Women in HIV Cure-Related Research

The Women’s HIV Research Collaborative
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Map showing locations in WA, TX, GA, IN, OH, PA, NC, MD, and DC.
Presentation Overview

- Women & HIV
- Overview: HIV Cure Research
- Women in HIV Cure Research
- Recommendations for HIV Cure Research
- Opportunities to Get Involved
Women Play Vital a Role in HIV Cure Research
Women & HIV
# HIV & Cisgender Women

<table>
<thead>
<tr>
<th>Category</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Total</td>
<td>38 million</td>
</tr>
<tr>
<td>Adults</td>
<td>36.2 million</td>
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<tr>
<td>Women</td>
<td>19.2 million</td>
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<tr>
<td>Men</td>
<td>17 million</td>
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<tr>
<td>Children</td>
<td>1.8 million</td>
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Global Prevalence, 2019  
(UNAIDS/WHO estimates)  

US  
(CDC)  

- Cis women made up 19% of new HIV diagnoses in the US overall.
- More than half of diagnoses among cis women occurred in the southern region of the US.
- Black/African Americans made up the majority of new HIV cases.
- 85% of cis women acquired HIV through heterosexual contact.
- 15% acquired HIV through drug use.

These disparities highlight the social and structural issues women face in the US.
Transgender Women & Viral Suppression

Viral Suppression Among Ryan White Clients (2016)

NHAS 2016 Target for Trans Women (74.7%)

79%  84.9%

Transgender Women  Overall

What does “HIV cure” mean to you?

**What does a ‘cure’ for HIV look like?**

397 people living with HIV in the U.S. surveyed. (Results exceed 100% because respondents were allowed to select more than one answer.)

- HIV is completely eliminated from the body: 68%
- No risk of transmitting HIV to others: 68%
- No more HIV treatment ever needed: 64%
- No risk of opportunistic infection: 47%
- No more HIV treatment needed now: 40%
- Negative HIV test: 30%
- Other: 11%

Cure: A Loaded Word

The NIH makes an important distinction:

- **Classic cure**: eliminating all cells with HIV from the body
- **Sustained ART-free remission**: HIV remains present, but at undetectable levels *without ART*

Cure: “the strategies that eliminate HIV from a person’s body, or permanently control the virus and render it unable to cause disease” (AVAC).

The concept of “cure” has multiple social/cultural connotations.

- In the context of clinical trials, “cure” may be defined by different endpoints or clinical measures (size of reservoirs, extent of immune response, etc).

In other words, “cure” doesn’t always mean the same thing to everyone!
Main HIV Cure-Related Strategies

Source: http://treatmentactiongroup.org/cure/trials
A Broad Spectrum of Strategies

- Treatment Action Group (TAG), with support from the Bill and Melinda Gates Foundation, conducted a landscape analysis of current HIV cure trials.
- There are presently 128 HIV cure-related trials grouped into 24 different categories, reflecting the breadth of strategies under consideration.
- Combined, the 128 studies plan to enroll a total of over 7,000 participants.
  - Individual studies’ recruitment targets are between 5 and 905 participants.
  - Most of these studies are early development trials (Phase I or Phase II).

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<tr>
<th>Latency-Reversing Agents</th>
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<tr>
<td><strong>Chidamide</strong></td>
</tr>
<tr>
<td>NCT02902185 (closed to enrollment)</td>
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<tr>
<td>Tang-Du Hospital</td>
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<td>Phase I/II</td>
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<tr>
<th><strong>Valproic Acid + Pyrimethamine</strong></th>
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<tr>
<td>NCT03525730</td>
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<tr>
<td>Erasmus Medical Center</td>
</tr>
<tr>
<td>Phase VII</td>
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<table>
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<tr>
<th><strong>Kansui (Traditional Chinese medicine containing Ingenols)</strong></th>
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<tr>
<td>NCT02531295</td>
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<tr>
<td>UCSF</td>
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<td>Phase I</td>
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<th>Proteasome Inhibitors</th>
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<tr>
<td><strong>Ixazomib</strong></td>
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<tr>
<td>NCT02594047 (closed to enrollment)</td>
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<td>Nathan W. Cummins, M.D.</td>
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<td>Phase VII</td>
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<th>Retinoids</th>
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<tr>
<td><strong>Acitretin</strong></td>
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<tr>
<td>NCT03763506 (not yet open for enrollment)</td>
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<tr>
<td>Ottawa Hospital Research Institute</td>
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<tr>
<td>Phase I</td>
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Source: https://www.treatmentactiongroup.org/cure/tri
A Major Investment by Participants

Many of the studies in TAG’s analysis require multiple study visits and at least one invasive procedure.

