

2024 COMMUNITY HIV CURE RESEARCH WORKSHOP

Saturday, March 2, 2024

Justice-Informed HIV Cure Trials with ATIs

The Critical Need for Socio-Behavioral Sciences and Ethics Research

Karine Dubé, DrPH

Outline

1. Justice-informed HIV cure-related trials with ATIs
2. What are we learning so far?
3. Brief discussion: How should we move forward?

Justice in Research Ethics



- Justice requires the fair and equal distribution of benefits and risks of participation in a research study.
- Recruitment and selection of participants must be done in a fair and equal manner.
- Justice forbids exposing one group of people to the risks of the research solely for the benefit of another group.

Call for justice-informed HIV cure trials with ATIs

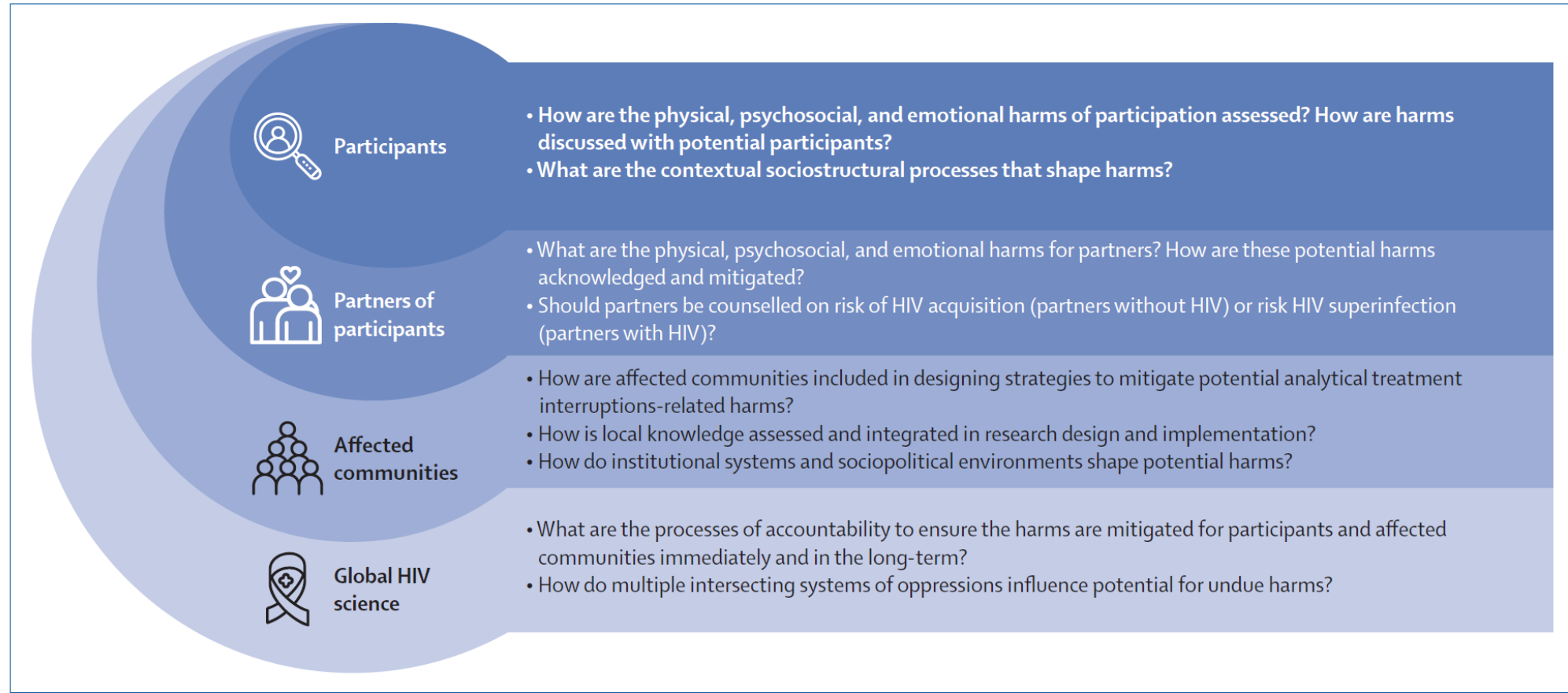


Figure: Key questions to mitigate potential harms related to HIV cure-related research with analytical treatment interruptions

WHY? SOCIAL SCIENCE

All That [NOT SO] 'Ancillary' Stuff

Help us understand:

- Research context and risk behaviors
- Factors that affect product acceptability and uptake
- Factors that affect feasibility of clinical studies
- Factors that affect participant recruitment/sampling, screening and retention
- Factors that affect involvement of diverse communities
- Participant experiences (e.g., quality of life)

Help us inform:

- Design of recruitment materials and informed consent documents
- Meaningful efforts to conduct community/stakeholder engagement – including dissemination of study results

Help us assess:

- Community knowledge and perceptions of specific HIV cure strategies

Help us ensure:

- Ethical conduct of research
- Patient/participant-centered biomedical research agenda

