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Inclusion of Trans Women in Pre-Exposure Phrophylaxis (PrEP): A Review

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Abstract

Trans women are at high-risk of HIV infection. We conducted a review to determine the extent to which trans women were eligible for inclusion in and enrolled into pre-exposure prophylaxis (PrEP) efficacy trials. Out of seven trials analyzing PrEP efficacy, we found that trans women comprised only 1.2% of one trial, and 0.2% of total trial enrollments. Although an additional PrEP trial to determine efficacy among trans women may not be warranted, further research is needed to determine the effectiveness of PrEP in this marginalized population, through observational and feasibility studies. These studies should focus on unique barriers that trans women may experience while obtaining access to PrEP, such as gender discrimination, transphobia, and violence.

Keywords

transgender; trans women; PrEP; HIV; marginalized population

Background

In countries around the world, transgender women (trans women), are at high-risk of HIV infection. A 2013 meta-analysis found that trans women across fifteen countries had 49 times the odds of being infected with HIV, compared with all adults of reproductive age (Baral et al., 2013). Recent studies demonstrate that trans women are less likely to be enrolled in antiretroviral therapy (ART) than non-transgender persons (Melendez et al.,

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2006), and among those on therapy, are less likely to be adherent to ART (Sevelius, Carrico, & Johnson, 2010). Highlighting this leaking treatment cascade, a 2014 study in San Francisco estimated that only 65% of trans women infected with HIV were on ART, the lowest ART coverage of any gender or high-risk group in San Francisco (San Francisco Department of Health, 2012; Santos et al., 2014).

In addition to risks from unprotected sexual exposures, substance use, sex work, depression, unstable housing, and high levels of victimization and violence are commonly reported by trans women (Duncan, Hatzenbuehler, & Johnson, 2014; Herbst et al., 2008; Hoffman, 2014; Santos et al., 2014), indicating the potential for multiple, concurrent HIV risks and underlying vulnerabilities. Structural forms of discrimination may contribute to these risk factors, possibly leading to poor outcomes such as unemployment or underemployment, and also create barriers to HIV preventive and other health services. For many of the same reasons, trans women may lack access to gender sensitive health services. Given this context, a biomedical intervention such as pre-exposure prophylaxis (PrEP), which can address risks from multiple types of exposure (i.e., sexual or parenteral), may be integral for comprehensive prevention packages. Due to the greatly elevated risk of HIV infection among this population worldwide, and the multi-level factors highlighted here, which may hinder access to regular preventive HIV services, biomedical intervention strategies may be particularly effective.

PrEP has been found to be efficacious in preventing HIV acquisition among several high-risk populations, including men who have sex with men (MSM) (Grant et al., 2010), serodiscordant heterosexual couples (Baeten et al., 2012), and people who inject drugs (Choopanya et al., 2013). Although trial results have spurred recommendations for PrEP among these high-risk groups (Centers for Disease Control and Prevention, 2011, 2012, 2013), research involving (and specific recommendations for) trans women have been largely absent, despite the elevated risk for HIV within these communities. A notable exception are the World Health Organization (WHO) PrEP guidelines, which do include trans women in the context of demonstration projects (2012).

Although results and enrollment characteristics from completed oral PrEP trials have been described elsewhere (van der Straten, Van Damme, Haberer, & Bangsberg, 2012), we have not been able to identify a summary of the inclusion and enrollment of trans women in these studies. To inform future research examining the use of PrEP among communities of trans women, we conducted a review to assess the extent to which trans women have been eligible for and included in previously conducted oral PrEP efficacy trials. We also sought to determine the potential for sub-groups analyses in this population.

Methods

We reviewed all published results from randomized controlled trials that included an analysis of oral PrEP (i.e., tenofovir or tenofovir/emtricitabine), as identified by a non-systematic literature review and from reference lists of summary publications (Baeten, Haberer, Liu, & Sista, 2013; Molina et al., 2013; van der Straten et al., 2012). Our results our limited to English-language publications. PubMed and Medline searches, and well as

reviews of HIV/AIDS conference abstract databases (e.g., IAS and CROI) were also conducted using search terms that included “transgender,” “trans women,” PrEP,” and “pre-exposure prophylaxis.” Studies examining the efficacy of only non-oral PrEP formulations (i.e., topical) were excluded. The online clinical trial registry, http://www.clinicaltrials.gov, was used where appropriate to supplement published information. For in-progress or halted trials, available descriptions of study enrollment criteria were used to determine inclusion of trans women in these studies. When information was not available, attempts were made to contact the study’s corresponding author.

