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Perceptions of risks and benefits of participating in HIV cure-related research among diverse young adults living with HIV in the United States: qualitative research findings

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Running Head: Perceptions on HIV cure research participation among YLWH

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Abstract

In the United States, young adults have the highest rates of new HIV infections, and are less likely to be aware of their infection, be engaged in care, or achieve HIV viral suppression. As biomedical HIV research increasingly focuses on achieving long-term suppression without antiretroviral therapy (ART) and finding an HIV cure, little is known about perceptions of young adults living with HIV (YLWH) regarding HIV cure research. We recruited a diverse sample of 20 YLWH (18-29 years old) to participate in individual semi-structured qualitative interviews to explore knowledge and perceptions of HIV cure research, and motivations and barriers to participation. Most participants had little knowledge of HIV cure research. Motivators of HIV cure research participation included altruism, stigma reduction, and the elimination of the clinical burdens of HIV. Barriers included potential physical side effects, psychological distress, the possibility of disclosure as a result of participating, and the amount of time required to participate. Most participants had concerns about analytic treatment interruptions (i.e., ART interruption to assess HIV remission), and indicated that they would want more frequent laboratory testing and protection for their sex partners during this time. Lastly, participants suggested that, if other YLWH are considering participation in cure research, they should first learn as much as possible about the research, then consider the potential personal benefits and the contribution that they could make to science and their communities. As HIV cure research advances, the participation of YLWH will be critical. Our study provides knowledge about how YLWH view HIV cure research. More socio-behavioral research is needed to ensure that those who are most likely to be the decision-makers and beneficiaries of an HIV cure are included at all levels of research.

Introduction

In 2018, young adults between 25–29 and 20–24 years of age had the first and second highest HIV infection rates, according to the US Center for Disease Control¹. Further, young adults are the least likely to be aware of their infection, are less engaged in HIV care, have lower viral suppression rates, and are less represented in HIV research compared to older adults²⁻⁶. As the high incidence of HIV among young people persists, and older people living with HIV (PLWH) continue to age and become ineligible for participation in HIV cure studies, young adults living with HIV (YLWH) will be spearheading decision-making related to HIV cure research studies. However, there is a dearth of data on their perspectives on HIV cure research.

Although antiretroviral therapy (ART) has sustained the lives of millions of PLWH worldwide, high levels of ART adherence remain low^{7,8}. Biomedical research towards an HIV cure is rapidly advancing and targeting the outcome of ART-free sustained viral suppression. As of March 2022, 250 interventional and observational studies for HIV cure were being conducted worldwide⁹. Though, little is known about the perceptions of risks and benefits involved in current HIV cure research, which are notable, the extant literature has largely focused on older PLWH^{10,11}. Perceptions of the risks and benefits toward different HIV cure research approaches vary based on age. For example, participants under 50 years of age were more likely to be demotivated by perceived social risk (e.g., stigma, discrimination, fear of HIV transmission during analytic treatment interruptions [ATIs; ART interruption to assess HIV remission]) compared with those over 50 years¹².

Due to their age, perception of risks and benefits of YLWH toward HIV cure research, ATIs, HIV disclosures, and HIV-related stigma may drastically differ from older PLWH. Additionally, YLWH may have different levels of trust toward medical establishments and altruistic attitudes toward participating in HIV research versus older PLWH who have lived through a historically different period of time¹³. Further, given the advancements in ART, YLWH have a different experience from older PLWH regarding ART because YLWH have benefitted from newer ARTs that have lower dosing frequency and fewer adverse effects. Some YLWH do not perceive cure strategies to be better than their current treatment^{12,14}. These differences in perceived risks and benefits between YLWH and older PLWH warrant further investigation to understand how factors such as stigma,

moral obligation to participate, and experiences with HIV medications can explain these differences.

Although YLWH will likely be most directly affected by future cure interventions, as they become available^{12,13}, currently available research on the perceived risks and benefits of HIV cure research may not be representative of young adults who share notably different views of HIV cure research^{13,15}. Future HIV cure research must include more perspectives from racial and ethnic diverse populations – who have been disproportionately affected by HIV¹ – and younger populations who will make up participant pools for future research. Engaging and recruiting younger populations into novel HIV cure studies will require an understanding of their motivations for a cure and perceived barriers to research. Therefore, we conducted semi-structured one-on-one qualitative interviews with diverse YLWH to gain insights into the perceived motivators and barriers to participation in HIV cure research.

Materials and methods

Study overview

The purpose of the Youth4Cure study is to explore the level of knowledge, interest, concerns, motivators, and deterrents of participating in HIV cure research among YLWH in the US. As the first step toward this goal, we conducted semi-structured individual qualitative interviews with 18–29-year-olds living in the US.

