



NATIONAL CENTER FOR
INNOVATION IN HIV CARE

TRANSGENDER WOMEN AND PRE-EXPOSURE PROPHYLAXIS FOR HIV PREVENTION:

What We Know and What We Still Need to Know

By Samantha Marquez
and Sean Cahill

¹ amfAR: The Foundation for AIDS Research (2014). Trans population and HIV: Time to end the neglect. Retrieved from: <http://www.amfar.org/issue-brief-trans-populations-and-hiv-time-to-end-the-neglect/>

² Grant R, Lama J, Anderson P. et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*. 363:27; 2587-2599.

³ Baeten JM, Donnell D, Ndase P, et al. (2012, August 2). Antiretroviral prophylaxis for HIV-1 prevention among heterosexual men and women. *New England Journal of Medicine*; 367(5); 399-410.

⁴ U.S. Centers for Disease Control and Prevention (2013, July). Bangkok Tenofovir Study: PrEP for HIV prevention among people who inject drugs. <http://www.cdc.gov/nchstp/newsroom/docs/factsheets/archive/prep-idu-factsheet-508.pdf>

Executive Summary

Transgender women are at elevated risk of becoming infected with HIV.¹ Pre-exposure prophylaxis for HIV prevention (PrEP) is effective in reducing the risk of HIV infection among men who have sex with men (MSM),² heterosexual men and women,³ and people who inject drugs (PWID).⁴ Transgender women have been included in some clinical trials of PrEP, but only as a small minority of participants in studies with non-transgender MSM. Until an analysis of transgender data from two research studies was published in November 2015, no study had shown PrEP to be effective in reducing transgender women's HIV risk.⁵ Low adherence is likely a major factor in this general lack of demonstrated efficacy.⁶ However, the analysis of the transgender samples of two PrEP clinical research trials published in *The Lancet* in November 2015 demonstrated some efficacy among transgender women who were adherent to PrEP.⁷

Questions have been raised about the interaction between feminizing hormones and the medication currently approved for use as PrEP for HIV prevention—emtricitabine and tenofovir disoproxil fumarate (FTC-TDF). More research is needed to demonstrate that PrEP is effective for preventing HIV infection among transgender women engaging in anal intercourse with men. Research is also needed to better understand the interaction of PrEP and feminizing hormones, and any potential impact on the ability of PrEP to build up in sufficient concentrations in rectal tissue. In the meantime, PrEP is a prevention option that transgender women should consider with their medical providers. PrEP could prevent HIV infection in transgender women.

⁵ Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. *The Lancet*. DOI: [http://dx.doi.org/10.1016/S2352-3018\(15\)00206-4](http://dx.doi.org/10.1016/S2352-3018(15)00206-4).

⁶ Ibid, p. 6.

⁷ Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. *The Lancet*. DOI: [http://dx.doi.org/10.1016/S2352-3018\(15\)00206-4](http://dx.doi.org/10.1016/S2352-3018(15)00206-4).

⁸ amfAR: The Foundation for AIDS Research (2014). Trans population and HIV: Time to end the neglect. Retrieved from: <http://www.amfar.org/issue-brief-trans-populations-and-hiv-time-to-end-the-neglect/>



Background:

⁸ amfAR: The Foundation for AIDS Research (2014). Trans population and HIV: Time to end the neglect. Retrieved from: <http://www.amfar.org/issue-brief-trans-populations-and-hiv-time-to-end-the-neglect/>

⁹ Ibid.

¹⁰ Ibid.

¹¹ UNAIDS (2013). Global report: UNAIDS report on the global AIDS epidemic 2013. Retrieved from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Global_Report_2013_en_1.pdf

Transgender Women at Elevated Risk of HIV Infection

Transgender women are 49 times more likely to be HIV-infected than the general population, with 19.1% of transgender women worldwide living with HIV and 21.6% of transgender women in the United States living with HIV.⁸ Rates of HIV infection are even higher for racial and ethnic minority transgender women in the United States.⁹ Black transgender women are approximately three times more likely to be living with HIV than their White and Latina counterparts.¹⁰ Despite the increased risk of acquiring HIV, transgender women are an underserved population, not only in terms of HIV treatment, but also in terms of HIV prevention and medical care of their HIV disease. There are many factors that contribute to the high risk of HIV infection for transgender women, including sexual risk-taking, discrimination, violence, poverty, high unemployment, and housing instability.¹¹

