

Medication Non-Adherence: An Overlooked Aspect in the Treatment of Bipolar Disorder

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ABSTRACT

Although pharmacotherapy is a cornerstone in effectively managing mood fluctuations in bipolar disorder, adherence to prescribed medications often remains a challenge in the long run, to prevent recurrent episodes and hospitalizations. Nearly half of the patients are known to either discontinue the therapy or fail to follow the prescription schedule consistently. This challenge usually arises due to multifaceted factors including, complicated dosing schedules, poor insight of the disorder, adverse effects and certain social stigmas. Patients with bipolar disorder should be routinely screened for Medication Non-Adherence to differentiate between actual treatment failure due to inefficacy of medicines and non-compliance to these medications. Several scales and methods have been developed, validated and used for the same. Following this, the barriers can be managed by introducing patient-centric approaches that include simplifying treatment regimens based on subjective complaints, educating patients and their family members regarding the benefits and repercussions, as well as making use of digital reminders and other tools. Implementing these strategies requires the collaborative efforts of psychiatrists and pharmacists. While psychiatrists focus on diagnosis and formulate a treatment plan, pharmacists can synergize the efficacy by providing counselling and reviewing medications. Rather than functioning independently, this collaborative approach creates a strong support system that targets all aspects of management and maximizes the benefits of achieving a therapeutic outcome.

Keywords: Bipolar disorder, Medication Adherence, Medication Non-Adherence.

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INTRODUCTION

The World Health Organization (WHO) reports Bipolar Disorder (BD) as one of the ten leading causes of disability worldwide (Başkaya and Demir, 2022). Globally, the estimated annual incidence of BD is 0.4%-0.5%, and the lifetime prevalence is 2.6%-7.8% (Swaroopachary *et al.*, 2018). The prevalence of BD in India ranges from 0.51 per thousand population to 20.78 per thousand population (Narayanan *et al.*, 2020). Medication Adherence (MA) is defined as the degree to which a patient follows their prescribed medication regimen accurately, including the correct timing, duration, dose, and frequency of medication. It is a complicated process, as it involves a series of interconnected steps

among patients, healthcare providers, and the overall healthcare system. When a patient fails to take at least 80% of the required dosage, the term “non-adherence” is used (Loots *et al.*, 2021). C. Everett Koop, US Surgeon General in 1985, quoted Medication Non-Adherence (MNA) as “Drugs do not work in patients who do not take them” (Koop, 1985).

Long-term pharmacological management of BD involves therapy with psychotropic medications to regulate fluctuations in mood and reduce the risk of relapse. However, adherence to these medications remains compromised (Tamene *et al.*, 2025). A large U.S. based database study reported that approximately 50% of the patients were non-adherent to lithium and other medications over a period of one year (Jawad *et al.*, 2018). Consistent adherence to safe and effective dosages of the prescribed drug is necessary for the long-term efficacy of any sustained preventative medication regimen. However, MNA is very common in patients with psychiatric disorders, as they are required to take medications for a long time. Non-compliance can lead to serious consequences for the patient's health, such as disease progression,



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risk of hospitalization, and death (Al Maqbali *et al.*, 2022). Hence, measuring MNA is very critical in this population.

Several validated tools are available to measure MNA, including scales, self-report questionnaires, monitoring devices and biological markers (Lam & Fresco, 2015). When MNA is not measured, non-adherence can mistakenly be attributed to treatment failure, leading to inappropriate changes in medications and unnecessary dose escalations (Jawad *et al.*, 2018). Pharmacists, along with other health care professionals, can improve the efficacy and quality of care by offering education plans regarding the illness and treatment options, thus preventing future hospitalizations (Aremu *et al.*, 2022).

METHODOLOGY

The search was conducted on PubMed, Scopus, and Google Scholar. The various search terms that were used were 'bipolar disorder', 'bipolar affective disorder', 'bipolar mood disorder', 'type 1 bipolar disorder', 'type 2 bipolar disorder', 'medication adherence', 'drug adherence', 'prescription adherence', 'medication non-adherence', 'medication compliance', and 'medication non-compliance'. The review included articles published over the last 20 years. Furthermore, no restrictions were placed on the types of studies included.

