HRSA CARE ACTION

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Identifying Emotional Barriers

Selecting a Regimen

Best Practices

Trust Leads to Success

PREPARING PEOPLE FOR TREATMENT SUCCESS

Starting treatment was a scary time for me. I'm a 'fast progressor,' which means that if I'm not on medication my HIV disease advances very quickly. So it was important that I get on medication as soon as I was emotionally ready. But I was so young—only 22 in late 2002 when I was first diagnosed—and I was very worried about the potential for horrible side effects such as disfigurement [which were more common at that time]. I selected a regimen mostly because it seemed least likely to cause severe effects. I actually wound up becoming manic [because of that medication], but I forced myself to stay on it, almost to the point that I was coming apart at the seams. I was just so afraid of having to take a different regimen. My doctors at the time were awesome; they were young too, so they really related to me on that level. But I still didn't want to open up and have an honest conversation about where I was at.

—Michael Hager, HIV patient

Beginning antiretroviral therapy (ART) can be a complicated process for many HIV-positive people. With new guidelines calling for starting medication therapy as early as possible, in the absence of a vaccine or cure for HIV, many more patients likely will be navigating that process over the coming years. At the same time, the renewed focus on testing as a result of the National HIV/AIDS Strategy and the increase in access to care because of the Affordable Care Act (ACA) will mean that many more people will learn their serostatus and begin care. Thus, the need

DID YOU KNOW?

- According to results from one cohort study, drug-resistant mutations can occur even among patients who report very high but not perfect adherence to antiretroviral therapy.[1]
- In a global pooled sample of adults taking HIV medications, only 62 percent of people achieved adherence of at least 90 percent of medication doses.[2]

U.S. Department of Health and Human Services
Health Resources and Services Administration

DIRECTOR'S NOTES

The decision to begin taking HIV medications requires careful consideration. While antiretroviral therapy (ART) can improve health outcomes dramatically for HIV-positive people, medication must be taken daily without interruption. People living with HIV/AIDS (PLWHA) who begin ART must understand that if they fail to take their medications on a regular basis for the rest of their lives, they face an increased risk of HIV progression, drug resistance, and infectiousness.

That's why it's so important for HIV care providers to support patients in making what is essentially a lifelong commitment. Whether patients are beginning ART for the first time or restarting treatment after a lapse, providers must thoroughly assess their readiness and involve them in the decision-making. What's more, the entire care team must collaborate effectively to identify and overcome any barriers to treatment that patients may be facing.

In this *HRSA CAREAction* newsletter, you'll find strategies and tactics that are helping providers accomplish these tasks for the varied populations they serve. Selecting the right drug regimen for each individual is one of the first steps, and this newsletter identifies factors that go into that decision. It also discusses practical and proven steps that providers can take to improve patients' adherence.

With thorough guidance and support, more patients can achieve a successful treatment outcome, living longer and healthier lives. And that's something we all want!

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Cover: Man checking medications.
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to prepare people for treatment and to provide support for them throughout treatment becomes increasingly urgent.

For many years, people living with HIV/AIDS (PWLHA) typically did not confront the choice to begin ART until their disease had progressed to a later stage, which meant that their immune systems had already been compromised. At that point, the benefits of beginning therapy often clearly outweighed the risk and inconvenience of taking medications. Today, the U.S. Department of Health and Human Services (HHS) guidelines—also known as the Public Health Service guidelines—recommend encouraging nearly everyone with HIV to take a combination of three or more medications from two different classes.[3]

Evidence is mounting that early initiation of treatment can both improve health outcomes for PLWHA and significantly reduce the risk of transmission between serodiscordant couples.[4,5] Indeed, results from a randomized clinical trial showed that achieving viral suppression through the early initiation of ART reduces transmission of HIV to an uninfected sex partner by 96 percent.[6]

Although these medications save lives, the decision to begin ART is still one that requires careful consideration. That's because patients must commit to taking a medication regimen daily—for the rest of their lives—without interruptions and despite the potential for side effects.

