

Medication adherence

Improve the health of your patients and reduce overall health care costs.



CME
CREDITS:
0.5

Marie T. Brown, MD, FACP
General Internist, Associate
Professor, Rush Medical College

Christine Sinsky, MD
Vice President, Professional Satisfaction, American
Medical Association and Internist, Medical Associates
Clinic and Health Plans, Dubuque, IA

How will this module help me successfully identify and prevent medication nonadherence in my practice?

- 1 Eight steps to improve medication adherence
- 2 Answers to common questions about how to involve staff and patients in identifying nonadherence and changing behaviors

Increasing administrative responsibilities—due to regulatory pressures and evolving payment and care delivery models—reduce the amount of time physicians spend delivering direct patient care. In the midst of a busy day, it is common to forget to ask questions about a patient’s prescriptions and whether they are adhering to their treatment plan. Identifying and correcting medication nonadherence is critical for patient health and safety as well as for the practice to deliver the most effective care possible. Encouraging adherence will improve the health of patients and reduce overall healthcare costs.

Medication adherence

Release Date: June 2015

End Date: June 2019

Objectives

At the end of this activity, participants will be able to:

1. Identify when a patient is not adherent to their medications
2. Create a blame free environment for patients to discuss medication nonadherence
3. Determine why the patient is not taking their medicine
4. Tailor the adherence solution to the individual patient

Target Audience

This activity is designed to meet the educational needs of practicing physicians.

Statement of Need

Many physicians are surprised that their patients are not open about their medication-taking behavior. In fact, patients are often reluctant to tell their doctors that they do not take their medicines as prescribed about half the time. In addition, approximately a quarter of prescriptions are never filled. Medication adherence is a growing concern to physicians and health care systems because of increasing evidence of noncompliance among patients and correlated adverse outcomes. Medication nonadherence can result in higher individual costs of care, potential harm to patients and unnecessary time-consuming work for the practice. Needless escalation of therapy, unnecessary hospitalization and emergency room visits caused by medication nonadherence can add to overall health care costs. This module provides step-by-step solutions to promote medication adherence by patients and recommendations for physicians and their teams to help them correct this problem.

Statement of Competency

This activity is designed to address the following ABMS/ACGME competencies: practice-based learning and improvement, interpersonal and communications skills, professionalism, systems-based practice, interdisciplinary teamwork and quality improvement.

Accreditation Statement

The American Medical Association is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation Statement

The American Medical Association designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credit*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Claiming Your CME Credit

To claim *AMA PRA Category 1 Credit*[™], you must 1) view the module content in its entirety; 2) successfully complete the quiz answering 4 out of 5 questions correctly and 3) complete the evaluation.

Planning Committee

Rita LePard – CME Program Committee, AMA

Ellie Rajcevic, MPA – Practice Development Advisor, Professional Satisfaction and Practice Sustainability, AMA

Sam Reynolds, MBA – Director, Professional Satisfaction and Practice Sustainability, AMA

Christine Sinsky, MD – Vice President, Professional Satisfaction, American Medical Association and Internist, Medical Associates Clinic and Health Plans, Dubuque, IA

Krystal White, MBA – Program Administrator, Professional Satisfaction and Practice Sustainability, AMA

Author(s)

Marie T. Brown, MD, FACP – General Internist, Associate Professor, Rush Medical College

Faculty

Marie T. Brown, MD, FACP – General Internist, Associate Professor, Rush Medical College

Jennifer K. Bussell, MD, FACP – Clinical Faculty, Feinberg School of Medicine, Northwestern Medicine, Chicago, IL

Umair Jabbar, MD – Attending Physician, Stroger Hospital of Cook County

Malaika Y. Peart, MD, FACP – General Internist, Cook County Hospitals and Health Systems

Patrika L. Smith, MD – General Internist, Fantus Clinic, Cook County Health & Hospitals System

Ellie Rajcevic, MPA – Practice Development Advisor, Professional Satisfaction and Practice Sustainability, AMA

Sam Reynolds, MBA – Director, Professional Satisfaction and Practice Sustainability, AMA

Christine Sinsky, MD – Vice President, Professional Satisfaction, American Medical Association and Internist, Medical Associates Clinic and Health Plans, Dubuque, IA

About the Professional Satisfaction, Practice Sustainability Group

The AMA Professional Satisfaction and Practice Sustainability group has been tasked with developing and promoting innovative strategies that create sustainable practices. Leveraging findings from the 2013 AMA/RAND Health study, *Factors affecting physician professional satisfaction and their implications for patient care, health systems and health policy*, and other research sources, the group developed a series of practice transformation strategies. Each has the potential to reduce or eliminate inefficiency in broader office-based physician practices and improve health outcomes, increase operational productivity and reduce health care costs.