REVIEW OF LITERATURE

Medication Non-Adherence

Medication Non-Adherence (MNA) is typically classified into two types: Primary and Secondary Non-Adherence. Primary Non-Adherence happens when a patient does not fill a new prescription and, because of this, does not start the medication, whereas Secondary Non-Adherence occurs when a patient fills their prescription but fails to take the medication as directed. This cause of non-adherence can be further classified into two types: unintentional and intentional. When patients attempt to follow their treatment plan but are unable to do so due to factors outside their control, such as forgetting to take the prescribed drug, having trouble taking it, misunderstanding the instructions, or financial limitations, it is known as unintentional non-adherence. Intentional Non-Adherence, on the other hand, is when patients deliberately choose not to take their medications as directed. This might be due to worries about side effects, doubts about the medication's effectiveness, personal values or views that don't align with the recommended course of treatment, or the conviction that the drug isn't needed. Intentional Non-Adherence is a deliberate act in which the patient consciously decides to reject the recommended course of therapy, whereas unintentional non-adherence is usually a passive occurrence brought on by negligence or oversight. Sometimes patients don't simply stick to or completely stop their treatment plans instead; they often make personal adjustments along the way. This might mean taking only some of their prescribed doses i.e. partial adherence

or going through periods where they start and stop treatment unpredictably i.e. irregular adherence. Rather than making an all-or-nothing choice, they tend to navigate treatment in a way that fits their own comfort or circumstances, even if it's not always consistent (Chakrabarti, 2016; Jayasree *et al.*, 2024). Figure 1 shows two types of Medication Non-Adherence.

Factors affecting Medication Non-Adherence

MNA is a common issue among individuals with mental illness and a significant contributor to relapse, particularly in BD. Understanding the factors that lead to poor adherence and exploring strategies to address them could greatly benefit individuals with BD and their families. Multiple studies have identified a range of factors contributing to Medication Non-Adherence in individuals with BD. Common reasons include forgetfulness, medication side effects, and drug expenses. Additional contributing factors involve a lack of social support, limited knowledge about the illness and its treatment, and lack of compassion for the condition. Some patients also stop medication prematurely due to the belief that their condition has improved (Delcine *et al.*, 2023; Mishra *et al.*, 2017).

Non-adherence is more common among certain demographic groups, such as men aged 46 to 60, individuals living in rural areas, those with a poor educational background, people who are working, younger individuals, unmarried individuals, and those with co-occurring substance abuse (alcohol and drugs). Emotional distress and a lack of insight into the illness also play a role (González-Pinto *et al.*, 2010). Other influencing factors include drug-related variables, the complexity of treatment including the use of multiple medications, treatment availability, social and familial support, and patients' perception of mental illness (Elhosary *et al.*, 2023). Notably, about one in four individuals with bipolar disorder do not adhere to prescribed medication during the maintenance phase after an acute episode. The likelihood of non-adherence during maintenance therapy was higher among those with psychotic symptoms, cannabis use, impaired insight, and those receiving antidepressant treatments. Figure 2 shows the factors that are associated with Medication Non-Adherence in bipolar disorder. Future therapies targeting modifiable risk factors will benefit from a deeper understanding of the causes of non-adherence in BD treatment (Lama *et al.*, 2012). Medication adherence among patients with bipolar disorder with promoting and hindering factors, is shown in Table 1.

