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Community HIV Clinicians' Perceptions about HIV Cure-Related Research in the Northwestern United States

Laurie Sylla[1,2], **Hursch Patel**[3], **Michael Louella**[1], **Jane Simoni**[4], **Karine Dubé**[3]

[1]·defeatHIV Collaboratory, 1100 Fairview Avenue North, E5-110, Seattle, WA, 98109, USA

[2]·University of Washington, School of Medicine, Division of Allergy and Infectious Diseases, Mountain West AIDS Education & Training Center, Mailstop 359932, Seattle, WA 98104

[3]·University of North Carolina Chapel Hill, Gillings School of Global Public Health, 4108 McGavran-Greenberg Hall, Chapel Hill, NC, 27599, USA

[4]·University of Washington, Departments of Psychology and Global Health, 3909 Stevens Way CE, Box 351525, Seattle, WA, USA

Abstract

Background: Research on stakeholder perspectives of HIV cure research has involved people with HIV (PWH), who generally cite the importance of HIV clinician advice in making decisions about trial participation. However, there has been little exploration of non-researcher community HIV clinician perspectives, which are clearly critical to the success of HIV cure-related research.

Objective: We aimed to learn how community HIV clinicians perceive HIV cure research and identify factors that would lead them to support or discourage HIV cure trial participation by their patients.

Methods: We recruited a purposive sample of 12 community HIV clinicians in metro-Seattle, WA to participate in structured interviews. We completed 11 interviews via teleconference and received one written response. We used conventional content analysis to analyze the data.

Results: Overall, community HIV clinicians were supportive of patient participation in HIV cure trials. Factors affecting support included knowledge of local trials, ease of referral, patient immune function and health stability, study risks and benefits, burden of study requirements, patient characteristics, patient life stability, potential impact on engagement in care, study communication plans, and beliefs that patients should have the autonomy to decide to participate. Participants had concerns about trials requiring treatment delays or interruptions and HIV transmission risk. While their knowledge of the field was limited, they were interested in learning more about open HIV cure trials.

Corresponding Author: Laurie Sylla MHSA (She/her), Director, Mountain West AIDS Education & Training Center, University of Washington, Mailstop 359932, Seattle, WA 98104, Phone: 206-221-4943, syllal@uw.edu.

Geolocation

This study was conducted in the greater Seattle area, Washington State, USA

Declaration of Interests

We have no competing interest to declare.

Conclusions: It would benefit the HIV cure research community if those leading HIV cure trials make stronger efforts to engage community clinicians who care for PWH, but are not active researchers, early in the trial design process. Such engagement prior to launching HIV cure trials will improve trial designs, leading to better enrollment and retention within these important studies.

Keywords

HIV clinicians; HIV cure-related research; analytical treatment interruptions; socio-behavioral sciences; HIV cure; cure; community clinicians

Introduction

HIV is now considered a manageable condition for those who can access suppressive antiretroviral therapy (ART) [1]. However, there is still no cure for HIV, and millions of individuals remain unable to access ART. With persisting toxicities associated with HIV medications [2] and continued stigmatization of HIV, the goal of finding a cure remains a priority [3]. To this end, HIV research funding has been growing globally [4], increasing by 272 percent from 2012 to 2019 [5]. Additionally, an estimated 320 clinical and observational studies towards an HIV cure have been completed or are currently underway [6]. Various modalities, such as cell and gene therapies, immune-based therapies, latency-reversing agents and combination approaches, are being tested [7] with the goal of either entirely removing the virus from the body or conferring sustained, medication-free durable suppression [8]. Regardless of the modality, to assess the efficacy of interventions, studies commonly utilize analytical treatment interruptions (ATIs) or the pausing of ART [9], a practice subject to ethical considerations [10–12]. For example, participants who undergo ATIs assume significant potential risks [9], such as viral load increase, CD4 count decrease, development of resistance to ART, and HIV transmission to sexual partners [13,14], while receiving limited direct clinical benefit [15,16].

We believe understanding the perspectives of people with HIV (PWH) is essential to HIV cure research. In a previous focus group study we conducted in the United States [17], we found PWH strongly value their medical providers' guidance regarding participation in HIV-related clinical trials. Approval from HIV medical providers would considerably influence potential participants' decisions regarding clinical research study participation[17–20]. HIV medical providers are considered key stakeholders in the pursuit of an HIV cure [8,21–23]. Throughout this paper, we use the terms medical provider, clinician, HIV clinician, and community clinician to denote physicians, advanced practice nurses, and physician assistants who are providing HIV medical care in the community and who are not also conducting clinical trials.

However, social sciences data on how HIV clinicians perceive HIV cure research remains scarce, with a few notable exceptions. Lau and colleagues conducted a global survey of health care providers asking for their tolerability for ATIs and found 18% (n=144) would not accept prolonged periods of any level of viremia [24]. In Europe, Protière and colleagues surveyed 164 physicians and found the highest reluctance in proposing HIV

cure-related trials with ATIs among physicians who were not research-oriented [19]. In a separate discrete choice experiment study, Protière and colleagues found that physicians and PWH had different preferences for certain attributes of HIV cure-related clinical trials [25]. Namely, physicians focused on patient safety outcomes, whereas PWH were more concerned with participation burdens such as side effects and the frequency of follow-up visits [25]. Such differences led to physicians preferring cure studies investigating immunotherapies alone and combined with latency-reversing agents, while PWH strongly preferred immunotherapy studies [25]. Moodley and colleagues also explored perspectives of HIV clinicians in South Africa and found limited awareness of HIV cure research among healthcare workers [26].

Given the high levels of trust established through long-term provider-patient relationships [27], HIV clinicians can educate, encourage, or potentially discourage PWH from participating in HIV cure research. Previous studies have found that clinician influence is one of the key factors involved in a patient's decision to participate in a clinical trial [19,28,29]. Specifically, patients may be likely to enroll in clinical trials if they have a positive relationship with their provider [30–32]. Conversely, patients are more likely to forgo clinical trials if their provider discourages participation [33], or if their provider seems to prioritize the study over patient care [34]. To ensure successful implementation of HIV cure trials, particularly those involving ATIs, it is essential to understand the perspectives of community clinicians regarding participation to ensure trials are acceptable to them as well as their patients.

As the number of PWH needed to participate in HIV cure studies increases [6] along with the number of cure studies that will require ART interruption, understanding clinician perspectives can help facilitate patient/participant engagement, recruitment and retention in trials. To date, most HIV social science studies on HIV cure research in the United States have centered on the perspectives of PWH [35–38]. In this qualitative, in-depth interview study, we sought to rectify a critical knowledge gap by uncovering the perspectives on HIV cure research held by HIV clinicians working in the Northwestern United States. Our ultimate goal was to generate considerations to meaningfully engage community clinicians in the research towards a cure for HIV.

