NO DATA NO MORE

Manifesto to Align HIV Prevention Research with Trans and Gender-Diverse Realities

AVAC
25 Years and Counting

July 2021

The *No Data No More Manifesto,* written and informed by trans and gender-diverse (TGD) advocates from Cape Town to Cologne, with support and solidarity from AVAC, offers practical and essential priorities for meaningful change. The future must include peer-led HIV prevention research with true ownership, acceptability and viability in TGD communities.

This manifesto for HIV prevention research for trans and gender diverse people (TGD) is authored by Max Appenroth, JD Davids, Cindra Feuer, Ricki Kgositau and Immaculate Mugo in partnership with AVAC and input from the ad hoc Technical Advisory Group members, with special thanks to Craig Hendrix, Asa Radix, Alexandra Rodriguez, Jae Sevelius and Leigh Ann van der Merwe; to NIAID's Cross-Network Transgender Working Group, including Clare Collins, Brian Minalga and Rona Siskind; and to artist Rory Midhani.

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PREAMBLE

From the Co-Authors

As a trans woman who is masculine-attracted, it often pains me to see how women like me (who have sexual and intimate relations with cis-het men, masculine gay men, trans men, and masculine-identified and -presenting women) are often ignored in research and programs because of presumptions about our bodies and lives.

Trans and gender-diverse persons construct, experience and express our various identities in nuanced ways. For example, trans women may identify as lesbians, and some trans men are gay or men who have sex with men (MSM). Some trans people prefer intimate partnerships with each other. There are also pansexual and gender nonbinary people, in addition to heteronormative and binary-identified trans people. For these nuances to be visible in data sets, it's important for trans-identified people to be on the forefront of research done about and for us—"nothing without us."

Trans-diverse communities have far too often experienced a lack of leadership and participation in compulsive binary and cis-heteronormative research and programming. Subsequently, our health outcomes and rights are further challenged—hence the need for this manifesto.

—Tshepo Ricki Kgositau, Cape Town

Based on who I am—a transmasculine person who has sex with cis men—I fall under two of the five designated WHO key populations (KP) that are most at risk for HIV. Yet my identity as a person placed in high-risk sexual networks is historically and consistently overlooked by the HIV establishment. Transmasculine and other assigned female at birth (AFAB) trans people have been neglected in HIV research and care for decades. Many of us identify as MSM. Some are sex workers; others inject drugs or represent a constellation of several KPs at once. Yet AFAB trans people are still not recognized enough by researchers and health care providers to investigate the specific risks to our community or to offer us medically appropriate and accessible care. If we aren't being discriminated against or even attacked, I and my community live with missing knowledge on the side of doctors or a lack of information based on insufficient research. One might better understand now why we often shy away from medical help, even when we need it. Or, why trans people are more often living with HIV and our general health status is comparably poor. The status quo is a burden to us as individuals and an impediment to the movement's attempt to control HIV. This is the reason we drafted this manifesto.

—Max Appenroth, Cologne

My years of working with, and for, the transgender movement at sub-regional and Pan-African levels have allowed me to appreciate and elevate diversity within trans communities. As a manager of trans-focused HIV programs on the African continent, I can testify to trans people lamenting a lack of appropriate and specific HIV prevention commodities and amenities due a lack of trans representation at decision-making tables. As a queer woman who has sexually intimate relations with transmasculine beings, transmen and masculine-expressing lesbian women—among the various masculine expressions I am attracted to—I have seen how programmers miss very significant HIV vulnerabilities of masculine and trans nonbinary persons' prevention needs.

Developing this manifesto has been an opportunity to inform and direct future research and advocacy around HIV prevention science for trans and gender diverse (TGD) persons. For trans-focused programs to be effective, trans people—who recognize the subtleties and nuances that often go overlooked—need to be in the leadership seat, informing in-depth analyses and recommendations to ultimately shift the way research informs policy and programs. This is the objective of this manifesto.

—Immaculate Nyawira Mugo, Cape Town

Around the world, we need HIV research that is accurate, comprehensive and free of the very stigma and biases that are at the heart of the decades-long HIV pandemic. Yet the majority of research protocols, articles and conference presentations still speak of "men" and "women", as if these binary designations include all people at risk of, or living with, HIV. This language and conduct are not only inaccurate—they risk the very integrity of HIV research itself and perpetuate the marginalization of trans and gender-diverse people. This will not be corrected by simply adding the word "cisgender" or extending research based on the assumption that trans people are in the "wrong bodies" or all seeking to emulate binary lives. It's far past time to put trans and gender diverse researchers and community members in positions of power in trial design, prioritization, funding and analysis. We don't need to waste any more time getting this wrong, as lives depend on it.

—JD Davids, Brooklyn

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SUMMARY

The *No Data No More Manifesto*, written and informed by trans and gender-diverse (TGD) advocates from Cape Town to Cologne, with support and solidarity from AVAC, offers practical and essential priorities to manifest meaningful change. We believe the future must include peer-led HIV prevention research with true ownership, acceptability and viability in TGD communities.

Specifically, this declaration sheds light on the TGD experience and the role of gender-affirming therapy, and the HIV prevention research landscape, including its historical gaps and recent progress. *No Data No More* provides a vision for a relevant and inclusive TGD research agenda, offering public recommendations to finally fulfill an inclusive HIV research future where TGD people flourish in all our diversity.

The stakes are high: Efforts to bring an end to the global HIV pandemic will fail if effective, accessible HIV prevention interventions don't reach TGD communities. Yet our people—who often face crushing stigma, marginalization, criminalization and violence, along with a disproportionate burden of HIV—continue to be overlooked, subsumed, underrepresented or excluded altogether from HIV prevention research and programs. Though there's been a recent uptick of TGD-inclusive scientific literature and trans-led research, it falls gravely short of what's needed.

Trans women bear a disproportionate burden of HIV globally with 19 percent living with HIV—49 times greater than the general population. HIV in trans men is woefully understudied and the absence of data leads to a false assumption that they bear little to no burden of the virus. Gender nonbinary people face even greater underrepresentation in HIV surveillance and research and related syndemics (the confluence of two epidemics with the potential to worsen outcomes for both). As such, we envision an HIV TGD research agenda that:

- Considers diversity, including the full range of participants along the gender spectrum.
- Tracks epidemiological data on HIV incidence and prevalence that accurately reflects the large and growing HIV acquisition rates of TGD populations, including in regions where little to no data has been collected thus far.
- Supports best practices in language use, informed by TGD researchers, TGD community advisory board members and TGD trial participants.
- Undertakes a global analysis of the data gap from TGD-relevant health programs and prevention research.
- Addresses structural barriers that limit TGD people's access to HIV prevention and the HIV research process.

Gender-affirming hormone therapy (GAHT) in all its forms is a building block of TGD health and well-being, including HIV prevention. Improved uptake and retention are a direct result of GAHT as it enhances an individual's self-worth and self-esteem. And yet, gender-affirming hormone therapy remains an unmet need and priority for many. Furthermore, for too many years, a lack of research into hormone and ARV drug interactions has raised concerns among some TGD people at risk for HIV and slowed their uptake of PrEP. As such, we call for an HIV research agenda that:

- Ensures all new PrEP compounds in development undergo drug-drug interaction studies with feminizing and masculinizing hormones to examine any possible drug variances.
- Resolves efficacy and safety questions about on-demand oral PrEP for trans people on GAHT.
- Provides GAHT across the HIV care and prevention research continuum, from early clinical trials through delivery.