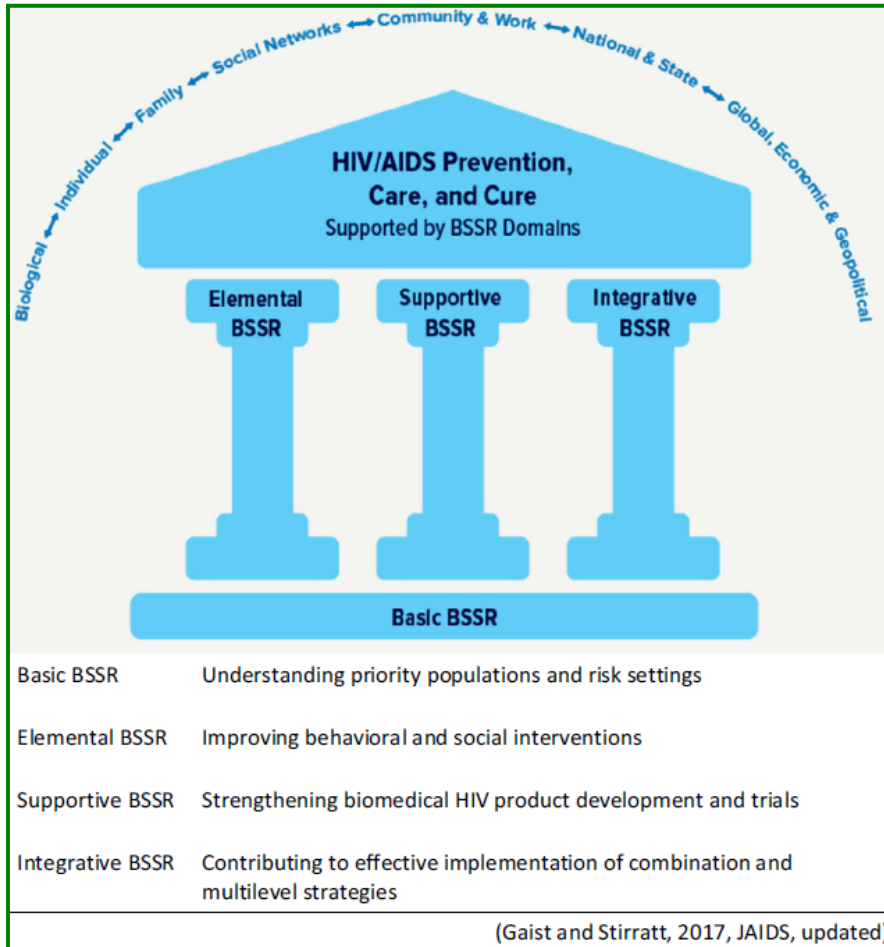
Help us enable:

- Inclusion of key essential and under-represented populations in research
- Shared decision-making

Help us avoid:

- Community opposition
- Strategies that may be unappealing

Applying the Behavioural and Social Sciences Research (BSSR) Functional Framework to HIV Cure Research



Basic BSSR: understanding behavioural and social factors

- Defining use of language to define HIV cure research
- Understanding community perceptions and knowledge of HIV cure research
- Framing expectations around HIV cure research
- Examining the construction and management of HIV-related identities
- Assessing the social meaning of finding a cure for HIV infection
- Understanding views of becoming detectable/undetectable and how the U = U movement shapes desires to engage in HIV cure research

Elemental BSSR: Advancing Behavioural and Social Interventions

- Designing counselling and support interventions to address psychological needs related to ATIs
- Implementing behavioural risk-reduction strategies during HIV cure and ATI studies to minimize third-party risks (e.g., counselling, PrEP provision, adherence to partner protection measures, HIV testing referral)
- Developing and implementing HIV stigma reduction interventions

Supportive BSSR: Strengthening the Design and Outcomes of Biomedically Focused Clinical Trials

- Determining desirable target approach and product profiles for sustained antiretroviral (ART)-free HIV cure regimens
- Examining acceptability of specific HIV cure research strategies
- Assessing PLHIV's (1) willingness to participate in HIV cure research, (2) risk acceptability thresholds for interventions and procedures, (3) barriers and motivators to participation, and (4) acceptability of ATI-related parameters
- Understanding HIV cure researchers' and HIV care providers' (1) willingness to refer patients, (2) role of patient-provider relationships, and (3) shared decision making for cure research participation

- Improving informed consent processes and understanding of risks and benefits of HIV cure research
- Integrating patient-reported measures during the course of HIV cure research participation to examine: (1) factors affecting decisions to participate in research (both acceptor and decliner assessments), (2) reports of longitudinal participant experiences (with HIV cure research interventions, ATIs, and study procedures), (3) psychosocial aspects of HIV cure research participation, and (4) participant-centred outcomes
- Assessing and supporting adherence to HIV testing and viral load monitoring schedules, as well as ATIs, in cure clinical trial protocols
- Integrating strategies to mitigate social impacts and harms during trial participation
- Understanding factors affecting or enhancing the engagement and involvement of diverse and under-represented populations in research, such as women and minority groups

Integrative BSSR: Advancing Implementation of Integrated, Combination, and Multi-Disciplinary Approaches

- Developing decision tools to help people living with HIV make informed decisions and choices about any available treatment and cure strategies
- Testing behavioural interventions to support patient retention and completion of future HIV cure regimens
- Anticipating research needs on factors affecting future real-world implementation of HIV cure research strategies, including, but not limited to: (1) infrastructure, staffing and training requirements, (2) monitoring of drug resistance and viral loads, (3) co-morbidities and poly-pharmacy, and (4) intervening factors such as injecting drug use, mental health issues, intimate partner violence, resilience and food security
- Developing HIV cure strategies with scalability considerations
- Integrating cost-effectiveness research and anticipating performance benchmarks for real-world implementation

Participant experiences in HIV cure-directed trial with an extended analytical treatment interruption in Philadelphia, United States



I was hoping to make it through the three-month period after being taken off of everything, but I only made it about six weeks because my viral load started going up again. So, I'm back on my

HIV medication now... I kind of feel like I let our community down. I mean, I'm not depressed about it, but I don't know. I was hoping I make it through the whole three-month area and then I could stay off my medications, but I don't know. I'm not saying I feel like a failure, but I just feel like I'd let the whole HIV community down.

I was hoping that there was a rare chance that these antibodies would really – like they were long-lasting but that they were really long lasting and that I would still be undetectable with just the antibodies, that's what I was hoping for. Like I knew it wouldn't last forever. So, I am grateful that from October to February without any antibodies maybe a little bit longer I was undetectable. That was exciting to me. Yeah so, I was just hoping it would be a little bit longer.

So, I'm back on a regimen that I didn't have to be on. So, it was depressing to me. I'm like, I need this to survive. I finished my interferon... and I think it was January or February. So not taking nothing to take even though I only take one pill to take in something like I said, I was depressed for a little over a week and I had to, I had to speak to the people that I use for sounding boards and for therapy. So, but it was depressing to me. Do I like taking [the pills]? No.

So, I felt like I was in safe hands and that always makes a person feel valued. That makes them feel like, I'm not just a guinea pig or I'm not just a number and grand number of participants. I wasn't just a participant, I was a person.

Participant experiences in HIV cure-directed trial with an extended analytical treatment interruption in Philadelphia, United States



Table 5. Considerations for future HIV cure-directed clinical research generated in collaboration with BEAT-HIV Community Advisory Board.