Methods

Study Setting and Participants

We used a purposive, non-probabilistic technique to recruit HIV clinicians working in the Seattle, WA area. By clinicians, we mean medical doctors, advanced practice nurses, and physician assistants engaged in providing primary HIV care who are *not involved in the conduct of HIV cure research*. In this manuscript, we use the terms "clinician" and "provider" interchangeably. From the patient perspective, the clinical person is providing care and is a provider to them, whereas providers usually self-identify as clinicians. Our goal was to reach those working in sizeable HIV practices, in a diversity of specialties (i.e.., infectious diseases, general medicine/family medicine, internal medicine and hematology) and in various medical settings (e.g., hospital-based clinic, private practice, community health centers, Ryan White clinics, and Federally Qualified Health Centers (FQHC)), with

varying time in the field, as those who provided care in the pre-ART era had very different clinical experiences influencing their perspectives than those who have entered the field more recently. Due to the exploratory nature of this topic, we used in-depth interviews [39] to elicit nuanced considerations for engaging community clinicians in HIV cure research.

Participant Recruitment

A research team member (LS) sent formal email invitations to 51 area HIV clinicians at 16 different health care organizations, asking them to participate. Once clinicians indicated interest in participating, they received informed consent and demographic forms to complete and return prior to their interviews. Through study team member personal knowledge, we developed a list of providers at some of the larger HIV practices and clinics in the greater Seattle area. Additional names were generated by asking participants who else they would recommend we interview. With permission, we used their names when we reached out to invite these additional providers. We intentionally avoided oversampling from any one particular clinic site, although we did speak to multiple providers at the largest HIV clinics. In total, we formally reached out in three waves to 51 clinicians, including 15 who were suggested to us by interviewees. Fifteen clinicians expressed interest in participating in an interview (30% response rate). Upon confirming the date and time of each interview, we sent clinicians a virtual conferencing weblink. As part of the original recruitment invitation, we offered the option to complete the interview in writing, rather than being interviewed live. Five clinicians elected to send written responses and we provided them with the interview guide as well as the informed consent and demographic forms. They were also given the opportunity to change their mind and schedule a live interview after seeing the interview guide. Of these five, one completed the written interview, one opted for a live interview, and three withdrew prior to completing the informed consent (#103, 109 and 111) due to time constraints. (Our outreach and interview schedule coincided with one of the peaks of the COVID-19 pandemic). In total, we completed 11 in-depth interviews, and one clinician provided responses in writing (#107).

Data Collection

From January through April 2021, an interviewer (LS) conducted interviews in English using a virtual conferencing platform, with fidelity to the approved guide. The guide covered provider experience with clinical trial referrals, perceptions of HIV cure research and the likelihood of cure discovery, perceptions of cell and gene therapy, importance of discovering an HIV cure, considerations for supporting treatment delay or treatment interruption to facilitate patient participation in a cure trial, and the best ways to engage with providers about HIV cure research (Supplementary Table 1). Interviews took between 30 and 50 minutes to complete. Following each interview, L.S. wrote detailed field notes about potential themes that emerged. Clinicians who completed their interviews were offered a $50 electronic gift card; some declined compensation.

Data Analysis

Interviews were recorded and automatically transcribed by the virtual conferencing platform. In addition, a research team member (H.P.) carefully reviewed each transcript against the audio recordings for accuracy and made corrections. We used only verified

transcripts to analyze the data. We destroyed audio files once transcripts were cross-checked for accuracy, quality, and authenticity. Given the exploratory nature of the research topic, we used conventional content analysis focused on inductive reasoning to analyze the qualitative interview data [39]. After listening to all interviews, two researchers (K.D. and L.S.) independently confirmed data saturation [40] had been achieved.

We compiled all de-identified text responses into one master document for manual coding. To realize the potential of the dataset, we analyzed data by question blocks or sections. We carefully reviewed all responses to each question, and extracted salient quotes, and ascribed codes or themes. Our codebook was inductive, and contained code names, brief descriptions, and examples. Coding occurred in three sequential waves. First, L.S. provided preliminary codes that emerged during the interviews from her field notes. Second, a separate researcher (K.D.) reviewed the transcripts and expanded on the initial codes. Third, L.S. reviewed the codes and associated quotes, and made final refinements. Codes were expanded and collapsed as needed, and discrepancies were resolved by consensus. Once the final codes were agreed upon, we summarized key patterns in the data and prepared narrative summaries. We also generated a list of supplementary quotes (Supplementary Table 2), and summarized considerations to facilitate engagement of community HIV clinicians in HIV cure research and improving communication between HIV clinician-researchers and community clinicians based on our findings (Table 3).

Ethics Statement

The University of Washington Institutional Review Board reviewed this study (#00009913). All participants provided written informed consent, as well as verbal consent, to be recorded.

Results

Clinicians participating included seven cisgender females and five cisgender males. Of these, 10 were Caucasian/White and two were of Asian descent. These demographics are reflective of clinicians providing most HIV care in the Seattle area. Clinicians worked in a variety of health care settings, and all but one had more than five years of experience providing HIV care. The majority (7/12) had more than 100 patients with HIV in their panel (Table 1). Most serve diverse patients with respect to race and ethnicity, sexual orientation, and gender, with the majority of patients being of lower socio-economic status.

Encouraging and Discouraging Clinical Trial Participation

All clinicians interviewed had prior experience supporting patient participation in clinical trials generally, such as for HIV treatment, hepatitis treatment, and COVID-19. A few had actively recruited patients for trials within their practices. Clinicians could rarely recall actively discouraging patients from participating in a trial, although some stated it was outside their purview to actively encourage trial participation or did not feel that they were well informed about available trial opportunities. Most indicated that patients should have the autonomy to make trial participation decisions, as long as the patient truly understood the intention of the study and what would be required. Those who had been in practice since the early days of the HIV epidemic recalled clinical trials as the best way for patients to

get access to promising treatments in development when there were no effective treatment options.

> *I can't think of a moment in which I have discouraged a patient. I have encouraged and have helped facilitate interested patients connecting to trials primarily.* #101

> *I think as long as somebody can really understand the risks and benefits, people have a right to make those decisions for themselves.* #113

Clinicians commented that often it is the patients themselves who initiate discussions about potential study enrollment.

> *I can think of moments in which I have encouraged participation, although frankly the impetus for that has most often come from patient inquiries or patients asking questions.* #101

> *Usually it's patients who have had long-standing HIV, not necessarily people who've been newly diagnosed, who have asked about potential studies that they could be in.* #105

There was convergence among providers about the various factors they would take into account in determining their support for trial participation. These included the patient's intrinsic attributes, motivations, study goals, study requirements and logistics, potential risks, potential clinical benefits to the patient, and potential impacts on the relationship between the clinician and their patient. Sometimes it was a combination of all of these factors.