If patients fail to take their medications on a regular basis, the potential results can be progression of HIV disease, including opportunistic infections, drug resistance, and/or increased infectiousness. It is vitally important, therefore, that providers find ways to help patients make that lifelong commitment. Patients also must understand that the first regimen selected typically offers them the best chance of long-term treatment success and prevention of drug resistance.[3]

To gain that level of commitment, providers must involve patients in decision-making and customize a treatment plan to meet their needs.[7] The process involves identifying any emotional concerns that a patient might have, taking time to establish a trusting relationship, making a thorough assessment of readiness for treatment, selecting the best regimen, and planning for adherence

"The idea of taking medications every day for the rest of your life is just a hard concept to wrap your head around."

support. Each step is critically important for maximizing the likelihood of treatment success.

IDENTIFYING EMOTIONAL BARRIERS

As a first step, providers must consider the emotional impact of diagnosis and the beginning of medication therapy. After all, receiving an HIV diagnosis can cause great emotional distress, and patients may not make a decision to begin medication therapy easily. Providers need to enable patients to talk about their feelings and provide them with links to counseling and support groups as needed.

Even patients who have known their serostatus for a while may struggle with conflicting thoughts that can affect their willingness to adhere to a medication regimen. For some patients, taking medications can be a negative daily reminder of their illness. Someone who otherwise feels healthy may simply be reluctant to take medications—especially if those drugs cause side effects.

"The idea of taking medications every day for the rest of your life is just a hard concept to wrap your head around," one HIV-positive person told regulators during a public meeting on HIV treatments held by the U.S. Food and Drug Administration (FDA) on June 14, 2013. "It's impossible to take anything *every* day," agreed Matt Sharp, an independent HIV advocate who attended the meeting and is HIV-positive.

Still others may worry about the long-term impact of taking ART and are distrustful of the medical community. One patient told FDA administrators at the public meeting that the regimens he has been on over the years have caused a few irreversible side effects. "It's maybe the lesser of two evils, but nobody told me about the potential [for side effects] at the beginning," he said.

Of course, fear is a major emotion for many PLWHA, especially those who are newly diagnosed. They also may be in denial about their HIV diagnosis because they have internalized HIV stigma, which may lead to unwillingness to take medications. In addition, if they are not disclosing their status to partners, family members, and others who need to know or who could support their adherence, they may struggle with maintaining privacy while taking daily medications.

"Many of our clients share rooms because of poverty, so they don't have space to hide medications from others," explains Eduardo Antonio, a treatment health educator for the Mission Neighborhood Health Center (MNHC) in San Francisco. MNHC, a Federally Qualified Health Center, has been offering HIV services since 1989 as Clínica Esperanza; and its primary focus is serving HIV-positive individuals in the Latino community.

TIME AND TRUST ARE KEY

It's important to engage with patients about their emotions from the very beginning. To establish trust, Dr. James Dwyer, medical director for NorthPoint Medical in Ft. Lauderdale, FL, shares something that a mentor taught him to say long ago. "I tell patients that 'as long as you're a patient of mine, you'll never go through this disease alone.'"

But "establishing a relationship in which patients feel comfortable opening up takes time," says Dr. Ann Khalsa, medical director for the McDowell Healthcare Center in Phoenix, AZ. For many providers, time is in short supply. The McDowell center currently serves about 3,000 HIV/AIDS patients with 13 full-time staff, including 2 physicians, 2 nurse practitioners, and a few part-time case managers and patient educators. "Right now, we are continuing to add 50 to 75 new patients every month," Dr. Khalsa adds. "We've been swamped."

Despite the high caseload, Dr. Khalsa has remained steadfast in her advocacy for extended appointments of at least 30 minutes for PLWHA. The first visit is especially important, according to HIV advocate and patient Matt Sharp. "In an era where we are trying to get people to start treatment as early as they can, physicians need to carve out that time no matter what," says Sharp.

HRSA recognizes the time pressures that providers are facing. The agency is committed to improving the supply and distribution of health workers to ensure access to needed care. In addition, the ACA established the National Center for Health Workforce Analysis Center (http://bhpr.hrsa.gov/healthworkforce/) to provide research and resources that support capacity decisions. Providers also can turn to the April 2010 issue of the HRSA CAREAction newsletter on *Workforce Capacity in HIV* (http://hab.hrsa.gov/newspublications/careaction newsletter/april2010.pdf) for additional insight.

