Landscape analysis & diversifying efforts

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Session 3: Cure advances globally
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

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

Prevalence (%) by WHO region
- Eastern Mediterranean: 0.1 [0.1–0.1]
- Western Pacific: 0.1 [0.1–0.2]
- South-East Asia: 0.3 [0.2–0.3]
- Europe: 0.4 [0.4–0.4]
- Americas: 0.5 [0.4–0.5]
- Africa: 4.2 [3.7–4.8]

Global prevalence: 0.8% [0.7–0.9]
Geographic distribution of cure-related studies

Number of cure-related studies, 2019
By country

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Geographic distribution of cure studies remained stable from 2018-2019.
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.

Smeaton *Clin Infec Dis* 2019
Roberts *AIDS Res Hum Retroviruses* 2022
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 into 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.

Received 18 September 2015; Revised 29 January 2016; Accepted 2 February 2016; Published 18 February 2016

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Policy considerations for cure-related research: NIH

1993
NIH Revitalization Act: Requires strengthening of inclusion guidelines

2000
NIH Revised Guidelines: Specifically addresses the inclusion of women and minorities in clinical research

Strengthens guidelines related to sex/gender analyses and publication of results

2000–2003
Increases attention to training, a new system for data collection, data analyses, and compliance

2016
SABV policy states NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies

2017
Inclusion across the lifespan policy requires studies to enroll individuals of all ages and report de-identified individual-level participant data by sex/gender, race, ethnicity, and the age at enrollment in progress reports
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

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

Barr & Jeffers, J Virus Erad 2020
### Enrollment in HIV cure-related research, as reported by survey respondents

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

*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

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.

“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.”
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

AIDS 2022 Affiliated Independent Event
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
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.
Researchers and advocates perceive existing research infrastructures as influential on diversity in cure-related research.
Acknowledgments

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