The Noncompliance Epidemic

Why Are So Many Patients Noncompliant?

Neil Chesnow | January 16, 2014

An Epidemic of Noncompliance

If you're baffled by how many of your patients, particularly those with chronic conditions, don't take their medications as prescribed -- if at all -- you're not alone. Doctors from coast to coast feel frustrated by the same thing.

In 2011, Consumer Reports published a survey of 660 primary care physicians, “What Doctors Wish Their Patients Knew.”[1] The number-one complaint by far: Patients didn’t take the doctors’ advice or otherwise follow treatment recommendations.

"Most of the doctors we surveyed said it affected their ability to provide optimal care," the editors wrote.[1] “Thirty-seven percent said it did so 'a lot.'"

In fact, the number of patients who are noncompliant has reached epidemic proportions, and doctors' inability to provide optimal care as a result has mushroomed into one of the most pressing problems in healthcare today.

• In the United States, some 3.8 billion prescriptions are written every year,[2] yet over 50% of them are taken incorrectly or not at all.[3]

• In a survey of 1000 patients, nearly 75% admitted to not always taking their medications as directed.[4]

• A study of over 75,000 commercially insured patients found that 30% failed to fill a new prescription, and new prescriptions for chronic conditions such as high blood pressure, diabetes, and high cholesterol were not filled 20%-22% of the time.[5]

• Even among chronically ill patients who regularly fill their prescriptions, only about half the doses taken are taken as their physicians intend.[6]

• Poor compliance accounts for 33%-69% of drug-related adverse events that result in hospital admissions.[3]

• Poor compliance with medication regimens is associated with up to 40% of nursing home admissions.[7]

• In a study of over 8400 senior health plan enrollees, only 1 in 3 of those who began treatment with concurrent antihypertensive and lipid-lowering drugs were taking both medications as directed or at all at 6 months.[8]

• In a study of over 240,000 patients who were given a new prescription for an antidepressant, less than 30% were still taking the medication 6 months later.[9]

• Compared with patients who follow instructions, patients who don't take their medications as intended have a risk for hospitalization, rehospitalization, and premature death that is 5.4 times higher if they have hypertension, 2.8 times higher if they have dyslipidemia, and 1.5 times higher if they have heart disease.[10]

• The number of patients with serious cardiac conditions who don't take their medications is especially baffling and problematic. In a study of 34,501 patients age 65 or older, only 26% of those who began a statin regimen to reduce the risk for coronary heart disease maintained a high level of use 5 years later; the greatest decline occurred during the first 6 months of treatment.[11]

• Even after a life-threatening event, compliance with medication regimens remains surprisingly poor. Within 2 years of initiating therapy, only half of patients hospitalized for acute myocardial infarction (MI) were still taking their prescribed statins, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs).[12]

One upshot: Poor medication compliance is implicated in over 125,000 US deaths per year.[3]

Yet compliance -- which is used interchangeably with the term “adherence,” although the latter is gaining ground -- has been exhaustively studied. More than 40,000 peer-reviewed papers on the subject have been published,[13] "yet the rates of poor adherence have not changed significantly over the past several decades and continue to remain at an
unacceptable level," observes URAC, a healthcare accreditation organization, in a white paper prepared for industry leaders.\(^{[13]}\)

Or, as former Surgeon General C. Everett Koop once put it with his customary forthrightness, "Drugs don't work in people who don't take them."\(^{[3]}\)

The $290-billion question -- $290 billion being how much poor compliance is estimated to cost the US healthcare system each year\(^{[14]}\) -- is, why?

An Unbelievably Complicated Problem

One reason noncompliance has been such a tough nut to crack is its daunting complexity. Patients don't take their medications for a multitude of reasons, many of them emanating from the murky depths of human psychology, and which the patients (not to mention medical researchers) may not fully understand.

To complicate matters, these reasons vary from patient to patient. That rules out a one-size-fits-all solution. Internist William Shrank, MD, MSHS, Chief Scientific Officer and Chief Medical Officer of Provider Innovation and Analytics at CVS Caremark, has served as lead author or coauthor in over 100 studies on patient compliance with medication. His conclusion: "There is no silver bullet."

