

## WOMEN IN HIV CURE RESEARCH:

# Advocating for, Discovering and Delivering a Cure

WOMEN'S RESEARCH INITIATIVE ON HIV/AIDS (WRI)



## HIGHLIGHTS

- **The Women's Research Initiative on HIV/AIDS (WRI) is an interdisciplinary and intersectoral group** dedicated to elevating, enhancing and expediting research on women and HIV. In 2016, the WRI convened a meeting focused on women in HIV cure research, including gaps and opportunities and strategies on how to address them.
- **Current HIV cure research is focused on the HIV reservoir**, the main barrier to a cure. HIV reservoirs are areas in which HIV persists and is not cleared by anti-HIV drugs or the immune system. HIV cure research strives to achieve the eradication of all virus that has the potential to cause disease.
  - Because women are severely underrepresented in this research, there is simply not enough data to truly understand sex differences impacting the development of an HIV cure.
- **Women living with HIV have mixed feelings about participating in HIV cure research.** Research and anecdotes suggest that while most people see value in pursuing HIV cure research, perspectives are much more varied and nuanced when it comes to personally participating.
- **There exists a lack of consensus among the scientific community** about the value of and need for women's participation in HIV cure research. There also appears to be a bias among some researchers that relevant sex differences are already understood, which is simply not the case.

## DEFINITIONS

### **Sustained remission (functional cure):**

ability to stop taking antiretroviral treatment (ART) without HIV becoming detectable

### **Sterilizing cure:**

eradication of HIV from all places in the body

### **Latent infection:**

viral DNA integrated into the DNA of cells that are not producing virus

### **HIV reservoir:**

cells containing HIV DNA in blood, organs and tissue throughout the body

## BACKGROUND

Finding a cure for HIV has been a goal of HIV research since the virus was first identified, more than 30 years ago. In recent years, funders have invested more resources into HIV cure research and while research is still in the early stages, progress has been made. HIV cure research is focused on the HIV reservoir, where HIV persists inside infected cells and is not cleared by anti-HIV drugs or the immune system. The HIV reservoir is the main barrier to a cure.

There are several known reservoirs, including immune cells in the gut, lymphoid tissue, blood, brain, genital tract and bone marrow. It is unclear when reservoirs are established, but recent research suggests that it could be as early as three days after initial infection. Research also suggests that the earlier a person receives HIV treatment, the smaller the size of their reservoirs. Early treatment may also prevent reservoirs from forming in some areas of the body. It is important to keep the reservoir size small because people with larger reservoirs experience greater and more persistent immune activation.<sup>1</sup>

Although antiretroviral therapy (ART) can stop the replication of HIV, latently infected cells persist and are not eliminated by ART. A cure is achieved when the reservoir is eradicated and there is no remaining virus with the potential to cause disease. Some of the main HIV cure research approaches currently include:

- ‘Shock and kill:’ shock the resting reservoir cells into producing virus, then ‘kill’ the newly activated cells. Once the cells produce virus, they are no longer hidden from the immune system. The substances that provide the ‘shock’ are called latency reversing agents, as they interrupt HIV’s ability to remain inactive within cells.
- Gene therapy – some approaches include:
  - Knocking “out” genes in the cell that allow the virus to enter and infect immune cells
  - Knocking “in” genes to immune cells that make them resistant to infection
  - Cutting out the genetic pieces of HIV that have become integrated into the DNA of infected immune cells

- Therapeutic vaccines: making the immune system capable of killing infected cells

## WOMEN IN HIV CURE RESEARCH

Women are severely underrepresented in HIV cure research, which means that there is simply not enough data to truly understand sex differences related to HIV cure. And yet, there appears to be a bias among some researchers that relevant sex differences are already understood. Research has shown a number of sex differences in HIV pathogenesis: men have higher immune activation and exhaustion while women have less residual virus activity, globally higher induction of type 1 Interferon pathways, lower initial viral load and higher CD4 counts, faster HIV disease progression and better response to vaccines. Estrogen has emerged as an important factor in latency reversal. As such, it is vital that women be addressed and included in HIV cure research.