Disclosure Statement

The content of this activity does not relate to any product of a commercial interest as defined by the ACGME; therefore, neither the planners nor the faculty have relevant financial relationships to disclose.

Media Types

This activity is available to learners through Internet and Print.

References

1. Sabaté E, ed. *Adherence to Long-Term Therapies: Evidence for Action*. Geneva, Switzerland: World Health Organization; 2003.
2. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA*. 2006;296(21):2563-2571.

3. Fischer MA, Choudhry NK, Brill G, et al. Trouble getting started: predictors of primary medication nonadherence. *Am J Med.* 2011;124(11):1081.e9-e22.
4. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. *J Gen Intern Med.* 2010;25(4):284-290.
5. Office of the Inspector General, US Department of Health and Human Services. *Medication regimens: causes of noncompliance.* Washington DC, US Dept of Health and Human Services; 1990. DHHS Publication OEI 04- 89-89121. <https://oig.hhs.gov/oei/reports/oei-04-89-89121.pdf>. Accessed April 7, 2015.
6. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care.* 2005;43(6):521-530.
7. Zolnierek KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care.* 2009;47(8):826-834.
8. Kesselheim AS, Misono AS, Shrank WH, et al. Variations in pill appearance of antiepileptic drugs and the risk of nonadherence. *JAMA Intern Med.* 2013;173(3):202-208.
9. Kesselheim AS, Bykov K, Avorn J, Tong A, Doherty M, Choudhry NK. Burden of changes in pill appearance for patients receiving generic cardiovascular medications after myocardial infarction: cohort and nested case-control studies. *Ann Intern Med.* 2014;161(2):96-103.
10. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation.* 2009;119(23):3028-3035. <http://circ.ahajournals.org/content/119/23/3028.full>. Accessed April 7, 2015.
11. Brown MT, Sinsky CA. Medication adherence: we didn't ask and they didn't tell. *Fam Pract Manag.* 2013;20(2):25-30. <http://www.aafp.org/fpm/2013/0300/p25.html>. Accessed April 7, 2015.
12. Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clinic Proceedings.* 2011;86(4):304-314. doi:10.4056/mcp.2010.0575.
13. Brown MT, Bussell J, Dutta S, et al. Medication adherence: truth and consequences. *Am J Med Sci.* 2016;351(4):387-399.



Introduction

What is medication adherence?

A patient is considered adherent if they take 80 percent of their prescribed medicine(s). If a patient takes less than 80 percent of their prescribed medication(s), they are considered nonadherent.

How common is medication nonadherence?

Patients don't take their medicine as prescribed about half the time.^{1,2}

Why is it important to assess adherence?

Patients are often reluctant to tell their doctor that they do not take their medicines. Unless a patient's medication-taking behavior is understood, therapy may be needlessly escalated. This results in increased costs to the patient and health care system, potential harm to the patient and unnecessary work on the part of the practice during the visit. Medication nonadherence can lead to unnecessary hospitalization and emergency room visits, which can add to overall health care costs. The practice team can help identify and improve patients' adherence to their medications.



Eight steps to improve medication adherence

1. Consider medication nonadherence first as the reason a patient's condition is not under control
2. Develop a process for routinely asking about medication adherence
3. Create a blame-free environment to discuss medications with the patient
4. Identify **why** the patient is not taking their medicine
5. Respond positively and thank the patient for sharing their behavior
6. Tailor the adherence solution to the individual patient
7. Involve the patient in developing their treatment plan
8. Set patients up for success

1

Consider medication nonadherence first as the reason a patient’s condition is not under control

Think about the possibility that the patient isn’t taking their current medications as prescribed when reviewing their medications, especially when considering escalating therapy or adding another medication. Many physicians are surprised to learn that:

- Patients do not take their medications half of the time
- Approximately a quarter of new prescriptions are never filled^{3,4}
- Most patients who decide not to fill a prescription or take a medicine will not tell their doctor

Escalating therapy when nonadherence is hidden can be very dangerous, costly and time-consuming. If a physician prescribes another medicine to an already nonadherent patient, this can have catastrophic results if the patient suddenly starts taking all of their medicines.