Researchers have analyzed the steps involved in compliance to better understand where the process breaks down.\(^{[15]}\) First the patient must receive the right prescription from a doctor or other provider. The new prescription must then be filled, the seemingly simple act of which can be a major barrier to compliance. The patient must then make it through the first 6 months on the medication, when the risk for noncompliance is highest. If the medication is for a chronic condition, it must then be taken as intended -- indefinitely.

"Adherence is the result of getting through these four steps successfully," notes the RAND Corporation, a nonprofit research organization, in a report aimed at policymakers in Washington, "and a single policy option is not going to address each of these challenges to adherence."

To thicken the plot, a patient's unique cluster of reasons for not complying at any given time isn't stable. With the loss of a job, for example, medications may become unaffordable, so the patient stops taking them, or cuts the pills in half to make them last longer, or skips some doses.

After a divorce, job loss, or any traumatic event, depression may set in; taking medication as directed may then be the last thing on the patient's mind.

Or a compliant patient may suffer a medication-related adverse event. As a result, she may stop taking her pills, as up to 20% of patients do because of perceived side effects.\(^{[16]}\)

Does the patient tell the doctor? Probably not. Why? The doctor is so busy; she doesn't want to be a bother. Or she doesn't like the doctor, so this is how she retaliates. Or she decides that her ill effects are a sign that she's taking too many drugs, so she goes off-regimen. Or she consults with a friend on a social networking Website for patients with similar chronic conditions, and the friend advises her to try alternative medicine instead.

"Is it widely known that adherence is a cluster of behaviors and not a single construct?" asks internist John F. Steiner, MD, MPH, Research Director at Kaiser Permanente's Institute for Health Research in Denver, and a thought leader on medication compliance issues. "No, that's actually a radical claim."

It may be radical, but researchers are putting patients, doctors, and the healthcare system itself under a microscope to better understand this ever-shifting cluster of behaviors and why it so often results in noncompliance. While many questions remain unanswered, here's what has been learned to date.

Patient Beliefs and Behaviors Are Often Barriers

Patients with chronic conditions may spend only a few hours a year in your office, but they spend roughly 5000 waking hours each year living the rest of their lives.\(^{[17]}\) During that time, out of touch with their doctors and generally unmonitored by the healthcare system, many are allowed to quietly, invisibly slip off their regimens.

In 2009, a team of researchers at Kaiser Permanente combed through much of the vast literature on compliance and distilled the sea of data down to several important patient-related barriers.\(^{[18]}\) They include forgetfulness; lack of knowledge about the medication and its use; cultural, health, and/or religious beliefs about the medication; denial or ambivalence regarding the state of their health; financial challenges; lack of health literacy; and lack of social support.
Forgetfulness is the number-one barrier to compliance, experts believe, although a survey of 10,000 patients found that only 24% ascribed noncompliance to forgetfulness. Up to 20% failed to take medications because of perceived side effects, 17% had cost issues, and 14% didn't feel the need to take medication; they believed it would have little or no effect on their disease.

Among patients with chronic conditions, such as high blood pressure and high cholesterol, noncompliance tends to be highest if symptoms aren't experienced.

Myopic? Perhaps. But when doctors are patients, they tend to act just like everyone else. Steiner likes to ask an audience of physicians for a show of hands of who has ever taken an antibiotic. Many hands are raised. He then asks how many doctors took the full course of antibiotics even after their symptoms abated. Many hands go down.

Even the Sickest Patients May Not Take Their Drugs

Noncompliance is plentiful in patients who exhibit symptoms too -- even for life-threatening conditions. Not even a brush with death is enough to get some patients to stick to their regimens. According to one study, after hospitalization for acute MI, about 24% of patients still had not filled their cardiac medication prescription a week after being discharged.

In another study, among patients discharged with prescriptions for aspirin, statins, and beta-blockers after an episode of acute MI, about 34% stopped at least 1 medication and 12% stopped all 3 medications within a month.

