

A Review of Medication Non-adherence in Chronic Diseases: Thin Line between Health, Harm and the Vital Role of Pharmacists

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ABSTRACT

Adherence to prescribed medication regimens is essential for the effective management of chronic conditions. Non-adherence to treatment plans undermine therapeutic effectiveness, increases healthcare costs and elevates the risk of complications. Non-adherence, however, is complex and often results from numerous interacting factors. Some of these factors may be related or unrelated to the individual. Adherence to medications comprises three interrelated stages: initiation, implementation and discontinuation. Patients who fail to initiate treatment and those who discontinue treatment prematurely often experience the worst clinical outcomes. Numerous studies on non-adherence have proposed models that help explain why patients fail to adhere to their medications. While there is a paucity of studies on the reasons patients prematurely stop taking their medications, existing research suggests that the decision is often based on a combination of social, environmental and personal factors including adverse drug reactions.

In the management of chronic diseases, there is often a delicate balance between effective disease control and clinical deterioration, underscoring the thin line between health and harm. It is therefore important for healthcare professionals, researchers, and stakeholders to prioritize efforts aimed at promoting adherence in individuals who suffer from chronic diseases. Pharmacists, as accessible members of the healthcare team, have a significant role to play. Some of their responsibilities include effective patient education and counselling, medication therapy management, monitoring and follow-up, use of medication management tools, collaboration with other healthcare providers, telepharmacy, integration of digital health technologies and tools, simplifying treatment regimens and community outreach and advocacy.

To effectively manage chronic conditions, medication adherence must be prioritized. Patients should be adequately educated on the significance of following their treatment regimen and the potential consequences of non-adherence. Individualized strategies that address patients' unique beliefs and barriers to adherence should also be adopted.

INTRODUCTION

Chronic diseases are medical conditions that last longer than six months despite treatment and may lead to disability or death. Annually, chronic diseases represent the leading cause of mortality and disability, accounting for nearly 41 million deaths, making up 74% of the total global death burden¹. Diabetes, hypertension and cardiovascular

diseases are examples of chronic diseases that constitute a serious public health crisis due to high rates of illness and death. A major challenge with the management of these conditions is medication non-adherence, as treatment is often prolonged, some lasting throughout a patient's lifetime². Although advancements have been made in the management of these conditions, optimal health outcomes

can only be achieved with a high level of medication adherence³.

The effectiveness of any prescribed medication in achieving therapeutic success depends largely on the extent to which the prescribed regimen is followed⁴. This is particularly relevant in chronic conditions, where medication-taking behaviour closely corresponds with treatment outcomes⁵. Evidence from Paterson et al.⁶ indicates that maintaining an adherence rate of 95% or greater in patients with HIV infection on protease inhibitor (PI) therapy is strongly associated with optimal viral suppression and a markedly lower risk of opportunistic infections and death. Similarly, Parikh et al.⁷ reported that among hypertensive patients on Renin-Angiotensin System Antagonists (RASAs) therapy, maintaining an adherence rate of 90% was most effective in preventing hospitalizations and emergency department visits, thereby reducing overall healthcare utilization and costs. Lim et al.⁸ also identified an adherence threshold ranging from 86% to 98% as the most strongly associated with achieving target HbA1c levels in patients with type 2 diabetes. Conversely, poor medication adherence among patients with chronic diseases has been shown to result in ineffective disease management and reduced quality of life². According to⁵, medication non-adherence also undermines therapeutic effectiveness, compromises patient safety and increases the overall economic burden of care, reflecting far-reaching consequences of non-adherence, especially in chronic disease management.

Without effective strategies to improve adherence, the burden associated with these conditions is expected to grow, underscoring the urgent need to address medication non-adherence amid the rising prevalence of chronic diseases⁹. Evidence from a systematic review¹⁰ indicates that even minor deviations below adherence thresholds can adversely affect clinical outcomes, highlighting the thin line between health and harm. In light of this, studies have shown that pharmacist-led interventions through patient counselling, use of educational materials, regular and timely follow-up, amidst others, can help strengthen medication adherence, and consequently, improve health outcomes and sustained therapeutic stability².