Participants were recruited through contacting clinic staff or organizations serving YLWH across the US to notify them of the study, re-contacting participants from prior studies who had consented to be contacted for future research, and peer referral. Young adults ages 18–29 living with HIV, residing in the US, who were English-speaking, willing and able to provide informed consent, and had access to a mobile telephone and/or a computer with internet access were included. Those who met inclusion criteria after telephone screening were asked to text message a photograph of an identification card to verify date of birth and a proof of HIV status (a letter of diagnosis, laboratory results, or HIV medication prescription). Participants were recruited purposively¹⁶ as we sought to ensure diversity in race, ethnicity, gender, and geographic location in the US.

Prior to initiation of the individual semi-structured qualitative interviews with YLWH, we asked participants to complete a brief online demographic survey using Qualtrics which was emailed or text-messaged to participants. The survey inquired about demographics (age, gender, race, ethnicity, sexual identity, time since HIV diagnosis, city/state of residence, education and work, and financial stability [including three responses: cannot get by on the money I have, can barely get by on the money I have, or have enough money to live comfortably]).

All interviews were conducted by one investigator and took place using a Health Insurance Portability and Accountability Act (HIPAA)-compliant videoconferencing platform to allow for flexibility in scheduling and audio-recording of the interviews. Verbal informed consent was received as approved by the University of California, San Francisco (UCSF) Institutional Review Board. Interviews lasted 45–60 minutes and followed an interview guide developed by study co-investigators (Supplement 1). Interview domains included perceptions of HIV cure-related research, facilitators and barriers of participating in HIV cure-related research, perceptions of HIV treatment interruptions, and considerations for engaging young people in HIV cure-related research. Participants were provided with a \$40 electronic gift card upon completion of the interview. We conducted interviews until three co-investigators who had listened to all interviews agreed that saturation had been reached^{17,18}.

Data analysis

Using the quantitative demographic survey, we describe the sample of participants using measures of central tendency (mean, standard deviation, etc.). Qualitative interviews were audio-recorded, anonymized, and stored on the university secure network. Interviews were then transcribed and the primary analyst wrote field notes immediately after conducting the interviews. A second and third analyst each successively listened to the audio recordings and while editing and building upon the previous analyst(s) notes and adding direct quotes. We then used these detailed notes to follow the procedures of Framework Analysis¹⁹, a health policy informed thematic analysis for qualitative research that involves specific questions. One investigator organized the research data into a framework matrix, which was used to identify overarching themes and findings. Three investigators discussed emerging patterns and themes, synthesized

results based on participant responses, and selected exemplary quotes to further elucidate important discussion points.

Results

From August–October 2020, we interviewed a select group of diverse 20 YLWH (Table 1). Participants had a mean age of 25.7 years (SD= 2.6), and mostly identified as male (65%), Black race (25%), gay (50%), and living in the Western region of the US (65%). Three individuals (15%) were HIV diagnosed at birth. Approximately 55% of participants had experienced financial instability.

Generally, most participants reported not knowing anything specific about HIV cure research except news article headlines (e.g., the “Berlin patient”). When asked about what comes to mind when they hear the phrase “HIV cure,” participants’ responses generally fell along “clinical impact” or “personal benefits” categories. Clinical impact responses were summarized as “going beyond undetectable,” “becoming negative again,” virus is “dormant,” “giving the immune system a break,” “completely resolve” or “eliminate” HIV. Examples of the personal benefits responses included: “No longer living with the complications of HIV;” feeling hopeful; relief from taking medications, doctor appointments, and insurance issues; having less stress and stigma; and no longer having to disclose HIV status. Main interview themes included **(1)** facilitators of HIV cure research participation, **(2)** barriers to HIV cure research participation, **(3)** ATI perspectives and concerns, and **(4)** what young adults should consider before participating in HIV research. Figure 1 contains key themes and sub-themes of the interviews.

Figure 1. Themes and sub-themes of the perceptions of HIV cure-related research among YLWH.

Facilitators of HIV cure research participation

The three themes of **(1)** altruism, **(2)** getting rid of stigma, and **(3)** reducing the clinical burden of HIV were the main reasons that participants noted as reasons why they might participate in HIV cure research.

Altruism

Most participants expressed the desire of wanting to be a part of the discovery of a cure for HIV, to “defeat the virus,” “contributing to something that would change a lot of lives in the future,” and changing “the world.”

