



Women in HIV Cure-Related Research

The Women's HIV Research Collaborative

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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

Total	38 million
Adults	36.2 million
Women	19.2 million
Men	17 million
Children	1.8 million

Global Prevalence, 2019
(UNAIDS/WHO estimates)

https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf



US
(CDC)

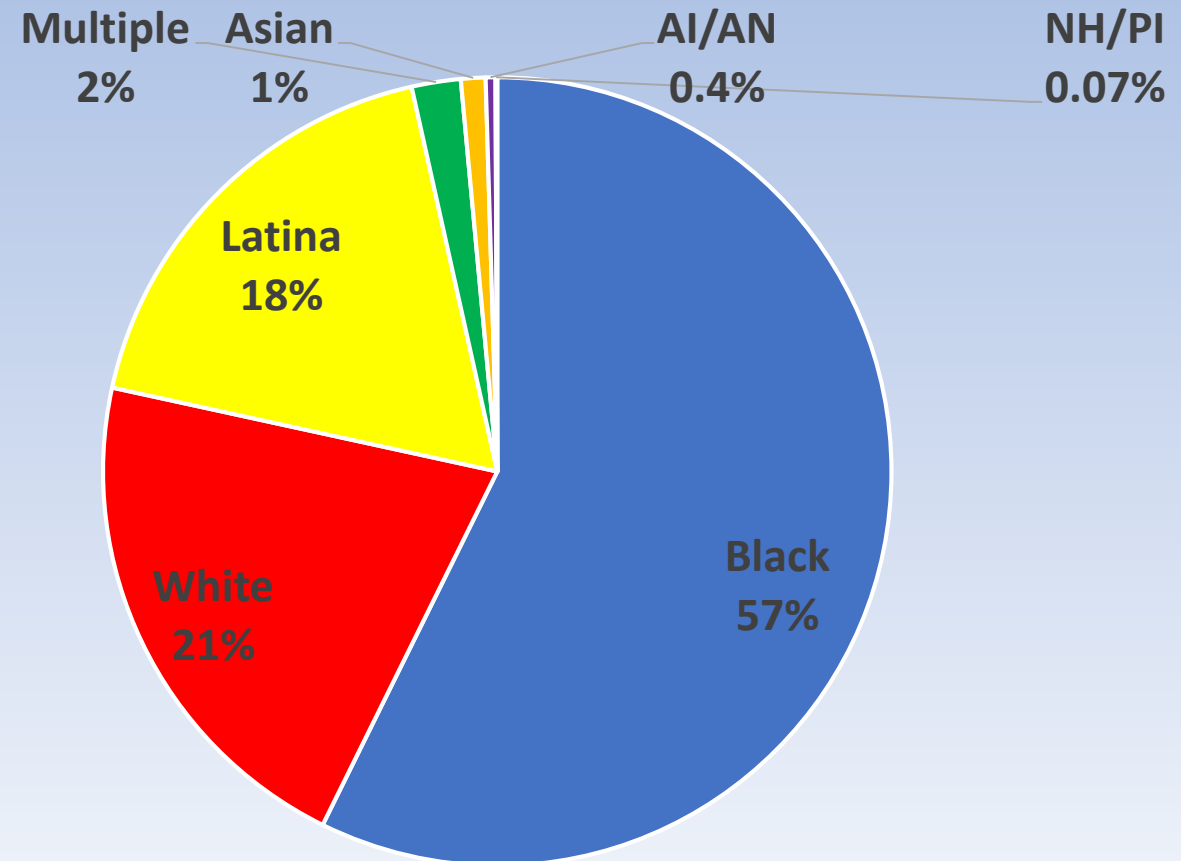
<https://www.cdc.gov/hiv/group/gender/women/index.html>

HIV Diagnoses: US Cisgender Women (2018)

- 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.

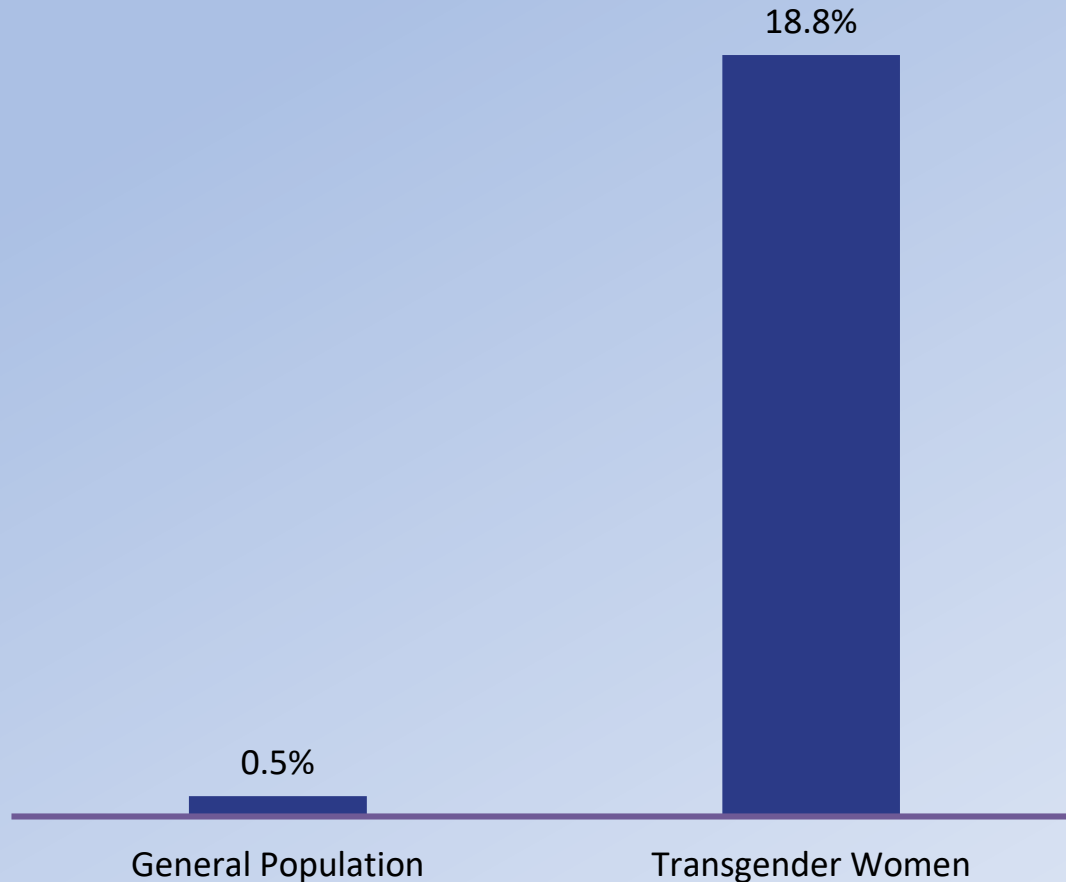
These disparities highlight the social and structural issues women face in the US.

