



# Analytical Treatment Interruptions (“ATIs”)

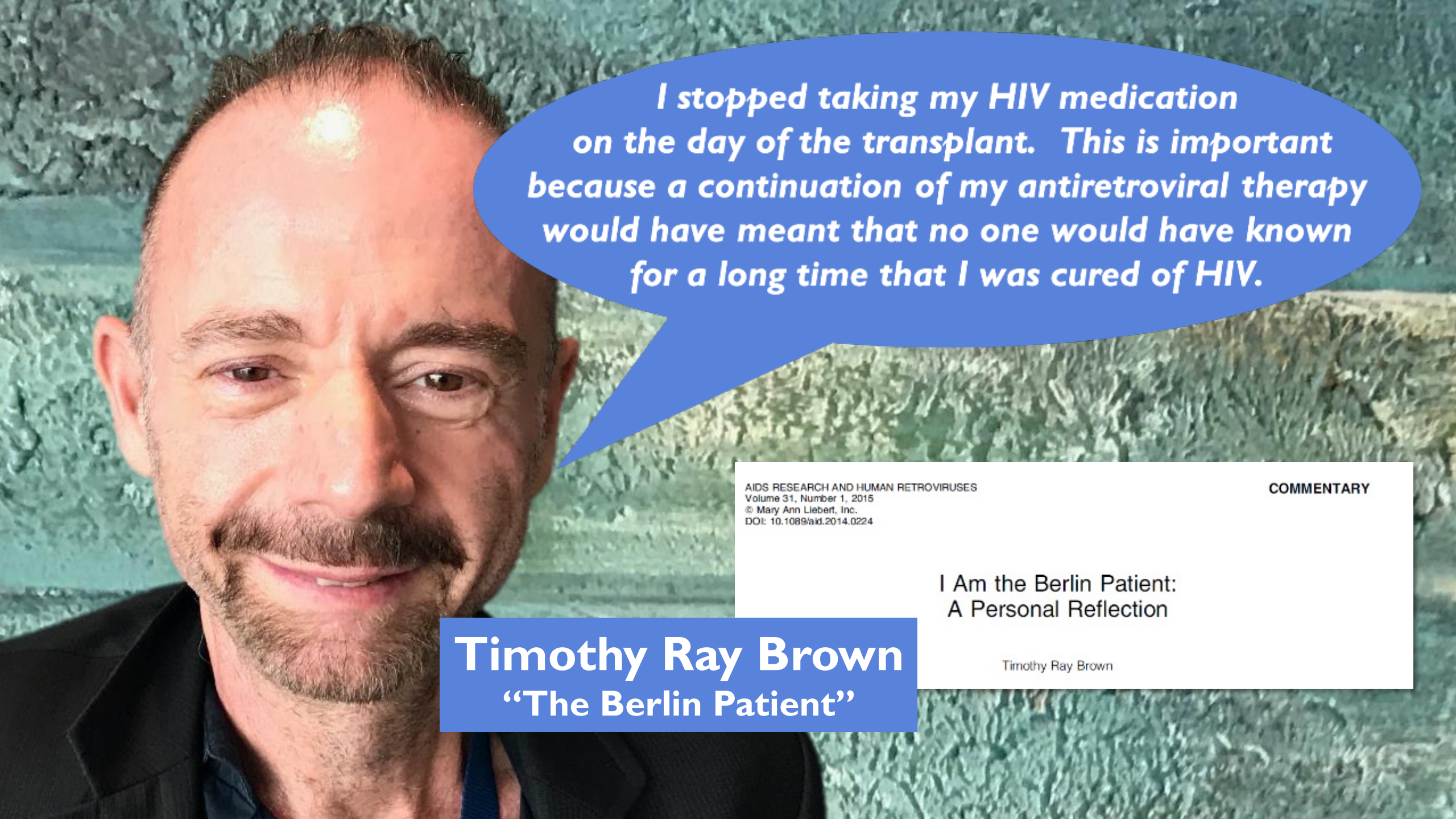


CUREiculum

This research training curriculum is a collaborative project aimed at making the science of HIV cure-related research accessible to the community and the HIV research field.

# Participant Testimonials



A close-up portrait of Timothy Ray Brown, a man with a mustache and goatee, smiling slightly. He is wearing a dark jacket over a blue shirt. The background is a textured, greenish-blue wall.

