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POSITIVELY AWARE
WINTER 2023

MORE THAN A GAME CHANGER

Long-acting injectables are taking HIV prevention and treatment to a new level—what people living with HIV and their care providers should know

ONE DOCTOR'S PERSPECTIVE

BLACK COMMUNITIES AND THE PROMISE OF LONG-ACTING TREATMENT

BECOME YOUR OWN ADVOCATE IN YOUR CARE

Jayr Washington shares how long-acting HIV treatment has freed them from worry and self-stigma

AUTUMN 2023

POSITIVELY AWARE · VOLUME 33 NUMBER 5 · positivelyaware.com · @posaware
SPECIAL ISSUE ON LONG-ACTING INJECTABLES

ABOUT THE COVER
JAYR WASHINGTON PHOTOGRAPHED BY JOHN GRESS

THIS ISSUE IS SUPPORTED BY FUNDING FROM GILEAD SCIENCES, INC.

POSITIVELY AWARE

LIVE LIFE POSITIVELY AWARE.
SINCE 1990, PUBLISHED BY
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TPAN was founded in 1987 in Chicago as Test Positive Aware Network, when 17 individuals living with HIV gathered in a living room to share information and support in response to the HIV/AIDS epidemic. POSITIVELY AWARE is the expression of TPAN's mission to share accurate, reliable, and timely treatment information with anyone affected by HIV.

BE GREEN.
SHARE OR RECYCLE
THIS MAGAZINE.

GUEST CO-EDITOR'S NOTE

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With the power to transform comes the need for transformation

In 1998, I got my first job in the HIV field as a peer education coordinator in Cleveland, Ohio. I was 23 years old. We were at the very beginning of implementing the very first wave of antiretroviral regimens. While this in and of itself was a revolution that saved countless lives, it was not without its challenges. These regimens involved medications, all taken at different times of day, some with food, some on an empty stomach. Some people got some pretty severe side effects from the early medications. Some of those side effects caused physical changes to the body and essentially "outed" people as living with HIV, which created another layer of stigma.

And here we are 25 years later, having moved from that place to single-tablet regimens, many with very few side effects. And then PrEP came along in 2012, revolutionizing HIV prevention, just as condom use was beginning to wane in the U.S. And now we're on the dawn of a new shift in HIV treatment and prevention: the era of long-acting injectables. In my 25 years of working in HIV, I could not have imagined these kinds of breakthroughs in biomedicine would be possible.

While these advances are something to celebrate, we are far from the end of the road. Technological gains only go as far as people know about them, and systems are developed, enhanced or created to ensure people have access. And this is where we as a nation, as a public health community and as a planet of humans struggle. Just like with the first ARV therapy, and the first PrEP pill for prevention, we're now four years into the FDA approval of the first long-acting ARV therapy and we are several years away from really implementing these long-acting medications to truly see the impact they can have on the lives of people (whether living with HIV or in need of PrEP) and on the HIV epidemic itself. It takes us far too long to move these innovative inventions to the point where they become medical miracles experienced by everyone who needs and wants them, regardless of race, ethnicity, national origin, religion, sexual orientation, gender identity, sex assigned at birth, pregnancy status or income.

When I started PrEP in 2015, I too became fully aware of all the barriers in place. It took two days and lots of phone calls from the time the prescription was written to get the meds. I was forced to call my insurer every month to get prior authorization before they fulfilled the prescription. And even then, I was forced to get my PrEP meds from a mail order specialty pharmacy. As someone who lives alone and travels a lot for work, this was sometimes a nightmare to coordinate every month. When I was going through these challenges with daily pill-form PrEP I often thought to myself, if I was 20 years old instead of 40 years old, and living at home or in a college dorm, I would have given up. I definitely would not have had the PrEP meds sent through campus mail or delivered to my mom's house. It gave me a greater appreciation for what people living with HIV and other chronic conditions have to go through, in their case, to survive.

In this issue of POSITIVELY AWARE, we take a look at long-acting injectable treatment and PrEP. The articles included speak to the humans involved downstream, and what their experiences as patients, researchers, advocates and medical providers of long-acting treatment or PrEP teach us about how useful these products can be. But the authors here also tell us how far we have to go before they reach their full potential. And the full potential to save lives, to prevent HIV diagnoses among people more vulnerable to HIV, has everything to do with our ability to transform systems of care to more quickly and easily implement these new tools.

It takes us far too long to move these innovative inventions to the point where they become medical miracles experienced by everyone who needs and wants them.

I have personally heard stories of people being newly diagnosed with HIV and refusing to take pill-form ARVs and that the injectable saved their lives. I've heard from providers that many cisgender women they speak to about PrEP refuse the pill, but are very interested in the injectable for the privacy it offers them. We hope that this issue of POSITIVELY AWARE generates discussion among patients, researchers, advocates and providers, and becomes another stimulus to create new and innovative access points. It took us nearly a decade to do so with both ARV therapy and with PrEP.

Let us do better, more and faster with each new innovation.

RYARMO PHOTOGRAPHY

Getting started

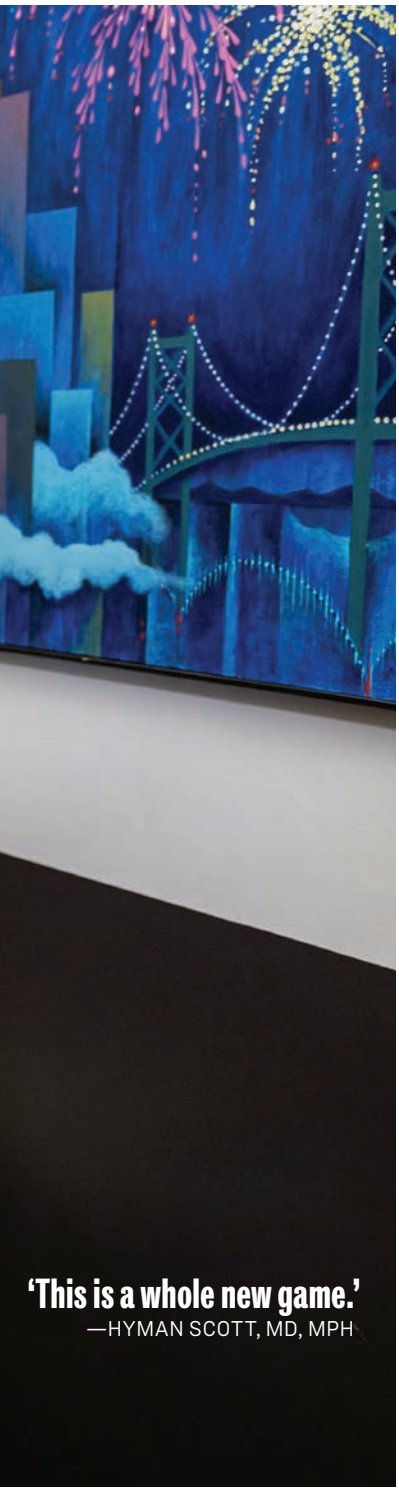
What individuals and care providers should know as they consider long-acting injectable treatment—'make it as simple as possible,' says **Dr. Hyman Scott**

INTERVIEW BY **RICK GUASCO** | PHOTOGRAPHY BY **ROBERT SILVER**

Someone walks into a clinic or the office of their care provider asking about a long-acting injectable, a new mode for HIV prevention or for treatment of their HIV. *What happens next?*

Instead of a daily pill, long-acting injectables (LAIs) are medications administered by injection that can remain effective for months. LAIs are not only a game changer, they are a whole new game in the fight against HIV. There are new players, new rules and new requirements.

Cabotegravir was approved in December 2021 by the U.S. Food and Drug Administration as the first long-acting injectable for PrEP. Known by its brand name, Apretude, it is initially



'This is a whole new game.'
—HYMAN SCOTT, MD, MPH

administered as a monthly shot for the first two months, and then as a single injection every two months. Before starting the injections, there's an optional pill version of cabotegravir that can be taken, although testing has shown this oral lead-in is not necessary.

For HIV treatment, cabotegravir is combined with another HIV drug, rilpivirine. Known as Cabenuva, it is the only complete treatment regimen in LAI form. Two shots of the combo are administered (one in each butt muscle) every two months, with an optional one-month oral lead-in.

Another long-acting injectable, lenacapavir, marketed under the name Sunlenca, is administered to the abdomen every six months, but daily oral antiretroviral medications must still be taken.

Located on the second floor of the Strut building in the Castro, Magnet is operated by the San Francisco AIDS Foundation in close collaboration with the city's department of public health. It is one of San Francisco's busiest sexual health clinics, providing PrEP to about 3,000 people—50 to 60 of whom are on long-acting injectable PrEP, says Hyman Scott, MD, MPH, Magnet's medical director. (Dr. Scott is also an infectious disease physician at Zuckerberg San Francisco General Hospital's Ward 86 HIV/AIDS clinic.)

What happens when someone asks about LAIs?

"If someone is interested in long-acting injectable PrEP, we do education about what it is, how it works, what the requirements are for getting started," Dr. Scott says. "And then there's quite a bit of insurance navigation that's required for long-acting injectables that is more intensive compared to oral PrEP."

TESTING, TESTING...

TESTING IS KEY to LAIs, whether for HIV prevention or treatment. People receiving cabotegravir for PrEP are given an HIV viral load test every time they receive an injection. That's because if a person has acquired HIV, it will be detected more quickly by a viral load test (which measures how much virus is in a person's blood) than an antibody antigen test, which detects the immune system's response to HIV exposure.

