OVERVIEW

The treatment landscape for prevention and management of patients with HIV continues to expand and provides patients with the option for novel therapies ranging from robust single-tablet regimens to 2-drug treatments, and now, long-acting agents. Despite extensive progress in prevention and management of HIV, the COVID-19 pandemic disrupted the delivery of many advances. Although the pandemic paved the way for the rapid adoption of telehealth, it further highlighted disparities among those living with HIV. Four case studies are discussed in this activity by Melissa Badowski, PharmD, MPH, and Monica Gandhi, MD, MPH, that provide insight on challenges encountered in everyday clinical practice. Their discussion highlights recent clinical advances in the use of antiretroviral therapy and preexposure prophylaxis, the role of telehealth in HIV services, and approaches to overcome health disparities. Join Drs. Badowski and Gandhi for this active dialogue to partake in a practice-based update on treatment and prevention services for patients with HIV in the era of COVID-19.

TARGET AUDIENCE

This activity is intended for HIV specialists, infectious disease specialists, primary care physicians, nurse practitioners, nurses, and other healthcare professionals who care for persons living with HIV.

LEARNING OBJECTIVES

- List the challenges in accessing HIV care in the face of the concurrent COVID-19 pandemic
- Discuss the impact of the COVID-19 pandemic on adherence to HIV treatment
- Identify opportunities to reduce health disparities for patients living with HIV by improving HIV care delivery
- Develop individualized HIV care plans for patients living with HIV that reduce disruptions to care, while optimizing newer treatment strategies

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CE INFORMATION

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Editor's Note: This is a transcript of a webcast presented in February 2022. It has been edited and condensed for clarity.

Case 1 Question 1

Case background

CS, a 35-year-old with newly diagnosed HIV, presents for rapid initiation of antiretroviral therapy (ART).

They previously took tenofovir alafenamide/emtricitabine daily for 1.5 years for preexposure prophylaxis (PrEP). During the COVID-19 pandemic, CS had intermittent follow-up for PrEP due to anxiety of being exposed to SARS-CoV-2. They also report unstable housing.

Their past medical history includes generalized anxiety disorder (prescribed lorazepam 0.5 mg twice daily as needed), hypertension (prescribed lisinopril 40 mg daily), and previous substance use disorder (last use 7 years ago).

Laboratory results reveal:

CD4	492 cells/mm^3
HIV-1 RNA	pending
HIV-1 genotype	pending
HLA-B*5701	pending
SCr	0.9 mg/dL
AST/ALT	25/27 U/L
HAAb	pending
HBsAg	pending
HBsAb	pending
HCVAb	pending

Question 1

Which of the following factors may be a barrier to adherence to ART in CS?

a. History of substance use disorder
b. Hypertension
c. Low baseline CD4 count
d. Generalized anxiety disorder

Answer rationale

The correct answer is **D**.

- Factors associated with poor ART adherence include uncontrolled psychiatric disorders, unstable housing, neurocognitive impairment, active substance use disorder, side effect concerns, nonadherence to clinic visits, and unfavorable social circumstances.[1] Other factors include food insecurity, poverty, lack of access to medical care, unstable insurance, and concerns regarding adverse effects.
- Although numerous barriers to ART adherence exist, they should not be seen as a barrier to initiating ART.[1]
- An interdisciplinary RAPID start model in an urban safety-net clinic with high rates of mental illness, substance use, and housing instability demonstrated that immediate initiation of ART (at first visit after diagnosis) was associated with > 90% virologic suppression based on last viral load after a median of 1 year of follow-up.[2]
- Similarly, data from the POP-UP program (from the same urban clinic) provided a clinical model to reduce barriers to accessing HIV care in patients who were homeless or had unstable housing. All patients had substance use disorder and 77% also had a mental health diagnosis. More than 75% restarted ART within 7 days of enrollment, 91% returned for a follow-up visit within 3 months, and 55% achieved virologic suppression at 6 months (all were unsuppressed at baseline).[3]
- Despite substantial advances in prevention and management of HIV achieved prior to and during the concurrent COVID-19 pandemic, patients were met with reduced access to and utilization of services for the prevention and treatment of HIV.[4] Virologic suppression rates decreased during the COVID-19 pandemic in urban clinics,[5] but preliminary data demonstrates that the rates of virologic suppression improved with concerted efforts to see patients via in-person care.[6]
- A recent modelling study found that deaths due to HIV could increase by up to 10% over 5 years, compared with if there was no COVID-19 pandemic, with the greatest impact estimated to be from interruption to ART that could occur during a period of high health system demand.[7]

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Faculty Comments

Monica Gandhi, MD

I thought we could discuss some of the barriers here for adherence.

One thing I would say is that the patient currently doesn't have substance use disorder, but that's a huge barrier to adherence, and it's been really challenging during COVID, with a lot of substance use and relapses. That the patient currently doesn't have substance use disorder. That mental illness and housing and food insecurity are huge barriers to adherence that we see in San Francisco at San Francisco General and our practice, and I was wondering about what are some of the barriers that you see to adherence? Probably the same?

Melissa Badowski, PharmD

A lot of patients, during the COVID pandemic, didn't want to access healthcare because they were almost fearful of, if they had to be on public transportation, that was a lot of their only way of accessing us. It wasn't necessarily only that we saw those barriers, but we also saw barriers to stopping treatment. We had a lot of rapid restarts within our population. For us, first and foremost, it's going to be a lot of the mental health disorder/illness that has been a barrier, but then also housing instability has been very high prior to and during the current pandemic.

Monica Gandhi, MD

I totally agree that everything seemed to worsen during this time and it really is these structural determinants, housing, there is food insecurity, there is increase in substance use, fear of going to the medical system. And then there's just literally the stigma of taking a pill every day, if you're living with other people—this particular patient had housing insecurity—you may not want to pull out that preexposure prophylaxis (PrEP) pill and show people. And there is stigma and shame and everything else that has goes into adherence problems. Generalized anxiety disorder in this particular patient led to concern about taking preexposure prophylaxis and now the concern is that these factors would contribute to poor antiretroviral therapy (ART) adherence. In this case, we really have to think about poverty and lack of access to medical care, unstable insurance, all of these other factors that are leading to ART adherence, but that never should be a barrier to starting ART and, in fact, in our program at Ward 86, which is we service essentially a publicly-insured population, so usually MediCal, which is Medicaid, Medicare or even no insurance. We're a municipal healthcare system, so it is a very vulnerable population. We started a rapid program in 2013 where we tried to get people who had been newly diagnosed in the city of San Francisco to get to our center. We would give them an Uber car to get them over to San Francisco General and try to start rapid ART on the same day. We performed an evaluation of our program and were really heartened to see that a lot of people, even with all of these adherence barriers, wanted to start ART on the same day of a new diagnosis, like this patient, because it led you to get a new diagnosis on a day and, by the end of the day, to have something to do about it. All of that counseling about how ART is so life-saving, how you can have a normal life span if you take these pills every day, and it takes a life-altering diagnosis and changes the equation for patients by the end of the day. We had really high adherence to our rapid ART program and at a median of 1 year out at Ward 86 from starting people, again with all of these concomitant challenges, on rapid ART, we still had 96% virologic suppression in our rapid ART program.

It was really heartening. And a lot of our patients are marginally housed, like you said there in Illinois as well, because we have, especially over these last couple of years, there's been problems with housing. We started up a program called the POP-UP programme which is for the homeless, a program for people living with human immunodeficiency virus (HIV) and marginal housing. We make it really low barrier for them to come in. We don't make appointments. We just have every afternoon totally free for them to drop in anytime if you're in the POP-UP programme to see the same group of providers and help support their adherence on ART. Even though people in the POP-UP programme started without any virologic suppression, about a year out we had a 55% virologic suppression rate. So, not certainly as high as we want, but better than where we started.

The other thing I wanted to mention about this is that there's been an incredible setback in HIV outcomes during the COVID pandemic and there was a recent modeling study that found that deaths due to HIV unfortunately could increase by up to 10% over 5 years because of the COVID pandemic. And I feel that for you and I, as HIV providers, this is the time to take back HIV, take back this focus on HIV around adherence, testing, all of our goals of ending the HIV epidemic and get back into it as the COVID pandemic becomes more manageable.