1. Community-based participatory practice (CBPR) approaches can enhance socio-behavioral research practices embedded as part of HIV cure research efforts.
2. HIV cure clinical trial participants are motivated by altruistic desires to help advance HIV cure science and the HIV community. It is important to manage participants' expectations, focus on participants' contributions, communicate uncertainty, and provide support to reduce feelings of having failed the research team and/or the HIV community following viral rebound.
3. At the start of the clinical trial, it is important to provide information to participants that the trial is addressing an unknown question (e.g. whether the experimental intervention will have an impact on ability to keep HIV suppressed in the absence of ART) and will most likely not cure them. Providing regular and accurate information to participants during the trial is important to reduce the risk of therapeutic (or curative) misestimation or misconception. There should be adequate support for partner protections during the ATI (e.g. referral to or provision of pre-exposure prophylaxis (PrEP) for partners without HIV).
4. It is important to emphasize time commitments, blood draws and procedures needed during HIV cure clinical trials.
5. Participants' experiences during ATI trials are heterogeneous. HIV cure clinical research teams should be attuned to participants' tolerance for physical and psychosocial side effects. Capturing side effects from the participants' perspectives can yield useful insight about how they experience clinical trials, and how to mitigate potential psychosocial risks during ATIs. Capturing participants' lived experiences can complement biomedical assessments.
6. The mental, emotional, and social impact of HIV cure-directed clinical trials on trial participants should not be underestimated. We recommend embedding frequent mental health checks as part of extended ATI trials involving viremia and ART restart periods, having health psychologists available as part of the trial team, and utilizing holistic person-centered clinical trial designs. Mental and emotional impacts can stem from the experimental interventions, ATIs (e.g. anxiety of being off ART) and even monitoring or additional procedures. Participants can be provided additional resources during the trial related to HIV or the ATI. We also recommend research teams to include some of the concerns of extended ATIs noted in this manuscript (e.g. anxiety of extended ATIs) as part of their informed consent forms.

Participant experiences in HIV cure-directed trial with an extended analytical treatment interruption in Philadelphia, United States



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Participant experiences in a combination HIV cure-related trial with extended analytical treatment interruption in San Francisco, United States



san francisco



PERSIST

I definitely had expectations. I definitely went on a rollercoaster of emotions, for sure. And so I don't want you thinking that I was flippant, or laissez-faire about this, or didn't have expectations—because I absolutely did. I posted a lot on social media about this ... I had this feeling of a lot of responsibility for all of these people. And to have to post that the experiment didn't work ... I felt like a failure ... It

took me a couple of days. And I think I even got back on meds before I could post to everyone—because it's not just my family and friends that I had to tell, but it was also these people in these other countries—my little pen pals, who, you know—some of them feel so desperate for there to be a cure and really needed this to work. And they were even more invested in it than me, okay? It kind of didn't work. You know, so that was a hard post, and those were hard conversations to have. Yeah. That was—I mean, you know, I could have chosen, obviously, to keep very private and never, ever post about that. So that would have all gone away, right? Like, that I did to myself. – Participant #06

What was anxiety-producing about it with me is, I didn't want the virus to spike. I was worried about, would I have a new seroconversion on this as it came back? And what if it spiked to 10,000, or, you know, 50,000 or whatever? Would I be laid up in bed? – Participant #06

What they told me was that the point of this particular study was to see what would happen when the viral load rebounded and that never happened. Well, it sucks because no one really knows ... no one wants to use the C word, the cured word, because going back to those other people that – people who thought they were cured. All these scientists said in the media and then, like, the virus came back. So it's, like, no one wants to use that word ... And then, you know, it just keeps me in limbo. If people ask me what's going on ... I have no idea. – Participant #02

Participant experiences in a combination HIV cure-related trial with extended analytical treatment interruption in San Francisco, United States



So, I'm dealing with the relationship piece, and then, a month of getting the test, and my partner is negative, and it's going to stay that way. The challenges in the relationship there, and then, navigating my body... It's been a real challenge for my partner during this journey, which I completely underestimated... I am in a relationship with a woman. And we have attempted to conceive during the time leading up to this... We were really arriving into this place where my partner is longing to try and conceive again. And that essentially requires unprotected sex... And that occurred right as I became detectable. So, once again, my partner had to go on to PrEP. She had to go through testing at that time, testing afterwards. It was a huge process for us and our relationship... It really affected our relationship, the trust piece. Essentially, I just had to take full ownership, like, "You're right. I should've said, 'No, we're not doing this right now.'" But I didn't... The practicality and the realness began to subside the deep elements of hope or ego, or just blind ambition, and the realness started coming into effect. – Participant #03

4/7 participants interviewed experienced difficulties around partner protections during extended ATI:

- Partner protections more difficult as time progressed
- Discomfort with intimacy
- Finding out whether partners are on PrEP was difficulty (“out of practice”)
- One partner took emergency PEP, provoking anxiety and need for additional support
- Partners had fertility desires (condomless sex – see quote)

SELF-REPORTED ANXIETY AND DEPRESSION RATINGS BEFORE, DURING, AND AFTER COMBINATION HIV CURE INTERVENTION TRIAL WITH AN ANALYTICAL TREATMENT INTERRUPTION IN SAN FRANCISCO, UNITED STATES

¹John A. Saucedo PhD, MSc, ¹Nadra E. Lisha PhD, ¹Lidia Rodriguez-Garcia, BA, ¹Elizabeth Nguyen, BA, ²Ana Korolkova, MS, BA, ²Fang Wan, MS, & ²Karine Dubé, DrPH, MPhil



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Background

The psychological experiences of participants in HIV cure-related trials with extended analytical treatment interruptions (ATIs) is unknown.

Limited literature suggests that ATIs may induce psychological distress given risks associated with being off HIV treatment.

Objective

To describe the psychological experiences of participants before, during, and after an extended ATI.

Parent Trial

Participants were recruited from JAWS – The UCSF-amfAR Combinatorial Therapy to Induce an HIV Remission trial (NCT04357821) over a 34-week period. ATI duration was up to 52 weeks.