A third study found that only about 40% of patients were still taking statins 2 years after hospitalization for acute coronary syndrome. Compliance was even lower for patients taking statins for chronic coronary artery disease.

A major reason why many patients go off-regimen is the cost of drugs. But even when patients are given drugs gratis, compliance improves only slightly. One much-discussed study looked at 2845 Aetna health plan members discharged from the hospital after an acute MI episode who were given all of their drugs -- statins, beta-blockers, ACE inhibitors, ARBs -- for free, comparing them with 3020 Aetna enrollees who had the usual prescription coverage. In the usual-coverage group, compliance rates were 36%-49%. But without the cost barrier, the rates were only 4%-6% higher.

What could account for this underwhelming result? Could depression play a role? Although the investigators noted cardiac-related comorbidities of patients at baseline, they didn't ask about depression. Yet a meta-analysis of 31 studies that collectively included 18,000 people found that depressed patients with a variety of chronic illnesses, including diabetes and heart disease, had 76% greater odds of being noncompliant compared with patients who weren't depressed.

At least you can understand why depressed patients may lack the motivation to stay on regimen, but, confoundingly, so do many patients who aren't depressed. As Shrank and cardiologist Lisa Rosenbaum, MD, noted in a 2013 paper:

Though patients may be forthcoming about the more practical challenges to adherence, the psychological barriers are tougher to identify and articulate. Patients don't generally tell their physicians, 'Every time I look at that pill bottle, it reminds me that I'm ill' or 'I tend to discount future benefits as long as I feel well today.' Such underlying psychological mechanisms probably contribute to nonadherence far more than we realize and help explain why existing interventions have brought only modest improvements.

Physicians' Role in Noncompliance

Once upon a time, patients followed the doctor's orders. Not anymore. The very notion of the doctor paternalistically telling the patient what to do is now politically incorrect. The term compliance, while still used interchangeably with adherence in the medical literature, is no longer preferred in white papers that think tanks churn out for healthcare decision-makers and policymakers in Washington.

"Compliance" implies that patients are passive actors in managing their chronic conditions. "Adherence," according to the World Health Organization (WHO), suggests just the opposite: that doctors and patients team up to help patients actively engage in maintaining their health.

In reality, though, the teamwork concept isn't working out too well. One reason is a chronic lack of time. The mean duration of a primary care visit ranges from 7.6 to 17.6 minutes. To be efficient, the doctor must control the conversation, with less time for listening and discussing topics such as medication reviews and preventive care.

Even if more time were available, it's not what every patient wants. In one study of doctor-patient relationships, behavioral economists used game-theory techniques to identify the factors affecting treatment decisions in patients with a life-threatening disease -- in this case, breast cancer -- who were considering adjuvant therapy. They found that when patients disregarded their doctors' treatment recommendations, the doctors responded by telling them in more
detail about the benefits of treatment. However, this produced a perplexing result: The more information the patients received, the less likely they were to be compliant.

"Patients want more specific disease and treatment information," the researchers conceded, but "the provision of this information might lead to therapy decisions which diverge from the physicians' recommendations."

But the larger problem is that too little information is offered to patients who want and need more. The average time that a doctor spends discussing all aspects of a newly prescribed medication is a mere 49 seconds.[28] Surveys show that no medication instructions are given by physicians in 19%-39% of prescriptions; in observational studies, 17%-25% of prescriptions are not accompanied by instructions from the doctor.[29] For a new prescription, doctors discuss dosing directions in fewer than 60% of cases, and they review potential adverse events -- a major reason why patients quit taking their drugs -- only 33% of the time.[29]

Nor do busy doctors typically have the time or skill to sit down with a patient and tease out his or her unique personal barriers to compliance, which is why so much of their advice goes in one ear and out the other, contends behavioral psychologist Kim Lavoie, PhD, Associate Professor at the University of Quebec at Montreal, Co-Director of the Montreal Behavioral Medicine Centre, and an expert on motivating patients to stick to their regimens.

"Health is not necessarily the patient's main priority," Lavoie observes. "If you have a 40-year-old woman who smokes and you want to get her to quit, what's likely to be her number-one concern? The answer," she says, "is weight gain. If the conversation doesn't address that obstacle, my prediction is that she's not going to quit."

