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DIGITAL AIDS TO ADHERENCE

New Tools Can Help But They Can't Replace a Physician-Patient Relationship Built on Trust

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Experts say digital tools might be useful when people want help taking their meds, but the aids can only supplement a physician-patient relationship built on trust

By Delia O'Hara

AS MANY as 100 different factors may go into determining whether patients take their drugs as prescribed. How many of those obstacles to adherence can be overcome with mHealth, mobile-based or mobile-enhanced healthcare technology, and other digital tools?

This is a good time to ask. The move to value-based healthcare, which incentivizes good outcomes, is creating new urgency around adherence that coincides with a proliferation of digital tools becoming available to consumers and healthcare systems.

In addition, the Centers for Medicare and Medicaid Services is poised to begin reimbursing next year for remote monitoring of patients, the Food and Drug Administration has declared its intention to "reimagine" its oversight role relative to digital health products, and the *21st Century Cures Act of 2016* will loosen regulation for some medical innovations to spur development.

A Shiny New Toy

But experts in the field of adherence caution providers against getting their hopes up that digital aids will solve the problem of non-adherence anytime soon.

"I'm afraid it's the new shiny toy syndrome," says Andrew Boyd, MD, associate chief health information officer for innovation and research at the University of Illinois at Chicago. Digital technology may eventually provide important tools for appropriate settings, but Dr. Boyd says he wants to see more trials and studies done to prove their usefulness. "We've tried lots and lots of things" for improving medication adherence, he says.

Some of the most successful interventions (up to 33% increase in adherence, according to one study) involve regular follow-ups by trained healthcare providers, but "that gets very expensive. Finding low-cost, effective measures is challenging," Dr. Boyd says.

Adherence is "the degree to which a person's behavior corresponds with the agreed recommendations from a health care provider," according to the World Health Organization. American doctors write nearly four billion prescriptions every year, but at least 20% of those are never filled. Half of drugs picked up from the pharmacy are taken incorrectly in terms of timing, frequency or dosage—or patients just stop taking them. These lapses cause 125,000 preventable deaths every year, not to mention incalculable damage to surviving patients, and cost the American healthcare system up to $300 billion.

But even the most effective interventions have not moved the needle much on adherence or treatment outcomes. That's one reason why digital systems are being developed to help.

Bottle Caps that Beep and Blink

Pillsy, for example, a HIPAA-compliant smart pill system (the bottle cap is the smart part) reports to a mobile phone application (app) when a patient opens the bottle, and can help a patient build up a robust medication routine, says Jeff LeBrun, co-founder and chief executive officer of Seattle-based Pillsy Inc. Forgetting to take pills is the most frequently reported reason for non-adherence, and research has shown that a new habit can take an average of about 66 days to take hold.

"That's where we can help," says LeBrun, adding that remote coaching can enhance the benefits of the device. The Pillsy Smart Cap beeps and blinks if it isn't opened within the set dosing period; alerts can also go to a user's smartphone. A consumer can buy the basic system on Amazon for $44.95 (smart phone and Bluetooth are extra), but LeBrun says Pillsy would like to deal with large provider systems rather than individual consumers.

Numerous studies have shown that digital reminders can help with adherence in various settings, LeBrun notes. However, a 2017 *JAMA* report on the REMIND trial, which studied 53,480 patients, showed that three low-cost reminder systems, including a digital timer bottle-cap, resulted in roughly the same shift toward optimal adherence the control group experienced—about 15%.

Proteus Discover does simple reminder systems one better, adding a sensor to the pill that activates in the stomach, signaling its arrival to a small wearable patch, a phone app and, in some cases, a provider portal. Rush University Medical Center was the first healthcare provider in Illinois to offer Proteus Discover, in 2017, to help patients manage hypertension.

Proteus and the drug manufacturer Otsuka American Pharmaceutical have joined forces on Abilify MyCite, a similar drug-delivery-plus-alert system for certain mental health conditions, including schizophrenia, approved by the FDA two years ago. It still is not widely available, and its ability to improve adherence has not been

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LEFT: Andrew Boyd, MD, is the associate chief health information officer for innovation and research at the University of Illinois at Chicago. RIGHT: Jeff LeBrun is the co-founder and chief exectuive officer of Seattle-based software maker Pillsy Inc.