***I stopped taking my HIV medication on the day of the transplant. This is important because a continuation of my antiretroviral therapy would have meant that no one would have known for a long time that I was cured of HIV.***

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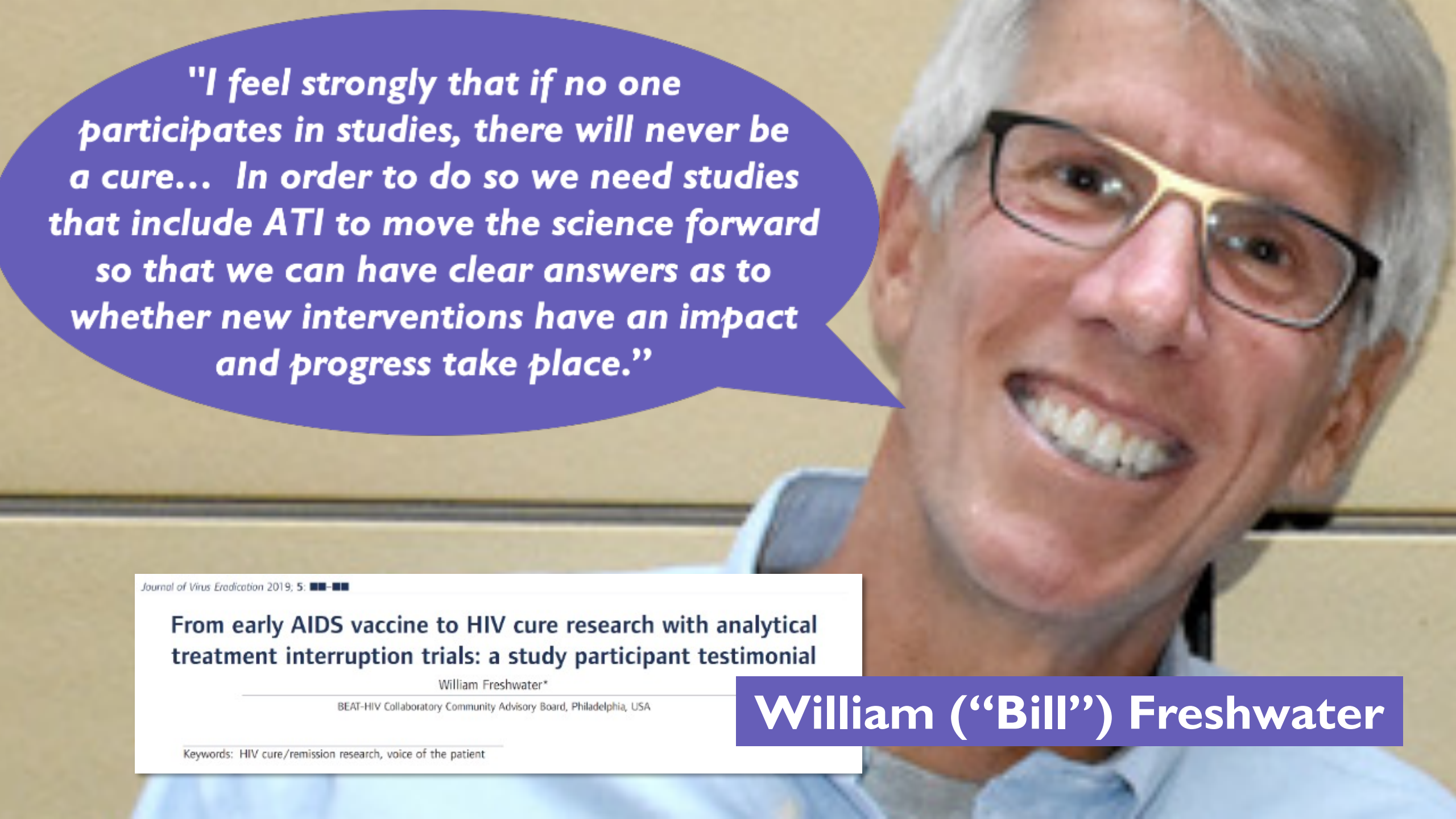
COMMENTARY

## **I Am the Berlin Patient: A Personal Reflection**

Timothy Ray Brown

**Timothy Ray Brown**  
**“The Berlin Patient”**



A close-up portrait of William Freshwater, an older man with white hair and glasses, smiling. He is wearing a light blue button-down shirt. The background is a plain, light-colored wall.

**"I feel strongly that if no one participates in studies, there will never be a cure... In order to do so we need studies that include ATI to move the science forward so that we can have clear answers as to whether new interventions have an impact and progress take place."**

Journal of Virus Eradication 2019; 5: ■■-■■

## **From early AIDS vaccine to HIV cure research with analytical treatment interruption trials: a study participant testimonial**