New HIV Diagnoses Among Cis Women in 2018 (CDC)

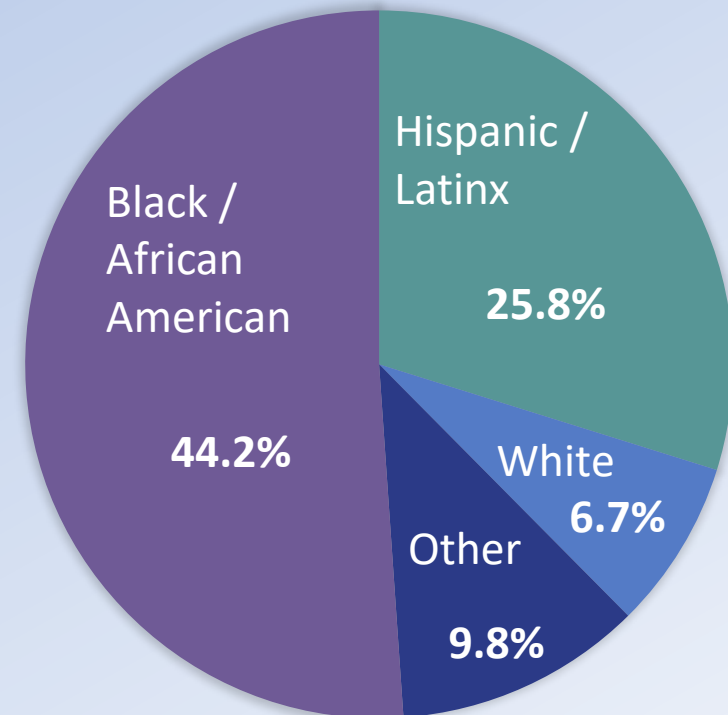


Transgender Women & HIV in the US

US HIV PREVALENCE



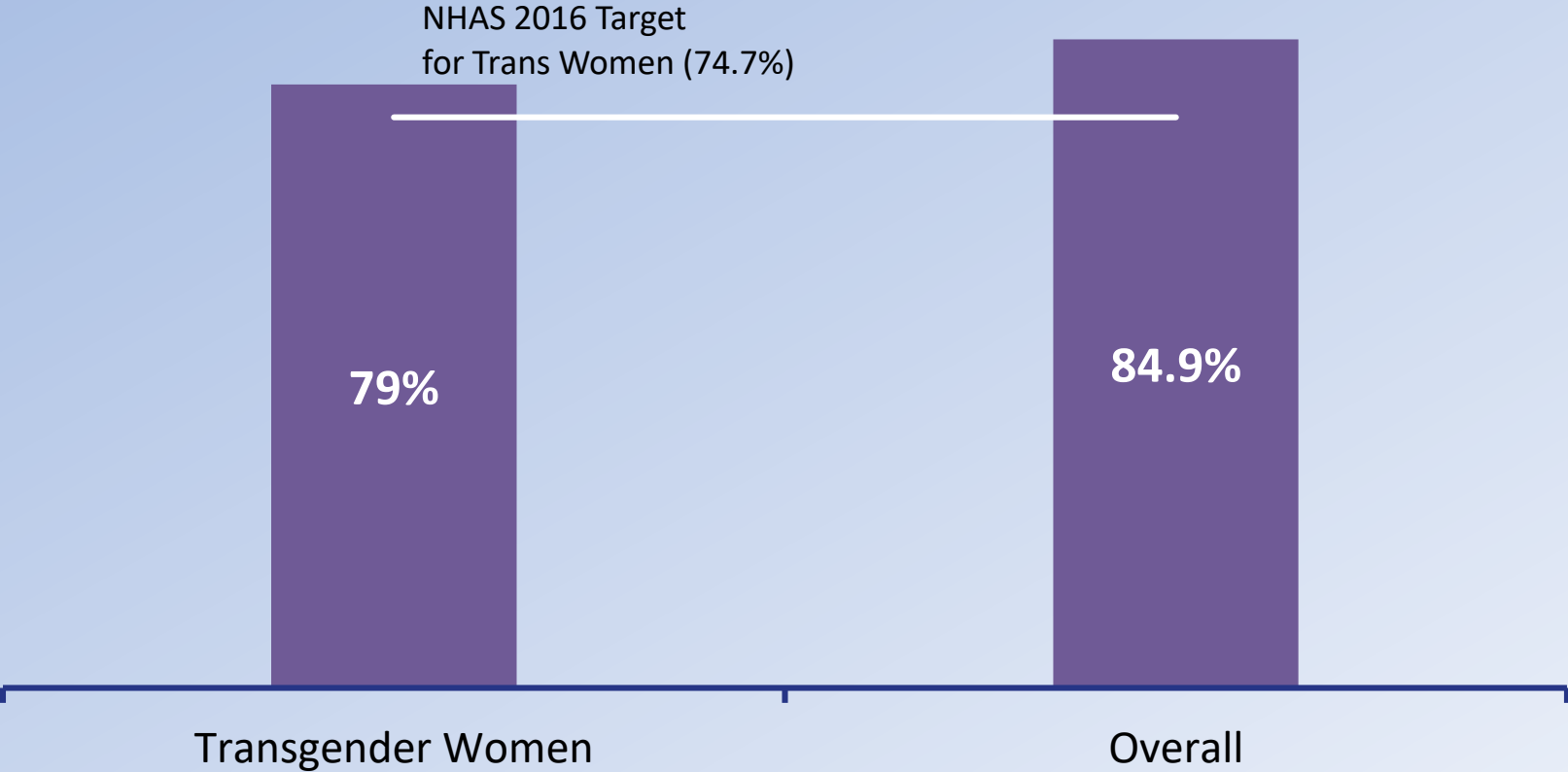
HIV PREVALENCE BY RACE/ ETHNICITY:
US TRANSGENDER WOMEN



Jeffrey S. Becasen, Christa L. Denard, Mary M. Mullins, Darrel H.Higa, Theresa Ann Sipe, "Estimating the Prevalence of HIV and Sexual Behaviors Among the US Transgender