanding of disease and drugs but also encourage the patients to express concerns regarding the side effects of the drug. Factors such as forgetfulness and disapproval are also of significance in this regard.[7]

Condition Related Factors

Just as understanding their medical condition can improve patients' adherence to medication, it can also lead to non-adherence. This is true particularly when the disease is severe or uncurable. Disease progression in spite of treatment or due to treatment itself (Selective serotonin reuptake inhibitors-associated apathy syndrome) can cost the patient's trust leading to non-adherence. Worsening disease and/or comorbidities induce a decline of functional capability of patients raising concerns of non-adherence.[7] Various factors affecting medication non-adherence is mentioned in Figure 2.

Techniques to Overcome Non-Adherence

As medication non-adherence is multifaceted, there is no one stop solution to overcome the hurdles; thus, our strategy should be multimodal. There are several options available, which include.[7]

Efforts from system

A method should be built to acquire continuous information in order to give individualized medicines and ensure information continuity. Simultaneously, the secrecy of patient data must be preserved. This should be implemented by system stakeholders to increase drug adherence.[7]

Efforts from Health Care Professionals

SIMPLE approach Simplifying regimen characteristics, imparting knowledge, modifying patient beliefs, Patient communication, Leaving the bias and Evaluating adherence.[7]

Printed Patient Information Leaflets (PILS)

To educate the patient about the medication and serve as a reference material if the patient has trouble remembering the instructions given by the HCP in the near future.

Accessibility in Remote Areas

Making pharmaceuticals available in outlying locations allow a huge number of patients to receive their medications on a regular basis, improving adherence rates.

Electronic Reminder

Reminding, alerting, educating, aiding treatment and administration, feedback, and reporting are some of the features of eHealth applications.[12]

Regimen Simplification

Once-daily dosing is said to have notably higher adherence rates compared to more frequent dosing schedules.[12]

90 Days Supplies

Providing patients with medications for 90 days instead of a week or a month can reduce the burden of frequent pharmacy visits whilst allowing pharmacist to keep track of patient medication consumption.[12]

Automatic Refills

Refilling prescriptions a few days ahead of the last dose of medication can prevent medication non-adherence, especially in geriatric patients and those who have physical or cognitive impairment.[12]

Side Effects

Priorly making patients aware of the potential side effects would result in higher adherence rates.[12]

Reducing Medical Costs

Medication costs can be reduced by providing medications under their generic names.[13]

Providing Incentives

Studies on incentive-based medication adherence for medications of alcohol dependence, have shown that incentives boost adherence by 20 percent.[14]

Patient Counselling

Genuine interaction with patients is an essential component of drug adherence. Pharmacists play a crucial role in patient education.[3]

Interactive "Gamification"

By converting healthy activities into games with rewards, it is possible to generate high-value interactions with patients by focusing on the psychological components of game mechanics.[6]

Efforts from Patient

(1) Patients who are motivated are more likely to stick to their regimen, hence counselling the patient is beneficial. (2) Taking medications at the same time every day may help in remembering and hence improve adherence. (3) Coupling medications with a routine activity like post or prior to meals or just before leaving for work. (4) Using reminders or containers with partitions for different times of administration would reduce perplexity in dose schedules. (6) Refilling pill containers at the same time weekly. For instance, every Sunday afternoon after lunch. (7) Purchasing timer caps for pill bottles and setting them 'on' when the next dose is due. (8) While travelling, packing medications for a few extra days to be prepared for unintentional extensions of the trip. (9) While flying, keeping medications in cabin baggage to avoid loss during baggage transfers or temperature fluctuations in the cargo leading to loss of chemical integrity of the constituents.[3]