Viral load tests are also checked for people receiving LAI for HIV treatment, but usually not at every injection.

In both instances, the point is to make sure that the individual is responding to their LAI and to get ahead of any acquisition of the virus or the virus developing resistance to the medication.

"If someone has delays or misses injections, we might be testing more frequently," Dr. Scott says. "We just want to be careful and make sure that if there's a problem, we identify it as early as possible."

The two-month injection schedule for long-acting PrEP does have some flexibility.

"There's about four weeks after the target date that we have to get someone in for their injections without them having to restart, without the extra reloading injection," he says. "We want to make sure that the levels of the medication for prevention stay high enough to keep someone protected. If it's more than four weeks after the target date, we have concerns that the levels have dropped such that someone may not have high enough protection."

If the client is not able to make it within the four-week window, they can be given oral medication until the next scheduled shot, Dr. Scott says. He adds that a client can receive their injection one week early if needed.

The main side effect has been pain and tenderness around the injection site lasting about two days, he says, which can be treated with ibuprofen or Tylenol if necessary. General fatigue and achiness can also occur, and usually goes away after a couple of days.

"I tell most people who are starting a long-acting injectable, *Yeah, this is gonna hurt your butt cheek for a couple of days*," he says. "And it's not something that's generally immediate. There's a little bit of inflammation response—that generally happens like the evening of or the next day."

RETHINKING EVERYTHING

THIS NEW MODE of treatment means many care providers, clinics and other facilities that administer LAIs need to rethink how they work.

"There's a new level of patient management that is required for injectables that is not as necessary for oral PrEP," he says. Some clinics have worked with infusion centers and pharmacies to offer patients more options and locations.

"My advice is always, make it as simple and as streamlined as possible," Dr. Scott says. "That'll be the best thing for our patients, but also for us as care providers. Oral lead-in, for example, is something that should be offered to individuals who want it, but it's not strictly necessary. Offering direct-to-inject and making testing as easy as possible for individuals is also really important."

For care providers and their practices, there are major differences between long-acting injectables and oral medications.

"Insurance was the biggest surprise for me," he says. "I thought we had figured out a lot of the things for getting people onto PrEP for the last 10 years, but this is a whole new game."

Scott's Magnet clinic has staff who have become experts in getting insurance approval for LAIs. "Our navigation team says they can eventually get it for everyone, but sometimes it can take four to six weeks, or even eight weeks for them to get through all the insurance hurdles that are put up for people who are privately insured as opposed to oral PrEP, where we can get access within 24 to 48 hours," he says. Insurance companies have also pushed back against injectable PrEP because of the availability of a generic version of oral PrEP (a combination of tenofovir DF and emtricitabine), he adds.

People on public health insurance such as Medicare or Medicaid (known as Medi-Cal in California) have a much easier time getting onto long-acting injectable PrEP because of government policies and laws supporting PrEP access. >>

'My advice is always, make it as simple and as streamlined as possible. That'll be the best thing for our patients, but also for us as care providers.'

"We talk a lot about starting PrEP, but staying on PrEP is also very important," he says. "When people stop, for whatever reason, it's often because of the hassle of staying on it—insurance, visits, testing costs. We have to remove the hassle factor from our implementation—at a policy level, a clinic level, a provider level."

ACCESSING TRANSFORMATION

WITH THEIR CHALLENGES and potential for change, how will LAIs affect accessibility and inequities in healthcare?

"I don't think we know overall yet, whether or not they make inequities worse," Dr. Scott says. "I think they have the potential to close some of the inequities that we see. My concern is that it depends on systems, clinical systems, and we know that those systems are not equitable. We've seen inequities worsen with oral PrEP. In clinical studies, we saw a very high efficacy among Black men who have sex with men and with transgender women on injectable PrEP. [LAIs] are a really powerful tool that can change the trajectory of the HIV epidemic in the United States. Oral PrEP was transformative, and I think this long-acting injectable option is also transformative. But we can't leave Black people behind, we can't leave Latinx people behind.

"The prevention tool itself is necessary, but not sufficient. What we need is to ensure that we have all of our systems in place to make sure that these tools are used in ways that can most benefit our communities. We know where the gaps are. The research has been clear about where we are and I think there's consensus about where we need to go. The challenge is how do we make that happen. What does it take to achieve those goals? Long-acting cabotegravir gives us an opportunity to think about some of the transformations that are necessary, because it takes a little bit more work to implement them. The data will tell us whether we're doing it or not. We will have an answer, and I just hope it's a different answer than we've had in the last 10 years for oral PrEP."

Working toward those transformations, Dr. Scott feels a personal connection.

"It's joyful to work with clients and patients; it's recharging in many ways," he says. "I love the connection with community, with my patients, with the work. I went into HIV because of the absolute connection between the community affected by HIV and the medical community. I haven't seen that type of a connection in many other places or with other conditions; it is a tremendous opportunity and privilege for me to be part of these communities." PA

Why I switched

from a daily pill to long-acting PrEP

BY **LUTFY MANDHIRY**

My journey to using long-acting injectable PrEP started in 2016. I'd been a longtime condom user as my mother educated my sister and me about the importance of safe sex at an early age. My mother was hopeful that by this age in my life, at least by the time I was 18, that there would be a cure for HIV. While she didn't necessarily know what my sexuality was at the time, and neither did I, she wanted us to be thoroughly aware. Thankfully she had this foresight, because I began to have sex at a young age and had the knowledge of protection with me. Coincidentally, one of my first partners was very big into safe sexual practices as well—which further reinforced what my mother had been teaching us all along.

In 2016, I decided that condoms were really not enough because a part of me wanted to participate in condomless sex, but I was always deathly afraid of any sexually transmitted infections (STIs), viruses, etc. I was speaking to my physician during a routine checkup when I casually began to express my concerns around the issue. My doctor then mentioned PrEP as a preventive method. I was hesitant as I really don't like taking pills of any sort, but with further consideration, I went into my local health department to further inquire about PrEP. It was there that I was introduced to Truvada. I used it for maybe a year or two but was experiencing some complications like head and stomach aches. So, my PrEP nurse switched me to Descovy. It was a smaller pill, and it was easier to swallow and had less side effects since it's processed by the body a little bit differently. So, after finding a PrEP medication that worked for me, what made me switch to a long-acting injectable PrEP med, Apretude?

I was living in Los Angeles at the time and had been receiving PrEP care at APLA Health's Charles Drew University/MLK Medical Campus. One of the PrEP nurses told me a few years ago that they were introducing Apretude. I was very apprehensive because it was fresh on the market, but it sounded like a better alternative. When you're on oral PrEP, you are supposed to take your pill every day—and sometimes it's just not possible. Sometimes you might stay out overnight unexpectedly, so you didn't think to pack your contact solution, your contact case, your hair products or your PrEP meds. Between the potential of missing a dose or running out of your pills, taking a daily pill is too tedious a task for a fast-paced or everyday life. In fact, this has happened to me before where I've just gotten down to my very last pill and wasn't paying attention. So, when Apretude was introduced to me, the idea of it sounded great because I did not have to remember to take a pill, and even though the alternative made sense, I was not entirely sold because I felt the research was still very limited. So, I sat on the idea for a while.

When I moved back to Baltimore, I continued my PrEP care through my city's health department. Access is easy—it's free and you don't have to wait long to be seen. I was still on Descovy, but one of the nurses mentioned that they were going to start offering Apretude; however, I'd have to get on the waiting list as only a few people would be able to receive it per their health insurance. After my chat with her, I decided to try it. About a day or two later, the specialty department at my pharmacy called me with the news that my application had been approved. They shipped it out to the health department, and within a week, I was receiving my first injection. I always tell people, if you're having problems getting access to PrEP, to check with your local health department as they may have a program to help you. Bonus: it might be at no cost to you.

I was still a little apprehensive when I went for my first dose, as there were still so many unanswered questions. My biggest concern was the time frame of when would I experience the full

INSTAGRAM

effectiveness of the medication. I rarely participate in condomless sex, so I didn't necessarily fear the initiation process, but I was extremely curious, nonetheless. The bonus here is that I'd no longer have to remember to take my PrEP daily. No more running out of pills or traveling with a rattling bottle of Descovy. The injection itself was pretty simple. One intramuscular injection to the upper buttocks and it's done! It didn't hurt any more than a flu shot. But after the second or third day, I was extremely sore around the injection area. A day or two later, though, the soreness wore off, and I was back to business. All in all, I feel the convenience is worth the few days of pain.

You never know when and where you may find yourself in a situation where you may 'slip up and slip in.'

Injectable PrEP is administered by your physician and has a short window for treatments. Knowing that, somebody like me, who's always on the go, might find trying to adhere to the window a little bit tricky. But just the ease of knowing that if I can make that appointment, get my injection and endure the soreness for a few days, then I can keep busy and stress-free—and no longer worry about keeping up with a pill.

As I began using Apretude, I thought it would be insightful to share my experience across my social media channels to create opportunities for conversation. My hope was to enlighten my people and my community who are unaware of this option or its accessibility. I wanted this to be impactful to those who were considering their PrEP options, either the long-acting injectable or the traditional oral treatment. After making a few videos, the comments started to roll in. Some commenters wrote things like:

Oh, you're allowing yourself to be a guinea pig?

In five years, you guys will all be on a commercial talking about how it didn't work.