> *I don't want to encourage people to go into trials for the wrong reason, in other words, for the stipend or they think that it will give them access to something that their peers won't have.* #106

There were additional study-specific factors that were of concern for providers if a trial was going to be cure-related.

> *I would want to know if it was a cure study or a remission study. I would want to know if it was going to involve a treatment interruption. I would want to know if it involved invasive procedures like lymph node biopsies and things like that. I would want to know what expectations were provided to the patient.* #102

One clinician who has also conducted research (not cure-related), and whose patient profile consists of individuals from groups traditionally under-represented in research, i.e., individuals who are transgender, homeless, women of color, etc., considered the need for more participation in research by individuals with these demographics.

> *I take into consideration the demographics of the patient, because I'm trying to encourage the people who don't often get included in the research to participate, so that we have better outcomes for people in their population.* #110

Clinicians also commented that, sometimes, how informed they are about locally available clinical trial opportunities would determine whether or not they refer patients to participate.

> *It's been rare that I have suggested a trial to someone, not because I wouldn't, but primarily because… I haven't always been super up to date on the ACTU [AIDS Clinical Trials Unit] studies and what's been going on.* #101

HIV Cure Trial Referrals—Most providers could not recall being asked by their patients about participating in any HIV cure trials or referring anyone to a cure trial. This could be because there have been very few HIV cure trials in the Seattle area. Providers reported, however, that patient interest in a cure was high.

> *I have a lot of patients who ask me about progress on a cure, if there's a cure… whether there might be a cure study they could participate in.* #101

> *I've had several patients ask,"Do I think that a cure will be possible in their lifetime? What are some of the things that are being done right now?" But I've never heard anybody ask me specifically for a cure trial.* #104

Overall, while clinicians expressed some concerns about referring individuals to HIV cure studies, all were willing to refer, taking into account the patient's clinical profile, study demands, and perceived risk-benefit of the study.

General Perceptions of HIV Cure-Related Research

Many clinicians interviewed believed it was possible that a "classic cure," defined as complete medication-free elimination of HIV from the body, would be discovered in their or their patients' lifetimes.

> *I think that it is possible that it [a classic cure] will happen in my lifetime, and I do tell patients that I think it's possible. I think that probably, more likely will be a combination of interventions that lead to sustained remission or some sort of sustained control of HIV that doesn't require antiretroviral therapy. [functional cure]*#101

A quarter of clinicians interviewed expressed skepticism that a cure for HIV would be possible.

> *Honestly, I think the chances are small, very small… You know, elimination of the virus [classic cure] is a huge challenge, because this is a virus that integrates into the host cells and genome… the problem is, if you have one cell left, it'll reignite the infection and you're back to zero completely, so that's why it's such a tall order.* #106

> *I have to say that I feel really skeptical, partly because the drug industry is so tied into the HIV practice community. There's a lot of money to be made in not healing people, and I know that sounds like a crazy conspiracy theory, but I think that's the kind of unconscious bias that can drive what kind of research gets done potentially.* #113

The rapidity of the discovery and development of highly effective vaccines against COVID-19 influenced at least one clinician's perception of what might be feasible with

respect to scientific discovery of an HIV cure. However, this clinician remained skeptical about the likelihood of accessibility of a cure, once discovered.

> *I feel like this has changed pretty radically in the past six months…, if you had asked me before COVID if I thought it was possible to develop a vaccine that was 95% effective in less than two years, I would have laughed you out the room… I really have a much brighter view of the capabilities of current science… So, I would say somewhere around 70% sure that it's possible to come up with a cure like that [classic cure] scientifically. Socially, like whether I think it's possible to come up with a cure like that, and then actually implement it in a way that's accessible to the general HIV positive population and I would tell you 30%.* #110

A number of respondents stated a belief that achieving ART-free durable suppression of the virus, sometimes referred to as a "functional cure," would be far more likely than an eliminating cure, although not every clinician agreed with this belief. One provider also wondered if durable suppression would overcome the chronic inflammation typically seen with HIV.

> *If you have antibodies that are suppressing the virus, are you also going to be dealing with the inflammation or maybe even have more inflammation, because you have these active antibodies around all the time that are kind of always swatting the virus down when it tries to pop up?* #106

Most clinicians expressed discovery of any type of HIV cure as being a long way off, although they believed it was possible. Some thought that ART-free durable suppression would be more easily achieved, yet would come with its own concerns. Many divergent points of view were expressed on this topic.

Value of HIV Cure Discovery

Even in the environment of highly effective, minimally toxic HIV treatment, nearly all respondents endorsed the value of discovering a cure for HIV from both medical and sociological perspectives, and commented it was important to pursue. Reasons they provided for the importance of a cure included patient desire, ongoing HIV stigma, questionable ongoing access to medication, adherence issues, long-term toxicities, and complications due to inflammation – such as increased risk of malignancies, organ damage, heart disease, and premature aging.

> *And then there also still are handfuls of individuals who are not able to adhere to therapy or have developed very complicated resistance or do still have more classic handfuls of pills and toxic medication; there still are long term effects of either the medications or of even well controlled HIV infections. I still think that a cure or other intervention would be extremely, extremely valuable and I, for one, would certainly support referring appropriate patients to such studies.* #101

> *Then the other piece is, I still think it plays a real, real difficult role in patient psyches that they have a chronic illness and even though we're in a much better place in 2021 with the stigma of HIV being far less than it was in 1985, it still has a stigma and it's still hard for people to live with that and I think that that's hard…*

> *I have patients tell me, my patients who have stopped therapy on their own, and when I recognize it when their viral load goes up and I asked them why they said, "I just wanted a time where I could pretend I didn't have a disease, where I didn't have to take a pill every day for something." So clearly there's stuff that's really emotionally important as well as maybe physically important.* #104

Several providers identified cure as something that was emotionally important to patients, and that would be valuable; however, they did not see it as an urgent priority, given the quality of current treatment.

> *HIV treatment options have grown to be more novel… more long acting, so that it's less of an inconvenience for the patient. I think that that makes it less pressing from a provider standpoint, and I think always from my standpoint it's less important than it is from a patient standpoint… But patients care so much about it and so I think that it is really important.* #112

Familiarity with the Current State of HIV Cure Research

None of the clinicians interviewed considered themselves to be experts on HIV cure research, nor did they prioritize keeping well informed of cure research developments. With an HIV cure being perceived as a distant possibility, providers preferred to remain current on evolving treatment practice above tracking new developments in the cure research field. Most respondents acknowledged having a basic knowledge, with a handful knowing a bit more. Most people rated themselves between 2 and 4 on a 5-point scale, with 5 being expert. Most were familiar with the two cases of cure via stem cell transplantation with HIV-resistant donor cells, and some had heard of CRISPR, bNAbs (broadly neutralizing antibodies) or latency reversal. A few acknowledged they found the science of HIV cure challengingly technical as well.

