

Patient adherence

Background

1-**“Keep watch also on the fault of patients which often makes them lie about taking of things prescribed.”** Hippocrates made this remark over 2000 years ago ⁽¹⁾.

Hippocrates advised the physician to “not only to do what is right himself, but also to make the **patient...cooperate**” ⁽²⁾.

Unfortunately, concern about how patients actually use their prescribed medications continues to this day ⁽¹⁾.

2-As former Surgeon General Dr. C. Everett Koop said, **“Drugs don’t work in patients who don’t take them.”** Prescription medications are only effective when they are taken ⁽¹⁾.

3-The terms **“compliance,” “adherence,”** and more recently **“concordance”** have been used to describe the relationship between patient medication taking behaviors and the regimens prescribed by providers ⁽¹⁾.

Definitions

1-Adherence to (or compliance with) a medication regimen is generally defined as the **extent to which patients take medications as prescribed by their health care providers** ⁽³⁾.

2-Often, the terms compliance and adherence are used interchangeably. However, they are somewhat different ⁽²⁾. The word **“adherence”** is **preferred** by many health care providers, because **“compliance”** suggests that the **patient is passively following the doctor’s orders** ⁽³⁾ while **adherence presumes the patient’s agreement** with the recommendations ⁽²⁾ and was intended to move away from viewing patients as individuals who simply did as they were told ⁽¹⁾.

3-More recently, the term **“concordance”** has been used. The concordance may be defined as **“an agreement reached after negotiation between a patient and health care professional that respects the beliefs and wishes of the patient in determining whether, when and how medicines are to be taken.”** ⁽¹⁾.

4-**Persistence** is defined as the **ability of a person to continue taking medications for the intended course of therapy**. A person is classified as **non-persistent** if he or she never fills a prescription or stops taking a prescription prematurely ⁽⁴⁾.

Incidence of nonadherence

1-Because of the difficulties in measuring adherence, no estimate of adherence or non-adherence can be generalized, **but poor compliance is to be expected in 30-50% of all patients, irrespective of disease** ⁽⁵⁾.

2-According to a 2003 report published by the World Health Organization (WHO), **adherence rates in developed countries** average only **about 50%**. In **developing countries**, the rates are **even lower**

3-The rate of adherence for **short-term therapy** was **much higher** at between 70% and 80% ⁽⁶⁾.

4-Furthermore, the rates of non- adherence with different types of treatment also differ greatly. Estimates showed that almost **50%** of the prescription drugs for the **prevention** of bronchial asthma were not taken as prescribed. Patients' adherence with medication therapy for **hypertension** was reported to vary between **50% and 70%** ⁽⁶⁾.

The Consequences of The nonadherence

1-Non-adherence to medications is considered as one of the largest drug related issues. WHO states that non-adherence to medications is a “worldwide problem of striking magnitude.” ⁽⁷⁾.

A-Poor medication adherence can cause negative health outcomes such as **worsening disease or even death** ⁽⁷⁾. Non- adherence is directly associated with poor treatment outcomes in patients with diabetes, epilepsy, AIDS, asthma, tuberculosis, hypertension, and organ transplants ⁽⁶⁾. For example:

- Nonadherence has been found to be the **primary predictor of rejection of transplanted organs** ⁽¹⁾.

- In **hypertensive** patients, **Nonadherence** is the most important **reason for poorly controlled BP**, thus increasing the risk of stroke, myocardial infarction, and renal impairment markedly ⁽⁶⁾.

- Up to 60% of patients with epilepsy are **non-adherents**, and this is the most **common reason for treatment failure** ⁽⁷⁾.

- Approximately 125,000 deaths occur annually in the US due to nonadherence with cardiovascular medications ⁽⁴⁾.

B-For infectious diseases, the consequences of non-adherence can include not only the direct impact such as treatment failures, but also the development of resistant microorganisms ⁽⁶⁾.

C-Poor medication adherence also may result in **increased health care cost** ⁽⁷⁾. More than **10% of older adult hospital admissions** may be due to nonadherence with medication regimens ⁽⁴⁾. Of all **medication-related hospital admissions** in the USA, 33

-69 % are due to poor medication adherence, with a resultant cost of approximately \$100 billion a year ⁽¹⁾.

Additionally, non- adherence would have **indirect cost** implications due to the **loss of productivity** ⁽⁶⁾.

D-Nonadherence with medication regimens may result in **increased use of medical resources**, such as physician visits, laboratory tests, unnecessary additional treatments, emergency department visits, and hospital admissions ⁽⁴⁾.

E-Additionally non-adherence has a **substantial negative effect** on **patient's quality of life** ⁽⁶⁾.