Efforts from Pharmaceutical Company

Pharmaceutical companies can play a crucial role by compounding medications with varied combinations for special populations and patients sensitive to certain ingredients and also for disease conditions that demand complex regimens. The role of pharmaceutical compounding in promoting medication adherence is underexploited. A few techniques curated for paediatrics are flavoured lollipops, lozenges and syrups are prepared to enhance the acceptance of medications and therefore increase medication adherence. When children get to choose among the flavours of their choice, the acceptability of medications will be notably increased. Drugs that can be fabricated into oro-dispersible formulations present the convenience of administration without the use of fluids as they can be easily chewed or swallowed as it is thereby improving adherence in general. Geriatric patients are often lifetime customers for pharmaceutical companies as they will be mostly under chronic medications. Simplifying regimens and diversifying dosage forms can significantly improve adherence as it reduces the imposition of ingestion of large numbers of tablets and pills. For example, mouthwashes for Chemo Induced Oral Mucositis (CIOM) are conventionally incorporated with diphenhydramine, lidocaine and antacids but now the addition of antibiotics like tetracycline or nystatin has become utilitarian in the treatment of various infections of the buccal cavity in cancer patients. Companies can adopt skillful methods in tailoring the constituents of a dosage form to enable utilization of the product by sensitive patients who are intolerant to various constituents. For example, methylcellulose can be used as a surrogate to lactose when patients are lactose intolerant.[15] Companies can make an invaluable contribution by manufacturing orphan medicines as these are the drugs used for managing conditions, like cystic fibrosis or acromegaly, affecting less than 200,000 people in a country.[15,16]

DISCUSSION

In this article, we have tried to assemble data on the assessment of medication adherence and common non-adherence. Medication adherence can be quantified directly or indirectly. Direct measurement includes drug/metabolite detection, smart pills and direct observation. Indirect measurement comprises patient interviews, pill count, questionnaires and many more. In clinical settings, assessing medication adherence can aid in revealing facts regarding the worsening of disease conditions or sometimes, the toxicity of drugs. This can be further analysed to alter the treatment plan to a more patient-centred therapy, counselling or suggestions to sign up for automatic refills which can play an intrinsic role in reducing repeated hospital costs.

Significant hurdles to effective drug use include illiteracy, family support, unemployment, time constraints, high patient count, complex regimens, polypharmacy and numerous other factors. These are often classified as socio-economic, system, therapy, patient and condition-related barriers. Overcoming these barriers can be attempted by revising the system, pharmaceutical company, HCPs' services and by patients themselves.

The articles pertaining to any disease condition were not considered as this was beyond the scope of our study. However, many studies that have focused on this area have been useful in elucidating the importance of adherence in the respective conditions. Only articles available in the English language were chosen which may lead to biased results.[3-9]

CONCLUSION

Medication adherence plays a vital role in healthcare as it has a direct impact on the health related outcomes of the patients. We use direct and indirect measurements to quantify the adherence. However, there are multiple factors negatively impacting medication adherence such as socioeconomic factors, system related factors therapy related factors, patient related factors and condition related factors. To limit these factors various strategies have been put We request you to add the conclusion part.

Up by the health care system and pharmaceutical companies. In developing countries, medication adherence is still a hurdle for the healthcare system and a clinical pharmacist can play a significant role by being a part of a multidisciplinary team.

ACKNOWLEDGEMENT

The authors express heartfelt gratitude towards the JSS College of Pharmacy, JSS Academy of Higher Education and Research (JSSAHER), Mysuru, for providing all the obligatory facilities for completion of this piece of writing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTION

SDS, ASKS, VBP, BSG and SP made significant contributions to the work reported, whether that is in the conception, execution, or acquisition, analysis, or interpretation of data, or all the areas; took part in drafting, revising, or critically reviewing the article; and gave final approval of the version to be published. All have read and agreed to the published version of the manuscript.

DATA AVAILABILITY

The data that support the findings of this study are available in standard research databases such as EBSCO, Google Scholar, the textbook DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition authored by *DiPiro et al*. and/or on public domains that can be searched with either keywords or DOI numbers.

ABBREVIATIONS

ARDS: Acute Respiratory Distress Syndrome; **BMQ:** Brief Medication Questionnaire; **CIOM:** Chemo Induced Oral Mucositis; **CMA:** Continuous, Multiple interval measures of medication Acquisition; **DAR:** Drug Adherence Rates; **EBSCO:** Elton B Stephens Company; **FDA:** Food Drug Administration; **HCP:** Health Care Professional; **IEM:** Ingestible Event Maker; **MARS:** Medication Adherence Rating Scale; **MEMS:** Medication Event Monitoring System; **PDC:** Proportion of Days medications Covered; **PILS:** Patient Information Leaflets; **WHO:** World Health Organization.