Methods to assess Medication Non-Adherence

Medication Adherence lacks a "gold standard" measurement method as all available approaches have their own set of limitations. Adherence can be assessed by either direct or indirect methods. Direct methods involve detecting the presence of drugs and its metabolites, or biological markers in blood or urine. These approaches are not commonly used due to their high cost, inability to provide real-time feedback during clinical visits, sensitivity to

factors unrelated to adherence such as drug-food interactions, physiological variability, drug half-life and dosing schedules. Indirect methods, on the other hand, focus on the behaviour of the patient to assess adherence. It involves pill counts, electronic medication monitoring, reviewing of medical charts, directly observed therapy, pharmacy refill records, clinician assessments and self-report questionnaires. Cost and limited accessibility are the main challenges in electronic monitoring, even though it can provide detailed information on adherence. Pill count methods are not reliable as patients may refill the prescription even before needed, forget dates of initiation of therapy, or may transfer drugs across containers. Despite all these limitations, indirect methods are widely used as they are affordable, quick to administer, applicable across various healthcare settings, and can be helpful in providing immediate feedback while identifying non-adherence factors (De Las Cuevas & Peñate, 2015).

Morisky Medication Adherence Scale (MMAS-8) is one of the self-report questionnaires that is being commonly used to evaluate medication intake behaviour (Lam and Fresco, 2015). This structured 8-item scale was developed to identify barriers to adherence and study the effects on behaviour associated with long-term use of psychiatric drugs. Both intentional (e.g., withholding medications due to side effects) and unintentional (e.g., forgetting to take medications) behaviours can be assessed using this scale (Tan *et al.*, 2014). The MMAS-8 has been translated into 33 languages that are currently available and being widely used in many studies.

Approaches to enhance medication adherence

Several evidence-based approaches have been identified to improve medication adherence that target barriers at both patient and healthcare system levels. Various methods to enhance medication adherence include (Jimmy & Jose, 2011).

- i. Patient education and counselling,
- ii. Simplified regimens,
- iii. Medication review,
- iv. Technological approaches.

Patient education and counselling

The main reason for MNA is forgetfulness and lack of proper follow up with the physician (Hugtenburg *et al.*, 2013). These challenges can be overcome by providing pharmaceutical care, which includes educating patients about their disease condition, treatment and lifestyle changes with the aid of Patient Information Leaflets or pamphlets, and modern audio visual tools such as videos and mobile health applications (Mishra *et al.*, 2017). Regular follow-up and reminder systems such as phone calls, Short Message Service (SMS) alerts, or app-based notifications, can further enhance adherence by reinforcing instructions and ensuring consistent communication between the patient and healthcare providers.

Table 1: Adherence to medication in bipolar disorder: Promoting and hindering factors.

Barriers/ Promoters	Factors
Promoters	An awareness of the illness
	Need for treatment perceived by the patient
	Attribution of causality to biological factors
	Collaboration in clinical decision-making
Barriers	The lack of belief that effective treatments are available
	Symptoms of adverse effects
	Social control

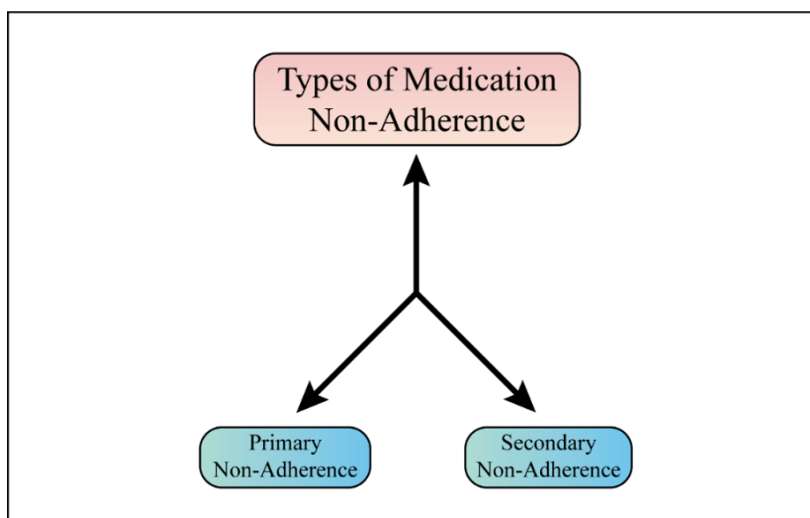


Figure 1: This figure shows the two types of Medication Non-Adherence (MNA), Primary Non-Adherence and Secondary Non-Adherence.

