

# Advancing the Meaningful Inclusion of All Women in HIV Research

## HIGHLIGHTS

- ▶ **The Women's Research Initiative on HIV/AIDS (WRI)**, a program of The Well Project, is a multidisciplinary and multisectoral effort dedicated to identifying gaps for women in HIV prevention, treatment, and cure research and policy. In 2022, the WRI convened a meeting to advance the meaningful inclusion of all women in HIV research, including but not limited to clinical trials.
- ▶ **Historically, women have been insufficiently included and involved in HIV research**, reflecting a form of paternalism that has sought to "protect" women, particularly those of child-bearing capacity, from potential harms from research. Such exclusion has resulted in limited knowledge about important aspects of women's experiences of HIV that would inform their active participation in decision-making about their health and well-being.
  - Specific populations of women (including women of trans experience, women who use drugs, and women who sell sex, among others) have been particularly marginalized and excluded from HIV research.
- ▶ **Deficits in HIV research among women impair the overall HIV response**; in order to successfully end the HIV epidemic, relevant experiences and circumstances of all affected populations must be understood.
- ▶ **In many cases, the tools to address these challenges already exist**; it is now imperative that necessary changes are implemented by policymakers, researchers, funders, industry, and other stakeholders to ensure the meaningful inclusion and engagement of all women in HIV research. Community engagement will play a fundamental role in these efforts.
  - For example, important work is being undertaken by advocates and clinicians to redress decades spent ignoring the needs of pregnant women and other birthing parents around HIV, including efforts to ensure their inclusion in HIV research and to enhance research on breast/chestfeeding in high-resource settings.

*The Well Project and the WRI define "women" as anyone who identifies as such across the gender spectrum. When appropriate, we strive to ensure that our programming is inclusive of broader gender identities, including men of trans experience, non-binary individuals, and others who could benefit from our resources and information. Our language herein reflects this approach, primarily referencing "women" but also using more inclusive language as appropriate, such as "lactating people" and "breast/chestfeeding."*

## WOMEN AND HIV RESEARCH: A PRIMER

While women have been affected by HIV from the beginning of the epidemic, their participation in HIV research, particularly clinical trials, has always been limited. In 1977, prior to the identification of the first cases of AIDS, the US Food and Drug Administration (FDA) recommended excluding women with childbearing potential from participating in phase 1 and early phase 2 clinical studies until reproductive toxicity studies were conducted and some evidence of effectiveness had become available. The recommended exclusion was broadly applied to any “premenopausal female capable of becoming pregnant,” but explicitly did not apply to women with life-threatening diseases. This policy was developed to reflect societal interests in protecting vulnerable populations but had the effect of drastically diminishing the number of women in clinical trials and knowledge about how treatments might affect women of childbearing potential. In biomedical science, evidence is foundational and without it, medicine lacks the ability to make appropriate recommendations about optimal therapy and the true risks of interventions. In an acknowledgment of this reality, the 1977 policy was reversed by the NIH Revitalization Act of 1993, which directed the National Institutes of Health (NIH) to establish guidelines for the inclusion of women in clinical research.

Addressing gender and sex in HIV research is vital to ensure that everyone living with HIV is afforded appropriate and accessible care. There are a host of biological, behavioral, and social issues related to gender and sex (including but not limited to genetics and epigenetics, hormones, the microbiome, exercise, stress, nutritional habits, anatomy, relationship dynamics, race, ethnicity, gender identity, sexual identity, stigma, and violence) that may influence a person’s experience of HIV. Recognizing that the terms “gender” and “sex” remain highly contested, it is important that researchers explicitly define them and describe the ways in which they will be addressed in their studies.

Unsurprisingly, HIV research that includes women has generated significant discoveries, including about sex-based differences in HIV transmission/acquisition, disease progression, co-infections, and mortality. We learned, for example, that vertical HIV transmission (from mother to infant) could be prevented with the use of antiretrovirals (ARVs) before, during, and after birth, and that HIV pathogenesis looks different between men and women (e.g., women were less likely to progress to an AIDS diagnosis than men). Notwithstanding these developments, and despite the 1993 policy change, women remain woefully underrepresented in HIV clinical trials. Many researchers still claim that it is difficult to recruit and retain women in studies due

### ***Specific research challenges related to women living with HIV***

***There are many ways to ensure the meaningful participation in research of women living with and vulnerable to HIV; examples include:***

- Designing studies from the outset to include women, rather than retrofitting the study design to accommodate women
- Conducting HIV research using a reproductive justice lens that reflects a commitment to bodily autonomy and acknowledges that agency to act on their own behalf rests with the participants
- Humanizing science and making it more accessible (e.g., through storytelling or other tools) to better reach women “where they are”
- Using multiple communications channels to disseminate information about opportunities to participate in HIV research to women, providers, and others
- Valuing women who participate in research as partners rather than subjects, and sharing the results of the research with them and their communities

to the complexities of their lives (e.g., raising children), even though this has been disproven over the years by multiple, successful clinical trials specifically focused on women, such as the GRACE study, which also demonstrated the value of engaging women living with HIV in the design of the trial itself.