Results

We identified seven trials that analyzed the efficacy of oral PrEP for HIV prevention. Three trials, FEM-PrEP (Van Damme et al., 2012), TFV Phase II (Peterson et al., 2007), and VOICE (Microbicides Trials Network, 2011), enrolled cisgender women (cisgender is defined here as those who identify with the gender they were assigned at birth). Two trials reported enrollment of MSM: iPrEX (Grant et al., 2010), and the Bangkok Tenofovir Study (Choopanya et al., 2013). Two other trials, PartnersPrEP (Baeten et al., 2012), and TDF2 (Thigpen et al., 2012), were designed specifically to analyze PrEP efficacy in preventing heterosexual transmission of HIV. One trial, the Bangkok Tenofovir Study, was designed to enroll people who inject drugs (PWID). According to published results, and a review of information available on http://www.clinicaltrials.gov, FEM-PrEP, TFV Phase II, and VOICE were the only trials which explicitly excluded the enrollment of trans women. One attempt was made to confirm enrollment and analytic data from a study author; however this was unsuccessful, and we instead relied on existing published information for our assessment.

Upon further review of trial data, only one study, iPrEx, was confirmed to enroll transgender people, and enrollment was limited to trans women. iPrEx was a multinational PrEP trial involving 2,499 MSM and trans women, among whom 29 (1.2%) self-identified as transgender at baseline (*Table 1*). Additionally, no trial reported enrollment of transgender men. Based on the small number of trans women identified in these trials, sub-group efficacy analysis was not deemed feasible.

Discussion

The results of this review demonstrate that inclusion of trans women in PrEP trials has been minimal. There are several potential explanations for a lack of transgender enrollment in these trials. The relatively small size of transgender communities throughout the world—possibly 1 in 500 persons worldwide according to a 2007 estimate (Olyslager & Conway, 2007)—may lead investigators to believe that the application of PrEP to this population may be of lesser priority. Whether or not the application of PrEP is perceived to be a lesser priority than other high-risk groups (i.e., MSM, commercial sex workers, serodiscordant couples, PWID), the potential impact of PrEP on incidence among trans women remains significant, given the very high risk for HIV within this population (Baral et al., 2013).

Finally, the difficulty of recruiting members of a low prevalence group may present a significant challenge to researchers. Among trials for which trans women were theoretically eligible, specific protocols to identify and recruit trans women did not appear to be in place, or could not be identified (Baeten et al., 2012; Choopanya et al., 2013; Grant et al., 2010; Thigpen et al., 2012). Often, trans women are categorized alongside MSM, which may lead to difficulties in their recruitment, since studies not seeking trans women independent of MSM may be viewed negatively by trans women, or otherwise ignored. Also, the trial settings themselves may have affected potential recruitment, as many took place in countries with high levels of stigma and discrimination experienced by transgender persons, which may have severely limited the capacity to recruit transgender participants.

As the most fundamental aspect of improving transgender enrollment, use of evidence-based recruitment strategies for this population must be considered in future studies. Although a previous study assessing the use of long-chain peer referral to specifically recruit MSM and trans women has demonstrated only limited success, further efforts to determine effective recruitment strategies may yield different results (Coombs et al., 2014). It is likely that without protocol designed specifically to enhance participation of transwomen in PrEP research studies, or HIV prevention studies as a whole, minimal enrollment will persist, leading to continued difficulty applying results and subsequent clinical recommendations to this population. Closely related to the difficulties of recruiting trans women, trial investigators may have been concerned with statistical ‘noise’ that may be introduced by enrolling small numbers of trans women among a larger cisgender population. Moreover, without sufficient enrollment to perform subgroup analysis among trans women, either within an individual trial or pooled across trials, the perceived benefits may have been minimal. However, we note that recruitment of trans women in PrEP studies may allow for pooled analyses in the future.

Despite limited participation of trans women in PrEP trials, observational studies regarding the use of PrEP among trans women have increased the body of knowledge regarding issues such as adherence (Golub, Gamarel, Rendina, Surace, & Lelutiu-Weinberger, 2013), risk-compensation (Golub, 2014; Marcus et al., 2013), acceptability (Galea et al., 2011; Golub, 2014; Yang et al., 2013), and epidemic impact (Gomez et al., 2012). Overall, this preliminary body of literature suggests that PrEP represents an important opportunity to prevent incident HIV infections among trans women; however, significant barriers to its effective use and retention among PrEP programs have yet to be overcome. Unfortunately the majority of the studies within this growing literature do not provide insights into the challenges faced specifically by transgender communities in accessing PrEP, instead conclusions tend to be directed simultaneously to MSM and trans women, which may obscure distinctions between the ideal application of PrEP programs between these populations.