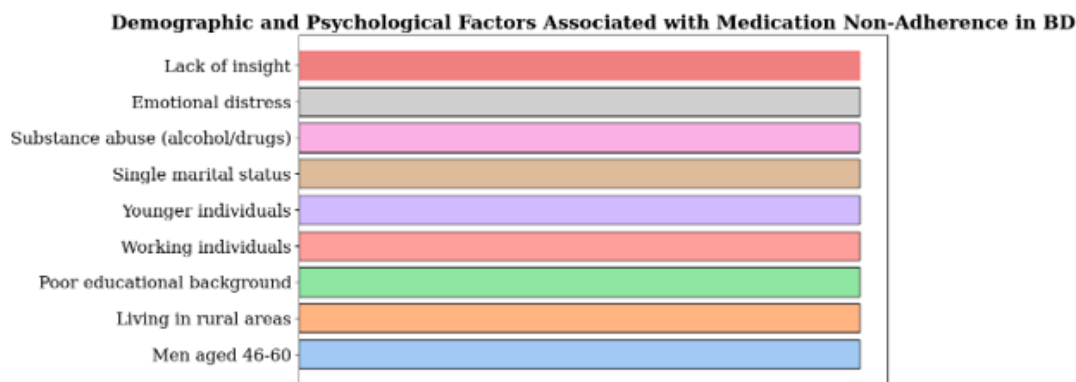


Figure 2: Common demographic and psychological factors linked to Medication Non-Adherence in bipolar disorder.

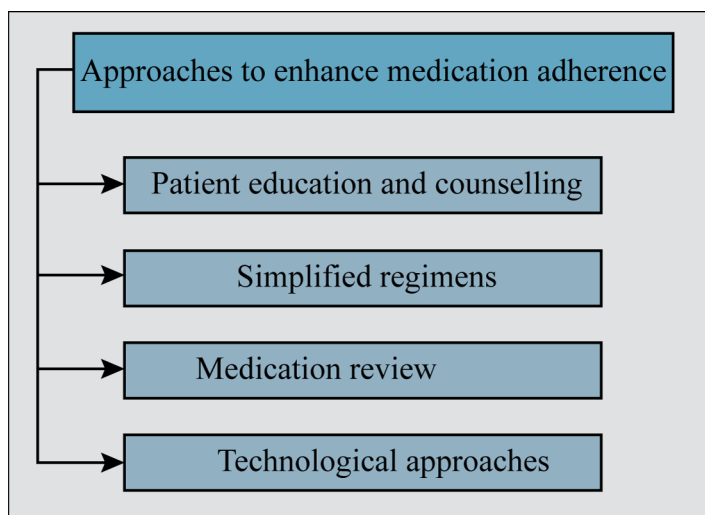


Figure 3: Key approaches to improve medication adherence.

Simplified regimens

Optimizing a patient's medication schedule can improve the medication adherence and therapeutic outcomes. This includes reducing dosing frequency, using fixed-dose combinations, switching to long-acting formulations, deprescribing unnecessary medications, and aligning dosing times with daily routines. By minimizing complexity and pill burden, simplified regimens help to reduce confusion, prevent medication errors, and enhance patient compliance with their therapy (Thorakkattil *et al.*, 2024).

Medication review and reconciliation

Through medication reconciliation, clinical pharmacists can learn about their patients' medications along with their indications, dosages, and duration of therapy. This enables the pharmacist to identify therapeutic duplications, drug omissions and interactions, side effects, and any other medication-related problems, which help to enhance the safety and efficacy of the therapy (Farag *et al.*, 2022; Soubolsky & Halpape, 2022).