The historic failure to conduct meaningful HIV prevention research with TGD populations is yet another act of systemic and institutionalized violence against TGD people. **It exacerbates the very health disparities that the HIV field has committed to addressing.**

Further, when TGD groups are included in research, their numbers are typically too small to measure statistically significant outcomes in the trans subgroup. While there are growing commitments to TGD-inclusion, this goodwill doesn't stretch far enough to ensure needed research is adequately funded or developed in partnership with TGD communities and answers critical questions. As such, we envision an HIV research agenda to overcome this historic disparity that:

- Improves TGD-inclusion in randomized clinical trials that is comprehensive and studies the differences among trial participant sub-groups.
- Adapts gender-inclusive enrollment criteria from the UNAIDS/World Health Organization's guidance (*Ethical considerations in HIV prevention trials*) to local contexts.
- Provides inclusion criteria for TGD people in clinical trials and reports how gender is defined by the study protocol, and how it is explained and communicated to potential participants.
- Explicitly includes trans men and other assigned female at birth (AFAB) trans people in the eligibility criteria of all PrEP trials—and all other HIV clinical trials.
- Includes TGD leadership in clinical research. TGD representatives must participate in study design and implementation through direct and meaningful inclusion in protocol teams, special advisory committees, trial teams and even as principal investigators.
- Funds and strengthens capacity of local research sites to recruit TGD participants and follow the Good Participatory Practice Guidelines by engaging with the local LGBTQ community, including transgender-led organizations.

To advance this vital work, **we offer our detailed global manifesto to HIV researchers, site-level staff and funders. This work demands immediate and sustained action. Join with TGD communities to envision, fund, and launch a body of research to finally redress decades of negligence. No data, no more!** Forty years into the global HIV pandemic, which is endemic to most trans communities, it's beyond time to align HIV prevention research with trans and gender-diverse realities.

BACKGROUND

The stakes are high: Efforts to bring an end to the global HIV pandemic will fail if effective, accessible HIV prevention interventions do not reach TGD people. Yet our people—who often face crushing stigma, marginalization, criminalization and violence, along with a disproportionate burden of HIV—continue to be overlooked, subsumed, underrepresented and/or excluded altogether from HIV prevention research. Though there has been a recent uptick of TGD-inclusive scientific literature and trans-led research in the field, it's far from adequate. It's important to rectify this troubling omission. As Jerome Singh, an ethicist from the University of Toronto and the University of KwaZulu-Natal noted in 2016:

> *"To date, there have been no HIV-endpoint trials that specifically focus on transgender individuals . . . Given their disproportionate burden of HIV, their historic and ongoing marginalization, and the knowledge gap related to HIV prevention specific to the transgender community, conducting focused HIV prevention research on transgender persons is an ethical imperative."*[1]

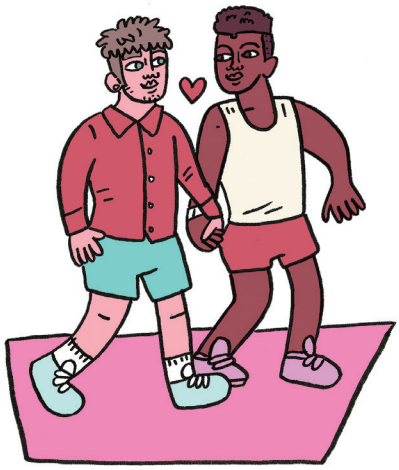
Trans women bear a disproportionate burden of HIV globally with 19 percent living with HIV—49 times greater than the general population. In some countries, HIV prevalence among trans women is 80 times higher than the general population.[2] Between 2010 and 2019, global HIV incidence rates in trans women increased by five percent, widely missing UNAIDS' target to decrease new HIV infections by 75 percent in this key population by 2020.[3]

HIV in transmasculine people is woefully understudied and the absence of data engenders a false assumption that they bear little to no burden of the virus. However, growing evidence shows just the opposite: A US meta-analysis found three percent HIV prevalence in trans men,[4] while another revealed 38 percent prevalence in trans male sex workers in Zimbabwe—numbers as high as their female sex worker counterparts.[5] Gender nonbinary people face an even greater dearth of representation in HIV surveillance and research and related syndemics. One US study estimated that nonbinary individuals make up more than 25-30 percent of trans populations.[6]

Further, when TGD groups are included in research such as in the iPrEx oral F/TDF and DISCOVER trials, their numbers are typically too small to conduct a robust cohort analysis: to measure outcomes statistically significant to the trans subgroup. While there is movement (e.g., TGD inclusion as a key pillar in US NIH reconfigured HIV research networks[7] and UNAIDS/WHO updated ethical guidelines[8]), goodwill does not stretch far enough to ensure the research is adequately funded or developed in partnership with TGD communities and answers critical questions.

LIVED TGD EXPERIENCES

- Drivers of HIV incidence in TGD people
- Cornucopia of TGD sexuality and identity
- More and better HIV surveillance
- On language
- Structural barriers



Drivers of HIV incidence in TGD people

The multiple and intersecting drivers of HIV among TGD populations include unprotected receptive anal and vaginal/front hole sex; higher sexually transmitted infection rates (in some cases potentially heightened by vaginal/front-hole atrophy from masculinizing hormones);[9,10] higher prevalence of injecting drug use; risks from hormone and silicone injection outside of medical care or supervision; high HIV prevalence in sex partner networks; high-risk criminalized environments for sex workers; houselessness and housing insecurity; and lack of legal protections.

Other health disparities and conditions include poor mental and physical health, delays in preventative health screening, and lack of access to culturally competent and gender-affirming medical care and social services.[11] The imposition of traditional cultural norms can also increase the risk of HIV for trans women. Examples include castration of hijra in India and of Xhosa women in South Africa.

Notably, widespread experiences of discrimination and violence among TGD people extend to healthcare settings. According to the 2015 US Transgender Survey:

> *"One-third (33%) of respondents who had seen a health care provider in the past year reported having at least one negative experience related to being transgender, such as verbal harassment, refusal of treatment, or having to teach the health care provider about transgender people to receive appropriate care."*[12]

Similar numbers are found in the European Union, where 34 percent of the TGD survey participants experienced discrimination when seeking help from medical or social services (compared to 13 percent of cis lesbian, gay or bisexual people).[13] Alienation from health care contributes to other drivers of HIV—decreasing opportunities for testing and treatment of STIs, or increasing the need to turn to sources outside of medical systems for hormones or injectable silicone.

We believe research addressing HIV in TGD populations has begun to identify key drivers of HIV incidence, though there's still a pressing need for research that adds to this knowledge base—including biomedical, social and structural factors specific to countries and regions.

Vision

- Key drivers of TGD HIV incidence are comprehensively identified—including biomedical, social and structural factors across countries and regions.

Cornucopia of TGD sexuality and identity

Assumptions and nuances about TGD sexuality and gender are not well understood or addressed in research, and both have implications for HIV risk. For example, in one TGD survey, only 15 percent of participants identified as heterosexual.[14] In the iPrEx oral PrEP study, 678 of a total 2,499 participants were identified as trans women. However, a post-study analysis revealed subgroups who identified as women (1 percent), trans women (12 percent), men using feminizing hormones (1 percent) and reports of nonbinary characteristics (14 percent).[15]

In terms of sexual expression, applying binary and cis-heteronormative assumptions to TGD communities are common mistakes with significant negative implications. This can result in limited or inaccurate data and understandings of TGD people and furthers their alienation. All sexual orientations and sex practices are represented and take place in TGD communities. TGD people may also desire or choose to partner with one another, rather than—as it is often assumed—desiring sexual acceptance and partnership with cisgender people. Many of the sexual practices of TGD populations are overlooked by data sets. This obscures the most acceptable and appropriate HIV prevention interventions, leaving communities having to extrapolate meaningful data from other cohorts.