For example, consider a patient who is hospitalized and has medications started according to their medication list. The provider in the hospital is unaware that the patient had not previously been taking all of his or her prescribed medications. Once all the medications are initiated, the patient may develop severe hypotension or hypoglycemia, resulting in the need for additional care and management.

Q&A

[If a patient is nonadherent, are they nonadherent to all their medications or just one?](#)

It depends. Patients may be adherent to one medicine and nonadherent to others depending on their beliefs and understanding about each medication.

[What is primary medication nonadherence?](#)

Primary medication nonadherence is failing to fill or take a new prescription. Before e-prescribing, physicians were not able to track whether a patient filled a new prescription, but with this technology some practices are able to identify medicines that were prescribed but never filled.

[How common is primary medication nonadherence?](#)

Approximately a quarter of patients never fill a new prescription.^{3,4}

2

Develop a process for routinely asking about medication adherence

When you ask your patients about their medication-taking behavior during a visit depends on your individual practice. Your team can save you time by helping with this decision.

One option is to have the receptionist offer the patient a pre-visit questionnaire at check-in that includes questions about his/her medication usage. The questionnaire may be accompanied by a list of the patient’s current medications with directions to cross out medications they are no longer taking and circle any they don’t take regularly or have questions about. You can then review this questionnaire with the patient during their visit.

Another option is to have the medical assistant (MA) or nurse gather additional information on potential medication nonadherence while rooming the patient and then alert the physician to discuss any potential issues during the visit.

Q&A

I'm already so busy. Won't this take a lot of time?

With the approach outlined above, much of the medication review is done during the patient's time in the waiting room and is completed before the doctor enters the room. The MA or nurse who rooms your patients or makes pre-visit phone calls can assist in reconciling medications and initiating the conversation about adherence with patients. In fact, identifying nonadherence before the visit may save time in the long run. For example, if you know that the current medicine is not being taken, rather than it being insufficient or ineffective, you may save time by not ordering another medicine or changing the dose.

I've learned that patients don't always remember or even know their medications when they come to the office. Do you have any suggestions?

Medication review does not need to occur while the patient is on-site. Staff may reach out to patients before their upcoming appointment to conduct an in-depth medication review and discuss medication-taking behavior during a pre-visit phone call. This can save time during rooming and has the additional advantage of allowing the patients to look at their medication bottles.

I've heard of practices that ask patients to bring in their medications. Could that work?

This is called a "brown bag review" and it works for some practices. Patients are asked to bring in all their medicines, including supplements, medications from other doctors and discontinued medications. During this review, medication nonadherence may be identified (e.g., too many refills left, pill counts may be off, last refill date can be noted). Medication duplication may also be identified. This is an effective way to understand all of the patient's medications, even ones that have been prescribed by other physicians or at other organizations or emergency departments.

How can I get patients in the habit of bringing in their medications or an updated list of their meds?

Some practices have their staff routinely call each patient on the day before their appointment to remind them to bring in their medication list or their medication bottles. Other practices include this message in automated reminder calls, letters, emails or messages sent via the electronic health record (EHR) patient portal.

3

Create a blame-free environment to discuss medications with the patient

The patient may have good reasons for not taking their medications and should be reassured that they can share their true medication-taking behavior without judgment.



Q&A

Why is it important to create a blame-free environment?

A blame-free environment encourages and allows patients to be honest with their physician. Patients want to please their doctor and may resume taking their medication a few days or weeks before seeing their doctor, giving the false impression that conditions are under control. By doing so, they can also honestly say "yes" when a staff member asks if they are taking their medicine. This behavior is known as "white coat adherence."

Can you give me examples of nonjudgmental approaches I can use to ask my patients about their medication-taking behavior?

Asking patients, “Why aren’t you taking the medications I prescribed?” is confrontational and suggests that you think the patient’s nonadherence is because they are defying your recommendations. Instead, try saying, “Many people have trouble taking their medications on a regular basis. Do you find this is the case for any of your medications?” This removes blame from the patient to allow them to open up about their particular situation.