Population: A Systematic Review and Meta-Analysis, 2006–2017", *American Journal of Public Health* 109, no. 1 (January 1, 2019): pp. E1-e8. DOI: 10.2105/AJPH.2018.304727.

Transgender Women & Viral Suppression

Viral Suppression Among Ryan White Clients (2016)



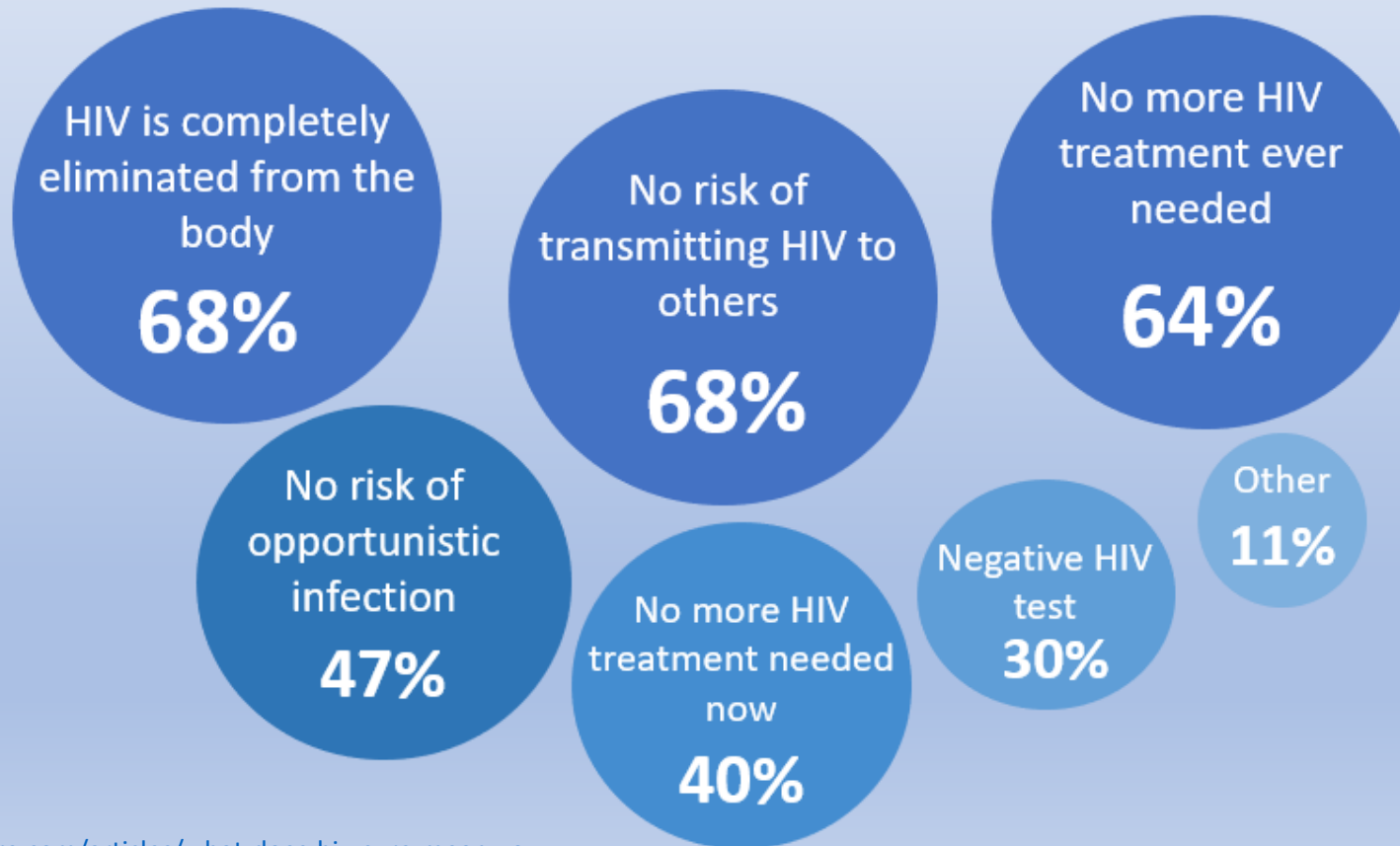
Source: Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2015. *HIV Surveillance Supplemental Report* 2017;22(No. 2).