Additionally, many trans people find themselves on a continuum of transition and, subsequently, HIV prevention, treatment, care and support may look different at each of their personal stages of transition. Data are also lacking on the small but growing populations of TGD youth who use hormone blockers and then cross-gender hormones in adolescence, thus preventing exposure to endogenous hormones and the development of the secondary sex characteristics they produce. Just as important, research in TGD populations often disregards or excludes those who have undergone “bottom surgery” (gender-validating surgeries on reproductive organs or genitals). Very little is known about HIV prevention interventions and experiences in these populations.

Given the sexual and gender diversity within TGD populations, we believe an equally diverse research and development agenda that includes implementation research is particularly important to fully characterize the varied research participants along gender and sexuality spectrums. This will illustrate how to best apply clinical research findings across the diversity of TGD people to increase uptake of newly proven HIV interventions.

Vision

- A research and development agenda includes implementation research and fully considers the range of research participants along the gender spectrum.

More and better HIV surveillance

In terms of gender expression, HIV surveillance data too often categorize people as one of two genders, thus obscuring HIV data that is representative of all TGD people. Globally, many countries—including the majority of those in Africa—do not even attempt to gather size estimates for TGD populations. Integrated Biological and Behavioral Assessment Studies, or IBBS, funded by The Global Fund and PEPFAR, help to develop countrywide and multiyear action plans to reduce HIV. They don't track TGD populations, yet generally do include other key populations—e.g., sex workers, cisgender men who have sex with men and people who inject drugs. The Global Fund and PEPFAR perpetuate this omission as fiscal sponsors of IBBS. As with surveillance data, the HIV continuum of care often lacks nuance in providing services across the gender spectrum.

We believe epidemiological data on HIV incidence and prevalence should more accurately reflect the population estimates of TGD people in all their diversity, including in regions where there is little to no data, such as sub-Saharan Africa and Eastern Europe/Central Asia. The Global Fund and PEPFAR should use their influence to include TGD populations in IBBS surveys. Recruiting trans-identified data collectors and researchers would result in more accurate data.

Vision

- Epidemiological data on HIV incidence and prevalence more accurately reflect HIV infection rates anong all TGD populations, including in regions where there is little to no data, such as sub-Saharan Africa and Eastern Europe/Central Asia.
- The Global Fund and PEPFAR use their leverage to include TGD populations in the IBBS survey.
- Trans-identified data collectors and researchers capture more accurate surveillance data.

On language

Precise and intentional language around gender in research is vital. It is fundamental to the goals of research itself. This includes greater accuracy in trial design and data collection, and in the interpretation, dissemination and application of results.

HIV requires that we understand both bodies and gender as complex, while also developing and establishing definitions that allow the field to conduct meaningful and comparable research. This requires the ability to define and categorize participants. HIV researchers must accurately and respectfully understand and describe a range of distinctions relevant to anatomy, physiology and endocrinology that can vary across the TGD spectrum. All these factors can increase or decrease the likelihood that HIV will reach particular cells, establish infection, and potentially lead to the transmission of the virus to others.

In 2015, a study of HIV testing events by the US Centers for Disease Control and Prevention (CDC) identified six subgroups of TGD populations.[16, 17] The subgrouping revealed distinct differences among categories that may have been missed when TGD populations are lumped together as simply trans women or trans men. For example, those assigned male at birth (AMAB) who identified as "trans women" had much higher HIV prevalence (4.3 percent) than AMAB individuals who identified as "women" (1.4 percent).

We believe it's imperative to support best practices in language use, informed by TGD researchers, community advisory board members and trial participants. We recommend researchers adhere to the US *NIAID HIV Language Guide*[18] along with the *Guidance on the Use of Gender-Inclusive HIV Research Practices: Protocol Design, Data Collection, and Data Reporting*,[19] drafted by NIAID's Cross-Network Transgender Working Group.

Vision

- All researchers adhere to the US *NIAID HIV Language Guide* along with the *Guidance on the Use of Gender-Inclusive HIV Research Practices: Protocol Design, Data Collection, and Data Reporting*, drafted by NIAID's Cross-Network Transgender Working Group.

Structural barriers

Around the world, TGD people face structural barriers to HIV prevention and treatment. First, the major HIV prevention programs in many regions prioritize cisgender heterosexual people and overlook the prevention needs of TGD communities. Second, in many regions TGD people cannot safely seek HIV prevention or treatment services because of social, cultural and legal barriers. Such barriers pose challenges to TGD participation in HIV research trials, perpetuating a vicious cycle of underrepresentation in HIV prevention services.

Low engagement of TGD people in HIV treatment and prevention must be addressed in clinical research, implementation research and health delivery systems. Lack of trans-centered research is among the most alarming failings in the HIV response. We believe global systematic analysis of gaps in data from TGD-relevant health programs and prevention research is a necessary next step. (A preview of such an analysis can be found later in this manifesto.) We believe future research must also address structural barriers that limit access to prevention strategies and research processes.

Discriminatory attitudes and punitive laws have hindered TGD research and services for decades, affecting global health at large. HIV will not successfully be controlled as long as people markedly vulnerable to HIV, as TGD people are, remain excluded. We support reaching the UNAIDS top-line target for 2025, aiming for "less than 10% of countries [having] punitive legal and policy environments that deny or limit access to services."

Vision

- A global systematic analysis of gaps in data from TGD-relevant health programs and prevention research.
- Research that addresses structural barriers that limit access to prevention strategies and the research process.
- Reaching the UNAIDS top-line target for 2025, aiming for "less than 10% of countries [have] punitive legal and policy environments that deny or limit access to services."

ROLE OF GENDER-AFFIRMING HORMONE THERAPY (GAHT)

- Hormone-associated HIV acquisition risks
- Hormones and ARVs: Treatment
- Hormone and ARVs: PrEP
- What about on-demand PrEP?
- Integrate gender-affirming hormone therapy (GAHT)

Hormone-associated HIV acquisition risks

Some TGD people use gender-affirming hormone therapy and/or surgical interventions to more closely align their bodies with their gender identity. While broadly safe, GAHT requires some monitoring. For example, trans people assigned female sex at birth taking testosterone may experience vaginal atrophy, posing a potential HIV risk to degenerated genital tissue.[20] Thinning tissue, tied to hormone use, might also affect rectal and penile mucosae. There's reason to believe that use of progestins for gender-affirming hormone therapy could increase HIV risk in trans women[21], as it is implicated in contributing to increased HIV risk in cis women.[22] Hormone-mediated changes to the genital tract could also increase the likelihood of other sexually transmitted diseases.[23] We believe dedicated research is needed to address the knowledge gap in hormone-associated HIV susceptibility.

Vision

- The HIV prevention field studies how hormones might affect HIV susceptibility.