Study Methods

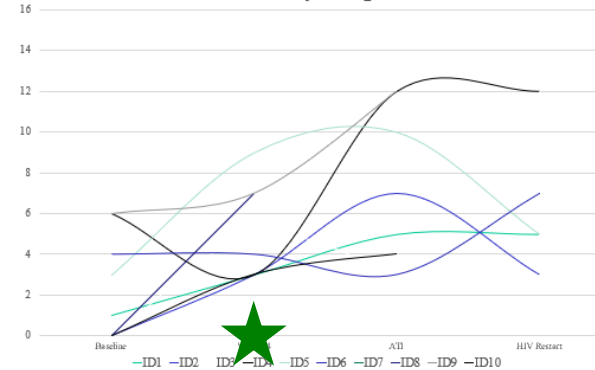
10 participants surveyed over time who participated in JAWS.

Time points aligned with trial study milestones:

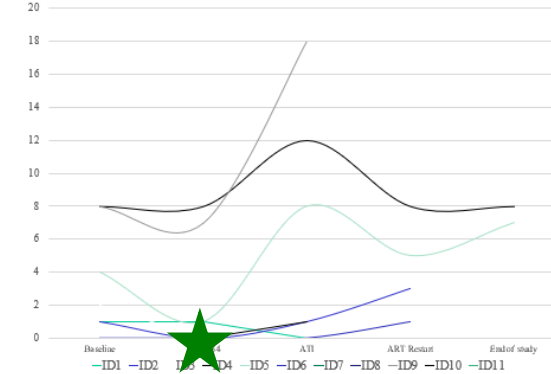
1. Baseline, 2. Week 34 (Prior to ATI),
3. ATI Visits (Monthly during ATI), 4. ART Restart Email, 5. Exit Visit.

Baseline anxiety – Generalized anxiety disorder 7-item measure (GAD-7), a past 2-week symptom rating.

Anxiety Ratings



Depression Ratings



Methods (Continued)

Follow-up anxiety – State-Trait Anxiety Inventory (STAI) 6-item measure. This is a measure of anxiety at the time of measurement, i.e., current state.

Depression – Patient health questionnaire (PHQ) w/8 of the 9 items. This is a past 2-week depressive symptom rating.

- Scores of 6 (anxiety) and 5 (depression) are considered mild severity

Results

- Nine of 10 participants were men, 1 was a transgender woman.
- All were >30 years of age.
- Five were Latino, 8 were of White race.
- **Baseline** PHQ (M=2.7, SD=3.09) and **GAD** scores (M=2.3, SD=2.5) were below mild severity.

Results (Continued)

- **Week 34** ratings were below the mild severity.
- **ATI PHQ** (M=5.3, SD=6.5) and **anxiety** (M=7.7, SD=4.3) scores were >mild severity.
- **ART restart PHQ** ratings were below mild (M=3.4, SD=3.2). **Anxiety** ratings fell but stayed above mild severity (M=6.4, SD=3.4).

Discussion

- Psychological distress was minimal; however, during the ATI, it reached a mild severity and reduced after re-starting ART.
- We recommend integrating self-ratings and close monitoring in new trials

For more details:

Acknowledgements:

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ATI Initiation

Participant experiences in a combination HIV cure-related trial with extended analytical treatment interruption in San Francisco, United States



Table 3. Summary of considerations for implementing combination HIV cure trials with extended ATIs.

Decision-Making Factors

- PWH may have several motivations for joining complex combination HIV cure-related trials, such as mix of scientific altruism, trust in the clinical research, and hope of achieving post-intervention control. It is important to guard against potential therapeutic or curative misconception when enrolling participants in HIV cure-related trials.
- PWH's backgrounds may influence their decision to participate (e.g., prior research participation or relationship with research team, time availability and resources to participate, personality types). Strategies will be needed to engage individuals in HIV cure-related trials who may not be as trusting of the clinical research establishment, with full-time responsibilities, or who are more risk-averse.

Trial Perceptions and Expectations

- Most participants perceived the likelihood of trial risks, although one participant was unable to accurately appraise risks. Close clinical monitoring mitigated potential worries around risks during the trial. Most participants perceived some trial benefits (e.g., psychosocial benefits such as sense of pride, purpose and optimism).
- Most participant had an accurate appraisal of the trial's purpose and no expectation of being cured. However, it is possible that PWH still hope to be cured or achieve sustained post-intervention control. For participants whose HIV do not rebound, there can be confusion or uncertainty about their trial outcome.

Experiences with Combination HIV Cure Trial

- Trial teams should find a balance between the frequency of clinical monitoring visits and providing peace of mind for participants, and accommodate trial visits to participants' unique circumstances when possible (e.g., travel schedules). There should be innovations in trial conduct to reduce trial intensity and burdens (e.g., home-based viral load test).
- There will be heterogeneity in how participants experience experimental interventions and procedures during the trial. There should an emphasis on safety and emotional health when undergoing experimental interventions.
- ATIs should be considered like a journey, on both physical and emotional levels. ATIs can be anxiety-provoking for participants who experience uncertainties around viral rebound. ATIs may not be as life-changing for participants who take daily pills for other medical conditions. Trial teams should carefully manage expectations around the state of durable ART-free control. Even the lack of viral rebound may not necessarily result in relief but can be a source of worry due to ongoing uncertainty. There should be a robust psychosocial infrastructure in place to take care of participants' needs before, during and after ATI trials.
- Participants will experience ART restart differently (e.g., sense of relief, defeat). Research teams should emphasize that participants have not failed the trial when resuming ART, but have helped answer scientific questions. Customized approaches may be needed to support participants with ART re-adherence behaviors post-ATI.

Psychosocial Factors

- Becoming and remaining detectable for HIV during ATIs can be a stressor. ATIs are accompanied with viremia-related worry, which will likely increase with higher viral load measures. Viremia-related worry may be lesser for individuals with prior experience with prior HIV detectable status, but will need to be thoughtfully considered in the era of U=U.

Behavioral Factors

- There can be many challenges associated with partner protections during ATI trials (e.g., conversations around condom use, trying to find out if partners are on PrEP, helping partners navigate PrEP, dilemma around whether to have sex, taking oneself out of U=U. etc.). Evidence-based partner protections support in the context of ATI trials are needed for participants and partners.

Logistical Factors and Study Conduct

- Research teams should offer as much logistical support and flexibility to participants as possible. The importance of mental health, emotional and psychosocial support systems around each participant should not be under-estimated.

