

# Literature Review: Determinants and Interventions for Optimizing Medication Adherence

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**Abstract**— This literature review synthesizes recent evidence on the determinants of medication adherence and the interventions most likely to improve it in chronic care. Using the initiation–implementation–persistence framework, it organizes barriers and facilitators across four levels: patient factors (health literacy, beliefs, motivation, mental health), therapy factors (polypharmacy, side effects, dosing complexity), provider factors (communication, shared decisions, follow-up), and system factors (cost, access, continuity, and fragmented services). The review compares intervention approaches, including tailored education, regimen simplification, motivational interviewing, pharmacist-led monitoring, multidisciplinary care pathways, and financial or logistical support. Particular attention is given to digital strategies—SMS reminders, mobile apps, telehealth, electronic refill prompts, and smart packaging—and the conditions under which they succeed or fail. Findings indicate that single, generic interventions rarely sustain adherence; combined, patient-centered and context-sensitive packages perform better, especially when aligned with local resources at Maaref University of Applied Sciences and similar settings, and evaluated with pragmatic outcomes and equity.

**Keywords**— Medication adherence; Initiation–implementation–persistence; Digital health interventions; Health literacy; Chronic disease management.

## I. INTRODUCTION

Medication adherence is a big and complicated issue in healthcare around the world. It means how well a patient follows the medicine plan that a doctor or healthcare provider suggests (Heidari et al., 2019). Adherence isn't just one action, it's a process with three connected parts: starting (taking the first dose), following through (sticking to the dosing plan over time), and staying with it (how long someone keeps taking the medicine before stopping) (Davis et al., 2015). When people fail at any of these steps, especially those with long-term health conditions like diabetes, high blood pressure, or heart disease, it's called a "silent epidemic." That's because the problems from not taking medicine as directed are serious but often go unnoticed (Heidari et al., 2019).

Not following a medicine plan can lead to worse health outcomes. Patients who don't take their meds as they are told may see their conditions get worse, treatments fail, and they face preventable health issues, which can even lead to more deaths (Davis et al., 2015). From an economic point of view, not taking medicine also costs a lot. In countries like the United States, it's linked to hundreds of billions of dollars in extra healthcare costs each year. This is mainly because of more hospital stays, emergency room visits, and dealing with problems that could have been avoided (Heidari et al., 2019). Globally, the World Health Organization says about half of all patients don't take their medicines as prescribed, showing how

widespread and serious this problem really is (Heidari et al., 2019).

Even though there have been many improvements in medicine and how healthcare is provided, the rate at which patients follow their treatment plans has not improved in a matching way. This means the problem is more than just not having good medicines or better healthcare systems. It shows that there are deeper reasons connected to how people behave, their social situations, and the bigger systems in place. Things like not knowing enough about their medications, having bad feelings about taking medicine, complicated treatment plans, not getting good advice from doctors, and not having enough money all play a part in whether or not someone follows their treatment (Davis et al., 2015). Because of this, taking medicine as prescribed is now seen as a complex issue that needs a full approach, not just simple education or isolated actions. Given these challenges, this review of recent research aims to closely look at what's been studied about taking medicine as directed. The review has two main goals. The first is to find and understand the main factors that affect whether people take their medications, using up-to-date ideas and real research. The second part is to look at how well the current approaches are helping to improve the way medications are used, with a particular focus on new digital tools and strategies that doctors, and healthcare workers are leading. Rather than just listing what has been studied, this review takes a closer look at how the methods work, the results they show, and the shortcomings or problems found in the studies.

**II. Review Methodology**

This review is a **Narrative Review** that aims to provide a critical synthesis of recent literature on medication adherence determinants and interventions for optimization. Unlike systematic reviews, this approach does not follow a strict, pre-defined search protocol but focuses on analyzing and interpreting key, influential research in the field.

**Search Strategy:** Research was identified through searches in major academic databases (e.g., PubMed, Scopus) using combinations of keywords including: "Medication Adherence," "Determinants," "Interventions," "COM-B framework," "Digital Interventions," and "Pharmacist-Led Interventions."

