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Considerations for Increasing Racial, Ethnic, Gender, and Sexual Diversity in HIV Cure-Related Research with Analytical Treatment Interruptions: A Qualitative Inquiry

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Abstract

Despite disproportionate incidence and prevalence of HIV among transgender individuals, cisgender women, and racial and ethnic minority groups, all remain underrepresented in HIV cure research. As HIV cure trials are scaled up, there is emerging research on ways to mitigate risks of HIV acquisition for sexual partners of analytical treatment interruption (ATI) trial participants. As such, it is imperative that HIV cure researchers consider the implications of implementing ATIs in populations that are disproportionately affected by HIV, but largely underrepresented in trials to date. In this qualitative study, we sought to derive triangulated perspectives on the social and ethical implications regarding ATIs and partner protection strategies during ATIs among under-represented populations. We conducted 21 in-depth interviews with 5 types of informants: bioethicists, community members [people living with HIV (PLWH) and their advocates], biomedical HIV cure researchers, sociobehavioral scientists, and HIV care providers. We analyzed the data using conventional content analysis and reduced the data to important considerations for implementing ATI trials in diverse communities and settings. Our study revealed the following key themes: (1) attention must be paid to gender and power dynamics in ATI trials; (2) ATI trials should be designed and implemented through the lenses of intersectionality and equity frameworks; (3) ATI trials may have both positive and negative effects on stigma for PLWH and their partners; and (4) partnership dynamics should be considered when designing ATI protocols. Our study generated actionable considerations that could be implemented in ATI trials to promote their acceptability to communities that have been underrepresented in HIV cure research to date. Research teams must invest in robust community and stakeholder engagement to define best practices. Paying attention to representation and equity will also promote better and more equitable implementation of HIV cure strategies once these become ready for rollout.

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Background

Globally, women and girls continue to represent more than half of the 38 million people living with HIV (PLWH) worldwide.[1] In the United States, Black/African Americans account for over 40% of new HIV diagnoses each year,[2] and an estimated 44% of Black/African American transgender women and 26% of Latinx transgender women live with HIV.[3] Despite disproportionate incidence and prevalence among transgender individuals, cisgender women, and people from racial and ethnic minorities, all remain underrepresented in HIV clinical research, especially HIV cure research.[4] This is due to structural barriers that compound individual barriers, such as lack of concerted efforts to create awareness about trials to these populations, trial designs and schedules competing with other priorities (e.g., women caring for dependents), provider referral bias, logistical barriers (e.g., transportation), and mistrust in biomedical research, given maltreatment of racial and ethnic minorities in medical settings and the legacy of medical experimentation.[4–7] Between 1995 and 2020, women represented a median of 11.1% of HIV cure trial participants globally, and only one participant has ever been reported to have identified as transgender.[8] In U.S.-based HIV cure studies, the majority of participants are white men,[9] which severely limits the generalizability of research findings.

By HIV cure research, we are referring to any regimen or intervention that could either completely eliminate HIV from the body or induce a state of antiretroviral treatment (ART)-free viral suppression.[10] Globally, over 250 HIV cure clinical studies have been implemented,[11] and a growing number of these require participants to temporarily interrupt their current treatment for the purpose of evaluating intervention effects.[12] These pauses in HIV treatment are called analytical treatment interruptions (ATIs) and carry significant risks to participants, such as elevated viremia and $CD4^+$ cell count decline,[12] as well as the risks to sexual partners, including unintended HIV transmission. Furthermore, by involvement in HIV cure trials, we mean active participation in clinical research as study participants. We acknowledge that PLWH can serve many additional roles in the research process, as advisors, reviewers, information providers, activists, and co-investigators.[13–16]

PLWH who have achieved an undetectable viral load cannot sexually transmit HIV to others—this is called Undetectable = Untransmittable (U = U).[17] In an HIV cure trial with an ATI, the U = U principle of viral suppression is invalidated, leaving sexual partners at risk of acquiring HIV. In these complex studies, sexual partners are not considered trial participants and behavioral risk reduction strategies typically fall outside the scope of these trials.[18–20] At least two unintended HIV transmissions have occurred in the context of HIV cure-related studies in Europe,[21,22] underscoring the urgency of widely acceptable partner protection approaches, as well as considerations for the unique needs of communities where there is a disparate risk of acquiring or transmitting HIV.[17–19]

As HIV cure trials are scaled up in the United States and abroad, there is emerging research on ways to mitigate risks of HIV acquisition for sexual partners of ATI trial participants.[12,19,23] For instance, a research team at the University of California, San Francisco (UCSF), proposed strategies to protect sexual partners, which included, among other recommendations, aggressive pre-exposure prophylaxis (PrEP) navigation.[12] Recognizing the burgeoning interest on this topic in response to documented HIV transmission events, it is imperative that HIV cure researchers consider the implications of implementing ATIs in populations that are disproportionately affected by HIV, but largely underrepresented in trials to date, such as cisgender women, transgender individuals, and racial and ethnic minority populations.

In 1993, the U.S. Congress passed the NIH Revitalization Act (PL 103-43) requiring National Institutes of Health (NIH)-funded investigators to ensure inclusion of women and minority populations in clinical research. Despite this law and the accumulating evidence for sex- and race-related differences in HIV treatment and cure research,[8,24–27] little progress has been observed over the last 30 years in increasing the involvement of women and gender-expansive and racial and ethnic minority populations in HIV clinical research. Diversity in clinical research representation not only allows data to be more generalizable but also ensures the safety and efficacy of products and interventions for all populations.[28] Furthermore, from a societal standpoint, fair representation represents a fundamental matter of equity and justice.[29]

In this qualitative in-depth interview study, we sought to understand the perspectives of a wide-ranging sample of stakeholders—such as bioethicists, community members (e.g., diverse PLWH and their advocates), biomedical HIV cure researchers, sociobehavioral scientists, and HIV care providers—regarding ATIs and strategies for protecting sexual partners of HIV cure trial participants. We sought to understand the social and ethical implications of ATIs and strategies for protecting sexual partners in a variety of contexts, particularly focusing on cisgender and transgender women, and racial and ethnic minorities. Our goal for this study was to generate actionable considerations that could be implemented in ATI trials to promote their acceptability to communities that have historically been underrepresented in HIV cure research.