Due to discrimination transgender women face from society, employment can be difficult. For many transgender women, sex work becomes a means of survival and/or a way to access otherwise prohibitively expensive gender affirming surgeries.¹² For this subgroup of transgender women engaging in sex work, HIV prevalence is two times higher than for transgender women not engaging in sex work.¹³ Transgender women also engage in receptive anal and vaginal intercourse without condoms at high rates, forms of intercourse that increase the risk of HIV.¹⁴

Transgender people experience widespread discrimination, including discrimination in health care.¹⁵ The National Transgender Discrimination Survey, which included more than 6,000 transgender and gender non-conforming individuals, reported that 50% of transgender individuals had

¹² Operario D, Soma T, Underhill K. (2008). Sex work and HIV status among transgender women: systematic review and meta-analysis. *J Acquir Immune Defic Syndr*, 48, 97-103.

¹³ amfAR: The Foundation for AIDS Research. (2014). Trans population and HIV: Time to end the neglect. Retrieved from: <http://www.amfar.org/issue-brief-trans-populations-and-hiv-time-to-end-the-neglect/>

¹⁴ Human Rights Campaign. (n.d.). Transgender people and HIV: What we know. Retrieved from: <http://www.hrc.org/resources/entry/transgender-people-and-hiv-what-we-know>

¹⁵ Reisner, S., Hughto, J., Dunham, E., Heflin, K., Begenyi, J., Coffey-Esquivel, J., & Cahill, S. (2015 September). Legal Protections in Public Accommodations Settings: A Critical Public Health Issue for Transgender and Gender-Nonconforming People. *Milbank Quarterly*, 93(3), 484-515.

“... transgender women are an underserved population, not only in terms of HIV treatment, but also in terms of HIV prevention and medical care of their HIV disease.”

to teach their healthcare providers about proper transgender care, and 28% of survey participants chose to postpone healthcare visits due to discrimination.¹⁶ Racial and ethnic minority transgender women experience discrimination based on their racial/ethnic identity as well as their gender identity. Poverty and limited access to health care and other resources are common experiences of transgender women, especially Black transgender women. Given these barriers, many transgender women, especially transgender women of color, do not access the most current HIV prevention methods, including pre-exposure prophylaxis for HIV prevention (PrEP).¹⁷

¹⁶ Grant, J. M., Mottet, L. A., & Tanis, J. (2011). *Injustice at every turn: A report of the national transgender discrimination survey*. Retrieved from: http://www.thetaskforce.org/static_html/downloads/reports/reports/ntds_full.pdf

¹⁷ Baeten JM, Donnell D, Ndase P, et al. (2012, August 2). Antiretroviral prophylaxis for HIV-1 prevention among heterosexual men and women. *New England Journal of Medicine*; 367(5); 399-410.

¹⁸ U.S. Centers for Disease Control and Prevention (2013, July). Bangkok Tenofovir Study: PrEP for HIV prevention among people who inject drugs. Retrieved from: <http://www.cdc.gov/nchhstp/newsroom/docs/factsheets/archive/prep-idu-factsheet-508.pdf>

¹⁹ Grant R, Lama J, Anderson P. et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*. 363:27; 2587-2599.

Biobehavioral HIV Prevention Strategies

Previous strategies to reduce new HIV infections have been centered on education regarding how HIV is transmitted, promoting safer sex practices—including using condoms and lubricant, and the use of clean needles while injecting drugs. There has also been a call to engage high-risk individuals more frequently with HIV and STD screening.¹⁸

Recently, those involved in HIV prevention methods have focused their attention on biobehavioral interventions—using anti-retroviral therapies to reduce an individual’s susceptibility to HIV infection if he or she is exposed. Pre-exposure chemoprophylaxis for HIV prevention (PrEP) first demonstrated efficacy in 2010, using emtricitabine and tenofovir disoproxil fumarate (FTC-TDF).^{19,20} This first PrEP study, iPrEx, included two populations: men who have sex with men (MSM) and transgender women. 2,499 participants were enrolled across

11 sites, all of whom were born male and reported having sex with men. Only 29, or 1.2%, identified as female at the time of the study. Of the entire sample in the double-blind, randomized, placebo-controlled trial, the participants who took oral FTC-TDF had a 44% lower rate of HIV infection than those who took the placebo. All were provided comprehensive HIV prevention services, including risk reduction counseling and HIV/STI testing. In a nested case-control study, among subjects with a detectable study-drug level (i.e. the most treatment adherent), there was a 92% lower rate of HIV infection than among those without a detectable level of FTC-TDF tested in the visit before seroconversion.²¹ Pharmacokinetic modeling indicates that with consistent medication adherence, PrEP could reduce HIV acquisition by up to 99%.²²

²⁰ Veloso, V. G., Mesquita, F., & Grinsztejn, B. (2015). Pre-exposure prophylaxis for men and transgender women who have sex with men in Brazil: Opportunities and challenges. *Journal of the International AIDS Society*, 18(3).