Hormones and ARVs: Treatment

It's necessary to understand the potential drug-drug interactions between hormones and HIV medications; the latter improve health outcomes for people living with HIV and can reduce the risk of transmission to sexual partners. International antiretroviral guidelines such as WHO's *Update of recommendations on first- and second-line antiretroviral regimens* suggest first-line agents for HIV treatment generally do not have a significant effect on gender-affirming hormone levels or vice versa. However, pharmacokinetic studies have shown that certain antiretrovirals (ARVs) such as protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and cobicistat, a cytochrome P450 3A inhibitor (marketed as Tybost), interact with ethinyl estradiol, the key estrogen component of many oral contraceptives. In trans women, it's unknown if such interactions can increase or decrease ARV or hormone levels, potentially resulting in loss of virologic suppression or inadequate feminization. Few studies to date have interrogated the interactions between antiretroviral therapy (ART) and the types and doses of estrogens and androgen blockers found in feminizing regimens.

We believe there is a need to further study the drug-drug interactions between hormone therapies and ART to help determine how each may influence the effectiveness of the other. Additional research is needed on hormone therapy, gender-affirming care and the long-term health outcomes of TGD people living with HIV. As more specifics of HIV treatment for TGD people become available, trans health guidelines need to be updated. The potential for drug-drug interactions between HIV drugs and gender-affirming treatments hold significant implications for trans people living with HIV. Given the high burden of HIV among TGD people, these interactions should receive focused scientific inquiry.

Vision

- Continued study of drug-drug interactions between hormone therapies and antiretroviral therapy to help determine how each may influence the effectiveness of the other.
- Additional research done on hormone therapy and gender-affirming care and the long-term health outcomes of TGD people living with HIV.
- Trans health guidelines are updated in response to any relevant findings.

Hormone and ARVs: PrEP

Likewise, the potential for drug-drug interactions (DDI) between HIV drugs and gender-affirming treatments hold significant implications for trans people taking PrEP. Uncertainty around DDI may discourage TGD people from using PrEP or fuel provider hesitancy in educating patients or prescribing PrEP. However, the data increasingly show that PrEP is indeed effective when combined with GAHT and importantly, that hormone levels are not altered with PrEP (see table on page 14).

Although there is increasing data available regarding the pharmacokinetics of F/TDF (Truvada) showing that hormones are stable with PrEP use among trans women, limited data exist for trans men and trans adolescents. We believe this lack of information inhibits the acceptance of PrEP among AFAB trans people and should be addressed by research and communicated appropriately as more data becomes available.

Specifically, a handful of studies have found that oral PrEP with F/TDF does not lower hormone (estradiol or testosterone) levels in blood. But conversely, some studies show estrogen can lower the F/TDF PrEP drug levels in plasma and rectal tissue.[24, 25, 26] The lowering mechanism is not clear. But, importantly, evidence increasingly shows that a drop in PrEP drug levels is not enough to weaken PrEP's protection. In other words, the lower drug levels are not clinically significant.

Two more studies released this year at the Conference on Retroviruses and Opportunistic Infections affirmed that PrEP with GAHT is safe and effective: One showed that PrEP did not lower GAHT in young trans people taking testosterone or estrogen. The other showed that while intracellular levels of PrEP drugs were lower in trans women than trans men, they were still well within the range of levels seen in similar studies of directly observed therapy with PrEP drugs in cisgender people.[27, 28]

We believe that all new PrEP compounds in development should continue to undergo DDI studies with feminizing and masculinizing hormones. These pharmacokinetic studies should assess different hormones, whose use varies across regions. Specifically, studies should include TGD people taking testosterone with possible frontal/vaginal atrophy, such as the pending iMACT trial in Thailand.[29] Other studies of drug levels should include neovaginal and neophallus tissues, as well as rectal tissues after douching (which can cause micro-abrasions). This research should inform national guidelines on PrEP along with requirements for specialized provider qualifications for care.

Vision

- All new PrEP compounds in development undergo drug-drug interaction studies with feminizing and masculinizing hormones. These pharmacokinetic studies look into different hormones, whose use varies across regions.

What about on-demand PrEP?

A clear data gap exists around "on-demand" PrEP for trans people on GAHT. Currently, studies indicate that cis women must take daily oral PrEP in order to reach and retain protective HIV drug levels—a recommendation extended to others who may acquire HIV from insertive frontal/vaginal sex. Yet some regulatory authorities have approved on demand oral PrEP—to be taken around the time of sex (before and after)—as an alternative to daily oral PrEP for some populations. On-demand is only for cis men exposed to HIV acquisition through anal sex. Until there is data about the influence of hormone therapy on the efficacy of on-demand PrEP regimens, it will remain unclear if on-demand PrEP could be used by TGD individuals taking hormones.

Vision

- Research determines efficacy of on-demand oral PrEP for trans people on GAHT.

Table: Drug-drug interactions between PrEP and gender-affirming hormone therapies (GAHT)

The studies are listed in chronological order, depicting the mounting evidence over time that daily oral PrEP with GAHT is safe and effective and neither influences the effectiveness of the other. There's a need for continued drug-drug interaction studies as new HIV prevention products are developed.

Study name	Date completed	Population(s)	Drug-drug interaction	Result	Take home
Finding the Right Tenofovir/Emtricitabine Regimen for PrEP in Transgender Women (Johns Hopkins)	May 2018	TGW CGM	TGW: estradiol with oral daily F/TDF CGM: oral daily F/TDF	TVF and FTC are both lowered by one third in TGW blood plasma compared to drug levels in CGM; estradiol not affected.	It's unclear whether a reduction in PrEP drug levels in blood plasma correlates with a decrease in HIV protection. On-demand (2-1-1) PrEP regimens with estradiol may result in PrEP concentrations too low for HIV protection.
Does Sex Hormone Therapy Decrease NRTI Active Metabolite Formation in Mucosal Tissues? (UNC)	Oct 2018	TGW CGW: post-menopausal CGM	TGW: estradiol with daily oral F/TDF	TFV level in rectal tissue is 7-fold lower (decreasing with increased estradiol) compared to cisgender participants. No differences were observed in the blood.	The degree of feminization may be an important consideration. Additional studies are needed to determine if it negatively impacts PrEP's efficacy.
iFACT Study Drug-drug Interactions Between Feminizing Hormone Therapy and PrEP Among Transgender Women (TRCARC)	Jul 2019	TGW	Estradiol (EV/CPA) with daily oral F/TDF	TFV in blood plasma lowered by a small but statistically significant reduction of 13%-27%; estradiol not affected.	Further studies are warranted to determine if reductions in TFV negatively impact PrEP's efficacy.