## ETHICAL ISSUES RELATED TO HIV CURE RESEARCH

The ethics of cure research is a critical topic to explore when preparing to recruit research participants. Key issues specifically related to HIV cure research include:

- There is likely to be no health benefit for current participants
- As with any early-phase clinical trial, researchers do not yet understand all the details of the effects of a product (in this case, a potential cure) and how safe it is
- Enrolling in HIV cure research studies may involve stopping treatment and risking adverse health outcomes
  - Data have suggested that there are few adverse events when treatment interruptions are shorter than three months
- Enrolling women who are or may become pregnant into clinical trials has historically been challenging due to safety concerns pertaining to current and/or future reproductive health, resulting in limited female participation in clinical trials.
- Consideration of access to a future cure must be factored into clinical trial design

## PERSPECTIVES ABOUT HIV CURE RESEARCH AMONG PEOPLE LIVING WITH HIV

Understanding perceptions, attitudes and beliefs about HIV cure research among people living with HIV is vital to the development of successful clinical trials. One study about the risks and benefits of cure research found that 80 percent of participants felt that contributing to HIV cure research is important and 95 percent said they would like to help find an HIV cure. While willingness to participate decreased as the intrusiveness of the intervention increased, 50 percent of participants were willing to join any type of cure research. People who were more recently diagnosed with HIV were three times as willing to participate in cure research. This was also true for people who self-perceived as less healthy.<sup>2</sup>

Anecdotal feedback also provides important insights. Among a panel of women living with

HIV who discussed their thoughts on the risks and benefits of HIV cure research, there was tremendous variation. While it was clear that these women were supportive of and saw a compelling need to pursue and improve HIV cure research for women, they were cautious about ethical issues related to the research and eventual cure. They were also varied in their opinions about whether they would personally participate in such research.

Areas of concern included limited benefit for research participants in early-stage research, potential health risks associated with stopping treatment and eventual access to a cure for people of color and those with limited/no income. In considering their own willingness to participate in cure research, the panelists ranged from willing to participate in even the most intrusive research intervention to clear disinterest in any participation based on possible negative health outcomes and emotional anxiety.

## QUESTIONS ABOUT HIV CURE RESEARCH FROM WOMEN LIVING WITH HIV

- 1 What does being cured mean?
- 2 Where will the research be done? Will it be accessible? Will women/people of color feel welcomed?
- 3 What are the potential benefits and harms and to whom?
  - What protections will exist for people who enroll in the research?
- 4 What are some of the long-term consequences of being cured?
  - Will the cure require adherence over time?
  - How will the cure interact with other medications?
  - Will it be permanent? Would my immune system be restored?
- 5 What are the social justice implications of a cure?
  - Who will have access?
  - Will it work the same for everyone?
  - How would a cure impact testing policy?
  - How will we adjust to it being “over”?

## RESEARCH, POLICY AND EDUCATION RECOMMENDATIONS

*The WRI identified a number of research, policy and education opportunities to advance HIV cure research among women so that it ultimately works for women and benefits all.*

- **Assemble and leverage a group** of researchers, women living with HIV and social scientists to develop a framework to include women in HIV cure research. Publish this “roadmap,” including a set of principles that address equitable access, the ethics of recruitment and the importance of including women in the design and execution of research studies.
- **Engage basic scientists** about the need to include women in HIV cure research by highlighting existing data and continuing gaps in information. Identify researchers to serve as “champions.”
- **Tap into networks** and resources that already exist (including PWN-USA and The Well Project) to more effectively disseminate information on HIV cure research for women.
- **Engage women living with HIV** in a systematic way to better understand what kind of basic science research they would like to see and potentially participate in.
- **Determine whether** the pharmaceutical and biotechnology industries are willing to share de-identified data to better understand efficacy for women.

- **Create a clearinghouse** that can serve as a central repository for the significant amount of information on HIV cure research that currently exists. Provide ease of access for both interested stakeholders and people living with HIV.
- **Engage clinicians** who are working with women to ensure they have a solid understanding of HIV cure research and understand how to link interested women to information and studies.
- **Create materials** to help clinicians and women living with HIV understand the basics of HIV cure research and why and how women can be more centrally involved.

## CONCLUSION

HIV cure research is a critically important field of research with the potential to radically change the HIV landscape. Women remain underrepresented and under studied in HIV cure research, which will ultimately impair the approval and rollout of any potential cure that may be discovered. There are a variety of opportunities to influence this research across the areas of policy, advocacy, patient care and education.

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### References

1. <http://www.thewellproject.org/hiv-information/finding-cure-hiv>
2. <https://www.ncbi.nlm.nih.gov/pubmed/28275457>

## ABOUT THE WRI

*Since 2003, the Women’s Research Initiative on HIV/AIDS (WRI) has advocated for “more, better and faster research” in HIV disease in women. The WRI brings together an extraordinary group of leaders in HIV to identify key opportunities to accelerate our understanding of HIV disease in women. WRI members represent a broad range of stakeholders in the fields of clinical care, research, academia, community-based services, advocacy, government, the pharmaceutical industry and women living with HIV. This diverse membership operationalizes the cross-disciplinary approach advocated by the WRI. By addressing issues that affect women through a variety of lenses, the WRI is able to expand understanding of effective treatment and prevention for women and girls living with or at risk for HIV.*