

Treatment Adherence in Integrative Medicine—Part One: Review of Literature

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Abstract

Treatment adherence is a topic that is well studied but not well understood. Low treatment adherence is a significant issue that limits the effective management and treatment of chronic conditions, creating significant health care burden, costs, and poor patient outcomes. This report provides a review of the factors that facilitate or create barriers to treatment adherence, as well as strategies recommended to overcome adherence barriers.

A total of 25 interviews were conducted with practitioners demonstrating both high (n = 16) and low (n = 9) treatment adherence rates. A total of 185 survey responses were received from high-treatment adherence rate practitioners (n = 21), low-treatment adherence rate practitioners (n = 83), and practitioners that were neither in the high- or low-treatment adherence rate range (n = 81).

Practitioner prescribing behaviors and adherence statistics were determined and stratified by high-treatment adherence rate and low-treatment adherence rate practitioners. From the interviews, 78% of low-rate practitioners mentioned that establishing trust is a primary best practice for optimizing adherence, and for high-rate practitioners, 69% thought that facilitating

trust was important to optimizing adherence. Both low- and high-adherence rate practitioners prioritized using a staged approach as a strategy to overcome barriers to adherence. From the total survey sample it was found that key strategies to improving adherence included the practice of booking follow-up appointments, using lab results to explain treatment plans, and using a staged approach for treatment plans.

Our research sought to elicit strategies and skills that can help improve treatment adherence in integrative medicine and our findings have identified several common practices that can help to improve adherence. Research taking advantage of mobile devices and the internet for adherence has started to expand within the last 10 to 15 years. Technology has the potential to lead the development and establishment of a centralized database that acquires adherence information and provides solutions to its practitioners and patients. Further work to advance the field of integrative medicine through additional research and interventions that support treatment adherence would be valuable to the effective treatment and management of integrative medicine patients.

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Key Findings

- Treatment adherence is conceptualized and studied predominantly within the realm of conventional (pharmaceutical) therapies, but themes may overlap with other medical models.
- Several terms related to adherence, including “compliance” and “concordance,” have been used interchangeably in the literature, but it is commonly accepted that they have slightly different connotations.
- There are several ways to measure treatment adherence, but there is no single gold standard. Comparison of adherence rates can be difficult as studies often do not use the same measures or define adherence according to the same parameters (eg, dichotomous vs continuous variables).

- Hundreds of factors may interactively influence the likelihood of adherence. Practitioners should identify the most relevant factors for each patient.
- Interventions that improve medication adherence may target various facets of treatment, but adherence rates generally decline over time. New technology will provide opportunities to improve assessment and the likelihood of adherence.

How to Improve Treatment Adherence

- Practitioner education
- Become familiar with the factors that influence treatment adherence
- Proactive screening
- Proactively identify barriers to adherence and provide strategies prior to treatment initiation
- Continue to measure adherence rates
- Use multiple measures to best capture adherence rates and reasons for non-adherence
- Implement key strategies
- Provide strategic interventions specific to the identified reasons for non-adherence

Literature Review Methodology

The literature review used a semi-systematic, mixed methods approach to assess the current state of knowledge and synthesize themes across multiple disciplines.¹ The primary search strategy combined the search terms “adherence” or “compliance” in PubMed with various keywords identified for this review (eg, assessment, patient, medication, diet) and yielded more than 2 million articles, including duplicates. The search strategy on interventions to improve medication adherence included a combination of the search terms “medication adherence[Mesh]” and “intervent.*”

The inclusion of systematic reviews and meta-analyses was prioritized, followed by clinical trials or other supportive articles where required. However, there were no rigid inclusion or exclusion criteria.

Search Entry Examples:

- Treatment adherence and compliance [Mesh]
- Medication adherence [Mesh] AND intervention
- Adherence AND measure
- Adherence AND barrier

Defining Adherence

Variability exists when defining and measuring “adherence” to a treatment.² There has been a shift from using the term “compliance” to the word “adherence” as

literature and medical practices have come to recognize the importance of the therapeutic alliance.⁷ However, despite subtle differences in their meaning, these terms have been used interchangeably.⁴

Therapeutic alliance

The relationship between a patient and practitioner that encourages agreement on treatment goals and tasks, as well as a positive personal relationship.

Compliance

Compliance is defined as the extent to which a patient’s behaviors follow a practitioner’s prescribed treatment plan (eg, medication, diet, lifestyle changes, etc.). It often implies a patient’s subservience to the practitioner’s recommendations and infrequently considers patient treatment preference or values.^{2,4}