Continued on the next page

Study name	Date completed	Population(s)	Drug-drug interaction	Result	Take home
iBrEATHe Study Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots (UCSF)	Aug 2020	TGM and TGW CGM&W as historic controls	TGM: testosterone with daily oral F/TDF TGW: estradiol with daily oral F/TDF	TFV-DP levels in dried blood spots were comparable across populations (but 23% lower in TGM compared to CGM) and expected to reach high protection levels; hormone levels were not affected.	First study to show F/TDF blood levels are stable across trans populations using gender-affirming hormones. Could have encouraging implications for on-demand (2-1-1) PrEP in trans people. The study also affirms earlier findings that hormone levels are not affected.
TDF/FTC in PBMC Among Transgender Adolescents Receiving Daily TDF/FTC (UC)	Mar 2021	Adolescent TGW and TGM	TGW and TGM: "stable dose of cross-sex hormone therapy" (not specified) with daily oral F/TDF	F/TDF levels in blood cells were lower in trans women than in trans men, yet were still well within the range of levels seen in similar studies in cisgender people.	Changes in F/TDF dosing are not necessary to achieve protective concentrations but for definitive answers, future studies should measure drug levels in tissue from mucous membranes.
Exogenous Hormone Pharmacokinetics in Transgender Adolescents Receiving Oral F/TDF (UC)	Mar 2021	Adolescent TGW and TGM	TGW: estradiol and spironolactone with daily oral F/TDF TGM: testosterone with daily oral TDF/FTC	Estradiol and testosterone serum levels were not significantly altered by F/TDF.	This study affirms earlier findings that hormone levels are not affected by F/TDF as PrEP.
Planned studies					
iFACT III (same as iFACT study above but with F/TAF) (IHRI)	2022	TGW	Estradiol with F/TDF or F/TAF	TBD	
iMACT Assessment of Drug-Drug Interactions Between Masculinizing Hormone Therapy and Antiretroviral Agents Concomitantly for Pre-exposure Prophylaxis Among Transgender Men (IHRI)	2022	TGM	Testosterone enanthate with F/TDF or F/ TAF	TBD	

CGM: cisgender men; **CGW:** cisgender women; **CM:** cis men; **CW:** cis women;
EV/CPA: estradiol valerate/cyproterone acetate; **F/TAF:** emtricitabine/tenofovir alafenamide fumarate;
TBD: to be determined; **F/TDF:** tenofovir disoproxil fumarate/emtricitabine; **TF:** transfeminine;
TFV: tenofovir; **TFV-DP:** tenofovir diphosphate; **TGM:** transgender men; **TGW:** transgender women;
TM: transmasculine

Integrate gender-affirming hormone therapy (GAHT)

Gender-affirming therapy in all its forms is a building block of TGD health and wellbeing, including HIV prevention, treatment and care in general. Improved uptake and retention are a direct result of GAHT as it enhances a TGD individual's self-worth and self-esteem. And yet, gender-affirming hormone therapy remains an unmet need and priority for many.[30, 31]

An intervention that delivers HIV prevention services with hormone therapy could significantly improve health outcomes, including a reduction in epidemic rates of HIV in TGD communities.[32] This is precisely the objective of HPTN 091[33] (see page 19 for details).

We believe GAHT should be a priority across the HIV care and prevention research continuum, from development and demonstration to delivery. As such, we believe the inclusion of transition-related medical services and trans-competent providers is integral to sexual and reproductive health and we support its scale-up as part of UNAIDS' 2025 AIDS targets.[34]

Vision

- GAHT integration is a priority across the HIV care and prevention research continuum from development and demonstration to delivery.
- Access to transition-related medical services and trans-competent knowledgeable providers is part of the SRH package, as stated in UNAIDS' 2025 AIDS Targets.

HIV PREVENTION RESEARCH

- Inclusion and trial design
- Oral PrEP
- Leadership and partnership
- Vaccines and Cure

Inclusion and trial design

Randomized clinical trials (RCT) and demonstration studies for HIV prevention to date have largely excluded TGD people or included trans women within a subset of sex workers or men who have sex with men.

The number of TGD participants in efficacy trials has historically been too small to derive statistically significant data, including trans-inclusive HIV prevention trials such as iPrEx and DISCOVER PrEP studies and the HVTN 505 vaccine study. The recent groundbreaking HPTN 083 study showing the effectiveness of cabotegravir as long-acting injectable PrEP is lauded for its 12 percent transfeminine (TGW) participation; it found similar trends of HIV, STIs and adherence between MSM and TGW participants. But no statistical inferences from this study could be drawn to conclude CAB-LA's efficacy in TGW due to the comparatively low numbers in the TGW cohort. The pharmacokinetic analysis is ongoing and could help determine if protection in TGW truly aligns with that in MSM.

The US NIAID's HIV Vaccine Trials Network has been exemplary in its Mosaico study (HVTN 706) inclusion criteria, specifically naming trans men, trans women, and gender non-conforming/nonbinary people. It's the first trial protocol to call for participant recruitment across the gender spectrum—with the exception of cis women who have their own trial (HVTN 705). All HIV prevention clinical trials should follow suit.

While praised for TGW inclusion, regrettably, HPTN 083 missed an opportunity to include transmasculine and other TGD people who may have been assigned female at birth but who identify as MSM and/or are in the same sexual networks and thus share similar heightened risk factors. The trial's exclusion further alienates the AFAB population. Confounding the situation is that ViiV, the manufacturer of long-acting cabotegravir injectable PrEP, seeks regulatory approval for cabotegravir for all populations—including AFAB trans people. This leaves providers and potential transmasculine PrEP users to extrapolate the possible implications of this new, powerful HIV prevention option and how it might affect the HIV risk, safety and hormone levels among trans masculine people and others who are AFAB.

Setting aside the oft-made but unproven assumption of lower HIV prevalence and risk in transmasculine people, HPTN missed an opportunity to improve access to sexual healthcare services to an AFAB cohort, gather missing data, challenge stereotypical assumptions about their sexual practices and reduce stigma and discrimination against this community.

We believe research should both improve TGD inclusion in randomized clinical trials and test for differences in trial participant sub-groups. If TGD enrollment numbers are indeed too low to allow for statistically significant sub-analyses, enrollment data should at the very least be acknowledged and reported so that researchers can learn more about the barriers to inclusion. Where measurable differences among subgroups might be expected, research should be extended with small, targeted studies.

Comparative or bridging studies or pharmacologic assessments can be implemented when TGD persons are poorly represented in RCT study populations. These approaches can provide important additional information, as can implementation studies.

UNAIDS/WHO's newly updated *Ethical considerations in HIV prevention trials* guidance recognizes the need for fair and inclusion criteria for study populations, calls for gender diversity, and states that arbitrary exclusion should be avoided:

> *Guidance Point 5: Researchers, sponsors and research ethics committees must recognize gender diversity in participating communities, and pay adequate attention to the distinct needs and contexts of individuals of all gender identities and expressions. Researchers and sponsors should include gender-diverse groups in trials in order to establish the safety, efficacy and/or effectiveness of interventions for these groups . . . arbitrary exclusion can result in trial results being less impactful as they exclude the people who would most benefit from them or exacerbate health disparities and may impact the roll-out of effective products to at-risk individuals and groups.*

We believe the UNAIDS/WHO's guidance on enrollment criteria—being inclusive of all gender identities—should be adapted to local contexts with the involvement of trans people, as put forth in the statement *Transgender HIV research: nothing about us without us*.[35] Furthermore, we believe HIV research should make it clear if and how TGD people were included and how gender was defined by study protocol teams and communicated to potential participants. Gender identities should be adapted to local contexts with the involvement of trans people that takes into account the usefulness of cultural terms such as *travesti, kathoey, waria, hijra*, among many others. Data should be analyzed by gender categories that reflect specific cultural definitions.

We also believe all publications and conference abstracts reporting on clinical trials should reveal all collected data, including participants' gender and sex assigned at birth (assessed using best practices), as legislated by the US 21st Century Cures Act and the NIH Revitalization Act of 1993.[36, 37] If not available, studies should articulate the reasons for such omissions as part of the limitations of the research.