Overview: HIV Cure Research

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.)



Source: <https://www.positivelyaware.com/articles/what-does-hiv-cure-mean-you>

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).

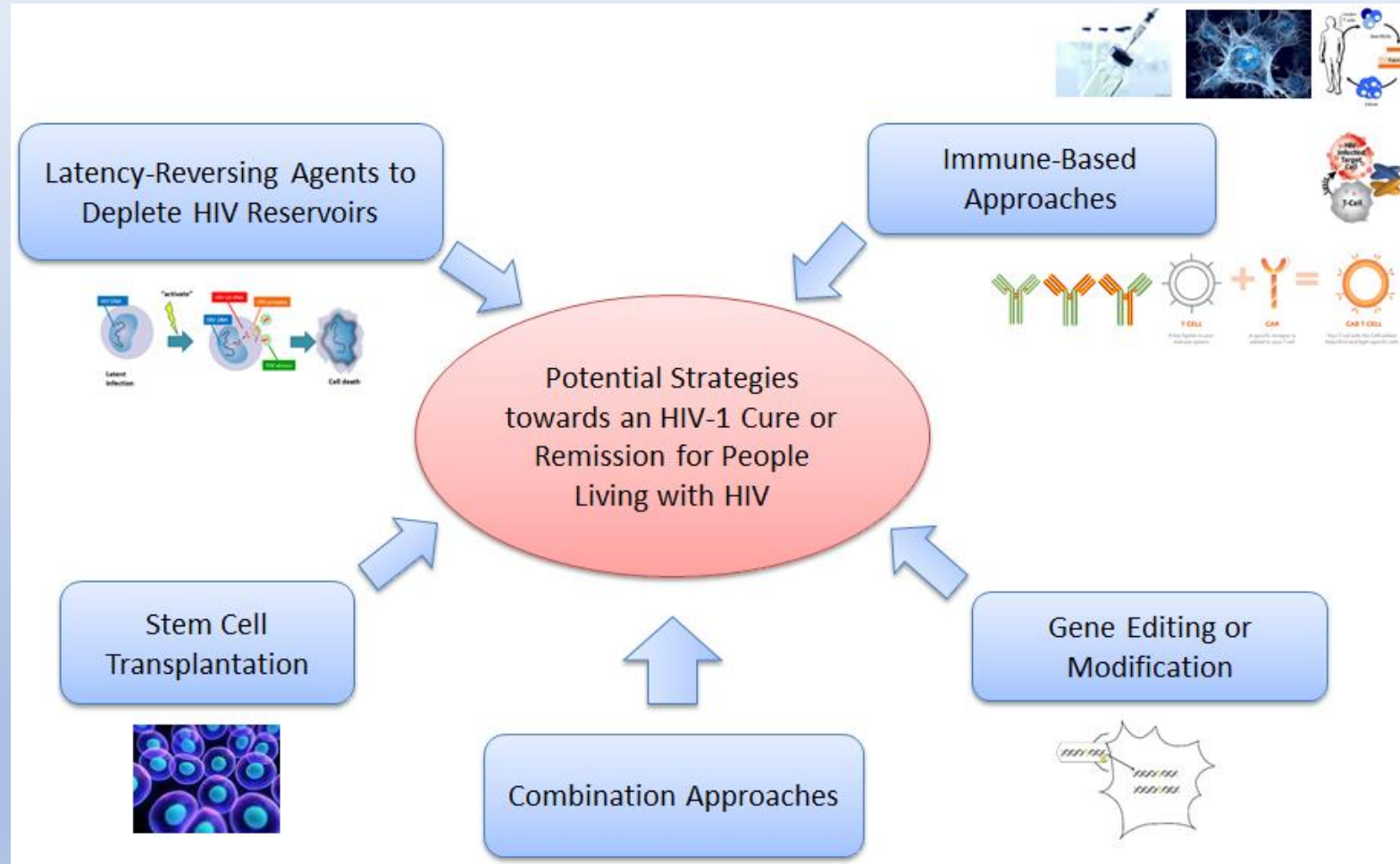
The concept of “**cure**” has multiple social/cultural connotations.

- 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).