Melissa Badowski, PharmD

All of the progress we made took a step back and we need to catch up and move on forward with it.

Case 1 Question 2

Case background

CS, a 35-year-old with newly diagnosed HIV, presents for rapid initiation of antiretroviral therapy (ART).

They previously took tenofovir alafenamide/emtricitabine daily for 1.5 years for preexposure prophylaxis (PrEP) During the COVID-19 pandemic, CS had intermittent follow-up for PrEP due to anxiety of being exposed to SARS-CoV-2. They also report unstable housing.

Their past medical history includes generalized anxiety disorder (prescribed lorazepam 0.5 mg twice daily as needed), hypertension (prescribed lisinopril 40 mg daily), and previous substance use disorder (last use 7 years ago).

CD4	492 cells/mm^3
HIV-1 RNA	pending
HIV-1 genotype	pending
HLA-B*5701	pending
SCr	0.9 mg/dL
AST/ALT	25/27 U/L
HAAb	pending
HBsAg	pending
HBsAb	pending
HCVAb	pending

Question 2

Which of the following regimens is most appropriate to consider for rapid initiation in CS?

a. Bictegravir/emtricitabine/tenofovir alafenamide
b. Dolutegravir/lamivudine/abacavir sulfate
c. Doravirine/lamivudine/tenofovir disoproxil fumarate
d. None. CS should wait until they have stable housing

Answer rationale

The correct answer is **A**.

- Rapid initiation of ART is recommended immediately, or as soon as possible, after diagnosis of HIV, regardless of CD4 count, HIV-1 viral load, psychosocial challenges, substance use disorder, or mental illness diagnosis.[1-4] Laboratory tests should be drawn on the day of diagnosis and medications changed if needed but ART still not delayed awaiting their results.
- Due to its lack of transmitted drug resistance and high genetic barrier to resistance, bictegravir, dolutegravir, or protease inhibitor-containing regimens may be considered for rapid initiation of ART before resistance testing is available whereas non-nucleoside reverse transcriptase inhibitors (ie, doravirine) are not recommended in this setting.[1] Abacavir can be used after the HLA-B*5701 testing has returned.
- Data on the use of the 2-drug regimen (2DR), dolutegravir/lamivudine, is beginning to emerge as a potential option for rapid initiation of ART. The STAT study evaluated the feasibility of starting daily dolutegravir/lamivudine within 14 days of HIV diagnosis in 131 participants without the availability of baseline laboratory results (ie, kidney function, HIV genotype, or hepatitis B (HBV) co-infection). Treatment was modified in 8 participants (6%) due to HBV-coinfection (n=5), baseline resistance (n=1), rash (n=1), and participant decision (n=1). Of 131 enrolled participants, 111 participants had an available HIV-1 viral load at Week 24 where 102 (92%) achieved a viral load of less than 50 copies/mL.[5]
- Rapid initiation of ART is recommended to increase utilization of ART, linkage to care, and decrease time in achieving viral suppression.[1-4,6,7]

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Faculty Comments

Melissa Badowski, PharmD

We recommend starting antiretroviral therapy as soon as possible after diagnosis. The traditional definition for rapid start is still within 14 days of diagnosis, but we want to move towards that more immediate start within the day of. This is irrespective of CD4 count, any psychosocial challenges, active or even past substance use or psychiatric illness. What we're using in our clinics are those that have higher genetic barriers to resistance, especially those anchor drugs, the second-generation integrase inhibitors. Bictegravir, dolutegravir and then pairing that with that traditional nucleoside reverse transcriptase inhibitor (NRTI) backbone. We can consider using protease inhibitors because they do have higher genetic barriers to resistance. All of those could be potential options for rapid start. It will depend on your model, what you're available to get, what your program offers and we tend to want to give them single-tablet regimens. Sometimes they have to settle for multiple-tablet regimens and we want to be as discrete as possible, but for this answer specifically, we would recommend bictegravir/emtricitabine with tenofovir alafenamide.

Although this one is a preferred option, we are still waiting for that HLA-B*5701 to come back. We could transition them to that if we consider that in the future, but we have to make sure that that was negative before starting. Lower on my list would be doravirine-based therapy because it's a non-nucleoside reverse transcriptase inhibitor (NNRTI), it has that lower genetic barrier to resistance. I would be concerned about missed doses.

Ultimately, we don't want to wait until starting initiation. Our old model of having the patient get their labs, then having them return months later, it's a way to lose the retention and care for our patients that we newly engaged in starting their services. We've all been from the school of thought about these 3-drug regimens and now there is data emerging in the area of 2-drug regimens, specifically with dolutegravir/lamivudine from the STAT study and this is based on a population of 131 people and rapid start was within 14 days, so there was a little bit more room instead of the immediate start. As clinicians, we want to make sure about their hepatitis serologies, we don't have it in this instance. What's their viral load? Because maybe we shouldn't be starting it based off of that package insert recommendation, but what the authors did find is that, out of that 131 patients, only 8 participants had to transition off of a 2-drug regimen from that rapid start with dolutegravir/lamivudine and, at 24 weeks, based off of available data, 92% of people were still virologically suppressed or at least achieved virologic suppression.

Movement for rapid start has really revolutionized antiretroviral therapy. I remember when we wouldn't be able to start somebody in the hospital because we were worried they wouldn't have access to it. But this has really increased the linkage to care and it has also decreased the amount of time, in terms of achieving virologic suppression and hopefully reducing transmission.

What regimen do you use in your clinic typically?

Monica Gandhi, MD

It's a great point about not only the STAT study but also there has been looks at like the DIAMOND study, just looking at even protease inhibitors (PIs) with tenofovir alafenamide (TAF)/emtricitabine (FTC). There's been a whole bunch of studies saying, what should be the first-line regimen? We don't use abacavir off the bat because we're waiting for that HLA-B*5701 and though bictegravir/TAF/FTC is a great option because it has that high genetic barrier to resistance. The way that we just happen to run our program is that we give patients their medication in the clinic, handing it to them even if they don't have insurance. That was a huge part of our rapid program which is to watch them take it and to give them what we call a starter pack of 7 days of medication. Since we ended up purchasing those starter packs and the reason we purchased them is sometimes patients can't get on emergency AIDS drug assistance program (ADAP) right away, can't go to the pharmacy and get them right away, so we thought this would increase adherence. Since we purchased those from clinic funds, we went for a little bit of a cheaper option which is really essentially the same thing. We give them dolutegravir and TAF/FTC. Two separate pills, but it ended up working out to be more cost- effective for us than buying bictegravir (bic)/TAF/FTC. I agree that starting an integrase strand transfer inhibitor (INSTI) and TAF/FTC is the one that makes the most sense while we're waiting to watch for adherence. The dolutegravir/lamivudine (3TC) option, we have been more wary of and waited and

ensured that we thought they had good adherence, especially if they had come off PrEP and failed PrEP because we don't yet know if they have an M184V. We have been a little bit more circumspect about using dolutegravir/3TC right away in our patient population and, if they don't have an M184V and if they do fine on the TAF/FTC and the INSTI, then we often simplify down to dolutegravir/3TC afterwards. We don't start NNRTIs as our first-line regimen with that lower genetic barrier to resistance, so doravirine-based regimens.

Case 1 Question 3

Case background

CS, a 35-year-old with newly diagnosed HIV, presented for rapid initiation of antiretroviral therapy (ART) 3 months ago. They report doing well on ART and deny any side effects, missed doses, or changes to their medications.

Laboratory results reveal:

	Baseline	Last Week
CD4	492 cells/mm^3	551 cells/mm^3
HIV-1 RNA	124,053 copies/mL	< 20 copies/mL
HIV-1 genotype	Wild-type	---
HLA-B*5701	neg	---
SCr	0.9 mg/dL	1.0 mg/dL
AST/ALT	25/27 U/L	21/20 U/L
HAAb	neg	---
HBsAg	neg	---
HbsAb	neg	---
HCVAb	neg	---

CS reports living in a shelter for the past 2 weeks and has increased anxiety about developing COVID-19. Initially, CS was hesitant in taking any vaccine against SARS-CoV-2 infection but reports receiving a vaccine that only required 1 dose 3 months ago when they learned they had HIV.