Vision

- Research improves TGD inclusion in RCTs and includes trial participant subgroups. If TGD enrollment numbers are too low to allow for statistically significant sub-analyses, enrollment data are acknowledged and reported.
- The recommendation from the UNAIDS/WHO guidance document on *Ethical considerations in HIV prevention trials* for the inclusion of all gender identities is adapted to local contexts with the involvement of trans people.
- HIV research reports if and how TGD people were included and how gender was defined by study protocol teams and communicated to potential participants.
- Publications and conference abstracts on clinical trials report all collected data, including those on participants' gender and sex assigned at birth (assessed using best practices). If not available, the reasons for these omissions are articulated as part of the limitations of the research.

Oral PrEP

WHO has recommended the use of PrEP for HIV prevention among all people at risk of HIV, yet most PrEP research has historically lacked significant or specific inclusion of TGD people.

For example, as noted in the HPTN 091 protocol:

> *"As of December 2018, only four of more than 37 US and international PrEP demonstration projects that include TGW [transgender women] are tailored specifically for transgender people; all others include TGW within a subset of MSM or sex workers, and samples of TGW remain insufficient for inference. Three studies that are transgender-specific are all being conducted in California in the US; one demonstration pilot is being conducted in Lima, Peru."* [38]

As with other HIV prevention research projects, PrEP efficacy and demonstration studies have typically miscategorized TGW as cis women or men who have sex with men and in some cases conflated trans women into sex worker cohorts. Trans men and other AFAB trans people have been explicitly excluded from PrEP efficacy studies thus far, although some are receiving PrEP in clinical practice, often based on information about PrEP dosing and efficacy drawn from studies in cis men and cis women. We believe trans masculine people should be explicitly included (listed in the eligibility criteria) in PrEP trials and all other HIV prevention trials, and if not included, medical or physiological reasons must be provided.

A recent US study showed that almost a quarter of TGD people could benefit from PrEP, but only three percent were using it.[39] The ongoing HPTN 091 trial in the US and Brazil is lauded as a breakthrough study to assess the acceptability and feasibility of PrEP and other HIV prevention services delivered with gender-affirming hormone therapy (GAHT) amongst trans women. The study is the first in HPTN's 21-year history designed specifically and exclusively for trans women. Furthermore, its protocol team includes trans leadership. The study began enrolling in early 2021 after delays due to COVID.

Vision

- All clinical trials for HIV prevention explicitly list trans men and other AFAB trans people in the eligibility criteria, or provide valid medical or physiological reasons for not doing so.

Leadership and partnership

We believe HIV research should include TGD leadership, as seen in HPTN 091 and the Botshelo Ba Trans study, the first HIV prevalence survey conducted in trans women in South Africa.[40] Both studies include trans co-principal investigators and the latter had several trans-identified data collectors. Often TGD people recruited to work on such studies only engage with the data at the level of collection and have no decision-making power over data analysis and dissemination, or its influence on policies and programs. At the very least, TGD representatives must participate in study design and delivery through direct and meaningful inclusion in protocol teams or special advisory committees.

We believe local research sites looking to recruit TGD participants should be funded and supported to follow the Good Participatory Practice Guidelines[41] by engaging with the local LGBTQ community, including trans-led organizations. Information should be provided and maintained on how research protocols affect the trans community via community forums, among other methods.[42] The research site should be populated by employees who represent the community and can competently offer trauma-informed care. To start with, research sites would benefit by acknowledging the historic mistreatment of the trans community, as their inclusion attempts to rectify decades of exclusion of people taking exogenous hormones. Now is the time for the research entities to demonstrate responsibility and foster trustworthiness.

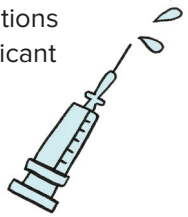
Training and educational opportunities in science and research for trans populations are needed—from basic laboratory research to clinical and translational research to policy formation. The US NIH, the largest funder of HIV research, recognizes underrepresented minorities for funding and training programs. Though trans identity may be considered for diversity-related funding, it's not currently explicitly included in the list of identities considered for more robust support with training. We believe this must change: All research entities offering training must proactively include TGD people to further develop their health-related science and research skills. TGD people must be trained, mentored, hired and promoted as research staff.

Vision

- TGD representatives participate in study design and delivery through direct and meaningful inclusion in protocol teams, special advisory committees and even as principal investigators.
- Local research sites are funded and supported to follow the Good Participatory Practice Guidelines and to engage with the local LGBTQ community, including trans-led organizations. The research site is populated by employees who represent the community.
- Research entities offering educational opportunities in science and research training must proactively include TGD people to further develop their health-related science and research skills. TGD people must be trained, mentored, hired and promoted as research staff.

Vaccines and Cure

Vaccines



As noted above, the Mosaico HIV vaccine trial is exceptional in its stated inclusion of populations across the trans-identity spectrum. It's too early to tell if its actual recruitment will yield significant findings as there are no specific recruitment targets. A recent study with trans women in New York City showed that a common barrier to their participation in HIV vaccine trials was "feelings of exclusion from biomedical research."[47] We believe and agree with the findings that trusting relationships with providers at research sites would facilitate study inclusion.

Cure

Structural impediments experienced by TGD people have led to challenges in maintaining HIV viral load suppression.[43] An HIV cure would potentially benefit them, but to date, only one trans women is known to have participated in such research.[44] In the study, *"I would really want to know that they had my back": Transgender women's perceptions of HIV cure-related research*, trans women were asked about their preferences for HIV cure strategies including latency reversing agents, gene modification and stem cell transplants and therapeutic vaccines. The greatest concern was voiced around vaccines due to negative past experiences. Overall, findings showed that most TGW have low medical literacy and education levels and their engagement with HIV cure research competes with more pressing personal priorities such as housing and financial security. We support the study's recommendation for broad education for trans people about HIV pathogenesis as well as HIV cure-related research with trans populations.[45]

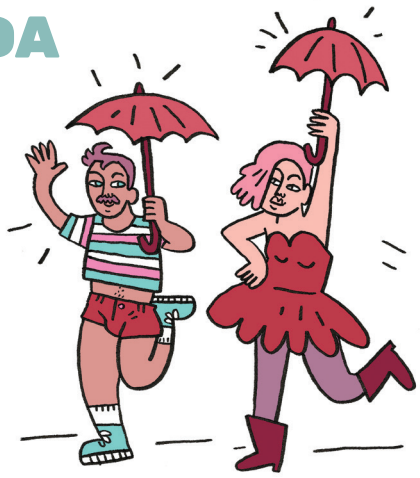
Trans people might even offer unique biologic traits for HIV cure research. One PrEP study looking at the drug-drug interactions between feminizing hormones and F/TDF found that estrogen receptors in rectal tissue could be acting as a deterrent to HIV transcription into the host genome. This led researchers to posit that "the influence of TGWs' unique hormonal environment on HIV replication may have important implications for HIV cure strategies."[46]

Vision

- Trans populations receive ongoing education about HIV pathogenesis as well as HIV cure-related research.
- Research sites facilitate inclusion and trusting relationships with trans communities.

A VISION FOR A TRANS AND GENDER DIVERSE RESEARCH AGENDA

- Lived TGD Experience
- Role of Gender-affirming Hormone Therapy (GAHT)
- HIV Prevention Research



Thanks in part to a 2015 Call to Action published in *JAIDS*[48] to center TGD people in HIV prevention, a baseline account exists of the small set of TGD-inclusive HIV studies at that time. This marked the beginning of HIV interventions proactively developed with TGD representatives and embraced by TGD communities. Yet six years later, TGD people's inclusion in HIV prevention research remains woefully inadequate, though there is a slow up-tick of trans-inclusive scientific literature in the field. While these new developments are welcome, we offer the following public recommendations to finally fulfill an inclusive HIV research future where TGD people flourish in all our diversity.