Participant experiences in a combination HIV cure-related trial with extended analytical treatment interruption in San Francisco, United States



Psychosocial Factors

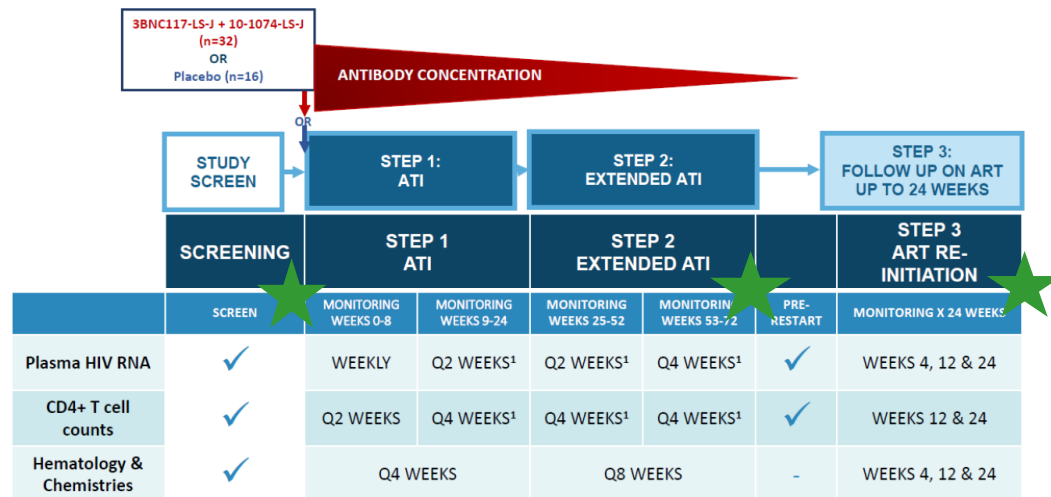
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Behavioral Factors

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A5416/HVTN 806/HPTN 108 SBR Component

A5416 Study Design



Three SBR Timepoints: ★

1. Entry/pre-ATI (Beginning Step 1)
2. Viral rebound or ART restart (or visit immediately after) (Beginning Step 3)
3. EOS or early discontinuation

¹OR WEEKLY IF VL > LLQ

- All 9 sites completing closed-ended surveys (CES)
- 5/9 sites completing In-Depth Interviews (IDIs)

A QUALITATIVE FOCUS GROUP STUDY

With this study we have hope that something is coming; Community Members' Perceptions of HIV Cure-Related Research in Durban, South Africa.

Karine Dubé^{1,2}, Deli Mthimkhulu³, Wiseman Ngcobo³, Deborah Mindry⁴, Luyanda Maphalala⁵, Vanessa Pillay⁵, Whitney Tran¹, Ana Korolkova¹, Thumbi Ndung'u^{6,7,8,9}, Krista Dong^{9,10,11}

IN THEIR OWN WORDS

AN ALTERNATIVE TO LIFELONG ART

It is a win-win situation, as studies are there to find a breakthrough, you see as much as it is scary, as people we can have doubts on what if it doesn't work, we mostly focus on a negative part of what if it doesn't, instead of what if it works and how many people who are on treatment will benefit, especially there are people who have been on ARVs for more than 20 years or 30 years who really needs this break, so yah it will be a breakthrough.

- Focus Group 3, Participant 16

REBOUND DURING ATI AND THE VIRAL RESERVOIR

[We] believe that it is something good but scary at the same time. It is scary because when you tell people to stop taking their ARVs, whereas as people who have knowledge, we know that the virus is hiding when you are taking your ARVs, but once you stop and use the bnAbs, the virus will come out in full force, and we do not know what will happen during that time. Even if we are going to be using something else instead, but we are still not sure if that something will work and bnAbs will be able to reach all the places where the virus is hiding.

- Focus Group 2, Participant 7

RISK FROM DISCLOSURE versus PARTNER PROTECTION

Yes, because where I see the danger... when I have an abusive partner who just comes and demands that we have sex and then... he gets infected... It is true that we change partners, and we are failing to disclose but we can't be forced to disclose. But since now it involves social workers and psychologists it will really help people to see what happens if I am hiding my status.

- Focus Group 3, Participant 17

LOCAL LANGUAGE TO UNDERSTAND HIV CURE.

I think that in terms of terminology or language, it depends on where you are. If it is going to be in Umlazi, it means that we will be speaking terminology that is always used on the street. It should be (developed by) someone who understands how we talk outside compared to us speaking here as we are formal. In short it depends on where you are. Amen.

- Focus Group 2, Participant 14



Community members, Dr. Karine Dube and the FRESH team



Focus Group Discussion




BEAT-HIV
DELANEY COLLABORATORY



1. University of California San Diego (UCSD) School of Medicine, Division of Infectious Diseases and Global Public Health (IDGPH), La Jolla, CA, USA 2. University of North Carolina at Chapel Hill Gillings School of Global Public Health, Chapel Hill, NC, USA 3. Integration of Tuberculosis in Education and Care for HIV/AIDS (ITEACH), Durban, South Africa. 4. Center for Gender and Health Justice, University of California Global Health Institute, Los Angeles, CA, USA. 5. Females Rising through Education, Support and Health (FRESH), Durban, South Africa. 6. HIV Pathogenesis Programme (HPP), The Doris Duke Medical Research Institute, University of KwaZulu-Natal (UKZN), Durban, South Africa. 7. Africa Health Research Institute (AHRI), Durban, South Africa 8. Division of Infection and Immunity, University College London, London, UK. 9. Ragon Institute of Massachusetts General Hospital (MGH), Massachusetts Institute of Technology (MIT) and Harvard, Cambridge, MA, USA. 10. Massachusetts General Hospital, Boston, MA, USA 11. Harvard Medical School, Cambridge, MA, USA