• At least 32 require an analytic treatment interruption (ATI).
• At least 67 require invasive procedures like rectal biopsies, lengthy imaging procedures, lymph node biopsies, lumbar puncture, leukapheresis, and/or stem cell transplants.

Currently, most cure studies offer no direct benefit to participants (e.g. they are not expected to actually cure participants of HIV).

• Sites and study teams will need to think carefully about how to engage communities that have been historically underrepresented in research.

*Information on study procedures was collected from the clinicaltrials.gov listings. It is possible that there are additional invasive procedures that were not submitted to the registry record.
Women in HIV Cure Research
NIH Revitalization Act of 1993

- NIH policy: women and minority groups must be included in all NIH-funded clinical research, unless a clear and compelling rationale establishes that inclusion is inappropriate.

- The inclusion of women must be addressed in research proposals, including the composition of the study population in terms of sex/gender and racial/ethnic group.

- Sex differences are strongly encouraged in results for all publications.

- Individuals of childbearing potential should not be routinely excluded.

- The NIH Director...
  - shall ensure that the trial is carried out in a manner sufficient to provide for valid analysis of whether the variables being studied affect women differently than other subjects.
  - shall conduct or support outreach programs for the recruitment of women and minority groups.

- Applicable to Phase III and pivotal Phase II and IV studies.

Source: https://grants.nih.gov/grants/funding/women_min/guidelines.htm
Sex Matters

**Sex Differences in HIV**

- Anatomic and hormonal microenvironment differences
- X chromosome gene dosage effects (TLR7, FOXP3)
- miRNA enrichment on the X chromosome
- Hormone responsive promoter elements
- Distribution of immune subsets
- Immune activation setpoints
- Efficacy of antiviral responses
- Hormonal modulation of function
- Distinct epigenetic landscapes
- Differences in establishing latency
- Direct estrogen effect on transcription and latency
- Immune modulatory function
- Microbiome in the genital tract: direct link with inflammation, acquisition risk/PrEP efficacy

Hormones & HIV Cure Research

Estrogen is a key mediator of the immune system.

“Estradiol at peak menstrual cycle levels is a potent inhibitor of viral reactivation suggesting important differences between [cis] men and women for viral replication and reservoir sizes.”

“The design of regimens for proviral reactivation needs to account for estrogen, and perhaps other hormones, as confounding factors affecting potency” (Karn, 2015).

Nearly a decade after demonstrating oral PrEP’s safety and efficacy overall, we are just now beginning to understand the role of hormones in PrEP effectiveness for cisgender and transgender women. We should start with hormones and other sex differences in mind as we explore HIV cure strategies for all women.

So, are women included?
So, what about transgender women?

There is only one transgender woman documented as having participated in an HIV cure clinical trial.

HIV cure research must become trans-inclusive in all aspects, including study design, data collection, recruitment and retention, analysis, reporting, and staffing.
The MOXIE Trial (ACTG A5366)

taMOXifen to Increase the Effects of vorinostat

First HIV cure-related study designed specifically for cisgender women with HIV.

- Testing two drugs to see if they can reactivate the “latent” HIV that can’t be detected by the immune system
- 30 participants: 20 women with tamoxifen plus vorinostat, 10 women with vorinostat alone
- All 30 women stay on their regular HIV treatment throughout the study
- Includes a socio-behavioral sciences component at study entry and exit

Lessons learned about recruitment:

- It is possible to recruit women in HIV cure-related research!
- Women greatly appreciated having a study dedicated to them.

BUT we shouldn’t have to create an HIV cure study specific to women!

- Sex/gender-based analyses should be built into all studies
- Need to set minimum enrollment for women
- Studies with female-relevant strategies should have a plan for inclusion of women
Why are women being excluded?

Common themes:
“Women are the same as men, so we don’t need them in trials.”
“Women are different from men, so we need to exclude them from trials.”

Are women the same or different?

Cis and trans women have a right to benefit from HIV cure research.