4

Identify **why** the patient is not taking their medicine

Most nonadherence is intentional. Patients make a rational decision not to take their medicine based on their knowledge, experience and beliefs. Top reasons for intentional nonadherence include:

- A** **Fear:** Patients may be frightened of potential side effects or side effects they had previously with the same or a similar medication. They may have witnessed side effects experienced by a friend or family member who was taking the same or a similar medication and believe that the medication caused these problems.
- B** **Cost:** Cost of medicine can be a barrier to adherence. Patients may not fill medications in the first place or ration what they do fill to extend their supply.
- C** **Misunderstanding:** Patients may not understand the need for the medicine, the nature of side effects or the expected time it will take to see results. This is particularly true for patients with chronic illness because taking a medicine every day so that “nothing happens” can be confusing. Failure to see immediate improvement may lead to premature discontinuation.
- D** **Too many medications:** The greater the number of different medicines prescribed and the higher the dosing frequency, the more likely a patient is to be nonadherent.
- E** **Lack of symptoms:** Patients who don’t feel any differently when they start or stop their medicine may see no reason to take it.
- F** **Worry:** Concerns about becoming dependent on a medicine also leads to nonadherence.
- G** **Depression:** Patients who are depressed are less likely to take their medications as prescribed.
- H** **Mistrust:** Patients may be suspicious of their doctor’s motives for prescribing certain medications because of recent news coverage of marketing efforts by pharmaceutical companies influencing physician prescribing patterns.

Source: AMA. *Practice transformation series: medication adherence*. 2015.

Q&A

Why wouldn’t a patient take medicine that would help them?

Physicians have a unique understanding of progressive illnesses and know that taking medicine now for an asymptomatic condition could prevent adverse outcomes in the future. Patients are often focused on short-term benefits and may not understand the future implications of medication nonadherence on their overall health.

How should I approach reasons for nonadherence that may embarrass the patient, such as needing help getting to a pharmacy, not being able to pay for a prescription or not understanding what the medication is for and being afraid to ask about it?

You may be able to uncover barriers to adherence by listing these issues and asking if any pose a problem for the patient. Also, saying that many patients experience similar challenges is helpful. Helping patients verbalize barriers to adherence is the first step in identifying and securing the supportive services they need. If a patient has difficulty with transportation to a pharmacy, the patient may benefit from a ride-share arrangement or having the prescriptions delivered to their home by their pharmacy or a mail-order pharmacy. If a family member is routinely picking up the medications for the patient, offer to send the prescription to a pharmacy conveniently located near that person. For patients who do not understand their medication or treatment plan, group classes or a one-on-one session with an educator about their condition and treatment could help close their knowledge gap.

Physicians and their teams can help patients understand that their concerns or challenges are experienced by many patients and can make patients aware of resources from the practice, organization or community that can promote medication adherence.

Why do patients stop their medicine once their condition is under control?

Physicians often assume that patients understand that they will need to be on a drug for a long time and therefore often fail to explicitly tell them that is the case. Once a patient's condition is controlled, such as when symptoms of depression improve with medication, the patient may think the problem has resolved and feel that they don't need to continue the medicine.

Will using generic medicines help increase adherence?

Prescribing generics may help some patients overcome financial barriers to adherence. However, patients and physicians are often not aware that the appearance of generic pills may change frequently—adding to confusion or general mistrust. Patients should be encouraged to ask the pharmacist about changes to their medication to confirm the pills and administration instructions are still correct. This is an opportunity for patients to engage in their own care.

Isn't forgetfulness a common unintentional cause of not taking a medication or missing a dose?

Forgetfulness might be a problem for some patients, but most nonadherence is intentional. Patients make a conscious decision not to take their medicine.

Is medication nonadherence ever unintentional?

Yes, nonadherence is occasionally unintentional. Unintentional nonadherence may result from forgetting to take the medication or low health literacy that can lead to misunderstanding about the purpose or use of the medication. Frequent changes in a patient's schedule, such as shift work, can also lead to unintentionally missing a dose of medication. Patients who tend to forget to take their medication or have irregular schedules can use pill boxes that organize medications by day of the week and time of day for each pill. These help keep the patient organized because they know in advance when each medication needs to be taken. Some patients also find that using an alarm or reminder on their phone or calendar can help them remember to take their medications at the correct time.



5 Respond positively and thank the patient for sharing their behavior

Physicians are often surprised to hear that their patient is choosing not to follow their advice. Once a patient shares their nonadherence with staff or the physician, the physician should respond positively: "Thank you for telling my staff that you are not taking the medicines I prescribed last time. Let's talk about why that is."

Responding by thanking them for their frankness and avoiding blame will make them more comfortable with sharing their reasons for not taking the medicine.

Q&A

How can I talk to patients in a way that improves their medication adherence?

Physicians' attitudes towards patients plays a critical role in medication adherence. As a physician engages and involves the patient in medication decisions and understands the patient's rationale for nonadherence, it becomes increasingly likely that adherence will improve.⁵ Good communication and medication adherence are connected. In fact, inadequate physician communication with patients may account for 55% percent of medication nonadherence.