I won't call it hate, just maybe some misunderstanding and miseducation. Whatever their responses are, I'm satisfied in seeing the conversation around safer sex practices beginning. Personally, I don't frequently participate in condomless sex, but there's a comfort in knowing that if I decided to, that I'd be better protected from HIV transmission. That same sense of peace is present when, and if, my condom breaks or slides off during sex.

So, if you're considering taking the long-acting PrEP injectable, what's my advice? Do it! What do you have to lose? You never know when and where you may find yourself in a situation where you may "slip up and slip in." There may also be moments of impaired judgment—under an influence of your choice—where your actions could lead you down the road of concern and regret the following day. And so, I would just say, know that your options are there. If you can get it, get it, and it may even be free.

Know your status and protect it. Your status is the only status that you can be accountable for, and you're going to be with you until the end. Your happiness and your health are your priority. Your health is your wealth, so be good to yourself and trust your instincts. If you can avoid the infection with a pill or shot, and help put an end to HIV, let's all do it together. PA

FOLLOW Lutfy Mandhiry on Instagram: @sincerely_lutfy.

Want to start long-acting injectable HIV treatment?

BECOME YOUR OWN ADVOCATE!

BY **JERRY L. WASHINGTON, JR.**

My journey living with HIV began 20 years ago and from that moment I became my own advocate in making sure that I received the quality of care I needed to thrive. It was early on when I learned very quickly the importance of health literacy and making your voice heard. It was in 2003 that I started my first HIV treatment regimen and during that time if your CD4 count was not less than 500, the doctor would not start you on meds. However, with all the information provided to me I made the choice to begin right away.

What I didn't know was that I was about to experience side effects that would be hard for me to tolerate. It was so bad that I asked my doctor multiple times to switch me to a different medication. Each time the doctor said no, and I felt like the doctor was not listening to me. So I began doing some research of my own by searching the internet, reading magazines, watching videos and asking different individuals within the community their personal experiences.

Since my doctor wasn't hearing me, I decided to take matters into my own hands and stopped taking medication. I knew it was risky because I learned that resistance could occur when you are not taking it as prescribed. This is where advocating for myself as it relates to care and treatment ignited.

Now the world looks even brighter and possibilities seem limitless to me because of new advances that are being made in medicine. It was almost two years ago when I began inquiring about taking injections for HIV treatment. The reason why I decided to be on the injectable is because I wanted to utilize the best or the most advanced science available. I wanted to be a part of that change that's happening within our community. And being on an injectable regimen is a life changing thing for me because it allows me the freedom not to really worry and stress about missing a dose or leaving my medication at home. I feel liberated and free to move about in life without worrying

about a bottle of pills. I can now receive treatment at my doctor's office every other month and it works for me.

However, it wasn't an easy process gaining access to the drug. I first learned about Cabenuva when I was a member of the Community Advisory Board at the University of North Carolina-Chapel Hill's Center for AIDS Research (CFAR). It's because of my engagement in CFAR programs that led me to having a conversation about getting on injectable HIV treatment once it became available.

The process to start involved a lot of work because my medical provider had to deal with my health insurance company and there was so much paperwork that needed to be completed. It took all of us working together to get things going. Then I contracted COVID-19 in 2020 and because I was sick for 30 days with no family around, I decided to move to Washington, D.C. to be closer to my family. However, before I left North Carolina, I finally got approved to take Cabenuva. Now, I found myself having to go back through the same process again in the DMV [metropolitan Washington, D.C. area]. It took me two years to finally be in a position to start my Cabenuva journey.

During those two long years, I went through a lot of emotions. I was angry, I felt disappointed. I often felt confused and overwhelmed about the process. One day I was being told one thing, and then subsequently being told another. I had to really push past all those emotions to get where I am today, taking long-acting injectable HIV treatment. But it took a lot of effort, patience and education about the whole process. Education can help eliminate some of the emotions that may come up for someone who wants to explore new treatment options, because it often may seem like the doctor is responsible for delays and barriers, whereas it's actually not even the doctor's fault that the process is taking so long. Often it is really the insurance company that is responsible for unnecessary hold-ups. I have seen some people get on Cabenuva quickly. But for me it took about a year for my current provider to finally process all the paperwork necessary for them to administer the medication to me. And when they began to give it out, I was the second patient in my health facility to obtain access to it.

When I give advice to people living with HIV who want to start long-acting injectable treatment, I tell them to be patient. It's not going to be an overnight thing because there is a process one must go through in order to get on it. So be patient, listen to your doctor, but still advocate for yourself and make your voice heard. And if the outcome is such that you are not able to take the medication for whatever reason, just know that there are other oral treatments that you can still be on, and perhaps there are treatment options that you can switch to that may be a better fit for you.

But again, be patient. This is a new way to do HIV treatment, and anything new takes time. But I'm hoping that the process to start taking the injectable becomes less complex so that eventually a person can get on Cabenuva within a day or two of receiving their lab results. For those of us who are long-term survivors, who started HIV treatment when pills were the only option, we do sometimes get tired. We get tired of popping a pill on a day-to-day basis. And so having an injection available where you can receive it every two months is life changing. It's life changing mentally, it's life changing physically and it's life changing spiritually as well. It just changes your life for the better. You no longer worry about missing a dose or leaving a medication at home and traveling and things like that. It really pushes you to assert even more control over your own health.

HIV treatment for me means that I have an opportunity to live my best and complete life. That means that I can still do all the things that I want to do.

...be patient. It's not going to be an overnight thing because there is a process one must go through in order to get on it. So be patient, listen to your doctor, but still advocate for yourself and make your voice heard.

Treatment allows me not to really worry about a lot of things and I can focus on achieving all the things that I want to accomplish in life.

Despite my frustration waiting to get approved for Cabenuva, I still stayed on my daily oral medication until the approval went through. But the biggest thing is that I didn't give up—that's my advice. Keep pursuing what you believe you deserve and is available to you, no matter how long it may take. PA

‘Liberating’

Long-acting HIV treatment frees **Jayr Washington** from worry and self-stigma

INTERVIEW BY **RICK GUASCO**
PHOTOGRAPHY BY **JOHN GRESS**

Twenty-eight-year-old Jayr Washington had been on PrEP for about a year and a half, adherent to his daily oral HIV prevention, when everything changed.

"When I first started taking PrEP, I was on it consistently because I was doing heavy sex work before finding other employment," Washington says. "Then the [COVID] pandemic shut down the city, so, it was really my only source of income. I started to miss doses. I was off PrEP for about a month and a half, taking doses here and there. As the year went on, I seroconverted."

Washington, who is gender nonbinary and uses the pronouns they and he, lives on the West Side of Chicago, working as a health system navigator and HIV prevention specialist, particularly with people who are transgender and nonbinary.

"When I was diagnosed, I wasn't really shocked," Washington says. "Because I didn't know how long I had been living with HIV, I needed to get into care as soon as possible. I didn't want it to affect my health or affect others." Within a week, they saw a care provider and were prescribed daily oral HIV antiretroviral treatment.

"I was like, *Well, this PrEP all over again*," they say. But not in a negative way at first. Like oral PrEP, they saw their new HIV medication as a one-pill-a-day solution against HIV. Over time, though, that pill became a daily reminder of their HIV status. As they became increasingly busy having started a new job, they began to worry about adherence and to fear that missing doses might lead to the virus developing resistance to the medication.

"It used to tear me down, like, *Damn, I gotta get up and take this pill in the morning*," they say. "That's when I had to sit down with my provider and I told them that I think I'm ready for the shot," they say, referring to long-acting injectable (LAI) treatment for HIV.

Currently, there is one complete LAI regimen, in the form of two injections, one administered to each butt muscle every two months, a combination of the HIV drugs cabotegravir and rilpivirine marketed under the brand name Cabenuva. Another LAI drug, lenacapivir (brand name Sunlenca) is a single shot administered every six months but must be accompanied by daily oral HIV medications for now.

After three and a half years on oral HIV medication, Washington started receiving long-acting treatment at Heartland Health Alliance's James West clinic, just west of downtown Chicago.

"I don't have to worry about re-traumatizing myself every day," they say. "Knowing my status is one thing, but when you see your medication, it's a different type of feeling."

"It was very liberating, because I'm taking care of myself," they say about their first visit to the clinic to receive treatment. "I was nervous at first, but I was like, *Let's get this over with*. There was more fluid in the shot than I expected. The first shot, on my right butt cheek, wasn't as painful as I thought it was going to be, but that second shot—I'm not used to shots on my left side. I was like, *Oh, I feel it, I feel it!* But at the end of the day, it was something that I knew would be very beneficial to me in the long run."

The bus ride home was somewhat painful. "Sitting down the first time was painful, but after I got home and massaged it and the medication started going through my body; after a day or two, it was cool.

"The space that I'm in now, I'm very happy," they add. "Yes, I know that I'm positive, but I'm in care. I'm healthy and I'm taking care of myself. I have to do what's best for me. Being on the injectable is the best and is the most effective treatment for me."

They credit their care provider and Heartland with much of that success. Although the clinic maintains normal business hours Monday through Friday, Washington is able to receive treatment on Saturday mornings, so that they don't have to miss work during the week, something they're not able to do with a new job. They acknowledge that without the clinic being available beyond normal 8-to-5 weekday hours, accessing long-acting treatment would be much more difficult.

Washington also stresses the importance of the patient-provider relationship.