Question 3

Which of the following vaccine recommendation is most appropriate for CS at this time?

a. Restart the entire COVID-19 vaccine series using either BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna)

b. Receive 2 additional doses of the viral vector COVID-19 vaccine (Johnson & Johnson's Janssen)

c. Receive a COVID-19 booster dose of either BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna)

d. No additional vaccination or booster against COVID-19 is currently needed

Answer rationale

The correct answer is **C**.

- A national survey performed in the US evaluated COVID-19 vaccination rates and attitudes in 496 people with HIV (PWH) between March and May 2021 where 64% received 1 dose of a COVID-19 vaccine. Vaccination was associated with older age, increased length of living with HIV, higher level of education, higher perceived risk of COVID-19 vulnerability, less hesitancy, sexual and gender minority cisgender men and transgender participants, and undetectable viral load.[1]
- Another study interviewed 101 Black Americans with HIV between May and July 2020 where 97% reported at least 1 COVID-19 mistrust belief and just over 50% a vaccine hesitancy belief.[2]
- Many similarities exist between these intersecting pandemics which include how misinformation and denialism can lead to morbidity and mortality and the lag time for interventions to reach vulnerable populations.[3]
- Cohort studies demonstrated the incidence of developing SARS-CoV-2 was similar or lower but large population-based cohorts established a higher risk of severe COVID-19 in PHW. Therefore, vaccination efforts should be prioritized in PWH.[4-6]
- For all adults who received Johnson & Johnson's Janssen vaccine at least 2 months ago or longer, individuals should receive a single dose booster of either Pfizer-BioNTech or Moderna COVID-19 mRNA vaccine.[7]
- With the rapid development of COVID-19 vaccines during the current pandemic, there is renewed hope in the discovery of a vaccine to prevent HIV potentially derived from mRNA technology by triggering an immune response.[8] The first human trial of an mRNA vaccine for HIV has just launched.[9]

- Similarly, advances in antiretroviral therapy for the management of HIV took more than a decade to develop while antiviral therapies (molnupiravir and nirmatrelvir/ritonavir) against COVID-19 took a mere 18 months. Many concepts were borrowed from HIV and its lifecycle by working to prevent viral reproduction.[10]

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Faculty Comments

Monica Gandhi, MD

I thought we could discuss this, since this is such an important part of management for people who live with HIV, and this is vaccination with COVID.

Melissa Badowski, PharmD

One of the things we've seen a lot within our community is vaccine hesitancy. It's like medication adherence. How I approach it is, let's talk about it at each visit if you're not vaccinated at this time. I agree with the single dose adenovirus, we would recommend the option where they would get a messenger RNA (mRNA) dose and they would receive that booster dose. This is something that's definitely evolving every week, every day, every month. In our practice, we would look towards telling them to receive that mRNA vaccine for a booster at this point for the patient so they are maximally making sure that they're covered against the coronavirus.

It's been really interesting to see that heterologous vaccine mixture and what it seems to do to increase antibodies and even T-cell responses. There's something about getting 1 dose and especially when you do the DNA first, followed by mRNA. The National Institutes of Health (NIH) mix-and-match study really showed that that really increased antibody levels to COVID-19. Anyone should be vaccinated, but certainly people living with HIV with lower CD4 counts, we have seen more severe COVID outcomes. We have to be really aggressive about vaccination.

Case 1 Question 4

Case background

Six months later, CS remains undetectable and brings their partner MK to clinic. They are in an open relationship. MK does not have HIV but is interested in starting PrEP. MK denies any symptoms of acute HIV infection, is not on any medications, and has no known drug allergies. MK reports being hesitant in taking a daily medication even though they feel fine.

Seven days later, MK returns to clinic to review their labs. Laboratory results reveal:

	Last Week
HIV Ag/Ab	Negative
HIV-1 RNA	undetectable
SCr	1.0 mg/dL
HAAb	Positive
HBsAg	Negative
HbsAb	Positive
HCVAb	Negative
RPR	Reactive (1:32)
Gonorrhea	Negative
Chlamydia	Positive

Question 4

Which of the following options is the most appropriate to offer MK at this time?

a. MK does not currently need PrEP since CS is undetectable

b. Initiate intramuscular (IM) cabotegravir once monthly

c. Initiate IM cabotegravir once monthly for 2 months, and every 2 months thereafter

d. Provide a 12-month prescription for oral tenofovir disoproxil fumarate/emtricitabine once daily to decrease the number of times MK needs to follow up

Answer rationale

The correct answer is **C**.

- PrEP is recommended in sexually active adults and adolescents who have had anal or vaginal sex in the past 6 months and their sexual partner has HIV (especially if the partner has an unknown or detectable viral load), is diagnosed with a sexually transmitted infection (STI) in the past 6 months, or the individual has inconsistent condom use with sexual partner(s). Of note, although CS has an undetectable viral load, the couple is in an open relationship. PrEP is also recommended in persons who inject drugs and share injection equipment, or their injecting partner also has HIV.[1]
- Oral PrEP with daily tenofovir disoproxil fumarate/emtricitabine or tenofovir alafenamide/emtricitabine (tenofovir alafenamide/emtricitabine: not approved for use in people assigned female at birth who are at risk of acquiring HIV from vaginal sex) or on-demand PrEP with oral TDF/FTC had been the only options for the prevention of HIV infection but long-acting cabotegravir recently received FDA-approval to be given as a single intramuscular (IM) injection every 8 weeks.[1,2]
- Based on data derived from HPTN 083 & 084, long-acting IM cabotegravir was superior to daily oral tenofovir disoproxil fumarate/emtricitabine in transgender women and cisgender men and women in preventing HIV.[3,4]
- Prior to starting long-acting cabotegravir for the prevention of HIV, an individual must be assessed for any signs or symptoms of acute HIV infection as well as have a documented negative HIV Ag/Ab test within 1 week on starting PrEP.
- Long-acting cabotegravir has the potential to reduce gaps in adherence to prevention medications, especially in the setting of the ongoing COVID-19 pandemic by reducing the need to be seen in clinic.

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Faculty Comments

Melissa Badowski, PharmD

PrEP is recommended in adults and adolescents who are sexually active, in somebody who's living with HIV. We know that the U equals U movement, so undetectable equals untransmittable, is where the patient who has HIV and they've been taking their antiretrovirals is very unlikely to transmit any virus to their partner. They are in an open relationship, so we don't know what other partners may be doing and this patient would be a great candidate for starting preexposure prophylaxis in this case.

Historically, we've only been able to do oral PrEP with tenofovir-based therapies and, a few caveats being that with tenofovir disoproxil fumarate and emtricitabine, that's approved in all populations. Cisgender males and females as well as transgender females, but at current time, tenofovir alafenamide with emtricitabine is only approved in cisgender males and transgender females. There is also the on-demand, the 2-1-1, where this is approved with tenofovir disoproxil fumarate and emtricitabine where there are 2 tablets that are taken 2-24 hours before a sexual encounter, 1 pill 24 hours after the first dose and then another pill 24 hours after that second dose. It's only currently been studied in men who have sex with men.

Until recently, patients only had those oral options that were available. Recently, intramuscular cabotegravir has been approved for PrEP and this is in all populations, cisgender males, females as well as transgender females. In fact, intramuscular cabotegravir was actually proven to be superior to oral preexposure prophylaxis based on studies from the HIV Prevention Trial Network 083 and 084.

Prior to initiating PrEP, it's imperative to assess any potential candidates for signs and symptoms of HIV, as well as make sure that we have that HIV-negative test within 1 week prior to initiation. And then make sure to reassess on an ongoing basis. If they're on oral PrEP, we wouldn't want to provide more than a 90-day supply, and we would want to check their HIV status within that 90 days before we renew it. Then for intramuscular cabotegravir, once they're on their regular schedule, it would be every 2 months that we would assess their HIV status.

For this patient, they would be an ideal candidate and based off their patient-specific factors, intramuscular cabotegravir would be ideal where we would start the patient on the intramuscular formulation with that initial dose, followed by 4 weeks later and we would get HIV testing again, and then every 2 months thereafter to make sure that they're testing negative as well.

What's your experience been in people returning to clinic for preexposure prophylaxis? In my population, some people don't return after that initial visit.