> *When I go to conferences there's so much to learn that I automatically have given myself permission to do this automatic filter of is this relevant to my day-to-day practice right now? And if it's not, I don't have brain space right now.* #113

> *I probably know more than the average person, and I know broad strokes of different potential targets but… I don't know where things are in current development and I don't know how successful some of those therapies have been and what else is new in the pipeline.* #115

Typically, clinicians' knowledge about developments in the HIV cure field stems from meetings they attend which summarize highlights from major conferences. Occasionally they heard about cure developments informally, via colleagues more closely connected to the field.

Perceptions of Cell and Gene Therapy (CGT): Knowledge and Concerns

Clinicians were generally aware of high-level information related to cell and gene therapy, but their knowledge was generally peripheral and somewhat vague. They most commonly had heard of CRISPR and the idea of engineering stem cells, or cutting something out of the DNA.

> *I don't feel like I have a really great working understanding of a lot of those therapies.* #110

However, two clinicians stated that they knew and understood a bit more about CGT due to their work in other specialties such as oncology, where CGT has been studied more broadly, or had exposure to the field outside of their medical education and clinical practice.

> *So, it runs the gamut from vaccine development to gene therapies and CRISPR technology, and I take care of a lot of HIV patients. I'm a [specialty], so it's all in the realm of what I do on a daily basis.* #108

> *It's the idea that you could cut the HIV out of people's genome or engineer their stem cells, so that they're no longer a viable host for the virus and that involves ways to actually change the person's DNA in some way and that's, in other disease states, that's at such an early stage, you know.* #106

Although respondents mostly had only minimal knowledge related to the field, they did have concerns (e.g., risks of CGT, such as off-target effects or immune side effects.) They also stated patients would likely have concerns about CGT as well.

> *Anyway, it's a little bit scary to me, gene therapy, and I think patients also, maybe rightly, would be a little bit wary of it.* #106

> *I can imagine people being freaked out about that… kind of alteration in particular of their own bodies, but I think we alter our own bodies on a regular basis with so many things that we do, prescribed or not prescribed, that I don't feel negatively about that inherently.* #113

Most clinicians had limited understanding of CGT, and also expressed worries about potential clinical risks. This may affect their willingness to support patients' participation in CGT trials, although no one reported being flat-out against it.

Willingness to Delay HIV Treatment for HIV Cure Trial Participation

Current best practice in HIV care is to initiate ART as soon as possible after diagnosis. While most HIV cure-related trials would not necessitate delaying treatment initiation, it is possible that there will be trials that could require participants to be treatment naïve, particularly if the study is trying to recruit people diagnosed during acute infection. Intervening during the acute phase of HIV infection could limit the size of the reservoir that gets established [41], thereby increasing the efficacy of interventions that target the reservoir. In that instance, a trial might require a treatment delay. We specifically asked how a treatment delay would impact clinicians' willingness to support patient participation in a cure-related trial. (**See** Supplemental Table 1: Interview Guide.) While most clinicians were not entirely comfortable with delaying treatment initiation to enable participation in an HIV cure trial, they were open to it. Their primary concern was the patient's overall clinical and immunological health. Additional considerations included potential risks and benefits of the trial, the duration of the delay, study details, patient stability, the research team's communication of lab results, and importantly, the likelihood of the patient remaining in care after the trial. Until recently, ART initiation was not typically immediate, with delays of

several weeks being common, and some clinicians noted that historically, treatment had been delayed much longer, with treatment initiation not an emergency for most people.

> *If a person had a relatively intact CD4 count and low viral load and the delay were not significant, and the person were very motivated to participate and the risks of the intervention were low, then I would have no issue with it. If the person already had very advanced immunosuppression and if the delay were longer, and if the intervention were riskier, it would certainly give me pause and I would hesitate.* #101

> *I can't think of any situation where starting HIV meds is a true emergency… Usually we wait for an HIV genotype and phenotype to come back and so, even in a perfect context, we'd wait a couple… until those tests come back and it often takes two to three weeks.* #108

Few clinicians acknowledged discomfort with the conflict between what they considered to be clinical best practice (immediate treatment initation) and delaying treatment for trial participation. They indicated they would support immunologically intact patients who expressed interest in delaying treatment for the opportunity to be part of a cure trial, but did not see themselves as promoting those trials. Some raised concerns about patient engagement in care, particularly for new patients, questioning their ability to discern between research and care, thereby potentially weakening adherence messaging and care engagement.

> *I would also have concerns about the message that it sends to the patient that being on the meds is not crucial.* #102

> *I've had some issues in the past where people have entered the primary infection studies and then just not shown up to care and just gone to study visits and so, because they think, well, that's good enough. I'm getting my meds from them. I'm getting labs from them. What else do I need? And so I just want to make sure that there's a clear understanding of the need for ongoing care.* #115

A couple of clinicians indicated that many of their patients might not want to delay treatment. PWH have been hearing for a while about the importance of starting medication as soon as possible.

> *Convincing somebody, after all the hype about starting treatment right away, convincing a patient that to be in a trial where they wouldn't start right away is, you'd have to have a lot of information that would convince the person that it's not a high risk to them.* #106

On the whole, clinicians were not at all comfortable with any HIV treatment delay for individuals with low CD4 counts or high viral loads. There was, however, quite a bit of difference in how much treatment delay clinicians felt comfortable tolerating for immunologically intact individuals, ranging from only a couple of weeks up to a year.

> *Again, it would really have a lot to do with the patient's health. If it seems like someone whose CD4 count is 1,000 and has a low viral load, I might be willing to do it for six months or a year.* #102

> *I think beyond a quarter, I think it would feel very uncomfortable, very uncomfortable. So, I would say a month I wouldn't feel bad, two months I would feel eh, and then three, beyond three months I just would not like that.* #112

Further, before advising patients on whether to delay, clinicians would want to know more about both patient-level factors (e.g., their medication access, psychosocial state, comorbidities, ability to adhere to partner protection measures, other lived experience) and trial-related factors (e.g., monitoring plan, communication plan, potential risks/benefits). Overarching concerns included the likelihood of a patient maintaining clinical stability and engagement in care, the potential for risk of transmission to others, and a clear understanding by patient and clinician of the study risks the patient would be undertaking.

> W*hat are the parameters that they get checked? Are they checked every month or they checked every three months as part of the study? Am I still going to be doing monitoring of their immune systems while they're in the study? What type of communication, if the study was doing the monitoring? Would I get the results right away? You know, just so I could still be their doc and make sure that they're there safely cared for.* #104

> *I think it also depends a little bit on the risk of the patient and… who their sexual partners are and what their level of sexual activity is going to be. Somebody who is very aware that they have active HIV and they don't want to spread it to their partners, and who isn't ready to potentially commit to a period of either abstinence or other forms of HIV prevention, then I don't think that would be, that they would be a good candidate to withhold ARVs [antiretrovirals].* #105

Few clinicians indicated they would feel more comfortable with later-phase studies. It was important to the clinicians that patients understood there is little likelihood of benefit to themselves other than the sense of scientific contribution, when participating in early-phase studies. Clinicians also believed the informed consent process would be important.