Building on the above, this review primarily examines medication non-adherence in chronic disease management, discussing existing knowledge on its impact, exploring the crucial roles of pharmacists in promoting adherence in patients with long-term conditions, and highlighting recommendations and future directions. The “thin line

between health and harm” is employed as a conceptual framework to illustrate how even small lapses in adherence can shift patient outcomes.

OVERVIEW OF MEDICATION NON-ADHERENCE

Medication adherence refers to the extent to which patients follow a healthcare provider's direction regarding how to take their medications⁹. It is an essential element in achieving desired health outcomes, especially among individuals living with long-term or chronic medical conditions^{11, 12}. Conversely, medication non-adherence occurs when a patient fails to take their prescribed medications or follow the instructions provided by their healthcare professional for taking the medicine¹³. Despite its critical importance, medication non-adherence remains a pervasive global health challenge, contributing to poorer clinical outcomes, greater risk of complications, increased hospital admissions, and significant financial strain on healthcare resources⁹.

Medication taking behaviour can be described in three interrelated phases: initiation, which involves taking the first dose of the prescribed medication; implementation, which refers to how closely the patient follows their treatment plan as directed; and discontinuation, which occurs when the patient prematurely ends therapy¹⁴. Studies also estimate that as many as one in three patients fail to fill their first prescription, and among those who do, nearly half do not follow the prescribed regimen¹⁵. Non-adherence to the recommended treatment plan can lead to deterioration of a patient's condition, treatment failure, lower quality of life, reduced life expectancy and increased need for the use of medical services and associated costs¹⁴.

Globally, non-adherence to prescribed treatment among individuals suffering from chronic illnesses remains a critical public health concern². In high-income countries, it is estimated that only about 50% of patients with chronic conditions consistently follow their long-term treatment regimens with the proportion significantly lower in low- and middle-income countries². In chronic conditions such as diabetes and hypertension, non-adherence to prescribed medications can lead to clinical deterioration, poor health outcomes and elevated risk of cardiovascular complications^{16, 17}. It has also been shown that non-adherence to medications to prevent cardiovascular disease (CVD) has been associated with a significant increase in the risk of premature death from any cause, CVD death, hospitalization for heart attack or heart failure and coronary revascularization procedures¹⁸. This indicates that non-adherence can significantly worsen the course of chronic

diseases by impairing disease management, increasing the risk of complications and death⁹.

Classification of non-adherence

Medication non-adherence is classified into two types: primary and secondary. When a patient does not initiate a prescribed treatment, it is considered primary non-adherence, while secondary non-adherence occurs when the medication is started but not taken as prescribed¹⁹. In general, non-adherence is typically classified as either intentional or unintentional. Intentional non-adherence refers to a deliberate decision by the patient to not follow their recommended treatment regimen. Unintentional non-adherence, on the other hand, occurs when an individual plans to follow their prescribed treatment but are prevented from doing so due to factors outside their control. These factors may include forgetfulness, complicated medication regimens, poor health literacy and financial constraints, among others¹⁹.

Factors influencing non-adherence

Non-adherence arises from multiple, interrelated factors, highlighting that it is not solely a patient-driven issue²⁰. Various elements can influence an individual's ability to take medications as prescribed, including socio-economic influences, presence and severity of comorbidities, treatment complexity, healthcare system limitations, and patient-related factors¹³. Contributing factors may involve cost of medication, busy schedules that make it difficult to take medications consistently, the time required to schedule and attend appointments, difficulties communicating with pharmacists or other healthcare providers, inadequate understanding of medication therapy instructions, disease severity, personal beliefs about illness, and expectations regarding medication effect. These factors may be further intensified by limited access to healthcare and pharmacy services, lack of trust and effective communication with providers, and limited patient involvement in shared decision-making¹³.

