

# Treatment Engagement and Adherence

## *A Review of the Literature*

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### Key Points

- Medication adherence is a complex series of behaviors and encompasses three phases – initiation, implementation, and discontinuation.
- Engaging patients and improving their treatment adherence requires consideration of factors across multiple levels (e.g. patient, provider, healthcare system) and phases of adherence.
- Successful interventions to engage patients and improve adherence must be tailored to deliver information that is relevant to a patient's specific barriers, at the appropriate time, and in a manner that meets a patient's unique health needs.

### Introduction: Defining Treatment Adherence

Adherence is a critical component of treatment effectiveness. For a treatment to improve quality of life, symptoms, and control disease it is important that treatments are followed as prescribed. As transitions from infectious diseases to chronic, non-communicable diseases occur, adherence has become a particularly salient issue. Management of chronic conditions may require long-term adherence to therapies. Previously, *treatment compliance*, *cooperation*, and *persistence* were used to describe treatment adherence. More recent definitions of treatment adherence recognize the benefits of patient-centered care with partnership between patients, their healthcare providers, and families and caregivers. Engaging patients, their families, and caregivers in the adherence process is key.

Adherence is not simply one stage, but instead is a series of interrelated behaviors. In the context of adherence to medications, these behaviors have been defined in three quantifiable phases: initiation, implementation, and discontinuation (Vrijens et al. 2012). In this taxonomy, initiation is when a patient takes the first dose of a prescribed medication. Discontinuation is when a patient stops taking the prescribed medication, either according to a healthcare provider's instructions, on their own, or for other reason. Implementation is the extent to which a patient's actual medication-taking behaviors, or dosing, parallels what was prescribed from initiation to discontinuation (Vrijens et al. 2012). While this taxonomy was designed to apply to medications, it can be used as a framework with which to view adherence to other types of treatments as well.

The barriers and reasons for non-adherence may vary across these phases (e.g. initiation, implementation, discontinuation). Different strategies may be needed to engage patients at each phase. Additionally, there may be different challenges in quantifying adherence across these phases. For example, it may be difficult to identify patients that never initiate a new medication that was prescribed by their provider (e.g. fill a prescription and begin taking it). In this chapter, we describe the magnitude of treatment non-adherence, describe factors influencing treatment adherence, and summarize key adherence findings by phase of adherence.

## **Magnitude of the Treatment Adherence Problem**

Approximately half of patients with chronic diseases fail to adhere to prescribed medications in the United States, and these adherence rates are consistent across the globe (Sabaté 2003). More than one in five new prescriptions remain unfilled (e.g. initiation phase), and adherence to treatment therapy is lowest among patients who suffer from chronic illnesses (e.g. implementation phase) (Sabaté 2003). While overall adherence rates are approximately 50%, individual adherence varies by disease type, patient demographic characteristics, and other clinical characteristics (Briesacher et al. 2008). Because of the complexity and duration of treatment, adherence is often lower among patients with multiple chronic conditions (Briesacher et al. 2008; Brown and Bussell 2011). For example, more than 60% of patients with cardiovascular disease are not adherent with their medications; suboptimal adherence is often more common among patients of disadvantaged socioeconomic backgrounds (e.g. uninsured or inadequately insured, low annual income, low health literacy, minorities). This worldwide problem of treatment non-adherence presents enormous challenges to patients with chronic conditions, their providers and caregivers, and the healthcare system that is supporting them.

Suboptimal adherence is associated with many negative outcomes – increased hospitalizations, lower quality of life, higher mortality, and increased potentially avoidable healthcare costs (Long et al. 2016; Sokol et al. 2005). Suboptimal adherence is also associated with substantial societal costs. Medication non-adherence is a \$300 billion problem in the US alone (Sokol et al. 2005). Each year, non-adherent behaviors to treatment therapy are implicated in at least 125 000 American deaths (Osterberg and Blaschke 2005). Poor adherence is associated with increased

healthcare use; it contributes to a 17% increase in emergency room visits and a 10% rise in hospital stays in patients suffering from diabetes, asthma, and gastric acid disorders (Goldman et al. 2004).

## Factors Influencing Treatment Adherence

Factors influencing adherence are multifactorial and multilevel (e.g. patient, provider, healthcare system). The World Health Organization has categorized these factors into five domains – social and economic, healthcare system, therapy-related, patient-related, and condition-related (Sabaté 2003). Because patients' needs span across these domains, factors influencing adherence should be considered holistically and longitudinal changes should be recognized. Effective solutions to improve treatment adherence must involve intervention across multiple factors and multiple levels (Zullig et al. 2013a). We will discuss each of these domains in the following sections.