**Inclusion and Exclusion Criteria:** Studies were included if they focused on literature reviews or recent empirical studies (from 2015 onwards) that offered a clear theoretical or practical contribution to understanding medication adherence. Studies focusing narrowly on a single, specific disease or those lacking in-depth analysis of determinants or interventions were generally excluded.

**III. Findings from Earlier Studies**

To deal with the problem of people not following their medication properly, it's important to understand all the different factors that are involved. Recent studies show that these factors are linked and involve things like the patient's personal traits, how the healthcare system works, and the type of treatment plan. Here's a summary of ten recent studies (published between 2024 and 2026) in a table, followed by a closer look at how each study was conducted, what they discovered, and the limitations of their methods.

| Author/s & Date        | Research Design   | Sampling / Data Collections       | Findings / Conclusions   | Limitations / Future Research   |
|------------------------|-------------------|-----------------------------------|--|---|
| Zhang et al. (2025)    | Systematic Review | Studies (2010-2024)               | Adherence is fundamentally shaped by the COM-B model: Capacity (knowledge, published skills), Opportunity (social support, resources), and Motivation (beliefs, personal goals). | Linguistic bias (English and Chinese only) may limit generalizability across diverse cultural settings. |
| Al-Ganmi et al. (2020) | Narrative Review  | Evidence on digital interventions | Digital interventions show promise, but success hinges on high levels of personalization and   | Implementation hurdles, issues of access, and the potential to exacerbate health inequalities           |

|                              |                                 |  |   |   |
|------------------------------|---------------------------------|--|---|---|
|                              |                                 |  | interactivity. Outcomes are often inconsistent.   | s. App quality requires better regulation.  |
| Sholihah et al. (2025)       | Scoping Review                  | 12 studies focusing on multimorbidity patients           | Pharmacist-led interventions (counseling, medication management) demonstrated effectiveness in 75% of the reviewed studies.     | Need for robust studies assessing the long-term sustainability of these interventions.  |
| Butt et al. (2016)           | Systematic Review of RCTs       | 8 Randomized Controlled Trials (2449 arthritis patients) | 62.5% of trials reported significant adherence improvement when utilizing digital tools (calls, texts, video).                  | Short follow-up periods and small sample sizes in some included trials compromise long-term validity.                           |
| Heidari et al. (2019)        | Analytical Report               | WHO data and recent reports                              | Non-adherence affects approximately 50% of patients; this failure significantly escalates mortality and healthcare costs.       | Reliance on broad, aggregated secondary data limits in-depth causal analysis.   |
| Algabbani & Algabbani (2020) | Analytical Study                | Elderly polypharmacy patients with chronic diseases      | Key determinants include polypharmacy, cognitive impairment, low health literacy, and socioeconomic status.                     | Generalizability is difficult due to the pronounced heterogeneity in the health and cognitive status of the elderly population. |
| Virrueta et al. (2025)       | Retrospective Cohort Evaluation | Population health quality improvement program            | Pharmacist-supported electronic outreach proved effective in the proactive identification and mitigation of adherence barriers. | The retrospective design introduces potential selection and measurement biases.   |

|                             |                           |                                   |  |  |
|-----------------------------|---------------------------|-----------------------------------|--|--|
| Newman-Casey et al. (2015)  | Systematic Review of RCTs | Standalone mobile applications    | Applications that integrate both reminder functions and educational content exhibit the highest efficacy.      | Significant variability in app quality; many lack a verifiable scientific foundation.                    |
| Davis et al. (2015)         | Comprehensive Review      | Patients with chronic diseases    | Barriers are categorized as patient-related, medication-related, and healthcare system-related factors.        | The necessity for disease-specific, tailored strategies highlights the complexity of a unified solution. |
| Milosavljevic et al. (2018) | Critical Review           | Two decades of adherence research | Patient knowledge regarding their illness and medications is identified as a pivotal, patient-centered factor. | The historical focus may lead to an under-representation of the latest technological interventions.      |