ASSESSING READINESS

In addition to helping patients work through emotional issues, providers must assess lifestyle and other factors that can affect patients' readiness for ART.

For example, if a patient has an unpredictable schedule or travels a lot, those factors can affect their ability to take medication consistently. Sharp emphasizes that PLWHA need to find a dosing regimen that fits into their lives. "I am a person who stays up late at night and I work from home," he explains. "So I take my doses at noon and midnight, which is really easy to remember for me."

When patients lack a support system, such as family or a network of friends, it is important for providers to direct those patients to appropriate supportive resources. For example, most of MNHC's clients are Latino immigrants for whom separation from family or lack of cultural support around their sexual orientation or HIV status often results in feelings of isolation. MNHC providers try to alleviate these feelings by building a sense of community within the HIV clinic through mixed-gender support groups and a drop-in arts and crafts group.

Comorbidities, such as depression or other mental illness, as well as active substance abuse, can also affect readiness to begin treatment—as can such problems as homelessness or unstable living conditions. After all, a person who is homeless who has to take medications with food may have trouble obtaining regular meals, and a person suffering from depression or a substance abuse disorder may have trouble following a consistent medication regimen. Treatment for behavioral health problems such as depression and substance abuse can remove these barriers to care.

Low health literacy and language barriers also can limit a patient's understanding about the importance of adherence. Taking time to assess these issues can alert providers to the need for extra education or translation services.

Finally, identifying patients' financial circumstances can help determine whether they need help paying for treatment and ensuring a steady supply of medication. "Financial access is a big barrier for many people," says Dr. Joanna Eveland, medical director of HIV services at MNHC. "They frequently don't seek treatment because they just assume that they won't be able to afford it."

Screening Protocols and Tools

Benefits counselors and patient educators are often tasked with assessing factors, such as literacy levels, language barriers, and financial needs. Case managers and behavioral counselors frequently perform a thorough psychosocial needs assessment in preparation for the initial visit with a clinician.

Many providers use written questionnaires to assess relevant lifestyle factors, providing assistance to overcome language and literacy barriers as needed. MNHC uses a patient acuity scale that was originally developed by Whitman-Walker Health in the District of Columbia. "We individualized it for our population," explains Dr. Eveland. The scale requires team members to give patients a numeric value for 19 areas of psychosocial functioning. Based on the results, patients are assigned to a care level that ranges from adherence support to intensive management.

Still, there is no substitute for providers' experience. "All of our providers [at McDowell] have been seeing HIV/AIDS patients for more than 20 years," says Dr. Khalsa. "When patients come in for a provider visit, we are all focused on assessing their readiness."

SELECTING A REGIMEN

HIV treatments have come such a long way that selecting a drug regimen is less about overall efficacy than about finding the best option for each individual. That's why it's so important for providers to work together with patients to identify what may work best for them. Factors to consider include the following:

- **Side effects.** For patients, a common barrier to optimal adherence is the willingness and ability to tolerate side effects. Providers can discuss coping strategies in advance, and they can direct patients to community pharmacists for valuable advice on coping with minor side effects. Pharmacist Kirsten Balano is an assistant professor of pharmacy at University of California, San Francisco (UCSF), a staff member at Vista Family Health Center in Santa Rosa, and a clinical faculty member of the San Francisco Area AIDS Education and Training Center. She says that pharmacists can recommend various over-the-counter (OTC), herbal, or even nutritional remedies that may be helpful for coping with minor side effects; they'll also recognize when a side effect is serious enough to require a physician's attention.
- **Dosing schedules and pill counts.** Common sense suggests that people will adhere better to less complicated regimens, and research generally confirms

this assumption. For example, some studies have compared identical ART components given once or twice daily and found that once-daily doses result in both improved adherence and "non-inferior" viral suppression rates.[8,9] The number of pills is important, too. Among regimens of equal efficacy and safety, fixed-dose combinations (in which multiple drugs are combined into a single pill) are associated with higher patient satisfaction and thus better adherence.[10,11]