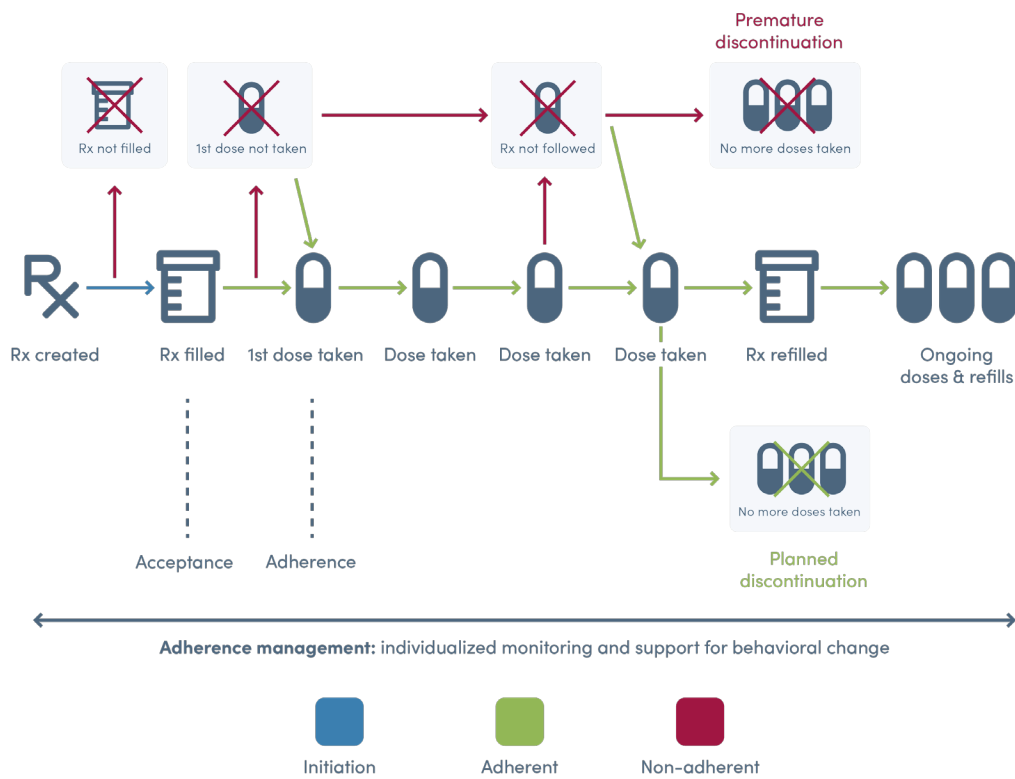
Adherence

Adherence is defined as the extent to which a patient’s behaviors follow an agreed-upon prescription or therapeutic regimen. It considers the patient’s views and choices, and it allows them to play a more active role in the development of the treatment plan.^{2,4-6}

Intentional Non-Adherence

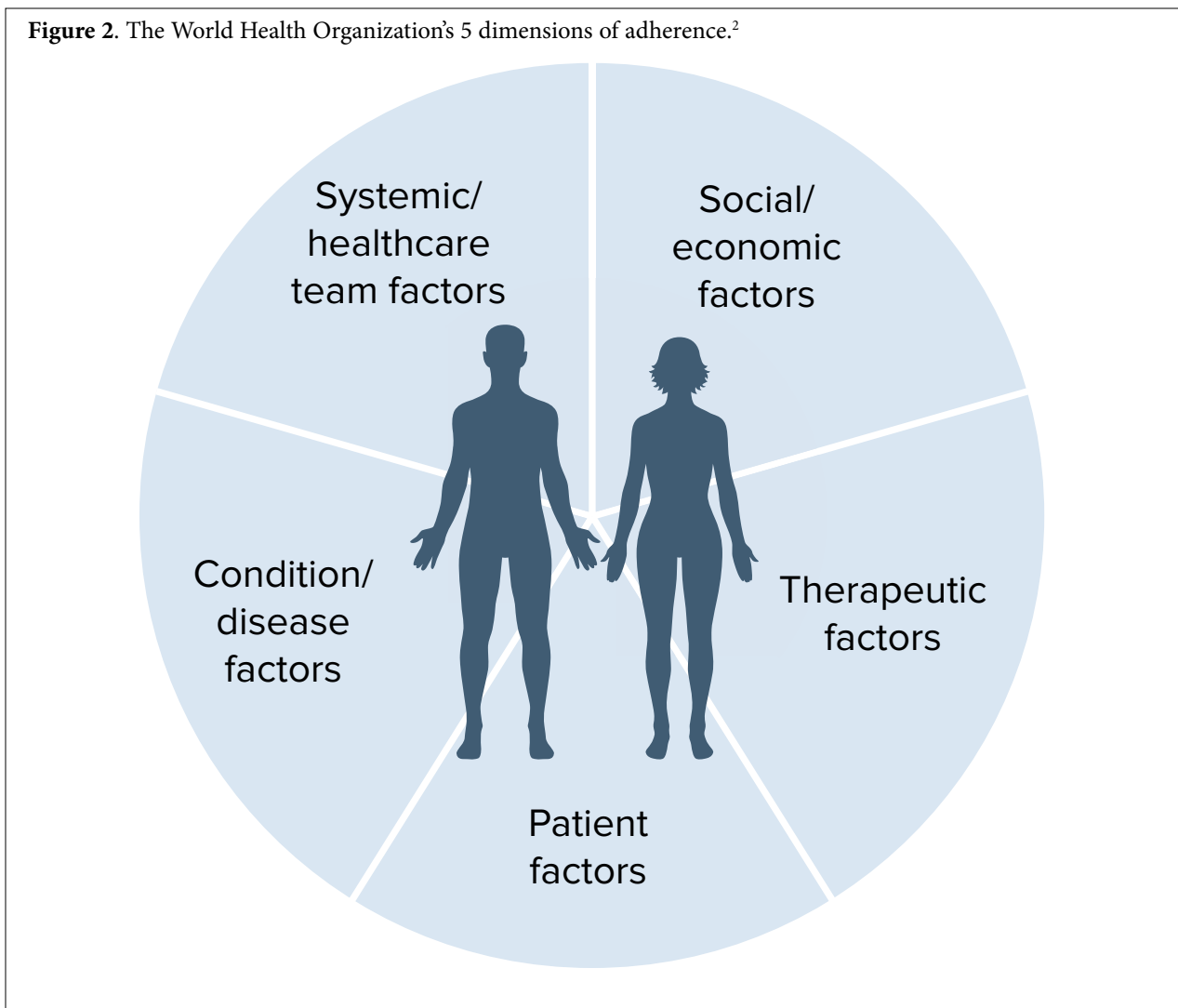
Deliberate abstinence from a therapy.