Several theoretical models provide a framework to understand these factors. The Perceptions and Practicalities Approach suggests that non-adherence arises from perceptual factors such as patient beliefs and emotional responses to their treatment, which leads to intentional non-adherence, as well as practical factors including medication cost and access, which contribute to unintentional non-adherence²¹. Similarly, the COM-B model posits that medication adherence is unlikely unless individuals possess the necessary physical and mental Capabilities

such as being able to swallow or remember doses, alongside adequate environmental and social Opportunities including stable housing or family support, and adequate Motivation, in the form of personal drive and belief systems²². For example, when applied to patients with rheumatoid arthritis, the COM-B model revealed that psychosocial influences and support systems were responsible for 66% of the observed difference in adherence behaviour²³. Another model that has been illustrated to describe medication adherence is the Medication Adherence Contexts and Outcomes (MACO) framework. The MACO framework presents medication adherence as a series of processes that involves various people, settings and outcome behaviours. It highlights that adherence is influenced not only by the patient but also by the people and the settings involved in supporting the patient's medication use such as doctors, pharmacists, caregivers, clinics, pharmacies, and the home²⁴.

A study also shows that an individual's decision to initiate therapy is influenced by their perceptions of the potential benefits and harms of medication, shaped by previous experiences and environmental influences²⁵. Although there is little known about the reasons patients discontinue treatment, existing research suggests that the decision is often a carefully considered one by the patient, influenced by a combination of social, environmental and personal factors including adverse effects²⁶. In summary, non-adherence is driven by a combination of patient-specific, therapy-related, healthcare system, and socioeconomic factors. Understanding these barriers is crucial for designing interventions, including pharmacist-led strategies, to improve adherence and reduce the health and economic burden of chronic diseases.

THE THIN LINE BETWEEN HEALTH AND HARM

The clinical consequences of medication non-adherence are particularly severe in chronic conditions. The achievement of optimal clinical outcome requires maintaining a minimum level of medication intake or adherence¹⁰. The World Health Organization emphasized that adherence rates above 80% are generally required to achieve desired therapeutic effects, and that even slight declines below this point often negate treatment benefits, particularly in chronic conditions requiring lifelong therapy²⁷. Similarly, in a retrospective longitudinal cohort study involving 557 patients diagnosed with heart failure with reduced ejection fraction, it was found that individuals with adherence levels less than 80% faced more than twice the likelihood of death and hospitalization due to

cardiovascular events²⁸. In a comparable study conducted in a primary care settings in Canada to examine the relationship between medication adherence and cardiovascular outcomes in patients with both diabetes and hypertension, it was found that high adherence (defined as 80% or greater) to anti-diabetics, anti-hypertensive drugs and statins was linked to a reduced risk of death whereas adherence below this threshold was associated with major cardiovascular complications including stroke, heart failure and coronary heart disease²⁹.

Building on this, research has shown that even modest reductions in medication adherence among cardiovascular patients markedly increase the risk of hospital readmissions, recurrent events and death, underscoring the delicate balance between adherence and harm³⁰. Evidence also shows that adherence is not a binary behaviour but a continuum; small deviations below optimal adherence thresholds can rapidly tip patients from stability to deterioration¹⁰. In a systematic review, Baumgartner et al.¹⁰ questioned the traditional 80% adherence benchmark and demonstrated that even minor shortfalls below this point can compromise therapeutic outcomes and lead to harm. This indicates that just a few missed doses may separate wellness from worsening disease. A similar study also demonstrated a gradient between adherence and clinical outcomes among patients on lipid lowering therapy, with risks of cardiovascular events and death increasing progressively as adherence dropped. Their findings emphasize that small drops in adherence, not complete treatment abandonment can cross that clinical threshold from health maintenance to harm, hospitalizations, or death³¹.

Recognizing the close relationship between adherence levels and health outcomes underscores the need for pharmacist-led, patient-centered interventions that sustain adherence well above critical thresholds. Through continuous counselling, regimen simplification, and regular follow-up, pharmacists can help patients maintain therapeutic stability and prevent minor lapses from progressing into significant clinical harm.