Please note, the visions listed below have been consolidated from the full manifesto: *No Data No More: Manifesto to Align HIV Prevention Research with Trans and Gender-Diverse Realities*.

Lived TGD Experience

We envision and believe in an HIV research agenda for trans and gender-diverse people that:

- Further identifies key drivers of HIV incidence—including biomedical, social and structural factors across countries and regions.
- Provides a diverse research and development agenda to fully consider the range of participants along the gender spectrum. Implementation research is particularly important to illustrate how to best apply clinical research findings across the diversity of TGD people for an increase in uptake of newly proven HIV interventions.
- Tracks epidemiological data on HIV incidence and prevalence to more accurately reflect the large and growing HIV acquisition rates among TGD populations, including in regions where there is little to no data, such as sub-Saharan Africa and Eastern Europe/Central Asia. Furthermore, The Global Fund and PEPFAR should use their leverage to include TGD populations in the IBBS survey. Recruiting trans-identified data collectors would also result in more accurate data capture.
- Supports best practices in language use, informed by TGD researchers, community advisory board members and trial participants, and adheres to the *NIAID HIV Language Guide* along with the *Guidance on the Use of Gender-Inclusive HIV Research Practices: Protocol Design, Data Collection, and Data Reporting*, drafted by NIAID's Cross-Network Transgender Working Group.
- Undertakes a global, and systematic analysis of the gaps in data from TGD-relevant health programs and prevention research as a necessary next step.
- Addresses structural barriers that limit TGD access to prevention strategies and the research process.
- Embraces the UNAIDS' top-line target for 2025 aiming for "less than 10% of countries [with] punitive legal and policy environments that deny or limit access to services."

Role of Gender-affirming Hormone Therapy (GAHT)

We envision and believe in an HIV research agenda for trans and gender diverse people that:

- Further explores how GAHT might affect HIV susceptibility.
- Further studies the drug-drug interactions between hormone therapies and antiretroviral therapy to help determine how each may influence the efficacy of the other, and to understand possible long-

term health outcomes, and updates trans health guidelines accordingly. Given the high burden of HIV among TGD people, these interactions should receive preferable, focused scientific inquiry.

- Sees all new PrEP compounds in development undergo drug-drug interaction studies with feminizing and masculinizing hormones to ensure any drug variances are not clinically significant. The pharmacokinetic studies should look into different hormones whose use varies in different regions. This research should inform national guidelines on PrEP.
- Addresses the urgent efficacy and safety questions of on-demand oral PrEP for trans people on GAHT.
- Prioritizes GAHT across the continuum of HIV care and prevention research, from development and demonstration to delivery. This agenda also supports the inclusion of transition-related medical services and trans-competent providers as integral to sexual and reproductive health services as part of UNAIDS' 2025 AIDS targets.

HIV Prevention Research

We envision and believe in an HIV research agenda for trans and gender-diverse people that:

- Improves upon TGD inclusion in randomized clinical trials while testing for differences among trial participant sub-groups. If TGD enrollment numbers are indeed too low to allow for statistically significant sub-analyses, RCT enrollment data should, at the very least, be acknowledged and reported so that researchers may learn more about barriers to inclusion.
- Adapts WHO's guidelines on enrollment criteria to local contexts, inclusive of all gender identities, with the involvement of trans people, as put forth in the statement *Transgender HIV research: nothing about us without us*.
- Reports if and how TGD people were included in clinical trials and how gender was defined by study protocol teams and communicated to potential participants.
- Reports on all collected data from clinical trials in all publications and conference abstracts, including those on participants' gender and sex assigned at birth (assessed using best practices), as legislated by the 21st Century Cures Act and The NIH Revitalization Act of 1993. If not available, articulate the reasons for these omissions as part of the limitations of the research.
- Explicitly lists trans men and other AFAB trans people in the eligibility criteria in all PrEP trials (and all other HIV prevention clinical trials), unless providing valid medical or physiological reasons for not doing so.
- Includes TGD leadership. At the very least, TGD representatives must participate in study design and delivery through direct and meaningful inclusion in protocol teams, special advisory committees and even as principal investigators.
- Funds and strengthens the capacity of local research sites that seek to recruit TGD participants to follow the Good Participatory Practice Guidelines. This necessarily involves engaging with the local LGBTQ community, including trans-led organizations. The research site should be populated by employees who represent the community and can engage competently through a framework of trauma-informed care.
- Offers educational opportunities in science and research training, proactively including TGD people to further develop their health-related science and research skills. TGD people must be trained, mentored, hired and promoted as research staff.
- Broadens education about HIV pathogenesis as well as HIV cure-related research with trans communities.
- Builds trusting relationships with providers at research sites to facilitate trans inclusion.

For more information on advocacy for TGD HIV prevention, go to avac.org/no-data-no-more

