

Elizabeth Barr, Ph.D., NIH ORWH
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Session 3: Cure advances globally

Landscape analysis & diversifying efforts



 **AIDS** 2022

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Conflict of interest

Elizabeth Barr:

The views expressed in this presentation are my own and do not necessarily represent the views of the National Institutes of Health or the United States Government.

Richard Jefferys:

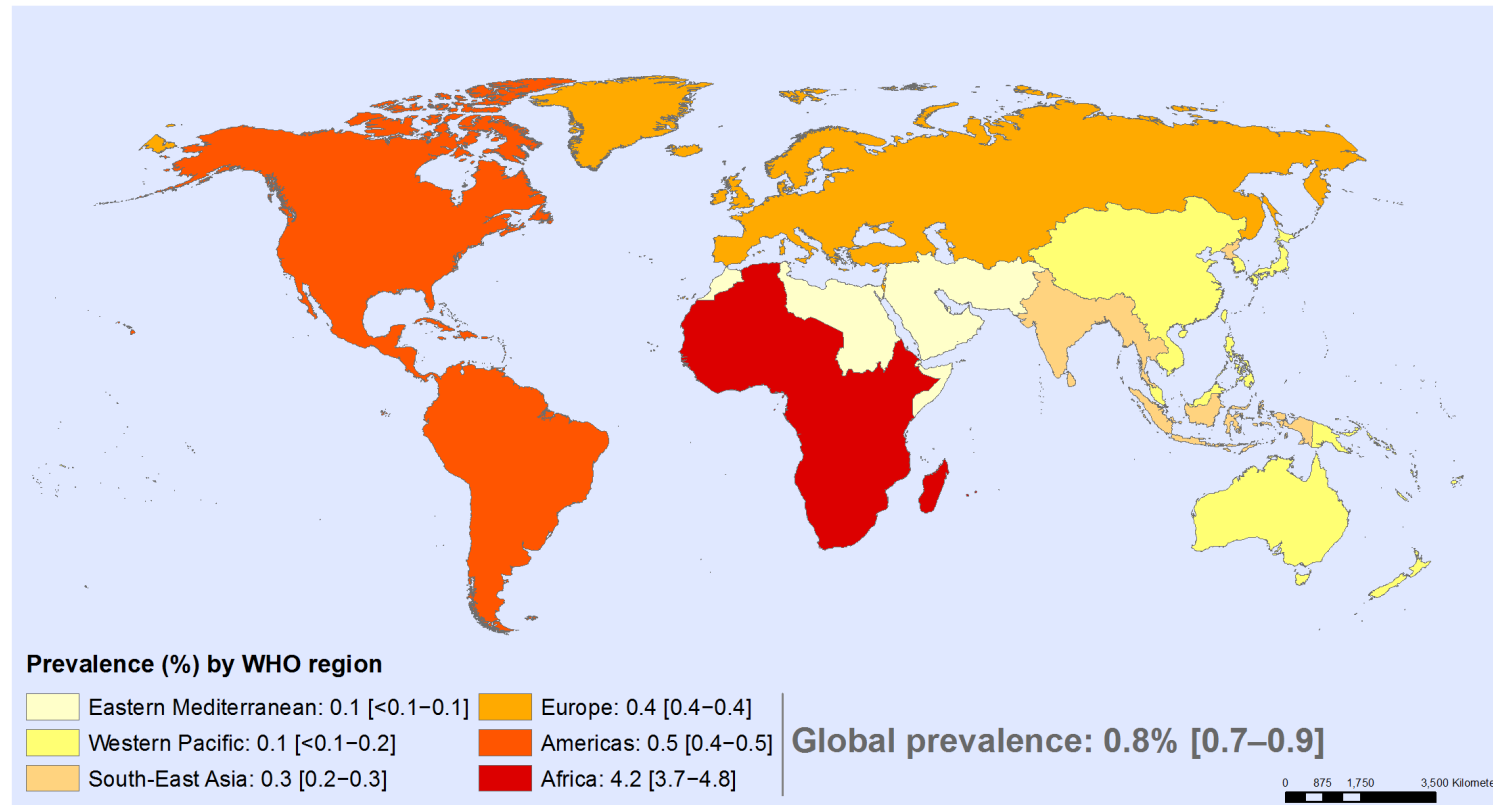
I have no relevant financial relationships with ineligible companies to disclose.