### Social and economic factors

Social and economic factors that influence adherence encompass poor socioeconomic status (e.g. annual income and poverty), health literacy, educational attainment, social support, distance from healthcare, transportation accessibility, medication cost, and racial, ethnic, and cultural background, among other factors (Sabaté 2003). We will not describe the literature for each of these factors at length. Instead, we will provide a general overview and highlight a few more newly recognized factors (e.g. health literacy and chaotic lifestyle).

*Socioeconomic status* While economic and structural factors may impact a patient's healthcare access, when evaluating the body of adherence literature, there is not a strong association between socioeconomic status and medication adherence (Alsabbagh et al. 2014; Falagas et al. 2008; Huang et al. 2013; Ungar et al. 2011). In fact, while low socioeconomic status may place patients at increased risk for suboptimal adherence, such patients are not guaranteed to experience adherence problems. When given access to medication adherence improvement and chronic disease management programs, patients from disadvantaged socioeconomic backgrounds may in fact have higher resilience and appreciation for medication adherence interventions than other groups (Bosworth et al. 2011; Jackson et al. 2012).

*Employment and education* Studies have identified that a patient's occupation, educational background, and income may impact access to healthcare and healthcare quality, including treatment adherence (Falagas et al. 2008; Huang et al. 2013; Ungar et al. 2011). Because many working-aged adults in the United States are insured through employer-sponsored health plans, employment status is intertwined with access to care, prescription drug coverage, and cost of therapy (which is described below) (Long et al. 2016). Patients with low educational attainment may be unable to secure employment with good health insurance options and/or may have difficulty interpreting prescription medication labels and, therefore, are at greater risk for treatment adherence problems (Dal-Fabbro 2005).

*Health literacy* Although educational attainment, literacy, and health literacy are separate constructs, they may all influence adherence. Health literacy is the ability to read and process health information and to make appropriate health decisions. Low health literacy is pervasive; up to 48% of English-speaking patients have low health literacy (Andrus and Roth 2002). Low health literacy is associated with poor overall health status, underuse and misuse of preventative services, and increased hospitalizations and healthcare costs (Andrus and Roth 2002). In the context of medication adherence, there is a weak, but significant, association between low health literacy and suboptimal medication adherence (Loke et al. 2012; Zhang et al. 2014). Patients who are already disadvantaged (e.g. racial and ethnic minorities, those with low educational attainment and/or low-income, and non-native English speakers) may be most at risk for health literacy problems (Andrus and Roth 2002). Simple graphical instructions, such as pictorial calendars, may be one strategy to overcome low health literacy and boost treatment adherence (Zullig et al. 2014).

*Social support* Social support can be emotional, tangible (i.e. financial support or caretaking), or informational. When patients have adequate support that is well-matched with their specific needs, they may be better equipped to overcome barriers to non-adherence (e.g. providing transportation, spouse reminding patient to take their medications). Strong social ties are associated with increased survival for patients with chronic diseases, perhaps because they are better able to cope with stressors that may interrupt the adherence process (Criswell et al. 2010; Ozbay et al. 2007; Scheurer et al. 2012; Simoni et al. 2006; Strom and Egede 2012; Wu et al. 2013). A systematic literature review identified that 28% of included studies (14 out of 50 studies) examined the relationship between emotional support and medication adherence; of these 14 studies, 42% (6 out of 14) were identified as having a significant relationship between emotional support and medication adherence (Scheurer et al. 2012). Most of the included studies showed a significant correlation between the provision of tangible means of support and medication adherence (Molloy et al. 2008; Scheurer et al. 2012). Tangible social support was effective in addressing systemic barriers such as inability to afford medication and difficulty reaching healthcare sites. Examples of tangible social support include paying for medications, providing transportation, and providing physical assistance when necessary (Ford et al. 1998; Heaney and Israel 2008; Strom and Egede 2012; van Dam et al. 2005).

*Prescription medication cost* Especially for patients who are under- or un-insured, the cost of prescription medications can be an adherence barrier. Express Scripts (at the time of this writing is the largest pharmacy benefits management organization in the US) reports that the average price for the most commonly used brand-name drugs in the US more than doubled (up 127%) between 2008 and 2014 (Miller 2016). Increased drug spending resulted from higher prices for specialty and biotech therapies and from the use of medications for a wider range of conditions and over longer periods of time (Eaddy et al. 2012). The cost of prescription drugs continues to rise because of lack of price controls, long waits to establish patents on drugs, limited competition among drug makers, developmental and production costs, and fewer generic medications on the market (Johnson 2015).