The HIV research enterprise has a long way to go to ensure that women are meaningfully and appropriately represented across all facets of the research process, as participants, study staff, researchers, funders, policymakers, etc. Additional work must be done to redress the following:

- Limited attention to specific populations of women (e.g., women who use drugs and alcohol, women who sell sex) in HIV research, particularly clinical trials
- Significant gaps in data collection related to women of trans experience, a population disproportionately affected by HIV
- Racial inequity and medical mistrust as they affect the participation of Black women and other women of color in HIV research

## INSIGHTS INTO SPECIFIC POPULATIONS OF WOMEN WHO ARE ESPECIALLY AFFECTED BY HIV

*While women in general have been underrepresented in the HIV response and in HIV research in particular, specific communities of women have been particularly marginalized.*

### WOMEN OF TRANS EXPERIENCE

Despite being profoundly affected by HIV, women of trans experience have long been marginalized in HIV research, including in one of the spaces that carries the most weight: data. While this is slowly improving, there is much ground to make up as women of trans experience have been miscategorized in data collection throughout the HIV epidemic. This has manifested in a variety of ways, including:

- Categorizing women of trans experience as men who have sex with men (MSM) (i.e., no questions are asked about gender identity)
- Categorizing women of trans experience as a subset of cisgender MSM (i.e., while the title might be about MSM, the study is also enrolling women of trans experience)
- Including women of trans experience and failing to disaggregate study findings (i.e., the title might include women of trans experience, but they are not described in the results)
- Including women of trans experience and failing to include questions specific to their experiences
- Categorizing heterosexual cisgender male partners of women of trans experience as MSM

***"A lot of time when we talk about social science research, those data don't come back to us after we have participated. We have to make sure it's the opposite – that my community gets the data first and knows how to connect it to their stories and work."***

**CECILIA CHUNG, Transgender Law Center**

The consequences of this miscategorization can be extreme. It can erase important identities, thereby contributing to marginalization, and it can perpetuate unsupported assumptions about sex, gender, and sexual behavior. Additionally, the miscategorized data can falsely elevate HIV incidence and prevalence among cisgender MSM, which may result in misallocating funds to cisgender MSM that should be addressing the needs of women of trans experience.

Beyond the issues created by miscategorization in data collection and analysis, there is a dearth of research specifically focused on areas of need for women of trans experience, such as the way that feminizing hormone therapy may impact HIV and its treatment, among many others. Much of this speaks to a lack of knowledge and experience among providers and researchers with addressing the health and realities of women of trans experience.

*There are relatively straightforward solutions to addressing these challenges:*

- People of trans experience must be involved across HIV research efforts, including as study leaders
- Sex and gender identity should be asked about in every study
- Researchers need to have a clear rationale and be explicit about study enrollment criteria and, wherever relevant, should actively recruit an adequate sample size of people of trans experience to ensure that findings are meaningful to that population
- Studies enrolling people of trans experience should include questions relevant to their experiences
- Researchers must do everything possible to ensure the physical and social safety of study participants of trans experience

*"As researchers, we need to be authentic, honest, trustworthy, and vulnerable, and get past this sense that we can't say 'I don't know.'"*

**TONIA POTEAT, PhD, MPH, PA-C,**  
University of North Carolina

## WOMEN WHO SELL SEX

Rates of HIV among women who sell sex may be as much as 30 times higher than those in the overall population. Factors driving this disproportionate impact occur at all levels, from the individual to the socio-structural. Examples include:

- **Individual:** economic and food insecurity, homelessness, trauma, unemployment, lack of agency, triaging of priorities
- **Interpersonal:** intimate partner violence, interactions with the police, partner drug use, relationship power imbalances, client condom refusal
- **Community:** vulnerable sex work locations, community impoverishment, condom and sterile injection equipment supply and availability, volatile drug and sex exchange markets
- **Socio-structural:** criminalization of drug use and sex work, structural violence, racism, sexism

Politics and policies significantly influence the HIV experiences of women who sell sex. For example, the President's Emergency Plan for AIDS Relief (PEPFAR), the US government's global HIV/AIDS program, requires all funded organizations to sign an anti-prostitution pledge, and those organizations that offer HIV support for women who sell sex are disqualified from receiving funding. And yet, while the issue of sex work garners significant political attention, women who sell sex are largely ignored. They are rarely addressed in HIV research and were not identified as a key population in the US National HIV/AIDS Strategy until 2020.