Geographic distribution of HIV

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Prevalence of HIV among adults aged 15 to 49, 2016
By WHO region



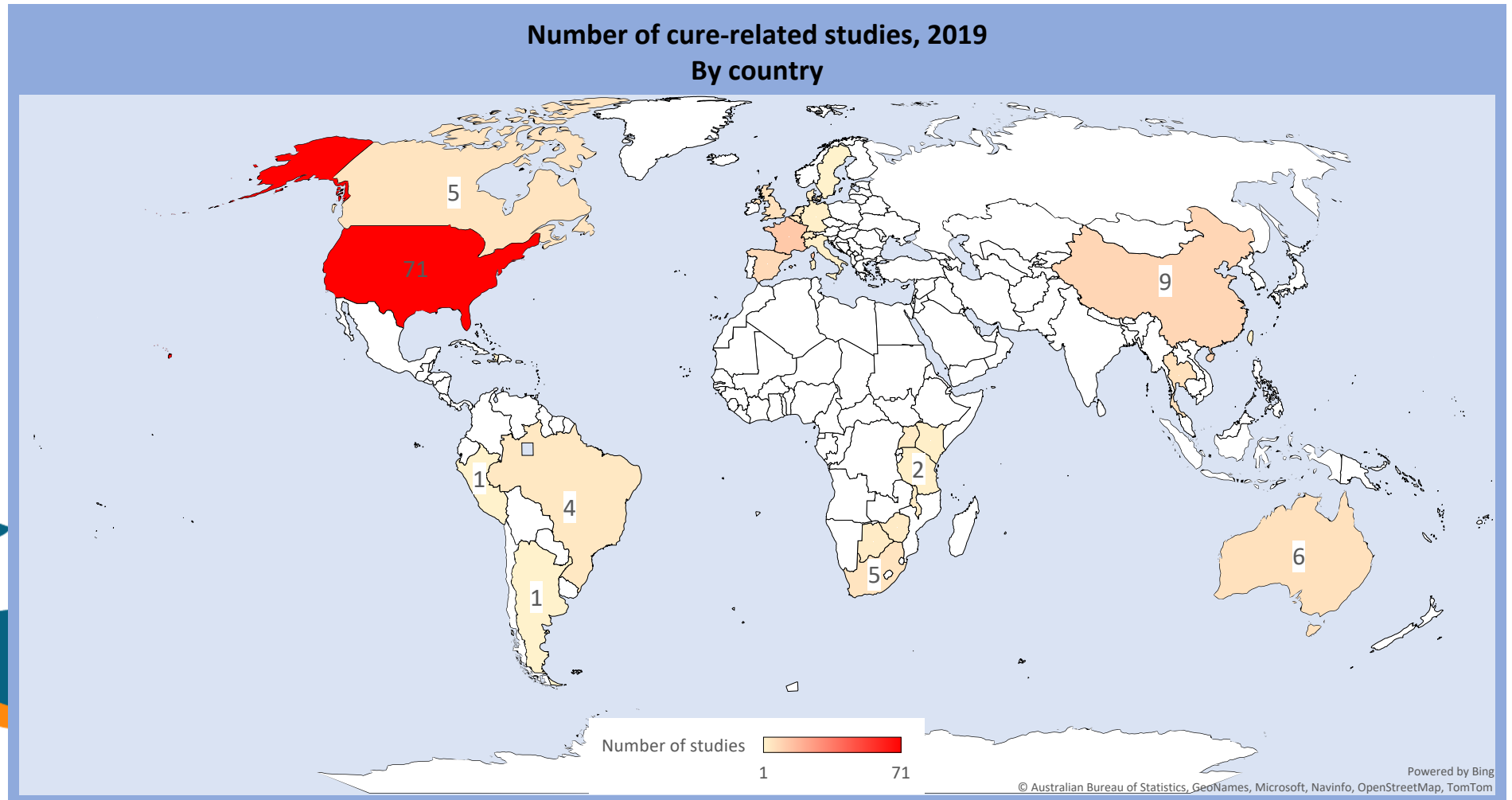