Several research studies have demonstrated that patients are sensitive to even small adjustments in co-payment costs and that reducing or eliminating out-of-pocket costs for prescription medications is associated with improvements in medication adherence

(Choudhry et al. 2008, 2011; Dusetzina et al. 2014; Ito et al. 2015). In a survey of over 14 000 Medicare beneficiaries, patients who chose not to fill at least one prescription reported reasons such as “thought it would cost too much” (55.5%), “medicine not covered by insurance” (20.2%), and they “didn’t think medicine was necessary for the condition” (18.0%) (Kennedy et al. 2008).

The use of oral anticancer drugs serves as an example of cost-related medication non-adherence. Innovative biologic treatments come with high price tags that may limit accessibility. Oral anticancer medications can average as much as \$7000 per month (Dusetzina 2016). Prescription medication costs have a significant impact on treatment adherence. Among patients with cancer who were receiving cancer care at a tertiary center, 27% of patients reported at least one form of medication non-adherence: skipping medications to extend prescriptions, taking less medication to extend prescriptions, or failing to fill a prescription because of the cost (Bestvina et al. 2014).

There have been several studies focusing on increasing prescription medication coverage and reducing patients’ out-of-pocket costs to improve medication adherence. While providing full coverage seems to improve medication adherence, this improvement does not necessarily equate to improvements in clinical outcomes (Choudhry et al. 2011; Njie et al. 2015), but may be associated with improvements in quality of life and reduced hospitalizations (Ito et al. 2015). A systematic review addressed the impact of 18 interventional studies designed to reduce patients’ out-of-pocket costs for medications to manage hypertension and hyperlipidemia. Adherence improved by a median of 3% and the proportion of patients achieving an adherence rate of 80% or more increased by 5.1% (Njie et al. 2015). While the effect sizes are small, when applied at the population level, even small improvements in medication adherence can have a meaningful impact on a population scale.

*Racial, ethnic, gender, and cultural background* Patient characteristics, such as race and gender, may interact with other factors to influence a patient’s medication-taking behaviors. For patients of minority racial and ethnic groups, perceived discrimination and trust or mistrust of healthcare providers and the healthcare system may moderate intervention effects and impact medication adherence behaviors (Dal-Fabbro 2005; Erwin and Peters 1999). Similarly, several studies have identified associations between gender and adherence, but the directionality of the association is uncertain. Some studies suggest that women are more adherent than men (Balbay et al. 2005; Choi-Kwon et al. 2005; Deeks et al. 2009; Fodor et al. 2005; Lertmaharit et al. 2005; Manteuffel et al. 2014), whereas other studies have suggested men are more adherent (Goldstein et al. 2016; Lauffenburger et al. 2014; Pearson 2013). Because men and women may have different healthcare-seeking behaviors and may interact with the healthcare system differently, gender may also play a role in treatment-effect heterogeneity. It is important to note that these characteristics do not occur in a vacuum but instead interact to influence a patient’s experience of adherence to medications.

### Healthcare system factors

At a healthcare system level, reimbursement and health insurance coverage, medication distribution systems, knowledge, training and capacity of healthcare providers, and system capacity all influence treatment adherence (Sabaté 2003). While patient-provider communication is an important factor in the treatment adherence equation

(Beach et al. 2015; Zullig et al. 2015), the largest body of literature regarding healthcare system factors and adherence addresses reimbursement and insurance coverage.

Healthcare policies and prescription medication insurance impact treatment access and cost. In the US, there are multiple avenues for offsetting out-of-pocket medication costs. Patients can receive assistance purchasing their prescription medications through medication subsidies, prescription caps, insurance benefits (e.g. co-insurance and cost sharing plans) and supplemental prescription drug coverage plans (Aziz et al. 2016). Value-based insurance designs, which were created to reduce access barriers to healthcare services while also de-incentivizing inefficient healthcare practices through high cost sharing, are increasingly common (Fendrick et al. 2010). Patients lacking insurance are more likely to not take medication as prescribed and are more than two times as likely to use alternative therapies; Medicare beneficiaries are more likely to buy prescription drugs from another country (Cohen et al. 2013).