²¹ Grant R, Lama J, Anderson P. et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*, 363:27, 2587-2599.

²² National Institutes of Health. (2010). *Questions and answers. The iPrEx study: Pre-exposure prophylaxis as HIV prevention among men who have sex with men*. Retrieved from: <http://www.niaid.nih.gov/news/QA/Pages/iPrExQA.aspx>



The iPrEx study was the first to show that PrEP could significantly decrease an individual's risk of HIV infection. Subsequent studies showed that PrEP could also be effective with heterosexual men and women,^{23,24} and people who inject drugs.²⁵ Since 2010, PrEP has revolutionized HIV prevention. In 2012, the Food and Drug Administration approved TDF-FTC for use as PrEP.²⁶

“When iPrEx was first reported in *The New England Journal of Medicine* in December 2010, the significant transgender participation in the study was not reported.”

²³ Baeten JM, Donnell D, Ndase P, et al. (2012, August 2). Antiretroviral prophylaxis for HIV-1 prevention among heterosexual men and women. *New England Journal of Medicine*; 367(5); 399-410.

²⁴ Centers for Disease Control and Prevention (no date; most likely 2011). TDF study of pre-exposure prophylaxis (PrEP) among heterosexual men and women in Botswana: Key facts. Retrieved from: <http://www.cdc.gov/hiv/prep/pdf/TDF2factsheet.pdf>.

²⁵ Centers for Disease Control and Prevention (2013, July). Bangkok Tenofovir Study: PrEP for HIV prevention among people who inject drugs. Retrieved from: <http://www.cdc.gov/nchhstp/newsroom/docs/factsheets/archive/prep-idu-factsheet-508.pdf>.

²⁶ Food and Drug Administration (2012). FDA approves first drug for reducing the risk of sexually acquired HIV infection. Retrieved from: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm>

Inclusion of Transgender Women in the iPrEx Study

When iPrEx was first reported in *The New England Journal of Medicine* in December 2010, the significant transgender participation in the study was not reported. A subsequent analysis of the iPrEx data presented at an International AIDS Society conference in Rome in July 2011 noted that nearly 14.6% of participants, some 366 individuals of the total 2,499 in the study, identified as “trans” or reported taking exogenous female hormones.²⁷ iPrEx Principle Investigator Robert Grant said in an interview published on YouTube June 19, 2015 that 366 participants in the iPrEx study described their current gender identity as female, said that they were transgender, and/or reported using feminizing hormones.²⁸ This finding that 14.6% of the iPrEx participants were transgender is much higher than the 1.2% who identified as female at the time of the study, which was originally reported in a December 2010 *New England Journal of Medicine* article.²⁹

The iPrEx study demonstrated drug efficacy among the overall sample, 85.4% of whom were cisgender (non-transgender) MSM. Among the transgender women sample (366 of the study’s 2499 participants), however, PrEP demonstrated no efficacy overall in preventing HIV among the subset who were considered transgender, with 11 new HIV infections among the transgender women sample taking TDF-FTC and 11 new infections among the group taking the placebo.³⁰ Grant, McMahan, Liu et al. stated in their presentation at the 2011 IAS conference that the lack of PrEP efficacy among transgender women might be the result of “hormonal effects on drug transport in the mucosa,” but also cited other possible factors, including chance, patterns of PrEP use (i.e. low adherence to daily oral PrEP), or sexual practices.³¹

²⁷ R. Grant, V. McMahan, A. Liu, J. Guanira, M. Casapia, J. Lama, T. Fernandez, V. Veloso, S. Buchbinder, S. Chariyalertsak, M. Schechter, L.-G. Bekker, K. Mayer, E. Kallas, P. Anderson, K.R. Amico, D. Glidden, for the iPrEx Study Team (2011, July). Completed observation of the randomized placebo-controlled phase of iPrEx: daily oral FTC/TDF pre-exposure HIV prophylaxis among men and trans women who have sex with men. International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention. Rome, Italy. WELBC04 - Oral Abstract Session. Retrieved from: <http://pag.ias2011.org/abstracts.aspx?aid=4800>.