THE ROLES OF PHARMACISTS IN MITIGATING NON-ADHERENCE IN CHRONIC DISEASES

Pharmacists can employ various interventions and approaches to enhance medication adherence among patients with chronic diseases, and several studies have shown that these interventions positively influence treatment effectiveness and the overall well-being of

patients^{9,32,33}. Some of these interventions include:

Patient Education and Counselling

Pharmacists play a vital role in improving medication adherence through patient education and counselling that strengthens patients' commitment to prescribed therapy⁹. By leveraging their professional expertise, pharmacists educate patients and caregivers on the purpose of each medication, the consequences of missed doses, proper administration techniques, potential side effects, and appropriate management strategies³². This knowledge translates into improved self-management, and consistent adherence to prescribed regimens, key factors that help patients maintain disease control, prevent disease complications and promote better health-related quality of life⁹. Effective communication and education empowers patients to actively participate in their recovery process and make informed decisions about their health³². Empirical evidence also shows that pharmacotherapeutic counselling by pharmacists improves medication adherence and reduces hospital readmission and emergency department visits related to disease progression, demonstrating that patient education and counselling can produce measurable clinical benefit³³.

Additionally, through effective counselling, patients can overcome misconceptions and feel less anxious about the prospect of managing a long-term illness and using drugs for an extended period of time. The treatment of a long-term condition frequently presents psychological exhaustion and treatment burden, but effective counseling offers essential emotional support that reduces this burden and sustains patient engagement and adherence to therapy^{9,32}.

Medication Therapy Management

Medication therapy management (MTM) services provided by pharmacists involves comprehensive activities such as collecting relevant medical and medication information, assessing the patient's condition and laboratory results, conducting thorough medication reviews and developing an individualized treatment plan. Pharmacists may also recommend adjustments to current therapy, monitor therapeutic outcomes, identify adverse drug reactions and educate patients to foster empowerment and active participation of the patient in their care³². These interventions are particularly beneficial for individuals managing comorbidities, where regimens are often complex, increasing the risk of errors and non-adherence. Through regular medication reviews, pharmacists not only enhance patients' understanding of their conditions and

therapies but also prevent drug-therapy problems, align treatment with clinical goals, and ultimately improve adherence and quality of care³⁰. A systematic review also found that MTM interventions may help reduce medication-related problems, including non-adherence and optimize therapy for patients with chronic diseases, however evidence regarding improvements in clinical outcomes remains limited³⁴.

Monitoring and Follow-up

Pharmacists play a vital role in monitoring for side effects, identifying drug interactions, prescription errors, and supporting medication adherence, thereby minimizing risks and improving medication safety practices³². Through regular follow-up, pharmacists can consistently assess therapeutic effectiveness, safety and the level of the patient's adherence³⁵. These interactions provide opportunities to reassess a patient's treatment plan, address any misunderstandings regarding their medications and offer important additional information. Empirical evidence also shows that timely follow-up is critical; for instance, delayed outpatient follow-up beyond the first six weeks after acute myocardial infarction has been associated with worse short-term and long-term adherence, highlighting that pharmacist engagements during early follow-up can directly influence adherence outcomes³⁶.

Consistent monitoring and follow-up also fosters trust between pharmacists and patients. This trust is vital as evidence suggests that trust and a strong therapeutic relationship are fundamental to the provision of quality healthcare, enhancing patient satisfaction and adherence, and consequently leading to more effective management of chronic diseases³⁷.

Medication Management Tools

Medication management tools like pillboxes have been shown to enhance adherence in chronic diseases. In a 2021 study, it was demonstrated that providing education and pillboxes to patients on long-term therapy significantly increases adherence compared to patients who are not given pillboxes³⁸. In the study, patients with diabetes mellitus were randomly assigned to three groups: control group, education-only group and a group provided with both education and pillboxes. The result from the study indicated that the group that received education in addition to the pillboxes had a significantly higher adherence rate, demonstrating the importance of integrating education with practical tools like pillboxes or pill organizers. Electronic pillboxes with reminders can also be used to improve

medication adherence, particularly among older adults who may face challenges with complicated treatment regimens³⁹. These medication management tools lower the chances of missed doses and support patients in adhering to their treatment plans.