Figure 1. The Fullscript model of adherence management



“Adherence management” refers to the ongoing assessment and support from healthcare systems, prescribing policies, communities and organizations, practitioners, family and caregivers and patients.⁴

Figure 2. The World Health Organization's 5 dimensions of adherence.²



Unintentional Non-Adherence

Sporadic or accidental lapses in the degree to which a treatment plan is followed.

Concordance

Concordance is the element of adherence that describes the state of cooperation and mutual agreement to a prescribed treatment plan between a practitioner and their patient. Concordance reflects the increasing emphasis placed on the shift from a patient's subservient acceptance of a treatment plan to the therapeutic cooperation between patient and practitioner.⁴

The use of shared decision-making strategies to empower patients in disease self-management and treatment adherence has been increasingly recognized.⁷⁻¹⁰

Frameworks of Adherence and Influencing Factors

Various theoretical models of treatment adherence have been proposed. Please note that the following examples are merely used to illustrate some of the types of theoretical models available to conceptualize adherence and are not meant to be a comprehensive or exhaustive list.

The Process of Medication Adherence and its Management

Within this framework, adherence to medications is the extent to which patients use their medication as prescribed during 3 phases:

- **Initiation** (primary adherence): the point at which a patient takes the first action, step, or dose, etc of a prescribed treatment plan^{4,11}
- **Implementation** (secondary adherence): the degree to which a patient follows their treatment plan from initiation to discontinuation⁴
- **Discontinuation**: the point at which the treatment plan halts regardless of the rationale or whether it was intentional or unintentional.⁴

The World Health Organization's 5 Dimensions of Adherence

The World Health Organization's (WHO) report on adherence describes 5 interacting dimensions that influence adherence to treatment plans in chronic disease states.² Non-adherence has been traditionally considered a

patient-centered problem. Therefore, interventions to improve adherence have primarily focused on targeting patient-related factors without critical reflection on the interplay of the other 4 dimensions.^{2,12-14}

Condition/disease factors

- Symptom severity
- Extent of physical, psychological, social, educational, or employment disability
- Development course or state of the condition
- Presence of co-morbidities
- Existence of treatments available

Patient Factors

- Forgetfulness
- Negative feelings like stress, hopelessness or anxiety towards treatment or the condition
- Level of motivation, self-efficacy or knowledge of the disease and therapy
- Perception of therapeutic expectations, effects, efficacy or need for treatment
- (Mis)understanding of the disease, diagnosis, or therapeutic protocol

Social/Economic Factors

- Age, race and gender
- Poverty or employment status
- Literacy level and education
- Social and family support
- Living location and transportation access
- Treatment cost
- Culture or social beliefs about the treatment or disease

Systemic/Healthcare Team Factors

- Patient-practitioner relationship
- Availability or scope of care/coverage
- Access to treatment
- Practitioner education, workloads, incentives and feedback
- Time constraints, follow-ups
- Systemic patient education
- Establishment of community support and self-management programs

Therapeutic Factors

- Protocol complexity
- Therapy duration
- (Un)success of previous treatment
- Frequency of treatment adjustments
- Speed of therapeutic benefits
- Presence of adverse events
- Availability of medical support for adverse events

It is important to note that these factors have been primarily studied within the realm of conventional medicine. However, the factors influencing adherence

transcend medical dogmas, whereby significant overlap of these factors similarly influences adherence to other treatment options including diet, physical activity or complementary and alternative medicines (CAM), including supplements.¹⁵⁻²³

Some factors that specifically relate to these alternative treatment options include:

CAM

- Strong belief in holistic health
- Positive attitudes or appreciation of CAM-based therapies
- Belief in environmental pollution as a negative health factor
- Perception that other treatments are costly¹⁶

Diet and nutrition

- Knowledge of specific diets, instructions, nutrition labels, and adapting recipes²⁴⁻²⁹
- Limitations of foods/supermarkets, cost^{24,25}
- Cultural connections with food, history of poor diet^{24,25,27,29-31}
- Intensity/difficulty of the diet, food palatability^{26,32}