"Doctors' communication style can positively influence [patient] beliefs and therefore lead to better adherence to recommendations," note the authors of a paper that analyzes the doctor-patient interaction.[30] "However, they are often unable to understand differences in patient preferences regarding information and participation during consultations. They often fail to listen to patients and explore their views on their disease and medication."

Explore their views? Who has the time for that? But doctors' failure to listen may not be just a function of time. Doctors, after all, are also psychological beings, who may at times act irrationally in counterproductive ways.

"The doctor, just as the patient, also experiences feelings during the consultation such as anxiety or anger, which have been shown to decrease the overall satisfaction of both parties with the consultation and also the patient's adherence to recommendations," researchers have discovered.[31]

Conflicting Perspectives on Compliance

When you prescribe drugs for patients with chronic conditions, or advise them to go on a diet, it's natural to assume that because patients come to you as their medical expert, you share the same goal: the patients' long-term health.

But this may not be the case. In fact, doctors and patients tend to have conflicting perspectives on the burden of adhering to the medication and lifestyle regimens that the doctors prescribe. Doctors "want to maximize patients' health outcomes in the future and are less interested in patients' anticipatory feelings in the present," one paper points out. [30] Patients "put more weight on leading an easier life now rather than thinking of the consequences of their future health status."

It might be easier to bridge this gap if the doctor-patient relationship still had the influence it once did, but with many patients switching health plans, and often doctors, on a yearly basis as premiums are raised, the relationship now is often perfunctory. The more patients you are forced to see to pay the bills, the less time you have to explore and address patient barriers to compliance.

Too-brief visits with the doctor and leaving with more questions than answers may be a reason why many patients seek medical advice elsewhere. The prospect of patients visiting healthcare Websites on the Internet (the quality of whose information can be highly variable), rather than trusting you to know what you're doing, may make smoke come out of your ears. But now patients are visiting social networking sites, specifically for patients with chronic diseases, where they compare notes.[32] They discuss their medications, dosages, and adverse events with each other, give each other advice, and often take that advice.

One study found that 55% of patients rely entirely on their physician to make treatment decisions.[33] That means 45% are seeking advice elsewhere. In another study, 68% of patients turned to other sources to validate information received from their doctors.[34] These other sources, needless to say, aren't other physicians.

Even when doctors take the time to explain things to patients, many patients have little or no idea of what the doctors are talking about. Nearly half of all adults in the United States -- 90 million people -- have trouble understanding what the doctor tells them about why they are sick and how to adhere to medication regimens, according to the Institute of
"Each patient, in reality, has his or her own unique barriers, which can vary by disease and medication," a team of RAND researchers concluded. Programs for improving adherence must find a balance between 'customized' interventions and effective programs that work for large groups or classes of patients.

"This is not to say that society needs thousands of different programs for each barrier," the researchers continued, "but it needs programs that can identify these barriers and take the diversity of individuals and barriers into account."

We are not there yet.

Medication Regimens Can Be Too Complicated

It's easy to lose sight of the fact, especially when dashing off prescriptions every 15 minutes, that the drug regimens being prescribed, even though they may be evidence-based, may not be easy for patients to follow even if they wanted to.

In a 2012 paper, Kaiser Permanente's John Steiner calculated how many behaviors per year are required of a hypothetical 67-year-old patient with well-controlled hypertension, diabetes, and hyperlipidemia. It came to more than 3000 behaviors. "And that's a conservative estimate," he says.

Writing in the New York Times, internist Danielle Ofri, MD, Associate Professor of Medicine at New York University School of Medicine, told of a small experiment that she conducted with a group of medical students. They wrote up prescriptions for several common medications: metformin, furosemide, albuterol, lisinopril, and ranitidine. Each student received 2 prescriptions and 2 boxes of Tic Tacs® and was instructed to take the "medicines" for a week.

"When we met for our next session, I asked them how they did, and they all had abashed expressions on their faces," Ofri writes. "Not one was able to take every single pill as directed for 7 days."