**3.1. Conceptual Frameworks and the Multifaceted Nature of Determinants**

Recent research consistently conceptualizes medication adherence as a complex health behavior shaped by multiple interacting determinants rather than a single patient decision. Among the reviewed studies, the systematic review by Zhang et al. (2025) provides one of the most structured and practically applicable approaches through its use of the COM-B (Capacity, Opportunity, Motivation–Behavior) framework. This model offers a clear behavioral lens for understanding why patients may fail to adhere to prescribed treatments and how such failures can be addressed.

Within this framework, Capacity refers to the patient’s psychological and physical ability to follow a medication regimen. This includes adequate knowledge of illness and its treatment, as well as the skills required to manage dosing schedules and administration techniques (Milosavljevic et al., 2018). Limited health literacy or misunderstanding treatment instructions can directly undermine adherence, particularly in patients with complex regimens (Zhang et al., 2025).

Opportunity encompasses external factors that enable or constrain adherence behavior. Social support from family members or caregivers plays a critical role in reinforcing adherence, especially among vulnerable populations. In addition, having enough money and being able to get healthcare services greatly affect how well a patient can get and keep taking their medicine (Zhang et al., 2025). These kinds of barriers show that not taking medicine as prescribed isn’t just about someone not trying hard enough, it’s often

because of bigger problems in the system and the way things are structured.

Motivation is the third part, and it’s about the inside feelings that push someone to act. What a patient thinks about whether their medicine is needed, worries about side effects, their own health goals, and how confident they feel about managing their treatment all play a role in whether they stick to their medication (Zhang et al., 2025). If someone doesn’t believe in the importance of their treatment or feels unsure about managing it, they might choose not to take their medicine, even if they have the chance and resources to do so. These findings match closely with the detailed review by Davis et al. (2015), which groups reasons for not taking medicine into things related to the patient, the medicine itself, and the healthcare system. While Patel et al. takes a more general approach, the COM-B framework gives a clearer way to design solutions. It helps researchers and doctors connect the problem areas directly to the right strategies.

**3.1.1. Comparison with Other Health Behavior Models**

Although the COM-B model is becoming more popular in research about following treatment plans, it is often used along with other established theories about health behaviors. The Health Belief Model (HBM) looks at how people see the seriousness of a disease, how likely they think they are to get it, and whether they believe the benefits of treatment outweigh the challenges (Milosavljevic et al., 2018). The Theory of Planned Behavior (TPB) focuses on how people decide to act, based on their attitudes, what others think, and how easy they feel it is to do the behavior (Zhang et al., 2025). While HBM and TPB are helpful for understanding why patients decide to take medicine, they mostly describe what happens rather than offer clear ways to create effective interventions. On the other hand, the COM-B framework is strong because it helps create real-world solutions. It connects behavior problems to specific issues like a person’s ability, the environment, or their motivation. For example, teaching patients can help if they lack knowledge, supporting them with policies or money can help if they face practical problems, and talking to them or encouraging them can help if they lack motivation. As Zhang et al. (Zhang et al., 2025) pointed out, this practical focus makes COM-B especially useful for today’s research on treatment adherence, where the focus has moved from just finding problems to building clear, effective interventions based on evidence.

**3.2. Adherence Challenges in Specific Demographic Cohorts**

Recent studies show that having trouble with taking medicine isn’t the same for everyone. Some groups, such as older adults and people with serious ongoing health issues, face bigger challenges in keeping up with their medications. These groups require special solutions that are made to meet their specific needs.