Monica Gandhi, MD

It's been really interesting. As you know, intramuscular (IM) cabotegravir just got approved, so we're super excited to start it. We have been using IM treatment, but really just going to start exploring IM cabotegravir for prevention. But in terms of returning to clinic for oral PrEP, we divide it into 2 categories. One is that usually people who are planning and know when they're going to have risk factors for HIV, that's where we're encouraging the 2-1-1 strategy because they know that it's going to be this weekend and they can do the 2-1-1 after a risk factor for HIV. But people who are more spontaneous, don't know when risk factors are going to occur, we encourage daily PrEP, either with TAF/FTC or tenofovir disoproxil fumarate (TDF)/FTC, the latter is the only one approved for vaginal sex. It's been harder during the COVID pandemic. We've been very good about saying, we're going to give you 3-months' supply, you only have to come in every 3 months, or even longer, to check creatinine and your HIV antigen-antibody. We're trying to make it easier for people to not have to come back to clinic and have PrEP for longer, so that will help adherence.

Case 2 Question 1

Case background

AZ is a 68-year-old person with HIV for more than 25 years who is currently taking daily dolutegravir/rilpivirine.

Initially, when the COVID-19 pandemic began, they had difficulty with follow-up due to extended work hours and a long commute on public transportation.

AZ was able to access follow-up HIV care through telephonic telehealth appointments for the last 12 months.

Question 1

Which one of the following was a common challenge that patients with HIV faced during the COVID-19 pandemic while accessing care through telehealth?

a. Obtaining labs

b. Reimbursement for telephone and video encounters

c. Scheduling medical visits

d. Lack of a secure and private connection through recognized telehealth platforms

Answer rationale

The correct answer is **A**.

- Mandates emerged from Congressional House Bill 6074 which allowed for the waiver of telemedicine restrictions, emergency waivers from the Centers for Medicare and Medicaid Services (CMS), and made way for the rapid expansion of virtual healthcare.[1]
- One unanticipated obstacle was having protocols in place to obtain or refer out for labs in people utilizing telehealth services.[2]
- Prior to the pandemic, challenges for reimbursement were often cited as a barrier to telehealth implementation. Due to the emergent need to reduce the spread of SARS-CoV-2 by limiting physical contact, Medicare's 1135 Waiver lifted various telehealth requirements. The CMS increased rates of reimbursement to be on par with video visits.[3,4]
- Ease of scheduling telehealth visits during the COVID-19 allowed for patients to access care with minimal interruptions. Although video is preferred to an audio-only visit, both telehealth modalities were available to retain patients in care.[1,5]
- The use of telehealth through HIPAA-compliant platforms permitted medical care through an encrypted telehealth platform allowing patient privacy to be ensured and maintained. Under emergency provisions, certain platforms were provisionally allowed to provide telehealth (ie, Apple FaceTime, Zoom, Skype, etc) but these applications can potentially lead to privacy risks.[6]

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Faculty Comments

Monica Gandhi, MD

There have been problems and challenges during the COVID pandemic for people living with HIV to access care through telehealth. Different clinics have had different experiences. We specifically were told to do telehealth for our patients when the first shelter in place order came around in March 2020, in San Francisco. We found that we had a pretty split population where there were patients who had access to telephones, who had access to privacy and were able to do telehealth, but there was a large portion of our population, because we do work in the safety net population, that didn't have complete access to phones or a private place to have a conversation with their doctor. We were concerned about their ability to get labs and needing those laboratory testing to see if they were able to take their HIV medications. We went back to in-person care quickly after the shelter in place order in San Francisco for the majority of our patients or anyone who wanted it. We masked, distanced, ventilated the clinic, had no transmissions in the clinic, but we did a lot of in-person care during the pandemic.

Telehealth was an incredibly important thing during the pandemic and I think it's going to last for a while because the Congressional House Bill 6074 allowed for waiver of telemedicine restrictions and emergency waivers from the Center of Medicare and Medicaid Services that allowed this rapid expansion of virtual healthcare. And I'm intrigued to see what ends up happening in our HIV setting as we go forward as the pandemic quells, how much is going to be telehealth, how much is going to be in-person care. In our clinic, we would lose that personal touch of not just the in-person care, but all the social services that were needed during this time.

Case 2 Question 2

Case background

AZ was able to access follow-up HIV care through telephonic telehealth appointments for the last 12 months and has gotten used to this for their medical appointments.

AZ's provider recommends an in-person visit since AZ has been without labs for more than 12 months and has complained about shortness of breath over the past couple of visits.

Question 2

Which one of the following has not been an observed benefit of using telehealth during the COVID-19 pandemic for patients with HIV?

a. Reduced waiting room time

b. Reduced potential exposure to COVID-19

c. Increased perceived access to services

d. Impaired clinical evaluation

Answer rationale

The correct answer is **C**.

- With the spread of COVID-19 came the reduction of in-person hospital and clinic visits and the rise of telehealth visits. The role of telehealth during the COVID-19 pandemic allowed access to care to be expanded, continuity of care to be sustained, and hours of availability to be more flexible. One limitation to telehealth is the inability to perform a physical exam.1 Moreover, some safety-net populations could not access telehealth readily and needed to be converted to in-person care.[2]
- Telehealth reduced travel times to and from the clinical setting as well as waiting room times. Furthermore, telehealth reduced potential exposures to COVID-19 by screening for symptomatic infection.[3]
- Data collected between April and May 2020 from the COVID-19 Disparities Survey assessed the relationship between the stringency of COVID-19 control measures and interruptions to HIV prevention and treatment services. More stringent responses were associated with decreased perceived access to services.[4]
- Additionally, fear of acquiring COVID-19 in healthcare settings discouraged travel and clinic attendance for the management of HIV.[5]

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Faculty Comments

Melissa Badowski, PharmD

For us, the role of telehealth in our population reduced wait times to see a provider, but it also reduced the amount of time a patient spent within the waiting room in clinic. It further reduced any potential exposures to COVID-19 for not only our patients, but also for providers and clinicians. It helped to preserve personal protective equipment (PPE) that was very limited initially. We started to think about alleviating those transportation-related exposures for a lot of our patients who relied heavily on it. That was just one of our benefits of it, but while telehealth helped to bridge care gaps and maintain continuity of care for many, vulnerability for our patient population, especially those who are most vulnerable, were unable to access it reliably a lot of times.

There was a disparity study that was conducted earlier within the pandemic. They demonstrated that the more stringent the response was, this was associated with perceived reduction in access to services. Patients thought there was a negative impact with the stringency of their responses so that they weren't able to access it and if they were vulnerable and did not have reliable internet or even telephone access, they could not receive these services.

Case 2 Question 3

Case background

After AZ's in-person encounter, they request to go back to telehealth like they had previously.

AZ's provider suggests a "hybrid-approach" to their HIV management and suggests using telemedicine where they can see each other virtually in real-time for the next visit. AZ agrees to give this approach a try.

As AZ's follow-up telemedicine visit approaches, they become increasingly more anxious about connecting to the telemedicine platform used by their clinic with their smartphone. AZ has had difficulty paying for Internet services during the pandemic due to irregularity in work hours.

AZ was able to connect with their provider, but the video continued to freeze during the encounter. AZ does not have any other device that they could connect at home. Therefore, AZ is unable to complete their scheduled visit.

Question 3

Which of the following interventions would make it easier for AZ to adopt telemedicine?

a. Provide written instructions on how to connect and troubleshoot any technology issues that may arise 30-minutes prior to the telemedicine encounter

b. Encourage the patient to connect 2 minutes prior to the telemedicine encounter to troubleshoot any last-minute issues that may arise

c. Reduce potential health disparities by informing patients about free or reduced-cost internet options in their area

d. Recommend the patient find a local Wi-Fi hot spot

Answer rationale

The correct answer is **C**.