> *It's a very altruistic kind of consent, where you'd really say this isn't going to help you. Don't have hope that this is going to cure your HIV, but if enough people like you participate in this kind of trial, we might be able to come up with a cure and your participation would be very valuable for that. Maybe present it that way. That'd be for Phase 1. As you get further, and get to Phase 3, it's a really different consent, because then you could say, well, it looks like this might cure HIV, but we don't know for sure, and it's a whole different kind of consent.* #106

Nonetheless, the trial phase mattered for a number of clinicians who would be much less comfortable with high risks of Phase I clinical trials. The inclusion of an ATI would also be of paramount importance.

Perceptions of Analytical Treatment Interruptions (ATIs)

While most clinicians expressed discomfort with treatment interruptions, they were supportive of their patients participating in them, provided they were clear on the risks, and that they would remain clinically and immunologically stable with close monitoring and clear ART restart criteria. Clinicians were more uncomfortable with trials that would allow

viremia to persist for a long time (e.g., a few months). Criteria related to perception of ATI safety, such as a robust CD4 cell count, absence of comorbidities, clinical history, and a means to address transmission risk, were similar to those for treatment delay. An additional concern specific to ATIs related to the possibility of developing resistance.

> *It gives me pause. I really worry about periods of viremia and long-term health effects… That said, in this setting with very close monitoring and a very strict protocol and in a research trial setting, if the person were very motivated and understood the risks and benefits and wanted to participate, I certainly would support that… But the longer the viremia, the more reluctant I feel.* #101

> *The person might become infectious, so depending if they're sexually active, that's going to be an issue. But beyond that, the concerns would have to do with, is it going to be harmful to the person's health to let the virus come back, might they develop resistance, might they suffer from CD4 suppression from having the virus back? People don't just instantly get sick when they have HIV. It's a long slow process, so I don't have terrible concern about a person's health if their CD4 is okay, for a few months.* #106

> Y*es. I think I feel a lot more comfortable with ATIs than I do with the delayed ART, just because I've heard about it more, read about it more, seen studies with ATIs and so, thus again, that's from a comfort level.* #112

One provider (#112) indicated they would feel more comfortable with a treatment interruption than a treatment delay. Further, some clinicians spoke to patients' lived experience and their depth of understanding about HIV and its potential seriousness, their prior research and clinical experience, and how their patients' current circumstances might impact their ability to participate in a treatment interruption.

> *If it was an HIV experienced patient and… this is not their first rodeo and they're very aware of the effects of this disease historically… I don't have as many concerns about them participating with that level of risk… They're invested at a different level in the significance of participating and giving back; whereas, millennial patients… they're like, yeah, you're gonna give me a pill and I'm going to be better… Like, I'm not super worried about this HIV thing… And so, I have hesitations about an ability to really fully incorporate the impact of what you're saying yes to, depending on your understanding of the disease and your experience with being positive.* #110

A few clinicians noted that whether it came to ATIs or to cure trial participation in general, ultimately, patients had the right to self-determination.

> *I think as long as somebody can really understand the risks and benefits, people have a right to make those decisions for themselves. I think that comes down to also letting a patient know; that letting a patient choose, and as long as they understand that some treatment interruptions have been shown to potentially create a more difficult long-term treatment plan.* #113

Clinicians provided possible safeguards to ensure ATIs were implemented safely and ethically. For example, they expressed participants should be in good immunological and

clinical condition, that there should be clear entry/exclusion criteria to this effect, as well as clear rules for stopping the interruption and restarting therapy. They commented close monitoring and good communication between the research team and the clinician were essential. They also stated the psychoemotional state of the individual was important, as well as life stability, since that affects monitoring and follow-up.

> *The person would need to be housed. The person would need to have a cell phone. The person would need to have access to come in as often as possible and then having very frequent lab draws. I don't know how many, but I think those are some of the safeguards that I would think about.* #112

> *I would think very close, very close monitoring of viral load and of the patients; very, very reliable ways to connect with the patients… We lose a lot of patients from studies that are lost to follow up, and these are not people you want lost to follow up.* #102

A significant concern in these days of U=U (i.e., Undetectable equals Untransmittable – meaning a person cannot pass on HIV to their sexual partners if their virus is undetectable) was that interrupting treatment created the possibility of viral rebound and inadvertent HIV transmission to sexual partners. By and large, clinicians thought that steady partners should be counseled and offered pre-exposure prophylaxis (PrEP) (one clinician noted it should be free). Most considered essential a robust informed consent clearly explaining possible transmission risk, for both the participant and their steady partner if they had one.

Most clinicians were less comfortable with someone with multiple partners undergoing an ATI than someone who was celibate or who had a steady partner that could be informed and prescribed PrEP. Some clinicians felt prior to undergoing an ATI that participants who had multiple or casual partners should agree to abstain from sexual activity during the treatment interruption and others stated that they should agree to use barrier protection. Some felt that individuals who had multiple sexual partners should not be part of a study that included an ATI. One noted the importance of individuals being able to opt out of the ATI component of the study if they were concerned about transmission to an HIV serodifferent partner.

> *Medical ethics point of view, I think I just have to believe people have the fundamental right to make terrible decisions and that's autonomy at its best in medicine. So, if I believe that's true, people also have the fundamental right to prove that they can make informed decisions and that's the best we can do. So just make it a real rigorous informed consent.* #106

> *Somebody who, for whatever reason, is engaging in a lot of sexual activity really probably should not necessarily be part of the study… That's probably more of a public health concern than it is for the actual safety of the patient themselves.* #105

While clinicians expressed support for patient self-determination in participating in HIV cure studies, including those with ATIs, they indicated they had multiple concerns regarding potential negative clinical impacts of an interruption, transmission risk and partner vulnerability, as well as assuring continued patient engagement in clinical care while participating in a study. They also identified additional psychosocial risks of HIV cure trial participation.

Perceived Risks – Including Unacceptable Risks

We asked clinicians about their perceptions of potential benefits and risks for patients who participate in HIV cure trials. Perceived benefits and risks were primarily psychosocial. Plausible benefits included positive effects of contributing to science, providing meaning after a difficult diagnosis, giving a sense of hope, and for those in trials with treatment interruption, providing a sense of freedom being ART-free. Possible risks included psychological stresses of being in studies, risk of losing HIV identities and potential disappointment if someone believes they may be cured and then they are not. Clinicians stressed the importance of setting very clear expectations to avoid creating false hopes. In addition to the emotional risks, a couple of clinicians expressed concern that people participating in studies with extended time off of ART might not come back to it very easily.