- **Adverse reactions and interactions.** Providers should assess the need for treatment of any comorbidities and the potential for drug/drug interactions. They will also need to identify any OTC, herbal, or vitamin supplements patients may be taking to identify the potential for adverse reactions and interactions.
- **Pregnancy.** If patients are pregnant or planning to become pregnant, they will still need to take HIV medications.[12] Providers will need to review or reassess medical status, however, to select the regimen best-suited for each individual's needs. Factors that providers will need to consider include the potential for different regimens to prevent mother-to-child transmission, changes in how the body absorbs medications during pregnancy, and the potential for some HIV medications to cause birth defects or other harm to the baby.[12] For more information, see the HHS perinatal guidelines available at http://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0 and the fact sheet "Anti-HIV Medications for Use in Pregnancy," available at http://aidsinfo.nih.gov/contentfiles/DrugRegimensPregnantWomen_FS_en.pdf.
- **Other situations.** Poor oral health and nutrition can also affect a patient's ability to swallow or absorb medications. Even the patient's age or life skills may play a role. For example, one MNHC patient had never learned to swallow pills, so the care team spent a considerable amount of time developing a combination of liquids and the smallest pills available.

BEST PRACTICES IN ADHERENCE SUPPORT

The first step in providing adherence support is empowering patients. "You [as a provider] are here to support them and provide information, but they are free to make the decisions that they deem best," explains Dr. Dwyer.

In fact, the more providers can actively engage PLWHA in their own treatment decisions, the higher the chances of success. Key characteristics of "patient-centered care" are that patients are in charge of their care and that clinicians and patients work together to adhere to patients' treatment choices. In one example of a patient-centered adherence protocol, the treatment process is managed through oral and written agreements (available at https://careacttarget.org/sites/default/files/file-upload/resources/01-Adherence-Protocol.pdf).

STRATEGIES FOR IMPROVING ADHERENCE TO ANTIRETROVIRAL THERAPY

- Use a multidisciplinary approach.
- Establish a trusting relationship with the patient.
- Assess readiness to start antiretroviral therapy (ART).
- Involve the patient in selecting a medication regimen.
- Identify potential barriers to adherence prior to starting ART.
- Provide resources (e.g., mental health and substance abuse treatment referrals and assistance in obtaining prescription drug coverage) as needed.
- Assess the potential for and prepare to treat adverse effects.
- Assess adherence at every clinic visit.
- Use educational aids, including pictures, pill boxes, and calendars.
- Identify the type of nonadherence and the reasons for nonadherence.
- Simplify regimens if possible.
- Implement automated refills.
- Send reminders through calls or text messages.

Adapted from U.S. Department of Health and Human Services. *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents;* Table 12. February 2013.

Providers can also take many practical steps to improve patients' adherence success rates. Some of those tactics are discussed in the sidebar, **Strategies for Improving Adherence to Antiretroviral Therapy,** on page 5.

Basic Tools and Tactics

Providers today are employing all kinds of hands-on tools—including prepackaged pill organizers, pill boxes, keyring pill containers, timers, and medication planners/calendars—to help patients remember to take their medications. Even stickers that indicate the number of pills to take or when to take them (e.g., using pictures of the sun and moon to indicate morning and evening dosages) are useful for helping patients overcome language or literacy barriers.

The bottom line is that these basic tools and strategies work for many kinds of patients. One study showed that the use of pill boxes was associated with increased adherence and viral suppression among both general and homeless populations.[13]

The use of electronic tools, such as text messages, smartphone applications, and patient Web portals, also results in significant adherence benefits.[14] (See sidebar, **Electronic Support: 'There's An App for That'.**)

Working With Pharmacists

Pharmacists can play an important role in improving adherence. As discussed previously, they can provide guidance to patients regarding managing minor side effects. Pharmacists also can alert physicians if prescriptions remain unfilled.

In addition, onsite pharmacists can assist with regimen selection. They often provide guidance as to what regimens might be most efficacious and durable for a patient given his or her lifestyle, and what regimens might provide protection from adverse drug interactions and drug resistance.

Many pharmacists can provide assistance to providers by conducting medication therapy reviews, which involve analyzing all current medications that patients are taking.[16] Such a comprehensive evaluation can be invaluable by helping to identify potentially harmful interactions between HIV medications and other prescription drugs or OTC supplements.