Spectrum of medication non-adherence ^(1, 4, 6, 8)

Medication nonadherence can include:

- 1-Failing to **initially fill** a prescription
- 2-Failing to **refill** a prescription as directed
- 3-**Omitting** a dose or doses (decreasing the frequency of doses) (Many patients are afraid of taking medications)
- 4-Taking **more of a medication** than prescribed (some patients may rely too heavily on medications and take more than prescribed)
- 5-**Prematurely discontinuing** medication
- 6-Taking a dose at the **wrong time**
- 7-Taking a medication **prescribed for someone else**
- 8-**Taking a dose with prohibited foods, liquids, and other medications**
- 9-Taking **outdated** medications
- 10-Taking **damaged** medications
- 11-**Storing** medications **improperly**
- 12-**Improperly** using medication **administration devices** (e.g., inhalers).
- 13- "**White-coat adherence**", which means "improved patient adherence to treatment around clinic visits"

In addition, it has been shown that almost all patients who had poor adherence with drugs **eventually dropped out of treatments completely**, and therefore did not benefit at all from the treatment effects.

Causes of medication nonadherence

1-The reasons for poor medication adherence are often multifactorial. Nonadherence to medications can be **intentional** or **nonintentional**.

A-Intentional nonadherence: is an active process whereby the patient chooses to deviate from the treatment regimen.

B-Unintentional nonadherence: is a passive process in which the patient may be careless or forgetful about adhering to the treatment regimen ⁽⁹⁾.

2-The common belief that **patients are solely responsible for taking their medications** often reflects a **misunderstanding** of how other factors affect patient adherence to treatment regimens ⁽⁴⁾.

3-The World Health Organization has categorized potential reasons for medication nonadherence into 5 broad groupings that include **patient, condition, therapy, socioeconomic, and health system–related factors** ⁽⁹⁾. (Figure-1). ⁽⁴⁾ Factors associated with each dimension are listed in Table-1 ⁽⁴⁾.

4-It is important to recognize that a person may have **multiple risk factors** for medication nonadherence and these factors **may change over time**.

Therefore, it is important to continually assess a person's adherence throughout the course of therapy ⁽⁴⁾.

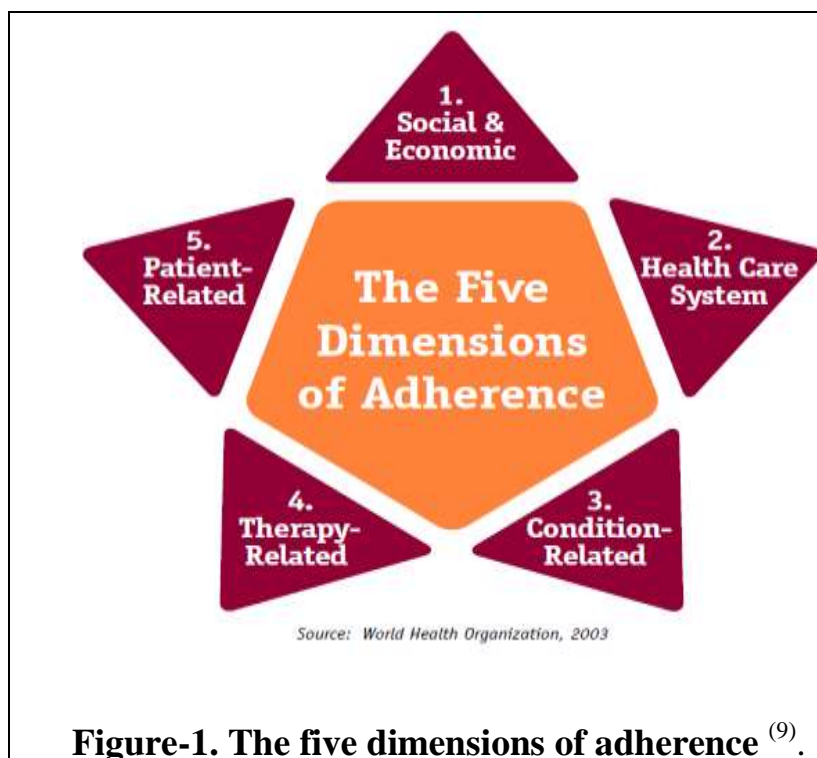


Figure-1. The five dimensions of adherence ⁽⁹⁾.

Table-1. Factors reported to affect adherence ^(4, 6).