Compliance, it turns out, is inversely proportional to the number of times a patient must take medication each day. For medication taken only once daily, the average compliance rate is nearly 80%; for medication that must be taken 4 times a day, the average rate drops to about 50%.

One study found that the average patient who takes a statin for dyslipidemia currently takes a total of 11 medications, makes 5 pharmacy visits over a 3-month period, and synchronizes -- that is, picks up multiple prescriptions at the same time -- half of his or her refills. However, 10% of statin users take 23 or more medications, make 11 or more pharmacy visits to 2 or more pharmacies over 90 days, have 4 or more prescribers, and only synchronize 10% of their refills.

Picture a Medicare patient whose memory may not be what it once was, and who may lack social support to get to the pharmacy regularly, trying to adhere to all of this.

"We're asking patients to adopt obsessive-compulsive behavior," admits internist Edmund Pezalla, MD, MPH, National Medical Director of Pharmacy Policy & Strategy for the health insurer Aetna. "Taking medication every day is hard to do. We're asking people to deal with the same boring situation over and over again. We're not programmed to do that. Machines do that. Humans don't do it very well."

Fragmented Care Is a Culprit

Even if doctors had more time to spend with patients and patients were more willing to take their doctors' advice, the healthcare system creates numerous obstacles to subvert their efforts. A major obstacle is fragmented care.

"In decades past, community-based physicians not only authorized a patient's admission to the hospital, they performed regular hospital rounds, supervised overall patient care, and authorized the patient's discharge," notes a report by the New England Health Policy Institute (NEHI). "In theory, medication management was seamless because the admitting physician, the discharging physician, and the 'receiving' physician in the community were the same individual."

That's not the situation today. Patients with chronic conditions now see primary doctors who in turn refer them to specialists. If they are hospitalized, a hospitalist likely as not will take over their care. Many patients are discharged not to their homes but to long-term acute care hospitals, inpatient rehabilitation hospitals, or skilled nursing facilities, where more doctors will prescribe medications for them.

"Transferring patients from short-term acute care hospitals to post-acute providers increases the number of times
information needs to be passed between providers and increases the opportunity for errors and medication errors in particular," the NEHI report points out. [39]

Other systemic barriers to compliance include lack of access to healthcare, inconvenience in obtaining prescription refills, wide variations in the cost of the same drugs from one health plan to another, and pharmacy policies that limit prescription size and require frequent refills.

Access to Pharmacy Data Is a Problem

Even in Accountable Care Organizations and integrated delivery systems, with resources far beyond those of the average doctor, care teams typically lack access to pharmacy data, such as the rate at which a prescription is filled and refilled by a given patient. [13] If you knew which of your patients weren’t picking up their drugs, you would know who needs help with medication compliance.

"For patients with coexisting conditions who take multiple medications prescribed by multiple physicians, there is a vital need to reconcile the prescribed regimen with what a patient is actually taking and to understand why there is a difference between the two," note David M. Cutler, PhD, and Wendy Everett, ScD, in a 2010 paper. [2] "But optimizing and reconciling medications require substantial investments of time by a skilled healthcare practitioner, as well as electronic data sharing among practitioners -- neither of which is widely available in today's model of healthcare delivery."

Even if time, skill, and electronic data sharing were widely available, the complexity of each patient's barriers, and the ever-shifting nature of those barriers, probably would still thwart many efforts to improve medication compliance.

"Although the multifactorial nature of nonadherence means there will never be a one-size-fits-all solution, interventions ranging from education to elimination of selected copayments to telephone-based counseling have achieved modest improvements in clinical trials," Rosenbaum and Shrank point out. [24] "But even if we had more robust interventions," they write, "we'd lack simple, cost-effective ways of targeting the right intervention to the right patient."

Why Research Hasn't Been More Helpful

Advances in medicine generally stem from peer-reviewed studies that produce statistically compelling, evidence-based data for doing one thing or another. The more studies, the better and more refined the evidence, or so one would think.

This has not, by and large, been the case with compliance. The ocean of data on the subject has stubbornly resisted attempts at synthesis into a statistically compelling, evidence-based, systematized plan or plans of action for overcoming barriers to compliance across a range of patients, drugs, and diseases.