Collaboration with other Healthcare Providers

Addressing medication non-adherence in chronic diseases requires a collaborative effort, with pharmacists contributing significantly alongside other healthcare professionals to promote adherence^{9, 32}. Physicians, pharmacists and nurses are all important in the efforts to improve adherence, through patient education and the provision of continuous support throughout therapy. At the stage of diagnosing and outlining treatment, the physician plays a key role, providing clear and thorough communication. The pharmacist reinforces adherence by offering further instructions and ensuring patient understanding. It is important that patients gain a clear understanding of both the importance of following their prescribed treatment plans and the dangers associated with not adhering to their prescriptions⁴⁰. Effective collaboration fosters better coordination between healthcare providers, encourages patient involvement in decision making, enhances a safer health system, and promotes more efficient use of resources. Furthermore, effective collaborations among healthcare professionals positively influences both patient satisfaction and adherence to therapy, leading to the achievement of treatment goals⁴¹.

Telepharmacy

Telepharmacy involves the use of information and communication technology (ICT) by pharmacists to deliver pharmaceutical care and communicate with patients remotely⁴². There has been a growing use of telepharmacy in the treatment and management of chronic diseases⁴³. By delivering pharmaceutical care remotely via telecommunication technology, telepharmacy has emerged as an essential means of expanding access to pharmacists and promoting adherence in patients with chronic diseases especially those in underserved or remote communities^{9, 44}. Through this intervention, pharmacists can engage in virtual consultations, oversee how well a patient adheres to their medications, and deliver real-time guidance. Patients with chronic illnesses that require continuous monitoring and regular oversight particularly benefit from telepharmacy. A study found that patients who used telepharmacy had approximately 122 times higher odds of adhering to their prescribed treatment plans compared to

those who did not use telepharmacy¹¹. Telepharmacy enables pharmacists to provide drug therapy education, which enhances the understanding of patients of their ongoing therapy. It also helps provide timely reminders for medication usage, regular monitoring, and follow-up, all of which contribute to improved adherence¹¹.

Digital Health Technology and Tools

A range of digital health technologies including telehealth services, mobile applications and telemedicine have been introduced to enhance the care of individuals with chronic illnesses. Pharmacists can take advantage of these tools to support ongoing care, improve medication adherence, engage with patients and caregivers and provide patient-centered education, especially for those managing long-term illnesses⁴⁵. Innovative digital health technologies like mobile health applications and electronic systems for tracking medication use have proven effective in promoting adherence. These tools offer timely medication prompts and real-time tracking of adherence. Research indicates that patients who use such technologies report higher adherence rates and feel more engaged in their care⁴⁶. By empowering patient to actively monitor their own health, mobile apps stand out amidst digital health technology. Common features of these apps include reminders for medication intake and educational resources for users. Mobile health applications can help improve adherence by enabling patients to follow a consistent dosing routine through alerts and reminders while providing timely feedback on their progress⁴⁷. Mobile digital devices like smartphones, tablets and personal digital assistants can also be used to disseminate health services and information⁴⁸. Findings from studies including digital health devices demonstrated enhanced adherence and self-management in conditions including hypertension, asthma, diabetes and chronic obstructive pulmonary disease⁴⁹. These digital health innovations deliver patient-centered, timely and tailored information to support the management of chronic diseases⁴⁵.

Simplifying Treatment Regimens

Simplifying treatment regimens is another key approach to improving medication adherence in patients with long-term illnesses. Patients with chronic diseases, especially those with other comorbidities often struggle to keep track of complex regimens with multiple daily doses. This is also further compounded when individual drugs are prescribed, which negatively impacts adherence, instead of fixed-dose combinations⁵⁰. Once-daily dosing or combination drugs,

can significantly enhance medication adherence in chronic conditions. Simpler regimens often lead to improved patient satisfaction and less burden from their therapy, helping the patient to manage their conditions more effectively with minimal interruptions to their daily lives. When treatment plans are made simpler and tailored to the individual patient, the chances of long-term adherence dramatically increases⁹. In patients with chronic diseases and comorbidities, taking multiple medications at the same time is common and it significantly contributes to medication non-adherence. Evidence from a recent study shows that people with chronic illnesses and who take several medications concurrently tend to be non-adherent, highlighting the importance of careful medication management in these patients⁵¹.