ELECTRONIC SUPPORT: 'THERE'S AN APP FOR THAT'

Electronic tools that support adherence are fast becoming "go to" resources for providers and patients. From text messages to smartphone applications, new tools are being developed to remind patients to take medications and track adherence results.

The U.S. Centers for Disease Control and Prevention (CDC) will soon be releasing a new mobile application to support adherence to HIV medications. In addition to providing dose and refill reminders, the new app, called "Every Dose Every Day," will also track medical visits and lab results. Some additional features will include enabling users to designate a "buddy," so a message can be sent if a user misses a dose, and providing a "Tip for the Day." The app will also allow users to enter information about other non-HIV health care providers, as well as any non-HIV medications or supplements they may be taking. And it will allow users to upload a photo of something or someone that inspires them to maintain adherence.

All information will be completely private, residing solely on the user's phone. The free app will be available for both Google Android and Apple iOS platforms and can be downloaded at the Google Play or iTunes stores or through the EffectiveInterventions.org Web site.

Many other free or low-cost adherence applications, that help patients adhere to HIV and other medications, are available. A list of 11 free applications was published in the June 2013 issue of *Pharmacy Today* at www.pharmacist.com/pharmacy-today-archives-2013.[15]

The number of people in the United States with access to smartphones is increasing dramatically each year. It makes sense to identify ways for patients to use these tools to improve adherence to treatment.

Note: References to specific smartphone applications are provided as examples and do not denote endorsement by the Federal government.

Studies show that patient education and counseling are generally effective at improving adherence.

According to UCSF's Balano, three common problem areas are heartburn medications, the supplement St. John's wort, and certain prescription cholesterol medications. Balano says that the least expensive statin medications, which most insurance companies prefer, can be contraindicated when a patient is taking HIV medications. "A provider might write a prescription for the preferred statin for someone on an HIV regimen, but the claim might get denied in the pharmacy," she explains.

Finally, community pharmacists frequently have considerable experience working with insurance companies and other payers to ensure consistent access to various therapies. "Although they don't always get paid to provide this kind of support, pharmacists often help with complex billing and access issues," says Balano.

Health Education and Peer Support Interventions

Studies show that patient education and counseling are generally effective at improving adherence.[17] Thus, many providers offer these services in-house or provide links to community services as a best practice.

At MNHC, a meeting with the health educator is part of the intake protocol for every new patient. "Part of what I do at the beginning is talk about the progression of HIV," says patient educator Antonio of MNHC. "I use visual materials to show patients how HIV reproduces in the cells, so by the time they see the doctor, they already understand what their labs mean and are getting ready to think about medication."

At McDowell, new patients always visit with a behavioral counselor who performs a thorough needs assessment before the first physician appointment. "If someone needs followup, we'll either get them back in for behavioral counseling or with the registered nurse for adherence monitoring," says Dr. Khalsa.

At the heart of patient education and counseling is communicating a defined message about why it's so important to take the medications. "What worked for me," says Sharp, "was my clear understanding that you had to take to the medications to keep the virus under control . . . period. It's so important for providers to communicate a simple, definite message about that."

Peers may be in the best position to reinforce that kind of messaging. Dr. Dwyer of NorthPoint Medical says that hearing from other patients who have been successful at medication therapy can be a powerful tool. "When patients speak with peers, they learn that they are not alone. Their life circumstances may be different and how they acquired HIV may be different, but everyone has this commonality," he explains.

Meeting and interacting with other PWLHA who are leading healthy, productive lives also increases self-efficacy. The idea is that peers can motivate attitudinal and behavioral change.[18] That's because when people believe that they can change their behaviors, they are more likely to do so; successful peers are uniquely qualified to provide that kind of positive example.[19]

Case Management to Facilitate Adherence

The reality is that when patients are struggling with psychosocial barriers—such as lack of stable housing and transportation, substance abuse and mental health disorders, and food insecurity—education, counseling, or peer support may not be enough to maintain adherence to a medication regimen. Providing referrals to appropriate support services through case management is therefore vitally important.