- Socioeconomic disparities prevent vulnerable populations from truly benefiting from telehealth innovations, creating a "digital divide" that must be breached in order to achieve equitable improvement in health outcomes.[1]
- Various socioeconomic issues & social determinants of health affect telemedicine readiness including income, housing instability, mental health, substance use, education, digital literacy, geography, broadband connectivity, and language spoken.[2]
- One study found that female gender, older age, income below $50,000 per year, and non-English speaking patients were more likely to complete a telephone visit compared to a video visit.[3,4]
- When developing and offering a telehealth intervention, every effort should be made to offer and provide the opportunity to every patient in order to reduce disparities.[5]
- Screen patients on their digital health literacy prior to their visit along with their ability to connect to a video visit (device, ability to connect to the Internet, availability of data, and access to a quiet and private area to conduct the visit).[5]
- Instructions for a successful telehealth visit should be provided in a timely manner prior to a patient's telemedicine encounter in their preferred language with enough time to review (ie, at least 24 hours).[6]
- Patients should be encouraged to connect at least 15 minutes prior to a video encounter to troubleshoot any last-minute issues that may arise.[6]

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Faculty Comments

Melissa Badowski, PharmD

When we think about our patients and who is really going to be the most affected by telehealth and who would benefit from it, we still find that many patients are really intimidated by the prospect of telehealth, especially if it's their first visit. They get anxious, nervous and this is why we really need to make sure that we're preparing patients for this virtual encounter and it can't just be an hour beforehand. It has to be well in advance.

Unfortunately, something that was also realized was the digital divide which has further highlighted socioeconomic disparities that prevent our most vulnerable populations from being able to benefit from the use of telehealth. Some of the factors that we're already well-aware of that really increase that social divide are lower income, unstable housing, and digital health literacy. We think of health literacy as being another potential barrier, but now looking to pair that digital aspect of it. Looking at geographic areas, where a patient resides, if they were in certain areas that didn't have broadband access, that could have negatively impacted if they could have video connection or even reliable connection at all. And then language barriers. How do we make sure that we overcome, if somebody speaks a different language, in providing those resources in the available language, and making sure that translator services are available.

The other thing that I had found is that there's a website that's the National Digital Inclusion Alliance and they provide great resources and information on low-cost or even free broadband plans that are available nationwide. I always encourage people who are saying that they're having issues with connectivity, paying for connectivity, to look at some of these resources and I helped to navigate if a patient would prefer to use telehealth, but they are unable to pay for it or have an area that's secure, quiet, and private.

We really want to look at how can we empower our patients to want to engage in telehealth. We want to reduce the barriers. I think that's the most important aspect of it and, again, providing available instructions in a good amount of time before they're seen so that maybe they can troubleshoot and connect to see would this work for me or not. There are some programs that did a really great job of providing services and it came from the Veterans Administration where they actually provided iPads that were cellularly enabled. This was over 50,000 iPads that were provided to their patients so that they could connect if they were living in a geographically-limited area so that they could get care. This was definitely a great model to use.

There were other programs that University of Michigan has used where they've also provided the opportunity navigate a telehealth visit before it even happens, 1 to 2 weeks beforehand. These are just some of the ways that we can really engage a patient into being able to adopt telehealth. How can we meet them where they are with their digital journey?

Case 3 Question 1

Case background

ES is a 42-year-old person who has been virologically suppressed on daily bictegravir/emtricitabine/tenofovir alafenamide for the past 3 years since diagnosis. This has been their only regimen, has never received PrEP, and CD4 count has consistently been over 500 cells/mm.[3]

In the future, ES is interested in reducing the number of medications taken for the virus but isn't ready to make the switch today.

In addition, ES would like to be able to take antiretroviral therapy more discreetly since they live in a halfway house and are concerned about privacy.

Question 1

Which of the following regimens is most appropriate to consider in ES?

a. Cabotegravir/rilpivirine intramuscularly

b. Darunavir/cobicistat + lamivudine orally

c. Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide orally

d. Doravirine + raltegravir orally

Answer rationale

The correct answer is **A**.

- The paradigm of 3-drug regimens with a dual-NRTI backbone plus an anchor antiretroviral agent is becoming modernized and replaced with 2DR. Long-term data on the safety and efficacy of 2DR in PWH are continuing to emerge.[1-5]
- Oral daily fixed dose 2-drug combinations available as single tablet regimens include dolutegravir/rilpivirine and dolutegravir/lamivudine while the long-acting monthly IM injection cabotegravir/rilpivirine is dosed every 4 weeks.[1-5] The FDA also recently approved IM cabotegravir/rilpivirine every 8 weeks for the treatment of HIV.[6]
- In the ATLAS and FLAIR studies, long-acting cabotegravir/rilpivirine was noninferior to current oral antiretroviral therapy in virologically suppressed participants without treatment failure leading to the development of antiretroviral resistance and no underlying resistance to cabotegravir or rilpivirine.[4,5]

- Long-acting injectables allow for discreet dosing, without food requirements, and once monthly or every 2-month dosing in the healthcare setting.
- Regimens containing PI-based and elvitegravir/cobicistat are recommended to be taken with food which may impair medication adherence and may make taking this medication less discreet. In addition, neither darunavir/cobicistat + lamivudine not doravirine/raltegravir has not been recommended as a first-line regimen. Doravirine + raltegravir is a multiple-tablet regimen with a lower genetic barrier to resistance compared to other options.

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Faculty Comments

Monica Gandhi, MD

This next question is really interesting about 2-drug therapy and specifically cabotegravir/rilpivirine intramuscularly which just got approved last January and a lot of work being done on using long-acting intramuscular every 4 weeks treatment. We had already been going towards 2-drug therapy with the dolutegravir/3TC regimens and dolutegravir/rilpivirine. And this was a natural extension of it. If we're going to be using 2-drug therapy and we have injectable, long-acting pharmacokinetically-stable agents, can we use cabotegravir and rilpivirine intramuscularly either every 4 weeks or every 8 weeks?

It was first approved, cabotegravir/rilpivirine intramuscularly every 4 weeks, and then, just very recently, with the results of the ATLAS 2M study showing that you can go from giving it every 4 weeks to giving it at a higher dose every 8 weeks, now the FDA has approved every 8-week formulations of IM cabotegravir and rilpivirine. The initial ATLAS and FLAIR studies really showed us that cabotegravir/rilpivirine every 4 weeks was noninferior to using oral regimens, usually 3-drug oral regimens in either treatment-naïve or treatment-experienced patients in FLAIR and ATLAS, respectively. And then the ATLAS 2M study, which we now have data from Conference of Retroviruses and Opportunistic Infections (CROI) 2022 out to 152 weeks, shows that after you've been suppressed or you stay suppressed on every-4-week IM cabotegravir/rilpivirine, that you can go to the every 8 week dosing. And virologic suppression rates were kept high.

We started a pilot program for IM cabotegravir/rilpivirine, not just in patients who are virologically suppressed, which would be how the clinical trials were designed. The FLAIR study, you were treatment-naïve, but you had to be virologically suppressed prior to going on the IM cabotegravir (cab)/rilpivirine. And in the ATLAS study, treatment experienced but already were virologically suppressed for at least 6 months before going on to therapy. We have had a group of patients who, in our pilot program, are not virologically suppressed but they really had no other options. They couldn't take oral pills because of multiple reasons, some included just the housing insecurity, using methamphetamine, it just was so difficult for them to take oral pills regularly. We have a very small program that we've been exploring over the last 7 months, where we started a group of patients who have a lot of concomitant challenges to adherence. They didn't start out with virologic suppression, but we went ahead and started IM cabotegravir/rilpivirine every 4 weeks. We have about 25 patients in our clinic total who are on IM cabotegravir/rilpivirine every 4 weeks and 14 of them started without virologic suppression, sometimes even really high viral loads. They couldn't have any rilpivirine-associated mutations. We went ahead and started it. We followed them really closely. We ensured they could come in every 4 weeks for their regimens and about 34% of them were homeless. We've had great success so far. It's a very small pilot program, but all 14 of those who started out virologically nonsuppressed are now virologically suppressed on the IM cabotegravir/rilpivirine. It gives you hope that we may be able to use this for a different patient population.

Melissa Badowski, Pharma

That's what we were hoping for initially when this was approved. This is definitely an area that is very needed for this patient population, especially because they are the most vulnerable and really need the most help.

Case 3 Question 2

Case background

Six months later, ES returns to clinic and is ready to switch antiretroviral therapy. They remain virologically suppressed on daily bictegravir/emtricitabine/tenofovir alafenamide. Together, the decision is made to initiate long-acting cabotegravir/rilpivirine, but ES is concerned with the potential for side effects.