William Freshwater\*

BEAT-HIV Collaboratory Community Advisory Board, Philadelphia, USA

Keywords: HIV cure/remission research, voice of the patient

**William ("Bill") Freshwater**



# What is an ATI?



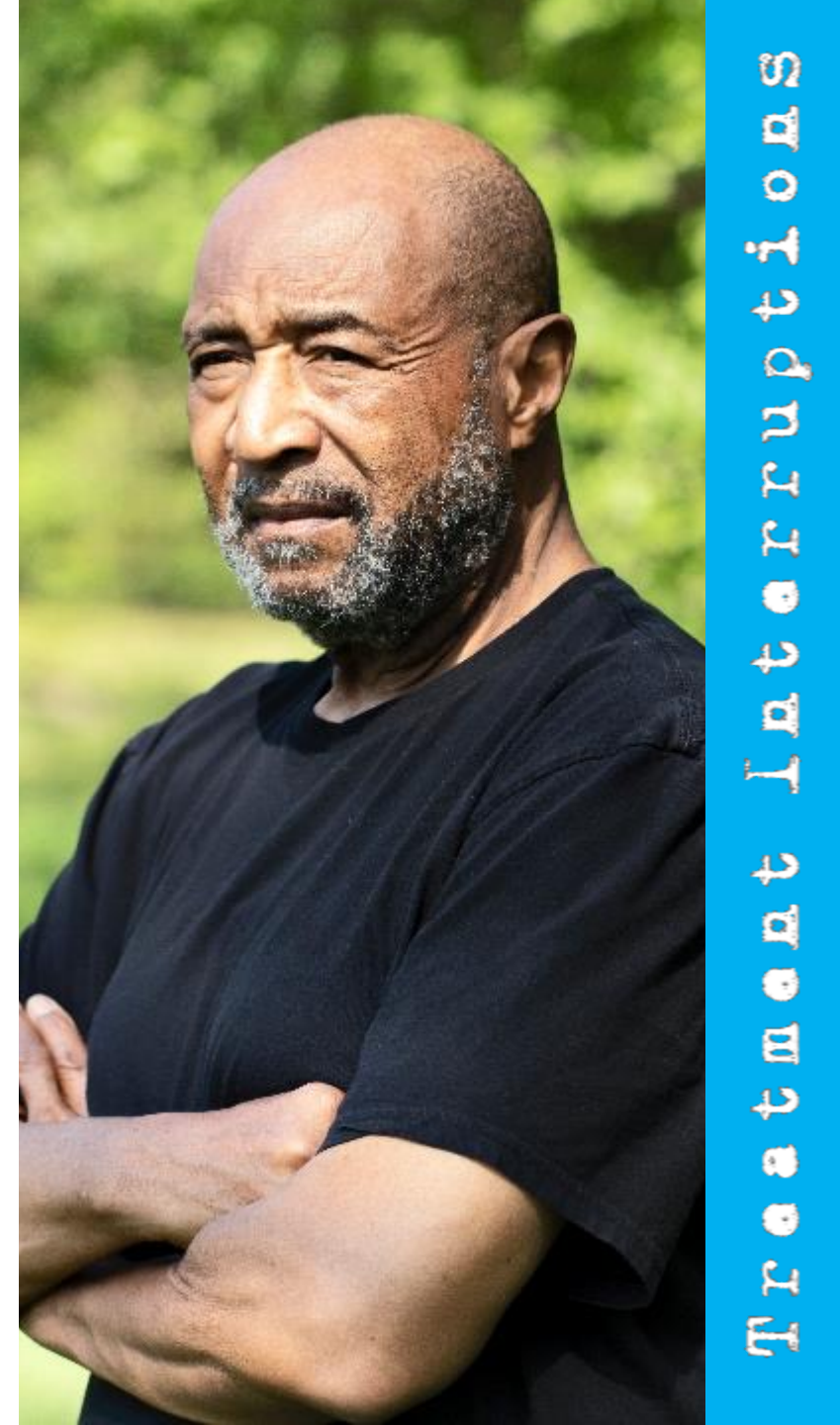
# What is an ATI?

- stands for **Anal<sup>y</sup>Treat<sup>m</sup>Inter<sup>r</sup>uption**
- also called **IMAP** – **Intens<sup>i</sup>Mon<sup>i</sup>ted Antiretroviral Pause**
- As part of participation in a research study, a volunteer/participant is asked to **pause their HIV medications** under careful observation from a doctor, researcher and/or healthcare team
- **Clinical status** and **safety labs** including viral load, CD4+ T cell count are monitored closely and frequently, usually through weekly blood samples
  - It remains important to stay in close contact with your primary care provider



# ATIs in Context

- **Short or brief ATIs:** *some treatment pauses may last days to weeks*
- **Restrictive ATIs:** *restart HIV medicines as soon as virus is detectable*
- **Extended or prolonged ATIs:** *may last weeks to months*
- **Permissive ATIs:** *may allow high levels of HIV under close monitoring for weeks to months before restarting HIV medicines*