²⁸ Dr. Bob Grant on transgender women and pre-exposure prophylaxis. Interview, June 19, 2015. <https://www.youtube.com/watch?v=08YEm7YcaIk>. Accessed October 22, 2015.

²⁹ Grant R, Lama J, Anderson P. et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*. 363:27; 2587-2599.

³⁰ Yang D, Chariyalertsak C, Wongthanee A, et al. (2013). Acceptability of pre-exposure prophylaxis among men who have sex with men and transgender women in Northern Thailand. *PLOS One*. 8(10): e76650. Citing Grant, McMahan, Liu et al., 2011.

³¹ Grant, McMahan, Liu et al., 2011.

Other PrEP Studies With Significant Inclusion of Transgender Women In Their Sample

The PrEP Open Label Extension (OLE) study enrolled 1,603 individuals from the iPrEx clinical trial and two other PrEP trials (the Adolescent Trials Network 082 study and the US Safety study). Some 175 of these individuals, or 10.9%, were transgender. All of the participants were offered PrEP. Ultimately 1,085 of the study's participants received PrEP, including 140 transgender women. Some 12.9% of the OLE participants who received PrEP were transgender women. The transgender participants in the OLE study had lower levels of tenofovir diphosphate in their blood than the non-transgender participants in the study. The authors of the study noted that:

The lower concentrations of tenofovir diphosphate among transgender women might be a result of lower adherence or different pharmacokinetics: more information is needed (panel).³²

³² Grant, R. M., Anderson, P. L., McMahan, V., Liu, A., Amico, K. R., Mehrotra, M., Hosek, S., Mosquero, C., Casapia, M., Montoya, O., Buchbinder, S., Veloso, V. G., Mayer, K., Charialertsak, S., Bekker, L., Kallas, E. G., Schechter, M., Guanira, J., Bushman, L., Burns, D. N., Rooney, J. F., & Gidden, D. V. (2014). Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: A cohort study. *The Lancet*, 14 (9), 820-829.

“Nearly half of the transgender women took oral medications regularly and nearly three-fourths of these participants feared that PrEP might interact with other medications, including female hormones.”

In a June 2015 interview, iPrEx OLE Principle Investigator Robert Grant said that this significant level of participation of transgender women in the iPrEx (14.6% of all participants) and iPrEx OLE studies (12.9%) demonstrates that transgender women are willing to take PrEP.

A study of PrEP acceptability among transgender women and MSM in Northern Thailand enrolled 131 MSM and 107 transgender women, meaning that the sample was comprised of 45% transgender women and 55% MSM. Nearly half of the transgender women took oral medications regularly and nearly three-fourths of these participants feared that PrEP might interact with other medications, including female hormones.³³ Yang et al., the

authors of the Thai acceptability study, concluded that the high prevalence of regular medication use among transgender women could be a resiliency factor that could be leveraged into improved adherence for PrEP. They also noted the critical importance of addressing transgender women’s concerns related to whether or not there are any interactions between PrEP and feminizing hormones in public education and outreach campaigns to educate transgender women about PrEP.³⁴ At this point we don’t know if there are such interactions. More research is needed to know for sure. What we can do now is present all the information we have to transgender women at risk for HIV infection and ask them to discuss whether or not to use PrEP with their health care provider.

³³ Yang, Chariyalertsak, Wongthanee, et al. (2013).

³⁴ Ibid.

A Recent Analysis of the Transgender Participants in iPrEx and iPrEx OLE

As this issue brief went to press (November 2015), a peer-reviewed article analyzing the experiences of the transgender participants in the iPrEx clinical trial was published in *The Lancet*.³⁵ This article reported a slightly lower number of transgender or gender variant participants than the earlier conference presentation: “29 (1%) identified as women, 296 (12%) identified as trans, and 14 (1%) identified as men but reported use of feminizing hormones, such that 339 (14%) reported one or more characteristics and are classified as transgender women for the purpose of this study.”³⁶ This unplanned exploratory analysis of the iPrEx data found 11 HIV infections among the transgender women who were randomized into the PrEP group and 10 HIV infections among those taking the placebo.³⁷

However, PrEP use in the subgroup of transgender persons with evidence of high medication adherence was protective; none of the transgender wom-

en who became infected in the iPrEx randomized, placebo-controlled trial had detectable drug at the visit where HIV infection was first detected.