“I am able-bodied enough and I have not had any adverse effects of any medication that I’ve been on... so I guess this would be a good baseline for trying new medication... so I guess the possibility that this could help other people...” (28-year-old, API, male)

“I would want to give my time and actually put my body on the front line to make sure that this cure is available to everybody who is living with HIV.” (29-year-old, White, genderqueer)

Getting rid of stigma

Most participants identified reasons for HIV cure research participation that was related to social implications of an HIV cure. They described the perpetual stigma of living with HIV described by young adults and that it would motivate them to participate in this research.

“...to release a burden of a stereotype of HIV that comes with it. For me personally, having this virus, you feel like you’re not wanted. You don’t feel as special as someone who is STD-free. When HIV comes to mind, they automatically assume AIDS. They assume it’s a gay disease. If they catch it they can die. It’s just so many things... you just feel like trash. Will you ever find that person to love you for you? Not everybody is mentally strong to pull themselves out that hole. When people hear HIV, they automatically assume death... nobody wants this...” (24-year-old, Black, female)

Some participants described how an HIV cure could eliminate their worry of others being afraid of them, bearing the burden of HIV, and worries about others seeing their medications.

“You are shunned. Seroconversion is painful enough but then you also have to deal with the psychological and emotional pain. Being a part of the study and helping to develop a cure would be one way to be free of that.” (26-year-old, multiracial, genderqueer)

Reducing the clinical burden of HIV

Similarly, participants identified challenges of HIV clinical impact as reasons for HIV cure research participation. These reasons included challenges with needing to take medications daily, going to frequent medical visits, and having to do laboratory tests. One participant summarized this as the fatigue of living with HIV and the possibility of living a life without it.

“I would like to join it because taking my medicine is tough... I’ve been taking medicine all of my life... [I’ve had] a monthly doctor visit... if there was a way for this to lessen, I would actually be happy” (23-year-old, Black, female)

Barriers to HIV cure research participation

While some participants were able to identify reasons to participate in HIV cure research, they questioned whether it was worth trading a care and treatment routine that they are accustomed to and that is effective, for an unknown strategy.

“I need to look at the long-term point of it... I’ve been on medication for this long... I’m okay being on medication for the rest of my life... [If the cure strategy proved ineffective], I would want to know why I messed that up when I was not having any problem right now... I would want to know why I messed my well-being when I don’t know the future of it... I know that the medications can only get better... is it good enough for me to do it [*cure research participation*] now versus me being on medication now that will continue to get better as time goes on” (23-year-old, multiracial, male).

“Now, just the comfortability that I have living with HIV... it’s like every day to me, it’s a part of me. I don’t know what my life would be without it...” (25-year-old, Black, female)

We asked participants’ reasons why they would not want to participate and what would constitute ‘too much risk’ to elicit perceived barriers to participation in HIV cure research. Risks such as disruption of daily life and death were mentioned by some participants. Surprisingly, a few participants stated that there was no risk that would be a barrier to their participation.

“I feel like participating no matter what will help improve a patient’s life... another young person’s life... it’s a reason to get involved” (23-year-old, Black, male)

The majority of participants identified concerns regarding risks and side effect of HIV cure research which may prevent their participation. Identified barriers included: **(1)** Physical health side effects, **(2)** psychological distress, **(3)** potential for HIV status disclosure, and **(4)** lack of time to participate.

Physical health side effects

Concerns about side effects as potential barriers to participation were common among participants. Examples including anything that would result in the individual to become sicker or develop a rash; impact their kidneys, liver, stomach, lungs, bones, or brain; result in cancer; or cause fatigue.

“If it has some damage to all the organs of mine, I might reconsider it... for example... stomach or liver or causing directly side effects to my body... for example if it makes me very fatigued and I cannot focus on work... that would be another reason.” (28-year-old, API, male)

Several participants described “too many side effects” (23-year-old, Black, female), “physical impairment” (29-year-old, White, male), “changes to your overall well-being [whereby] your family and friends notice a change in your behavior” (29-year-old, White, male), or effects on overall health as ‘too much risk.’

Psychological distress

Several participants expressed concerns regarding a connection between HIV cure research participation and psychological distress. For some, participation and the strategy being investigated could be an additional stressor that may exacerbate their current depression, stress, anxiety, or trauma.

“If anything were to affect my mental health... When I was younger... my medication made my depression worse... I would want to make sure that this stays healthy as well because it’s part of everything” (28-year-old, API, male)

Others worried about the possibility of getting their hopes up and being let down if the experimental cure intervention was unsuccessful. They noted the emotional trauma and the “let down” after the time and effort dedicated to a failed result as being difficult to bear.

“I would not want somebody telling me that I am cured, and then the cure falls through... it would mess with my mentality... then you have the whole mixture of emotions” (24-year-old, Black, female)

For some, the psychological distress associated with participation constituted ‘too much risk.’