One observational study in the United States showed that case management to address food insecurity, housing, and transportation needs was associated with improved adherence and CD4+ cell counts in marginally housed populations.[20] Another study showed that intensive case management for adolescents and young adults—focused on increasing feelings of personal empowerment and improving support networks—was highly effective at improving appointment adherence.[21]

In addition, anecdotal evidence supports the idea that offering in-house case management services is ideal. "We found that it was a significant barrier to refer people out to other agencies. Onsite and close communication with case managers has made a big difference," says Dr. Eveland of MNHC.

Service-Delivery Interventions

Key populations often require a high degree of service-delivery intervention. Many providers stress that the most successful interventions are tailored to individual needs.

"It's about working together with the client to see what they need," says Antonio. "I will keep medications for them. I will call them if needed. I will set up an alarm

ONLINE RESOURCES

Connecting to Care: Addressing Unmet Need in HIV, Adherence Protocol
https://careacttarget.org/library/adherence-protocol

Guide for HIV/AIDS Clinical Care, Adherence
http://aidsetc.org/aidsetc?page=cg-406_adherence

Guidelines for the Use of Antiretroviral Agents in HIV–1-infected Adults and Adolescents
http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0

Prevention With Persons (PWP) With HIV, Initiation of and Adherence to Treatment as Prevention
http://cdc.gov/hiv/prevention/programs/pwp/art.html

for them on their phone or enroll them in a free program that sends automatic text messages . . . whatever they need."

Antonio is even prepared, if necessary, to hand-deliver medication for homeless or homebound patients. One homeless patient has been virally suppressed for a year because Antonio secured the man's permission in advance to find him and bring his medicine to him if he misses an appointment. Similar interventions have been effective with MNHC's patients who are active substance users.

Enrollment Assistance

The inability to access a steady, affordable supply of medication presents a large adherence barrier for many patients. For this reason, HIV care providers frequently offer enrollment assistance for insurance benefits or financial support programs such as the AIDS Drug Assistance Program (ADAP).

According to Patrick Byers, a medication assistance program coordinator in Louisiana, many people do not even realize that financial support is available. "They will go to the pharmacy and then come to me and say, 'I just tried to get this filled and it was $1,800,'" he explains. "They don't know that we can help them find other avenues to get their medicines—and get them at a cheaper price or free if we can."

For patients who are not eligible for financial support or who end up on an ADAP waiting list, most HIV pharmaceutical companies will provide immediate vouchers or application-based patient assistance. In 2012, to simplify the process of accessing antiretroviral medications, HHS—in collaboration with seven pharmaceutical companies, the National Alliance of State and Territorial AIDS Directors, and various community stakeholders—developed a common application for pharmaceutical company assistance programs. For more information, please go to http://www.hab.hrsa.gov/patientassistance/index.html.

Patients often require help, however, in obtaining and maintaining pharmacy benefits. Providing documentation and renewing their enrollment is a challenge for many patients—particularly those with addiction, language barriers, and mental illness, or those who are marginally housed. This is where Byers and other Ryan White providers like him frequently step in and provide necessary support.

TRUST LEADS TO SUCCESS

Preparing people for treatment starts with building a trusting relationship. Providers need to put aside their own assumptions and biases, and work with each person wherever he or she is. Patients, for their part, need to give doctors the benefit of the doubt and be active participants in their care.

"Patients need to know that you are going to be there for them, but that you're not going to take away their decisionmaking ability or their individuality," says Dr. Dwyer. "If you can do that and earn their trust, you're golden."

REFERENCES

[1] Health Resources and Services Administration, HIV/AIDS Bureau. Guide for HIV/AIDS clinical care. June 2012. Available at: http://aidsetc.org/aidsetc?page=cg-406_adherence. Accessed July 11, 2013.

[2] Ortego C, Huedo-Medina TB, Llorca J, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. *AIDS Behav*. 2011;15:1381–96. doi: 10.1007/s10461-011-9942-x.

[3] U.S. Department of Health and Human Services (HHS). Guidelines for the use of antiretroviral agents in HIV–1-infected adults and adolescents. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Accessed August 1, 2013.

[4] Evans D. HIV test and treat: challenges to overcome. March 10, 2011. Available at: www.aidsmeds.com/articles/hiv_test_treat_2581_20054.shtml.