Furthermore, among transgender women who participated in the post-trial open-label extension study (iPrEx OLE) where all participants were offered PrEP, quantitative analysis of drug exposure, measured in dried blood spots, revealed that seroconversion occurred only among transgender women having drug concentrations commensurate with using less than two tablets of emtricitabine plus tenofovir disoproxil fumarate per week on average. No HIV infections occurred among transgender women with drug levels consistent with taking 4 or more tablets per week.³⁸

The lack of protection against HIV infection among the 11 transgender women taking PrEP who seroconverted during the study “seems to be primarily a result of low adherence leading to low drug exposure, as measured by drug concentrations.”³⁹

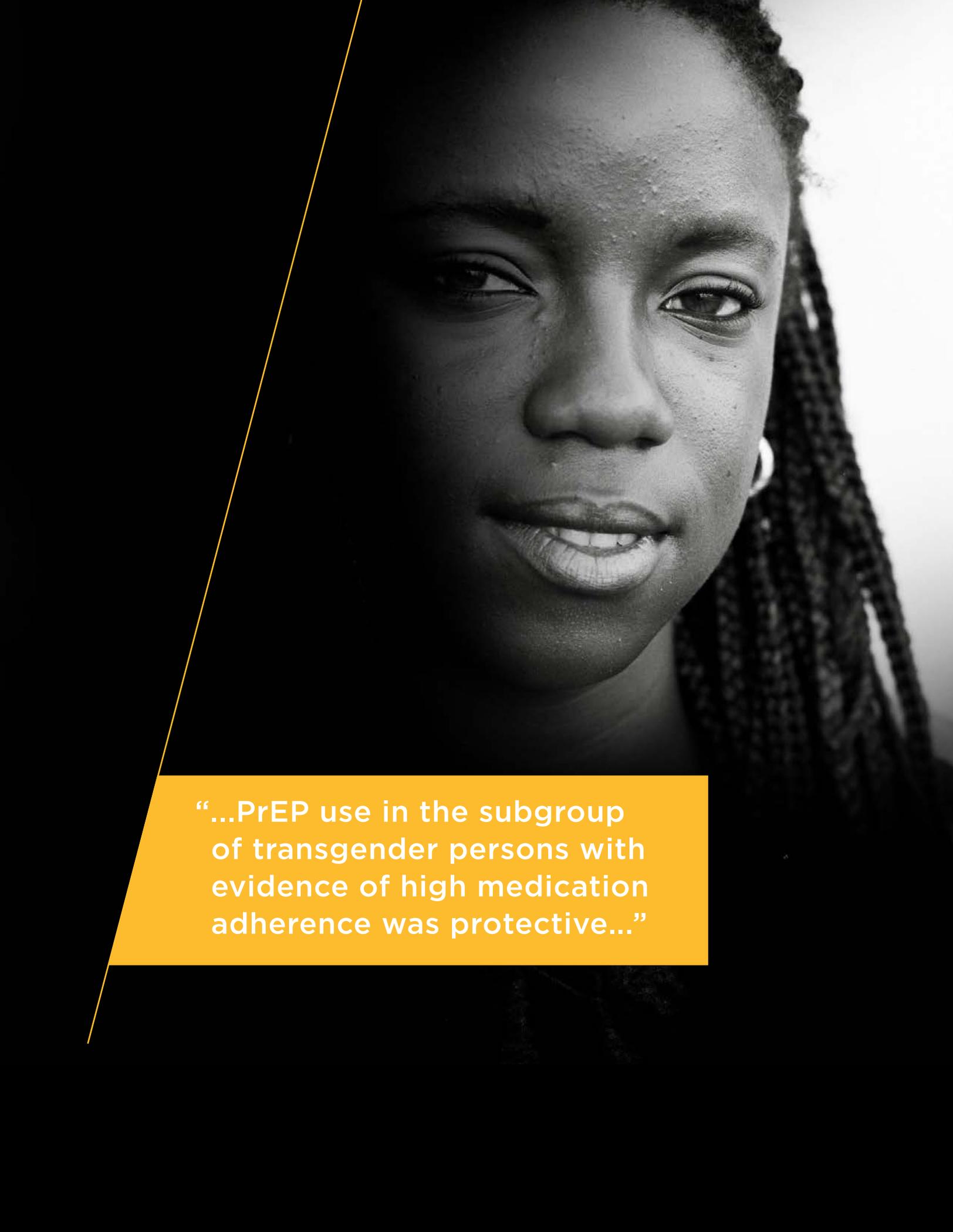
³⁵ Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. *The Lancet*. DOI: [http://dx.doi.org/10.1016/S2352-3018\(15\)00206-4](http://dx.doi.org/10.1016/S2352-3018(15)00206-4).