“I would probably lose my mind at that point. I got my hopes up... actually took the chance, and already convinced myself. Yeah, I took this cure, regardless of whether I’m comfortable living with HIV or not. I already pre-planned some things that I envisioned so much, to just be told it didn’t work. It’s a beat down. For me, I wouldn’t be upset, and it’s just another day. The disappointment would just trigger people, like the loss of a job. It’s a crush, because you already convinced yourself in your mind. You were ready to go, and you were let down. It would probably be a traumatic experience for a lot of people.” (25-year-old, Black, female)

Potential for HIV status disclosure

Given the persistence of HIV stigma, some participants expressed high level of concern about any possibility that participating in an HIV cure trial might lead to others knowing about their status. They noted that the inadvertent disclosure may be due to seeing people they know in the program or having their identity publicized, and having their friends and family reject them, take pity on them, or treat them differently. This was considered to be too much risk for them.

“I do want to get involved, but it’s still something that I have not even fully disclosed to my own relatives. I am still apprehensive about being extremely public about it, but I do feel comfortable sharing with like researchers or being in groups with other people with the same condition. My main deterrent, at this time, I don’t see myself being on TV, or doing a press conference...Something a little behind closed doors for the time being... Just having to expose my relatives is an ongoing fear of mine, it’s something I’m working on personally” (27-year-old, Latino, male)

Lack of time to participate

Several participants identified logistical challenges as potential barriers. Specifically, the time that might be required for study participation was a concern due to conflict with school, job, or life events.

“If it’s something that may be... too much for me... I’m going through too much that week or that month... or it’s conflicting my time” (23-year-old, Latino, male)

Analytic Treatment Interruption (ATI) perspectives and concerns

The majority of participants expressed some level of fear or concern about potential negative consequences of pausing ART as part of the HIV cure trial methods, i.e., ATIs. For some, these fears were largely informed by messages from public health experts and providers emphasizing the importance of viral suppression via high levels of ART adherence. Three of the four participants who were HIV diagnosed at birth indicated that they were happy to continue taking their current medication. They noted being used to taking daily medications and worried about the risk of stopping ART given the length of time they have lived with HIV.

“If I miss my medication for 30 days, I don’t know what’s going on internally. I just don’t know how strong my immune system is by itself... I don’t know how that’s affecting my body. That’s a lot of what-if factors. (24-year-old, Black, female)

“I’m sure it’s okay for others who have not had it as long... for me who had HIV for so long... I have background noise... I am undetectable... I don’t know if I’d want to take that risk... I’d be worried about becoming non-undetectable and be spiking when I’ve controlled it my entire life” (23-year-old, multiracial, male)

A few participants indicated that they understood the need for ATIs and, while they identified some concerns, that would not prevent them from participating in HIV cure research.

“I feel like it’s important for the research... I just see the logic... I guess [my concern] goes back to that whole opportunistic infections, but if it goes back to controlled research, and everyone is following the protocol, there shouldn’t be much of a concern” (26-year-old, multiracial, genderqueer)

“I understand that this is a part of research, and to evaluate the success of that cure, we have to see if the body can handle the medication, I would talk to the researcher about the plan B, what if the virus comes back, what is the other medication I have to take... so it’s gonna be a lot of conversations, and I have to do a lot of research, and I have to have Plan B and Plan C” (28-year-old, API, male)

Participants concerns centered around **(1)** ATI safety and monitoring, **(2)** restarting ART, and **(3)** protections for sexual partners during an ATI.

ATI safety and monitoring

Some participants expressed concerns about how ATIs might affect their health, both related to HIV care specifically and their overall well-being. One participant discussed their worry of a shorter lifespan if they discontinued ART (29-year-old, White, male).

Another worried about the time until virologic rebound:

“I’m not sure what exactly stopping medication would look like, and how my virus would respond to it, like would it be replicating right away, or would it be gradual, or, would it take maybe one month to get anything significant in terms of replication?” (27-year-old, Latino, male)

We asked participants what strategies they would want to see implemented to make them feel safe if they were asked to temporarily stop ART. They described how often they would want their HIV viral load and CD4+ cell count monitored, what would make them decide to resume ART, and what safety measures they would want implemented for their partners.

There were wide variations in the frequency with which participants wanted their HIV viral load monitored. Several indicated that they would want their bloodwork done once a month, at minimum, with others indicating that they would prefer to be monitored even more frequently. Several participants discussed their interest in getting monitored very frequently initially and then gradually spacing out monitoring visits if there were no laboratory abnormalities.