> *If they go in thinking I'm in a cure study, I have a 50% chance of being cured, when we know this is more very early exploratory, then that could be very psychologically damaging. It could be that they never think that they need to be on meds again. I guess the psychological benefits are that they're helping participate in research and advancing science. But I do think there's very significant potential for psychological risk.* #102

> *My worry would be that somebody looks at that and says, "I'm going to be cured," and the emotional risk… it'll almost be like being diagnosed twice, except for worse… and I think that worst case scenario impacts somebody's ability to take the medicine that they need for the rest of their life.* #113

When asked to identify what would constitute "too much risk" for them to support trial participation, most clinicians focused on clinical risk, such as excessive toxicities or tumor formation. Some spoke to unknown risks of early trials, while others identified risks due to ATIs, such as the potential to become resistant or ill due to viremia, and the potential to transmit HIV. A number of clinicians appeared more concerned about the risks associated with an ATI than with the interventions themselves. A few noted risks of poor trial implementation, such as inadequate consent or monitoring.

> *If there were breaks in protocol that didn't protect their safety or their identity. If the consent process was shoddy and patients weren't going through high level informed consent decision making. All the things that we expect in clinical trials would need to be in there for this one too.* #108

> *I would not feel comfortable with extended treatment interruptions if their health was not absolutely excellent. I would not think that it would be an appropriate level of risk if there was going to be transmissions of HIV during these treatment interruptions.* #102

To engender clinician support for patient participation in cure trials, trialists should have clearly delineated inclusion/exclusion criteria that address clinical history, medication resistance profiles, and lab parameters. They should also have a robust safety monitoring plan, partner risk mitigation strategies, and protocols for clinical data sharing and communication with primary HIV care providers.

Keeping Clinicians Informed about (and Engaged with) HIV Cure Research

For the most part, HIV clinician interest in HIV cure research was secondary to their interest in prevention and treatment developments that are likely to impact the care they provide in the immediate to near future. They expressed being challenged by lack of time, and by how much information they were inundated with via email and other sources. That said, they wanted to know about major developments in the field. They had great interest in knowing about opportunities for their patients to participate in trials and how to refer them, and they wanted to be able to answer patient questions about a possible HIV cure. Several noted it would be significantly more difficult to keep community-based providers informed and engaged than those affiliated with academia.

Clinicians identified possible strategies for keeping them engaged, such as pre-trial launch communications, podcasts, luncheons, and presentations at staff meetings. Several agreed to be added to an existing HIV cure listserv. They were also interested in having trial information in a format they could easily share with patients.

> *I've always thought it would be useful to have a repository of local clinical trials… Whether it's a website or an app… Something where I could just hit a button and everything that's currently open with a bullet pointed list of inclusion and exclusion criteria… If there were trials available, the other thing that tends to be useful is just having a card to hand a patient with some basic and contact information.* #101

> *Continue to have sessions about this at big HIV conferences and to make sure that those sessions are accessible to people who aren't scientists… having like a dumbed down version… just ensuring that the cure content can be talked about in an accessible way is important.* #112

For the most part, clinicians indicated that their primary interest in HIV cure research was being kept abreast of major developments in the field at a high level, explained in easy-to-understand terminology. They favored more detailed, personalized communication for information about cure studies their patients could enroll in, and expressed great interest in learning about these opportunities. Clinician-driven considerations for keeping them informed about HIV cure research are summarized in Table 2.

Discussion

This study sought to identify HIV clinician perspectives on HIV cure research, including their willingness to support patient participation in HIV cure-related trials. By focusing on their perspectives – a scarcely documented viewpoint – our study extends the current HIV cure research literature that highlights the key influence clinicians hold over a patient's decision to enroll in a clinical trial [17, 22]. Clinician influence in this context, coupled with the growing demand for PWH to enroll in HIV cure clinical trials, creates the necessity to understand community clinician perspectives on HIV cure research [6]. Such insight can help generate ethical ways to facilitate further participant engagement and recruitment into HIV cure trials, as clinicians can be important gatekeepers to patient participation [19,20]. Furthermore, our study rectifies a critical knowledge gap in HIV cure research, as very little has been published about clinician perceptions and considerations regarding the conduct of

HIV cure research, particularly in the United States. In summary, effective engagement of non-researcher HIV clinicians by cure researchers will be an essential step for successful recruitment of participants into HIV cure clinical trials and eventual adoption of curative interventions.

Through this qualitative exploration, we found that most of the HIV clinicians we interviewed had a general knowledge of the HIV cure research field, did not follow the field closely, and were not motivated to do so. Our findings align with those of a qualitative study conducted in South Africa in 2014 among key stakeholders (including doctors and nurses), which showed limited awareness of HIV cure research [26]. While putting the onus on busy trialists to initiate communication, develop provider-centric and patient-centric recruitment materials, and to find multiple methodologies for sharing developments in the field may feel unbalanced to some, given the differing levels of motivation and pressures on those engaged in running a trial and those whose primary goal is clinical care, it is likely researchers will need to accept this responsibility to successfully build bridges with clinicians not actively involved in HIV cure research. Sullivan, et al., conducted a study assessing HIV patient satisfaction with their primary care physicians and found that a patient's perception of their provider's knowledge regarding HIV was a key factor in patient satisfaction [42]. As such, we believe that it will be important to further engage with clinicians in the context of HIV cure research.

Furthermore, the clinicians we interviewed generally considered their knowledge of cell and gene therapy to be vague, yet they expressed some concerns related to the associated risks of off-target effects or immune side effects. Some of their concerns were rooted in pre-existing biases and general lack of information about a field that pushes people beyond their comfort zones because of the enormity of possibility and the enormity of what remains unknown. Given the recent growth of HIV studies involving CGT, it will be essential to increase clinician comprehension of and comfort with CGT as an approach to garner their support for their patients participating in CGT-based HIV clinical trials [7].

The majority of clinicians interviewed indicated that their patients often asked about an HIV cure. While their general perception was that an accessible intervention may be developed in their or their patients' lifetimes, they did not think one was on a nearby horizon. Skepticism for most who expressed it, was rooted in both their understanding of the complexity of eliminating the reservoir and the potential for viral reactivation. While one participant raised the possibility that companies might not want to invest in a cure since they were profiting from selling lifelong therapies, it is likely that if an acceptable, scalable HIV cure were discovered, it could be made profitable and the industry would pivot, as was the case with hepatitis C.

Several clinicians indicated that ART-free durable suppression of HIV would be a more realistic goal in contrast to a cure that removes HIV from the body in its entirety. Yet fundamentally, the overwhelming majority agreed that a cure for HIV is essential to pursue for both medical and sociological reasons, despite current advances in HIV treatment [3], a viewpoint which is consistent with that expressed by Protière et al. [23]. Specifically, clinicians identified barriers to treatment access, treatment failure in heavily treatment-

experienced long-term survivors, adherence fatigue, HIV stigma, ongoing inflammation, increased comorbidity despite viral suppression, long-term toxicities, and emotional well-being as reasons to pursue a cure. Here is an area of common ground between researchers and community providers.