³⁶ Ibid, p. 1.

³⁷ Ibid, p. 1.

³⁸ Ibid, p. 5.

³⁹ Ibid, p. 6.



“...PrEP use in the subgroup of transgender persons with evidence of high medication adherence was protective...”

Feminizing Hormones and Antiretroviral Medications

Researchers should explore whether exogenous female hormones interfere with the effectiveness of PrEP. Low adherence is also most likely a major factor in PrEP's lack of efficacy with transgender women in the clinical trials to date that have included transgender women. Other researchers have suggested that the lower efficacy of PrEP in transgender women may be the result of lower rates of adherence due to more complicated employment, housing, and access to care factors.⁴⁰

In 2011 the Center of Excellence for Transgender Health at the University of California, San Francisco reviewed the possible impact of antiretroviral medications on cross-sex hormone therapy and determined that there was no scientific reason why the drugs would interact:

There is no evidence or clinical studies of potential drug interactions between different classes and combinations of antiretroviral medications (ARV) and cross-sex hormone therapy (csHT) used by transgender women for gender transition and feminization.⁴¹

⁴⁰ Escudero, D. J., Kerr, T., Operario, D., Socias, M. E., Sued, O., & Marshall, B. D. L. (2015). Inclusion of trans women in pre-exposure prophylaxis trials: A review. *AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV*, 27(5), 637-641.

⁴¹ University of California, San Francisco. (2011) Review of literature relating to possible drug interactions between antiretrovirals and estrogen therapy used for MTF gender transition. Retrieved from: <http://transhealth.ucsf.edu/trans?page=protocol-hormones-arvs>.

“...as nucleoside reverse-transcriptase inhibitors (NRTIs)—the umbrella term for the type of drugs used in PrEP—and estrogens/progestins are metabolized through different pathways, it is unlikely that any interactions could occur...”

These conclusions were drawn from several studies of potential interactions between antiretroviral medications and oral contraceptives (which contain estrogen and/or progestins).⁴² These studies showed that, as nucleoside reverse-transcriptase inhibitors (NRTIs)—the umbrella term for the type of drugs used in PrEP—and estrogens/progestins are metabolized through different pathways, it is unlikely that any interactions could occur.⁴³ It’s important to note that the hormone drug levels in oral contraceptives are much lower than the hormone drug levels in feminizing hormone therapy.

The UCSF analysis found that some protease inhibitors decrease blood levels of synthetic estrogen (ethinyl estradiol), while others cause an excess. UCSF notes that:

...the key clinical indication is to monitor patients for evidence of estrogen excess or deficiency...Clinical surveillance for estrogenic symptoms will likely improve compliance and retention with ART [anti-retroviral therapy] and csHT regimens...

⁴² Ibid.

⁴³ Ibid.



The UCSF analysis also addresses PrEP head on, indicating that there is no reason to think that using feminizing hormones interferes with the effectiveness of PrEP:

PrEP (Preexposure prophylaxis) uses the drug Truvada, which is a combination of antiretroviral drugs tenofovir disoproxil fumarate [TDF] and emtricitabine [FTC]. Both TDF and FTC are NRTIs, and do not impact P450 activity.⁴⁴ TDF is renally eliminated, subject to active tubular secretion, and does not appear to have an effect on hepatic function.⁴⁵ FTC is eliminated via plasma, and there are no studies that specifically measure interactions between FTC and hormonal contraceptives.⁴⁶

Because NRTIs and estrogens are metabolized differently, there is no reason to expect that PrEP and csHT would interact. However, no data currently exists on the interaction between OCP [oral contraceptives] or csHT [cross-sex hormone therapy] and PrEP.

⁴⁴ P450 is an enzyme that metabolizes estrogens as well as protease inhibitors and non-nucleoside reverse-transcriptase inhibitors.

⁴⁵ Kearney, B. P., Flaherty, J. F., & Shah, J. (2004). Tenofovir Disoproxil Fumarate: Clinical pharmacology and pharmacokinetics. *Clin Pharmacokinet*, 43 (9), 595-612.