To address the high rates of HIV among women who sell sex, research on individual, interpersonal, community, socio-structural, and policy factors that drive their vulnerability should be expanded, as should interventions to address these factors. Structural and community interventions outside the US have been shown to be effective, but little of this knowledge has been applied to women who sell sex in the US. The success of these interventions is attributable to their focus on altering the risk environment in which women who sell sex live and work, rather than attempting to change individual behavior one woman at a time.

## PREGNANT AND LACTATING WOMEN AND OTHER BIRTHING PARENTS

There are gaps and challenges in research related to women and other people living with HIV who experience or plan to experience pregnancy, birth, and/or breast/chestfeeding. Chief among these is the longstanding exclusion of such people from research, particularly clinical trials of ARVs. This exclusion originated with the aim to protect women and their babies from physical harm, in light of historical examples of experimental drugs (e.g., thalidomide) causing birth defects, but it has resulted in:

- Disincentives for industry, funders, and researchers to include women and other pregnant and lactating people in studies
- A lack of pre-clinical reproductive toxicity data until late in drug development, which delays the point at which women and other pregnant and lactating people can begin to participate in research
- Limited systematic post-marketing surveillance or observational studies evaluating pregnancy and other outcomes following drug licensure and widespread use

Thankfully, the paradigm has recently shifted and there is increasing acknowledgement among researchers that it is unethical not to include women and other pregnant people in research. The World Health Organization (WHO) and IMPAACT (International Maternal Pediatric Adolescent AIDS Clinical Trials Network) brought together stakeholders in two meetings in 2020 and 2021 to address the delayed study of ARVs among women and other people who are pregnant or lactating. They identified issues that affect the ability of researchers to enroll women and other pregnant people in HIV clinical trials and made a series of important recommendations:

- Developmental and reproductive toxicology studies should be conducted earlier in drug development, enabling pregnant people to participate in research sooner and ensuring that safety and efficacy findings are available to inform future use
- All new ARVs should have a specific pharmacokinetic (PK)/safety study that enrolls pregnant people to evaluate safety and tolerability in the short-term, as well as PK and drug exposure levels among pregnant people
- Safety should be the primary focus of pregnancy trials – they do not need to establish efficacy in pregnancy as long as drug exposure is adequate

(For more details about the WHO and IMPAACT's recommendations, [click here](#). Additional information is available in a special issue of the [Journal of the International AIDS Society](#).)

In order to transform the involvement of women and other pregnant and lactating people in HIV research, it will be necessary to incentivize these changes. Options include making specific data in pregnant people both a requirement for drug approval and mandated by funders, when appropriate, and requiring researchers to justify the exclusion of women from their research when such exclusion occurs.

### Research for women who acquired HIV perinatally

The experiences of women and others who acquired HIV perinatally (at birth, during breastfeeding, or otherwise) are often invisible. While this population shares experiences and concerns with other long-term HIV survivors, there are important differences related to the impact of HIV and its treatments that have not been adequately addressed. Any holistic research agenda addressing HIV among women across the life course must include attention to salient medical, psychological, and social factors influencing the experiences of those who acquired HIV through perinatal transmission.

# Jumpstarting research into breast/chestfeeding with HIV



Prior to the availability of ARVs, the rate of HIV transmission through breastfeeding was approximately 16 percent, which led policymakers (and consequently providers) to discourage breastfeeding by women living with HIV when possible. The advent of ARVs, however, significantly changed the landscape. Recent clinical trials in low-resources settings (e.g., PROMISE) show that when a woman's viral load is suppressed, the risk of transmission is less than 1 percent. Research is limited in high-resource settings, due in part to guidelines in those areas that recommend against breastfeeding. Providers in high-resource settings often consider the risk of any HIV transmission as the only factor when counseling about infant-feeding decisions, which ignores challenges related to health disparities; family and cultural values, and economic concerns; and potential health benefits.