In response to the mounting prescription drug costs, public and private insurers have become selective in certain drugs and the extent of coverage they offer for prescription drugs. In 2012, 16 states imposed limits on the number of drugs Medicaid recipients could receive, with states such as Arkansas, California, Kansas, Louisiana, North Carolina, and Texas opting to restrict the list of drugs they covered (Galewitz 2012). These policy changes have potential to impact patients' initiation and persistence with medication regimens.

### Therapy-related factors

Therapy-related factors include the complexity and duration of the regimen, previous treatment failures, changes in the regimen, side effects, among other factors (Sabaté 2003). Concurrent treatment for multiple conditions increases treatment complexity, which in turn may make paying for and correctly implementing medications particularly challenging. An example of treatment complexity is polypharmacy (e.g. prescribed three or more daily medications); 30–40% of elderly patients take five or more medications (Furberg et al. 2010). Routine medication review among patients using multiple medications could reduce inappropriate or duplicative prescribing, thus reducing patients' medication-taking burden, and improving adherence (Tarn et al. 2009). Interventions have successfully reduced inappropriate prescribing and polypharmacy among the elderly using a variety of strategies (e.g. medication review), but these interventions have not clearly impacted measured outcomes (e.g. hospital admissions) (Christensen and Lundh 2013; Cooper et al. 2015).

Another strategy to reduce the burden of polypharmacy is medication packaging systems, such as blister packs. Systematic reviews confirm that blister packaging, reminder packaging, and calendar packaging improve medication adherence (Conn et al. 2015; Mahtani et al. 2011; Zedler et al. 2011). Compared to other intervention strategies to improve adherence (e.g. increasing coverage to reduce patients' out-of-pocket costs), medication packaging may be a relatively low cost solution to address many common adherence barriers. Packaging strategies may be particularly helpful in the context of polypharmacy where remembering complex medication regimen instructions may be challenging.



### Patient-related factors

Patient-related factors include knowledge, attitude, beliefs, perceptions, expectations, and resources (Sabaté 2003). Many patient-related factors are centered around a patients' belief system about their health and healthcare.

*Health beliefs* The Health Belief Model (HBM) is one framework in which to consider these patient-related factors. The HBM posits that a person's health behaviors are determined by their understanding of the perceived threat and benefits of diseases and treatments (Bosworth and Voils 2012; Dal-Fabbro 2005; Erwin and Peters 1999; Gatti et al. 2009). Culture, religion, ethnicity, and other spheres of relation influence individuals' health beliefs and practices. An individual's understanding of the seriousness and risks associated with the disease or treatment and the benefits and barriers to treatment impacts adherence (Bosworth and Voils 2012). The HBM additionally includes cues to action, motivating factors, and self-efficacy as concepts that influence an individual's health belief system. Health beliefs have been associated with adherence behaviors in several clinical conditions including transplantation and management of dyslipidemia (Al Hamid et al. 2014; Buckley et al. 2016; Kung et al. 2012; Shiyambola et al. 2013; Zullig et al. 2016). Adhering with treatment recommendations is largely based on a patient's perceptions of the benefits of the treatment. Patients who view the potential benefit of treatment as outweighing their perceived negative consequences are more likely to adhere (Hayden 2014). High self-efficacy, a patient's belief in themselves to follow through with an action, is also associated with better adherence (Bosworth and Voils 2012; Chlebowy and Garvin 2006; Hayden 2014). Successful strategies to shape and change patients' health beliefs and promote treatment adherence include health coaching (Wolever et al. 2010), shared decision-making, and motivational interviewing.

*Healthy adherer effect* Related to health beliefs is a concept coined the "health adherer effect," also known as "compliance bias." A meta-analysis reported an association between adherence to a placebo and improvements in mortality (Simpson et al. 2006). The authors suggested that adherence to medications may be a proxy measure for general healthy behaviors. In other words, people who are adherent may exhibit different health beliefs which impact their lifestyle behaviors. These health beliefs may be different among adherent and non-adherent patients. In fact, adherence to placebo has been associated with improved clinical outcomes and mortality in several studies (Avins et al. 2010; Curtis et al. 2011; Simpson et al. 2006). Traditionally, most studies have not considered the potential for a health adherer effect in their study design or interpretation of results. This may be an avenue for future research.

*Chaotic lifestyle* A non-traditional patient-related factor influencing adherence is a chaotic lifestyle. Having a chaotic lifestyle, including the lack of flexibility to schedule medical appointments, may be an important barrier to obtaining regular medical care and has been associated with suboptimal medication adherence among post-myocardial infarction patients and those with HIV/AIDS (Wong et al. 2007; Zullig et al. 2013b). Life chaos may be a modifiable determinant of medication adherence and represents opportunity for further research that seeks to address the structural and individual stressors that negatively impact patients' ability to adhere.