LATENCY-REVERSING AGENTS				
Chidamide	NCT02902185 (closed to enrollment)	Tang-Du Hospital	Phase II/III	December 2018
valproic acid + pyrimethamine	NCT03525730	Erasmus Medical Center	Phase I/II	April 2020
Kansui (traditional Chinese medicine containing ingenols)	NCT02531295	UCSF	Phase I	December 2019
PROTEASOME INHIBITORS				
ixazomib	NCT02946047 (closed to enrollment)	Nathan W. Cummins, M.D.	Phase III	September 2019
RETINOIDS				
acitretin	NCT03753867 (not yet open for enrollment)	Ottawa Hospital Research Institute	Phase I	May 2019
STEM CELL TRANSPLANTATION				

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.

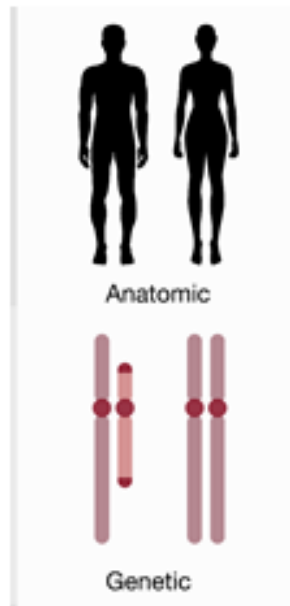
Women in HIV Cure Research

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.

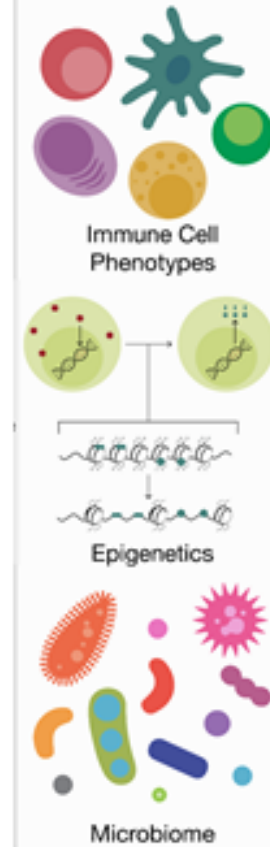
Sex Matters

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

SLIDE CREDIT: Ndung'u T. HIV Cure Research in Women. Community Cure Workshop. Saturday July 21, 2018.

Scully, *Curr HIV/AIDS Rep*, 2018

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?