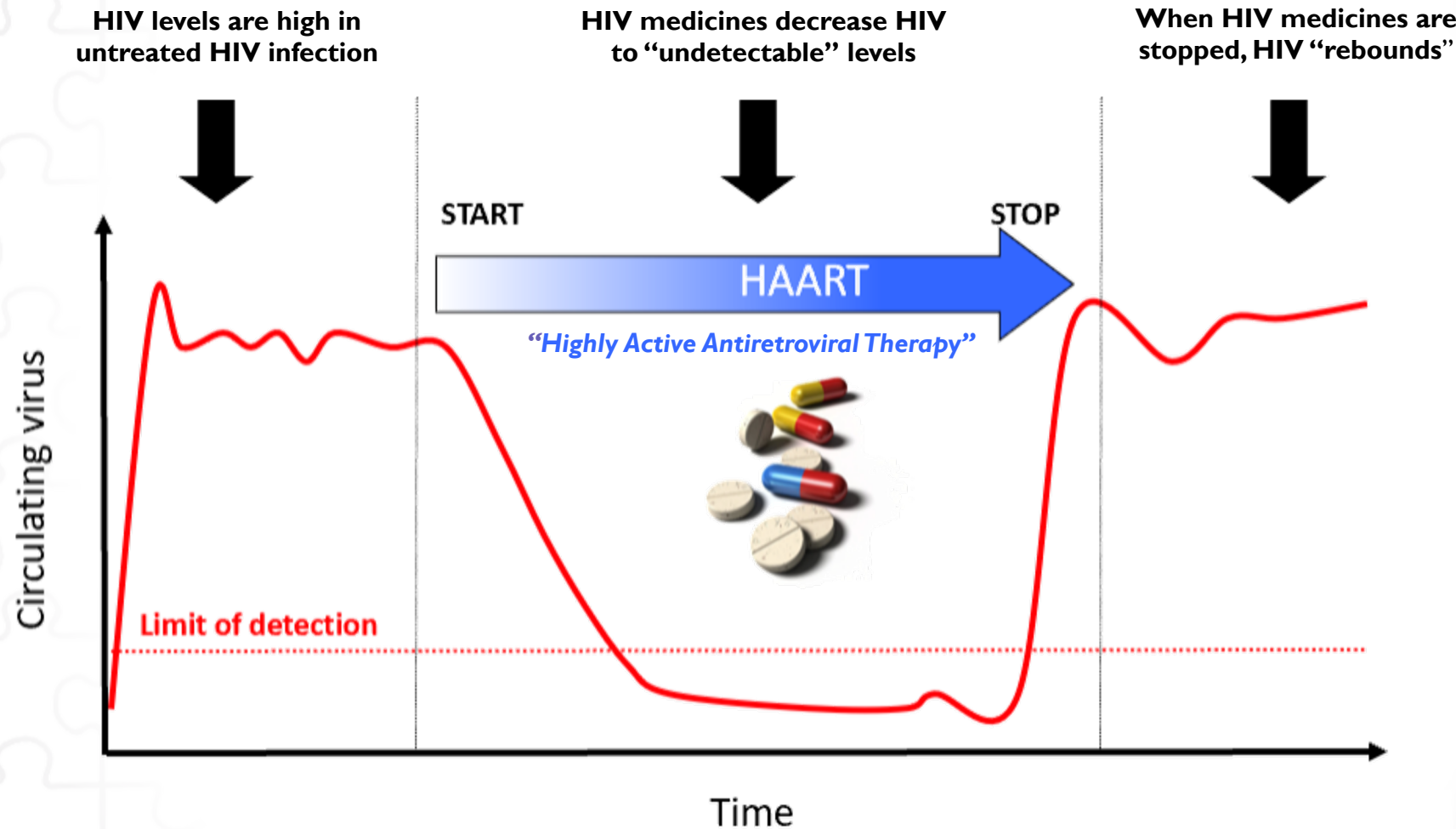


# If HIV medicines are effective, why pause them?

- HIV reservoir: **HIV** that is “**hidden**” in different cells and tissues
- Goal of many “HIV cure” studies: **reduce the reservoir** and **teach the immune system** to control reservoir
- There is currently **no other way to know for sure** if any decreases in reservoir size or changes in immune function caused by a cure intervention have enhanced a person’s ability to control HIV
- So, ATIs are needed to determine whether a cure intervention has **enhanced a person’s ability to control HIV** in the absence of HIV medicines



# Current Medicines **Do Not** Eliminate HIV



**WHY?** Because HIV hides in a “**reservoir**” that is not cleared by HIV medicines



# What do we **learn** from an ATI?

- Is the volunteer a **post-treatment controller** (someone whose HIV levels stay low without HIV medicine)?
- Has the **HIV reservoir** been **decreased**?
- Has the **immune system** been **taught** to control HIV?
- What may the study teach us about the experimental intervention?
  - The **effects** of the intervention **on participants' health**
  - The ability of the intervention to **control or eliminate HIV**





# Types of Experimental Therapies Where ATIs Might Be Necessary

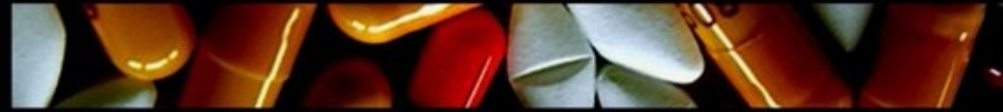
- Immune-based approaches: **jump start** the immune system
- Broadly neutralizing antibodies: defend the body from infectious particles and **kill infectious particles**
- Cell and gene therapy: change immune cells in order to **prevent HIV from entering the body**
- Combination approaches: mixing **different approaches together**