In recent years, though, there has been an increased recognition of the need for research around breast/chestfeeding and HIV in high-resource settings. Advancing this research, and thus support for women living with HIV in their infant-feeding decision-making, requires that a variety of efforts be undertaken, including:

- Qualitative studies to understand the lived experiences of women and other pregnant/lactating people and clinicians around infant-feeding decisions
- Understanding the ideal frequency of checking maternal viral load/baby testing
- Evaluating real-life scenarios
- Evaluating different pediatric preventive regimens currently being used

## POTENTIAL RESEARCH QUESTIONS INCLUDE:

- Who is considered a good candidate for breast/chestfeeding?
- How do pediatricians navigate the role of standard infant prophylaxis beyond the first 4-6 weeks?
- What levels of HIV viral load or pro-viral cell-associated HIV exist in the breastmilk of a lactating parent living with HIV? How infectious is cell-associated HIV?
- What are the levels of maternal ARVs in breastmilk?
- How long does someone have to have an undetectable viral load before it is "safe" to breast/chestfeed?
- Are breast/chestfeeding and formula both being used (mixed feeding but no solids)?
- How do we best reach clinicians and parents to share evolving guidance on breast/chestfeeding and HIV?

In addition to advancing research, it is necessary to revise policies (including updating federal guidelines around breast/chestfeeding) to better acknowledge the right to bodily autonomy, support informed infant-feeding decision-making among women living with HIV, and decrease criminalization. For more information and resources on this topic from The Well Project, [click here](#).

## ELUCIDATING WOMEN'S EXPERIENCES IN HIV RESEARCH

Much attention to the inclusion of women in HIV research has been focused on clinical trials for HIV treatment and prevention. Randomized clinical trials are considered the gold standard of methodology to determine if a specific intervention works in the context of a controlled study, but they have their limits, particularly when it comes to demonstrating whether said intervention is effective in the “real world.” Whether women take up HIV interventions that have demonstrated efficacy depends on factors at play in their everyday lives, including their access to information; access to healthcare; relationship dynamics; social network and community norms; and other concerns.

Thus, it is imperative that research examine and address the whole of women's lives and experiences as they interact with HIV prevention, care, and treatment. This requires employing research methodologies beyond clinical trials, particularly qualitative approaches. These include storytelling and personal narratives, observational studies, interviews, focus groups, and ongoing, collaborative discussions.

Context is a crucial part of all research. Understanding the realities that inform and influence the experiences of study participants (both those specific to study participation and occurring in the “rest of their lives”) through all phases of the study enables the development and incorporation of relevant study questions and a meaningful research and analysis framework.

### Structural power

Structural power is an aspect of research that is not often acknowledged or studied but that ultimately affects the conduct of research (including but not limited to HIV) and the experiences of participants. To ensure that women are not just represented in HIV research but also are treated fairly with respect to both the conduct and outcome of it, a number of questions should be considered:

- Who holds decision-making power in research design and implementation and how transparent is this?
- Who is funding and sponsoring the research?
- Who is included and excluded, who decides, and why?
- How does research address the structural inequities (i.e., the actual social determinants of women's health) within which research is constructed?
- Are women demonstrably valued and respected in ways that are tangible and quantifiable?

Regardless of the kind of research undertaken and the methodology employed, women living with and vulnerable to HIV must be engaged in all phases of a study, from its development, through its execution, to the dissemination of results and their implementation in programming. Engagement and inclusion mean more than just “showing up,” but also feeling valued and understood.

## RECOMMENDATIONS

Based on the landscape and challenges described above, the WRI identified a series of recommendations related to education, advocacy, research, and policy that aim to ensure better representation and involvement in research of women living with and vulnerable to HIV. The WRI is committed to working collectively with all relevant stakeholders to advance these efforts.

## ENGAGE AND CENTER COMMUNITY

- Work with funders to undertake a series of efforts to ensure that the perspectives of women living with and vulnerable to HIV are reflected in HIV research
  - Create a mechanism through which diverse groups of women living with and vulnerable to HIV can provide input into the research priorities of HIV research networks and other structures of the National Institutes of Health (NIH), Centers for Disease Control (CDC), and other funders; elevate the value of subject matter expertise
  - Create a model that reimagines the process for development of research questions to ensure that they represent the needs of women living with and vulnerable to HIV; work with NIH and HIV research networks to adopt
  - Create and promote a speakers' bureau of women living with HIV who can provide community perspectives to help guide research
  - Promote meaningful partnerships between HIV researchers and women who sell sex
- Engage the advocacy community to develop programming that amplifies the need for greater involvement of women in HIV research
  - Develop a communications mechanism (e.g., a listserv) that disseminates employment opportunities around HIV research to people living with HIV; promote widely among organizations engaged in HIV research, treatment, prevention, policy, and other programming
  - Create and disseminate a series of educational materials about HIV research to women living with and vulnerable to HIV; create trainings that can be provided by and for women living with HIV
  - Develop and disseminate a series of communications highlighting the work of underrepresented women with careers in HIV research and policy
- Work with academia to create a framework through which researchers can develop partnerships with local community-based organizations, enabling their research to benefit from their expertise and engagement with local populations