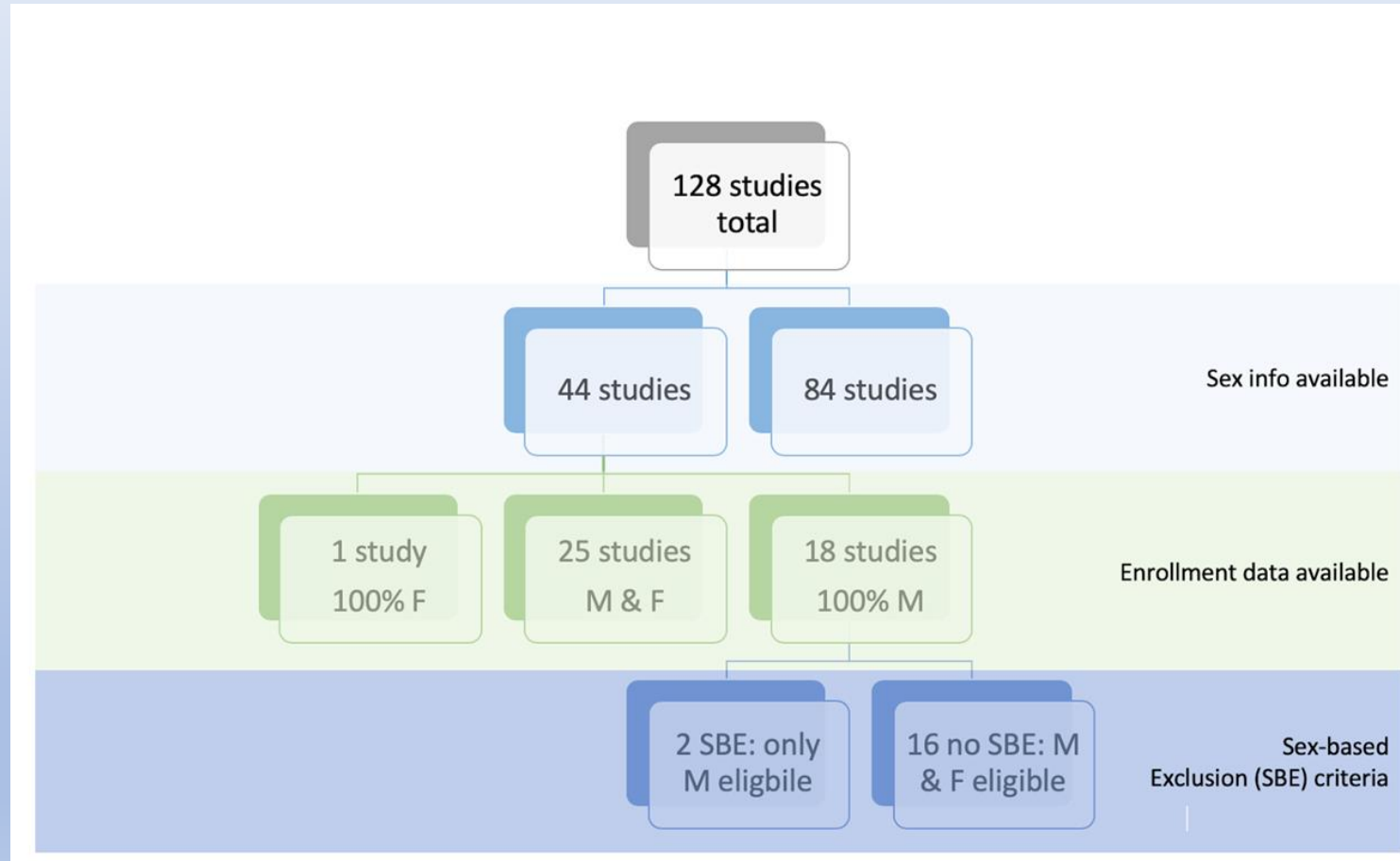


Image credit: Liz Barr

Participants' sex from TAG's Analysis

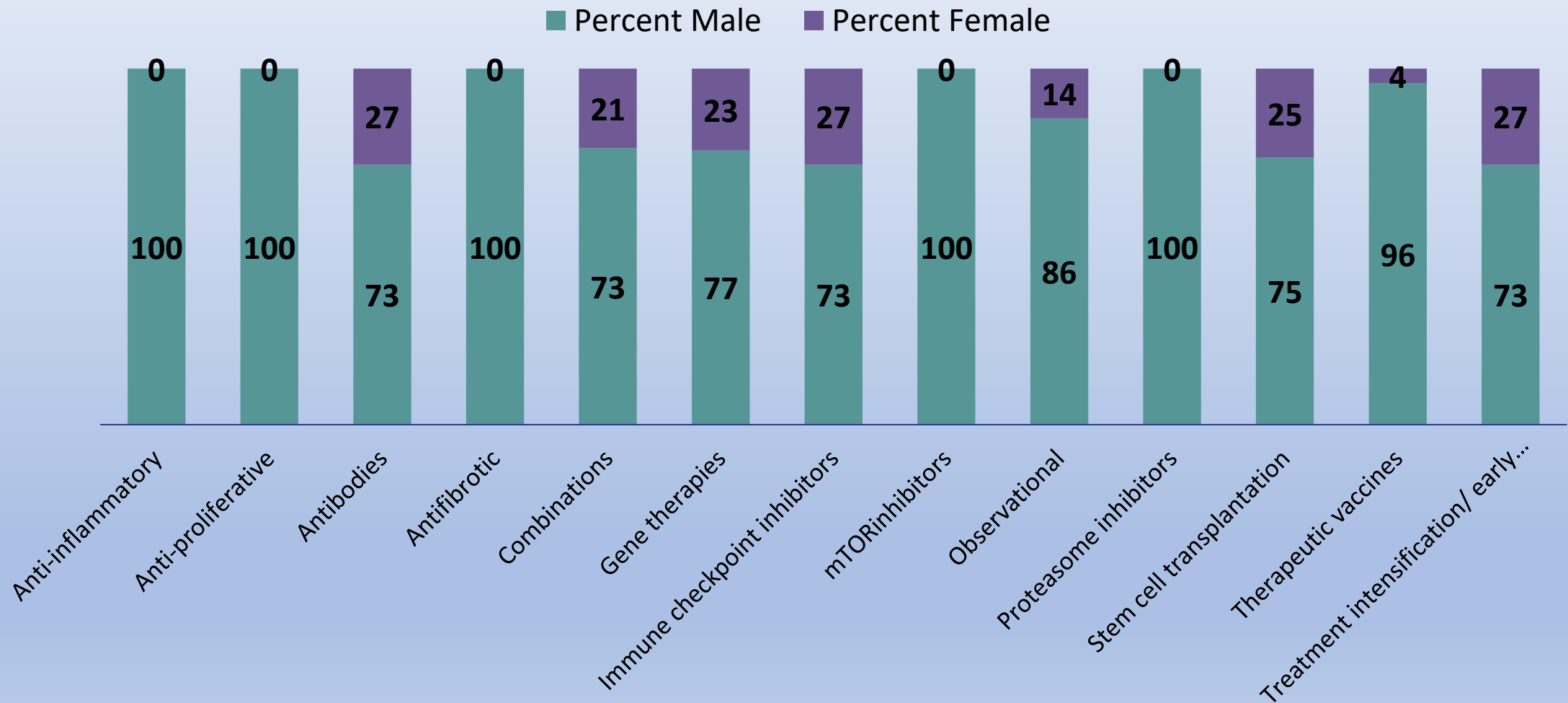


Image credit: Liz Barr

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.



- 1. What is your current gender identity?**
 - Genderqueer
 - Gender Variant, Gender Non-conforming
 - Man
 - Transgender Man/Trans Man
 - Transgender Woman/Trans Woman
 - Woman
 - Additional category, please specify _____
 - Decline to answer
- 2. What was your sex assigned at birth?**
 - Female
 - Male
 - Intersex
 - Decline to answer

The MOXIE Trial (ACTG A5366)

ta**MOX**ifen to **I**ncrease the **E**ffects 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.”