6

Tailor the adherence solution to the individual patient

Each patient may have a unique reason for not taking their medicine. By identifying and discussing these unique reasons you can develop a personalized approach that promotes adherence in the future.

Q&A

One of my patients skips his medications because of shift work and a busy schedule—despite reminders and pillboxes. What should I do?

Using “forgiving drugs” is often helpful in addressing this form of nonadherence. These are drugs with longer half-lives that may be given once a week or once a month and have little if any symptoms upon discontinuation. For example, fluoxetine has a long half-life compared to other commonly used antidepressants and may be a good choice for treating depression in this situation. It may also be helpful to inquire about the patient's schedule and identify any aspects of their daily routine that are fixed and could provide an opportunity to take their medications.

How can I simplify a treatment regimen to encourage adherence?

Adherence increases as the frequency of dosing decreases. You can try simplifying a patient's dosing schedule by adjusting medicines so that they can all be taken at the same time of day. Choosing long-acting drugs is also useful if the dosing burden is too complex. If possible, consolidate medicines by using combination products.

If I inform the patient of potential side effects of a medicine, won't that scare him and add additional reasons for nonadherence?

Patients want and are entitled to know what might happen when they take a medicine. Informing patients of potential side effects develops trust, engages the patient and gives the physician and patient the opportunity to identify the best treatment plan together.

Cost of medication is an issue for many of my patients. What can I do to help?

If cost is a barrier to adherence for your patients, try using generic medicines. You should also check that the drug you're prescribing is on the patient's insurance formulary. Often patients are embarrassed to tell you that they cannot afford a drug. Selecting and prescribing medications known to be on a discount list through major pharmacies can decrease cost regardless of insurance. Pharmacy price comparison websites such as [GoodRx](#) are an additional resource to help reduce medication costs. Ask a care manager or someone in financial services at your practice to help patients find financial assistance plans and insurance plans that may offer better prescription coverage.

7

Involve the patient in developing their treatment plan

Patients who are included in decisions about the medications they are prescribed are more likely to adhere to their treatment plan. Before starting a new medication, you might offer the patients a choice: “We could either start a blood pressure medication today or you could make some other changes and we can see if you can control your blood pressure without medication. To control your blood pressure without medication, you can work on getting more exercise and start a low salt diet. It’s also important that you monitor your blood pressure at home three times a week to make sure you’re on track. When you come in for your check up in six weeks, we can see whether you’ve gotten your blood pressure under better control and discuss options. Which would you prefer?”

Q&A

How do I know if my patient understands their treatment plan?

The “teach-back” method is a good way to find out if the patient understands their medications and the treatment approach you recommend. During the expanded discharge process at the end of the visit (see the [rooming and discharge module](#) for more information) someone on the team, such as the nurse or medical assistant, asks the patient to describe the next steps as they understand them. The patient thus “teaches” the staff about the next steps. This gives the nurse the opportunity to fill in any gaps in the patient’s understanding of their treatment plan, medication regimen and provide any additional explanation that is needed. The staff should also ensure that the patient has written instructions to help them adhere to their medication regimen.

One of my patients has consistently elevated blood pressure yet remains nonadherent to prescribed medications. I’d like to see if a new medication improves adherence. Do you have any suggestions?

As described previously, patients have numerous reasons for intentionally not taking their medication. Start by trying to understand why this patient is not regularly taking the medication. Sometimes it helps to negotiate with the patient and agree to stop a less essential medication, at least for a time, while the patient tries the new medication. Another option is to offer lifestyle changes to address the elevated blood pressure, such as increasing exercise and decreasing salt intake. Alternatively, you may suggest starting with a lower dose of a new medication to acclimate the patient to the potential side effects. Finally, you might suggest a brief trial of the medication with a plan to reassess together in a few weeks. This will reassure the patient that if the medication doesn’t agree with them they will be able to stop taking it. If the patient is still hesitant to take the medicine, accept their reluctance with plans to re-evaluate together in the near future.

8

Set patients up for success

Make it easy for patients to adhere to their medication regimen. One simple way for your practice to achieve this is to give patients an updated medication list at the end of each visit that highlights any changes to their treatment plan. If the patient agrees, you may also ask if the family or caregiver would like an extra copy.

Q&A

How can I predict which patients won’t take their medication?