Question 2

Compared to their previous regimen, which of the following side effects is more likely to occur with cabotegravir/rilpivirine?

a. Dyslipidemia
b. Increased serum creatinine
c. Peripheral neuropathy
d. Injection site reactions

Answer rationale

The correct answer is **D**.

- Due to the injectable formulation of cabotegravir/rilpivirine, injection site reactions (ie, local pain or discomfort, nodules, swelling, etc) were commonly reported in patients receiving long-acting cabotegravir/rilpivirine but only 1% led to discontinuation. Most injection site reactions lasted a median of 3 days.[1-4]
- Patient-reported outcomes were collected in both the ATLAS and FLAIR studies for long-acting cabotegravir/rilpivirine. In both studies, > 90% of participants preferred the long-acting injectable formulation over previous oral therapy.[4-6]
- Dyslipidemia, elevations in serum creatinine, and peripheral neuropathy were not reported side effects in clinical trials.[1-6]

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Faculty Comments

Melissa Badowski, PharmD

With our patient they are thinking about switching over to therapy and compared to previous regimens, we start to think about side effects. I know there's always that question, a lot of hesitancy around patients wanting to switch over because they're thinking I already know what I'm experiencing from this regimen, what if I feel something different from a different regimen. That's where it's our job to alleviate those concerns and fears. It is not the bad old days of HIV anymore where there are handfuls of pills and numerous side effects. These medications are amazing in the sense of tolerability and safety for these agents.

While dyslipidemia, increased serum creatinine and peripheral neuropathy were not reported in clinical studies, since this is an injectable, you would expect injection site reactions. In clinical studies, 83% of individuals reported injection site reactions where it was either pain, nodules or swelling near the injection site. The good thing is this went away in about 3 days and it only caused about 1% of individuals to discontinue intramuscular injections. The clinical trials that secured approval for this long-acting medication also collected patient-reported outcomes. That was another thing in previous studies we had never really seen, but when looking at intramuscular injection vs oral therapy, at least 90% reported that they'd rather do this as opposed to oral therapy. This is going to be for certain patients who are interested in switching over, maybe for improving discreetness of taking their therapy.

Other noted side effects were benign and mild. Pyrexia, headache or fatigue was something that was associated with cabotegravir/rilpivirine IM injections, but this is small and pales in comparison to the benefit of the medication. What has been your experience with side effects and patient tolerability with these regimens, the intramuscular particularly?

Monica Gandhi, MD

We have had injection site reactions but they pale in comparison to being able to not take a pill every day and to be able to not think about it for 4 weeks. We will be changing some patients over to every 8 weeks now that we have the ATLAS, the FDA approval to do so. There definitely was more pain at the beginning, but not nodules like we used to get with enfuvirtide, and it's really quite tolerated. One thing which is really interesting is there was a study from the European AIDS Meeting that showed that people with high body mass index (BMIs), the longer the needle you used, the better pharmacokinetics you got in terms of higher cabotegravir levels. Because we have seen some failures in people with high BMI and it could be because you need to get past that initial layer with a longer needle, get into the deeper intramuscular level, and then we saw some higher cabotegravir levels. We have been using a longer 2-inch needle in our patients who have high BMIs of over 30.

Case 3 Question 3

Case background

ES has been receiving the IM injection for more than 6 months without any tolerability issues. Unexpectedly, ES had to travel out of town and missed their injection of cabotegravir/rilpivirine. Their last dose was 5-weeks ago.

Question 3

Which of the following recommendations is most appropriate for ES at this time?

a. Restart cabotegravir 600 mg/rilpivirine 900 mg IM followed by cabotegravir 400 mg/rilpivirine 600 mg IM every month thereafter

b. Resume cabotegravir 400 mg/rilpivirine 600 mg IM as soon as possible

c. Change ES back to daily oral cabotegravir and rilpivirine

d. Resume daily oral bictegravir/emtricitabine/tenofovir alafenamide

Answer rationale

The correct answer is **B**.

- Since the missed injection was 2 months ago or less, long-acting cabotegravir 400 mg/rilpivirine 600 mg IM should be given as soon as possible.[1,2]
- Long-acting cabotegravir/rilpivirine have long half-lives (cabotegravir: 6-12 weeks; rilpivirine: 13-28 weeks). Concentrations may be detected >12 months after the last IM injection is administered.[1,2]
- If the missed injection was more than 2 months ago, the patient would need to re-initiate long-acting cabotegravir 600 mg/rilpivirine 900 mg IM for 1 month, then resume long-acting cabotegravir 400 mg/rilpivirine 600 mg IM monthly, thereafter.[1,2]
- If this had been a planned interruption (ie, planning to miss scheduled injection by >7 days) oral therapy (cabotegravir 30 mg and rilpivirine 25 mg once daily with a meal) can be taken for up to 2 consecutive months. The oral medications should be used until the day the IM injection is restarted.[1,2]
- At this time, it would not be appropriate to resume daily oral bictegravir/emtricitabine/tenofovir alafenamide unless the patient was no longer interested in receiving monthly long-acting cabotegravir/rilpivirine IM injections.[2]

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Faculty Comments

Monica Gandhi, MD

This person had missed a dose and we did resume the cabotegravir. This is really important to discuss about getting it every 4 weeks. Clinical trials did allow some leeway on that. If you looked at FLAIR and ATLAS, they allowed out to 5 weeks for their injection, but if an injection is too long ago, if you missed out to 8 weeks, then we do need to go to the higher dose and reinduce our patients with induction-based dosing which is the cabotegravir 600 mg, rilpivirine 900 mg if you wait too long until your next injection. That's what our protocol is in our clinic, that we allow a certain amount of missed weeks but if it goes too long, out to 2 months, we reinduce them with the higher dose.

If there's a planned interruption, that someone's going to be out of town, they can't come in for their injection, then we give oral bridges to cabotegravir/rilpivirine in between. What we've been doing in our clinic is we don't actually give them the cabotegravir/rilpivirine oral as their oral bridge in between because rilpivirine has a relatively low genetic barrier to resistance and it is 2 pills. We go back to what they were taking before. If they were on a darunavir-based regimen, if they were on dolutegravir/abacavir/3TC, if they were on bictegravir/TAF/FTC, if they really needed oral bridge in between, we usually do a 1 pill, once a day regimen in between for their bridge that has a higher genetic barrier to resistance, and then resume the IM cabotegravir/rilpivirine when they get back from their hiatus.

Melissa Badowski, PharmD

The every-2-months, that's going to revolutionize a lot for these patients. Some of the concern is that you'd have to come in every 2 months to get an injection. The other nice thing is you can pair those visits with a provider visit, but it's also a nice way to check in with the patient. For those who are really motivated to be on this, and who don't have a lot of other options, this will be great and revolutionize the care that they receive.

Case 3 Question 4

Case background

Three months later, ES ends up getting arrested and detained at a county jail. On intake, they remain virologically suppressed and all other labs are within normal limits. The county jail does not carry long-acting cabotegravir/rilpivirine on its formulary and does not have a process in place to obtain or administer it.

Question 4

What is the most appropriate recommendation for the management of ES's virus based on the jail's formulary?

a. Hold antiretroviral therapy

b. Start dolutegravir + abacavir + lamivudine

c. Start darunavir/cobicistat + emtricitabine/tenofovir alafenamide + dolutegravir

d. Start any oral ART regimen the patient prefers and to which his virus is sensitive

Answer rationale

The correct answer is **D**.

- Since dolutegravir + rilpivirine have similar properties and mechanisms of action to cabotegravir/rilpivirine, this could be a comparable ART regimen for the patient; however, any oral ART regimen which the patient prefers and to which the virus is susceptible is appropriate.[1,2]
- Over the course of the COVID-19 pandemic, 1 study evaluated the COVID-related impact on long-acting cabotegravir/rilpivirine clinical trials. Of 27 participants using alternative oral ART in place of cabotegravir/rilpivirine, 11 (41%) took dolutegravir with rilpivirine.[1]
- Holding ART is not recommended because it is not clear how long the patient will be detained. Holding ART would lead to loss of virologic suppression, decreased immunologic function, and could lead to transmission of HIV.[2]
- It is unknown what the patient's HLA-B*5701 is at this time. Therefore, abacavir-containing regimens should not be initiated without knowing the patient's allele due to the risk of developing a hypersensitivity reaction.[2]
- Although darunavir/cobicistat + emtricitabine/tenofovir alafenamide + dolutegravir is not unreasonable ART, the patient has not demonstrated resistance or the need for this regimen at this time.[2]

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Faculty Comments

Melissa Badowski, PharmD

We look at our patient who unfortunately gets detained and this is something that happens a lot within my population where we have a patient who maybe didn't show up to clinic for a little bit and then we hear that they had gotten incarcerated or they're detained, but the other thing that we're up against is that if they were on this intramuscular long-acting injectable, what should they do once they go into the correctional or jail setting? Unfortunately it happens all too frequently, but sometimes based off the formularies and the formulary within our current prison system, they do not have IM cabotegravir/rilpivirine at this point.