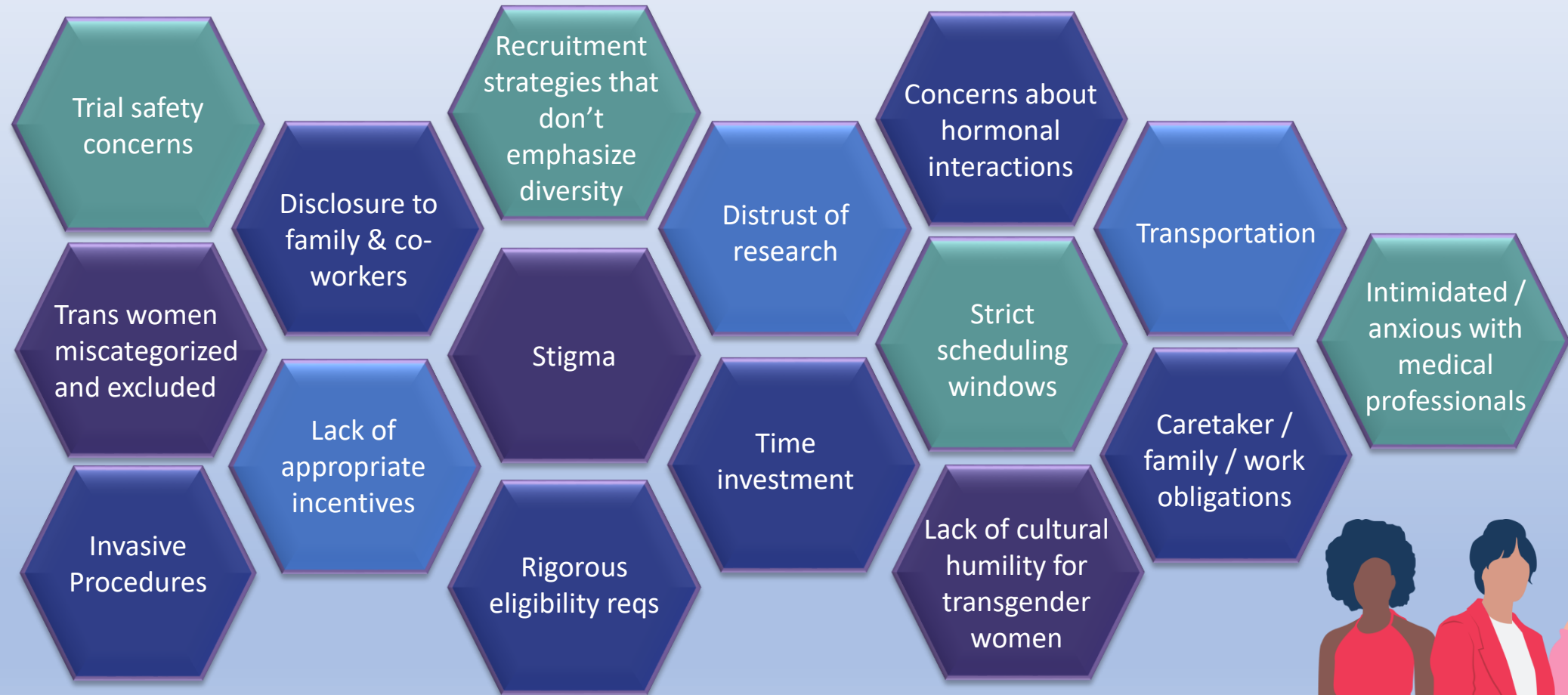
Are women the same or different?

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



Adapted from Rowena Johnston (amfAR)

Barriers for Women



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**



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

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

The screenshot displays the DAIDS Learning Management System interface. At the top, there is a navigation bar with links for HOME, COURSES, RESOURCES, and HELP. Below this, the system title 'DAIDS Learning Management System' is visible. A user login bar indicates the user is logged in as 'Rina Siskind' with a 'Turn editing on' button. The main content area shows the course details for 'An Introduction to Transgender Communities Course', including its title, duration (1 hour), and description. The course is divided into two steps: 'Step 1: Presentation' and 'Step 2: Certificate of Completion'. A sidebar on the right contains a 'Toolkit' with icons for 'Browse Courses', 'Transcripts', and 'My Courses', and an 'Administration' section with options for 'Course administration', 'Edit settings', 'Turn editing on', 'Course completion', 'Users', and 'Filters'. The Windows taskbar is visible at the bottom of the browser window.

<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

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>

HIV within Latinx Communities in the US: Needs, Priorities, and Assets

Dr. Scott Rhodes, Wake Forest School of Medicine; Jose Bauermeister, University of Pennsylvania; Omar Martinez, Temple University; Jorge Benitez, Columbia University Medical Center. July 3, 2017.

Our People are Not a Study: A Community Perspective on Engaging Researchers

Jontraye Davis, FHI 360; Miguel Hunter, Triangle Empowerment Center; Terry Munn, Triangle Empowerment Center; Kareem Alexis, Triangle Empowerment Center; Kate MacQueen, FHI 360; Mehri McKellar, Duke University Medical Center. August 16, 2017.

Our People are Not a Study: A Community Perspective on Engaging Researchers (Slides Only)

Jontraye Davis, FHI 360; Miguel Hunter, Triangle Empowerment Center; Terry Munn, Triangle Empowerment Center; Kareem Alexis, Triangle Empowerment Center; Kate MacQueen, FHI 360; Mehri McKellar, Duke University Medical Center. August 16, 2017.