Footnotes

[1] Singh JA. Ethical issues to consider in the design of HIV prevention trials involving transgender people. J Acquir Immune Defic Syndr. 2016;72:S252–S255.
[2] Transgender people, WHO, 2021 (https://www.who.int/hiv/topics/transgender/about/en/).
[3] Prevailing against pandemics by putting people at the centre. Geneva: UNAIDS; 2020.
[4] Becasen J, Denard CL, Mullins MM, Higga DH, Sipe TA. Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis, 2006-2017. Am J Public Health. 2019;109(1):e1-e8.
[5] Kloek M, Van Noord L, Chabata ST, Musemburi S, De Vlas S et al. HIV prevalence and risk in male, trans male, and trans female sex workers in Zimbabwe. Abstract 879. Conference on Retroviruses and Opportunistic Infections. March 8-11, 2020.
[6] James SE, Herman J, LRankin S, Keisling M, Mottet L et al. The report of the 2015 U.S. transgender survey. Washington, DC: National Center for Transgender Equality; 2016.
[7] Siskind RL, Andrakik M, Karuna ST, Broder GB, Collins C et al. Engaging transgender people in NIH-funded HIV/AIDS clinical trials research. J Acquir Immune Defic Syndr. 2016; 72(Suppl 3): S243–S247.
[8] Ethical considerations in HIV prevention trials guidance document. Geneva: UNAIDS and WHO; 2021.
[9] MacCarthy S, Poteat T, Xia Z, Roque NL, Kim A et al. Current research gaps: a global systematic review of HIV and sexually transmissible infections among transgender populations. Sex Health. 2017;14(5):456-468.
[10] McFarland W, Wilson EC, Raymond HF. HIV prevalence, sexual partners, sexual behavior and HIV acquisition risk among trans men, San Francisco, 2014. AIDS Behav. 2017;21(12):3346-3352.
[11] Callander D, Wiggins J, Rosenberg S, Cornelisse VJ, Duck-Chong E. The 2018 Australian trans and gender diverse sexual health survey: report of findings. Sydney: The Kirby Institute, University of New South Wales; 2019.
[12] James SE, Herman J, LRankin S, Keisling M, Mottet L et al, The report of the 2015 U.S. transgender survey.
[13] A long way to go for LGBT equality, LGBTI II – survey data explorer. Vienna: European Union Agency for Fundamental Rights (FRA); 2020.
[14] James SE, Herman J, LRankin S, Keisling M, Mottet L et al, The report of the 2015 U.S. transgender survey.
[15] Deutsch MB, Gilden DV, Sevelius J, Keatley J, McMahan V et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEX trial. The Lancet. 2015;2(12);E512-E519.
[16] Mulatu M. HIV testing, seropositivity and linkage to care among transgender persons in CDC-funded testing sites in the United States, 2012-2013. 2015 National HIV Prevention Conference, 7 Dec 2015. Abstract 1559.
[17] The six categories were: male at birth and identifying as a transgender woman (M-MTF); male at birth and identifying as a woman (M-F); male at birth and identifying as other/unspecified (M-OTH); female at birth and identifying as a transgender man (F-FTM); female at birth and identifying as a man (F-M); female at birth and identifying as other/unspecified (F-OTH).
[18] NIAID HIV language guide, 2020 (https://www.hptn.org/resources/HIVLanguageGuide).
[19] Guidance on the use of gender-inclusive HIV research practices: protocol design, data collection, and data reporting, 2019 (https://daidslearningportal.niaid.nih.gov/local/pages/?id=17).
[20] Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2009;94:3132–3154.
[21] Radix A, Sevelius J, Deutsch MB. Transgender women, hormonal therapy and HIV treatment: a comprehensive review of the literature and recommendations for best practices. J Int AIDS Soc. 2016; 19(3 Suppl 2):20810.
[22] Haaland R, Swaims A, Evans-Strickfaden T, Lupo LD, Hart C. Progesterone increases are associated with HIV suseptability factors in women. Conference on Retroviruses and Opportunistic Infections, 23¬¬-26 Feb. Abstract 860.
[23] Transgender people and sexually transmitted infections (STIs). San Francisco: USCF; 2016 (https://transcare.ucsf.edu/guidelines/stis).
[24] Hiransuthikul A, Janamnuaysook R, Himmad K. Drug-drug interactions between feminizing hormone therapy and pre-exposure prophylaxis among transgender women: the iFACT study. J Int AIDS Soc. 2019 Jul; 22 (7): e25338.
[25] Cottrell ML, Prince HMA, Schauer AP. Decreased tenofovir diphosphate concentrations in a transgender female cohort: Implications for Human Immunodeficiency Virus Preexposure Prophylaxis. Clin Infect Dis. 2019 Nov 27;69(12):2201-2204.
[26] Shieh E, Marzinke MA, Fuchs EJ. Transgender women on oral HIV pre-exposure prophylaxis have significantly lower tenofovir and emtricitabine concentrations when also taking estrogen when compared to cisgender men. J Int AIDS Soc. 2019 Nov;22(11):e25405.
[27] Yager JL, Brooks K, Brothers J, Reirden D, Malhotra M et al. Exogenous hormone pharmacokinetics in transgender adolescents receiving oral TDF/FTC. Conference on Retroviruses and Opportunistic Infections, 6-10 March 2021. Abstract 366.
[28] Yager JL, Brooks K, Brothers J, Reirden D, Malhotra M et al. TFV-DP and FTC-TP in PBMC among transgender adolescents receiving daily TDF/FTC. Conference on Retroviruses and Opportunistic Infections, 6-10 March 2021. Abstract 367.
[29] ClinicalTrials.gov, NCT number: NCT04593680
[30] Reisner SL, Radix A, Deutsch MB. Integrated and gender-affirming transgender clinical care and research. J Acquir Immune Defic Syndr. 2016;72 Suppl 3(Suppl 3):S235-42.
[31] Sevelius J. Gender affirmation: a framework for conceptualizing risk behavior among transgender women of color. Sex Roles 68. 2013;675-689.
[32] Sevelius JM, Deutsch MB, Grant R. The future of PrEP among transgender women: the critical role of gender affirmation in research and clinical practices. Journal of the International AIDS Societ. 2016;19(7Suppl 6), 21105.
[33] HPTN 091 (https://www.hptn.org/sites/default/files/inline-files/HPTN_091_Protocol_Final_Version_1.0_13Apr2020.pdf).
[34] Prevailing against pandemics by putting people at the centre. Geneva: UNAIDS; 2020.
[35] Scheim AI, Appenroth MN et al. Transgender HIV research: nothing about us without us. Lancet HIV. 2019;6(9):e566-e567.
[36] 21st Century Cures Act, 42 USC 201, 2016 (https://www.nih.gov/research-training/medical-research-initiatives/cures)
[37] National Institutes of Health Revitalization Act of 1993 Subtitle B—Clinical Research Equity Regarding Women and Minorities (https://orwh.od.nih.gov/sites/orwh/files/docs/NIH-Revitalization-Act-1993.pdf).
[38] HPTN 091 (https://www.hptn.org/sites/default/files/inline-files/HPTN_091_Protocol_Final_Version_1.0_13Apr2020.pdf).
[39] Sevelius JM, Poteat T, Luhur WE, Winston E, Reisner SL et al. HIV testing and PrEP use in a national probability sample of sexually active transgender people in the United States. J Acquir Immune Defic Syndr. 2020;15.84(5):437-442.
[40] Cloete A, Wabiri N, Savva H, van der Merwe L, Simbayi L. The Botshelo Ba trans study: results of the first HIV prevalence survey conducted amongst transgender women (TGW) in South Africa. 9th South Africa AIDS Conference, Durban ICC, KwaZulu-Natal, 11-14 June 2019.
[41] Good Participatory Practice Guidelines. New York, Geneva: AVAC, UNAIDS; 2011 (https://www.avac.org/good-participatory-practice).
[42] Poteat T, Aqil A, Corbett D, Evans D, Dubé K. “I would really want to know that they had my back”: Transgender women’s perceptions of HIV cure-related research in the United States. PLOS ONE. 2020; Vol 15, No. 12.
[43] Bukowski LA, Chandler CJ, Creasy SL, Matthews DD, Friedman MR et al. Characterizing the HIV care continuum and identifying barriers and facilitators to HIV diagnosis and viral suppression among black transgender women in the United States. J Acquir Immune Defic Syndr. 2018;79(4):413–20.
[44] Curno MJ, Rossi S, Hodges-Mameletzis I, Johnston R, Price MA et al. A systematic review of the inclusion (or exclusion) of women in HIV research: from clinical studies of antiretrovirals and vaccines to cure strategies. J Acquir Immune Defic Syndr. 2016;71(2):181–8.
[45] Poteat T, Aqil A, Corbett D, Evans D, Dubé K, “I would really want to know that they had my back”: Transgender women’s perceptions of HIV cure-related research in the United States.
[46] Cottrell ML, Prince H, Schauer AP, Sykes C, Maffuid K et al. Decreased tenofovir diphosphate concentrations in a transgender female cohort: Implications for human immunodeficiency virus preexposure prophylaxis. Clin Infect Dis. 2019; 69(12): 2201–2204.
[47] Taylor NK, Young MR, Williams VD, Benitez J, Usher D et al. Assessing knowledge of HIV vaccines and biomedical prevention methods among transgender women in the New York City Tri-State Area. Transgend Health. 2020; 5(2):116-121.
[48] Mayer KH, Grinsztejn B, El-Sadr WM. Transgender people and HIV prevention: What we know and what we need to know, a call to action. J Acquir Immune Defic Syndr. 2016;72 Suppl 3(Suppl 3):S207-9.

About AVAC

AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit www.avac.org.

Illustrations: Rory Midhani