"Thank goodness I have a great provider who understands me, who listens to me," they say. "Even though the doctor is not of my demographic, she can relate to me because she's had so many patients who are trans, nonbinary; she's very familiar with the community. I need to be around a provider who's culturally competent and who's familiar with my community, who understands my community's needs and not what *they* think we need. I feel that in order to be a great provider, you have to be able to listen, actively listen, and understand what your clients are telling you."

Washington slips into their activist role as they call out providers whose lack of knowledge or personal biases can negatively affect patient care.

"I've worked with clients who had providers who didn't know what PrEP was. *You're a doctor; how don't you know about PrEP or PEP?*" They share the experience of one client, a cisgender woman, who asked her physician that she be tested for HIV. The doctor was dismissive. "The doctor told her, *What do you want to get tested for? That's a gay thing, that's your least concern*," Washington says. "The *H* in *HIV* stands for *Human*. Anyone is HIV possible."

'Knowing my status is one thing, but when you see your medication, it's a different type of feeling.'

It's in this role as activist, on the West Side, among trans and nonbinary folk and on social media, that Washington is finding themselves.

"I've seen a lot of my friends pass away from not taking their medications," they say. "The fact that I'm being open and vulnerable about it, maybe that can rub off on someone else to be comfortable enough to share their story, especially in our community."

At 28, they see themselves in a unique position—between older generations "that paved the way for me to be my authentic self" and a younger generation "who will look up to me because I'm right before them and see that it is okay to live with HIV.

"This is a pivotal moment in my life right now, when I'm being vulnerable and resilient about my status," they add. "I've never talked about it much. I'm in care, I'm healthy. I'm active, still doing what I used to do, but more honestly. This is very liberating for me. I love that word. *Liberating*." PA

Promise?

GETTING PREPPED: RECEIVING LONG-ACTING PrEP AT WHITMAN WALKER IN WASHINGTON, D.C.

Making good on the potential of long-acting injectables for Black communities

BY **DANIELLE M. CAMPBELL, MPH**, AND **JOHN W. MEADE, JR., MPH** | PHOTOGRAPHY BY **JIMELL GREENE**

Nearly four decades of HIV activism in the United States has demonstrated a movement with strong foundations in fighting for access to lifesaving prevention and treatment. Unfortunately, these efforts have not equitably benefited communities disproportionately impacted by HIV, in particular, Black people. We bear the brunt of the HIV burden, experience the worst care outcomes across the HIV care continuum and are characterized as lower utilizers of biomedical HIV prevention technologies including oral PrEP. So, let us heed the wise words of the late U.S. Representative John Lewis and build a movement for Black people by Black people to fight for what we deserve.

Recently, the U.S Food and Drug Administration (FDA) approved the first non-oral, long-acting injectable treatment (cabotegravir and rilpivirine, brand name Cabenuva). A long-acting injectable prevention option (cabotegravir, brand name Apretude) resulting from findings of key research studies led by the HIV Prevention Trials Network (NPTN 083 and 084) promises to reconsider paradigms of pill burden and challenges to medication adherence among groups who are undoubtedly overrepresented among incident and prevalent HIV diagnoses.

In a press release about the new drug approvals, the FDA declared that long-acting formulations offer "a tremendous opportunity to narrow racial disparities in HIV incidence."

As folks who advocate with Black-focused social justice and health equity-oriented lenses, we offer that statements like these overstate the perceived benefits of long-acting prevention and treatment. They oversimplify complex historical systems of exclusion that limit equity in access to HIV treatment and prevention advances and threaten to perpetuate narratives that medicalize adherence while ignoring social contexts that facilitate negative health outcomes among Black people.

As long-acting options enter the HIV treatment and prevention landscape, we are challenged by the current state of affairs of HIV treatment and prevention among Black people. For example, more than 10 years after the approval of the first oral biomedical HIV prevention strategy in the U.S., data from the CDC says that only 11% of Black people with

an indication for PrEP have actually been prescribed it. Indeed, Black communities may not have felt the the "game changing" benefits of oral PrEP once promised by the field. What we experience instead are provider biases, barriers to medication coverage by insurers and high lab costs, to name a few. It remains to be seen whether or not Black communities will benefit from the benefits of long-acting injectables. As of the time this article was written, we were unable to locate any online data sources that provided any demographic data on long-acting injectable users for prevention or treatment. This is abhorrent. For data on global PrEP, we recommend PrEPWatch, a global resource for PrEP information and resources.

To make good on the promises of long-acting HIV prevention and treatment, stakeholders working in HIV must support community-derived strategies for Black people led by and developed by Black people to support our collective improved health. As a matter of health justice, we demand the continued acknowledgement and remedying of historical social and structural factors that limit Black people's sustained engagement in HIV care.

The history of exploitation, subjugation of and experimentation on the Black body must be addressed, or the cycle will continue. James Marion Sims's (the "Father of Gynecology") exploitation of the Black female body, the U.S. Public Health Service study "Untreated Syphilis in the Negro Male" at Tuskegee and the stolen cancer cells from Henrietta Lacks, which were used to advance modern science, are just a few examples of why there is a culture of distrust in research, medicine and new health technologies, including long-acting injectables.

The impact that anti-Black racism, discrimination, generational poverty and sexism has had in limiting our ability to equitably access HIV care is beyond calculation. As it relates to long-acting modalities, we can only predict the same negative impacts will limit Black people's utilization. Specifically, anti-Black racism and discrimination, medical distrust and the fact that many providers do not treat Black patients the same as White counterparts continue to have a detrimental impact on the ability of Black people to access HIV prevention and treatment options.

PrEP in Black America Coalition

In the spirit of seeking change to ameliorate the devastating impact of HIV in Black communities through biomedical HIV prevention, Black leaders from across the nation established the PrEP in Black America (PIBA) Coalition in 2022. We offer as a remedy to these historical injustices reimagined interventions and strategies designed for Black people by Black people. Further, we advocate for interventions and strategies as described in Goal 3 of the National HIV/AIDS Strategy for the United States, 2022-2025, that "Reduce HIV-related disparities as health inequities" while increasing the recognition of racism as a public health crisis.

We acknowledge the work of PIBA as a model for effective community engagement and mobilization through an HIV prevention lens with features that are fully translatable to the HIV treatment space. Since its establishment, the PIBA coalition has organized two summits that brought together over 250 Black HIV prevention leaders and public health practitioners to discuss strategy, interventions and policy as it relates to access to HIV prevention tools in the Black community.

It is important that we learn from our experience with treatment and prevention inequities and apply them to the rollout and implementation of long-acting injectables. To get to the root of these inequities that affect the Black community, we must address medical mistrust of the health care system. This is a phenomenon that has been apparent throughout U.S. history stemming in large part from the medical mistreatment and abuse of Black people dating back to slavery.

Black people are not categorically challenged by medication adherence. The public narrative around PrEP and treatment adherence among Black people obscures root causes, like racism and medical mistrust, making these trends appear natural and inevitable. Our ability to effectively maintain adherence and secondarily viral suppression exists within a system that does not support our lived experience.

And to be clear, if we are to benefit from access to long-acting injectables, they must be accessible and affordable.

As public health practitioners and founding members of the PrEP in Black America Coalition, we engage with colleagues and allies to raise, nurture and articulate an effective social justice public narrative that supports a common agenda to achieve health and racial equity. Without a clear and concise consideration of the social and ecological contexts of Black people, we will continue to miss the proverbial boat and risk not benefiting from long-acting prevention and treatment modalities.

There is a social and moral obligation for systemic change. PA

"If you see something that is not right, not fair, not just, you have a moral obligation to do something about it."
—U.S. REPRESENTATIVE JOHN LEWIS
(1940—2020)

IN OUR 2022 REPORT, "For Us, By Us: PrEP in Black America—A Master Plan for HIV Prevention in Black America," PIBA organizers lay out a framework centered by Black people to address PrEP disparities in Black communities with three key recommendations, defined through strategic partner engagement with stakeholders.

RECOMMENDATION 1
Efforts to address HIV prevention in Black communities must be led by Black people at all levels.
We believe this approach to be directly translatable to efforts that will improve HIV treatment, viral suppression and HIV-related health outcomes among Black people. The messenger, from the community health worker to the principal investigator, matters!

RECOMMENDATION 2
A well-resourced multi-pronged effort to educate Black people about PrEP is needed.
We believe this approach is directly translatable and should be considered through a co-joined effort as outlined below.

RECOMMENDATION 3
Support a federally-funded national PrEP program.
Support is needed for the development of culturally tailored implementation science research to communicate knowledge and perceptions of PrEP options among Black people, led by Black people.

Black public health professionals, advocates, activists and organizers can **SUBSCRIBE TO** the PIBA listserv, tinyurl.com/pibalistserv. **FOLLOW** @prepinblackamerica on Instagram and @PrEPInBlkUS on X (formerly Twitter).

DANIELLE M. CAMPBELL, MPH, is a community advocate living in Los Angeles and a founding member of the PrEP in Black America Coalition.