Methods

Study setting and participants

We conducted 21 interviews with 5 types of informants: (1) bioethicists, (2) community members (e.g., diverse PLWH and their advocates working with underrepresented communities), (3) biomedical HIV cure researchers, (4) sociobehavioral scientists, and (5) HIV care providers. Informants were affiliated with academia, community advisory boards (CABs), community-based organizations (CBOs), government, industry, and nongovernmental organizations (NGOs). We recruited participants in a purposive, nonprobabilistic manner due to their prior involvement with HIV

cure research, ATIs, and/or HIV prevention research. Our objective was to derive triangulated perspectives regarding ATIs and partner protection strategies during ATIs. We focused this inquiry on informants who were already actively engaged in the HIV cure and prevention research fields, rather than prospective trial participants or affected communities. While our qualitative study did not recruit transgender individuals, we interviewed informants who work closely with these populations. Furthermore, because little was previously known about this topic, we conducted in-depth interviews to obtain rich narratives and nuanced considerations that are characteristics of qualitative research and one-on-one interactions.[30]

Participant recruitment

An external scientific advisory board proposed a list of potential informants for this research project. We sent formal e-mail invitations to all potential informants asking them if they were willing to participate in our study. E-mail correspondence included the purpose of the study, the institutional review board (IRB)-approved informed consent form, a demographic questionnaire, and the interview guide. We contacted 30 possible informants; 21 agreed to an interview (response rate: 70%). Each informant received a Health Insurance Portability and Accountability Act (HIPAA)-compliant virtual videoconferencing weblink upon confirmation of the date and time of the interview.

Data collection

Two trained interviewers (K.D. and J.K.) conducted interviews that lasted between 30 and 60 min. All interviews were conducted in English and followed the IRB-approved interview guide (Table 1). As an incentive for their participation, we provided a U.S. $20 electronic gift card to all PLWH and community representatives (from CABs, CBOs, or NGOs). Participation by informants from academic institutions, government, and industry was not incentivized.

Table 1. Institutional Review Board-Approved Interview Guide: Considerations for Involving Diverse Participants in HIV Cure-Related Research with Analytical Treatment Interruptions

Introduction
• First, thank you so much for your time.
• Can you please describe your involvement in HIV-related research?
Considerations for diverse pools of participants:
• What might be some considerations specific to women undergoing ATIs?
• What might be some considerations for involving minority or diverse populations in ATI studies?
Additional considerations
• Do you think HIV treatment interruptions might affect stigma for people living with HIV?
• Do you think partnership dynamics should be factored in prevention measures during ATIs?
• How can we best engage people living with HIV around mitigating risks during ATIs?
• How can we best engage communities around mitigating risks during ATIs?
Wrap up and closing
• Would you like to add anything or make additional comments?

ATI, analytical treatment interruption.

Data analysis

All interviews were transcribed verbatim. Transcripts were reviewed for accuracy by a research team member (J.K.). Because little was previously known about considerations for implementing ATI trials in diverse communities and settings, we used conventional content analysis involving inductive reasoning to analyze the qualitative data.[30,31] Conventional content analysis provided a flexible and systematic approach to parse out data. We focused on reducing data to important considerations for implementing ATI trials in diverse communities and settings.

We compiled all de-identified data into one document for manual coding and further organized responses received by informant types, which allowed us to review the range of responses obtained. We analyzed the data by question blocks, ascribing key themes and extracting salient quotes to illustrate each theme. Two members of the research team (K.D. primary coder and J.K. secondary coder) coded the data and organized text units under each theme. Our codebook was inductive, including the code name, description, and exemplar quotes. Themes were expanded and collapsed during the coding process, and coders resolved discrepancies by constant comparison and consensus. Once the coding process was completed, we wrote narratives to contextualize the data.

Ethics statement

Our study was approved by the University of North Carolina at Chapel Hill (UNC-CH) IRB (study #19-0522). All participants provided verbal consent to be interviewed, and interviews were audio recorded. All interviews were confidential, and participants could use pseudonyms in the recordings if preferred. We deleted audio files upon verifying transcripts for accuracy and fidelity.

Results

We interviewed 21 participants, including 11 cisgender men and 10 cisgender women. Of these, 13 were White/Caucasian, 7 were Black/African American, and 1 was Hispanic (Table 2). We interviewed nine community members, six biomedical researchers, three sociobehavioral researchers, two bioethicists, and one HIV care provider. Informants worked in the field of HIV for a mean of 20.4 years (SD = 9.1 years) and in the field of HIV cure research for a mean of 6.8 years (SD = 6.1 years).

Our study revealed the following key themes: (1) paying attention to gender and power dynamics in ATI trials and (2) influencing ATI designs through the lens of intersectionality and equity frameworks. This lens and framework force researchers to recognize the differential experiences of oppression and privileges related to intersectional positions (i.e., age *and* race *and* gender), which may lead certain populations to be more or less distrustful of biomedical research; (3) identifying how ATI trial participation may positively/negatively affect stigma for PLWH and their partners; and (4) considering partnership dynamics to

Table 2. Demographic Characteristics of Key Informant Interview Participants (United States, 2020)

Participant number	*Sex*	*Race/Ethnicity*	*Informant type*
01	Male	White/Caucasian	Biomedical researcher[a]
02	Male	White/Caucasian	Biomedical researcher
03	Male	White/Caucasian	Bioethicist
04	Female	Black/African American	Community member
05	Female	Black/African American	Sociobehavioral researcher/epidemiologist
06	Male	White/Caucasian	Community member
07	Female	Black/African American	Community member
08	Female	White/Caucasian	Biomedical researcher
09	Male	Black/African American	Community member
10	Male	White/Caucasian	Biomedical researcher
11	Male	White/Caucasian	Biomedical researcher[a]
12	Male	White/Caucasian	Community member
13	Male	White/Hispanic	Community member
14	Male	White/Caucasian	Sociobehavioral researcher/epidemiologist
15	Female	Black/African American	Community member
16	Male	Black/African American	Community member
17	Female	White/Caucasian	Community member
18	Female	White/Caucasian	HIV care provider
19	Female	White/Caucasian	Bioethicist
20	Female	White/Caucasian	Biomedical researcher
21	Female	Black/African American	Sociobehavioral researcher/epidemiologist

[a]Biomedical researchers with active HIV care responsibilities. For this study, they were interviewed as biomedical researchers.

minimize the potential for social harms, including accounting for intimate partner violence and engaging in trauma-informed research.

Considerations for involving women in HIV cure-related trials with ATIs

We inquired about considerations for both cisgender and transgender women. We also queried for thoughts on possible risk mitigation strategies for HIV transmission during ATIs if the participants and/or their sexual partners were women. Most informants recognized the need to pay attention to gender and power dynamics, regardless of whether women were ATI trial participants or sexual partners.

Bioethicists (#03, #19) reported that including women in HIV cure trials was crucial, even for early-phase trials enrolling small numbers of volunteers, and that research teams should be concerned about the current underrepresentation of women as a matter of health equity and justice. A bioethicist (#19) identified two countervailing moral concerns: women need to be represented, but it may be more difficult to protect them from undue harm—including social harm.

> [W]e have these two countervailing moral considerations, right? We need women to be in the research for the sake of women, and we need women to be protected and it's harder to protect women sometimes than men. —Bioethicist (#19)

Bioethicists (#03, #19) also suggested research teams seek to understand how HIV cure research participation fits within the context of women's lives to minimize risks to them and their partners.