Community Outreach and Advocacy

Through targeted outreach and advocacy initiatives, pharmacists also contribute meaningfully to promoting adherence in patients with chronic diseases. The easy accessibility and regular patient interactions position pharmacists to identify barriers to adherence and implement tailored interventions. For example, a study was carried out by pharmacists in community pharmacies across rural Montana, United States. This program was tagged “Team Up. Pressure Down.” The pharmacists provided consultations and shared educational materials. As a result, adherence to blood pressure medications increased from 73% to 89% among patients who were involved in the program within that community⁵².

Beyond patient care, pharmacists also advocate for broader reforms by shaping health policies and contributing to system-level changes across healthcare. In low- and middle-income countries, for instance, pharmacists have advocated for their inclusion into primary healthcare teams to better manage long-term illnesses. Evidence from a review suggests that interventions by community pharmacists in these settings greatly enhanced medication adherence, highlighting the need for policy reforms to institutionalize the role of pharmacists in the management of chronic diseases⁵³.

RECOMMENDATIONS

According to the World Health Organization, adherence is the primary modifiable factor capable of undermining therapeutic success²⁷. It is therefore important that clinicians, researchers, and policymakers prioritize efforts to address the issue of medication non-adherence, especially in chronic diseases. The emergence of electronic

medical records, digital technologies, and artificial intelligence presents an opportunity to integrate individualized care tailored to each patient's potential barriers to adherence and personal beliefs²². Ensuring continuity of care is also an important strategy to improving medical adherence in patients with chronic conditions, achievable through maintaining structured appointment scheduling systems.

Operations research methodology also offers a way to improve adherence in patients with long-term illnesses. Operations research can be used to develop appointment scheduling systems that decrease missed visits, ensure timely medication refills and allocate resources effectively for patient follow-up⁵⁴. For example, pharmacy or insurance records can be used to indicate if a patient procured their drug(s) in sufficient quantity to be able to follow their prescribed dosing regimen, in both frequency and duration. Following the assessment of the patient's adherence levels, appropriate interventions can then be implemented if non-adherence is identified. In addition, by providing financial support for treatments and outpatient visits, healthcare systems can reduce cost barriers and improve adherence to prescribed medications, self-monitoring and scheduled care. When individuals with chronic conditions fail to attend scheduled visits, their health may worsen due to the absence of timely clinical monitoring, increasing the likelihood of emergency interventions or hospital admissions⁵⁴.

CONCLUSION

Interventions to improve medication adherence remain essential for optimizing chronic disease management and achieving treatment success. To maximize effectiveness, these interventions should be systematically applied and tailored to address both the treatment initiation and treatment implementation phases of medication taking behaviour. Ensuring patients initiate therapy requires adequate counselling and simplification of complex treatment regimens. To promote sustained use of medications over time, medication management tools (eg pillboxes) and telepharmacy should be employed^{4,44}. Given that suboptimal adherence can lead to worsening clinical outcomes, it is essential that all parties involved prioritize proactive strategies to mitigate preventable harm. Pharmacists, as accessible healthcare providers, are crucial in promoting adherence in patients with chronic conditions by providing medication therapy management and continuous monitoring and follow-up, in partnership with other members of the healthcare team^{35, 41}. Integrating

patient education with interventions such as medication management tools and the use of electronic medical records to monitor adherence, can also enable healthcare systems identify and address gaps in medication taking behaviour, thereby supporting patients in maintaining therapeutic stability and preventing complications associated with poorly managed chronic conditions. Ultimately, sustaining adherence demands a patient-centered approach that recognizes how easily therapeutic progress can shift when consistency falters.

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