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MEADE: SAM HOLLENSHEAD

Making a SPLASH

For people living with HIV who are experiencing homelessness or unstable housing, long-acting injectable treatment holds great promise—how **Ward 86** makes it work

BY **ELIZABETH IMBERT, MD, MPH**, AND **MONICA GANDHI, MD, MPH** | PHOTOGRAPHY BY **ROBERT SILVER**

DR. GANDHI, MEDICAL DIRECTOR OF WARD 86

People living with HIV who are experiencing homelessness or unstable housing face disparities across the HIV care continuum. In 2021, 17% of people living with HIV in the United States reported homelessness or unstable housing (HUH).[1] People experiencing HUH remain significantly less likely to achieve viral suppression than people with stable housing, even among those who access care.[2] In San Francisco, people experiencing homelessness account for 24% of people newly diagnosed with HIV and only 27% of people experiencing homelessness were virologically suppressed in 2021 (compared to 75% of those with stable housing).[3]

People experiencing HUH face significant challenges to adhering to daily oral antiretroviral therapy (ART). Common causes for non-adherence among people with HUH include lost or stolen medications; medications taken by law enforcement during encampment sweeps; lack of food access; stigma; competing basic subsistence needs; forgetting to take medications; insurance lapses or prohibitive co-pays; transportation issues; or the impact of co-existing mental health or substance use disorders. Expanded access to affordable housing is essential to address HIV disparities among people experiencing HUH; however, treatment and care models must respond now to support patients while housing solutions are being proposed and implemented.

Long-acting injectable antiretroviral therapy (LA ART) holds great promise for the treatment of HIV among people experiencing HUH. The U.S. Food and Drug Administration approved injectable cabotegravir (CAB) and rilpivirine (RPV) for dual administration every 4 weeks in both antiretroviral therapy-naïve and antiretroviral therapy-experienced patients in January 2021, and approved a higher dose every 8 weeks in March 2022.[4] However, the research trials that led to the approval of LA ART for the U.S. and Europe examined the use of the combination regimen only in study participants who were already virologically suppressed on oral ART. Given that limitation, we need better data to demonstrate if we can use LA ART in patients with challenges to taking oral ART due to housing insecurity or other barriers.

Data on long-acting cabotegravir and rilpivirine in people with detectable viral load who face challenges to adherence are currently limited.[5] In 2021, Ward 86, the public HIV clinic in San Francisco, launched the SPLASH (Special Program of Long-Acting Antiretrovirals to Stop HIV) to administer LA ART therapy to our patients. In our demonstration project, where we tracked data carefully and presented it, and we enrolled individuals with detectable viral load who face adherence challenges.[6] Many of these patients are seen in the Ward 86 POP-UP program (Positive-health Onsite Program for Unstably-housed Populations), a low-barrier drop-in care model that serves people living with HIV who experience HUH, are not virally suppressed, and have difficulty attending scheduled appointments.[7]

Studying LA ART for homeless or unstably housed patients with detectable HIV—the SPLASH study

THE SPLASH TEAM at Ward 86 (which includes clinic leadership, the pharmacy supervisor, a pharmacy technician, researchers and leadership of the POP-UP program) created a protocol for eligibility, referral, injection administration, follow-up, laboratory monitoring and late injections.[8] Between June 2021 and November 2022, 133 people living with HIV were started on long-acting injectable antiretroviral therapy, 76 of whom had virologic suppression while using oral ART and 57 of whom had viremia. In this initial cohort, 77 (58%) were unstably housed and 11 (8%) were living on the street; about a quarter of the patients in our initial SPLASH cohort were enrolled in the POP-UP program. Among people with viremia, 54 of 57 had viral suppression, one showed the expected 2-log reduction in HIV RNA level and two experienced early virologic failure. The current virologic failure rate of 1.5% in the cohort was similar to that across registrational clinical trials at 48 weeks.

Our follow-up data of the first 243 patients on LA ART at Ward 86 is still being analyzed, but the overall virologic success rate among those on LA ART who started with viremia remains high (about 85%). This compares to a rate of only 33% virologic suppression in people who traditionally cannot take oral ART for a variety of barriers, including homelessness, despite incentives and other interventions.[9] This project demonstrates the ability of LA ART to achieve virologic suppression among people living with HIV, including those who experience HUH, have viremia and face challenges to adherence.

Our project has led thought leaders in HIV medicine to call for the addition of long-acting ART for individuals who are not virally suppressed to the Department of Health and Human Services (DHHS) Antiretroviral Treatment guidelines when oral pill form medication is not possible due to a variety of challenges.[10]

LA ART programs still need supportive services

WHILE LA ART in and of itself can assist homeless and unstably housed people who struggle with medication adherence, it's not just the injection itself that may make the difference. The POP-UP program worked with the SPLASH team at Ward 86 to facilitate people experiencing HUH starting LA ART. Facilitators who helped patients stay in care included a patient cohort who developed a trusting relationship with the POP-UP team; using the same nurse to administer the medications in the clinic, which also builds up trust; call reminders when injections are due; drop-in access that allows patients to come to the clinic to receive their injections when it is convenient for them; a mobile team who can go and find patients if they are late for injections; and an existing multi-disciplinary meeting to discuss patients and develop individualized care plans.

When considering using long-acting injectables in people living with HIV who are experiencing HUH, there are several key considerations. It is important to conduct a rigorous clinical review, reviewing all prior treatment regimens and genotypes (resistance testing) to ensure that the patient does not have drug resistance with any integrase or rilpivirine mutations. If individuals have chronic hepatitis B, they must continue oral medications for hepatitis B. We have also started to use a combination of a novel long-acting capsid inhibitor (lenacapavir)[11] with cabotegravir for patients with underlying resistance to rilpivirine or non-nucleoside reverse transcriptase inhibitors (NNRTIs).

'Our project has led thought leaders in HIV medicine to call for the addition of long-acting ART for individuals who are not virally suppressed.'

The 101 for patients

WE ASK PATIENTS to commit to taking long-acting injectables before enrolling in our program. It is our practice to counsel patients on the long half-life of the injectable medications, and share that if they stopped injectable medications, adherence to oral ART would be key to preventing additional resistance development. Given this, for individuals who face challenges with adherence, we emphasize that this is not a medication to start and then discontinue shortly after. We counsel about the importance of on-time injections and collect contact and location information to ensure that we can reach patients if they are late for their injections. We ask patients to agree to come to the clinic to receive the injection or in rare cases, our team will work with existing resources to deliver injections to the patients where they live. For example, the SPLASH program has partnered with nurses in a San Francisco-based street medicine program or nurses who visit patients in health-at-home programs at low-income housing units in the city. It has been key to have a pharmacy technician to both help acquire the injectable ART regimens from the patients' medical insurance (which has been easier for patients on public, rather than private, insurance programs in the U.S.) and track when patients are due for their injections. Finally, it is our practice in the POP-UP program to perform in-person outreach if patients are late for their injections. We have started to co-administer the long-acting ART with long-acting medications for psychotic conditions or long-acting medications for substance use disorder treatments when indicated.

Summary

HOMELESSNESS AND UNSTABLE housing are major barriers to HIV care engagement and achieving population-level Ending the HIV Epidemic goals.[12] Long-acting injectable medications provide a much-needed alternative strategy for people experiencing homelessness who face significant barriers to adherence to oral ART. While long-acting injectables can be a game-changer for individuals who face challenges to adherence to oral therapy, it is important to deliver them within a clinical program that can support rigorous clinical review, counseling, adherence support and in-person outreach when needed. We think the use of long-acting ART in patients with multiple structural barriers to taking oral ART can be accomplished and will increase rates of virologic suppression in hard-to-reach populations. We encourage clinicians to reach out to us for any questions about our programs for vulnerable populations living with HIV. PA

ELIZABETH IMBERT, MD, MPH, is medical lead of POP-UP program at the University of California-San Francisco's Ward 86 HIV Clinic.

MONICA GANDHI, MD, MPH, is medical director of the Ward 86 HIV Clinic at UCSF.

For footnotes, GO TO positivelyaware.com/LAI-HUH.

IMBERT: UCSF · GANDHI: ROBERT SILVER

What trans folks should consider

Hormone therapy appears safe with injectables, but other questions remain

BY **FINN SCHUBERT, MPH**

Long-acting injectable medications for HIV treatment and prevention have been an exciting development, offering the option of an every-other-month injection instead of a daily pill. Studies have shown that long-acting injectables are safe and highly effective, and many people view them as a convenient alternative to a pill-based regimen.

But folks in the trans community may have a few more questions in order to consider this option. What do the studies say about these medications for trans folks, and what might they need to keep in mind when considering whether these medications are a good fit?

The injectables

For HIV treatment, the only complete injectable regimen currently available is a two-medication treatment (cabotegravir and rilpivirine, given in two separate shots), which can be given monthly or every other month, brand name Cabenuva. For HIV prevention, the injectable is cabotegravir (brand name Apretude) alone, which can be given every two months.

These medications are safe and effective in general—in studies of the HIV treatment option, fewer than 2% of people had a detectable viral load after taking the medication for 48 weeks. Serious side effects are very rare, although many people do experience mild injection site reactions such as pain or swelling. For PrEP, the cabotegravir injectable was shown to be slightly more effective than the TDF/FTC (Truvada) pill in preventing HIV infection, though both options are highly effective when taken appropriately.

But are these safe and effective for transgender people? In general, the answer is yes, but let's look at some considerations about hormone therapy and silicone fillers.

Hormones are safe to take

A MAJOR STUDY regarding cabotegravir for HIV prevention included 570 transgender women, 330 of whom were taking estrogen treatment during the study. The study reported similar efficacy in transgender women and cisgender men (which were the only two populations in the study). In a small sub-study, investigators found no difference in drug concentrations between those who were and were not on hormone therapy, suggesting that estrogen treatment does not decrease the effectiveness of cabotegravir for PrEP. There is no specific experimental data currently available for transgender men.