**3.2.1. The Geriatric Population and Polypharmacy**

A study by Algabbani (2020) looks closely at why older adults with long-term illnesses might not follow their treatment plans. The study shows that taking many medicines at once, trouble remembering things, and not understanding health information are big reasons for not following the treatment. Taking five or more medicines at the same time makes it harder to keep track of when and how to take them. This can lead to mistakes in taking the right dose, and it can confuse the patient (Algabbani & Algabbani, 2020). All of these things make it harder for the person to stick to their medicine plan. When someone has trouble thinking clearly, even a little, it can affect their ability to

remember, pay attention, and make decisions. Afkhami et al. (Algabbani & Algabbani, 2020) say that just giving information isn't enough for older people because their thinking ability may be limited. It's better to make the medicine plan easier, use easy-to-read labels, and get help from people like family members or tools that remind them to take their medication. The results show that older adults usually don't stop taking their medicine on purpose. Instead, they have real difficulties in managing their health because of their age and how the healthcare system works. So, any support for this group should take into account both their personal needs and the help they receive from their environment.

### 3.2.2. Socioeconomic and System-Level Barriers

In addition to age-related issues, factors related to a person's social and economic background, as well as the structure of the healthcare system, greatly affect whether someone follows a treatment plan. A report by Heidari et al. (2019) says that not following a treatment, or non-adherence, is a serious problem around the world, affecting about half of all patients. The report uses data from the World Health Organization to show that things like the cost of medicine, limited access to healthcare, and uneven drug supply can all make it hard for people to follow their treatment. In poorer and middle-income countries, money is often the biggest problem when it comes to following treatment, even if people are motivated or know what they should be doing. Even in wealthier countries, costs that people pay directly or restrictions on insurance can lead them to skip doses or stop treatment altogether (Heidari et al., 2019). These findings show that simply focusing on the patient isn't enough to fix the problem. Pruitt et al. (Heidari et al., 2019) suggest that to make real progress in improving adherence, there needs to be action at the policy level. This includes things like helping pay for medicine, expanding healthcare coverage, and improving primary care systems. From the COM-B framework's point of view, these strategies mainly deal with opportunity-related barriers, showing the importance of looking at bigger system issues as well as individual actions.

### 3.3. Evaluating the Efficacy of Targeted Adherence Interventions

Because medication non-adherence is a common and complex problem, recent studies have looked more closely at special kinds of programs that help people follow their medicine plans.

The most studied types of these programs are digital tools and efforts led by healthcare providers. Both kinds of programs aim to deal with the many reasons people might not take their medicine as prescribed.

#### 3.3.1. Digital Interventions

Digital health tools, like apps, text messages, and telehealth communication, have become very popular as ways to help improve medication adherence on a large scale.

Recent studies show that these tools can work, but how well they work depends a lot on how they are designed and used.

Moon and Walsh (2025) (Al-Ganmi et al., 2020) studied digital adherence tools and found that having only technology isn't enough to make a big difference.

Tools that just send automated reminders often only help a little and only for a short time.

However, tools that integrate educational content and personalized feedback, as noted by Newman-Casey et al. (2015), show greater efficacy. A systematic review by Butt et al. (2016) of eight randomized controlled trials found that digital tools, including calls, texts, and video support, were used. The results show that these tools can work well in various ways, especially when long-term self-care is needed. Even though the results are positive, there are still some difficulties to overcome. Many studies have short follow-up periods and small groups of people, which makes it hard to know if the improved medicine-taking lasts over time (Butt et al., 2016). Also, as Moon and Walsh (Al-Ganmi et al., 2020) noted, not everyone has equal access to digital tools, which could make health differences worse. This shows that when creating these programs, it's important to consider fairness and equality.

#### 3.3.2. Pharmacist-Led Interventions

Alongside digital methods, pharmacist-led interventions have become a very effective way to help patients take their medications as prescribed, especially those with complicated treatment plans. A scoping review by Sholihah et al. (2025) found that pharmacist-led actions, such as giving medicine advice and managing treatment plans, helped improve medication adherence in about 75% of the studies they looked at. Pharmacists are especially good at finding issues with medications, making treatment plans simpler, and helping patients deal with concerns about side effects and how well their treatment works. The success of pharmacist involvement is also shown by a study done by Virrueta et al. (2025). Their work showed that when pharmacists helped with electronic outreach in population health programs, they were able to find and solve problems with medication adherence before they led to treatment failure.