Clinicians stated that they presently prioritize focusing on new clinical developments in HIV therapeutics that have more immediate impacts on their practice, rather than tracking HIV cure research developments. Until there are breakthroughs suggesting a scalable HIV cure is within view, HIV cure researchers will need to vie with competing priorities for clinician attention. Clinicians were, however, interested in high-level advancements in HIV cure research. Of note, they stated that their knowledge of HIV cure developments largely stems from plenary sessions or post-conference summaries from major conferences such as the Conference on Retroviruses and Opportunistic Infections (CROI) and the International AIDS Society (IAS). This suggests that providing clinician-friendly summaries from major conferences is an important way to sustain interest in developments within the HIV cure field. Inviting and encouraging community clinicians to attend the “Young Investigators Symposium” that occurs as a pre-CROI session would provide an excellent means for these clinicians to access HIV cure research information presented in terms more comfortable than in some of the more detailed, heavily jargoned scientific sessions held during the main conference.

Overall, clinicians we interviewed had experience with and were supportive of patient referrals to clinical trials. Encouragingly, several clinicians spoke to patient rights to self-determination. They expressed concern that people participate for the “right” reasons, which they identified as altruism, or the desire to contribute to cure discovery, rather than believing they were likely to be cured because of participation or for any compensation they might receive. In making determinations about supporting patient trial participation, HIV clinicians would heavily weigh the individual’s clinical profile, the risks the participants would be facing, the burdens of participation such as frequency of visits and procedures, intrinsic patient characteristics and external life circumstances, and the appropriateness of an individual for a specific trial. Clinicians felt strongly that individuals who did not have stable living situations and who could potentially become lost-to-follow-up should not be in trials that involved treatment interruptions, nor should individuals who had difficulty achieving viral suppression or with a complex HIV resistance profile. Our findings echo those of Protière et al., which showed physicians most worried about the possible clinical and social impacts of HIV cure trials with ATIs were also most reluctant to propose them to their patients [19]. Of note, however, as previous studies have found in the context of HIV, it will be important to find a balance between shared decision making among providers and patients, while avoiding an overly paternalistic approach to research recruitment [43]. Further, given their concerns and biases, it is important for community clinicians to become knowledgeable about any local HIV cure studies accruing enrollment, including CGT-based studies, prior to engaging in patient discussions encouraging or discouraging enrollment.

In relation to the limited current literature on provider perspectives on HIV cure research, Protière et al. found quality of life issues, such as side effects and study requirements were important for both French clinicians and PWH as factors influencing participation in HIV

cure trials, with physicians giving somewhat greater weight to the potential for participants to successfully maintain an ATI [23,44]. Our results show that clinicians in the Northwestern United States considered many of the same aspects – potential risks, study logistics, and study requirements – that physicians and PWH considered in France, as revealed from the work of Protière and colleagues [19,23,44].

Another significant finding was clinicians reporting a lack of knowledge about local cure trial opportunities and a willingness to refer patients if they knew about them, the referral process was easy, and they believed their patients suitable for participation. Despite availability of trial information on large repository websites such as ClinTrials.gov (https://clinicaltrials.gov/) and the Treatment Action Group HIV cure trial listing (https://www.treatmentactiongroup.org/cure/trials/), this finding highlights a need for HIV cure researchers to regularly engage with HIV clinicians to keep them informed of current local research opportunities, especially considering the previous findings of patient satisfaction being directly linked to a provider's knowledge about the field of HIV [42]. Consequently, keeping HIV clinicians informed about research opportunities could lead to positive clinical experiences for patients with HIV. Furthermore, by keeping HIV clinicians informed about ongoing HIV cure trials, clinicians can take an active role in recruiting patients who are traditionally underrepresented in research – such as cisgender and transgender women and people from racial, ethnic and sexual minorities [45–47] – a desire expressed during our interviews. Clinicians stated an interest in learning about local HIV cure trials with easily accessible and comprehensible information on open trials for themselves and their patients (e.g., websites, brochures, postcards, summary sheets, etc.).

Among clinicians' biggest concerns was the potential negative impact participation in a cure trial may have on an individual's engagement with clinical care, particularly if treatment delays or interruptions were involved. Clinicians in our study expressed trepidation that patients who receive experimental intervention(s) and laboratory results from the research team may be less inclined to see their HIV providers. Congruently, Moodley et al. found key informants in South Africa (including four clinicians) expressed concerns that ATIs might disrupt established routines of ART adherence [18]. Clinicians expressed a desire not only for timely communication from the study team with laboratory results and other clinical information, but also for the team's plans to reinforce engagement with care. Here it would likely be advantageous for both HIV cure trialists and community providers to carve out time for direct communication before and during ATI trials, either in person or via videoconferencing platforms, as personal connection could be an important means of building trust. We also believe it will be important to have conversations about remaining engaged in care with future HIV research participants as part of the informed consent process to ensure that research participation does not detrimentally impact an individual's retention in clinical care. While some providers did not view it as an emergency, immediate treatment initiation is the current clinical practice standard with numerous studies demonstrating clinical benefit to initiating treatment immediately upon diagnosis [48,49]. For trials that would involve either treatment delay or interruption, some providers expressed concern about the mixed message that would send regarding the importance of medication adherence. Clinicians stressed the necessity that participants understand that adherence outside an ATI study would still be essential in the absence of cure. A few

expressed doubts that patients would be willing to forego their medications after years of adherence messaging. The contradictory nature of ATIs will indeed require a robust, continuous informed consent process throughout the duration of a given clinical trial, along with close monitoring, to ensure participants are fully informed and to prevent therapeutic or curative misconception [18,50]. Furthermore, clinicians recommended that only clinically stable patients participate in trials involving ATIs, and that research teams collect extensive locator information to ensure retention and enforce robust safety monitoring. These findings are consistent with a recent consensus statement guiding the safety and ethicality of ATIs [9]. Consistent with the ATI consensus statement guidelines [9], clinicians were also more cautious when tolerating extended periods of viremia [9,13]. This finding further corroborates a recent global survey of 114 HIV care providers who expressed caution with extended ATIs that called for sustained periods of viremia [24].

Finally, of particular concern to the community clinicians interviewed herein, was the potential risk of ATI trial participants transmitting HIV. This concern has also been expressed in prior socio-behavioral research on ATIs in a variety of settings [14,18,24,44]. Clinicians recommended that steady partners be provided or referred for PrEP. They voiced a greater concern about non-steady partners, with some believing participants should either commit to abstinence or the use of barrier protection while off-ART or be excluded from particular trials. Nevertheless, it will be important for clinicians to engage in conversations with patients to reinforce understanding of a protocol's requirements for preventing secondary HIV transmission [14]. In summary, ensuring participants can be closely monitored and can implement safety precautions for sexual partners will be important to gain community clinician support for HIV clinical trials involving ATIs.