Physical activity and exercise

- Availability of exercise facilities, equipment³³⁻³⁸
- Level of fatigue, physical limitations/injury^{34,35,38-40}
- Observed or perceived lack of time, weight loss or change in body composition^{35,36,38,39}
- Cultural/social perspectives on appropriateness of exercise^{33,37,39}
- Lack of enjoyment of exercise or knowledge/training^{35,39}
- Type of exercise, whether it is supervised, performed in groups etc.^{34,35,41,42}

Supplements

- High number of pills, frequency of doses^{15,22,43}
- Low frequency of clinical visits/follow-up¹⁵
- Forgetfulness^{15,22}
- Presence of fear of adverse events^{15,22}
- Modes of administration (eg, capsule, tablet, liquid, injection)²²
- Supplement characteristics (eg, size, taste, smell, color, taste fatigue)^{22,44,45}

Measuring Adherence

Adherence may either be measured as a binary/dichotomous or continuous variable. As a binary variable, the individual may either be adherent or non-adherent. As a continuous variable, adherence is measured as the degree to which the patient precisely follows the treatment plan.

For example, suppose a patient is provided with 3 recommendations in their treatment plan. In this case, he/she may be adherent to 1 aspect of their plan, may

choose not to initiate or fulfill another, or may not demonstrate persistence with the third portion of the recommendation. Following only some aspects of the treatment plan would make the individual partially adherent where adherence is a continuous variable.⁶

Adherence can be measured quantitatively or qualitatively, but there is no single gold standard to measure

adherence as individual treatment adherence measures have their strengths and limitations.⁴⁶ Knowing the benefits and limitations of various measures, practitioners can strategically combine numerous measurement methods to more accurately gauge adherence.⁴⁷ Tables 1a and 1b provide an overview of methods for measuring treatment adherence.^{2,14,48-50}

Table 1a. An Overview of Subjective Measures Used to Measure Medication Adherence

Subjective Measure: Validated scales may provide quick and simple measures of adherence, as well as insights into potential causes of non-adherence.	
Self-rated adherence behaviors	Patients answer questions relating to their adherence behaviors and potential barriers to adherence
Pros	<ul style="list-style-type: none"> • Patients indicating that they have not followed a treatment plan are typically accurate • Provides real-time adherence behavior feedback
Cons	<ul style="list-style-type: none"> • Patients denying non-adherence are typically inaccurate • Can have poor measurement sensitivity or specificity • Subject to communication, interpretation and literacy barriers or survey design flaws
Practitioner-rated adherence behaviors	Practitioners evaluate the adherence behaviors of their patients using standard scales or questionnaires.
Pros	<ul style="list-style-type: none"> • May remove self-reporting bias • Provides real-time adherence behavior feedback
Cons	<ul style="list-style-type: none"> • Practitioners tend to overestimate patient adherence • Can have low measurement sensitivity or specificity • Subject to communication barriers or survey design flaws

Table 1b. An Overview of Objective Measures Used to Measure Medication Adherence

Objective Provides adherence data with low risk of bias, but can be limited to gaining insight into behaviors related to adherence or for understanding reasons for non-adherence	
Equations of medication adherence	Mathematical formulae present a straightforward interpretation where adherence is often defined as the use of >80% of doses.
Pros	<ul style="list-style-type: none"> • Applies to pharmaceuticals, supplements, or other treatments that use a discrete and planned number of treatment units • Avoids problems of reporting or subjective evaluation bias
Cons	<ul style="list-style-type: none"> • Overestimation/underestimation of adherence may occur • Assumes patient actually used the treatment as prescribed • Some do not account for gaps between refills or surpluses of previously available medication. • Determination of adherence can be arbitrary (ie, >80%) • Does not provide qualitative treatment information, including adherence to dose timing, the handling of missed doses, the reasons for non-adherence, etc.

Table 1b. (continued)

Electronic medication containers	Records time and date of when the medication container is opened/ accessed and can send data to practitioner databases
Pros	<ul style="list-style-type: none"> • Higher accuracy than other measures such as pill counts (ie, lower ability to skew adherence patterns/data) • Data on non-adherence sporadicity or consistency with real-time monitoring/feedback on adherence behaviors • Reminds patient to use or refill prescriptions
Cons	<ul style="list-style-type: none"> • Expensive and may be relatively bulky • Assumes patient actually used the treatment as prescribed • Constant surveillance may cause additional anxiety/stress • Overestimation of adherence may occur with accidental container opening
Dispensary databases and EHRs	Centralized systems or EHRs can manage patients, schedule, create prescriptions, record prescription fill and refill data, observe insurance claims, etc.
Pros	<ul style="list-style-type: none"> • Records whether treatment plans are filled, refilled, or prematurely halted, and can provide multi-therapy adherence data • May identify/target patients at high risk for non-adherence
Cons	<ul style="list-style-type: none"> • Does not provide qualitative treatment information and assumes that treatment was actually used as prescribed • Data can be limited by non-synchronized dispensaries • May underestimate adherence if medication is acquired outside of the centralized database or not verified
Biochemical measures	Biomarkers that provide evidence of use of the prescribed treatment; compares standard responses or pharmacokinetic data with the observed response from the patient (eg, blood/urinary measures, biopsies to seek dyed indicators)
Pros	<ul style="list-style-type: none"> • The presence of metabolites or other biomarkers in the body may provide a direct measure of engagement
Cons	<ul style="list-style-type: none"> • Factors may skew the interpretation of adherence (eg, drug-interactions, differences in pharmacokinetics) • Invasive
Directly observed therapy	Whereby a practitioner is present to administer or supervise the patient's administration of a treatment
Pros	<ul style="list-style-type: none"> • Very accurate measure; low risk of mismeasurement
Cons	<ul style="list-style-type: none"> • Expensive, requires the consistent presence of a practitioner and not as generalizable • Patients may hide medications (eg, under the tongue) • May foster feelings of distrust; ethical concerns

Abbreviations: EHR, electronic health record.