A 2007 Cochrane review of interventions for enhancing medication compliance didn’t mince words: "With the astonishing advances in medical therapeutics during the past two decades, one would think that studies of the nature of non-adherence and the effectiveness of strategies to help patients overcome it would flourish," the authors wrote. [40] "On the contrary, the literature concerning interventions to improve adherence with medications remains surprisingly weak."

"There probably is a set of general principles that might emerge from the literature," suspects Kaiser Permanente's John Steiner, "but they're not intuitively evident because of the way the studies are designed and carried out."

Even the definition of compliance is subject to debate. Is compliance mainly taking one's medications as instructed, a narrow definition adopted by most researchers because it simplifies research to study only one variable at a time, even if it sacrifices environmental complexity? Or should the definition be broader: "the extent to which a person's behavior -- taking medication, following a diet, and/or executing lifestyle changes -- corresponds with the agreed recommendations from a health care provider," as WHO maintains? [25]

Steiner tells of his 93-year-old father, who embodies this definitional dilemma. "He discovered to his great delight that as long as he took his statin, he could eat anything he wanted," Steiner says. "By being adherent with his medication, he didn't need to be adherent with his diet. Those are different adherence behaviors, but in his case, one trumps the other."

"The problem is with the way the scientific literature evolves," Steiner reflects. "It's reductionistic. You want to do a study on adherence with antihypertensive drugs, for example, and you disregard the 6 other drugs that the patient is taking."

"That can make the literature seem fragmented," he says. "We don't tackle the adherence problem at the patient level. We tackle it at the drug or disease level. It's easier to study at that level. Measurements are easier. Costs are lower."
How Much Compliance Is Enough?

The Centers for Medicare & Medicaid Services has introduced uniform standards for compliance outcomes with its 5-star rating system for Medicare Advantage plans. The top rating is awarded to plans that achieve 70%-80% compliance in hyperlipidemia, hypertension, and cholesterol management in their members.[41]

But this raises another niggling issue: From a population-based perspective, how much compliance is enough? Setting optimal compliance rates across the board at 80% is arbitrary and potentially counterproductive, John Steiner believes.

"There's almost no evidence that can allow us to set those sorts of thresholds in a scientific way," he asserts. "For example, for first-generation antiretroviral drugs, studies showed that you needed adherence of 95% or greater to knock out the virus. An 80% adherence threshold would not have been stringent enough for those old drugs.

"The converse is also true. Years ago, when rheumatic fever was common, doctors prescribed penicillin to knock out strep throat, because that triggered rheumatic fever. However, studies showed that you only probably needed to take a third of the doses to knock out all the strep. So for that kind of situation, 30%-40% adherence was probably just fine. If it were 80%, you would increase the risk for side effects, as well as the cost, without increasing the clinical benefit."

"If lower levels of adherence are sufficient to achieve clinical goals, pursuit of higher adherence is wasteful," Steiner wrote in the *Annals of Internal Medicine* in 2012,[36] "and if higher levels are required, even these adherence targets will not suffice."

**Moderate Progress on Compliance Issues**

Despite a tsunami of unanswered questions, this is not to suggest that the enormous amount of research that has gone into compliance has largely been a waste of time. On the contrary, it has produced some valuable insights. The second article in this series looks at the healthcare industry's initiatives to improve compliance on the basis of this research.

With more than 40,000 peer-reviewed studies on the subject conducted over several decades,[13] you'd think we'd at least be at Compliance 2.0 by now in the state of our knowledge. In reality, it's more like Compliance 1.5. We are not on the verge of solving this immensely complex problem. The outlines of what is, at best, a partial solution are only just starting to emerge.

Despite moderate progress, "the heterogeneity in how adherence is assessed, measured, and defined is a major limitation to the data on barriers of adherence," investigators at RAND concluded in 2009.[15]

In 2014, that continues to be the case.

**References**


Medscape Business of Medicine © 2014 WebMD, LLC

Cite this article: Why Are So Many Patients Noncompliant? Medscape. Jan 16, 2014.