

ADHERENCE TO ANTI-SEIZURE MEDICATIONS

Avani C. Modi, Ph.D. and Aimee W. Smith, Ph.D.

WHAT IS ADHERENCE?

Adherence is defined as the extent to which a person's behavior coincides with medical or health advice.^{1,2}

WHY DOES ADHERENCE MATTER?

The consequences of non-adherence can be severe for patients with epilepsy. Non-adherence can lead to any of the following:

- Continued seizures⁸⁻¹⁰
- Poor quality of life^{11,12}
- Unnecessary ASM changes¹³
- Higher healthcare costs¹⁴
- Higher healthcare utilization¹⁴⁻¹⁶
- Pharmacoresistance¹⁷
- Death^{5,18}/sudden unexpected death in persons with epilepsy¹⁹

HOW DO YOU MEASURE ADHERENCE?

There are a variety of methods to measure adherence, both clinically and in research. In the table below, strengths and weaknesses of the various approaches are listed.

Table 1: Strengths and Weaknesses of Different Adherence Measurement Methods

Type	Strengths	Limitations
Self-report	• Easy to obtain • Assesses patient perception • Inexpensive • Comprehensive • Can obtain multiple perspectives	• Social desirability • Recall biases • Cannot be obtained from young children
Provider Estimate	• Inexpensive • Easy to obtain • Simple	• Generally an overestimate • Poor accuracy
Pill Counts	• Inexpensive • Objective	• Variable prescription sources or unknown source • Does not account for samples • Presumptive dosing • Potential for medication discarding • Requires patients bring prescriptions back to clinic
Prescription Refills/ Medication Possession Ratio	• Easy to collect in managed care setting • Inexpensive	• Presumptive dosing • Potential for medication discarding
Electronic monitors	• Continuous measurement of adherence • Provides precise data • Provides objective data	• Expensive • Technical problems • Lost monitors • Presumptive dosing
Blood serum levels	• Objective • Quantifiable • Sensitive to dosing regimens	• Affected by pharmacokinetic variation • Short-term-only reflects past 48-72 hours • Invasive
Hair serum levels	• Objective • Quantifiable • Sensitivity • Less invasive than blood serum testing	• Debatable effectiveness • Affected by pharmacokinetic variation
Saliva concentration	• Objective • Quantifiable • Painless (no venous access needed)	• Debatable efficacy • May be affected by pharmacokinetic variation • Needs calibration to individual saliva production

The most frequently used adherence measures in clinical practice are self-report, provider estimate, and blood serum levels. Blood serum levels are the most objective but only reflect adherence in the 48-72 hours prior to the blood draw. While self-report and provider estimates are easy to obtain and inexpensive, they are notoriously inflated and inaccurate unless a validated and reliable questionnaire is used. For example, the Morisky Medication Adherence scale²⁰ is a commonly used 4-item self-report measure. Epilepsy-specific self-management and adherence measures are also valuable, including the Pediatric Epilepsy Medication Self-Management Questionnaire²¹ and the Adult Epilepsy Self-Management Measurement Instrument.²² If clinicians cannot use validated instruments, open-ended and non-judgmental questions can be asked, such as:

“Most people miss doses of their medication at some point in time, what has your experience been with your ASM in the past week? How many doses do you think you have missed?”

In the research context, we highly recommend using either the Medication Possession Ratio (MPR) or electronic monitors, depending on the type of research being conducted. For example, electronic monitoring data can provide specific and individualized information for intervention, while MPRs can provide population estimates of adherence.

WHAT PUTS A PATIENT WITH EPILEPSY AT RISK FOR NON-ADHERENCE?

A model of risk factors and outcomes for non-adherence is presented in Figure 1. The model is not exhaustive, but represents major drivers of adherence in patients with epilepsy. Predictors or factors that influence adherence fall into four major categories: sociodemographic, medical, individual/family, and healthcare system. It is notable that a recent paper highlighted racial/ethnic differences in adherence barriers such that Black families experience more system and community-level barriers compared to White families. This is important for:

Figure 1. Adherence Model in epilepsy

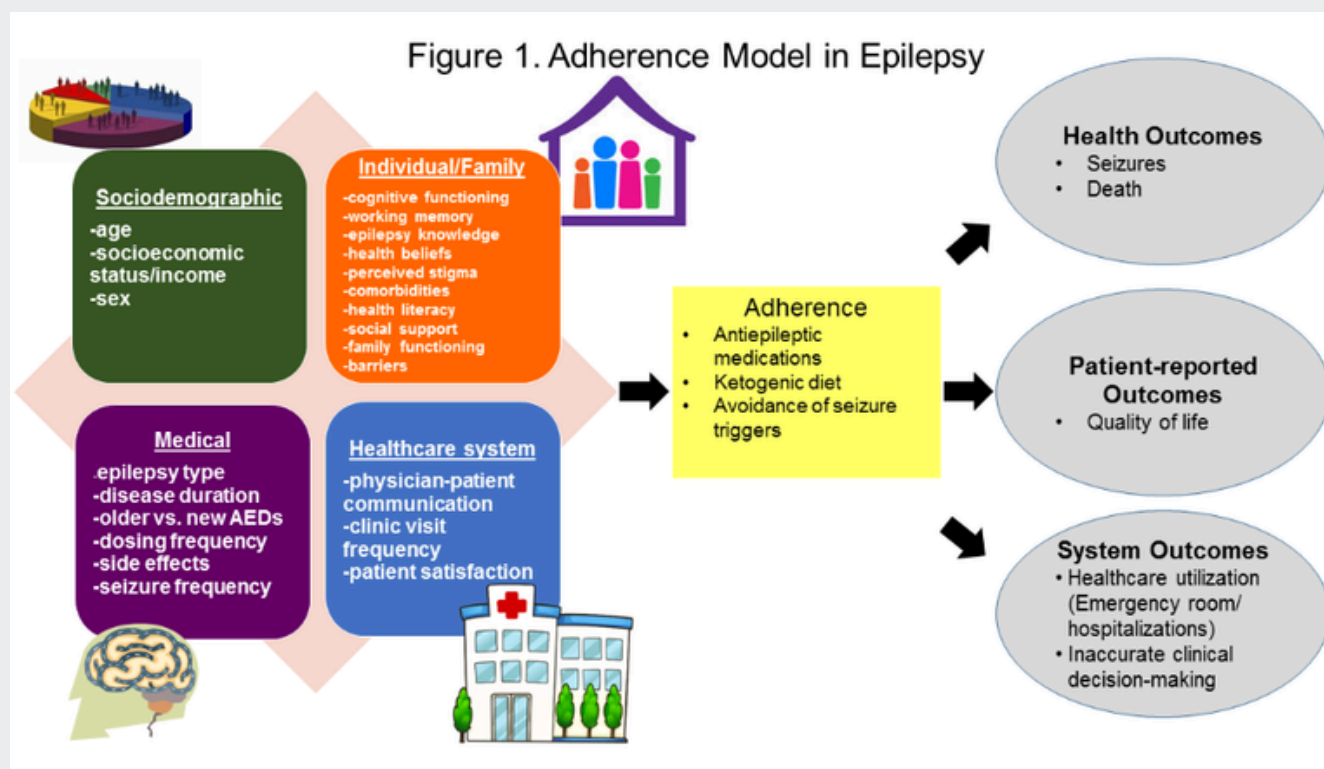


Figure from “Smith, A.W., Gutierrez-Colina, A.M., Guilfoyle, S.M., & Modi, A.C. (2020). Pediatric Epilepsy. In A.C. Modi & K.A. Driscoll (Eds). Adherence and Self-Management in Pediatric Populations (pp. 207-227). Cambridge: Elsevier S&T Books” used with permission from Elsevier.

Sociodemographic Factors and Social Determinants of Health:

- **Age.** Adherence is worse for adolescents and young adults^{23,24} compared to other age groups.
- **Socioeconomic status/Income.** Low income or socioeconomic status is associated with non-adherence.²⁵⁻²⁸
- **Sex.** No major sex differences have been found consistently; however, adherence needs to be carefully examined in pregnant women who may worry about the effects of ASMs on the fetus²⁹.
- **Race.** Black individuals with epilepsy experience higher rates of suboptimal adherence³⁰ and more system and community level adherence barriers compared to other racial groups.^{31,32}

Medical Predictors:

- **Epilepsy Type.** Some studies find lower adherence for individuals with localized seizures¹⁶ whereas others find lower adherence for generalized seizures.^{24,33}
- **Disease Duration.** Adherence typically declines over time,^{34,35} with the best adherence exhibited in the first 6 months.
- **Older versus newer generation ASMs.** Higher adherence is associated with the use of newer versus older ASMs.^{3,16}
- **Dosing Frequency.** Less frequent dosing is ideal to improve adherence⁶, with non-adherence being worse for dosing that is greater than 2 times a day.³
- **ASM Side Effects.** Real or perceived side effects of ASMs is related to non-adherence.³⁵⁻³⁸
- **Seizure frequency.** Although seizures are usually considered an outcome of poor adherence, they may also negatively influence adherence behaviors.³⁹⁻⁴¹

Individual and Family Predictors of Adherence:

- **Cognitive Functioning.** The patient's and family's ability to think clearly and problem-solve barriers that impact adherence⁴² (e.g., change in schedule, titration or switch in medicines) results in better adherence compared to individuals or families with cognitive difficulties (e.g., low IQ⁴³).
- **Executive Functioning.** Better memory is associated with better adherence.⁴⁴
- **Lack of Knowledge.** Knowledge about epilepsy and its treatments is associated with better adherence.^{42,45,46}
- **Health Beliefs.** Patient beliefs and perceptions about their health and their illness impact adherence behaviors.^{39,47-50} For example, believing epilepsy is a spiritual/psychological problem is associated with higher use of complementary and alternative therapies over ASM adherence.⁵¹
- **Perceived Stigma.** Perceived stigma is associated with worse adherence.^{35,52}
- **Psychological Comorbidities.** Depression,^{44,53,54} anxiety⁵⁴, and behavior problems⁴³ negatively impact adherence. Parental fears and stress are also predictive of ASM non-adherence.^{55,56}
- **Health Literacy.** Lower health literacy (e.g., the degree to which individuals have the capacity to obtain, process, and understand basic health information and the services need to make appropriate health decisions⁵⁷) is associated with poorer adherence.⁵⁸
- **Social support.** Increased social support is a predictor of better adherence.^{35,50,59}
- **Family functioning.** Better family problem-solving and communication are significant predictors of adherence in children^{27,42} and adolescents.⁶⁰
- **Barriers.** Individual and family-identified barriers can impede adherence and include forgetting^{21,36,37,39,61-63}, difficulty obtaining medication^{37,64}, difficulty swallowing pills, poor ASM taste, embarrassment in taking ASMs in front of others, and competing activities/inconvenience. Barriers are different depending on patient developmental stage and race.^{31,65}

Healthcare System Predictors of Adherence:

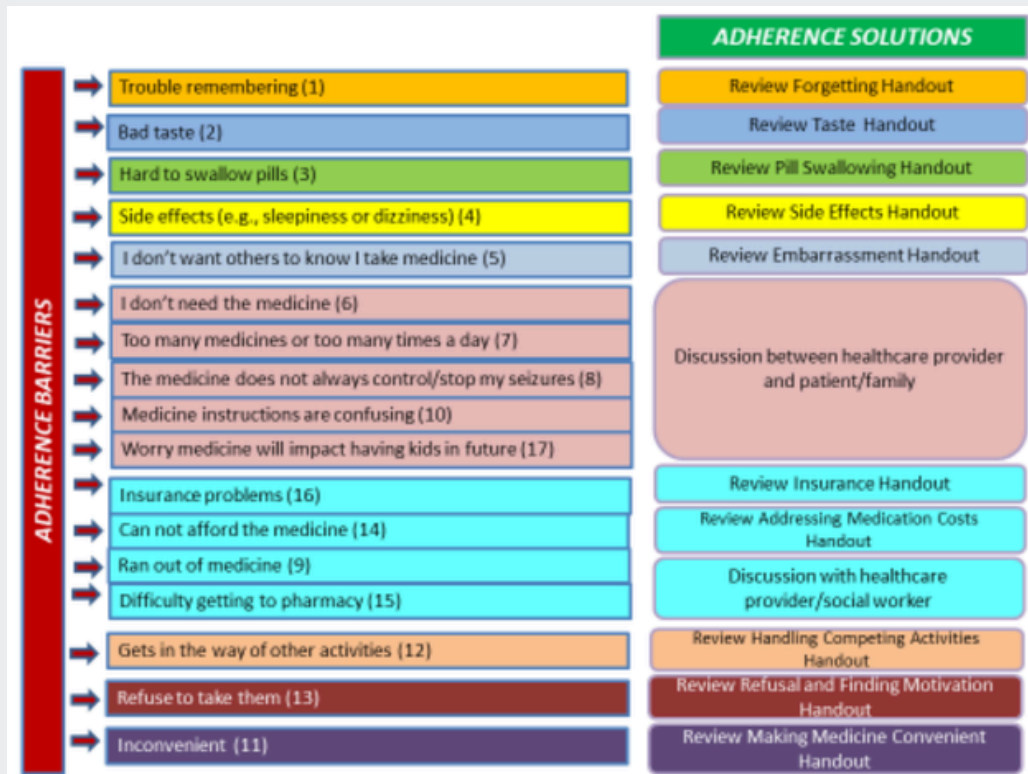
- **Physician-Patient Communication.** Poor communication between providers and patients results in worse adherence (e.g., misunderstanding dosing).³⁸
- **Clinic Visit Frequency.** More frequent clinic visits typically results in better adherence,^{66,67} which may be due to more frequent monitoring or white coat adherence (e.g., adherence increases prior to and after clinic visits).
- **Patient Satisfaction.** A positive relationship between patient and physician results in better adherence.^{37,50} Additionally, patient satisfaction with the healthcare they receive more broadly (e.g., shared decision making) can improve adherence.⁵⁶

HOW CAN WE IMPROVE ADHERENCE?

A 2020 Cochrane review of adherence interventions in epilepsy identified 20 studies, with 13 focused on adults, five focused on children and/or caregivers, one focused on adolescents, and one focused on all ages.⁶⁸ The review indicated that intensive reminders and multi-component interventions (e.g., education, problem-solving) demonstrate positive results. However, higher evidence-based interventions to improve adherence are still needed.

Notably, strategies to improve adherence should be tailored to individual patients and their relevant risk factors. Figure 2 identifies the most common adherence barriers and highlights ways for healthcare providers to address these barriers in the clinical setting. The Epilepsy Learning Health System, in conjunction with the Epilepsy Foundation, has created shared-decision making and patient handouts to address common adherence barriers (<https://www.epilepsy.com/tools-resources/forms-resources/medication-tools>). These can be useful for caregivers of children and the elderly, as well as adult patients.

Figure 2. Adherence Barriers and Solutions



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