⁴⁶ Wang, L. H., Begley, J., St. Claire, R. L., Harris, J., Wakeford, C., & Rousseau, F. S. (2004). Pharmacokinetic and pharmacodynamic characteristics of emtricitabine support its once daily dosing for the treatment of HIV infection. *AIDS Research and Human Retroviruses*, 20 (11), 1173-1182.



iPrEx and OLE Principle Investigator Robert Grant, M.D., cites other reasons to believe that feminizing hormones should not interfere with PrEP. In a June 2015 interview, Grant said:

We know that efficacy in women in the Partners PrEP study that was done in Africa was not different among women using female hormones for contraception versus women who were not using female hormones. So that's encouraging. We also know that there [were] no interactions between tenofovir, one of the components of Truvada, and oral contraception. But we do not yet have specific studies about drug-drug interactions between emtricitibine and female hormones or the interactions in transgender women who are using female hormones for feminization.⁴⁷

⁴⁷ Dr. Bob Grant on transgender women and pre-exposure prophylaxis. Interview, June 19, 2015. <https://www.youtube.com/watch?v=08YEm7YcaIk>. Accessed October 22, 2015.

Current Guidance Regarding PrEP and Transgender Women

The U.S. Centers for Disease Control and Prevention (CDC) released interim guidance for PrEP use among MSM in January, 2011. The interim guidance stated that, until safety and efficacy are shown among heterosexuals and people who inject drugs (PWID), “PrEP should be considered only for MSM.”⁴⁸ Subsequent studies showing PrEP efficacy among heterosexuals and PWID led to updated guidance that explicitly recommends that PrEP be considered a prevention option for high-risk individuals who are heterosexual and/or PWID.⁴⁹ There is currently no specific guidance regarding PrEP use with transgender women.⁵⁰

In the absence of data demonstrating the effectiveness of PrEP among transgender females, the federal clinical practice guidelines will not make any rec-

ommendation for (or against) indications for PrEP use. Until *The Lancet* article published in November 2015, research had demonstrated PrEP’s effectiveness for men who have anal sex with men, and for men and women who have vaginal sex, but not specifically for transgender women having anal sex. It is possible that the analysis published in *The Lancet* in November 2015 and described above may change this.

In 2012, the World Health Organization (WHO) released recommendations for the use of PrEP with MSM and transgender women who are at high risk of HIV. The guidelines state that PrEP “may be considered as a possible additional intervention” to prevent HIV among MSM and transgender women who have sex with men.⁵¹

⁴⁸ Centers for Disease Control and Prevention (2011, January 28). Interim guidance: Preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR. 60(03);65-68. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a1.htm?s_cid=mm6003a1_w. Accessed October 24, 2011.

⁴⁹ Centers for Disease Control and Prevention (2014). United States Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2014: A clinical practice guideline. Retrieved from: http://www.cdc.gov/hiv/pdf/prep_guidelines2014.pdf

⁵⁰ Ibid.

⁵¹ The World Health Organization (2012). Guidance on pre-exposure oral prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV: Recommendations for use in the context of demonstration projects. Retrieved from: <http://apps.who.int/iris/bitstream/10665/75188/1/9789241503884eng.pdf?ua=1>.

“There is currently no specific CDC guidance regarding PrEP use with transgender women.”

The WHO judged the quality of the evidence in support of PrEP to be “high,” and noted that “studies conducted among MSM-TG [transgender women] in several settings...generally supported the availability of PrEP.”⁵²

In September of 2015, the WHO issued updated guidelines for the use of PrEP.⁵³ The new guidelines state that PrEP should be “considered for people at substantial risk of acquiring HIV rather than lim-

iting the recommendation to specific populations.” “Substantial risk” in this context is defined as an HIV incidence rate greater than 2 per 100 person-years. Though this recommendation increases the likelihood that healthcare providers will offer PrEP to their transgender women patients who are at high risk for HIV infection, the guidelines also note that more information about PrEP in transgender populations is needed.⁵⁴

⁵² Ibid.

⁵³ The World Health Organization (2015). Treat all people living with HIV, offer antiretrovirals as additional prevention choice for people at substantial risk. Retrieved from: <http://www.who.int/mediacentre/news/releases/2015/hiv-treat-all-recommendation/en/>

⁵⁴ The World Health Organization (2015). Guideline on when to start antiretroviral therapy and pre-exposure prophylaxis for HIV.

Recommendations

Further research should be done to determine if PrEP interacts with cross-sex hormone therapy and decreases the efficacy of PrEP.