"A lot of people don't believe they have hypertension. Or maybe they believe it, but they want to deny it."

demonstrated. A 30-day supply of Abilify MyCite wholesales for $1,650.

Electronic health records (EHRs) have long been thought to have potential for helping improve adherence, especially for patients who take more than one type of medicine. More complex drug regimens—more pills, possibly more doses, more side effects, more trips to the pharmacy—are associated with lower levels of adherence. One in four Americans has multiple chronic conditions.

In some settings—and there are still plenty of limitations due to incomplete connectivity—EHRs can now allow providers to see some pharmacy fill data, a big improvement over patient self-reporting, said Stephen Persell, MD, MPH, a health services researcher and internist at Northwestern Medicine in Chicago.

However, EHRs don't tell doctors what patients are doing with the pills at home, and the data creates problems of its own, Dr. Persell says. "Who is going to respond to that information clinically, even if it comes to us?" Dr. Persell says. "Whose workflow is it going to fit into?" in a clinical staff that's already working at capacity.

Making Adherence Fun

One intriguing aspect of some digital adherence aids is "gamification," that is, the ability to make taking drugs as prescribed more engaging and enjoyable. The term comes from the video-game design world.

Gamification will be a feature, going forward, of My Personal Health Guide, now in development at the University of Illinois at Chicago to improve adherence and retention in care among gay or bisexual black men with HIV, who accounted for more than one-quarter of new HIV diagnoses in 2017.

HIV, a lethal disease that can be "silent" for years, can be controlled by drugs; however, adherence is critical to maintaining health. HIV-positive black men who have sex with men, as a group, have low levels of viral suppression. Ideally, drugs for HIV can reduce the virus in the body to undetectable levels, a major treatment goal both for the individual, and for stopping the spread of HIV.

Most of these men are young. Mark Dworkin, MD, associate director of epidemiology in UIC's School of Public Health, who co-developed the app, hopes users will want to explore it more with gamification. "People enjoy winning something, even if it's virtual," he says.

The UIC team obtained a five-year $3.5 million grant from the National Institutes of Health after a pilot version of My Personal Health Guide showed promise. Features of the app, which takes advantage of the smartphone's ubiquity, include the private delivery of information, reminders, prompts and supportive messages, plus an avatar that evokes an African American male healthcare provider. (A white nurse avatar is also in the works; patients wanted the choice.)

Dr. Dworkin, principal investigator in the study, worked with members of UIC's department of computer science to develop the app. One of its goals is to increase health literacy among users. "If they knew things that they don't currently know, they might make different decisions," Dr. Dworkin

LEFT: Mark Dworkin, MD, is associate director of epidemiology in UIC's School of Public Health RIGHT: Avatar of an African American healthcare provider, which is part of an app co-developed by UIC.

says. "The app could be useful to anyone else with HIV who struggles with adherence." The app also aims to increase motivation, which is where the gamification comes in. Positive motivational language is "peppered throughout the app" as well, Dr. Dworkin says.

My Personal Health Guide is one of thousands of apps that promise to help with adherence, but it is rare in terms of the science that has gone into its development. One 2018 study of 805 adherence apps found that only about 10% were developed with input from anyone trained in medicine or pharmaceuticals, and that less than 1% of the apps had any evidence base for effectiveness.

Patient Centered Conversations

Experts in adherence say digital tools might be useful when people want help taking their meds, but adherence is rarely that simple. "Taking medication for a chronic condition is as complicated a behavior as anyone can ask someone to do," says Ira Wilson, MD, a researcher in adherence, chairman of health services, policy and practice, in the public health program at Brown University in Providence, Rhode Island. "A lot of people don't believe they have hypertension. Or maybe they believe it, but they want to deny it," Dr. Wilson says. "There is nothing digital, ever, that is going to be able to solve this problem. Only one human being talking with another human being can engage with this issue."