This mix of methods shows how using professional knowledge along with digital tools can give early, targeted care that focuses on the patient's needs. From a behavior standpoint, pharmacist-led interventions are really helpful because they address multiple factors at the same time. By helping patients understand their condition better, making treatment plans simpler to follow, and providing support, pharmacists help patients feel more capable and more willing to stick to their treatment plan. They also help overcome barriers that are related to opportunities. These findings show that including pharmacists should be a key part of any complete plan to help patients stick to their medications, not just extra service.

#### 3.4. Methodological Limitations and Weaknesses in Adherence Research

Even though recent studies on taking medicine as prescribed have given us some useful information, there are some common problems with how these studies are done. These issues mostly involve how they measure adherence, how long the studies last, and whether the results can be applied to real-world situations.

A main problem in the way things are studied is how well people take their medicine as prescribed. Different studies use various ways to check if people are taking their medication, like asking people directly looking at how often they get refills from the pharmacy, counting pills or using electronic devices that track when medicines are taken. Asking people directly is easy and cheap, but it can be tricky because people might not remember correctly or might say they take their medicine even if they don't. Looking at pharmacy records tells us if people get their medicine

but not if they actually take it. Electronic devices give more accurate results, but they are expensive and might make people act differently which can affect the results. Since different studies use different methods it's hard to compare them directly and the results might not be consistent. Another issue is that many studies don't follow people for long enough, especially when testing digital tools. For example some studies only check results for a few months which isn't enough to see if improvements last over time, especially for diseases that need medicine for life. Other studies also show that it's not clear how long the effects of pharmacist help last. Without longer follow-up it's hard to tell if changes are just temporary or real and lasting. Also the results from studies may not apply to everyone because they were only done in certain places or with certain groups of people. For example some studies only looked at research done in English or Chinese which might miss important information from other parts of the world. This makes it harder to use the findings in different settings or with different people in other linguistic and cultural contexts. In addition, retrospective evaluations, such as those conducted by Virrueta et al. (2025), are inherently vulnerable to selection bias and may reflect context-specific outcomes that cannot be readily generalized to other healthcare settings.

These methodological problems show that there is a need for more standard ways to measure how well people follow treatment plans longer times to track how things go and studies that include a wider range of people. Fixing these issues is important to make the research more solid and the results more trustworthy.

### 3.5. Study Methodologies, Theoretical Contributions, and the Role of Motivation

Looking more closely at the methods and ideas from the studies reviewed, we can see how each one helps us understand better why people take their medications as prescribed. At the same time, these studies also show where there are still unanswered questions in the research. Together, they stress the need to connect behavioral theories with real-world approaches to improve medication adherence. Zhang et al. (2025) did a thorough review that added important theory by using the COM-B framework. This framework helps break down the reasons why people don't take their medications by looking at three areas: their ability, the opportunities they have, and their motivation. This organized way of thinking is a big improvement over earlier models that just described the problem without offering clear solutions. However, the study's focus on a limited set of languages made it less useful for people around the world. Many studies now focus on how digital tools can help with medication adherence. Moon and Walsh (2025) (Al-Ganmi et al., 2020) point out that these digital tools work best when they focus on changing people's motivation, not just reminding them to take their pills. Likewise, Newman-Casey et al. (2015) found that apps which include educational material are more effective at keeping people on track because they help patients understand their condition and feel more involved. While these findings show how important it is to use behavioral theories in digital tools, there's still a lot of variation in how well the studies are designed, which is a problem.