It is very difficult to predict which patients will be nonadherent. Most patients will not tell a doctor that they do not plan on starting a medicine. Encourage your patients to contact you if they decide not to fill the medicine. Let them know that they can tell you this without judgment and that you are committed to understanding their concerns about their medication and any barriers they may have to adherence. If the patient does call in, primary nonadherence can be addressed. Preventing primary nonadherence is particularly important with certain cardiovascular drugs, such as antiplatelet therapies after a stent is placed.

If I start a patient on a new medication for chronic illness, should I tell them that they will be on it indefinitely?

Yes. Patients are often unaware that medicines should be taken for an extended duration, especially when the directions on the label state “take one pill a day for three months.” The patient may interpret this as instructions to stop taking the medicine after three months. Physicians are often reluctant to tell a patient of the need for long-term therapy because they fear it will increase patient’s resistance to treatment or make the patient depressed. Some or all of those fears may be realized, but it is always best to be clear with your patients about the importance of their medication and the role it plays in improving their health.

I am the CEO of an Accountable Care Organization (ACO)—why should I care about medication adherence?

Increasing medication adherence may be good for the bottom line of an ACO. Medication nonadherence is responsible for one-third to two-thirds of all medical hospital admissions, over 10 percent of hospital readmissions and nearly one-third of preventable ER visits.^{6,7}



AMA Pearls

Remember to ask

If we ask, patients will be more likely to tell us about their medication adherence.

Spend to save

Every dollar spent improving adherence saves seven dollars in total healthcare costs.^{6,7}

Conclusion

Addressing medication nonadherence is critical for patient health and safety and for your practice to deliver the most effective care possible. This module provides an overview of reasons for medication nonadherence and suggestions for how to broach this subject with your patients. Use the strategies and tactics in this module to promote medication adherence by your patients.



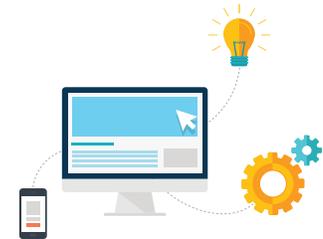


To demonstrate completion of this module and claim *AMA PRA Category 1 Credits™*, please visit:

www.stepsforward.org/MedicalAdherence

Get implementation support

The AMA is committed to helping you implement the solutions presented in this module. If you would like to learn about available resources for implementing the strategies presented in this module, please call us at (800) 987-1106 or [click here](mailto:StepsForward@ama-assn.org) to send a message to StepsForward@ama-assn.org



References

1. Sabaté E, ed. *Adherence to Long-Term Therapies: Evidence for Action*. Geneva, Switzerland: World Health Organization; 2003.
2. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low density lipoprotein cholesterol: a randomized controlled trial. *JAMA*. 2006;296(21):2563-2571.
3. Fischer MA, Choudhry NK, Brill G, et al. Trouble getting started: predictors of primary medication nonadherence. *Am J Med*. 2011;124(11):1081.e9-e22.
4. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. *J Gen Intern Med*. 2010;25(4):284-290.
5. Office of the Inspector General, US Department of Health and Human Services. *Medication regimens: causes of noncompliance*. Washington DC, US Dept of Health and Human Services; 1990. DHHS Publication OEI 04-89-89121. <https://oig.hhs.gov/oei/reports/oei-04-89-89121.pdf>. Accessed April 7, 2015.
6. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-530.
7. Zolnierok KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care*. 2009;47(8):826-834.
8. Kesselheim AS, Misono AS, Shrank WH, et al. Variations in pill appearance of antiepileptic drugs and the risk of nonadherence. *JAMA Intern Med*. 2013;173(3):202-208.
9. Kesselheim AS, Bykov K, Avorn J, Tong A, Doherty M, Choudhry NK. Burden of changes in pill appearance for patients receiving generic cardiovascular medications after myocardial infarction: cohort and nested case-control studies. *Ann Intern Med*. 2014;161(2):96-103.
10. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation*. 2009;119(23):3028-3035. <http://circ.ahajournals.org/content/119/23/3028.full>. Accessed April 7, 2015.
11. Brown MT, Sinsky CA. Medication adherence: we didn't ask and they didn't tell. *Fam Pract Manag*. 2013;20(2):25-30. <http://www.aafp.org/fpm/2013/0300/p25.html>. Accessed April 7, 2015.
12. Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clinic Proc*. 2011;86(4):304-314.
13. Brown MT, Bussell J, Dutta S, et al. Medication adherence: truth and consequences. *Am J Med Sci*. 2016;351(4):387-399.