### Condition-related factors

Condition-related factors include burdens placed on patients that are specific to their disease(s) or condition(s). According to the WHO, these factors include severity of symptoms, level of disability, rate of disease progression and severity, as well as the availability of effective treatments (Sabaté 2003). Comorbidities (e.g. depression, diabetes, HIV/AIDS, drug and alcohol abuse) may be condition-related factors that are likely to modify treatment adherence behaviors (Sabaté 2003).

## Medication Adherence in the Context of Three Adherence Phases

The factors influencing treatment adherence have been well documented, and there are many evidence-based interventions to improve adherence (Gellad et al. 2011; Nieuwlaat et al. 2014; Sabaté 2003). Traditionally, adherence has often been viewed as a single behavior or event. Among the adherence research community, there is an increasing recognition of the need to frame and describe adherence interventions within the framework of the phases of medication adherence (e.g. initiation, implementation, discontinuation) (Helmy et al. 2017; Vrijens et al. 2012). In the following sections, we describe methods for measuring adherence, studies to improve adherence, and approaches to engage patients and their caregivers in healthy adherence behaviors in accordance with the three adherence phases.

### Measuring medication adherence

There are many direct and indirect methods of measuring adherence which include subjective and self-report assessments, pill counts, electronic monitoring (e.g. smart pill bottles and caps, and ingestible pill sensors), log books and diaries, and pharmacy-based and claims measures, among others (Clifford et al. 2014). While there is no gold standard for measurement, a combination of direct and indirect methods is often best (De Geest et al. 2014). Additionally, interventions that seek to improve adherence must take a multilevel approach, integrating strategies at the patient, provider, and other levels (De Geest et al. 2014). Thus, decisions about approaches for measuring adherence should consider the context, intended purpose, available resources for measurement, and phase(s) of adherence that are of interest (Zullig et al. 2017).

Some measures may be better suited for measuring adherence at different phases than others. For example, pharmacy and claims measures may be very informative for evaluating persistence with a medication regimen over time, but may be unable to detect medications that are never initiated (e.g. first prescription is never filled).

### Existing interventions by adherence phase

As measurement strategies vary by adherence phase, so too do many barriers and intervention strategies to overcome them. We describe a purposive sample of



interventions by phase (e.g. initiation, implementation, discontinuation) that have successfully improved adherence (Vrijens et al. 2012).

*Initiation phase* Researchers at an integrated healthcare system conducted a randomized controlled trial to improve non-initiation of bisphosphonate therapy for osteoporosis (Cizmic et al. 2015). Adults with a new bisphosphonate order that was not filled within 14–20 days were randomized to either a control group (e.g. no outreach) or an intervention group. The intervention group received an interactive voice response phone call. If patients did not initiate therapy within one week, a follow-up letter was mailed. Approximately 31% of patients in the control group and 49% of patients in the intervention group initiated bisphosphonate medication within 25 days of study randomization. When adjusted for demographic and clinical characteristics, the odds ratio for initiation in the intervention versus control group was 2.3 (95% CI 1.34–3.94) (Cizmic et al. 2015). This suggests that an interactive voice response and follow-up letter system may be helpful to improve initiation of new therapies such as bisphosphonates. It is worth noting that, relative to available interventional literature in the implementation phase, less is known about strategies to improve initiation. A partial explanation for this is that identifying non-initiators can be challenging. Studies of initiation are often limited to integrated healthcare systems and/or countries that have integrated, single-payer systems (Cizmic et al. 2015; Halvorsen et al. 2016).

*Implementation phase* The bulk of interventions to improve adherence have focused on the implementation phase, the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose is taken (Vrijens et al. 2012). While a variety of intervention strategies have been used to improve adherence (Nieuwlaat et al. 2014), we will describe two randomized controlled trials – a full coverage, cost-reducing trial (Choudhry et al. 2011) and a multifaceted, pharmacist-led intervention (Ho et al. 2014).