A-Social and economic dimension	B-Therapy-related dimension
1-Low health literacy ^{**} . 2-Medication cost. 3-Cultural and lay beliefs about illness and treatment. 4-Unstable living conditions; homelessness 5-Lack of family or social support network 6-Limited access to health care facilities 7-Lack of health care insurance 8-Inability or difficulty accessing pharmacy 9-Elder abuse 10-Inability to take time off work	1-Complexity of medication regimen (number of daily doses; number of concurrent medications) 2-Treatment requires mastery of certain techniques (e.g. inhalers) 3-Duration of therapy 4-Frequent changes in medication regimen. 5-Lack of immediate benefit of therapy 6-Medications with social stigma attached to use 7-Actual or perceived unpleasant side effects 8-Treatment interferes with lifestyle or requires significant behavioral changes 9-Route of administration 10-Taste of the medication
C- Condition- related dimension	
1-Chronic conditions 2-Lack of symptoms 3-Severity of symptoms 4-Depression 5-Psychotic disorders 6-Mental retardation/developmental disability	

D-Patient-related dimension	
Physical Factors	Psychological/Behavioral Factors
1-Visual impairment 2-Hearing impairment 3-Cognitive impairment 4-Impaired mobility or dexterity 5-Swallowing problems	1-Knowledge about disease 2-Understanding reason medication is needed 3-Expectations toward benefit of treatment 4-Confidence in ability to follow treatment regimen 5-Motivation to manage the disease 6-Fear of possible adverse effects 7-Fear of dependence 8-Feeling stigmatized by the disease 9-Frustration with health care providers
E-Health care system dimension	
1-Provider-patient relationship 2-Provider communication skills (contributing to lack of patient knowledge or understanding of the treatment regimen) 3-Disparity between the health beliefs of the health care provider and those of the patient 4-Lack of positive reinforcement from the health care provider 5-Weak capacity of the system to educate patients and provide follow-up 6-Lack of knowledge on adherence and of effective interventions for improving it 7-Patient information materials written at too high literacy level 8-High drug costs, copayments, or both 9-Poor access or missed appointments 10-Long wait times 11-Lack of continuity of care	

****** Health literacy means patients are able to read, **understand, remember** medication **instructions**, and act on health information ⁽⁶⁾.

False Assumptions about Medication Adherence ⁽¹⁾.

The following are some common issues that should be kept in mind.

1-Do not assumes that **once patients start taking their medications correctly, they will continue to take them correctly in the future**. Often patients adhere to regimens while providers monitor adherence closely but lapse into nonadherence as provider attention decreases.

2-Do not assume that **when patients do not take their medications correctly that they "don't care,"** . Many patients want to take their medications correctly but are not able to do this due to a variety of reasons

3-Do not assume that **if patients are having problems in taking their medications, they will tell pharmacist or other health care providers (Patients may be embarrassed to admit having problems in taking their medications)**.

Measurement of medication adherence

1-Adherence to medication regimens has been monitored since the time of Hippocrates⁽³⁾.

2-The methods available for measuring adherence can be broken down into **direct** and **indirect** methods of measurement. Each method has advantages and disadvantages, and no method is considered the gold standard (Table-2)⁽³⁾.

3-**Direct** methods mostly used for patients under **single-dose therapy** or **intermittent administration** and **hospitalized**⁽⁸⁾.

Table-2. Methods of Measuring Adherence^(3, 8).

	Test	Advantages	Disadvantages
Direct methods	Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; impractical for routine use
	Measurement of the level of medicine or metabolite in blood or urine (e.g. serum level of antiepileptic drugs)	Objective	Variations in metabolism and “ white coat adherence ” can give a false impression of adherence; expensive
	Measurement of the biologic marker in blood *	Objective; in clinical trials, can also be used to measure placebo	Requires expensive quantitative assays and collection of bodily fluids
Indirect methods	Patient questionnaires, patient self-reports	Simple; inexpensive; the most useful method in the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
	Pill counts (Counting the number of pills that remain in the bottles).	Objective, quantifiable, and easy to perform	-Data easily altered by the patient (e.g., pill dumping) -No information on other aspects, such as dose timing -Unfeasible in assessing those medication taken as needed (prn)
	Rates of prescription refills;	Objective; easy to obtain data	A prescription refill is not equivalent to ingestion of medication requires a closed pharmacy system
	Assessment of the patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
	Electronic medication monitors (recording and stamping the time of opening bottles, dispensing drops, or activating inhaler)	Precise; results are easily quantified; tracks patterns of taking medication	-Expensive; requires return visits and downloading data from medication vials -Do not document whether the patient actually ingested the drug or correct dose -Pressure to the patient

	Measurement of physiologic markers (e.g., heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., increased metabolism, poor absorption, lack of response)
	Patient diaries	Help to correct for poor recall	Easily altered by the patient
	When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

*Non-toxic biological markers can be added to medications and their presence in blood or urine can provide evidence that a patient recently received a dose of the medication under examination ^(4, 6).

3-Patient self-report or questionnaire is one of the important indirect methods of measuring medication adherence and it's the most commonly used method in the clinical setting. Although it's simple and easy, studies show it can measure medication adherence effectively ⁽⁷⁾.