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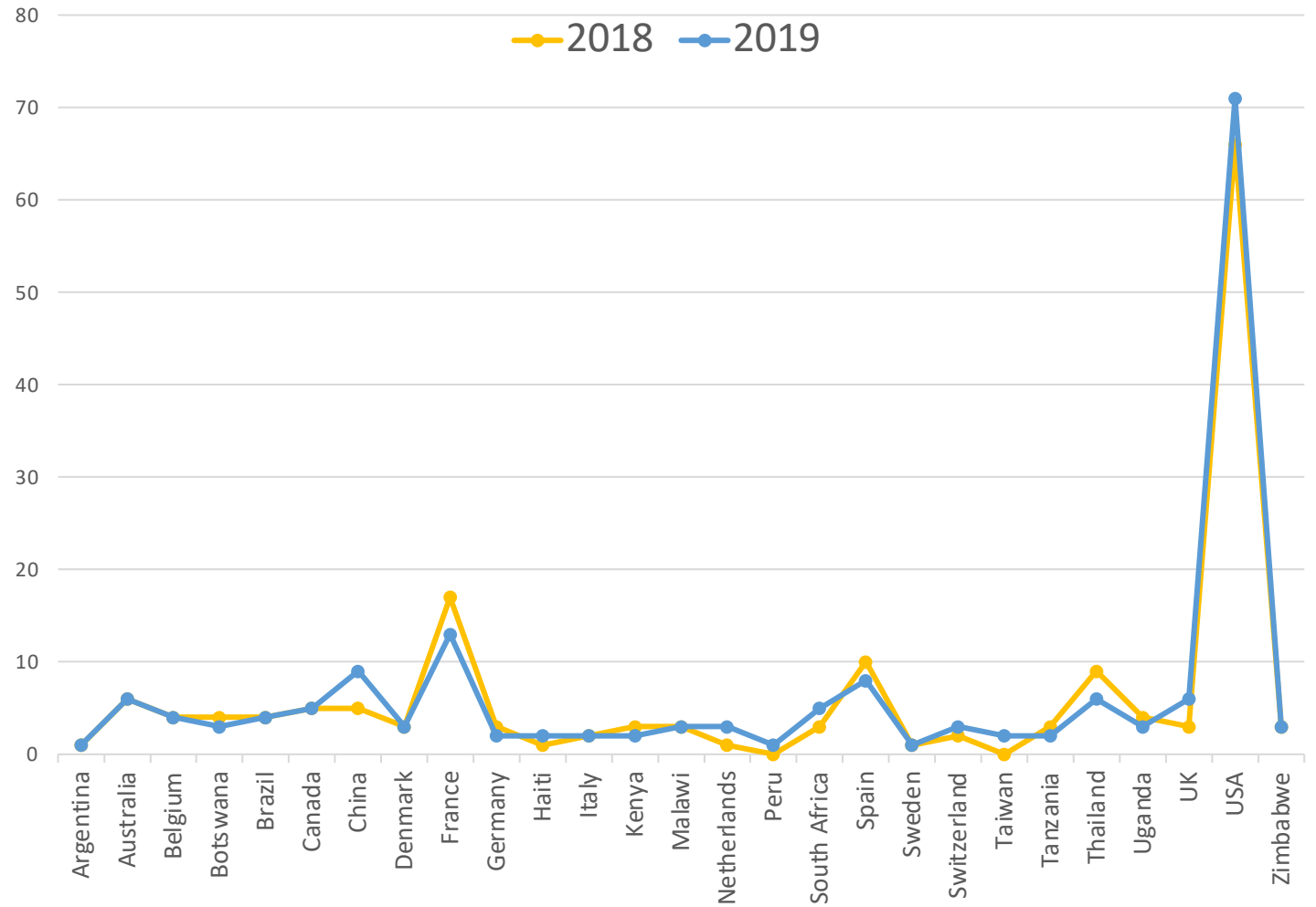
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Geographic distribution of cure-related studies