Technological approaches

In the modern era, it is important to incorporate technology in pharmaceutical care as it helps in improving medication

adherence and enhances clinical outcomes. The technological approaches practiced in pharmaceutical care include patient education with audio visual materials, mobile applications, smart pill boxes, SMS reminder systems, smart devices and AI enabled disease specific devices and applications. These practices connect the patients with healthcare providers in real time and are able to provide the services as per their current needs, enhance the treatment efficacy and are able to achieve the proposed treatment goals (Chong *et al.*, 2025). Various approaches to enhance medication adherence are shown in Figure 3.

Challenges in medication adherence for patients with Bipolar Disorder

In India, there is a limited provision of medication usage information during the dispensing process, coupled with a shortage of clinical pharmacists available to provide patient counselling, which poses significant challenges in preventing Medication Non-Adherence, treatment discontinuation, and the associated complications commonly seen in psychiatric patients. Enhancing MA remains a challenge due to a lack of consistent monitoring of adherence, as well as the scarcity of research on effective strategies (Sajatovic *et al.*, 2004). One of the major challenges in MNA is 'Technological implementation barriers' as



Figure 4: Major challenges affecting medication adherence among patients with bipolar disorder in India.

many tools fail to successfully transition from research settings to routine use (Figueiredo *et al.*, 2025; Moon & Walsh, 2025). Even though technologies like AI-based reminders, smartphone apps, electronic pill bottles, dispensers and smart inhalers can facilitate adherence, the effect is often limited by gaps in training, insufficient infrastructure, poor interoperability, cost and difficulty in incorporating them in daily clinical practice (Lehne *et al.*, 2019). Concerns about privacy and data security are also known to reduce trust among patients as well as healthcare professionals (Backes *et al.*, 2021). Additionally, timely reminders may become less effective due to alarm fatigue, and the majority of the tools depend on self-reporting or indirect measures, rather than confirming actual intake of medication (Figueiredo *et al.*, 2025). Hence, the barrier is not just the existing technology, but also whether it is practical and implementable in a real-world setting (Mason *et al.*, 2022). To address these challenges, collaborative approaches between clinical pharmacists and other healthcare professionals are essential to enhance MA among patients with BD. A study by Mishra *et al.* (2017) found that when pharmacists and psychiatrists collaborated, statistically significant findings showed better patient care and outcomes. Figure 4 illustrates the challenges in medication adherence among patients with bipolar disorder in India.

CONCLUSION

Non-Adherence to medication is one of the major barriers in the management of BD. There have been advancements in pharmacological treatments, but the benefits of these

medications are often negated due to poor adherence. This can lead to disease relapse, hospitalization, increased medical costs, and poor quality of life for both patients and their caregivers. It is crucial to understand that treatment failure often arises due to non-adherence, rather than inefficacy of medicines. Hence, the application of validated tools and scales must be routine while treating BD patients. Clinical pharmacists can collaborate with psychiatrists to manage factors contributing to Non-Adherence through optimizing pharmacotherapy, conducting medication reviews, providing patient education, and offering direct counselling.

FUTURE DIRECTIONS

Future research should focus on the practical implementation and scalability of technological approaches like AI-based monitoring and telepsychiatry in real-world settings.

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ABBREVIATIONS

BD: Bipolar Disorder; **MNA:** Medication Non-Adherence; **MA:** Medication Adherence; **WHO:** World Health Organization; **SMS:** Short Message Service; **AI:** Artificial Intelligence; **MMAS-8:** Morisky Medication Adherence Scale.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

A Ashvil, Lenora Katherine Crasto and Diya Kiran: Writing original draft; **Bipin Shaji and Shivaprasad Sirimalla:** Methodology and Supervision; **Mariyammathul Afeeza and Deepak C G:** Conceptualization; **Allen Pinto:** Project administration; **Juno Jerold Joel, Uday Venkat Mateti and Shrinivasa Undaru Bhat:** Contributed to the final review of the manuscript. All authors read and approved the final manuscript.

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