Community members, in turn, provided a rich set of considerations for involving women in HIV cure trials with ATIs. Members agreed that women should be involved in developing strategies that work for all populations. Furthermore, one community member advised researchers to agree on gender-inclusive practices for all participants at all stages of clinical trial implementation.

> So, I think the starting place for that is… make sure that there's agreement about what the definition of women is, and whether you mean someone who was assigned that sex at birth, or whether you mean someone who now currently has that identity. Because there are some women who have a penis, and so their needs are not necessarily the same as women who have a vagina… I think that that's the first place to start is making sure that there's a clear understanding and that your consent languages are gender inclusive as appropriate to whatever your study objectives are… the staff [should] know what pronouns… you like to use, and what name you like to be called and that sort of thing. —Community member (#17)

For individuals assigned female sex at birth, who desire pregnancy, it was recommended to discuss pregnancy-related considerations, including, but not limited to the prevention of vertical transmission of HIV, particularly if the trial involves an ATI that potentially may increase the risk of transmitting HIV to the fetus. All people of reproductive potential should be informed about the possible risk of HIV transmission to infants. A community advocate warned, however, that some may not always be able to control their ability to prevent pregnancy in the context of clinical research.

> [F]or people who were assigned female [sex] at birth, it's really important to focus on what are the issues associated with their ability or inability to have children? We need to really spend time talking about the importance of using some sort of birth control for the entire time that they're on [the] ATI but off of meds and making sure that they clearly understand the risk to the fetus, that you could pass HIV to your child. —Community member (#17)
>
> But… you don't always have control over your ability to not become pregnant… And we have to do better as an infrastructure to contend with that reality. Pregnancies hap-

> pening, they're going to happen, so how will a study team deal with it, right? Until we get past that, we'll continue to debate this issue. We're now 40 years into this epidemic… I have to say that we've miss[ed] the mark when we speak broadly about including women and not having a basic plan in place to meaningfully include women aside from making her promise to not get pregnant, well she does not impregnate herself. — Community member (#15)

Community members distinguished women as participants and women as partners in their responses. In both cases, there should be clear screening questions to identify possible risks of HIV transmission and/or risks of HIV acquisition in the context of HIV cure trials involving ATIs. Community members noted that, when PLWH interrupt treatment during an ATI, they likely will experience viral rebound and this increases the risk they will pass HIV to their partners.

> If she's having insertive sex with a male, vaginal sex with a person who is [male]… is she having sex with someone where there's a likely high transmission risk, even if she is detectable? What type of sex is she having? What's going on with her partner? I think we need to dig more deeply into these things with women, and it might result in having different types of screening questions or different kinds of scripts that will be more effective. —Community member (#04)

Community members recommended that disclosure conversations around ATI research participation apply a gender lens that is sensitive to people's unique circumstances. They believed attention should also be paid to gender dynamics and power imbalances.

> We know that a person might not have disclosed to their partner, and now they may, again, if we're considering this study, now this might change the dynamics of things… [W]omen living with HIV are at high risk of having violence perpetuated upon them than a woman with a different serostatus. There's just a lot, and there's not enough trauma-informed care out there already, and I think there are a lot of women that are in situations where there's an imbalance of power in their relationship. — Community member (#04)
>
> [Y]ou want to be very sensitive to the challenge of sexual networks and sexual partner negotiations in cultures, irrespective of geography, where women may be less empowered to really navigate and have control over those. So, it may be very different in an ATI study with women who may not be as open and able to drive the partnership discussions as much as a man might. —Community member (#12)

Community members suggested carefully evaluating what it would mean for women participants to ask their male partners to get tested for HIV and take PrEP in the context of ATI trials. They recommended weighing possible consequences for both the trial participants and the partners such as the possibility of intimate partner violence and navigation of gender dynamics.

> [I]t brings together so many colliding issues, right? When you talk about the rates of domestic violence or intimate partner violence against women with HIV, they are exponentially higher than that of the general population. And so, to bring into play a partner's participation in her trial… it just, it increases her level of vulnerability… We want to do the ethical thing and offer PrEP to a partner, but we must first evaluate the woman's ability to have an open dialogue with her partner about her participation in the clinical trial. — Community member (#15)

Community members recommended that women be involved in HIV cure trial design and as reviewers of clinical trial protocols. They also recommended applying an intersectionality and/or gender justice framework to HIV cure trials and involving community organizations that are well versed in various gender and sexual diversity issues. This was perceived to be of particular importance when involving transgender women, due to the greater potential for social harm (e.g., physical violence).

> [A]pply a gender and racial justice framework to the whole thing. Which means you then have to look at all of the intersections that individuals come into the study with and be able to address their concerns, their needs, and the concerns for participation in the study with those intersections. — Community member (#07)

Biomedical researchers recognized the difficulty in involving women in HIV cure trials involving ATIs, given childcare and other responsibilities they may have in their lives. They also recognized that HIV research environments were not always very welcoming for women. Two biomedical researchers (#01, #08) were adamant that pregnancy should be prevented through the use of reliable birth control to prevent vertical HIV transmission to their offspring.

> Obviously, if the [cisgender] woman could come up with a new STI during a cure trial, they can also become pregnant during a cure trial, and acute infection and rapid viral replication during early pregnancy would be a disaster for mother-to-child transmission. But for a baby, I think that's kind of non-negotiable… for cure trials, female participants have to be on reliable birth control, just full stop. —Biomedical HIV cure researcher (#08)

Biomedical researchers also made a distinction between women as ATI trial participants versus women as sexual partners of trial participants. When women are ATI trial participants, there should be adequate protection strategies for their sexual partners, such as PrEP referral and/or provision and access to other HIV prevention methods (e.g., external or internal condoms). In situations where PrEP and biomedical HIV prevention uptake are low, another proposed strategy was the use of self-test kits to determine if partners were at risk of acquiring HIV in the context of an ATI.

> It's so challenging. I've seen such low [PrEP] uptake… and men are much harder to reach than women are. My favorite go-to [is]… the self-test kit… Self-test kits are just such a high level of acceptability, willingness to use them, and desire to have them… It's one of my favorites for partner engagement. —Biomedical HIV cure researcher (#08)

However, biomedical HIV cure researchers perceived PrEP awareness to be lower in cisgender women compared to cisgender men. Additional considerations given by these researchers included balancing the need for disclosure of HIV status or ATI participation with equitable access to research participation, if for any reason disclosure was not possible for women.