Pharmacist-led interventions show strong real-world results, especially for patients with multiple health issues. Sholihah et al. (2025) and Virrueta et al. (2025) both show that professional medication management can help with several

adherence problems at once. These interventions are effective because they improve patient knowledge, make treatment plans easier to follow, and offer personalized support, which helps build both the ability and the desire to stick with treatment. However, most studies in this area aren't randomized or prospective, which means more careful trials are needed. A common theme in literature is the importance of motivation and self-efficacy in adherence. Milosavljevic et al. (2018) point out that knowing about medication isn't enough on its own—people also need confidence in their ability to manage their treatment. Interventions that build self-efficacy through skill development, reassurance, and setting small, achievable goals are more likely to lead to long-term adherence. This idea fits well with the COM-B framework, where motivation plays a key role in driving lasting behavior change. Overall, the studies reviewed show a trend from just observing behavior to creating focused interventions based on established theories. However, there are still limitations, including study design, how long the studies follow patients, and how diverse the groups are. Fixing these issues will be important for turning adherence research into practical, lasting improvements in clinical care.

### IV. Conclusion

Pharmacist-led interventions show strong real-world results especially for patients with multiple health issues. Sholihah et al (2025) (Sholihah et al., 2025) and Virrueta et al (2025) (Virrueta et al., 2025) both show that professional medication management can help with several adherence problems at once. These interventions are effective because they improve patient knowledge make treatment plans easier to follow and offer personalized support which helps build both the ability and the desire to stick with treatment. However most studies in this area aren't randomized or prospective which means more careful trials are needed. A common theme in the literature is the importance of motivation and self-efficacy in adherence. Milosavljevic et al. (2018) point out that knowing about medication isn't enough on its own—people also need confidence in their ability to manage their treatment. Interventions that build self-efficacy through skill development, reassurance, and setting small achievable goals are more likely to lead to long-term adherence. This idea fits well with the COM-B framework where motivation plays a key role in driving lasting behavior change. Overall the studies reviewed show a trend from just observing behavior to creating focused interventions based on established theories. However there are still limitations, including study design how long the studies follow patients and how diverse the groups are. Fixing these issues will be important for turning adherence research into practical lasting improvements in clinical care. Digital tools like mobile apps and electronic tools can help people take their medicine as prescribed (Al-Ganmi et al., 2020) (Butt et al., 2016) (Newman-Casey et al., 2015) But these tools work best when they are well-designed and tailored to individual needs. Apps that include educational materials and adjust based on user input are more effective than those that just send reminders. Still there are worries about unequal access to technology and poor quality of apps so these digital solutions should support not replace professional medical care. In short taking medicine as directed is key to making sure treatments work and health improves. Better adherence improves lives and helps healthcare systems by preventing problems and cutting costs (Davis et al., 2015). The research shows that future efforts should focus on creating interventions that are based on strong theories centered on patients and aware of how healthcare systems work. To move forward researchers and practitioners must fix methodological

issues work across different fields and make sure that adherence strategies are both effective and fair for all kinds of people.

## V. Future Studies

Based on the issues found in the research that has been reviewed, there are several important areas where more study is needed. First, there is a strong need for long-term studies that look at how well adherence programs work overtime, especially beyond one year. Many current studies, especially those looking at digital tools, only check results for a short period, which makes it hard to know if these tools are really effective in the long run (Sholihah et al., 2025) (Butt et al., 2016). Second, future research should focus on creating and using standard ways to measure how good and effective digital adherence tools are. Having common ways to evaluate these tools would help compare them across different studies and make sure that they are based on solid theories about behavior, not just on what's commercially popular (Newman-Casey et al., 2015). Third, more attention needs to be given to fairness and access in healthcare. Programs should be designed and tested in groups that are often left out, like older people with memory problems and people in areas with few resources, to stop existing health gaps from getting worse (Al-Ganmi et al., 2020) (Algabbani & Algabbani, 2020). Lastly, new technologies like artificial intelligence and machine learning should be studied more. These tools could help predict when someone might not follow a treatment plan and allow for customized, timely support based on how patients behave (Zhang et al., 2025).

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## Human Participants

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## Originality Note

The authors confirm that the manuscript is their original work, and if others' works are used, they are properly cited/quoted.

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