# Risks & challenges of an ATI



**TREATMENT INTERRUPTIONS**



**ARE CURRENTLY PART OF**



**MANY CURE RESEARCH STUDIES**



**BUT THERE'S MUCH UNCERTAINTY**



**ABOUT THE POTENTIAL RISKS**



# The Risks of ATIs

## Risk to Participants

- “Undetectable” status lost
- CD4+ T cell decrease
- Increased inflammation and other health effects
- Acute retroviral syndrome
- Anxiety and social stigma

## Risk to Partners

- Risk of sexual partner acquiring HIV from a trial participant who is experiencing a HIV rebound while on an ATI

**NOTE:** Risks are directly related to ATI duration and the highest level (peak) of increased HIV during rebound.

# Specific Challenges of ATIs

## Participants

- Difficulty **disclosing** HIV status
- Difficulty **disclosing** ATI participation
- Generic/**Vague counseling**
  - “Your partners will be at risk.”
  - “Avoid having sex.”

## Partners of Participants

- Are **NOT** part of the research study
- Are **not recognized** in law or medicine **as participants**
- **No** direct **information provided** on HIV risk reduction and **challenges understanding** any **information** received



# Recent ATI Transmission Cases

- France: **male to female** transmission
- Spain: **male to male** transmission
- PrEP (Pre-Exposure Prophylaxis) unavailable during either study
- Shows the **urgency** of efforts to mitigate transmission risk in the context of clinical trial

Make every attempt to **proactively ensure that PrEP & PEP (post-exposure) are available and accessible** to all identified participants' partners

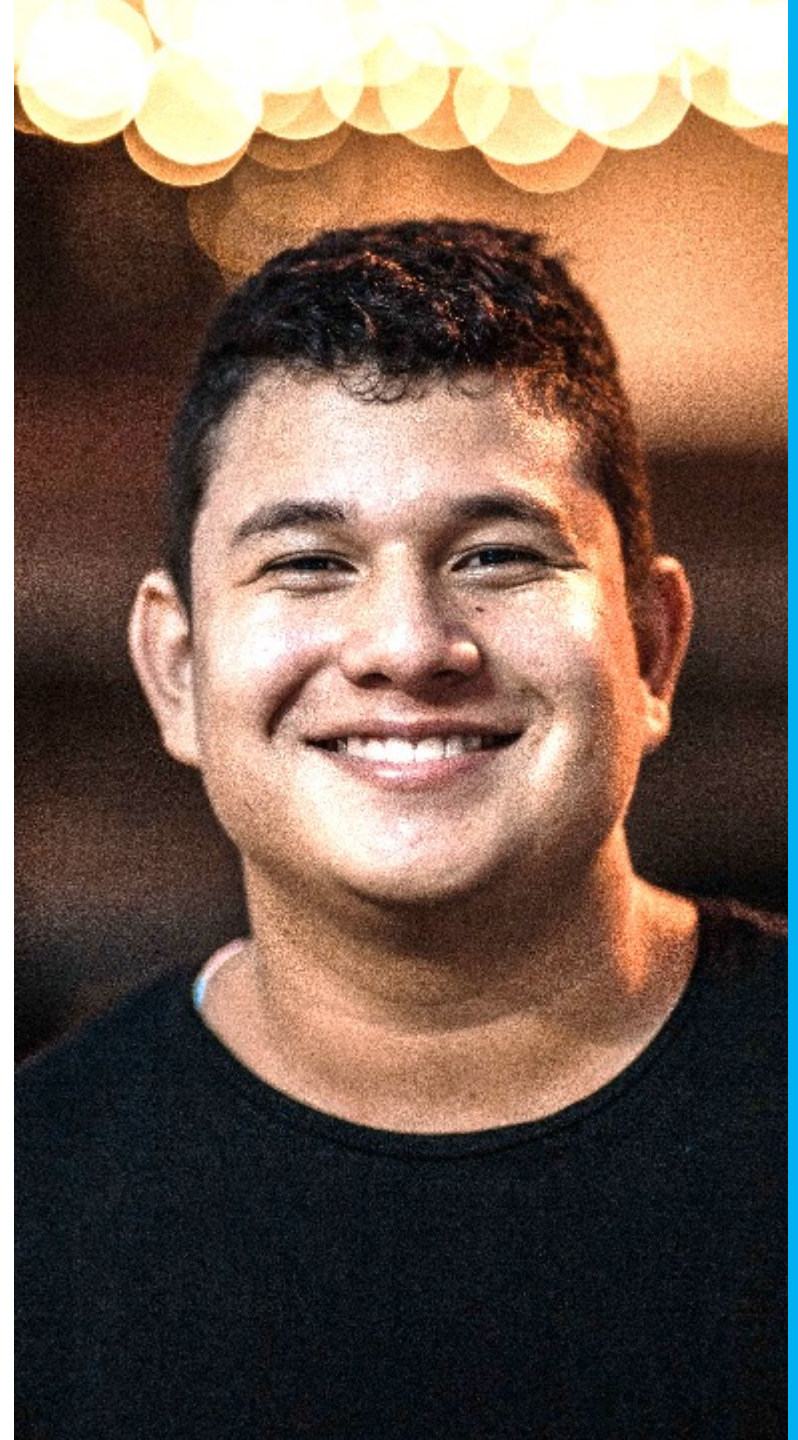


# Designing an ATI



# Designing an ATI: Key Considerations

- **Ragon Institute meeting:** 2018 meeting of experts to reach to consensus on how to implement ATIs safely
  - Community reps helped organize the meeting and participated
  - All attendees has an opportunity to comment and vote on all key focus areas
- **Key focus areas:**
  - **Inclusion & exclusion criteria** for clinical trials
  - How frequently to **monitor viral load** during ATIs?
  - When to **restart ART** after HIV rebound?
  - How to **decrease HIV transmission risk**?