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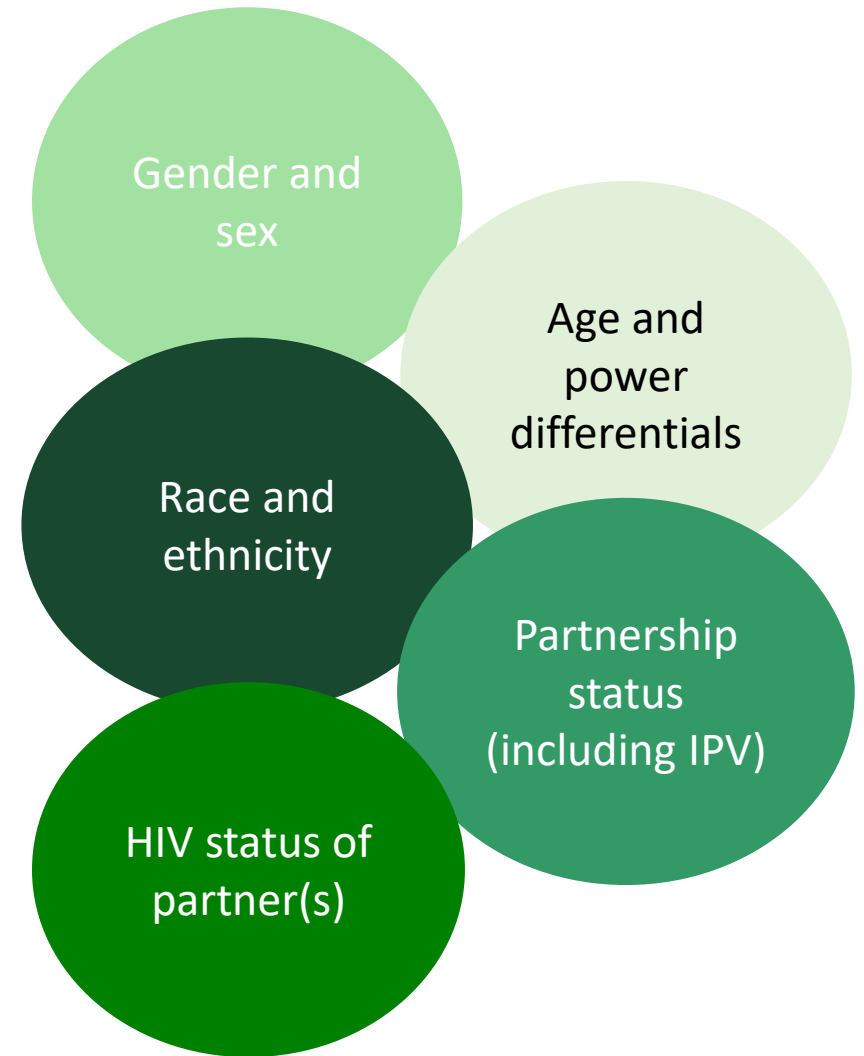
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SOCIO-BEHAVIORAL

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

Key Findings

- Attention must be paid to **gender** and **power dynamics**
- ATI trials should be designed and implemented through lenses of **intersectionality** and **equity**
- ATI trials may have both **positive** and **negative effects** on **stigma** for PLWH and partners
- **Partnership dynamics** should be considered
- Need to **bridge HIV cure-related research with HIV prevention**
- **Socio-behavioral research** should be mandated (and funded) as part of biomedical HIV cure protocols involving extended ATIs



A partner protection package for HIV cure-related trials involving analytical treatment interruptions



Karine Dubé, Tia Morton, Lawrence Fox, Lynda Dee, David Palm, Thomas J Villa, William Freshwater, Jeff Taylor, Gail Graham, William B Carter, John A Saucedo, Michael J Peluso, Annette Rid

Enable and encourage participants to protect their partners

Provide information or counselling on HIV testing,²¹ HIV prevention (eg, barrier protection, PrEP,^{7,9,13,17,18,21,31,85} and PEP^{7,21}) with use of evidence-based materials and approaches in a range of formats (eg, fact sheets, presentations, videos, and text messaging) that are tailored to diverse individuals (eg, with respect to gender, sex, age, sexual orientation, education level, etc) and specific locations⁹

Provide or refer to HIV prevention options (eg, no cost barrier protection, PrEP referral for partners)

Encourage participants to inform their partners and provide counselling^{7,9,21} on HIV and ATI trial participation disclosure,^{7,9,21} provide sample disclosure scripts,⁹ offer disclosure role playing sessions as needed

Encourage participants to include their partners in trial visits (eg, optional site visits and discussions with the trial team)^{9,21}

Provide mental health support or counselling referrals as needed^{18,21}

Offer peer support¹⁷ (eg, former ATI trial participants)

Encourage partners to communicate with the trial team^{9,17} (eg, provide written information tailored to partners, invite partners to accompany participants during trial visits in person or via telehealth)²¹

Offer information or counselling on HIV prevention (eg, barrier protection, PrEP,^{7,9,13,17,18,21,31,85} and PEP^{7,21}) with use of evidence-based and partner-specific materials and approaches in a range of formats, including fact sheets, presentations, videos, and text messaging²⁵

Provide HIV testing, PrEP,^{7,13,18,31,85} and PEP^{7,21} referrals and navigation assistance⁹ (eg, refer partners to full range of PrEP options)

Facilitate access to mental health support^{18,21,53} or counselling as needed

Engage the local community in discussions about trial involving ATIs⁹

Promote broader community engagement about ATI trials and consider health promotion and social marketing campaigns to raise awareness about HIV prevention needs for partners of ATI trial participants

Key messages

- Analytical treatment interruptions (ATIs) are used to evaluate the effects of experimental HIV cure-related interventions. During ATIs, sex partners of trial participants might be at risk of acquiring HIV.
- This Review proposes a partner protection package (P3) to address concerns around onward HIV transmission during trials involving ATIs.
- Our P3 proposal is informed by a series of community-driven conversations and two focused literature reviews.
- The prototype P3 delineates three basic considerations for protecting participants' sex partners during ATI trials: (1) ensuring the scientific and social value of the ATI and the trial, (2) reducing the likelihood of unintended HIV transmission, and (3) ensuring prompt management of any acquired HIV infection.
- The prototype P3 also outlines possible ways of implementing the three basic considerations and highlights ethical limitations or tradeoffs with specific approaches.
- A comprehensive P3 framework could help make a crucial contribution to the successful and ethical conduct of HIV cure-related trials involving ATIs, and ultimately, the development of effective HIV cure strategies.