Geographic distribution of cure studies remained stable from 2018-2019

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Diversity in cure-related research

- Women remain dramatically underrepresented in all HIV research (including cure); data suggests not due to screen failures
- Data on race and ethnicity is underreported and, when reported, diversity is suboptimal

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Population Representation in HIV Cure Research: A Review of Diversity Within HIV Cure Studies Based in the United States

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Abstract

HIV is experienced across diverse populations, with gender and racial/ethnic minority populations bearing a significant proportion of disease. With National Institutes of Health (NIH) placing a priority on the enrollment of women and racial/ethnic minorities into studies, it is important to understand the diversity of participants in research. We sought to characterize how HIV cure research studies report data on diversity. A sampling frame of publications with funding provided by the Martin Delaney Collaboratories for HIV Research in 2019 was reviewed for reporting of demographic data. Of 55 publications that included research on humans/human specimens, only 51% provided any demographic description. There often is insufficient consideration of diversity of populations in HIV cure research. Ameliorating gaps in this regard will require recruitment of diverse populations/specimens and specifications to report demographic data in articles. This will ensure inclusion of diverse participants in HIV cure research from earliest laboratory to eventual phase III studies.

Keywords: diversity, generalizability, representativeness, HIV cure research

Smeaton *Clin Infec Dis* 2019

Roberts *AIDS Res Hum Retroviruses* 2022

Barriers to a cure for HIV in women

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Gianella S et al. *Journal of the International AIDS Society* 2016, **19**:20706
<http://www.jiasociety.org/index.php/jias/article/view/20706> | <http://dx.doi.org/10.7448/IAS.19.1.20706>



Review article

Barriers to a cure for HIV in women

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Abstract

Introduction: Distinct biological factors exist that affect the natural history of HIV and the host immune response between women and men. These differences must be addressed to permit the optimal design of effective HIV eradication strategies for much of the HIV-positive population.

Methods and results: Here, we review the literature on sex-based differences in HIV pathogenesis and natural history in tissues and anatomic compartments, HIV latency and transcriptional activity, and host immunity including the role of sex hormones. We then outline the potential effects of these differences on HIV persistence, and on the safety and efficacy of HIV eradication and curative interventions. Finally, we discuss the next steps necessary to elucidate these factors to achieve a cure for HIV, taking in account the complex ethical issues and the regulatory landscape in the hopes of stimulating further research and awareness in these areas.

Conclusions: Targeted enrolment of women in clinical trials and careful sex-based analysis will be crucial to gain further insights into sex-based differences in HIV persistence and to design sex-specific approaches to HIV eradication, if required.

Keywords: HIV eradication; HIV cure; women's health; immune system; female genital tract; anatomic compartments.

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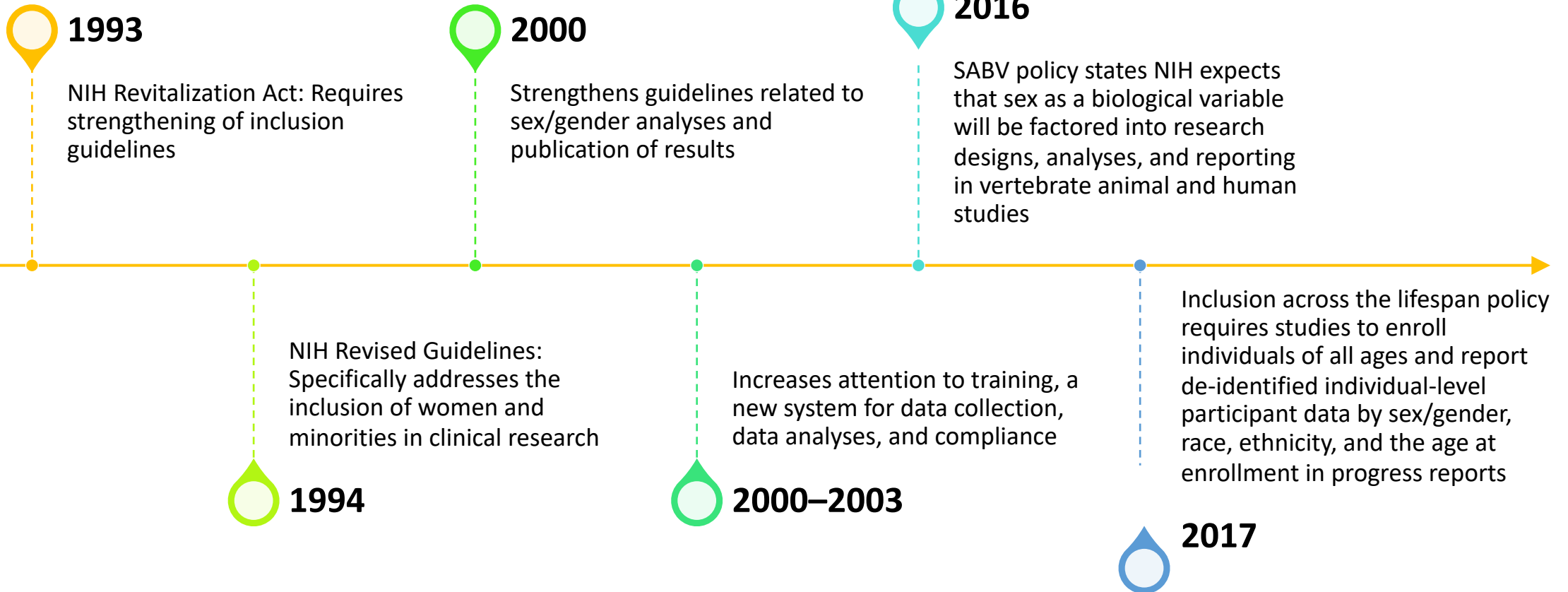
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Conclusions