> That brings to light a lot of issues about power dynamics and relationships and safety and risk that a participant is potentially taking on by A, disclosing or B, not disclosing. It's really, really complicated. I think that in order for ATIs to be done successfully, it is best for them to be done as openly as possible. But I think answering the questions about how to

> make ATIs feasible for people for whom that disclosure may not be as easy is really important to ensure that there is equitable access to participation in research. —Biomedical HIV cure researcher (#11)

Similarly, sociobehavioral scientists (#05, #21) strongly recommended paying attention to gender and sexual power dynamics, particularly around HIV/ATI disclosure. They also pointed to important gender disparities in HIV viral suppression rates that may affect willingness to engage in ATI trials.

> [T]here's a lot of gender and sexual power dynamics that come into play when you're talking about HIV, STIs, anything in that realm whether it's cure research, treatment adherence research… Even though women tend to be much more engaged in healthcare, in other words more willing to go to the doctor, to get preventive screening… they still do not experience as much from HIV treatment services as men do. In general, women have more complications when it comes to sustained viral suppression. And if you're talking willingness to be involved in an ATI study, they might reap less benefit when there's already so many challenges that they're dealing with in the first place. —Sociobehavioral scientist (#05)

Sociobehavioral scientists described potential issues for people with multiply marginalized identities (i.e., race, ethnicity, gender, and age) that may influence their willingness to engage in research. These include concerns around medical mistrust and discrimination. Sociobehavioral scientists cautioned, for example, that stigma related to multiple interlocking experiences of oppression (i.e., racism, sexism, and transphobia-related discrimination) were heightened in transgender populations.

> [I]f you add in the element of race, African American women, for example, pretty much are doing the worst when it comes to reaping the benefits of all of these advancements in HIV treatments… So I think there's an intersectional issue of racism and also sexism when it comes to why Black women are experiencing some of those challenges… We're also talking about issues around medical mistrust and also very real healthcare discrimination when they do access care. There are problems with Black women having undiagnosed mental illness related to HIV which is complicating their treatment outcome… There are some things that should be thought about for all of those, disclosure, inviting partners, doing HIV testing, all of that. —Sociobehavioral scientist (#05)

Sociobehavioral scientists further explained that women may have different types of sexual partnerships (e.g., steady partners vs. not steady) and differing comfort levels disclosing HIV/ATI participation based on those types of partnerships. The age difference between partners was also crucial in shaping abilities to implement partner protections around ATIs, such as PrEP referral. Overall, sociobehavioral scientists (#05, #21) recommended that women participants should be given tailored support and/or counseling during the ATI, particularly around issues of HIV/ATI disclosure and sexual autonomy, to balance their own safety with that of sexual partners. The HIV care provider (#18) recommended adequately compensating women to help them overcome barriers to research participation.

In sum, informants framed the inclusion of women in HIV cure trials as a matter of equity and justice. Consideration should be given to whether women are ATI trial participants versus partners of participants. There should be close attention paid to gender dynamics and power imbalances, particularly around HIV/ATI disclosure and PrEP referral issues. Tailored support/counseling may need to be offered to help women participants balance their safety with that of sexual partners.

Considerations for involving racial and ethnic minorities in ATI trials

Another topic of inquiry related to considerations for involving racial and ethnic minorities in ATI trials. Most informants highlighted the importance of integrating racial and ethnic equity frameworks into HIV cure trials, but recognized the difficulty of engaging communities that may have mistrust toward biomedical research.

A bioethicist (#03) was less concerned about minority underrepresentation in ATI trials involving high risks and no direct clinical benefits to participants. This bioethicist explained that small early-phase studies may not be powered to detect clinically meaningful differences (discussed further below).

> I am a little less concerned than others in the sort of HIV cure ethics or maybe HIV research ethics area about the diversifying of the pool of participants. In a word, in the setting, study participation is hardly a benefit. Arguably just really risky and so it's not… when I root for minority rights or women's rights or whatever, I usually do that for benefits, not for harms. It's a little more complex… it's not a case of some huge benefit that we're depriving people of. And in terms of study design… a lot of researchers would say a study that is underpowered is simply uninformative. —Bioethicist (#03)

Community members provided rich considerations for involving racial and ethnic minorities in ATI trials, and offered two specific recommendations related to clinical trial design: (1) being intentional around diversity in the clinical trial protocol, including specific benchmarks around diversity, and (2) allowing more inclusive and less discriminatory entry criteria.

> [D]esigning with intentionality around diversity is critical. And, we have very few examples of that, honestly, in HIV most trials have typically [been] enrolling older, whiter populations, and men. I think the HPTN 083 trial that just is now ending early for injectable cabotegravir as prevention had specific benchmarks for both age and diversity. —Community member (#12)

Another set of considerations related to meeting ''populations where they are'' (#16). For example, community members recommended partnering with CBOs that have established relationships with diverse communities (#04) and leveraging satellite sites that have gained the trust from racial and ethnic minority participants (#04, #09).

> [T]his is where it's crucial for research teams to partner with trusted community-based organizations, grassroots community-based, maybe health and social services or whatever organizations… situated in the community whose staff looks like the community, who speak the language and who understand the nuances, and maybe there's also other, maybe there's wrap-around care offered here like transportation… If you partner with these entities, I think you'll have more buy-in. —Community member (#04)

In addition, community members expressed desires to engage with research staff who were diverse and with ''peer mentors who are also members of racial or ethnic minority

communities, or peer navigators, who could provide someone that they might trust'' (#04). They also advocated for more flexible hours for research visits (#04) and ''cultural literacy for researchers'' (#07). One community member (#07) was adamant that HIV research teams should embrace a social justice framework that would require valuing people's lived experiences, changing the narrative around mistrust in biomedical research, building basic research literacy, and protecting people's hope around finding a cure. This community informant (#07) argued that promotion of medical research literacy, and researchers' embrace of a social justice framework, should go beyond simple discussions of medical mistrust stemming from the infamous U.S. Public Health Service Syphilis Study at Tuskegee (hereafter referred to as the USPHS Syphilis Study).

> That they have to see and know and trust… that we value their lived experiences… The second part… being very intentional about changing the narrative of how we talk about mistrust, right? … So, for example, changing the narrative means that when that comes up, the question then becomes is, do you know why informed consent exists? Tuskegee. Do you know why institutional review boards exist? Tuskegee. Do you know why community engagement and community advisory boards are so important now and are required? Tuskegee…. [T]he health and research literacy is key, extremely key so that we… can change the narrative of how we talk about it… The [next] one of course is protecting the hope… knowing that as hard as this is, at the end of the day, we all really want to get to the cure. —Community member (#07)

Community members appreciated and respected the complexity of issues surrounding medical and research mistrust. They suggested implementing clinical trials that account for the health disparities and intersectional oppression that participants experience, and not oversimplifying the issue of mistrust and racism.