Five of the more commonly used and validated self-report questionnaires for medication adherence include^{47,51}:

- The 8-item Morisky Medication Adherence Scale (MMAS-8)⁵²⁻⁵⁷
- The Brief Medication Questionnaire⁵⁶
- The Hill-Bone Compliance Scale^{57,58}
- The Medication Adherence Rating Scale (MARS)⁵⁹⁻⁶¹
- The Self-Efficacy for Appropriate Medication Use Scale (SEAMS)⁶²

It is important to note, regardless of treatment regimen, that limitations in measurement methods and variance in how adherence is defined are also pervasive across the literature for physical activity and exercise,^{42,63-68} diets,^{18,27,28,69-72} and CAM, including supplements.^{44,45,73-76}

Physical Activity and Exercise Adherence Measures

- Questionnaires
- Exercise diaries
- Session attendance
- Accelerometers
- Heart rate monitors
- Direct observation

Specific Exercise Measures

- Frequency
- Duration
- Intensity
- Type
- Progression

Diet Adherence Measures

- Weighing food containers
- Anthropometrics
- Stool testing
- 24-hour urine testing

Specific Diet Questionnaires

- Mediterranean
- DASH
- Gluten-free

Rates of Adherence

Broadly speaking, rates of adherence to the treatment of chronic disease are approximately 50%. This is a widely cited statistic regardless of whether regimens are based on conventional medicines, targeted lifestyle factors including diet or physical activity and exercise or complementary and alternative therapies, including supplements.

Medication Adherence

Approximately 15% to 30% of new prescriptions (ie, primary adherence) are never filled.⁷⁷⁻⁸¹ Ultimately, a lack of adherence in this context is indicative of the existence of a gap between what occurs before, during, and

immediately after a medical consultation and the point at which a prescription is either initially filled or not.^{4,48}

- 15% to 30% average rate of non-adherence to new treatment
- 50% average rate of non-adherence to the treatment of chronic disease

Adherence to chronic disease treatments is cited to be approximately 50% (ranging from 40% to 60%) and mainly refers to secondary adherence in the implementation phase.^{2,13,49,82-84} Even in clinical trials for chronic disease, in which patients receive more attention within controlled environments, adherence still only improves to 43% to 78%.^{12,49,85}

Other analyses have reported primary medication non-adherence data using electronic prescribing transactions or pharmacy claims (see Figure 3). Additional analyses have been conducted to predict the likelihood of non-adherence between different drug classes of drug therapies, such as oral diabetic,⁸⁵ anti-hypertensives,⁸⁷ and statin medications⁸⁸ (see Figure 4).

Figure 3. Primary non-adherence to various medications (%)^{11,79}

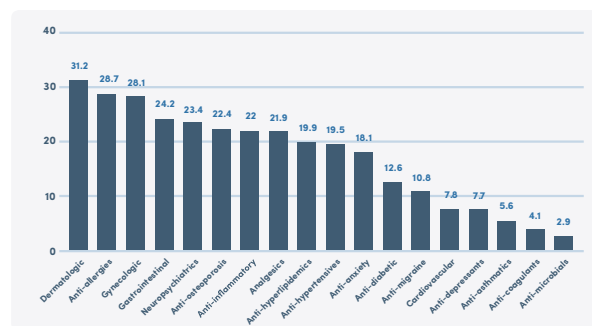
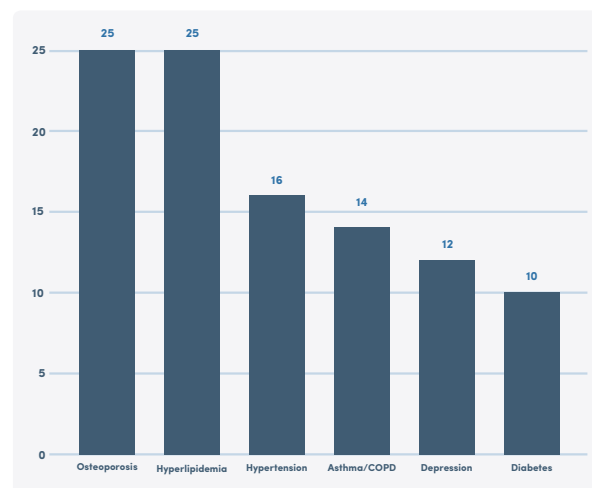


Figure 4. Primary non-adherence across chronic conditions (%)⁷⁷



Condition-Specific Rates of Adherence

Adherence rates in acute conditions are considered higher than those in chronic disease, as adherence rates substantially drop within the first 6 months of treatment.^{2,89-91} In the realm of chronic disease management, adherence appears to vary widely based on particular conditions.