There are distinct sex-based biological differences that affect the natural history and immune pathogenesis of HIV infection. These factors likely affect the establishment and distribution of the HIV reservoir and need to be considered in the design of future strategies to cure HIV. Current strategies for cure require identification of the size and location of the latent HIV reservoir. Profound differences in the HIV reservoir may exist between men and women and need to be addressed. Latency reversing agents that are to be used in a “kick and kill” strategy may be partially inhibited by estradiol-mediated mechanisms and therefore less effective in women. Immunological approaches targeting HIV-infected cells might work differently in women because both cell- and antibody-based immunity contain differences between sexes. Moreover, fluctuating hormonal status represents an additional variable that needs to be carefully considered when designing curative interventions. Targeted enrolment of women in clinical trials and careful sex-based analysis will be crucial to gain further insights into sex-based differences in HIV infection and to design sex-specific approaches to HIV eradication, if required.

Policy considerations for cure-related research: NIH

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Additional policy considerations for cure-related research

Horizon Europe

“the integration of the gender dimension into research and innovation content is a requirement by default, an award criterion evaluated under the excellence criterion, unless the topic description explicitly specifies otherwise”

CIHR Sex- and Gender-Based Analysis Plus Policy

SGBA Plus “is an intersectional approach to assess how factors such as sex, gender, age, race, ethnicity, socioeconomic status, disability, sexual orientation, cultural background, migration status, and geographic location interact and intersect with each other and broader systems of power...Applying SGBA Plus enables the Health Portfolio to formulate responsive and inclusive health research, policies, services, programs and other initiatives to promote greater health equity.

Enrollment in HIV cure-related research, as reported by survey respondents

Category (N=respondents)	#/total	%
Total participants (N=60)	2754	---
Female participants-sex (N=31)	260/1549	16.7%
Women participants-gender (N=20)	230/1241	18.5%
Transgender (N=20)	18/1233	1.4%
Participants over 50 (N=16)	49/731	6.7%

Barr & Jefferys, *J Virus Erad* 2020

Enrollment in HIV cure-related research, as reported by survey respondents

Category (N=respondents)	#/total	%
White participants (N=21)	117/843	13.9%
Black participants (N=21)	71/843	8.4%
Asian participants (N=21)*	629/843	74.6%
Hispanic participants (N=21)	26/843	3.1%
White participants (N=20)**	117/219	53.4%
Black participants (N=20)**	71/219	32.4%
Asian participants (N=20)**	12/219	5.5%
Hispanic participants (N=20)**	26/219	11.9%

*617 of the 629 Asian participants were enrolled in a Thai study

** Data excluding that Thai study

Treatment Action Group Focus groups

Four focus groups in late 2021/early 2022
(2 with US/UK advocates, 2 with researchers)



How to increase diversity: US/UK advocates

“30 years and we are making the same demands”

“The divide is widening between research and community.”

“If a trial doesn’t have enough people of color and women for significant information to be obtained, then they need to stop the trial until they do. That should be the order of the day.”

1. Research agenda: integrate sociobehavioral research early and often; move away from framework of “early diagnosed, early treated”
2. Advocates: build internal advocacy infrastructure and train newer advocates.
3. Researchers: shift paradigms around community engagement.
4. Funders: increase support for community engagement.

How to increase diversity: Researchers

“Compared to 10 years ago, recruitment has become more difficult. The trials have become more difficult. [ATIs] really take part of the potential study population out of the equation.”

“We keep talking about the same things over and over again. We need resources. We need staff dedicated to this, and we need time.”

1. Studies: Build planned diversity-powered enrollment increases if interim analyses in small, exploratory studies are promising
2. Sites: Dedicated staff with protected time to engage with diverse populations
3. Networks: Increased communication and collaboration between large networks and single-center studies
4. Community: Researchers can continue engaging in outreach and education to build trust

Next steps

- Additional focus groups with advocates in Africa, Asia, South America (Summer/fall 2022)
- Meeting to explore data sharing (Fall/winter 2022)
- Updated landscape analysis of cure-related research in 2022



Conclusions #1

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Participant demographics in cure-related research do not reflect the demographics of people living with HIV.



Researchers & advocates are supportive of efforts to increase diversity

Conclusions #2

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**Researchers and advocates
perceive existing research
infrastructures as influential
on diversity in cure-related
research**

Acknowledgments

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- Treatment Action Group
- Focus group participants
- Mike McCune
- Conference organizers

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