THE ROLE OF HIV VIRAL SUPPRESSION IN IMPROVING INDIVIDUAL HEALTH AND REDUCING TRANSMISSION

POLICY BRIEF



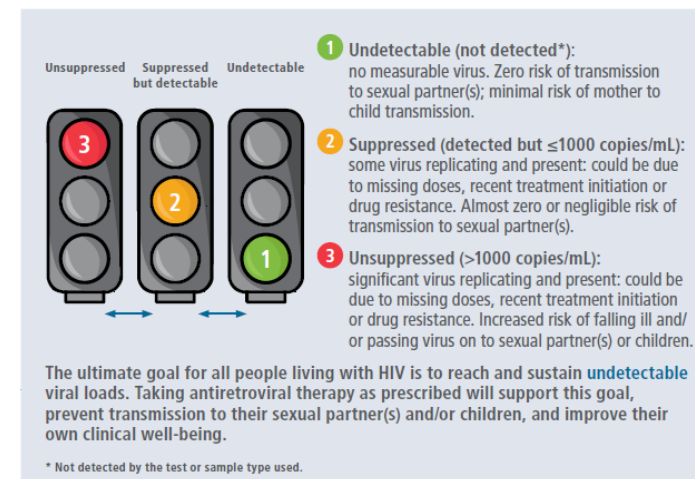
3. THE UPDATED TREATMENT MONITORING ALGORITHM AND ITS THREE CATEGORIES OF VIRAL LOAD LEVELS

3.1 Updated treatment monitoring algorithm

WHO's HIV treatment monitoring algorithm was updated in 2021 to support people living with HIV to achieve viral suppression, with the ultimate goal of maintaining an undetectable viral load (2). The updated algorithm introduced two distinct thresholds: >1000 copies/mL to identify people living with HIV who are unsuppressed and for whom treatment might be failing; and undetectable to identify people living with HIV whose viral load cannot be detected. This policy brief aims to explain the rationale behind these thresholds and to provide additional information regarding implementation considerations.

3.2 Three categories of viral load levels

There are three key categories of viral load suppression: unsuppressed, suppressed, and undetectable. The viral loads of people living with HIV can fluctuate between these categories depending on their access and adherence to antiretroviral therapy. These are illustrated and detailed in the figure below.



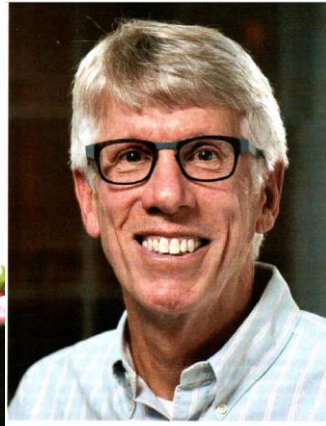
The 2025 Global AIDS Targets calls for all people receiving antiretroviral therapy to achieve viral suppression by 2025. (3). People living with HIV with an undetectable viral load as well as those with a suppressed viral load (detected but ≤ 1000 copies/mL) should be included in the numerator when calculating the last 95 (viral suppression) target.

Anyone with a detectable HIV viral load, even if suppressed (≤ 1000 copies/mL), should be supported with adherence counselling and follow-up viral load testing (see Annexes 1 and 2 for the updated treatment monitoring algorithm and implementation considerations for treatment monitoring of pregnant women and breastfeeding women, respectively); however, only those with persistent unsuppressed viral loads¹ should be considered for a treatment regimen switch.

¹ Two consecutive viral load tests performed three months apart that are >1000 copies/mL, with adherence counselling between tests.



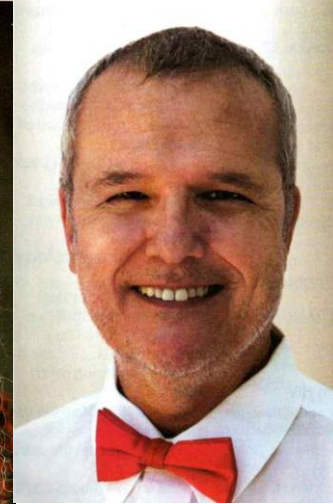
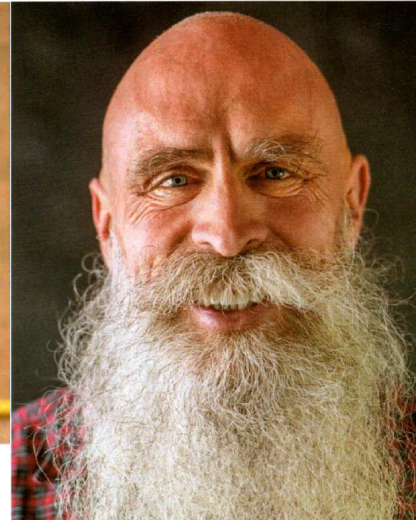
GAIL GRAHAM
A positive experience



BILL FRESHWATER
Make participants feel like partners

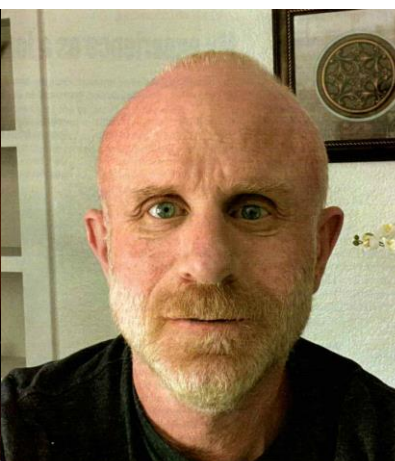
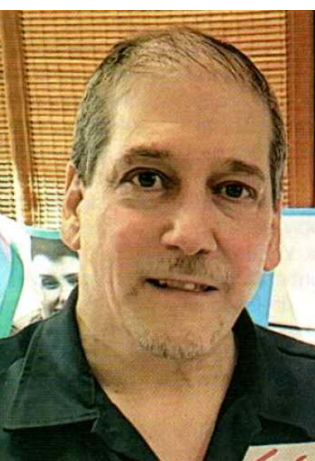
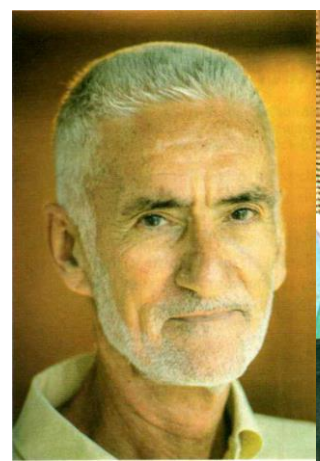
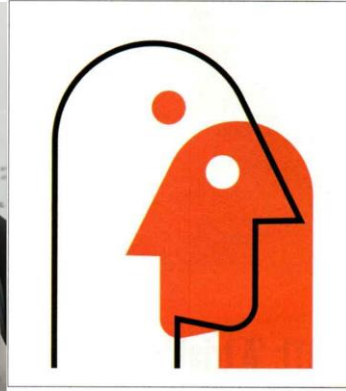