> [W]e tend to simplify this issue… [P]eople that has been suffering from access to care or… health disparities…if I've been a person that has suffered from health disparities my whole life, is it fair to be asked to participate in a clinical trial in which I'm gonna risk my life? … I don't know if that's fair to ask minorities to join clinical trials in which we're not very clear about how it's gonna benefit them… [Y]ou need to think about intersectionalities. —Community member (#13)

Community members also recommended leveraging social networks and pre-existing relationships, such as trusted bonds between patients and their HIV care providers, who would need to be on board with HIV treatment interruptions used in HIV cure trials (#16). Community members also advised investing in culturally appropriate community engagement efforts. Similarly, biomedical HIV cure researchers recognized that more should be done to engage diverse communities around HIV cure research. They also advised engaging HIV care providers who have established trust with their patients.

> [T]he real necessity of trust and communication between provider or researcher and participant, and the fact that many researchers aren't from those communities. So I think that establishing and building that kind of trusting relationship that really facilitates safe conduct in these studies, and safe participation in these studies… So, I think that's really quite crucial. —Biomedical HIV cure researcher (#20)

One biomedical HIV cure researcher (#20) highlighted the necessity of acknowledging historical and cumulative traumas, particularly in communities that may be more ''vulnerable'' to experimental or exploratory medicine.

> Given where the cure field is… sometimes I certainly hear treatment interruptions or cure studies characterized as ''more experimental'' than other kinds of research… And I think that communities of color, trans individuals, members of particularly vulnerable and under-represented populations are particularly vulnerable to exploratory and experimental research, and/or that kind of lights up historical trauma from that work in the past. So, I think that just requires great deal of sensitivity and consideration as we move forward. —Biomedical HIV cure researcher (#20)

Likewise, sociobehavioral scientists encouraged acknowledging the sociohistorical past of biomedical research (#14, #21). The fact that the USPHS Syphilis Study involved withholding of treatment makes for a complicated picture for ATI trials (#14).

Sociobehavioral scientists described four concrete recommendations: (1) engaging trusted community advisors on how to frame ATIs in HIV cure research for the community to which they belong, (2) creating vignettes of PLWH who have carefully weighed the risks and benefits of ATIs and who represent diverse populations (e.g., local champions), (3) conducting adequate formative research before implementing ATI trials in affected communities, and (4) reporting the findings of such studies back to affected communities. The HIV care provider (#18) advised including clinical research sites that are geographically located within predominantly Black or Latinx communities. Furthermore, the HIV care provider (#18) stated some Latinx PLWH may be concerned with immigration issues and deportation, particularly in states with severe immigration policies and practices, so it is important for them to feel safe in the clinical research environment.

Overall, any strategy must first start with acknowledging the sociohistorical past of biomedical research, medical mistrust, and existing health disparities. Recommendations to increase diversity in research included the following: creating trial designs with diversity and inclusion criteria, meeting communities where they are (e.g., CBOs and satellite sites), having staff and peers who are reflective of the communities researchers are seeking to enroll, reducing logistical barriers (e.g., site hours and transportation), advocating for social justice, building cultural literacy of researchers, and engaging HIV care providers who serve diverse communities. Informants also advised investing in community engagement efforts, involving past participants and geographically diverse sites.

Stigma and ATI trials

Factors associated with increased stigma stemming from participation in ATI trials included potentially becoming viremic and feeling pressure to disclose one's HIV status and/or ATI participation. However, informants also advised that participating in HIV cure research, including trials that include ATIs, could help reduce HIV-related stigma because participants would be contributing to the larger cause of advancing science toward a cure.

A bioethicist (#03) reported not yet having seen any evidence of the effect of HIV cure trials on societal stigma, however, and that HIV transmission in the context of ATI trials may have the untoward effect of exacerbating stigma for PLWH.

> I haven't come across huge evidence of big effect on societal stigma in general. So, one could speculate that it could go in different ways… of course, if there is an incident of infection, that could affect it negatively. —Bioethicist (#03)

Three community advocates (#04, #06, and #13) expressed concern that ATI trials could increase stigma for PLWH who become detectable for HIV even as they contribute toward advancing HIV cure science, particularly if their altruism is misunderstood in the community.

> I can see a stigma from the people that are hard core believers in U=U. You know?… It's like the goodness of a person is measured by their viral load, right? … [T]here are big chances that a stigma is developed around this person, right? That if they don't understand what I said about altruism and the way you are putting your body and yourself for the good of the whole community… And if you are letting yourself become detectable, you know, some people may see that as irresponsible if the person cannot explain why. Right? —Community member (#13)

Another community member (#16) explained the stigma would be akin to that faced by HIV-negative individuals who develop vaccine-induced HIV seropositivity because of their participation in HIV vaccine trials. In addition, partners of ATI trial participants may also face stigma because they would need to take PrEP. ATI trials also have implications for HIV criminalization, particularly in racial and ethnic minority populations.

> [T]he stigma of coming off of one's medication in order to participate in an ATI-involved study has huge ramifications for HIV criminalization laws in this country, in the United States and globally… That's a huge, you know, structural and systemic barrier to engaging under-represented communities, and I'm specifically naming Black communities, who already have, disproportionate involvement, or shall I say are, disproportionately, inequitably, targeted by the criminal justice system in the United States. —Community member (#16)

Once again, community members raised the critical importance of community engagement to help counteract stigma in the context of ATI trials.

> I think where community engagement becomes so vital… So it's important to understand and to be able to communicate clearly, like why is the ATI an appropriate research strategy to answer whatever this particular question we have is, and why is this the right way to answer the question? … And if people can understand why, then they can be accepting of the fact that somebody might choose this… And then I think the next layer of that is understanding how are they being protected?… I mean, stigma is born out of people not understanding. —Community member (#17)

A biomedical researcher (#02) pointed out that stigma around having a detectable HIV viral load remains a key challenge in implementing ATI trials due to the pervasive messaging many PLWH receive about maintaining an undetectable viral load, specifically to prevent HIV transmission.

> What's going on is U=U. We've hammered into everyone's head that if you are undetectable, you're not transmitting. You're healthier… it's way better to be undetectable. There's no question about that, period… And now you're telling us the exact opposite after hammering into us that U=U… It's completely counter intuitive right now…It's this discomfort… I think it's more psychological. —Biomedical HIV cure researcher (#02)

In turn, sociobehavioral scientists noted that HIV-related stigma remains difficult to measure, define, and reduce. They indicated that HIV-related stigma could be affected in two ways in ATI trials: (1) it could be increased in the short term due to viral rebound and pressures to disclose HIV status or (2) it could be decreased in the long term as a result of participating in research that could eventually lead to a cure.