Three things are necessary before patients will adhere to their medication regimens, Dr. Wilson says:

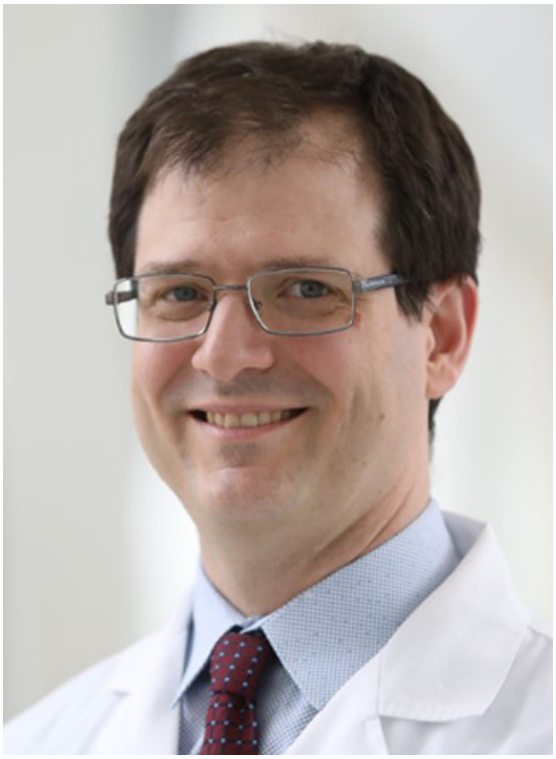
- The patient has to agree he or she has the condition.
- The patient has to be convinced this is the right treatment now for the condition in her case. Planning to start exercising to bring down one's cholesterol levels is an example of a patient with her own ideas about treatment. Choosing Chinese herb therapy over the prescribed drug regimen is another.
- The patient has to be able to take the therapy—to afford it, remember to take it, handle the logistics, bear the side effects, and manage all the other considerations that go into committing to, and following through on, a particular treatment.

"Digital aids can only help with certain aspects of that third phase, with people who want to take the drug but need help with oversight," Dr. Wilson says. With every other aspect of adherence, only a patient-centered conversation with a provider will be effective, he says. "These conversations take a long time and they can change over time" as the disease progresses, or upsetting symptoms go away, or new drugs are added for new co-morbidities, and so on. "Tools can only supplement a trusting relationship."

But there aren't enough providers out there to give that kind of attention to every patient. When Dr. Wilson gets new patients—he is an internist at the Veterans Affairs Medical Center in Providence—they wait three months or more to see him for the first time. And provider shortages are only one aspect of our healthcare system that reliably and deeply cut into adherence, Dr. Wilson notes. Another is that "the cost of medication is insanely high and rising," even for generics, he says.

"People enjoy winning something, even if it's virtual."

LEFT: Stephen Persell, MD, MPH, is a health services researcher and internist at Northwestern Medicine in Chicago. RIGHT: Ira Wilson, MD, is a researcher in adherence and chairman of health services, policy and practice, in the public health program at Brown University in Providence, Rhode Island.



Will Adherence Give Way to Compliance?

And now the healthcare system is gearing up to incentivize providers for good outcomes, with improved ways of documenting whether patients have been taking their medications. UIC's Dr. Boyd worries that there will be pressure to replace "adherence," in which the patient owns taking his medicine as prescribed, with the old idea of "compliance," the expectation of a more passive acceptance of providers' recommendations handed down from on high; or to try compelling patients to take their medications—say, an insurance company not paying for treatment if the patient did not take drugs as prescribed, or not approving a patient's return to work unless she could show she was regularly taking her medication.

MHealth makes possible "a new level of intrusion, a new level of monitoring that is not common in the current doctor-patient relationship—and new companies, new parties that have access to that data," Dr. Boyd says.

Ultimately, all that could damage the optimal doctor-relationship, he says. Human nature being what it is, it could also motivate patients to develop ingenious ways to cheat, like the workers who put their Fitbits on pets to log additional steps for workplace fitness challenges. That's not the direction Dr. Boyd wants to see medicine take. "As a doctor, I want the best for my patients," Dr. Boyd says. "But at the end of the day, patients do get a choice."

When Technology Helps

MHEALTH CAN help people who want to take their medications but have trouble with the logistics, says adherence researcher Ira Wilson, MD, but only a patient-centered conversation with a provider will be effective with other causes of non-adherence.

Some reasons for unintentional non-adherence include:

- Forgetting to take medication
- Running out of the medication
- Poor understanding of medication or dosing
- Inadequate health literacy
- Inability to pay

Some reasons for intentional non-adherence include:

- Rejection of the diagnosis
- Denial about the diagnosis
- Rejection of the treatment
- Commitment to an alternative treatment
- Deciding to stop or modify the treatment, perhaps because symptoms have gone away
- Unwillingness to pay for a drug that could be afforded
- Unwillingness to endure side effects, whether they are mild, moderate or severe