Some of our patients don't necessarily disclose their status, so there may be an interruption to care. We would not want to interrupt care if we can make sure to get around that. And then some of the other jail formularies will split doses or split medications apart. In our prison setting, we refrain from doing that. We do single-tablet regimens. The most appropriate thing here is that we're going to be able to give a patient what they want and, it is so important that it's bringing the patient into these decisions. When we start somebody on antiretroviral therapy, I never tell them you're going on this. It's what do you want to go on out of all of these options. We also have to make sure that the patient's virus is sensitive to this.

While it's easy to consider going to dolutegravir/rilpivirine because it would be pretty similar to cabotegravir/rilpivirine, it could be what they were on in the past and what they've been taking before. That provides a lot of options for the patient. What we see all too commonly is once they go into the jail setting, maybe they don't have medications, they're not aware of their status, some of our jails still don't provide antiretroviral therapy but again it's really how do we make sure that we continue the patient on an appropriate regimen. When we give different options to the patient, we lay it out for them, what do you want to continue on and once we're able to do IM long-acting within the Department of Corrections or even within the jail setting, that'll make continuity of care and that transition of care so much easier.

Case 4 Question 1

Case background

Over the course of the COVID-19 pandemic, many treatment and prevention efforts were interrupted. A public health intervention is being developed in an urban area which is considered to be a priority area for ending the HIV epidemic due to its high incidence of new infections.

Question 1

Which of the following populations should be targeted for HIV testing?

a. Those who identify as heterosexual
b. Those who identify as transgender
c. Those residing in a retirement community
d. Those residing in a homeless shelter

Answer rationale

The correct answer is **D**.

- Approximately 13% of people living in the US are unaware of their HIV status.[1]
- Black and Latino communities along with gay, bisexual, and other men who have sex with men, are disproportionately affected by HIV.[1]
- Of 37,968 people who were diagnosed with HIV in 2019, only 2% (601) were among transgender people while 23% were among heterosexual people.[1]
- Creating and maintaining research and community interventions are vital in reducing health disparities in HIV testing and treatment. These interventions must be centered upon key underserved populations at risk for acquisition and transmission of HIV.[2]
- Targeted and intentional interventions that address different needs and preferences of diverse communities are needed in order to reduce gaps in social determinants of health (ie, economic stability, education level and access, housing stability, etc).[2]
- Unfortunately, with the rise of SARS-CoV-2, many interventions had to pivot to telehealth, but in order to be successful, significant time and resources had to be invested to build trust in these vulnerable communities.[2]
- UCLA and UCSF HIV Disparities Centers created and piloted interventions in populations experiencing health disparities and worked with members of the medical, faith-based, and at-risk communities to develop interventions ranging from drop-in clinics, telehealth, mobile testing sites, and educational events offering HIV testing with DJs and gospel choirs.[2]

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Faculty Comments

Melissa Badowski, PharmD

We have many interventions that are available to us, and throughout the COVID-19 pandemic, treatment and prevention efforts have definitely been interrupted. When we're looking at different areas of where we can promote, do testing, engage and link patients to care, there are a lot of different populations we think about and definitely the homeless and those vulnerable populations are going to be really where we want to target a lot of interventions. We still have 13% of people who are unaware of their HIV status, and this still affects many of the minority communities as well as bisexual men and men who have sex with other men who are still disproportionately affected. When we think about those who are transgender and having an HIV diagnosis, based on most current statistics, only about 2% actually had a new HIV infection, whereas in somebody who identified as being heterosexual, those rates were about 23% of new incidents of HIV infection, but men who have sex with men (MSM) still remains the highest at about 38%.

Even though these are statistics of where we want to provide a lot of our interventions, any intervention that we prevent even 1 infection is a great stride in prevention as well moving forward. For this answer in particular, those residing in the homeless shelter would probably have the greatest benefit, especially because we could reduce some of the gaps in social determinants of health by hopefully providing care there, but unfortunately a lot of our prevention efforts had to pivot towards telehealth and some of those screening events that we normally would hold were no longer available because you couldn't congregate in a community setting. There's a lot of centers in California that have disparity centers and they're able to pair with the community as well as medical leaders, clinical staff and even faith-based organizations to provide these interventions. Now that we're starting to be able to come out again, these testing efforts will be really important and just in getting those off the ground again. Those in high-risk communities are really going to be important and a lot of what you said about pop-up clinics or where you can come in when you need to, that's just as important as meeting patients where they are. We have mobile testing that's being launched and resumed and just going to these communities that are high-risk, especially if you look at the CDC ending the HIV epidemic, those counties and areas within the United States that are most afflicted with HIV. These are going to be the sources where we need to identify so we can start to make strides in meeting that goal of ending the HIV epidemic.

Have there been any particular interventions for testing in the communities that you serve that have been great at identifying those who are living with HIV who maybe didn't know?

Monica Gandhi, MD

Yes, one thing that happened in the City of San Francisco is there was large testing sites set up for COVID-19, but our HIV testing rate dropped by almost 90% at the beginning of the pandemic. And we are still down in our HIV testing rate by 44%, even to this day. And so, 1 testing initiative that was started in San Francisco was to do HIV testing at COVID testing sites. At the University of Chicago and some sites in Chicago, I was very impressed with their programs, that they showed us at ID Week about testing for HIV in ERs because people were coming in with COVID symptoms or coming in with nonspecific viral symptoms and that could be acute retroviral syndrome. I thought that was a very creative program to test simultaneously by drawing a blood tube while you're doing your COVID swab and test for HIV as well.

Case 4 Question 2

Case background

The public health intervention was successful in identifying new HIV infections.

QR, a 52-year-old, exhibited signs and symptoms of acute HIV infection but was afraid to get tested based on the stigma associated with having HIV. Their baseline CD4 count was 234 cells/mm3, HIV-1 RNA 29,739 copies/mL, and genotype revealed wild-type virus. QR has a past medical history of depression but denies any treatment at this time. QR reluctantly began daily bictegravir/emtricitabine/tenofovir alafenamide at time of diagnosis but was concerned with continuous access to the medication due to their living situation.

Through the assistance of interdisciplinary interventions provided by his clinic, QR was able to achieve virologic suppression, begin medication treatment and counseling for depression, secure stable housing, access medical and prescription insurance, and, eventually, obtain employment.

During the COVID-19 pandemic, QR experienced the loss of their mother, the only person who knew they were living with HIV. This caused them to turn to daily alcohol use, lose their job and medical insurance, and stop coming to clinic and taking all of their medications at once because "I was tired of dealing with everything."

Question 2

Which of the following factors is most important to address first?

a. Alcohol use

b. Unemployment

c. Death of their mother

d. Loss of insurance coverage

Answer rationale

The correct answer is **C**.

- Stressful life events, as in this case, the loss of QR's mother led to alcohol use, unemployment and, ultimately, cessation of ART. Although alcohol use, unemployment, and loss of insurance coverage can lead to health disparities and worse clinical outcomes in PWH, the trigger for QR's being lost to follow-up stems from a single event.[1-3]
- Stressful life events have been linked to loss of virologic suppression and faster progression of HIV.[1-3]

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Faculty Comments

Monica Gandhi, MD

It's been a difficult and tragic time during the COVID pandemic and in this case, the death of the patient's mother had them turn to daily alcohol use, lost their job, lost medical insurance and it has been a time for stressful life events and those stressful life events can trigger many aspects in someone's life that reduces ART adherence because everything that's going on. We saw a lot of people lose their jobs during COVID-19 and that led to loss of insurance coverage and though we take patients without insurance coverage, it was hard to find a way to a new clinic. That really lead to health disparities in San Francisco and lost to follow-up during the time of COVID-19. That is not just related to COVID-19. Stressful life events have always been linked to this loss of virologic suppression and faster progression of HIV because when there's so much going on, it's hard to remember to take a pill every day. We really have to keep on top of anyone who has stressful life events to try to bring them back into the fold of care.