“I think monthly... well I think it can go from like... you would start weekly, when bi-weekly, then monthly... to whatever macrolevel... I actually feel like that would be the best.” (26-year-old, multiracial, genderqueer)

A few participants wanted to be monitored relatively less frequently but wanted a complete bloodwork more often than every three months, which was their current HIV viral load monitoring frequency. One participant, who had a fear of needles, was not fond of the idea of frequent blood draws, but expressed a willingness to give an ATI a trial run.

“If they have to do extra monitoring, they’d have to poke me!... probably not the best for me... just because I don’t like needles, I hate getting poked... Maybe I’d do

it if we check it in two months, and then I'll go back on my medications." (23-year-old, multiracial, male)

Restarting ART

Several participants noted their worry around developing drug resistance to their current ART once they have discontinued and therefore being unable to go back to this regimen if they needed to restart.

"What if this treatment does not work, and my virus... [no longer responds] to the medicine I'm so used to taking, and now I'll be switching to a new medicine... if I'm able to understand all the possibilities, and all the situation you might experience after you stop the medicine, and how much it's affecting your body, if I don't have those super clear data, I'm definitely not comfortable. Even though I have all these data, it does not stop my worries... (27-year-old, API, male)

Nearly all participants referenced CD4+ cell count decreases, HIV viral load increases, or negative physical or mental health effects as the criteria for resuming ART. The negative health effects were noted to be particularly problematic if they continued daily and were disruptive to an individual's daily life.

"I do feel that if people start feeling a sense of depression or they may need therapy, they should restart medication... I just believe that if your results are fluctuating too much, you should probably just go back on your medications... we don't want the person's life to be at risk just for the research..." (23-year-old, Black, male)

Protections for sexual partners during an ATI

Several participants expressed concern for how not being on ART could place their sexual partners at increased risk of HIV acquisition. They identified PrEP, condoms, and resources for obtaining PEP or PrEP as potential ways to prevent transmission if they did not have an undetectable HIV viral load.

"... if one of the partners isn't taking their meds in the relationship, maybe the partner needs to be on PrEP and take it constantly and every day... so that nothing happens in the future" (23-year-old, Black, male)

What young adults should consider before participating in HIV research

We asked participants what they thought other young adults should think about before deciding to participate in HIV cure research. Participant responses were categorized into three themes: **(1)** knowledge of study details, **(2)** personal meanings and benefits of participation, and **(3)** altruism.

Knowledge of study details

Most emphasized that young adults should be very thoughtful about all aspects of research and ensure that they are fully informed about such things as study pros and cons, emotional strain, side effects, and logistics. One participant noted the importance of a reputable referral source and investigators. Several participants suggested that young adults should learn as much as they can before participating.

“Ask questions, a lot of time people see the big informed consent form, like it’s just a formality... I kinda connect with someone to run questions by, what this actually means, I think that would be wise. A lot of times what scares people is they can’t relate to it, they can’t understand the terminology...” (29-year-old, Black, male)

“make sure you read everything... make sure you’re comfortable with the choices you are making... just know we’re not sure of anything yet... don’t expect too much... have hope but don’t expect it to work the first time around... we’re not sure if that’s how that works...” (23-year-old, multiracial, male)

In addition, participants suggested that young adults should consider all that may be required of them including logistics and study procedures (e.g., blood draws, study visits), as well as side effects of the study interventions.

“I would tell them to definitely you know go over the pros and cons, ask if there are side effects, ask how long this study is, but also put their best foot forward, because this would help the community and the world at large if we do get an HIV cure, but definitely ask questions and be their own advocate, and have an open mind... and making sure that they’re taking care of during the study, not just when they’re being experimented on, researched on, but also being monitored holistically” (29-year-old, White, genderqueer)

Personal meanings and benefit to participants

Some participants felt that young adults should base their decision about cure research participation on their personal definition of what living with HIV meant to them and what a cure would mean in their lives. In this regard, they would find peace in their decision instead of basing it on what society would want or expect from them.

“... define what HIV cure means to you, do not base that on what the primary care physician or what society tells you... what it means to you, and accept the fact that you have it, and you are living with HIV... I would take a dive deep into research in terms of the progress and advancements of technology of HIV... and how it’s so currently advanced, and how it’s not a bad topic to discuss as it was back then... and not look at HIV from an emotional standpoint...” (25-year-old, multiracial, male)

“... considering all aspects of the cure, I’d think about life after the cure, the real reason about why they want to get the cure. If the real reason is about what other people think, instead of what they think, I would not suggest they get the cure... It’s their health, their look on HIV, anything related to self versus the world or other people” (25-year-old, Black, female)

Others emphasized that young adults should consider how cure research participation can benefit them personally. These benefits included getting connected to other people living with HIV, finding helpful resources and services, learning more about HIV, and being paid for research participation.