## A collaborative, multidisciplinary approach to HIV transmission risk mitigation during analytic treatment interruption

Michael J Peluso<sup>1\*</sup>, Lynda Dee<sup>2,3,4,5</sup>, Danielle Campbell<sup>3,4,5,6</sup>, Jeff Taylor<sup>3,5,7,8</sup>, Rebecca Hoh<sup>1</sup>, Rachel L Rutishauser<sup>9</sup>, John Saucedo<sup>10</sup>, Steven G Deeks<sup>1</sup> and Karine Dubé<sup>11</sup>

- Provided a **practical starting point** to reduce HIV transmission risk during ATIs
- Described strategies in a cure trial that **may be applicable to other urban areas** with university based medical centers and accessible PrEP
- Included **extensive community involvement**





# Integrating **Risk Mitigation** into Protocol

- **Script and checklists** for discussion of transmission risk during ATI
- **Standardized counseling at enrollment prior to ATI**
  - For both study participants and partners
- **Build counseling into study protocol**
  - Hands-on PrEP referrals made for partners whenever possible





# Testing and Disclosure

- **Counseling materials** help to facilitate discussion about **HIV status** and ATI between participant and partner(s)
- **Directs partner(s)** who don't know their HIV status **to local HIV testing resources**

# Focus on PrEP (Pre-Exposure Prophylaxis)

- **Passive navigation** to PrEP and **providing condoms** is not enough
- ***Mandatory protocol provisions for PrEP education and active navigation to PrEP are necessary***
- **De-stigmatizing PrEP** and **PEP Information sheets**, including information specific to women and trans communities must be provided





# Study Team Engagement

- Encourage participants to **engage partners whenever and if possible**
  - Invite to study visits
  - Partner participation encouraged at least 4 weeks prior to ATI
- **Hands-on** study team engagement with partners
  - Access to study physician to discuss PrEP issues
  - Initial and repeated **transmission counseling**
  - **Direct referrals** to local PrEP and PEP sites
  - **Warm hand-off** to directly connect partner to PrEP and PEP clinics



# PrEP (Pre-Exposure Prophylaxis) for Cisgender Women

## What is PrEP (Pre-Exposure Prophylaxis)?

Truvada for PrEP is a tool women can use to take active control of their sexual health to prevent HIV without requiring their partner's cooperation!

## Is PrEP for you?

- Truvada for PrEP may be for you if you:
  - Want to take it
  - Have sex without using condoms
  - Are unsure of your partner's HIV status
  - If a partner with HIV is not regularly taking their HIV medication
  - Recently had a sexually transmitted infection
  - Inject drugs
  - Are worried about your risk for HIV

## Is it safe to use?

- Truvada is a daily oral medication that when taken regularly is more than 99% effective at preventing HIV. For women, Truvada for PrEP works best when taken every day.
- Research studies have shown that Truvada for PrEP is safe to use in women. It does not interfere with hormonal contraceptives. It is safe to use if you think you might become pregnant or are breastfeeding.

## How can I get Truvada for PrEP?

- Truvada for PrEP resources are available online at [www.pleaseprepme.org/women](http://www.pleaseprepme.org/women) and NURX ([www.nurx.com](http://www.nurx.com)).

**We are happy to answer any questions you may have!**

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# PrEP (Pre-Exposure Prophylaxis) for Partners



## What is PrEP (Pre-Exposure Prophylaxis)?

PrEP is a medicine that prevents HIV. We recommend that participants in our trial talk with their HIV-negative sexual partner(s) about PrEP. This is because volunteers may no longer have "undetectable" HIV when they stop taking HIV medications during part of the trial. They may be able to transmit HIV to partner(s) during this period.

## How can my partners and I learn more about PrEP?

The study team can provide information to help you or your partner(s) learn more about why PrEP is an important consideration for HIV-negative partners. If a participant or their partner(s) want more information, ask us about this anytime! We are happy to discuss this with you and recommend having this discussion in first 6 months of the trial.



## How can partners of study participants access PrEP?



There are several different ways to access PrEP. The best way will depend on a partner's insurance and where they receive medical care. We can help navigate this. A good place to start is to see whether the partner's primary care doctor can prescribe PrEP.

## What are some other ways to access PrEP? Ask our team for help!

If your partner is a **San Francisco Department of Public Health** or **Community Health Network** patient, they can contact Miguel Ibarra at 415-206-2411 for assistance with accessing PrEP.