Melissa Badowski, PharmD

I couldn't agree more, especially with the loss of insurance. A lot of times, patients are afraid to tell us that they lost their job, lost their insurance. They don't know that there are so many resources that are available from drug companies that we can provide in the clinic setting and we often don't find out for a month or 2 that they were unable to access their antiretroviral therapy. There are a lot of patients who had interruptions to therapy and saying, it's okay but this is why we're here, proving that it's okay that you may not know how to do this, this is our specialty, this is what we're here is to get you access to those medications.

Case 4 Question 3

Case background

QR, a 52-year-old, exhibited signs and symptoms of acute HIV infection but was afraid to get tested based on the stigma associated with having HIV. Their baseline CD4 count was 234 cells/mm^3, HIV-1 RNA 29,739 copies/mL, and genotype revealed wild-type virus. QR has a past medical history of depression but denies any treatment at this time. QR reluctantly began daily bictegravir/emtricitabine/tenofovir alafenamide at time of diagnosis but was concerned with continuous access to the medication due to their living situation.

Through the assistance of interdisciplinary interventions provided by his clinic, QR was able to achieve virologic suppression, begin medication treatment and counseling for depression, secure stable housing, access medical and prescription insurance, and, eventually, obtain employment.

During the COVID-19 pandemic, QR experienced the loss of their mother, the only person who knew they were living with HIV. This caused them to turn to daily alcohol use, lose their job and medical insurance, and stop coming to clinic and taking all of their medications at once because "I was tired of dealing with everything."

Question 3

Which of the following interventions is most likely to assist in keeping QR engaged and retained in HIV care and treatment?

a. Job training
b. Weekly virtual visits using long conversations to identify barrier to medication adherence
c. Interdisciplinary interventions including cognitive behavioral therapy
d. 90-day supply of antiretroviral therapy

Answer rationale

The correct answer is **C**.

- Interdisciplinary clinic interventions coupled with cognitive behavioral therapy to overcome the grief QR is experiencing due to the loss of their mother would assist in retention of HIV care. Merely providing QR with job training or a 90-day supply of ART would not likely retain them in care without other available interventions.[1-3]
- Although transportation was not reported as a barrier to accessing HIV care for QR, PWH who are not retained in care report more transportation-related challenges (such as transportation costs, unreliable public transportation, and travel distance) compared with those who are retained in care.[3,4]
- Barriers to being engaged and retained in care include other stressful factors such as hunger, unstable housing or homelessness, violence, stigma, and fear of disclosing HIV status.[5,6]
- Although telehealth may assist in enhancing retention in HIV care, this approach may not be feasible for all and may require a hybrid approach for certain populations. In addition, engaging in brief conversations at each visit can assist in improving adherence to ART.[7,8]

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Faculty Comments

Melissa Badowski, PharmD

When we think about this patient, again based off of a lot of what they dealt with, we think about some of the interventions of what we can do in terms of making sure that they stay in our healthcare system, make sure that we are able to overcome some of those psychosocial issues they've had, but we always want to provide nonjudgmental care. Whenever our patients come in, I try to show the upside of things, like you're doing a great job, you made your virologic suppression, you've continued this, this has been 2 years, 3 years. But a lot of people are beat down a lot of times about what they're not doing correctly and so we try to celebrate and emphasize what they are doing well. To bring them a little bit more hope. It's not just going to be one thing that helps to benefit a patient. Job training could be a good thing since they may have lost their job. We think about medication adherence and so we don't want to do anything that's very lengthy in terms of medication adherence discussion. It's brief conversations at every visit. So, they're used to hearing us talk about this.

For the option with the interdisciplinary intervention with cognitive behavioral therapy, this is the most important thing that we can offer to a patient. Again it's going to be on their terms, when they feel most comfortable in being able to do it. I don't want to just give them their medication, write a prescription, have them sent to their pharmacy and what do we do with this. We really want to talk them through it and check in on them.

What we will make sure to do is refer a patient to social work or case management in settings of where we think they can use a little help, especially if they are struggling with anxiety or depression, then we would recommend that they be seen by psychiatry. At every given point, somebody is dealing with something and while most of the times, they're doing just fine, we always want to be checking in with our patients to see how they're doing and making sure that if we can provide any assistance, maybe they don't need it today, but they know that they can come to us in the future if they should need it.

Case 4 Question 4

Case background

QR returns to clinic after being off ART for 9 months. They are interested in "starting fresh." QR saw commercials about a long-acting treatment for HIV and is wondering if they would be a candidate.

Pertinent labs reveal the following:

	12-months ago	Today
CD4	863 cells/mm^3	pending
HIV-1 RNA	35 copies/mL	pending
HIV-1 genotype	---	pending
SCr	1.1 mg/dL	pending
AST/ALT	32/29 U/L	pending
HAAb	pos	---
HBsAg	neg	---
HbsAb	pos	---
HCVAb	pos	---
HCV viral load	undetectable	---

Question 4

Which of the following recommendations would be most appropriate to consider in QR at this time?

a. Start darunavir/cobicistat/emtricitabine/tenofovir alafenamide + dolutegravir

b. Re-start bictegravir/emtricitabine/tenofovir alafenamide

c. Start oral lead-in with cabotegravir/rilpivirine

d. Wait until QR's genotype returns before restarting antiretroviral therapy

Answer rationale

The correct answer is **B**.

- Since QR stopped ART all at once, they may restart ART with their previous regimen while waiting for genotype results. Since bictegravir has a high genetic barrier to resistance, it is unlikely that any mutations developed.[1,2]
- Although the patient does not have prescription insurance, numerous avenues exist to provide the patient with ART (ie, patient assistance programs, HIV/AIDS drug assistance programs, samples, etc).[1]
- Rapid initiation of ART whether a new diagnosis or in someone returning to clinic is recommended to increase utilization of ART, linkage to care, and decreased time in achieving viral suppression.[1-5]
- For those returning to care, a close review of prior treatment history, concomitant medications, and resistance should be completed to reduce the risk for the development of resistance.[1]

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Faculty Comments

Monica Gandhi, MD

This is a very important and very common situation where someone has stopped therapy all at once. Stopped therapy, have been off ART for 9 months and really wants to restart. We will be discussing in the future with this patient intramuscular cabotegravir/rilpivirine because they're expressing interest in this, but in this case the question that comes out is are you worried, after they've stopped their bic/TAF/FTC 9 months ago, resistance, and do you need to start a more intensifying regimen? Because bictegravir has a high genetic barrier to resistance, because they stopped all of their ART at once and wasn't taking just half sometimes and half the rest of the time, this patient will not have developed any resistance to these high genetic barrier resistance drugs, like bictegravir or tenofovir, and you can go ahead and restart the old regimen which is bic/TAF/FTC while you're waiting for the labs.

The patient doesn't have prescription insurance and there are barriers to providing the patient with ART and what we need to do to circumvent those barriers are aid them with patient assistance programs, HIV drug assistance programs, giving them samples, giving them medications that you have in the clinic to get them on that rapid ART restart while you're getting them back on insurance and getting them to something more stable. Rapid initiation of ART is not just in the setting of a new diagnosis. We're working hard to rapidly restart if someone has been out of care and has chosen to come back into care and, at least in our clinic, really do start that ART right away, even if we're giving them samples or medications that we have left over from others while we're working on their insurance.

Essentially for those returning to care, you want to review, did they really stop their ART all at once. What was their prior treatment history? Were they taking off and on concomitant medications? Any question of resistance while you're waiting for that genotype and deciding what to start. In this case, we're good with restarting the old regimen.

Melissa Badowski, PharmD

That's what we definitely do in our clinical practice. We've done a really great job of educating patients. It's the all or nothing approach because the number of patients who come in now and say that they are intermittently taking their therapy to make it last is far less than it used to be. That's been a definite change, but I agree, we would start the same thing as well.