“If you’re down about your symptoms, I would suggest participating... Learning more can make you feel better... when I hear this word [undetectable] I felt better... I wouldn’t make people sick.” (29-year-old, White, male)

Altruism

Some participants placed emphasis on how other young adults should consider that dedicating themselves to this cause could contribute to the greater good, make them proud to be a part this research, and help other people.

“We are human being, we live as a social connection, so everything we do, every action we do is related to other people... you can choose to be a better person, for other people as well, for the community. It’s kinda like my mantra. I want to be

better for other people. I want to change the world by doing some things like I am capable to do, I can have the privilege to do.” (28-year-old, API, male)

“I think the first thing is definitely thinking about what you can bring to the group, the new way of thinking... you might bring a totally different way of understanding things... (27-year-old, API, male)

Discussion

To our knowledge, this is the first socio-behavioral study on perceptions of HIV cure-related research to focus exclusively on YLWH. We found wide-ranging perceived motivators and barriers to participation in HIV cure research among interviewees. First, very few participants had ever heard of HIV cure-related research, and several of them raised important questions around trading established treatment and care routines versus the uncertainty of participating in HIV cure-related research. Even though most were engaged in care, few had little prior awareness of HIV cure, one of the most important priorities for the National Institutes of Health²⁰, which reveals a clear need for further education and outreach on HIV cure research. Second, many YLWH expressed ideas regarding altruism and research participation. While narratives about giving up their bodies to science or to advance a cure have been documented in studies with older populations¹¹, including in the end-of-life studies²¹, we have yet to find these narratives among YLWH. Third, despite having exclusively experienced ART with low pill burden and few adverse effects, most participants were eager to receive an HIV cure without the consideration of any upper thresholds of acceptable risk. Fourth, psychological distress was a prominent theme that was expressed by nearly all participants as a barrier to participation in HIV cure research. Finally, most participants expressed fear or concern over the seemingly contradicting messaging between Undetectable=Untransmittable^{22,23} and need for ATIs. ATIs were particularly concerning for YLWH who had acquired HIV perinatally.

The majority of YLWH in our study had not previously heard of HIV cure-related research. This finding is consistent with prior focus groups conducted among predominantly older Black/African Americans in the US²⁴. When probed about an HIV cure, participants also conceived of a cure as completely resolving or eliminating HIV, or relief

from HIV medications, corroborating results from prior studies in older adults living with HIV^{14,25,26}. Interestingly, there were additional insights gained by some YLWH. For example, some viewed benefits of a cure as not having to live with HIV complications, taking ART, attending doctor appointments, dealing with insurance issues, as well as having less stress, stigma, or fear of disclosure. An important caveat is that HIV cure research participation may require more frequent clinic visits to monitor safety (e.g., HIV viral load rebound)²⁷. For YLWH who have benefited from the availability of potent ART, it will be important to adequately manage expectations about when efficacious HIV cure-related regimens would be available²⁸. Additionally, participation in HIV cure trials that require ATIs may also place YLWH in situations where they have to disclose their participation to sexual partners²⁹. This is because with ATIs, there are extended periods of time where participants are off ART and may experience viral rebound²⁷. Having sufficient support regarding disclosure processes, PrEP for sexual partners, and counseling are services being considered necessary for HIV cure research²⁹, which were also echoed in our data.

Interestingly, although 55% of young participants in our study reported being financially unstable, compensation did not surface as a strong theoretical motivator to participation^{30,31}. However, altruism emerged as an important facilitator for HIV cure research participation among YLWH, concordant with previous research on willingness to participate in older adults^{32,33} and accounts from prior trial participants^{34,35}. Importantly, engagement and recruitment efforts around HIV cure-related research will need to be focused on long-term scientific and societal benefits of participation³². The social implications of participation – including reducing stigma – emerged as an important motivator, which is also consistent with prior research conducted among diverse women living with HIV in the US³⁶, as well as research on theoretical willingness to participate^{25,37}. What will be important to consider for future purposes is the nuanced issue that current HIV cure strategies under investigation are not completely eliminating HIV from the body, and thus, whether YLWH would view themselves as free of stigma and disclosure requirements¹¹. More research will be necessary to understand how HIV cure research participation, particularly ATIs, affect both internal and external stigma in YLWH³⁸.

Most YLWH viewed physical side effects as a barrier to participation, congruent with prior socio-behavioral sciences research showing high thresholds of safety would be

necessary for HIV cure-related research interventions to remain acceptable to diverse PLWH^{14,39}. In our study, the potential for long-term toxicity or opportunity costs of participating in earlier studies (versus later studies when interventions may show more efficacy) did not emerge as important topics, but we suspect these considerations will remain important for PLWH. Ethically problematic was a subset of participants who did not place any upper thresholds of acceptable risk in their calculation whether to participate⁴⁰.