CDC's Response to HIV-related Disparities among African American Gay and Bisexual Men in the U.S.: Update 2017

Dr. Eugene McCray, Director of CDC's Division of HIV/AIDS Prevention (DHAP) - July 11, 2017

Privilege & Power in Healthcare: Unpacking the Black Experience

Dr. Michele Andrasik, HIV Vaccine Trials Network. February 6, 2017.

Women & HIV Cure Series: Barriers and Facilitators to Women's Participation in HIV Cure (Part 3)

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Women & HIV Cure Series: What Cure Means to Women, What Women Mean to Cure (Part 2)

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Women & HIV Cure Series: Where are We? Women in the HIV Cure Landscape (Part 1)

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Community Engagement in HIV Clinical Research (Part 3)- Microbicide Update: Gels, rings, and other things

Drs. Sharon Hillier and Ian McGowan, Microbicide Trials Network. September 8, 2016.

Community Engagement in HIV Clinical Research (Part 2)- Black MSM & Transgender Persons

DaShawn Usher- NY Blood Center; Michele Andrasik- HIV Vaccine Trials Network on June 22, 2016

ACTG & IMPAACT



ACTG: AIDS Clinical Trials Group

<https://actgnetwork.org/>

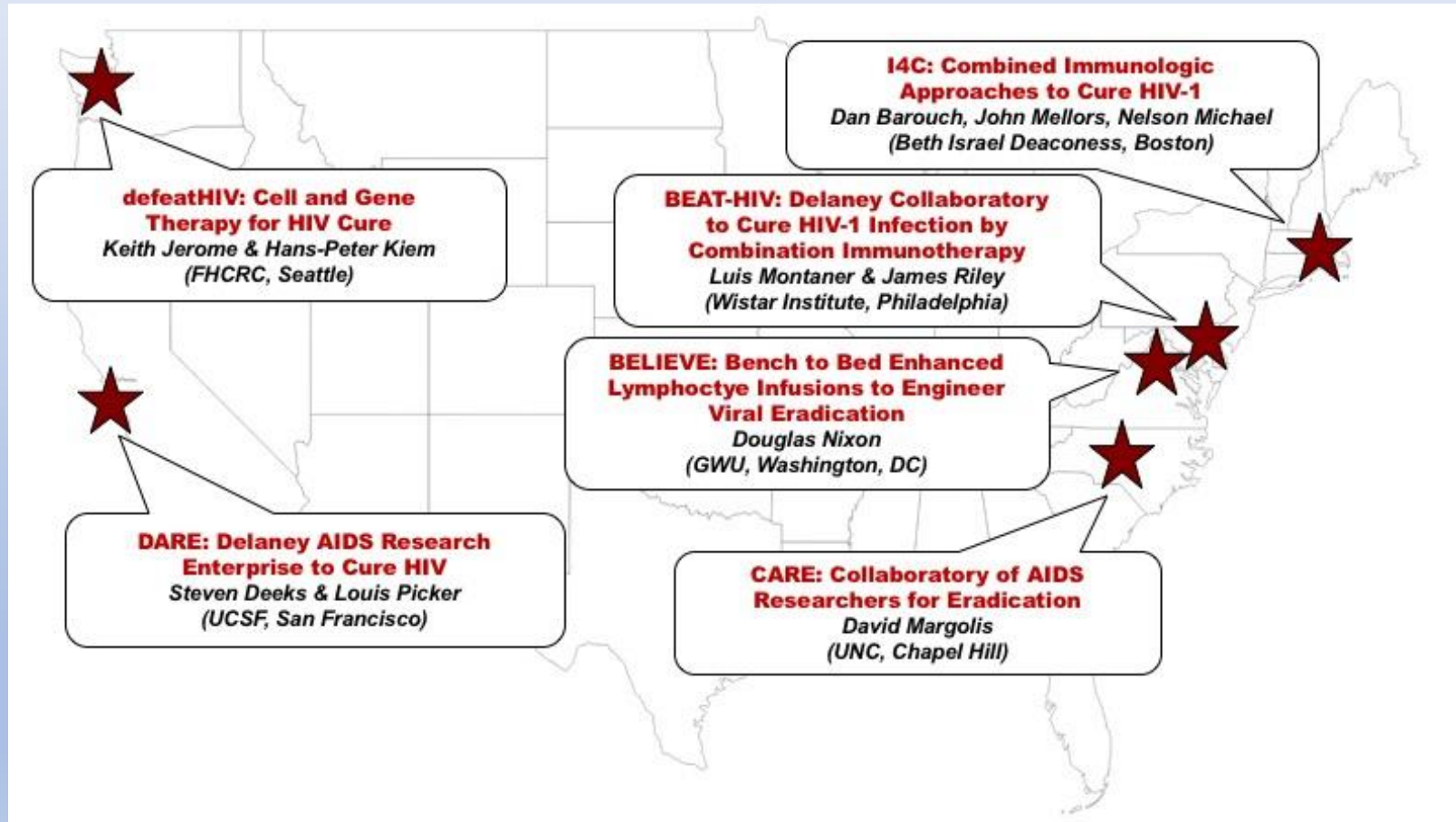
IMPAACT: International, Maternal, Pediatric, Adolescent AIDS Clinical Trials Network

<https://impaactnetwork.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)



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=jmaaMv1PaIA>



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/>

Treatment Action Group - <http://www.treatmentactiongroup.org/cure>

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

TheBody.com - <https://www.thebody.com/category/curing-hiv>

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

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

Acknowledgments

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