Our considerations for both trialists and care providers for engaging HIV clinicians in HIV cure research can be found in Table 3.

We acknowledge limitations to our study. First, the purposive nature of the interviews may have introduced a sampling bias. Since the study was implemented during the COVID-19 pandemic, several clinicians were unavailable to participate (30% response rate), which may have further skewed the sample. Clinicians were not diverse with respect to race or ethnicity, yet were largely representative of those serving PWH in the Seattle area. As with much qualitative research, findings should be viewed as hypothesis generating. Since data were collected in one U.S. city, they are not generalizable to all infectious diseases or other HIV clinicians in the United States. Additional research will be needed to understand clinician perspectives across a diversity of settings using different methodologies.

Conclusions

HIV clinicians in our study were generally supportive of HIV cure research. With appropriate participant protections, easily accessible trial information, and well-defined communication plans between research and care teams, HIV clinicians appear willing to be engaged as partners in facilitating patient access to HIV cure trials. The data suggest there is value for HIV cure trialists to foster relationships with local treatment providers in advance of trials opening for enrollment and to sustain these relationships over time to enhance

long-term trust in the HIV cure research endeavor. Indeed, the adoption by clinicians of an efficacious intervention will be essential for optimal roll out of any HIV cure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability

All data relevant to this study have been provided in the text and in the Supplementary Appendices.

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Table 1:

Demographic Characteristics Infectious Diseases Clinicians (Seattle, WA, United States, 2021)

Demographics		
	n	**%**
Gender		
Male	5	42%
Female	7	58%
Ethnicity/Race		
Caucasian/White	10	83%
Black/African American	0	0%
Latinx	0	0%
American Indian, Alaska Native, Native Hawaiian, Other Pacific Islander	0	0%
Asian Descent	2	17%
Type of Provider		
Infectious Diseases Specialist (MD)	5	42%
Family Practice/General Medicine (MD)	2	17%
Advanced Registered Nurse Practitioner	2	17%
Physician Assistant/PharmD	1	8%
Internal Medicine (MD)	1	8%
Hematology/Oncology/HIV (MD)	1	8%
Health Care Setting		
Hospital-Based Clinic	3	25%
Private Practice	3	25%
Community Health Center (CHC)/Ryan White Clinic	1	8%
Federally Qualified Health Center (FQHC)/Ryan White Clinic	1	8%
Mixed Settings	4	33%
Time Providing HIV Care		
3 - 5 years (#107, 110)	2	16%
>5 - 10 years (#s105,112, 114)	3	25%
>10 - 25 years (#s 101, 102, 113, 115)	4	33%
More than 25 years (#s 104, 106, 108)	3	25%
Number of Patients		
11 - 25 patients (#104)	1	8%
26 - 50 patients (#s 105, 107, 110, 113)	4	33%
50 - 99 patients	0	0%
>100 patients (#s 101, 102, 108, 112, 114, 115)	7	58%

Notes:

Clinicians 103, 109 and 111 withdrew from the study due to time constraints.

One provider gives gender-affirming care.

Table 2:

Clinician Suggestions for Keeping HIV Providers Informed about HIV Cure Research

Trial referrals	Easily navigable, searchable website or app with information on open HIV cure trials, entry criteria, study aims, etc.
	Trial brochures/postcards to give patients
	Laminated sheet summarizing open trials
	Brief talks at provider meetings providing study overviews
	Phone numbers of a designated staff member to answer questions if patient/provider wants to learn more about a specific trial
Advances in HIV cure research	General review of cure research developments in major conference update presentations (Conferences on Retroviruses and Opportunistic Infections/International AIDS Society/Infectious Diseases Society of America)*
	Review updates at national conferences*
	HIV cure research updates at community-oriented conferences, e.g., Ryan White*
	Local/regional seminars (preferably with Continuing Medical Education (CME) credits)*
	Online seminars that can be accessed any time*
	Single day pre-conferences at national or international conferences*
	Email/listservs (although recommended, several noted that they are inundated with too many emails)
	Monthly email update customized for clinicians
	Publications in clinician-oriented journals
	Podcasts/Twitter feeds (free of pharma influence)

* Use language that can be understood by non-scientists

Table 3:

Suggestions for Bridging the Divide Between Community Clinicians and Trial Investigators Engaged in HIV Cure Research

Suggestions for Trial Investigators	Suggestions for Community Clinicians
Set up an easily searchable online repository of local open HIV cure trials, including inclusion/exclusion criteria	Learn about HIV cure-related trials open to enrollment at ClinTrials.Gov (https://clinicaltrials.gov/) and the Treatment Action Group HIV cure trial listing (https://www.treatmentactiongroup.org/cure/trials/)
Devise simple trial referral mechanisms that include contact information (a phone number or email address) and a live person from the study team to interact with	Become familiar with local trials, their aims, and requirements, prior to advising patients on participation
Create study recruitment materials that follow plain language and people-first principles that include a phone number for talking with a study team member that clinicians can give to their patients; refer to the NIAID HIV Language Guide https://daidslearningportal.niaid.nih.gov/local/pages/?id=17	Take advantage of opportunities to learn about HIV cure research progress via mechanisms designed to be accessible to non-scientists, such as the "Young Investigators' Symposium" at CROI, or post conference community summary presentations
Inform local providers about current or upcoming studies, via calls, staff meeting presentations, webinars, or community-wide in-person presentations; begin education and building relationships prior to study launch	Invite local HIV cure trial investigators to present their study at a team meeting if there are locally available open trials
Develop a written plan for how/when study labs and other information of clinical importance will be shared with clinicians whose patients are enrolled; share this with clinicians when introducing the study	Share any concerns about a specific local trial with the investigators, and any recommendations that would make the trial more palatable to refer patients
Generate a Frequently Asked Questions (FAQs) document, simplified protocol, or other summary document detailing study goals, expectations of participants, labs, safety monitoring plan, clinician communication plan, and how participants will be encouraged to remain engaged with their clinical care; include ATI rationale, monitoring plan, ART restart plans, partner safety plan, if trial includes ATI	Share study recruitment/explanatory materials with patients who express interest in HIV cure research
Eliminate burdens on referring clinicians as much as possible; invite their ongoing feedback to identify these challenges to the referral process	Subscribe to an HIV cure listserv or digest
Design participant education materials that emphasize the importance of staying engaged with their clinical care teams while in the study. If there is an ATI or treatment delay involved, education materials should also include information on why the ATI or delay is needed, how their safety is being protected, and the importance of taking their medications correctly post ATI or ART initiation delay.	