While the methodology of the 2011 Center of Excellence for Transgender Health/UCSF review was sound, further research on interactions between antiretroviral medications and cross-sex hormone therapy would clarify whether there is any interaction between the two classes of drugs.⁵⁵

As PrEP research continues and the drug is evaluated for continued effectiveness, researchers should include more transgender women in study populations.

Of all the completed clinical research studies done on PrEP in the past five years, only iPrEx and OLE were confirmed to have enrolled transgender women. There is still doubt in the minds of some scientists and public health professionals that PrEP will be effective for transgender women. The only way to draw conclusions is through further research. For this reason, it is imperative that future PrEP trials include a larger transgender

⁵⁵ Human Rights Campaign. (n.d.). Transgender people and HIV: What we know. Retrieved from: <http://www.hrc.org/resources/entry/transgender-people-and-hiv-what-we-know>



female population within the sample. Robert Grant, PI of the iPrEx study, recommends that transgender women be studied separately from gay and bisexual men and other MSM. Leading researchers at the Center of Excellence for Transgender Health—including Madeline Deutsch, Jae Sevelius, and Joanne Keatley—joined Grant to make similar recommendations in the November 2015 *Lancet* article:

Studies of PrEP use in transgender women populations should be designed and tailored specifically for this population, rather than adapted from or subsumed into studies of MSM.⁵⁶

⁵⁶ Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). *The Lancet*. DOI: [http://dx.doi.org/10.1016/S2352-3018\(15\)00206-4](http://dx.doi.org/10.1016/S2352-3018(15)00206-4)

Research studies with targeted recruitment of transgender women should be used when testing all new forms of HIV prevention and/or treatment, as they are a population at high risk for HIV acquisition.

It is important that transgender women be included in research, not just in the context of PrEP efficacy, but also when other methods of HIV prevention and treatment are being analyzed. Although both MSM and transgender women may engage in unprotected receptive anal intercourse, the two populations have different needs—needs that are not addressed effectively when they are not a major, central focus of research. By targeting studies and study recruitment at transgender women, we will have a better understanding of the effects of the intervention on the population, as well as their unique barriers to access and adherence.

Guidelines and recommendations for the use of PrEP should include information about the cost-effectiveness of using the intervention with each population.

As transgender women can be difficult to engage not only in research studies, but also in medical care, it is important that HIV prevention methods outlined by organizations like the CDC and WHO include information about the most effective ways of reaching each population that presents a high risk of HIV infection and ensuring they can access these new biobehavioral prevention approaches through health insurance and access to culturally competent, affirming care.

This publication was produced by the National Center for Innovation in HIV Care, The Fenway Institute, Fenway Health with funding under cooperative agreement #U69HA27176 from the U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau. The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of HHS or HRSA.

“...it is imperative that future PrEP trials include a larger transgender female population within the sample.”

Transgender women should consider using PrEP as a prevention approach that could reduce their chance of becoming infected with HIV, and providers should discuss PrEP with their transgender female patients.

While more research is needed, in the meantime, transgender women should discuss PrEP with their medical provider as an option that could help them stay HIV-negative. Providers should be prepared to discuss PrEP as an option with their transgender female patients, weigh the risks and benefits in each case, problem solve any PrEP access issues if applicable, and emphasize the importance of adherence in PrEP's efficacy.

Authors:

Samantha Marquez

Samantha Marquez is a Research Fellow at the Fenway Institute. She is currently pursuing an MSW degree at Wheelock College.

Sean Cahill, PhD

Sean Cahill, PhD, is Director of Health Policy Research at the Fenway Institute, Director of Curriculum and Policy at the National Center for Innovation in HIV Care, and Visiting Scholar at the School of Public Policy and Urban Affairs at Northeastern University.

Reviewers:

Emilia Dunham, The Fenway Institute

Ryan Kruis, MSW, The Fenway Institute

Harvey Makadon, MD, The Fenway Institute

Designer:

Elizabeth Gruber

This publication was produced by the National Center for Innovation in HIV Care, The Fenway Institute, Fenway Health with funding under cooperative agreement #U69HA27176 from the U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau. The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of HHS or HRSA.



 **NATIONAL CENTER FOR
INNOVATION IN HIV CARE**

1340 Boylston Street, 8th Floor
Boston, MA 02215
617.927.6028 | nationalhivcenter.org
nationalhivcenter@fenwayhealth.org