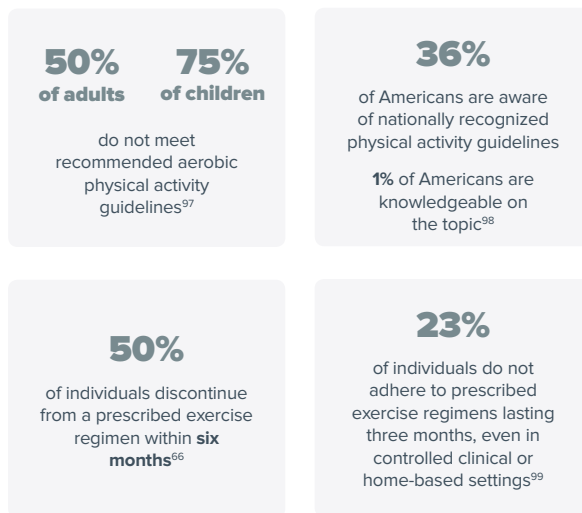
For example, a meta-analysis comprising data from 519 971 patients compared primary medication non-adherence rates using prescription fill data over the course of 1 year across 6 conditions (see Figure 4).⁷⁷

Concerning secondary non-adherence, a longitudinal study with 706 032 patients using medication possession ratios exceeding 80% (drawn from insurance claim data) compared rates of non-adherence among 7 conditions over 1 year (see Figure 5).⁹²

Adherence to Physical Activity and Exercise Recommendations

Studies on adherence to physical activity or exercise also commonly refer to the definition provided in the WHO’s report, which states, “the extent to which a person’s behavior—taking medication, following a diet, and executing lifestyle changes—corresponds with agreed recommendations from a healthcare provider,”² despite the report’s focus on pharmacologic adherence. However, many studies refer to other definitions or do not explicitly define adherence at all.⁶³ Specifically applied to physical activity and exercise, some iterations add to the WHO’s

report by further capturing the extent to which prescribed intensity, duration and frequency of physical activity and exercise is accurately performed.⁹³ As shown in the following infographics, low rates of adherence to physical activity guidelines are widely problematic. Low rates of exercise adherence are also extensively observed across states of chronic disease.⁹⁴⁻⁹⁶



Adherence to Dietary Recommendations

Compliance with recommended diets or healthy nutrition plans also falls within the WHO’s definition of adherence. Studies within the realm of diet and nutrition refer to the WHO’s estimation that 50% of individuals are broadly non-adherent to their treatment plans.^{2,18}

It may be important to note that although there is limited evidence to compare adherence rates between personalized diets and standardized diets, there is some evidence that personalized diets may be more effective. For example, patients with type 2 diabetes who received standardized app feedback about the total intake of calories and dietary fat over the course of 3 months were shown to have lower adherence each month than a group of patients who received personalized feedback on total caloric intake and predicted glycemic scores based on their specific meals.¹⁰⁰ In a similar fashion, scores reflecting adherence to the Mediterranean diet were greater in patients who received personalized nutrition advice, particularly when this was combined with advice based on genetic testing, compared with patients who received standard dietary advice.¹⁰¹

Adherence to Complementary and Alternative Medicine

There is very little information directly comparing broad adherence rates between conventional care and complementary and alternative medicine or integrative medicine therapies such as supplements. One systematic review indicated that adherence to herbal therapies and other remedies was also approximately 50%.¹⁶ Overall, regardless of the medical model, non-adherence is described as a “universal” issue.¹⁰²

Figure 5. Secondary non-adherence in chronic conditions (%)⁹²

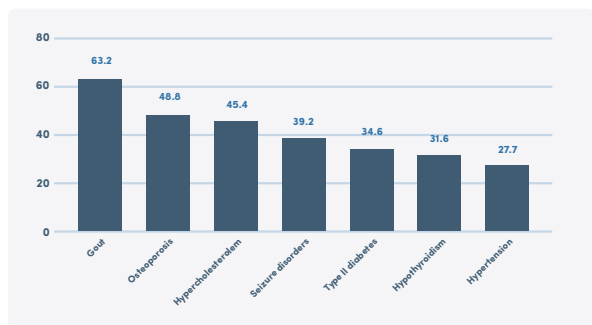
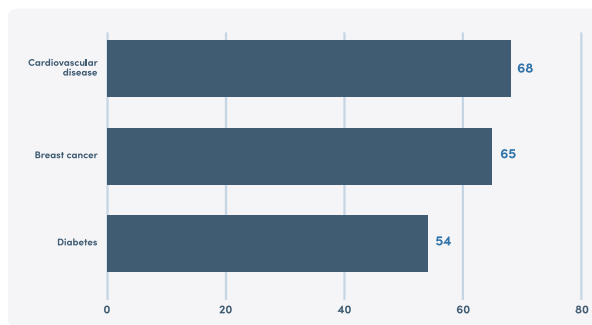


Figure 6. Adherence to physical activity guidelines



Researchers and clinicians should not discount the possibility of underlying influential differences between supplements and pharmaceuticals that may lead to dissimilarities in low adherence risk. There may be inherent behavioral differences between individuals actively seeking to manage their health through supplementation⁵ as opposed to conventional approaches. For example, inherent motivations for the use of supplements may influence adherence, suggesting that there may be an association between the self-determined use of supplements (independent from any advice provided by a practitioner) and an inherent health-seeking behavior.