If your partner receives healthcare through **Kaiser**, the **Chinese Community Health Plan**, or the **VA**, they should contact their clinic to access PrEP.

If your partner **does not have insurance** or **does not have a regular doctor**, they can contact the San Francisco City Clinic at 415-487-5537.

## Where else can my partner access PrEP?



**www.PleasePrEPMe.org** is a searchable online resource that can help find a PrEP provider according to specific geographic or insurance needs.

PrEP can be accessed via telehealth through **Nurx.com** and **PlushCare.com**. Computers are available at the study site!



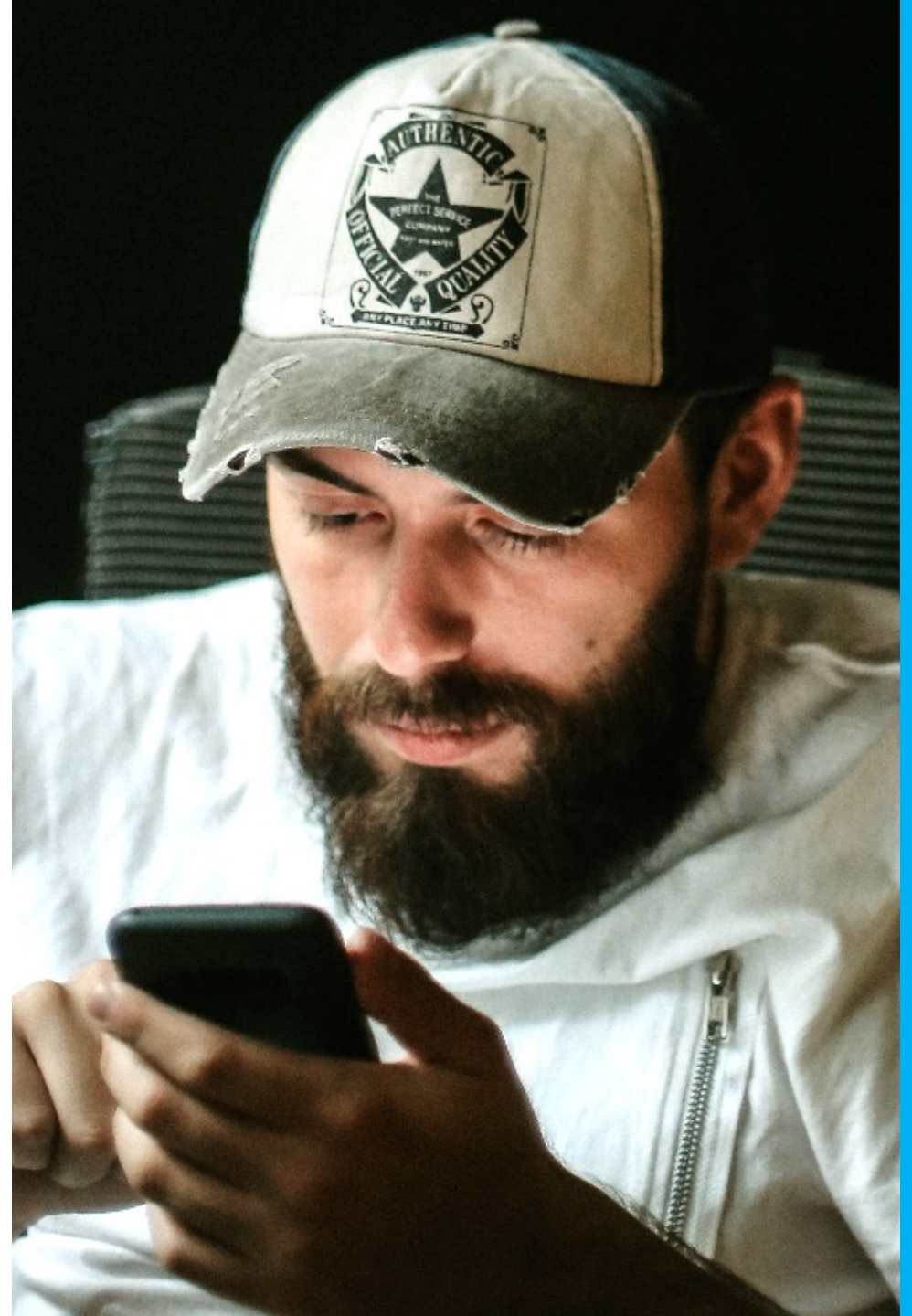


# Specific Anticipated Challenges

- PrEP use considerations in **women, communities of color & trans communities**
- Multiple or anonymous partners
- Unwillingness of participants **to disclose HIV status** or **ATI participation**
- Unwillingness of participants **to involve partners**

# Navigation to PEP

- In cases with **known possible HIV exposure without PrEP**
- **Rapid PEP navigation assistance** (< 72 hours)
- Study team will facilitate PEP via **established pathways** at the study site and in the community