## Demystifying policy

While advancing and improving research is crucial to achieving the goals described throughout this brief, it needs to be accompanied and complemented by policy work at all levels (local, regional, federal). It is important to recognize that policy is many things, and many of us are already undertaking efforts that impact policy whether we realize it or not.

Policy can be formal and informal, it can operate at multiple levels, it can be incremental and it can be revolutionary, it can be visible and invisible. Policies matter because they structure and determine our lives and facilitate or hinder access, in this case to HIV prevention and treatment. By influencing policy, we can change people's lives. It is important to highlight the multitude of ways individuals can engage and influence policy, including:

- Voting in all local, state, and federal elections
- Advocating for legislation/getting laws passed or changed
- Influencing a report or a plan
- Serving on an advisory committee
- Speaking at a public meeting
- Requesting a meeting with officials
- Writing to elected representatives
- Analyzing an issue/options
- Generating data



## ENGAGE STUDY SPONSORS TO LEVERAGE FUNDING MECHANISMS

- Tie milestones associated with enrolling members of specific populations (e.g., cisgender women, women of trans experience, women who use drugs, Black women and other women of color, women who sell sex, women who acquired HIV at birth, etc.) to payment of installments of grants or other modes of financial support
- Require justification for the exclusion of women in funding requests
- Establish conditions for funding that encourage community engagement
  - Normalize inclusion of a line-item in grant applications for community consultants
  - Mandate meaningful, compensated engagement with community partners (e.g., capacity building, staff support and training) as a condition of funding
  - Establish scoring criteria that reward engagement with specific priority populations, including women

## UNDERTAKE MULTIDISCIPLINARY EFFORTS TO ADAPT AND PROVIDE SUPPORT FOR RESEARCH EFFORTS

- Work with high-profile journals to encourage the inclusion of authors from affected populations in publication submissions
- Develop best practices guidance that addresses logistical hurdles to clinical trials participation, such as:
  - Providing translators
  - Developing education to train site staff to recruit and retain women in HIV research
  - Simplifying the informed consent process
- Support ongoing efforts by the WHO and IMPAACT, among others, to expand inclusion of women and other pregnant and lactating people into HIV research efforts; encourage inclusion of those who may not identify as women, including men of trans experience and non-binary individuals
- Create and promote a database featuring a diverse group of researchers including Black women and other women of color, women of trans experience, etc. to participate in and lead research efforts
- Develop a research agenda to increase research among people who acquired HIV perinatally, including women

## ENGAGE THE ADVOCACY COMMUNITY TO EDUCATE STAKEHOLDERS

- Create a mentor program to connect community members interested in increasing their involvement in HIV research with seasoned community representatives as mentors about involvement in HIV research
- Create best practice guidance on engaging community members in HIV research; address compensation (monetizing subject matter expertise) and define criteria to avoid tokenization

## CONCLUSION

Ensuring truly meaningful and equitable engagement of all relevant populations of women in HIV research, and including attention to the biomedical, behavioral, and social aspects of HIV specific to women's lives, are vital to ending the HIV epidemic. While there have been significant strides made over the last four decades, including recent efforts to include in clinical trials women and other people living with HIV who are pregnant or breast/chestfeeding, there is still considerable work to be done. Success in this work requires concerted partnerships among and between all HIV research stakeholders that center the lives and experiences of diverse populations of women.

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## ABOUT THE WELL PROJECT AND THE WRI

*The Well Project is a non-profit organization whose mission is to change the course of the HIV/AIDS pandemic through a unique and comprehensive focus on women and girls. Its program, the Women's Research Initiative on HIV/AIDS (WRI) is a multidisciplinary and multisectoral effort dedicated to identifying gaps for women in HIV prevention, treatment, and cure research and policy. For more information, please visit [www.thewellproject.org](http://www.thewellproject.org).*