4-In 2008, a modified eight item **Morisky Medication Adherence Scale (MMAS-8)** developed from the original four item Morisky scale was published. Afterwards, MMAS-8 has become popular and commonly used in various clinical settings and different populations, as well as been translated in foreign countries ⁽⁷⁾.

Prerequisites for adherence to medication regimens ^(4, 6)

Berger and Felkey (2001) summarized the prerequisites for adherence to medication regimens. Adherence requires that a person:

- 1-Show interest in his or her health and **understand the diagnosis**
- 2-Understand the **potential impact of the diagnosis**
(The adherence was better when patient believes that the illness or its complications could pose severe consequences for his health)
- 3-Believe that the **prescribed treatment will help**
- 4-**Know exactly how to take the medication and the duration of therapy**
- 5-Find ways to **fit the medication regimen into his or her daily routine**
- 6-**Value the outcome of treatment** more than the cost of treatment
- 7-Believe that he or she **can carry out the treatment plan**
- 8-Believe that the health care practitioners involved in the treatment process truly care about him or her as a person rather than as a disease to be treated.

Enhancing adherence

- 1-The WHO, in its 2003 report on medication adherence, states that **“increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment”** ⁽¹⁰⁾.

2-Table-3 lists some simple strategies for optimizing a patient's ability to follow a medication regimen. Enhancing **communication** between health care providers and the patient is a key and effective strategy in enhancing adherence ⁽³⁾.

3-Studies show that **no single intervention is adequate to ensure medication adherence** ⁽⁹⁾ (simplifying a dosage regimen is unlikely to affect a person who does not believe that taking medications is important or that the therapy will improve his or her health, and the available evidence shows that knowledge alone is not enough for creating or maintaining good adherence). A **combination of approaches** is the most effective ⁽⁴⁾.

Table-3. Strategies for improving Adherence to a Medication Regimen ⁽¹⁻⁴⁾.

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| <ol style="list-style-type: none">1-Assessing the person's understanding about the disease and the treatment regimen and then providing information where knowledge gaps exist2-Emphasize the value of the regimen and the effect of adherence.3-Provide simple, clear instructions and simplify the regimen as much as possible (minimizing the frequency of dosing, prescribing fixed-dose combination pills when possible).4-Encourage the use of a medication-taking system (adherence aids like Medication package for daily or weekly doses, wristwatch alarms can also be programmed to signal when medication doses are due to be taken, telephone reminder).5-Listen to the patient, and customize the regimen in accordance with the patient's wishes.6-Obtain the help from family members, friends, and community services when needed.7-Consider more "Medications with long half-life, depot (extended-release) medications, and transdermal medications" medications when adherence appears unlikely.8-Identify poor adherence with encouraging blame free environment (I know it must be difficult to take all your medications regularly. How often do you miss taking them? : Look for markers of nonadherence: lack of response to medication, and missed refills. |
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Arabic version of Morisky Medication Adherence Scale (MMAS-8)

السؤال	نعم	كلا
هل تنسى أحيانا تناول الدواء الخاص بمشكلاتك الصحية؟		
لا يتناول الناس أحيانا الأدوية الخاصة بهم لأسباب أخرى غير النسيان، هل كان هناك اية أيام على مدى الأسبوعيين الماضيين لم تتناول فيها الدواء الخاص بمشكلاتك الصحية؟		
هل سبق لك أن خفضت أو توقفت عن تناول الدواء الخاص بمشكلاتك الصحية دون أن تخبر طبيبك وذلك لأنك شعرت بأن حالتك الصحية أصبحت اسوء عندما تناولت الدواء؟		
عندما تسافر أو تغادر المنزل، هل تنسى أحيانا اصطحاب الدواء الخاص بمشكلاتك الصحية؟		
هل تناولت الدواء الخاص بمشكلاتك الصحية بالأمس؟		
عندما تشعر بأن (المشكلة الصحية لديك) تحت السيطرة، هل تلجأ أحيانا الى التوقف عن استعمال الدواء؟		
تتناول العلاج بشكل يومي قد لا يروق لبعض الناس هل تشعر بعدم رضا أو امتعاض أو تشويش بسبب التزامك اليومي بالدواء؟		
كم من الأحيان تواجه صعوبة في تذكر تناول جميع أدويةك؟	نادرا /أبدا	أحيانا قليل عادة دائما

Each No answer is scored with 1 point except for the fifth question where the Yes answer is scored with 1 point. The 8th question is scored from 4-0 respectively, and then the answer is divided by 4 to get the question score. The total MMAS-8 score is calculated by the sum of the 8 questions scores. According to the scores adherence is classified into 3 categories: Low adherence (score <6), Medium adherence (6 to <8) and high adherence (score = 8). Based on adherence levels, patients classified as adherent (MMAS-8 score = 6-8) and Non-adherent (MMAS-8 score <6).

وبعض المصادر تصنف أي سكور أقل من 8 على أنه Non-adherent