Furthermore, supplement users are more likely to pursue health and wellness-related characteristics or behaviors, including wholesome nutritional patterns, increased levels of regular exercise, regulation of healthy body weights, and lower rates of alcohol and tobacco use, and are more likely to have health insurance.^{5,103} As widely described in health promotion literature, intrinsic motivation is associated with both initial engagement of health behaviors and long-term adherence.¹⁰⁴ A total of 23% of individuals indicated that their use of supplements was based on recommendations from a practitioner.¹¹

However, differences in adherence to supplements compared with conventional medicines may be attributed to reasons other than internal motivations. For example, patients with high cholesterol have been shown to be 30% more likely to persistently use supplements for 2 years compared with statins.¹⁰⁵ Meriva[®]-formulated curcumin products have also shown greater adherence levels than conventional analgesics.¹⁰⁶ Explanations for this difference may include greater perception of long-term safety, lower cost for its relative efficacy, or reduced prevalence of adverse events.

Much of the literature has focused on whether CAM improves or reduces the rate of adherence to conventional medicines; however, this remains inconclusive.^{17,20,23,107-110} For example, some studies have shown that CAM has been associated with lower rates of adherence to prescribed conventional medication, indicating that the use of supplements can also be a negative modifier of conventional medical adherence. Possible reasons may include individual

beliefs, patient preferences, substituting modes of care, or costs of therapy.^{20,111}

In some cases, concomitant use of supplements can also potentially reduce the risk for a conventional therapy's adverse events, thereby reducing the likelihood of premature treatment discontinuation.^{112,113} Unfortunately, patients also often elect not to disclose their use of complementary and alternative medicines to their practitioners, leading to the possibility of drug-supplement interactions and/or adverse events.¹¹⁴⁻¹¹⁶ Possible drug-drug, drug-supplement, and drug-food interactions have the potential to lead to higher rates of non-adherence.¹¹⁷

Practitioner-Related Adherence

Treatment adherence is directly linked to practitioner factors, although this is often overlooked compared with patient-related factors. The mere temporal proximity of a clinical appointment with a practitioner has been shown to affect treatment adherence. Adherence rates generally decline with time between check-ups.¹¹⁸

White coat adherence: Higher observed adherence just before or immediately after an appointment

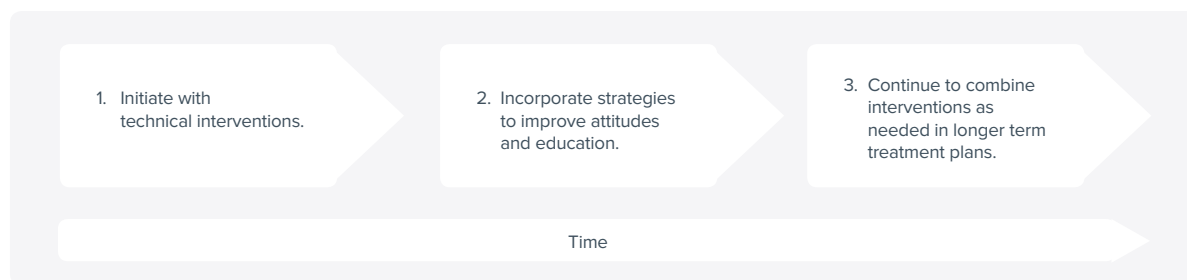
Adherence rates may vary by practitioner modality or specialty, although evidence is limited. For example, primary care providers (PCPs) or general practitioners may have less time available to address factors related to non-adherence, while other practitioners may be able to dedicate more time to navigating patient behavioral barriers.^{119,120}

Rates of medication adherence are often described as similar between practitioner designations. One meta-analysis showed that physicians, pharmacists and nurses had similar patient medication adherence rates.¹²¹ Also, nurse practitioners and PCPs had similar adherence rates for anti-diabetic medications, renin-angiotensin system antagonists and statins.¹¹⁹

In general, the integration of multiple practitioner designations, such as pharmacists, dieticians or health coaches, into patient care improves adherence and patient health outcomes.^{110,122-126}

Table 2. Intervention Strategies for Improving Medication Adherence

Strategy or Approach	Target or Area of Focus
Attitudinal	Patient beliefs, motivations or emotions
Behavioral	Patient behaviors
Educational/cognitive	Patient knowledge of treatment, conditions and importance of adherence
Multifaceted	Incorporates 2 or more interventions from different classifications
Psychosocial	Social circles or communities
Rewards	Positive or negative reinforcement of adherence
Structural	Healthcare system, practitioners, policies or other systemic factors
Technical	Aspects of the treatment itself



Interventions for Improving Medication Adherence

One of the most widely studied topics related to adherence is the efficacy of interventions to improve medication adherence. Intervention strategies generally target a specific aspect of adherence (see Table 1).¹²⁷

Interventions to improve adherence typically have small effect sizes, are transient¹²⁸ and are relatively similar across conditions.¹²⁸⁻¹³⁴