An important finding in our study was the frequently discussed psychological distress that may be associated with HIV cure research participation. The possibility of developing or exacerbating depression, stress, anxiety, and trauma emerged as important concerns, and underscored the urgency of incorporating mental health assessments and counseling and support interventions to address psychosocial needs during trial participation^{14,38}. In particular, ATIs have been associated with anxiety in both theoretical^{41,42} and actual³⁴ HIV cure-related research with older PLWH. The mention of emotional trauma around being let down if a cure regimen did not work was a salient one. Prior participants have expressed disappointments following relapse of virus⁴³.

Additional deterrents included the potential for HIV status disclosure and the social risk of being recognized as someone living with HIV. Ethically, HIV cure research teams must have robust confidentiality protections for PLWH participating in this research⁴⁴. Logistical aspects such as time commitments and transportation should also be taken into account³⁶. While structural racism and discrimination did not emerge as major themes in our study, we acknowledge that these issues remain critically important in decisions to engage in biomedical research, particularly for Black/African American people living with HIV, and will need to be further explored⁴⁵.

Other barriers to HIV cure research participation were framed in terms of concerns around trading a known treatment and care routine with uncertainty. This is a salient finding, because ART adherence has traditionally been a challenge for PLWH⁴⁶. This perceived contradiction between the need for ART adherence and trial designs that require disruptions in ART have been noted elsewhere^{24,26,42,47,48}. This finding is also consistent with results from older Black/African American individuals who reported being satisfied with life on ART²⁴. Participants who acquired HIV perinatally discussed their content with continuing taking their current medication given the duration of time that

they have lived with HIV and not knowing a life without HIV⁴⁹. The perceptions of YLWH who acquired HIV perinatally may also more closely align those of long-term survivors who have experienced a long journey towards becoming virologically suppressed.

The need for robust partner protection measures also appeared paramount for YLWH, including PrEP and condoms for sexual partners, consistent with prior research^{47,48}. While consensus has not been achieved on acceptable risk mitigation packages for sexual partners of ATI trial participants, various approaches have been proposed^{29,50}. These are also ethically relevant and align with the principle of non-maleficence. Finally, a topic that was unexplored in our study was the need to integrate HIV and reproductive health services for YLWH, particularly women living with HIV^{51,52}.

Our research is limited in that we captured the voices of 20 diverse YLWH from across the US; however, due to this relatively small sample size, our results may not be generalizable to all YLWH, especially those in other countries. There are currently no published studies comparing hypothetical and actual willingness to participate in HIV cure studies; therefore, it is unknown how results from this study will translate into actual study participation. However, we believe that these data can help shed light on motivators and deterrents of YLWH to participate in HIV cure trials and allow researchers to consider strategies to minimize low participation and retention rates.

Conclusions

YLWH remain vastly under-represented in HIV cure-related research and are less engaged in HIV care than older adults; yet will be key decision-makers in advancements of the HIV cure agenda in years to come¹³. It will be critical to involve a new generation that is less engaged in research and did not witness the early days of the HIV epidemic, while carefully managing expectations around scientific advancements. Optimizing engagement, recruitment, and retention efforts around HIV cure-related research will require involvement of young people of color in all aspects of clinical trials^{13,53}. Given the need for more social sciences research in this area, we have and will continue to use the results from this study to inform a larger survey of YLWH in the US to further explore interest in participating in HIV cure research. Similar research will also be important in international contexts as more trials are set to begin in low- and middle-income countries in years to come⁵³.

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Table 1. Characteristics of the participants.

Characteristics	Sub-categories	N= 20
Age, mean years (SD, range)		25.7 (2.6, 20–29)
Gender, N (%)		
	Male	12 (60.0)
	Female	5 (25.0)
	Genderqueer/Non-binary	3 (15.0)
Race/Ethnicity, N (%)		
	Black	5 (25.0)
	White	4 (20.0)
	Asian/Pacific Islander (API)	3 (15.0)
	Latino	2 (10.0)
	Multiracial	4 (20.0)
	Other	2 (10.0)
Sexual identity, N (%)		
	Gay	10 (50.0)
	Bisexual	6 (30.0)
	Heterosexual	2 (10.0)
	Queer	1 (5.0)
	Pansexual	1 (5.0)
Time since HIV diagnosis, mean years (SD, range)		7.9 (7.7, 10 months–26 years)
HIV diagnosed at birth, N (%)		3 (15.0)
Place of residence, N (%)		
	West	13 (65.0)
	Midwest	3 (15.0)
	South	2 (10.0)
	Northeast	1 (5.0)