WILLIAM B. CARTER
Don't cut off my dreams of a cure



If I have a suggestion to the study clinicians, it's make the participants aware of psychological things they might experience, how it may change their romantic and sexual interaction with partners. Be repetitive. Researchers go over all the physical risks, be very thorough with that. The mental health component has to be considered, too. Someone can describe a situation, and you think you're prepared for it, and then you enter into it. I was feeling alone and isolated. What

-Luis Canales





Elements of Comprehensive Participant Readiness and Resilience Framework – A journey approach to HIV cure research

Creating a framework that supports study participants throughout their experience—and beyond

Before ATIs

Reframe the approach to informed consent to a person-centered framework (e.g., decision support around ATI trial participation, availability of peer navigators for decision support).

Enhance the informed consent process (e.g., multi-media/multi-modal informed consent process to accommodate disparate learning styles, literacy levels and cultural, linguistic and socioeconomic backgrounds of prospective participants).

Provide clear information about known and potential risks of ATIs (based on previous trials), risks of experimental interventions and risks of monitoring procedures.

Explain to prospective participants the legal liabilities that may result from not disclosing their HIV status to sex partners during an ATI.

Discuss the potential long-term adverse events that can result from an ATI.

Ensure that treatment costs for adverse events due to the ATI are not borne by the participant.

Conduct pre-ATI assessments to determine a prospective participant's understanding and psychosocial readiness.

Plan and provide support around partner protection measures (for HIV-serodifferent relationships).

Multi-center trials must have a single lead institutional review board; there should be only one informed consent for the participant to sign.

During ATIs

Conduct close monitoring without overburdening trial participants.

Build support around partner protection measures.

Understand and consider the relationship dynamics and potential risks, including the risk for intimate partner violence.

Conduct psychosocial and mental health assessments and support—particularly addressing anxiety around being off HIV treatment.

Assess the impact of ATI participation on other people in participants' immediate social circles.

Develop and provide home-based viral load testing to self-assess transmissibility potential.

In case of unexpected intercurrent events (e.g., COVID-19, mpox pandemics), establish a mechanism for consultation with ATI participants, participant-centered communications, mental health safety screening and guidance to reduce risks to trial participants.

After ATIs

Conduct a mental health follow-up after the ATI period and study have ended.

Establish regular check-ins with participants following an ATI or the study's completion every six months.

Monitor for potential long-term effects of ATIs.

Provide ART resistance testing and assistance with ART regimen change if needed.

Disseminate research outcomes to participants in a way that is accessible to them.

Provide medical journals and other publications in which the study's findings appear free of charge to study participants.

Continue to check in with participants who have resumed ART after an ATI period has ended.

For participants who are post-intervention controllers, provide continued psychosocial support around being off ART and provide partner protection support.

For participants who are cured, provide psychosocial support around the anxiety of potentially having to relive the experience of an HIV diagnosis if they are no longer cured; offer support systems to maintain the social benefits they had received during the time they were living with HIV (e.g., housing benefits) and offer guidance around PrEP uptake if needed.

"This is actually a really unique moment in time":
Navigating Long-Acting HIV Treatment and HIV Cure
Research with Analytical Treatment Interruptions –
A Qualitative Interview Study in the United States



Image: Michael Louella

"This is actually a really unique moment in time":
Navigating Long-Acting HIV Treatment and HIV Cure
Research with Analytical Treatment Interruptions –
A Qualitative Interview Study in the United States



Image: Michael Louella

- Unique window of opportunity to counsel PWH about ATIs before switching to LA HIV treatment
- Need to support PWH's decisions and to help navigate rapidly evolving landscape of novel HIV therapeutics
- Heterogeneity in treatment and research preferences for PWH

"This is actually a really unique moment in time":
Navigating Long-Acting HIV Treatment and HIV Cure
Research with Analytical Treatment Interruptions –
A Qualitative Interview Study in the United States



Image: Michael Louella

- Pay attention to psychosocial and structural factors that may create systemic inequities in access to novel interventions
- Urgent need for educational opportunities aimed at HIV care providers
- Still a role for HIV cure research
- Critical to acknowledge the social context

Sources of Hopes



- An increasing number of biomedical researchers are recognizing the **importance of socio-behavioral sciences** to facilitate and inform **recruitment, retention** and **support** of HIV cure trial participants.
- At the FRESH site in South Africa, SBR is increasing our understanding of how to **safely navigate** women **through their ATIs**, including measures to **support disclosure** (when desired) and **partner protections** and how to implement a **trauma-informed/healing-centered trial**.
- **2024 consensus meeting** in Nairobi, Kenya will help **update guidelines around ATIs**.
- Increasing number of **groups** recognizing **critical importance of SBR and ethics research**.

Sources of Worries



- **Limited formative research** in resource-limited settings where ATIs are planned to be scaled-up
- **Limited infrastructure to perform SBR** and **ethics research** where ATIs are planned to be scaled up.
- **Lack of SBR** and evidence gathering around **effective partner protections+** and **lessons learned** in real-time.
- Expectations that SBR scientists should apply for “**separate**” **grants** that may not run parallel to ATI trial timelines
- SBR and ethics research **not adequately built into grants or protocol** – usually an afterthought.
- Assumption that other people will “take care of it”
- *CROI rarely accepts socio-behavioral research focused on HIV cure research (small sample sizes)

DEAR REVIEWER:



Years of HIV campaigns (in Africa and globally) have pounded home the message that adherence to a daily pill is critical to avoid development of resistance.

For those whose circumstances enable them to embrace high level treatment adherence – and we would argue that even those who have occasional or even frequent periods of treatment default – the idea of knowingly stopping treatment may produce anxiety.

PROPOSED DISCUSSION QUESTIONS



What does justice-informed HIV cure research with ATIs mean to you?

Should socio-behavioral research be embedded as part of ATI trials?

What should be some of the key socio-behavioral research questions?