A key study regarding cabotegravir/rilpivirine for HIV treatment reported on participants by sex assigned at birth, and did not separately report data for trans participants; however, expert consensus is that medications like cabotegravir and rilpivirine (which are an integrase inhibitor and a non-nucleoside reverse transcriptase inhibitor, respectively) are unlikely to interact with gender-affirming hormone therapy.

So, while hormone therapy should not be a barrier to trans people who want to use long-acting injectable HIV treatment or PrEP medications, there are some other things to consider.

Other considerations

SPECIFICALLY, the shot goes in your glute (the muscle of your butt), and it is not currently approved for injection at any other site on the body. This means that if you've had silicone injections or other fillers in your booty, this medication probably won't be an option for you at this time. If you are doing any gluteal intramuscular injections at home (some people inject testosterone intramuscularly), let your provider know about your injection sites and timing.

Keep in mind that you'll need to receive the injection at your provider's office every two months within a 7-day window before or after your target injection date. Will you be able to fit more frequent provider visits into your schedule? If you're currently receiving gender-affirming hormone therapy from a provider different from the provider who manages your HIV treatment or HIV prevention (for example, if you're seeing an endocrinologist for hormone care and an infectious disease physician for HIV care), would it be possible to reduce some of your visits

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If you're interested in the injectable, but worried about starting on a long-acting medication that you haven't tried before, there is the option of taking the same medication in pill form to try it before switching to the injection.

by finding one provider who can manage both medications? Hormone therapy and PrEP care can both be managed by a primary care provider who is trained to do so, and some HIV specialists or infectious disease providers will manage hormone therapy alongside HIV treatment.

There are some other considerations that aren't specific to trans folks, but are probably still worth mentioning if you're considering taking a long-acting injectable for PrEP or for treatment. Many people who struggle with taking a daily pill are excited to switch to cabotegravir/rilpivirine for HIV treatment, but it's important to know that this treatment is currently only approved for use in those who are already virally suppressed.

Also, the medication isn't a good fit for people who have liver problems, or individuals who are pregnant or chestfeeding. Since the medication is long-acting, some of it can remain in the body for 12 months after the last injection—someone with a uterus who might be considering a pregnancy for later might want to keep this in mind.

If you're interested in the injectable, but worried about starting on a long-acting medication that you haven't tried before, there is the option of taking the same medication in pill form to try it before switching to the injection. The pill form of the medication can also be used if you expect to miss a scheduled shot due to upcoming travel or other reasons.

With these medications, access can be an issue. Some state ADAP programs cover the long-acting injectable HIV treatment, and others do not. For the PrEP injectable, some people have experienced insurance challenges, including high co-pays and difficulty getting approval for coverage of the medication. Fortunately, injectable PrEP has recently received a grade A recommendation from the U.S. Preventive Services Task Force, and will be required to be covered at no cost to patients beginning in 2025.

Dealing with insurance issues can sometimes be extra stressful for trans folks who haven't changed their name legally or who maintain their health insurance with a sex designation that they no longer identify with. Some community organizations or healthcare facilities may have a case manager or navigator who can help you navigate these insurance issues so that you don't have to do it all on your own. For people who are uninsured, patient assistance programs may be a potential option to access these medications.

Summary

OVERALL, although it would be useful to have more data about long-acting injectable medications for trans and gender diverse folks, what we do know about these medications suggests that they may be a good option for some who would prefer an injection instead of a pill-based regimen. The injection offers privacy and flexibility, since you don't have to have pills around for someone to find, or remember to bring them with you if you're away from home. At the same time, some people don't mind taking a daily pill (or already take other pills daily anyway) but hate the idea of adding any more doctor visits to their schedule. Since both pills and injectables are safe and effective when taken appropriately, it's okay to choose based on which will work best for you. PA

FINN SCHUBERT, MPH (*he, him*) is a writer, consultant and former HIV program director living in New York City.

NEW POSSIBILITIES

Snapshots of HIV prevention and treatment drugs under development

BY **ANIRUDDHA HAZRA, MD**

The landscape of HIV treatment and prevention has been revolutionized by the emergence of long-acting drugs. Since 2021, we have had long-acting injectable anti-retroviral therapy (ART) and pre-exposure prophylaxis (PrEP) agents approved for use by most people living with or vulnerable to HIV, respectively. Cabotegravir/rilpivirine (Cabenuva) for treatment and cabotegravir (Apretude) for PrEP can be administered by intramuscular injection at monthly or bi-monthly intervals. Just as the introduction of single-tablet regimens transformed and challenged our perception of HIV treatment nearly two decades ago, these long-acting agents are doing it again, and it's only the beginning. Several other medications are working their way through the drug development pipeline with the goal of providing our communities what they have long been asking for—multiple options and modalities that align with our individual needs to promote care engagement for all people impacted by HIV.

Lenacapavir

Lenacapavir (Sunlenca) belongs to **a new class of drugs called capsid inhibitors that work by stopping HIV from replicating at multiple points** of its life cycle. It can be administered by subcutaneous injection every six months and is being studied for both HIV treatment and prevention. As it is given subcutaneously (just beneath the skin), lenacapavir has the potential to be self-administered. This, in addition to its twice-yearly dosing, makes it a very exciting option that bypasses many of the constraints noted with Cabenuva and Apretude—mainly their need for patients to attend injection appointments at a clinic or infusion center every two months.

Lenacapavir was approved for use in December 2022 for treatment-experienced adults with multidrug-resistant HIV who are unable to maintain virologic suppression on their current regimen. However, lenacapavir cannot be given on its own for treatment—it needs to be combined with an optimized ART regimen. This would typically require other oral drugs; however, there is a study proposed to the AIDS Clinical Trials Group to examine lenacapavir with long-acting cabotegravir in people with drug resistance. If proven to be successful, this combination of treatment would have a global impact. The World Health Organization (WHO) estimates 10% of people living with HIV worldwide carry resistance to non-nucleoside reverse transcriptase inhibitors including rilpivirine; this is a dealbreaker to the implementation of Cabenuva specifically in sub-Saharan Africa and Asia. However, a treatment combination of lenacapavir and cabotegravir would provide a scalable long-acting ART option for the world.

COURTESY OF UC MEDICINE

Lenacapavir for PrEP

After showing promise in early clinical trials, lenacapavir has entered two large Phase 3 trials evaluating its use as PrEP. As a Phase 3 trial, **researchers will work to confirm lenacapavir's effectiveness in preventing HIV**, monitoring its side effects compared to commonly used PrEP drugs in large groups of people.

PURPOSE 1 is evaluating the safety and efficacy of lenacapavir compared to oral emtricitabine/tenofovir (brand name Truvada) in preventing HIV infection in adolescent girls and young women.

PURPOSE 2 is a similar study assessing the safety and efficacy of lenacapavir as PrEP in cisgender men, transgender men, transgender women and nonbinary individuals vulnerable to HIV. Positive data from these trials would support FDA approval for lenacapavir as PrEP.

The availability of a twice-yearly, potentially self-administered option for PrEP would be a game changer for the field of HIV prevention in our ongoing efforts to de-medicalize PrEP and improve its accessibility to people who need it the most.

Islatravir

Islatravir belongs to **a new class of drugs called nucleoside reverse transcriptase translocation inhibitors that work by stopping reverse transcription, a key stage in HIV replication**. It has been studied in both treatment and prevention through multiple modalities including daily oral pill, weekly oral pill, monthly oral pill and ultra-long-acting drug-eluding implant. Islatravir was undergoing multiple studies as options for both long-acting treatment and long-acting prevention until trials were placed on hold in 2021 due to declining CD4 counts and total lymphocyte counts (TLC) observed in both its treatment and prevention trial participants. After looking at these cases closely, it was determined that this was likely a side effect of using too high a dose of the drug. The lower doses that were also being studied were not associated with this side effect.

A Phase 3 HIV treatment study evaluating a daily oral regimen of islatravir at a lower dose with doravirine (Pifeltro) has resumed in people living with HIV. Regarding its long-acting formulation, an early Phase 2 HIV treatment study has been initiated evaluating the safety and efficacy of islatravir in combination with lenacapavir as a once-weekly oral ART regimen in virologically suppressed people with HIV. If shown to be safe and effective in this smaller trial, once-weekly oral islatravir and lencapavir will proceed to a larger Phase 3 study.

Unfortunately, the future of long-acting oral islatravir for PrEP is much less certain. Many see this option as dead in the water since the study examining monthly oral islatravir as PrEP has been formally discontinued with no future studies looking at lower-dose islatravir for HIV prevention planned.

Islatravir for PrEP

However, an islatravir-eluding subdermal implant has completed a Phase 1 study in which researchers determined its potential as an effective and well-tolerated PrEP modality. **Data show that the islatravir implant could provide protection from HIV-1 for longer than a year, comparable to long-acting reversible contraceptives** (LARC). A Phase 2 study examining the islatravir-eluding implant for PrEP has been announced. Of note, the islatravir implant is based on the design used for [the LARC] Nexplanon and can be implanted by the same device. This sets up a future in which long-acting PrEP and LARC can be co-administered; prioritizing co-location of PrEP and reproductive services is critical to bridge the PrEP gap in cisgender women and other individuals of childbearing potential.

