Causes of medication nonadherence

“Between 100 and 250 factors have been observed to be associated with medication nonadherence [41,42], thus making the importance of tailoring management to individuals’ needs and using a multifaceted approach very apparent [43].”

Adherence research has unsuccessfully tried to find clear correlations between fixed patient characteristics, such as age, gender, or education, and adherent or nonadherent behavior [44,45]. However, when moving beyond these sociodemographic variables, modifiable patient characteristics, such as behavior and attitudes, have been shown to be barriers to medication adherence. For example, forgetfulness, fear of undesired side effects, reservations toward drug taking, and insufficient educational information and understanding about drug therapy or drug holidays have been found to be related to medication nonadherence [46].

A report by the WHO addressed the general importance of improving adherence to long-term medical treatments [1]. The WHO report concluded that adherence is the result of a complex interaction of the social environment, patients, and healthcare professionals. It has been shown that low adherence to long-term treatment often occurs when the treatment is complex or when the disease is asymptomatic (such as hypertension). Previous studies have reported that poor adherence to too many drugs is due to patient perception that the disease is not significant, adverse drug effects, lack of treatment effectiveness, and the patient’s...
poor or incomplete knowledge of the disease [47]. Known barriers can be characterized in at least three [42] ways:
1. Health literacy barriers related to not knowing what to do and why.
2. Behavioral barriers that address not having the skills necessary to accomplish medication management in the context of everyday life.
3. System or administrative barriers related to access and fragmentation of care.
Thus, the most effective interventions use a combination of approaches and address literacy, behavior, and organizational issues. System or administrative factors are derived from a patient’s inability to afford or difficulty in affording their medication and may include, for example, lack of adequate healthcare coverage, unemployment, retirement, and indigence.

**Patient-level factors related to medication nonadherence**
The most common reasons given by patients for not taking their medications are forgetfulness (30%), other priorities (16%), deciding to omit a dose (11%), lack of information (9%), and emotional reasons (7%); 27% of patients give no reason [48]. Factors that are associated negatively with adherence include increased complexity or duration of a medication regimen, side effects, very old age, extreme poverty, social isolation, and psychiatric diagnoses, especially paranoia [49]; a study on adherence in HIV-positive individuals, which included these patient-level factors, found that older HIV-positive patients with neurocognitive impairments or drug problems were at an increased risk of suboptimal medication adherence when compared to their younger counterparts (Figure 1) [50]. The risk of nonadherence is especially high when multiple predisposing factors converge, such as cognitive impairment and the use of numerous medications for multiple chronic conditions in the elderly.

In general, important predictors of adherence in single conditions include the use of simple and short regimens, particular classes of medications favored by consumers, and a high severity of disease and symptom score [12]. Older adults’ and consumers’ beliefs that therapy will help are additional predictors of adherence [12]. Key reasons for nonadherence include adverse effects or other problems with medications, such as poor
Cognition and medication adherence among younger and older HIV-positive adults

Figure 1 Cognition and medication adherence among younger and older HIV-positive adults. 1-day, 1-day self-report; 30-day, 30-day self-report; Attent, attention; Exec, executive; Mem, memory; Qual, qualitative self-report. Standardized values shown. Reproduced with permission from Gorman AA et al [50].
instructions, poor memory, inability to pay for medications, disagreement about the need for treatment, and weak relationships between patients and healthcare professionals [19]. Other reasons for nonadherence include polypharmacy [51], low literacy [52,53], “silent” conditions (such as hyperlipidemia, hypertension, and osteoporosis) [54–56], cultural factors [57], inadequate social support [58], and depression [59]. These barriers to adherence can often be improved upon or overcome by patient efforts independent of healthcare professionals.

Medication adherence appears to be a patterned behavior established through the creation of a routine and a reminder system for taking the medication [60]. Medication nonadherence may often be a rational response to the information patients are given, and many factors that drive nonadherence are beyond the control of patients.

**Health literacy**

Health literacy, defined as the “ability to understand and act on health information” [61], is one of the primary determinants of medication comprehension and a potentially significant predictor of medication nonadherence. However, in the USA, for example, over 90 million adults (39% of all adults) lack the literacy skills to effectively function in the current healthcare environment [62], a number that has not changed significantly over time [63]. Low health literacy is found in many different healthcare settings [64,65] and is most common in older patients, those with lower education levels, immigrants, and racial/ethnic minorities [66]. Numeracy, or the ability to understand numbers, is especially critical in the health domain, where understanding or not understanding what numbers mean may have life-altering consequences. Numerical competence is needed to understand and weigh the risks and benefits of treatment, to decipher survival and mortality curves, and to navigate medical insurance forms and informed consent documents [67].

Patients are required to read medical information and comprehend what to do and when to do it. Patients may also be required to perform
numerical tasks, including calculating the number of tablets for a single dose of medicine. They are expected to monitor themselves for both beneficial and adverse effects of their medications, know what to do if they miss a dose of medication, and master when, if, and how to obtain refills [68]. Chronic illnesses often require following an intensive and complex medical regimen (eg, medications, daily monitoring, routine physician visits, and tests), such that the adverse consequences of low health literacy may be particularly pronounced and thus require serious consideration [69]. Methods for screening for health literacy include a number of measures as well as asking patients if they have a problem understanding written health materials (see Figure 2) [70,71].