Choudhry and colleagues enrolled patients recently discharged from the hospital post-myocardial infarction clinic and randomly assigned their insurance plan sponsors to full prescription coverage or usual prescription coverage for statins, beta-blockers, angiotensin-converting-enzyme inhibitors, or angiotensin-receptor blockers (Choudhry et al. 2011). The primary outcome was a major vascular event or revascularization, and medication adherence was a secondary outcome. While there was no improvement in the primary outcome, medication adherence (e.g. mean medication possession ratio calculated from pharmacy data) was improved for all drug classes (e.g. ACE inhibitors or angiotensin-receptor blockers, beta-blockers, and statins). Across all three medication classes, the odds of full adherence to the study medications significantly increased by 31–41% ( $p < 0.001$ ) and there was no difference in adherence to other medications for which co-payments were not changed (Choudhry et al. 2011). The authors applied simulation modeling techniques and reported that patients who received full prescription coverage were estimated to have better health outcomes (e.g. quality-adjusted life years) and lower anticipated healthcare costs (Ito et al. 2015).

The second example of evaluating an intervention focusing on the implementation adherence phase was a multifaceted, pharmacist-led intervention. The intervention, which encompassed medication reconciliation and tailoring, patient education,

collaborative care between pharmacist and patients' physician, and voice messaging, increased adherence (Ho et al. 2014). The one-year intervention enrolled patients from four Veterans Affairs Medical Centers. The primary outcome was pharmacy-based medication adherence (e.g. proportion of days covered). In the intervention group, 89.3% of patients were adherent compared with 73.9% in the usual care group ( $p = 0.003$ ). The mean medication adherence was also higher in the intervention group (0.94 vs 0.87;  $p < 0.001$ ) (Ho et al. 2014).

These trials both demonstrated improvements in implementation and increased persistence with medication-taking behaviors over time. However, they involved complex interventions that might be difficult to translate into real-world settings and to sustain over time.

*Discontinuation phase* Patients may prematurely discontinue treatment against providers' instructions for many reasons. For women with hormone receptor positive breast cancer, long-term adherence to adjuvant endocrine therapy (AET) is critical to prevent breast cancer recurrence and reduce breast cancer-related mortality. Adherence rates to AET are low and are often related to medication side effects that prompt patients to discontinue AET therapy. A randomized clinical trial is enrolling 400 women with breast cancer who are prescribed AET and is seeking to reduce their discontinuation of AET through a multicomponent behavioral intervention (Shelby 2016). The intervention involves nurse-delivered skills training for managing symptoms, behavioral strategies for improving medication adherence, and symptom and medication education. If proven effective, this intervention has the potential to improve medication adherence, by targeting discontinuation reduction, and improve long-term health outcomes of women with breast cancer.

## Patient Engagement

Across all phases of medication adherence, it is critical that patients, their family members, and caregivers be engaged in their treatment decisions. When patients buy in to the goals of their therapy, they are more likely to follow providers' recommendations. Person-centered care focuses on providing patients with choices about their treatments and appreciating their roles as healthcare consumers with their own beliefs, values, and preferences (Bosworth et al. 2017). The average American may spend one or two hours annually with their healthcare provider, but they spend the remaining part of their lives (over 5000+ waking hours) elsewhere (Asch et al. 2012). Thus, it is critical that clinicians and researchers employ innovative strategies to better understand and improve patient engagement outside of the traditional healthcare setting. These strategies may include increased use of wireless devices and changes in financial incentives for healthy behaviors at home (Asch et al. 2012; Volpp et al. 2008, 2011). To ensure person-centered care, it is important that patients understand their health conditions, medication regimens, and general instructions. Patient information resources, health literature, and prescription information should be developed with patient readability in mind. It is important that information be delivered with "the right information in the right form at the right time, to the right person."

From the healthcare system perspective, person-centered care could also be prioritized through tighter coordination of patient history between pharmacies and hospitals. Providing healthcare providers with an accurate history of a patient's adherence through facilitation of patient information between these two health systems could aid not only in accurately tracking adherence history but also in assisting providers to develop more informed treatment therapies. Part of this communication requires an informed dialog between the healthcare team, their patients, family members, and caregivers who are best equipped to make decisions that are concordant with the patients' values (Bosworth et al. 2017).

In summary, medication adherence is a complex series of phases and behaviors. There are numerous factors that interact at multiple levels to influence treatment adherence behaviors. There is an array of methodologies to measure adherence, interventions to improve it, and strategies to engage patients in improving their adherence – but there is no gold standard method for adherence measurement or intervention. The best approaches for improving adherence require multilevel interventions tailored to the specific factors and barriers that are relevant for a particular patient. Selecting these approaches requires careful attention to phase(s) of medication adherence and an individual patient's unique health beliefs, barriers, and treatment adherence-related needs.

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