Broadly neutralizing antibodies (bnAbs)

Broadly neutralizing antibodies (bnAbs) are another newer category of HIV drugs. They are actively being studied for both treatment and prevention. These **antibodies target a part of the virus that does not change or mutate very much** and should remain effective for most people with HIV. Similar to neutralizing antibody therapy used to treat COVID-19 and RSV, bnAbs bind to the virus to effectively stop HIV replication and its spread.

There is a Phase 2 HIV treatment study examining the safety and efficacy of two bnAbs in addition to lenacapavir dosed every 6 months in virologically suppressed people with HIV. Initial Phase 1 data demonstrated that 90% of participants who transitioned to this regimen of two bnAbs with lenacapavir remained virologically suppressed at six months, showing promise in a twice-yearly ART regimen.

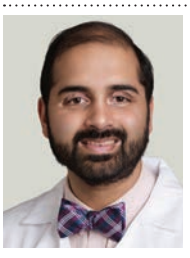
bnAbs for PrEP

Data for bnAbs in HIV prevention are a bit more disappointing. Two large Phase 2 PrEP studies found that use of a single bnAb did not prevent HIV acquisition, but the **study data did provide proof-of-concept that bnAb prophylaxis could be effective, and may need to be used in combination with other bnAbs**. There are several Phase 1 studies evaluating the safety and tolerability of multiple bnAbs administered together. Pending these results further trials studying combination bnAbs as PrEP may occur.

Future directions and lessons learned

This is an incredibly exciting time for HIV treatment and prevention; in addition to these new drug classes, there are many more long-acting modalities in early stages of development. These include drug-eluding implants for a variety of agents, including dolutegravir, which have the potential to work for a year if not longer.

However, inequities seen in access to existing HIV treatment and prevention options will only be magnified with the approval of these long-acting agents if we don't have reductions in prescription drug costs. The pricing of the only approved long-acting PrEP drug, Apretude, has been shown not to be a cost-effective option for PrEP. This impacts drug coverage by both private and public payors, ultimately placing it out of the reach of populations most impacted by HIV. We must ensure newer options are made available at scale with consideration of drug pricing and community-informed implementation. Doing so enables long-acting HIV treatment and prevention strategies to reach the people who need them and shortens our distance to ending the HIV epidemic.



ANIRUDDHA HAZRA, MD, is an assistant professor at the University of Chicago's Section of Infectious Diseases and Global Health and serves as a clinical ambassador for the CDC's *Let's Stop HIV Together* campaign.

Freedom to choose

Three public health experts show us what we need to succeed

BY **RUPA R. PATEL, MD, MPH**; **KIRK GRISHAM, MPH**; AND **JUNE GIPSON, PHD**

Long-acting injectables represent a transformative advancement in HIV prevention. However, for that transformation to be realized, we must first address emerging and longstanding barriers to HIV prevention that limit access to these new modalities. POSITIVELY AWARE convened three national experts—**Rupa R. Patel**, **Kirk Grisham** and **June Gipson**—with varied expertise and experience to explore the importance of long-acting injectable cabotegravir for PrEP, the policies needed to increase access, lessons learned from oral PrEP programs and other critical considerations for scale-up. Patel has over 15 years' experience in clinical medicine, research and public health program development in HIV prevention and is affiliated with Washington University in St. Louis. Grisham is a social science researcher and policy analyst with over 10 years' experience in academic- and community-based public health settings. Gipson is the president and CEO of My Brother's Keeper, Inc. and has worked in public health for over 20 years, guiding the establishment of Mississippi's first LGBTQ+ primary healthcare clinic.

What is important about long-acting injectable cabotegravir PrEP?

KIRK GRISHAM: What strikes me as important about long-acting PrEP is that this new modality offers users a real choice, between daily pill taking and an injection every couple of months. For some, such as those who find adherence to ongoing pill taking challenging and folks who are unstably housed, this is a PrEP option that may be especially helpful.

JUNE GIPSON: As Kirk mentioned, the primary game-changing attribute of these injectables is their extended dosing intervals. Patients no longer need to remember a daily pill, significantly reducing pill burden. This not only enhances convenience but can also improve adherence, making it a pivotal development in the ongoing effort to prevent HIV. Just as the evolution of HIV treatment to a single pill and the introduction of PrEP in 2012 revolutionized access and utilization, long-acting injectables further elevate this progress, aligning with the fast-paced and technologically advanced world we inhabit.

RUPA PATEL: Long-acting injectable PrEP represents a shift in how we, as a healthcare ecosystem, can better support retention and adherence by engaging in directly observed therapy (DOT). It holds promise for those who face pill stigma or forget their pills. When a PrEP client reports they desire taking a pill every day but cannot, this may help. Cabotegravir (name brand Apretude) is highly efficacious, has minimal side effects, is taken every two months and may evolve into an even better product. For instance,

at some point we may be able to inject fewer doses over a year, we could evolve to smaller dose volumes and we may be able to administer the injections in multiple sites on the body so it can be given by partners or oneself.

Describe the current barriers to implementing long-acting cabotegravir for PrEP.

GIPSON: There are multiple challenges despite its promising potential. First and foremost, the cost is a significant hurdle. Cabotegravir is prohibitively expensive. If insurance companies don't provide coverage or only offer limited coverage, many people may find it unaffordable. Furthermore, the healthcare landscape in the South and other areas of the U.S., with vast rural areas, poses another challenge. Due to a shortage of primary care providers in numerous regions, many people already grapple with accessing basic healthcare, let alone injectable PrEP.

PATEL: For this product to have so many advantages, national rollout has been rather slow. This is due to several intersecting things, including complex workflows related to insurance-related coverage and paperwork, insurance reimbursement, organizational financial risk for medication purchases, logistics related to medication shipment and documentation and appointment scheduling. The need for a properly trained workforce to deliver the injections, overall staff shortages and prescriber awareness and comfort also come into play. Community awareness and comfort with the intervention remain challenging.

GRISHAM: As June and Rupa mention, one of the biggest barriers to implementation, and future long-acting PrEP, is capacity. Administering this is a heavy lift. For many sites already doing this work, there is a single "champion" making sure all moving parts are working to ensure people get their shots. What happens if this single champion leaves? It's not sustainable. We really need to develop policy solutions that reduce provider burden, among other things!

What policies are needed to accelerate implementation of cabotegravir and future long-acting options for PrEP?

PATEL: We need to empower trained professionals to deliver it in locations outside of traditional clinic settings. Policies need to focus on task shifting so an array of professionals who are not doctors or nurses can perform intramuscular injections. We need to be able to deliver this product, nationally, as a billable service in community settings, mobile vans, pharmacies and street locations by trained peers to reach those who are largely left out of PrEP services. Insurance and other kinds of coverage must include laboratory tests and staff time as well as the medication.

GRISHAM: Rupa is spot on. Long-acting injectable PrEP should be a billable service in a variety of settings. A lot of us are talking about the de-medicalization of PrEP, which is critical, but we also need to talk about de-stigmatization and undoing the siloing of HIV-related services. In terms of policy, we need the PrEP shot to be as accessible as a flu or COVID shot. I live in Washington D.C. and when I wanted my flu shot and my COVID booster, I was able to walk 10 minutes down the street and get both without delay. Granted, cabotegravir cannot be as easily administered as these vaccines, but people are working on adapting its administration, and we could soon have a long-acting injectable version of PrEP that will be administered subcutaneously (lenacapavir). The communities most impacted by COVID are often also impacted by HIV. It makes sense to integrate these services.

GIPSON: To effectively reduce barriers across the U.S., several policy interventions are imperative. Firstly, a key concern is limited healthcare access in many states. Addressing this requires the expansion of Medicaid. Without Medicaid expansion, a significant portion of a state's population has no healthcare coverage, leading to reduced access to essential services, including HIV prevention and care. However, even if Medicaid were to be expanded, many folks face a dearth of healthcare professionals, particularly those specialized in HIV. As a remedy, more policies should be crafted to incentivize healthcare professionals to provide HIV services in underserved regions. Such incentives might include loan forgiveness programs, tax breaks or competitive compensation packages.

Equally vital is the need to bolster public awareness about HIV. Comprehensive campaigns that educate residents about HIV prevention, testing and treatment options, including injectable PrEP, should be launched. Collaborating with community leaders, religious figures and influential personalities in the state can help in shaping public opinion and reducing HIV stigma.

What do we need to consider from the PrEP user perspective?

GIPSON: From the user's perspective, several factors play a pivotal role in the acceptance and sustained use of injectable PrEP. Foremost is accessibility. If the medication is marketed as a breakthrough but remains out of reach, due to insurance constraints or a provider shortage, it can breed distrust. This can dampen enthusiasm, hindering the adoption of this new intervention. Equally significant is the method of administration: injections. It's crucial to gauge the community's comfort level with receiving regular injections. While the idea of forgoing a daily pill may seem appealing to some, it introduces a different kind of inconvenience. Users would need to make regular visits to a clinic for their injections. In states like Mississippi, where transportation can be a significant challenge, this could be a deterrent and especially burdensome in rural areas, where clinics may be few and far between. The logistical challenges of frequent clinic visits need to be weighed against the benefits. Taking these considerations into account helps ensure injectable PrEP programming resonates with users' needs and concerns.

PATEL: PrEP users also have different needs and desires over time. We must offer choices at each visit. People may want to switch between oral, injectable and other future options. We must build PrEP services around the ability to offer PrEP choices.