> I do think that people who were living with HIV who achieved viral suppression have some relief from that feeling of pathology that in some ways sustained viral suppression feels like a type of cure or relief… —Sociobehavioral scientist (#14)
>
> I can also see it being like this point of feeling a lot of pressure to disclose to people, for whatever reasons, whether it's family members, sexual partners, what have you, that you're part of this trial, and then in saying, ''Oh. I'm part of this trial,'' disclosing your status, and so I think then it could increase stigma… And then I could also see, on the other end, feeling very proud about being part of this kind of work; to be part of a curative research. —Sociobehavioral scientist (#21)

Sociobehavioral scientists suggested that HIV cure research should frame their work as contributing toward reducing HIV stigma. The HIV care provider (#18) suggested building robust community awareness of ATI trials to reduce stigma. Overall, concrete suggestions included measuring stigma for PLWH as part of ATI trials and building robust community awareness and understanding the necessity of ATIs to advance development of efficacious HIV curative strategies.

Partnership dynamics: violence- and trauma-informed research

Concerns emerged predominantly from community members and biomedical HIV cure researchers who strongly recommended focusing an intersectionality- and trauma-informed research lens to minimize social harms in HIV-related research.

Community members expressed the importance of considering the types of violence their particular populations may face, such as intimate partner violence, gender-based violence, and physical, emotional, or structural violence. Although men may also face intimate partner violence, this consideration is especially critical to women's involvement (#06). Wherever there is the potential for partner violence, research teams will need to assiduously help ATI participants to thoroughly evaluate the various risks versus benefits of their participation.

> The risk of him getting infected versus the risk of him beating her. If I were a clinical participant, I'd want to be the one making that judgment. I think this is about empowering [the] individual to help her help us navigate through that scenario. I think it's somewhat paternalistic for the trial team to say, ''Oh. We don't want you in the trial because we're afraid you might get beaten up or because we think you might transmit.'' … [W]e're grappling with your safety and his HIV potential seroconversion. Let's talk about that. How would you like to handle that? —Community member (#12)

A community member recommended adopting an intersectionality- and trauma-informed research lens akin to trauma-informed care.

> [W]e need trauma informed research… That the whole history, whether it's based on gender or whether it's based on race, or even in some instances, whether it's based in geography, we don't know where people have come from and we don't know what they all walk with… But there are so many different kinds of traumas and it's not just about women and it's not just about Black and Brown people… That the diversity is what we want, the intersectionality is what we have to understand. —Community member (#07)

Moreover, a biomedical researcher recommended taking the time to understand the communities that are being engaged in research without making sweeping generalizations about individual participants.

> To know that kind of dynamic in a community where you're conducting and ATI up front, will inform the kinds of counseling and conversation that you have in the informed consent with a potential participant who is living in that community, who may or may not be living in that specific dynamic, but is living in that community… but you do not know the dynamics that that particular individual is in. — Biomedical HIV cure researcher (#20)

Another researcher suggested having forward-looking discussions with participants depending on the length of the ATIs and the perceived risks and benefits of participation for the individual, and this is part of the ''art and science'' of informed consent.

> [We need] kind of a forward-looking discussion, maybe particularly depending on how long [the] ATI is… [I]t really just comes down to having a robust, informed consent conversation. These are the risks, here are some situations that could heighten those risks. Can you imagine yourself in this situation? Have you been in those situations before? How did you navigate that? Those kinds of things… Otherwise we end up contributing to science with communities that may not need it as much… We really have to be able to engage the most vulnerable individuals if we're going to help the most vulnerable individuals. But how to do that in a way that's safe, again I think it's art and science, and part of both of those things come up in the informed consent conversation. — Biomedical HIV cure researcher (#20)

Similarly, sociobehavioral scientists (#05, #21) advised understanding as much as possible about partnership dynamics to help ATI participants navigate adequate partner protection strategies. The HIV care provider (#18) recalled patients in complex partnerships whose dynamics would complicate HIV disclosure and ATI research participation. Altogether, informants converged on the idea that understanding partnership dynamics was critically important to effectively implement ATI trials. An intersectionality- and trauma-informed research lens may help minimize social harms.

Additional considerations for engaging diverse pools of participants in ATI trials

A bioethicist suggested making sure research teams emphasize ATIs are only in the context of research and are not included in the current standard of care (#03). Community members proposed building strong and trusting relationships with study participants (#06) and providing ongoing information about clinical research, not just at the point of recruitment for clinical trials (#06, #09, #16). Additional suggestions from community members included carefully managing expectations about HIV cure science (#07) and using coalition-building approaches to engage organizations that serve underrepresented communities (#16). Biomedical researchers' considerations focused on providing education to CABs about clinical trials since members act as ''protectors of the participants'' (#08).

Discussion

We found that engaging diverse communities in HIV cure research with ATIs will require closer attention to issues of equity, trust, and outreach in the design of such research (e.g., enrollment targets, recruitment efforts, and promoting safety and well being), as well as gender, power, and partnership dynamics in plans that are used in this research to reduce the likelihood of harm (i.e., asking partners to seek PrEP). Ideally, ATI trials are also implemented within a racial and social justice equity framework, where there are genuine community partnerships built to earn the trust of communities due to lasting sociohistorical traumas involving experimental medicine.[6,7] Furthermore, more sociobehavioral research will be necessary to understand the effect of ATI trials on stigma for PLWH and their sexual partners, including with PLWH of diverse racial, ethnic, sexual, and gender identities.[32] Finally, partner protection strategies should also be acceptable to both participants and their sexual partners, and robust community engagement will also be necessary to ensure acceptability.

Underrepresentation of women has led to significant gaps in knowledge about whether women respond differently to HIV cure research strategies, including biological differences, side effects, acceptability outcomes, and social impact, as well as other outcomes of interest.[9,24–26,29,33–35] The example of Descovy® for PrEP,[36] which conflated results from transgender women with cisgender men and excluded cisgender women and transgender men from efficacy trials, provides an important lesson about potential pitfalls in the field of HIV cure research. A more comprehensive understanding of how HIV cure research participation fits within the contexts of women's lives is critical to increasing the capacity of research teams to practice gender inclusivity and help women overcome barriers that may be unique to them.[29,35] Our findings suggest that HIV cure research needs to meaningfully address participant pregnancy-related considerations, including power and gender dynamics of pregnancy, as well as protection of pregnant women as a potentially vulnerable population. Attention will also need to be paid to gender and power dynamics when negotiating HIV/ATI disclosure and partner protections.[37–39] Counseling and support will need to be tailored to balance sexual autonomy and safety in the context of ATI trials, especially as women may be required to negotiate safe sex, ask partners to use PrEP, and/or HIV self-test kits with partners.[40] When HIV-negative women are partners of ATI trial participants, it will be critical to link them to effective HIV prevention resources, such as oral or injectable PrEP, and have plans that consider costs and medical insurance. Although promising, PrEP has remained underutilized in women around the world.[41,42] The growing number of ATI trials elevate the level of urgency for optimizing PrEP awareness and uptake for women at higher risk of HIV acquisition, particularly since women face intersecting risks of stigma and partner violence.[41,42]