### Self-efficacy

The key to self-management of chronic conditions is self-efficacy, or the confidence to carry out behaviors necessary to reach a goal identified by the patient [72]. Self-efficacy has been reported to improve medication adherence in studies employing survey and/or focus-group methods [73]. Studies using interview techniques have reported numerous medication compliance problems in people with multiple chronic conditions [74–76]. For example, medications for one condition can negatively affect another condition, and managing schedules that require medications at different times as well as pill burden can be major deterrents to achieving adherence [77]. A synthesis of qualitative studies of why there is resistance to taking medications showed that people were concerned about taking medications for long-term chronic conditions.

<table>
<thead>
<tr>
<th>Medication knowledge</th>
<th>Patients answering correctly (%)</th>
</tr>
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<tbody>
<tr>
<td>Dose</td>
<td>65.6</td>
</tr>
<tr>
<td>Frequency</td>
<td>49.2</td>
</tr>
<tr>
<td>Indication</td>
<td>19.7</td>
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<table>
<thead>
<tr>
<th>Monitoring method</th>
<th>Patient adherence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEMS measurement</td>
<td>30.0</td>
</tr>
<tr>
<td>Prescription refill assessment</td>
<td>38.0</td>
</tr>
</tbody>
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Figure 2 Patients’ understanding of their medication and adherence. MEMS, Medication Events Monitoring System. Reproduced with permission from Hauptman [71].
because of potential adverse effects. As a result, they “actively resisted” taking their medications rather than being forgetful, as cited by other researchers [77].

**Physician-level factors related to medication nonadherence**

Perhaps because patients take the medications, most of the attention on medication nonadherence focuses on the patients themselves; however, Tarn et al suggest that physician behaviors may critically contribute to medication nonadherence [78]. Not only is the ability of physicians to recognize nonadherence poor, they often lack adequate training to alleviate problems. Tarn et al documented major deficits in the information and education that physicians give to patients when prescribing new medications [78]. Physicians frequently omitted critical information, such as the name of the medication, purpose of the medication, duration of treatment, dosing schedule, and associated adverse effects of new medications. The data showed that in over 65% of all cases, at least one critical piece of information was not provided [78].

Barriers to adherence may also be related to poor interactions and/or communication between patients, healthcare providers, and the healthcare system. Traditionally, physicians and designated healthcare workers have played a key role in achieving adherence by providing patients with the rationale for treatment and involving family and caregivers whenever possible; however, it is time and resource intensive for providers to assess and influence adherence alone on a timely and ongoing basis. There remains an unmet need for reliable and broadly utilizable ways to accurately assess and manage a patient’s medication adherence.

An ideal system for improving adherence would not only engage the patients themselves, but also leverage their selected healthcare providers, caregivers, and communal support network. The system would also allow a secure exchange of reliable and robust information among patients and clinical decision and support systems [79].
Healthcare system-level factors related to medication nonadherence

For many patients, the cost of medication directly affects their level of medication adherence. In the USA, for example, the coverage gap in Part D for patients on Medicare may be a financial challenge, particularly for expensive medications; however, sometimes generic alternatives provided at lower cost can provide a solution. Additionally, several studies have shown a strong and consistent relationship between copayments and medication adherence [80–83]. A substantial portion of medication nonadherence is driven by out-of-pocket costs of multiple medications [84–86]. Patients with chronic illness are likely to skip or discontinue their medications in response to copayment increases [81,87]. Unfortunately, those with multiple chronic conditions (and presumably using more medications) are more susceptible to cost-related nonadherence [84], which may exacerbate chronic conditions, generate adverse health events, and increase healthcare use [88,89].

Payers and healthcare plans could turn this information to an advantage. Payers could selectively reduce or eliminate copayments for highly beneficial medications for some patient subgroups, such as statins in patients with heart disease or diabetes or blood pressure-lowering medications for those with hypertension. This has led to a movement, known as “value-based insurance design,” to reduce copayments for the most effective, high-value medications [90,91]. Observational studies have found that reducing copayments for highly effective chronic therapies can substantially improve adherence [91,92]. Moreover, studies suggest that adherence improves when physicians prescribe generic or lower-cost medications [93].

Others have posited that simply reducing copayments may not be sufficient, and have proposed that providing financial rewards for better adherence may be an even more effective mechanism for promoting behavior change. Volpp et al found a significant impact from financial incentives to improve smoking cessation rates [94], as well as for promoting weight loss [95]. While physician pay-for-performance has received substantial attention in the medical literature, patient pay-for-performance is a concept that needs further research in order to understand its long-term effectiveness and cost-effectiveness.
Moving toward adherence-dependent quality and performance measures

Consistent with current emphases on quality, access, and equity of care [96], the literature focuses on performance measures in which medication adherence contributes to quality scorecards, including mortality, more intermediate treatment targets such as blood pressure and lipid control, and decreased symptom-associated readmissions [97–101]. The link between medication adherence and treatment targets is robust, although practical approaches that help patients improve medication adherence are lacking. For this reason, the WHO has distinguished between modifiable and nonmodifiable risk determinants. In a clinical setting, nonmodifiable factors might serve as “flags” to alert providers to communicate carefully with patients, whereas modifiable factors might serve to trigger specific interventions for patient-associated adherence problems [139].
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