GRISHAM: Exactly! Similarly, not everyone is going to want to receive PrEP in a de-medicalized context. For some, traditional forms of engagement with a doctor in a clinic is preferred. For others, there may be more interest in hybrid models, perhaps doing a telehealth visit and then receiving their injection in a secondary space by a traditional provider. What is most important is that we increase user agency and autonomy so there is choice when it comes to engaging their provider on how their PrEP is administered. We want to provide multiple points of entry for the diversity of prevention users.

How to apply the lessons learned from current oral PrEP programs to long-acting options?

GRISHAM: Some of the most promising oral PrEP programs involve telehealth and/or pharmacies to deliver PrEP. Telehealth has a role in the rollout of injectable PrEP, but there is still the matter of administering the injection. One of telehealth's greatest strengths is the ability to engage with PrEP users who may not have access to a brick-and-mortar provider. There is a critical need to build up networks of sites connected to telehealth that can administer injectable PrEP, including pharmacies.

PATEL: We must build PrEP injection programs inspired by the community-facing oral PrEP programs that encompass one-stop, same-day, hybrid/telehealth, self-collection lab kits, delivery in diverse settings (e.g., homes, vans, pharmacies

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FROM LEFT: **JUNE GIPSON, PhD**, is the CEO of My Brother's Keeper, Inc. **KIRK GRISHAM, MPH**, is an associate with the O'Neill Institute for National and Global Health Law, Georgetown University Law Center. **RUPA R. PATEL, MD, MPH**, is a research associate professor of medicine (Voluntary), Division of Infectious Diseases, at Washington University in St. Louis.

or other community locations) and provision by a varied workforce (e.g., pharmacists, medical assistants, trained peer workers and nurses). We must develop user-focused programs that combat stigma, medical mistrust, discomfort, cultural insensitivity and product misinformation. Today, we still have some provider discomfort with oral PrEP and we need to continue to address this barrier and incorporate injectable PrEP in skills-based education for providers. PrEP has been an important gateway to care and other services that foster overall well-being. Therefore, all types of PrEP provision must be developed in tandem with provision or referrals to an array of services including mental health, substance use, food and housing, employment, insurance, legal, vaccination and primary care.

GIPSON: Successfully including injectable PrEP into PrEP programming involves not only logistical changes but a deep understanding of the needs and concerns of healthcare providers and clients. Healthcare providers need thorough training regarding injectable administration, its distinct advantages, potential side effects and monitoring protocols.

On the client front, clear communication about the distinctions between the kinds of PrEP are crucial. This includes discussing the convenience of fewer doses with injectable PrEP against the commitment to periodic injections, which can be a decisive factor. Healthcare providers should have a system in place that not only monitors the well-being of patients on injectable PrEP, but also collects their feedback. This allows for real-time adjustments based on client experiences. The role of case management is central. Case managers can assist with adherence to injection visits by tracking clients' injection schedules, offering reminders and addressing concerns. Lastly, while injectable PrEP is an innovative addition to HIV prevention services, and it might be a game-changer for many, it's not a one-size-fits-all solution. Some might find oral PrEP more suitable or may prefer it in certain life stages or circumstances. Recognizing and respecting client choice must remain at the heart of successful and sustained prevention strategies.

Are we re-medicalizing PrEP by incorporating an injection? How do we de-medicalize prevention?

GRISHAM: I think this is an important question. PrEP advocates have been making great strides to decrease barriers and increase access to HIV prevention for oral PrEP. Provider administered prevention, on the other hand, relies heavily on medical systems. Yet if we see de-medicalization as a continuum, we can push for models in and outside of the clinic that decrease barriers and de-medicalize injectables. These may be hybrid models where telehealth is used to prescribe and a brick-and-mortar location is used for administration, or even at-home delivery/administration. Pop-up testing and vaccination as well as mobile clinics were crucial to the COVID response and will be critical to de-medicalized models for injectable prevention.

PATEL: Introducing injections, and other future forms of injections and implants, have the potential to "medicalize" PrEP. We need to be hyperaware of building programs that involve peer community staff, safe spaces and welcoming environments. We also must move injection delivery out of the conventional clinic setting and closer to where PrEP users are—e.g., homes, shelters, bars, meet-up venues, stores, HIV/STD testing locations and other community areas. We can learn a lot from global medicine programs in Africa and South Asia, and look at family planning injections, voluntary male medical circumcision and various maternal and child health programming which have successfully de-medicalized complex care to better serve communities.

GIPSON: De-medicalizing access to injectable PrEP, while a promising approach in certain contexts, faces significant obstacles across the U.S., particularly in southern states. Primarily, the challenges lie not just in the administration of the medication but in the broader healthcare infrastructure. Many states grapple with pervasive insurance issues; many residents lack adequate coverage, and even if access to injectable PrEP were simplified, the cost barrier remains insurmountable for many. Moreover, the shortage of physicians, particularly those specialized in HIV, exacerbates this challenge. Simplifying who can administer the injection, while logical, doesn't address the root problem. If patients can't afford the treatment or don't have easy access to healthcare due to various constraints, the change in administration doesn't fundamentally shift the accessibility paradigm. Without addressing the core issues of insurance coverage and the lack of healthcare providers, the move to de-medicalize PrEP administration in Mississippi might be akin to putting a band-aid on a deeper wound. PA

GIPSON: BRANDON HOLMES

GUEST CO-EDITOR'S NOTE

Jim Pickett

Beyond injectables

Way back in the mid-'90s, I tested positive for HIV and started writing about my experience for a pre-internet Chicago queer zine called *Babble*, and then called *Gab*—not to be confused with current online platforms using these names. POSITIVELY AWARE associate editor Enid Vázquez, a force of nature who has been with the magazine literally forever, took notice and charmed me into writing a semi-regular column for the magazine featuring my ramblings, bloviations and screeds cleverly called "Pickett Fences."

What a treat it has been, then, to be brought back into the cozy, warm folds of POSITIVELY AWARE and to collaborate with editor-in-chief Rick Guasco and guest co-editor Kenyon Farrow on this very special issue.

Before I could pronounce the word "microbicide" I got hooked on HIV research that was exploring novel ways to prevent infection. In 2005 I co-founded a global advocacy network called IRMA to demand greater investment into the development of rectal microbicides—products such as lubes or douches that could prevent HIV right where the action is for people who enjoy booty sex.

And there are a lot of us!

While we have learned that delivering an HIV prevention drug via "booty butter" (lube) is probably never going to make it to prime time, I am doing cartwheels and high kicks (in my mind) knowing that the HIV Prevention Trials Network (HPTN) is moving forward a rectal douche concept that pairs hygiene and ARV drugs into a potential new, "behaviorally congruent" means of HIV prevention. It's a fabulous idea that has been studied for years by visionaries at Johns Hopkins led by Dr. Craig Hendrix, and I am hopeful that the Phase II study the HPTN will launch in 2024 leads to efficacy studies and licensure and super deluxe rectal douches that prevent HIV and leave you feeling clean as a whistle, in every bathroom cabinet.

When I tested positive in 1995, I thought I had 10 years left. Almost three decades later, I am still here—thanks, science and yes, thanks to pharma as well. The world has witnessed dramatic improvements in HIV treatment, and in the last decade plus we have revolutionized HIV prevention—never again will condoms be our only choice to prevent the sexual acquisition of HIV.

Today we have options for both treatment and prevention that involve a handful of injections every year—no pills—and there are improved injectable modalities undergoing rigorous development. There are also long-acting pills, implants, films, and yes, rectal douches in the research mix.

Choice is the name of the game

I've long been a vocal critic of the NIH's research agenda, which has devoted most of its HIV prevention research dollars into studies developing systemic, long-acting, longer-acting, and even longer-acting-still drugs and delivery systems that attempt to remove the messiness and irrationality of the human condition from the equation. For me, the focus is too narrow, the focus removes individual agency, the focus limits true choice. The focus also falls prey to magical thinking, as if a fancy new injection will make everything better. LOL. As if.

That said, I love that we have options that provide protection for long periods of time that don't require daily behaviors. I love that we have options that mean people living with HIV don't need to be tethered to their pillbox forever and ever. Talk to me when we have a treatment shot that can be given twice a year, or less, and I will be first in line.

But everything can't be about longer and longer-still when we imagine the future of HIV prevention. We need prevention options that are short-acting, we need prevention options that don't require a trained clinician to deliver, we need prevention options that stay where you put them—where the action is and nowhere else. Not all HIV-negative people who are seeking options to maintain their sexual health want drugs coursing through their entire bodies for long periods of time when they could have drugs exclusively focused on their front or back doors—where sexual transmission actually occurs—for limited and discrete amounts of time, determined by the individual.

It is imperative we collectively demand a robust choice agenda. Such an agenda considers different drugs and delivery modalities and doesn't defer to only long-acting and systemic options. We must have an equity-focused, community-led agenda that recognizes the diverse needs of a wide array of races, genders, sexual identities, sexual preferences, ages and communities; that recognizes human rights and bodily autonomy; that places a premium on pleasure and that truly listens. We need fulsome implementation choices ("differentiated service delivery") and we need to banish once and for all the shiny-new-thing phenomenon (magical thinking) that seems to come along with any new technology.

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It is imperative we hold governments, other funders, the research establishment, pharma, organizations, policy makers, program implementers, advocates and each other accountable for this choice agenda. And we need to do this work with equal amounts integrity, vigor, savvy, resilience, perseverance, courage and thick skins.

Are you with me?

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