REFERENCES

1. Evidence for action [Internet]; 2003. Available from: http://apps.who.int/iris/bitstream/10665/42682/1/9241545992.pdf.
2. Basu S, Garg S, Sharma N, Singh MM. Improving the assessment of medication adherence: challenges and considerations with a focus on low-resource settings. Ci Ji Yi Xue Za Zhi. 2019;31(2):73-80. doi: 10.4103/tcmj.tcmj_177_18, PMID 31007485.
3. Center for Drug Evaluation and Research. Why you need to take your medications as prescribed or instructed [Internet]. U.S. Food and Drug Administration; 2016. Available from: https://www.fda.gov/drugs/special-features/why-you-need-take-your-medications-prescribed-or-instructed.
4. Park JY, Li J, Howren A, Tsao NW, De Vera MD. Mobile phone apps targeting medication adherence: quality assessment and content analysis of user reviews. JMIR mHealth uHealth [Internet]. 2019;7(1):e11919. doi: 10.2196/11919, PMID 30702435.
5. Stay on top of Your Treatment – Abilify MYCITE® System [Internet]. Available from: http://www.abilifymycite.com. Available from: https://www.abilifymycite.com/.
6. Medication Adherence innovative strategies [Internet]. Available from: https://www.elsevier.com/__data/assets/pdf_file/0005/991724/5A_4127_EL_Medi_Adherence_Whitepaper_FINAL_DIGI-112119.pdf.
7. Lin FJ, Huang YM, Ho YF. Medication adherence [Internet]. McGraw-Hill Medical; 2023 [cited Aug 26 2023]. Available from: https://accesspharmacy.mhmedical.com/content.aspx?sectionid=269767978&bookid=3097&Resultclick=2.
8. Patel H, Rajput DS, Vaghasiya J. Medication adherence assessment scale by Mrs. Hajra Patel and Dr. Jitendra Vaghasiya. J Young Pharm [Internet]. 2023;15(2):334-7. doi: 10.5530/jyp.2023.15.44.
9. Wong ZS, Siy B, Lopes KD, Georgiou A. Improving patients' medication adherence and outcomes in nonhospital settings through eHealth: A systematic review of randomized controlled trials [preprint]. J Med Internet Res. 2019.
10. Measuring medication adherence [Internet] [cited Aug 26 2023]. Available from: medicine.musc.edu. Available from: https://medicine.musc.edu/departments/family-medicine/research/rcmar/medication-adherence#:~:text=They%20recommend%20that%20clinical%20trials%20involving%20topical%20applications.
11. Mansukhani SG, MacLean EA, Manzey LL, Possidente CJ, Cappelleri JC, Deal LS. Development of a new patient-reported medication adherence instrument: concerns influencing medication adherence. Patient Preference Adherence [Internet]. 2021;15:1991-2007. doi: 10.2147/PPA.S318030, PMID 34526767.
12. Carolina JK, BCACP CP. Assistant, PharmDPGY2. Greensboro: Director Book Company of Pharmacy Education Area Health Education Center, North Carolina Assistant Professor of Clinical Education. Chapel Hill, NC: University of North Carolina Eshelman School of Pharmacy Clinical Pharmacist Practitioner. Greensboro: Cone Health Internal Medicine Center, North Carolina Kelsy Combs Ambulatory Care Pharmacy Resident Triad HealthCare Network Greensboro, North Carolina Jonathan Downs, PharmD Pharmacist Walgreens Pharmacy Mebane, North Carolina Frank Tillman III, PharmD Candidate Student Pharmacist University of North Carolina Eshelman School of Pharmacy Chapel Hill, North. Medication Adherence: The Elephant in the Room [Internet]. www.uspharmacist.com. 2018. Available from: https://www.uspharmacist.com/article/medication-adherence-the-elephant-in-the-room.
13. Center for Drug Evaluation and Research. Generic competition and drug prices [Internet]. U.S. Food and Drug Administration; 2019. Available from: https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/generic-competition-and-drug-prices.
14. DeFulio A, Silverman K. The use of incentives to reinforce medication adherence. Prev Med. 2012;55;Suppl:S86-94. doi: 10.1016/j.ypmed.2012.04.017, PMID 22580095.
15. Carvalho M, Almeida IF. The role of pharmaceutical compounding in promoting medication adherence. Pharmaceuticals (Basel). 2022;15(9):14248247. [Internet]. doi: 10.3390/ph15091091, PMID 36145312.
16. Research C for de and. Orphan products: hope for people with rare diseases. FDA [Internet]; 2019. Available from: https://www.fda.gov/drugs/information-consumers-and-patients-drugs/orphan-products-hope-people-rare-diseases.

Cite this article: Seetharama SD, Shriya ASK, Pawar VB, Gupta B, Palaksha S. Assessment of Medication Adherence and Common Non-Adherence: A Routinely Overlooked Hurdle. Int. J. Pharm. Investigation. 2024;14(4):1079-84.