# Our Ultimate Goal

- In some settings, it may be feasible for studies to **include access to PrEP and PEP**
- Universal **HIV testing, PrEP and PEP education**
- **More behavioral research** to understand values, motives, and prevention practices
- Increased focus on **women, communities of color & trans communities**
- More research to **identify partners' experiences/preferences**

# Our Recommendations

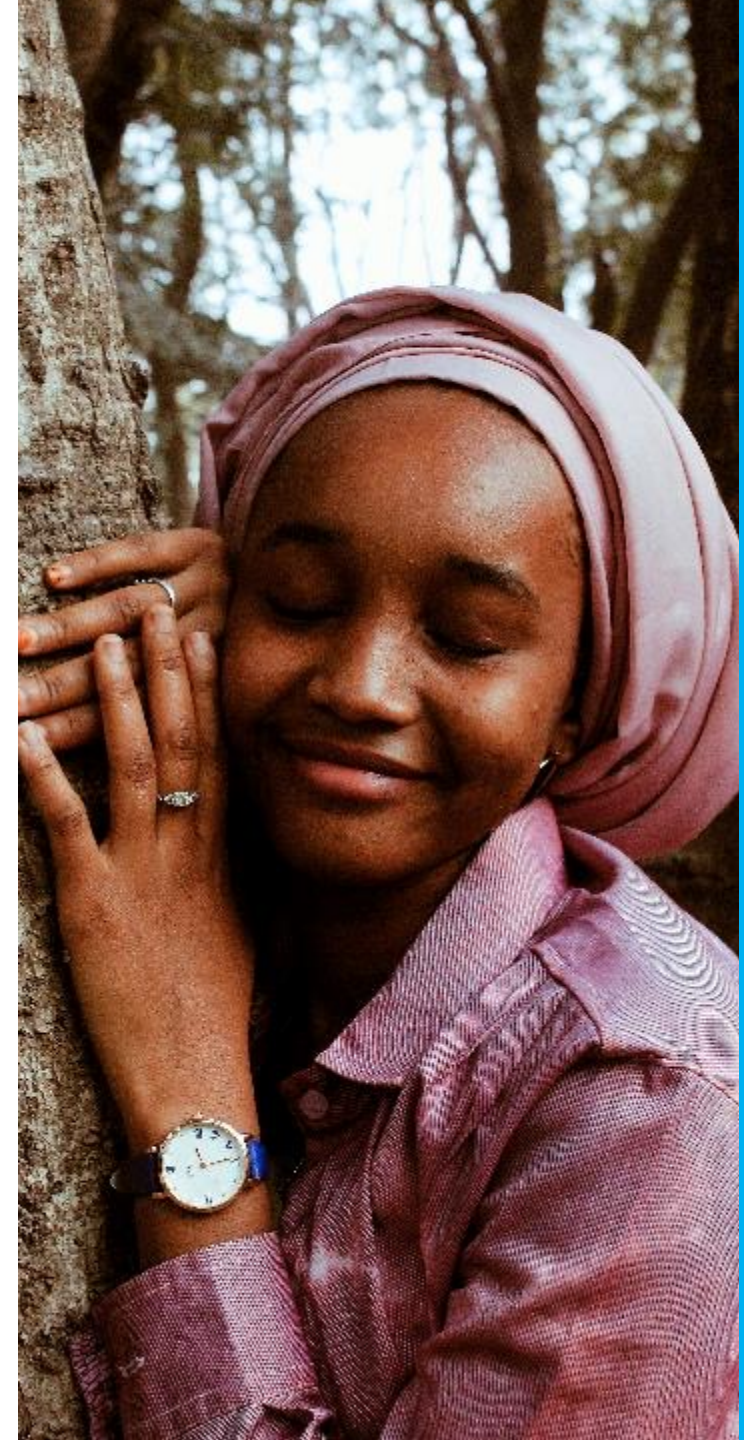
## “Standard of risk reduction” packet

1. Integrate risk reduction/mitigation into study protocol  
Risk reduction/mitigation concerns and practices should be integrated into the design of cure research studies
2. Promote and support testing and disclosure in couples where only one person is HIV+ (serodiscordant couples) or when someone’s HIV status is unknown
3. Focus on providing and accessing PrEP and PEP
4. Foster collaborations between study team, participant, and partner(s)
5. Provide Navigation to PrEP and PEP
6. Promote open and honest communication between participants, researchers, and study team



# Limitations of Recommendations

- **Recommendations** are based on **widespread understanding** of HIV transmission risk, universal testing, access to treatment, and PrEP and PEP for prevention
- Strong **stakeholder support** available and political will to address issues on local level
- **Community engagement**, including **Community Advisory Boards (CABs)** are essential
- Researchers **collaboration with local communities** to **create plans** that are **consistent with local needs and cultures**, including gender and sex dynamics, structures are essential to help prevent racial discrimination, social stigma and intimate partner violence.







# ACKNOWLEDGMENTS



## Module developers

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*Their caring support of the CUREiculum 2.0.  
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of people living with HIV*



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