[5] Severe P, Juste MA, Ambroise A, et al. Early versus standard antiretroviral therapy for HIV-infected adults in Haiti. *N Engl J Med*. 2010;363:257–265. doi: 10.1056/NEJMoa0910370.

[6] HIV Prevention Trials Network. HPTN 052: Initiation of antiretroviral therapy (ART) prevents the sexual transmission of HIV in serodiscordant couples [fact sheet]. July 2011. Available at: http://www.hptn.org/web%20documents/HPTN052/HPTN%20Factsheet_InitiationART4Prevention.pdf. Accessed July 11, 2013.

[7] Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009;49(4):1335–1374. doi: 10.1002/hep.22759.

[8] Flexner C, Tierney C, Gross R, et al; ACTG A5073 Study Team. Comparison of once-daily versus twice-daily combination antiretroviral therapy in treatment-naïve patients: results of AIDS clinical trials group (ACTG) A5073, a 48-week randomized controlled trial. *Clin Infect Dis*. 2010;50:1041–52. doi: 10.1086/651118.

[9] Molina JM, Podsadecki TJ, Johnson MA, et al. A lopinavir/ritonavir-based once-daily regimen results in better compliance and is non-inferior to a twice-daily regimen through 96 weeks. *AIDS Res Hum Retroviruses*. 2007;23:1505–14. doi: org/10.1089/aid.2007.0107.

[10] Eron JJ, Yetzer ES, Ruane PJ, et al. Efficacy, safety, and adherence with a twice-daily combination lamivudine/zidovudine tablet formulation, plus a protease inhibitor, in HIV infection. *AIDS*. 2000;14:671–81. doi: org/10.1097/00002030-200004140-00006.

[11] Bangsberg DR, Ragland K, Monk A, Deeks SG. A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people. *AIDS*. 2010;24:2835–4. doi: 10.1097/QAD.0b013e328340a209.

[12] HHS. Anti-HIV medications for use in pregnancy [fact sheet]. Available at: http://aidsinfo.nih.gov/contentfiles/DrugRegimensPregnantWomen_FS_en.pdf. Accessed August 18, 2013.

[13] Petersen ML, Wang Y, van der Laan MJ, Guzman D, Riley E, Bangsberg DR. Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: a marginal structural model analysis. *Clin Infect Dis*. 2007;45:908–15. doi: 10.1086/521250.

[14] Hardy H, Farmer E, Kumar V, et al. Assess and remind: a personalized cell phone reminder system is superior to a beeper to enhance adherence to antiretroviral therapy. Presented at the 4th International Conference on HIV Treatment Adherence, Miami, Florida, April 5–7, 2009. Abstract 289.

[15] Arya V, Alam R, Zheng M. Medication adherence: there's an app for that. *Pharmacy Today*. June 2013;34.

[16] American Pharmacists Association, National Association of Chain Drug Stores Foundation. *J Am Pharm Assoc*. 2008; 48(3):341–53.

[17] Thompson M, Mugavero M, Amico KR, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an international association of physicians in AIDS care panel. *Ann Intern Med*. 2012;156:817–833. doi: 10.7326/0003-4819-156-11-201206050-00419.

[18] Population Council. Horizons Project. Peer education and HIV/AIDS: past experience, future directions. Available at: http://www.popcouncil.org/pdfs/peer_ed.pdf. Accessed July 26, 2013.

[19] Bandura A. Social cognitive theory and exercise of control over HIV infection. 1994, 3–58. DiClemente R, Peterson J (Eds.) *Preventing AIDS Theories and Methods of Behavioral Interventions.* New York and London: Plenum Press.

[20] Kushel MB, Colfax G, Ragland K, Heineman A, Palacio H, Bangsberg DR. Case management is associated with improved antiretroviral adherence and CD4+ cell counts in homeless and marginally housed individuals with HIV infection. *Clin Infect Dis*. 2006;43:234–42. doi: org/10.1086/505212.

[21] Davila J, Miertschin N, Sansgiry S, et al. Centralization of HIV services in HIV+ African-American and Hispanic youth improves retention in care. Presented at the 5th International Conference on HIV Treatment Adherence, Miami, Florida, May 23–25, 2010. Oral Abstract 62911.