Education, N (%)		
	High school/GED or less	9 (45.0)
	More than high school/GED	11 (55.0)
Employment, N (%)		
	Full-time	8 (40.0)
	Part-time	4 (20.0)
	Not working	8 (40.0)
Financial stability, N (%)		
	Cannot get by on the money I have	4 (20.0)
	Can barely get by on the money I have	7 (35.0)
	Have enough money to live comfortably	8 (40.0)
	Decline to answer	1 (5.0)

GED: General Educational Development; SD: standard deviation

Figure legend:

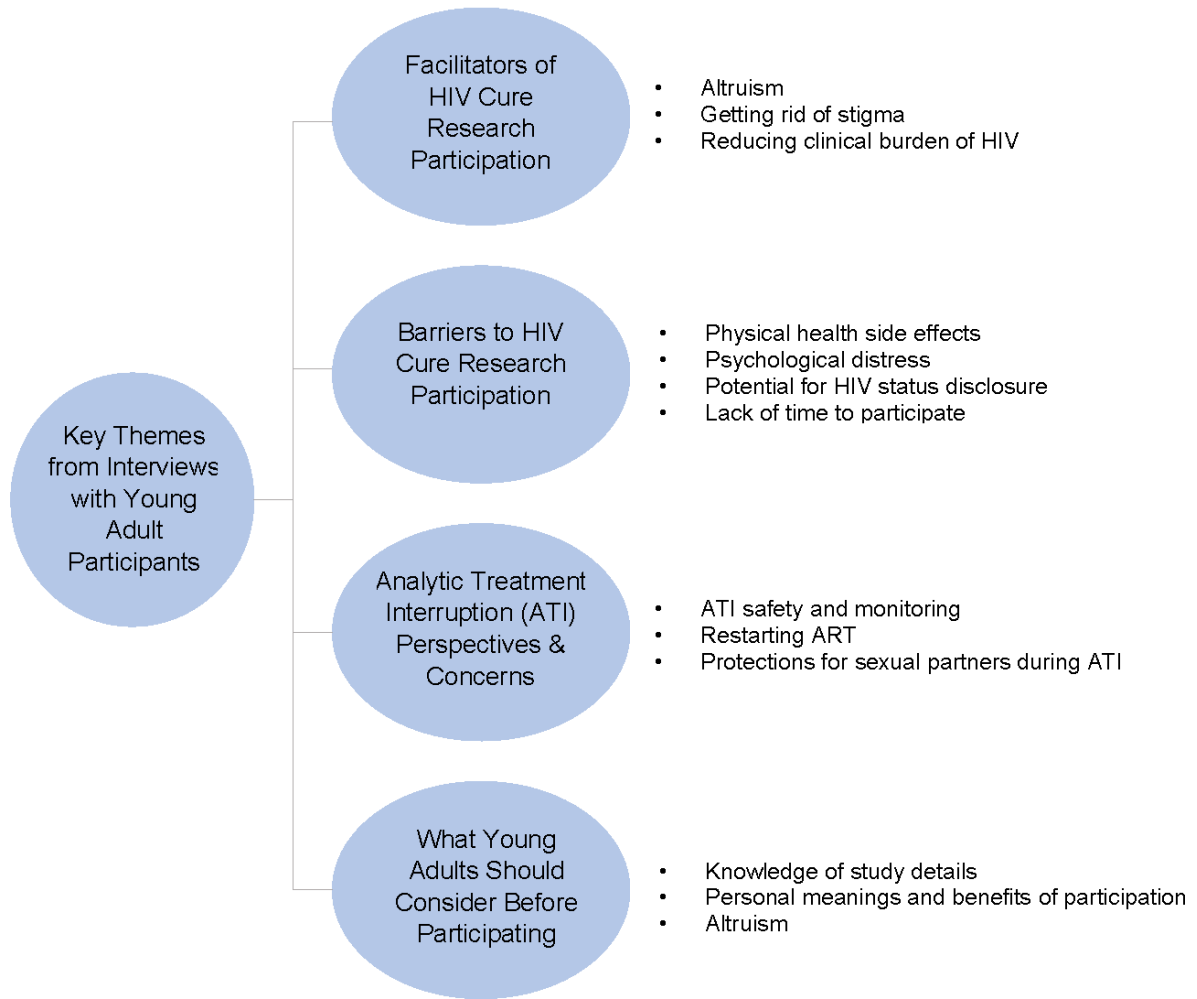


Figure: Themes and Sub-themes of the Perceptions of HIV Cure-related Research among YLWH