Technical interventions have been shown to provide consistent and reliable benefits to adherence, at least across brief time periods, while attitudinal and educational strategies were found to increase adherence over time in longer interventions up to 10 months. However, multifaceted interventions were required to continue to improve adherence past this time point.¹²⁷

- 4% to 14% potential average improvement in adherence with interventions^{128,132,134}
- 1% Potential reduction in adherence-improving efficacy of interventions each month¹²⁸

A recent umbrella review identified a few key interventions that have been shown to improve medication adherence across a variety of population groups. It was determined that the top interventions to improve medication adherence were dose simplification, patient education, electronic reminders, and cost reduction/rewards provision.¹³⁵

Dose Simplification

How:

- Reduce dose frequency^{107,129,130}
- Use sustained-release formulations¹⁰⁷
- Suggest combination pills or multi-ingredient formulations^{129,136}
- Suggest products with compartmentalized packaging^{129,130,137}

Adherence:

- 13% to 36% via daily dose vs twice per day¹³⁸
- 22% to 41% via daily dose vs thrice per day¹³⁸
- 5% with combination pill vs individual pills¹³⁶
- 3% with sustained-release formulations, 10% more days with correct dosing vs regular-release¹⁰⁷
- Packaging strategies commonly reported to improve adherence, but may be inconsistent^{129,130,134}

Electronic Reminders

How:

- Suggest text messages or other automated cues set to specific dose times via applications^{139,140}
- Personalize texts or use 2-way communication¹³⁹
- Consider electronic packaging devices that provide real-time dose use and feedback data¹⁴¹⁻¹⁴³

Adherence:

- 18% to 22% with mobile devices and reduces likelihood of missing appointments by 10%^{144,145}
- In 40% to 65% of trials using mobile device reminders^{139,144-146}
- 10% to 20% using strategies with feedback^{128,147,148}
- Electronic packaging strategies commonly reported to improve adherence, but may vary¹⁴⁹

Patient Education

How:

- Provide verbal or written content tailored to the specific condition or barriers to adherence^{81,150,151}
- Use information leaflets to improve health literacy¹⁵²
- Provide education on how to self-monitor and self-manage the condition^{151,153}

Adherence:

- 16% vs 10% among strategies without education¹²⁸
- Education strategies may need to be combined with other interventions to be optimized^{127,153-155}

Cost Reduction and Rewards

How:

- Support value-based insurance designs, which reduce costs for highly effective treatment vs less effective treatments¹⁵⁶⁻¹⁶⁰
- Explore financial reward options (eg, discounts, loss of percentages of “financial bonuses” for each lapse in adherence)^{161,164}

Adherence:

- Up to 14% with value-based insurance designs^{156-158,160}
- With reduced out-of-pocket expenses^{150,157-159,163}
- Financial reward strategies may have moderate to large effects on adherence, but may not extend beyond the incentivization period^{161,162}
- Greater frequency of rewards may be more effective than lower frequency (at same value)¹⁶²

Interventions for Practitioners

Interventions that target practitioners are also effective, particularly if they incorporate more than one of the following¹³²:

- Education (eg, uncovering barriers and finding solutions, improving their patient's adherence knowledge and using adherence checklists)
- Communication (eg, active listening, asking adherence-related questions, motivational interviewing and supportive communication)
- Assessment and monitoring (eg, using monitoring systems, pharmacy refill data, asking patients about adherence and recording answers)
- The therapeutic alliance/relationship (eg, health agreement negotiations)
- Integration of care and coordination between practitioners
- Increasing time with patients and the continuity of care
- Improving access to providers (eg, physical proximity to patients or provision of telehealth)
- 5% Improvement in patient adherence with practitioner-targeted interventions

Example: Motivational Interviewing

Motivational interviewing is a communication technique that may improve medication adherence.¹⁶⁴ It helps guide patients by identifying and focusing on the patient's own intrinsic motivations to improve their health.^{165,166} Motivational interviewing uses themes that recognize the partnership with the patient, accept and value the patient's perspective and efforts, provide compassion to reinforce healthy behaviors and evoke the patient's own understanding and knowledge of their behavior rather than imposing such behaviors. For example, practitioners are encouraged to ask open-ended questions, make affirmations to encourage the patient, give reflections to challenge deeper thought about the behavior and provide summaries to allow for simple understanding.¹⁶⁷ Motivational interviewing is just 1 example of a strategy for improving behavioral change overall and will be further explored as part of Fullscript's treatment adherence research program.

- 12% Improvement in patient adherence with practitioner-targeted communication interventions¹⁶⁸
- 17% Improvement in patient adherence when practitioners are trained in motivational interviewing¹⁶⁵

Conflicts of Interest

The authors of this report are employed by Fullscript as part of the Integrative Medical Advisory (IMAT) and Insights teams. They received no additional compensation for the production of this report and are not affiliated with any particular brands, products, or institutions. The authors aimed to provide an unbiased review of the literature in this area with the ultimate goal of providing practitioners with the knowledge and tools to help improve treatment adherence and subsequent outcomes for their patients. Our hope is that this report supports the continued development of research in the area of treatment adherence, particularly as it pertains to integrative medicine.

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