We also found that specific considerations should be given to involvement of transgender people in HIV cure trials involving ATIs, as well as efforts to fill gaps in knowledge with respect to how transgender individuals perceive HIV cure trials. Informants in this study recognized these as critical future directions for HIV cure research and spoke to the unique social-structural factors faced by transgender and gender-expansive individuals that may influence their ability or willingness to participate in cure research. A recent willingness to participate in a survey conducted in Brazil among 118 transgender women showed a strong aversion (91%) toward ATIs.[43] Research teams must recognize that ATIs may add more layers of social and structural vulnerabilities for both transgender participants and their partners. Another qualitative interview study conducted by Poteat and colleagues in the United States demonstrated transgender women face several competing priorities, such as gender affirmation, ART adherence, navigating relationships, physical safety, addiction, employment, mental health, and general well-being.[44]

Evidence from these studies dovetail with perspectives from informants in this study, and suggest that researchers using ATIs will need to consider leveraging counseling and supportive services to avoid undue harms resulting from participation in their studies, as well as integrating interventions to address social-structural barriers that may complicate transgender and gender-expansive people's ability to do so. When transgender individuals are included as sexual partners of ATI trial participants, it will also be important to link them to HIV prevention resources. Significant barriers, however, remain with PrEP and HIV prevention uptake among transgender individuals, including isolation, limited awareness, gender minority and HIV-related stigma, and medical mistrust,[45] as well as structural barriers, particularly in racial and ethnic minority groups.[46–48] For meaningful involvement of transgender individuals in HIV cure trials, research teams will need to incorporate intersectionality-informed approaches that account for factors that may influence representation by people with multiple socially marginalized identities (i.e., gender *and* sexual minority status *and* race *and* socioeconomic position)—factors that are established in the most recent trans-inclusive research frameworks.[49]

Regarding racial and ethnic minorities in ATI trials, it will be important to recognize how structural racism has reinforced systems of exclusion in the form of recruitment and screening processes, study inclusion criteria, designs, and schedules of events that may not be fully scientifically justified and do not favor working adults and caregivers. Rethinking barriers to entry will be required to fully construct a system of research that welcomes and prioritizes involvement of racial, ethnic, sexual, and gender minorities throughout the process of implementing HIV cure clinical trials.[50] For example, there should be intentionality around diversity in clinical trial design, such as more permissive inclusion criteria and involvement of underrepresented communities in the development and review of protocols.

Furthermore, informants suggested that intentional approaches to inclusivity would benefit from directly acknowledging the sociohistorical traumas and existing disparities, adopting social justice frameworks such as centering the perspectives of historically marginalized groups, building and sustaining trust with communities through long-term and meaningful engagement, and partnering with HIV care providers who may be more trusted and serve underrepresented communities. These findings parallel recent U.S. Food and Drug Administration (FDA) guidance for enhancing diversity of clinical trial populations related to enrollment and retention practices that enhance inclusion, cultural competency, and community engagement.[51]

Moreover, suggesting that study participation is ''hardly a benefit'' may represent a narrow view that does not reflect the multitude of ways in which people might potentially benefit from research participation, and these perspectives contradict prior evidence produced on the topic of participation in biomedical HIV research.[35,52–54] We contend that, even in early-phase studies, it may be too short-sighted to focus solely on detecting ''clinically meaningful differences'' as a primary purpose of diversifying participant pools. Clinical research participation may also confer psychosocial and other perceived benefits,[34,35,52,55,56] some of which have yet to be identified.

One way to move beyond a clinically meaningful difference threshold is through the integration of sociobehavioral science questions and methods, such as making qualitative inquiries a more routine practice in ATI trials. Such activities may yield critical insights from participants themselves about pre-existing or emergent risks related to their participation, may further increase understanding of their perceived benefits, and may potentially facilitate their retention in studies by improving their satisfaction with their decisions to participate.

Our data suggest that mistrust in clinical research does not stem only from the legacy of abusive medical experimentation in the United States (e.g., the USPHS Syphilis Study, Henrietta Lacks, and other ethical violations). Informants also mentioned ongoing health care inequities as a source of distrust. It is critical that efforts to build trust with historically underrepresented groups are not tokenistic or enacted for the sole purpose of increasing their participation in clinical trials. Researchers must demonstrate trustworthiness[57] and sincere commitment to advancing equity in health care and health research. Meaningful engagement of diverse populations in HIV cure trials—which encompasses, but is not limited only to increasing participation by women and racial, ethnic, sexual and gender minority groups—requires clinical researchers to contend with sexism, racism, gender binarism, and heterosexism that drive health inequities.[58] Ultimately, as the perspectives shared by our study's informants support, increasing trust in science and medicine necessitates restructuring health systems and research infrastructures to address fundamental roots of health inequities.[58]

We also explored two cross-cutting issues related to involving diverse populations in ATI trials: stigma and partnership dynamics. It remains unclear how ATI trials will affect stigma for diverse PLWH and their partners, and more research will be necessary in the context of ongoing ATI trials to ascertain these effects. Qualitative research conducted in China revealed that HIV cure research may have limited effects on stigma because of the layered and entrenched stigma facing specific groups, such as men who have sex with men and injecting drug users.[59,60] While diversity in HIV cure-related trials, broadly speaking, is a matter of justice and equity, without adequate attention to unique issues facing specific groups of participants, these values may also be in conflict with the ethical principle of nonmaleficence (doing no harm). For example, due to state laws that criminalize HIV transmission, having a detectable viral load may create heightened vulnerabilities for racial, ethnic, and gender minorities, who are disproportionately impacted by involvement in the criminal

Table 3. Summary of Considerations for Involving Women and Racial, Ethnic, Sexual, and Gender Minorities in HIV Cure-Related Research with Analytical Treatment Interruptions

Considerations for involving women in HIV cure-related trials with ATIs
- Inclusion of women in HIV cure-related clinical trials should be recognized as a matter of equity and justice.
- Research teams should seek to understand how HIV cure research participation fits within the contexts of women's lives and should practice gender inclusivity at all stages of clinical trial implementation (e.g., use of proper pronouns).
- For ATI participants who can become pregnant, the risk of transmitting HIV to their fetus should be minimized through robust informed consent and barrier protections. Research teams should recognize that people may not always have control over their ability not to conceive.
- When women are ATI trial participants, they should engage and/or refer HIV-negative sexual partners to receive protection measures whenever possible (e.g., PrEP and condoms).
- When women are partners of ATI trial participants, they should be offered PrEP and other HIV prevention measures.
- Research teams should apply a gender lens to ATI trial participation and carefully weigh possible clinical and social consequences for participants and their partners. Attention should be paid to gender dynamics and power imbalances for issues of disclosure and partner protection.
- Women should be involved as part of HIV cure research teams and as protocol reviewers to help guide research implementation.
- Research teams should consider involving community organizations well versed in gender and sexual diversity issues.
- To facilitate participation, research teams should help women overcome barriers to participation (e.g., adequate compensation).
- Tailored support and/or counseling should be offered to women around issues of HIV/ATI disclosure and sexual autonomy if/when needed.