Adapted from Rowena Johnston (amfAR)
Barriers for Women

- Trial safety concerns
- Recruitment strategies that don’t emphasize diversity
- Trans women miscategorized and excluded
- Disclosure to family & co-workers
- Stigma
- Lack of appropriate incentives
- Rigorous eligibility reqs
- Distrust of research
- Time investment
- Concerns about hormonal interactions
- Strict scheduling windows
- Transportation
- Caretaker / family / work obligations
- Intimidated / anxious with medical professionals
- Lack of cultural humility for transgender women

Facilitators to Women’s Participation

- Flexible schedules
  - Open early/stay open late

- Provide transportation assistance
  - Bus pass, parking fees, cab vouchers, Uber/Lyft
  - Better (closer, safer) parking

- Resources for children and family on site
  - Coloring books, DVD players
  - Wi-Fi
  - Food, snacks, drinks

- Appreciation and recognition of women’s efforts to participate

Adapted from Kate Starr on behalf of the WHRC
Facilitators to Women’s Participation

Compared to men, **cis and trans women are more likely** to be motivated by:

- Feeling good helping others like themselves
- Getting special knowledge about their own health
- Engaging with research teams
- Having regular access to study nurses
- Being compensated
- Receiving money for transportation
- Having someone to speak to about their HIV status
- Being treated as a special patient
- Receiving support from family and friends
- Being offered a meal

Adapted from Dubé, K and Evans, D. 2018 NIH-sponsored Workshop on HIV Cure.
Recommendations for HIV Cure Research
Transgender Training Curriculum for HIV Research

At the very least...

- Use the 2-step method for data collection
  - Gender identity
  - Sex assigned at birth
- Always describe study populations accurately in protocols, publications, and other study documents
  - *Cisgender* and *transgender*
  - Assigned Male/Female/Intersex at birth

https://daidslearningportal.niaid.nih.gov
Research Recommendations (continued)

• Reprioritize the vision of the NIH Revitalization Act
• Design studies with strategies relevant to cis and trans women
• Build sex- and gender-based analyses into protocols and statistical analysis plans
• Require minimum enrollment for cis and trans women
• Report results by sex and gender (even with 0 women enrolled)
• Include social scientists to address issues related to women’s enrollment and retention
• Pay attention to what women need and want
• Engage women and community members at all stages of HIV cure research
• Actually enroll and retain women

Source: Regulation of Clinical Research Related to HIV Cure meeting in Bethesda, MD (January 2018).
Get Involved!
Join the WHRC!

Contact Brian Minalga:
bminalga@fredhutch.org
www.facebook.com/HANCLEgacyProject

Recent Topics:
• Women and HIV cure research
• HIV prevention research for cis and trans women
• Pregnancy and lactation in HIV clinical trials
• Mental health, HIV, and gender
• Screening for intimate partner violence in HIV research
• Women of color in research
• Building partnerships with other women-centered organizations
WHRC’s Webinars

See the WHRC’s three-part webinar series on women & HIV cure research:

https://www.hanc.info/cp/resources/Pages/Legacy-Project-Webinars.aspx
ACTG & IMPAAACT

ACTG: AIDS Clinical Trials Group
https://actgnetwork.org/

IMPAACT: International, Maternal, Pediatric, Adolescent AIDS Clinical Trials Network
https://impaaactnetwork.org/index.htm

Consider engaging with:
• Community Advisory Boards
• Community Scientific Subcommittee (CSS)
• Women’s HIV Inter-network Scientific Committee (WHISC)
Martin Delaney Collaboratory Programs & CABs (2016-2021)

- I4C: Combined Immunologic Approaches to Cure HIV-1
  Dan Barouch, John Mellors, Nelson Michael
  (Beth Israel Deaconess, Boston)

- BEAT-HIV: Delaney Collaboratory to Cure HIV-1 Infection by Combination Immunotherapy
  Luis Montaner & James Riley
  (Wistar Institute, Philadelphia)

- BELIEVE: Bench to Bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication
  Douglas Nixon
  (GWU, Washington, DC)

- CARE: Collaboratory of AIDS Researchers for Eradication
  David Margolis
  (UNC, Chapel Hill)

- DARE: Delaney AIDS Research Enterprise to Cure HIV
  Steven Deeks & Louis Picker
  (UCSF, San Francisco)

- defeatHIV: Cell and Gene Therapy for HIV Cure
  Keith Jeromel & Hans-Peter Klein
  (FHCRC, Seattle)
International Workshop on HIV & Women

Recent Topics:

• HIV cure research: considerations for women
• Current controversies for ART use in women of childbearing potential and in pregnancy
• ART in women overall
• New drug delivery systems: are they right for women?

https://www.virology-education.com/event/upcoming/9th-hiv-women-workshop/
Participate In A Trial!

https://www.youtube.com/watch?v=jmaaMv1PalA
Get Informed

amfAR (Foundation for AIDS Research) -
Consortium on HIV Eradication: https://www.amfar.org/cure/
Institute for HIV Cure Research: https://www.amfar.org/Cure-Research-Institute/


POZ.com - https://www.poz.com/tag/cure


International AIDS Society - https://iasociety.org/hivcure

Positively Aware - https://www.positivelyaware.com/
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