Considerations for involving racial and ethnic minorities in ATI trials
- Research teams should be intentional about diversity in clinical trial design (e.g., diversity benchmarks and more inclusive criteria, such as higher body mass index).
- Research sites should be located in geographically diverse areas as much as possible.
- Research teams should meet communities where they are (e.g., partnerships with established CBO satellite sites).
- Attention should be paid to diversity research staff and cultural literacy of researchers.
- Diverse peer mentors/counselors to support participants should be considered. Research teams should engage trusted advisors on how to frame ATIs for specific populations and create vignettes of past trial participants to facilitate recruitment.
- Logistics should be taken into account to help participants from minority groups overcome barriers to participation and include such things as flexible research site hours and transportation for participants.
- Research teams should embrace a social justice framework that values people's lived experiences and that accounts for pre-existing disparities in access to health and intersecting sociohistorical traumas.
- Research teams should build trust with HIV care providers from diverse communities.
- There should be sustained investments in culturally appropriate community engagement efforts, including dissemination of research findings back to communities.
- Research teams should recognize that having a detectable viral load may create heightened vulnerabilities with respect to criminalization of HIV transmission. Ethical principles of equity and justice should be balanced with those of nonmaleficence (doing no harm). Using Kipnis' factors approach to vulnerability,[62] protections should be offered to ATI trial participants corresponding to specific sources of vulnerability.
- Increasing trust in clinical research and medicine should be much more about interrogating deeply rooted sources of health inequities and fundamentally about changing how health systems and research infrastructures operate.

Stigma and ATI trials
- Research teams should recognize that HIV cure trials could affect stigma in different ways: (1) stigma could be increased as a result of becoming viremic and being at risk of transmitting HIV to partners and/or (2) stigma could be reduced as a result of helping advance the search toward an HIV cure.
- Robust community engagement and awareness will be necessary to help counteract stigma, including tools to help people understand why ATIs are needed.

Partnership dynamics—intimate partner violence and trauma-informed research
- Research teams should adopt an intersectionality- and trauma-informed research lens that accounts for different kinds of traumas to minimize the risk of possible social harms when implementing ATI trials.
- ATI participants should be empowered to evaluate trade-offs during the informed consent process.

Patient and community engagement
- Research teams should clearly emphasize ATIs are conducted in the context of research, not care.
- Sustained patient/community education and engagement are critical at all stages of the research process, and not just before recruiting for ATI trials.
- Patient and community engagement should also be directed toward managing expectations about HIV cure science.

CBO, community-based organization; PrEP, pre-exposure prophylaxis.

justice system in the United States. Biomedical HIV cure research teams should be attuned to such vulnerabilities of ATI trial participants and provide additional support to those who represent these groups. In accord with Kipnis' factors approach to vulnerability, protections should be offered that correspond to specific sources of vulnerability.[61,62]

When looking at partnership dynamics, two themes emerged from our study: those related to partner violence and the need for trauma-informed research. Recent global estimates revealed one in three women have faced physical and or sexual violence by an intimate male partner,[63] and evidence supports women with such histories perceive value in participating in violence-related research.[64,65] However, it is not fully understood how experiences of partner violence will affect decisions to participate in HIV cure research. Simultaneously, applying a trauma-informed approach to HIV cure research aligns with the established trauma-informed HIV care and treatment model, which aims to promote a sense of safety among participants, while interrupting cycles of violence, addiction, and mental health challenges, and addressing structural trauma such as racism and poverty. Applied to HIV cure research, past traumatic experiences may shape an individual's response to future interactions with and mistrust of research staff, causing retraumatization.[66] Research staff should foster collaborative, transparent, trusting, and supportive interactions with participants, achieved through application of the ''3R's,'' which include (1) realizing the high rates of different forms of trauma, (2) recognizing the effect of trauma on participants and research staff, and (3) responding appropriately to trauma.[66,67]

To ensure inclusivity and influence study designs, it is critical to understand that additional resources and effort will be required if researchers are truly to strive for inclusivity, and add additional processes to already complex trials.[68,69] Through the lens of intersectionality, brought to fore is the concept of 'centering the margins,' which requires that groups of people who are rendered intersectionally invisible[70] and excluded from the work instead have critical decision-making power over the implementation of trials. Future research should build on our findings by elevating true diversity, that is, by meaningfully engaging PLWH who represent a wider range of racial, ethnic, sexual, and gender backgrounds. Future work in this area should also further examine the perspectives of researchers working to engage these groups, particularly those who may themselves be members of historically underrepresented or socially marginalized populations.

Our summary of considerations for implementing ATI trials in diverse pools of participants can be found in Table 3. This list is not exhaustive.

Limitations

We must acknowledge a number of limitations to our study. We conducted interviews with a relatively small sample, therefore, it is possible that we did not reach thematic saturation.[71] We did not interview any transgender or gender-expansive individual, and this is a major limitation of our study. To complement findings from this study, we intend to do so in the future. The individuals interviewed were not all representative of those who would face the barriers to participation discussed therein; therefore, there is a need to further amplify the voices of those who would be potential participants in ATI trials. Because our study took place during the COVID-19 pandemic, we were able to interview only one HIV care provider because few HIV/infectious diseases health care providers were available to participate in our study due to their clinical duties. The topic of engagement in ATI trials will require broad and ongoing stakeholder input and robust community engagement in diverse settings and contexts.

Conclusions

Our study provided considerations for implementing HIV cure trials involving ATIs in diverse communities and settings. We hope findings from this work will be shared with communities of interest to generate meaningful dialog around adequate and inclusive ATI trial designs in complex relationships and social contexts. To effectively and ethically implement ATI trials with historically underrepresented groups, research teams must invest in robust community and stakeholder engagement to define best practices. Paying attention to representation and equity will also promote better and more equitable implementation of HIV cure strategies once these become ready for actual rollout.

Author's Contributions

K.D. drafted the initial version of this article.

J.K., C.C., C.B., A.C.M.B., D.M.C., M.A.R., J.K.S., T.P., M.J., P.S., and J.A.S. reviewed the article for intellectual contents.

All authors read and approved the final article.

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Availability of Data and Material

Relevant quotes have been included in the Results section of this article.

Ethics Approval and Consent to Participate

The Institutional Review Board of the University of North Carolina at Chapel Hill approved this study (Study No. 19-0522). All interview participants included in this study provided informed consent.

Consent for Publication

Participants provided informed consent to publish de-identified data.

Author Disclosure Statement

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