Although this analysis focused on trans women alone, it should be noted that published literature concerning HIV risk and subsequent prevention modalities for trans men is extremely scarce. This understudied population may also benefit from increased research attention, since presently not even adequate estimates of HIV risk or risk behavior are available.

Given the growing evidence of PrEP efficacy in MSM and other populations, a specific randomized clinical trial for trans women may not be needed, and such a study may even violate the principal of clinical equipoise. However, in light of evidence that the inclusion of trans women in PrEP trials has been limited, we recommend that, to ensure optimal uptake of PrEP among this population, concerted efforts should be made to include trans women in acceptability, implementation, and evaluation studies. Such studies will be critical to informing clinical, programmatic and policy decisions regarding the use of PrEP by trans women, as it has previously been with other populations, such as MSM, serodiscordant couples, and PWID. Some barriers to PrEP effectiveness among trans women have already been identified, such as the complex and heterogeneous psychosocial motivations for engaging in risk compensation among trans women (Golub, 2014), as well as many correlates to poor PrEP adherence (Golub, et al., 2013). Particular attention should also be paid to unique barriers that trans women may experience while obtaining access to PrEP, such as gender discrimination, transphobia, and violence, which have been observed to play an important role in reducing acceptability of and access to other HIV testing, preventive and treatment services (Golub & Gamarel, 2013; Golub et al., 2013; Sevelius, Patouhas, Keatley, & Johnson, 2014; Sevelius, Saberi, & Johnson, 2014).

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References

Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, Celum C. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012; 367(5):399–410. doi: 10.1056/NEJMoa1108524. [PubMed: 22784037]

Baeten JM, Haberer JE, Liu AY, Sista N. Preexposure prophylaxis for HIV prevention: where have we been and where are we going? J Acquir Immune Defic Syndr. 2013; 63(Suppl 2):S122–129. doi: 10.1097/QAI.0b013e3182986f69. [PubMed: 23764623]

Baral SD, Poteat T, Stromdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. Lancet Infect Dis. 2013; 13(3):214–222. doi: 10.1016/S1473-3099(12)70315-8. [PubMed: 23260128]

Centers for Disease Control and Prevention. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR Morb Mortal Wkly Rep. 2011; 60(3):65–68. doi: mm6003a1. [PubMed: 21270743]

Centers for Disease Control and Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. MMWR Morb Mortal Wkly Rep. 2012; 61(31):586–589. doi: mm6131a2. [PubMed: 22874836]

Centers for Disease Control and Prevention. Update to Interim Guidance for Preexposure Prophylaxis (PrEP) for the Prevention of HIV Infection: PrEP for Injecting Drug Users. MMWR Morb Mortal Wkly Rep. 2013; 62(23):463–465. doi: mm6223a2. [PubMed: 23760186]

Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, Vanichseni S. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2013; 381(9883):2083–2090. doi: S0140-6736(13)61127-7. [PubMed: 23769234]

Coombs A, McFarland W, Ick T, Fuqua V, Buchbinder SP, Fuchs JD. Long-chain peer referral to recruit black MSM and black transgender women for an HIV vaccine efficacy trial. J Acquir Immune Defic Syndr. 2014 doi: 10.1097/QAI.0000000000000197.

Duncan DT, Hatzenbuehler ML, Johnson RM. Neighborhood-level LGBT hate crimes and current illicit drug use among sexual minority youth. Drug Alcohol Depend. 2014; 135:65–70. doi: 10.1016/j.drugalcdep.2013.11.001. [PubMed: 24326203]

Galea JT, Kinsler JJ, Salazar X, Lee SJ, Giron M, Sayles JN, Cunningham WE. Acceptability of pre-exposure prophylaxis as an HIV prevention strategy: barriers and facilitators to pre-exposure prophylaxis uptake among at-risk Peruvian populations. Int J STD AIDS. 2011; 22(5):256–262. doi: 22/5/25610.1258/ijsa.2009.009255. [PubMed: 21571973]

Golub SA. Tensions Between the Epidemiology and Psychology of HIV Risk: Implications for Pre-exposure Prophylaxis. AIDS Behav. 2014 doi: 10.1007/s10461-014-0770-7.

Golub SA, Gamarel KE. The impact of anticipated HIV stigma on delays in HIV testing behaviors: findings from a community-based sample of men who have sex with men and transgender women in New York City. AIDS Patient Care STDS. 2013; 27(11):621–627. doi: 10.1089/apc.2013.0245. [PubMed: 24138486]

Golub SA, Gamarel KE, Rendina HJ, Surace A, Lelutiu-Weinberger CL. From Efficacy to Effectiveness: Facilitators and Barriers to PrEP Acceptability and Motivations for Adherence Among MSM and Transgender Women in New York City. AIDS Patient Care STDS. 2013; 27(4): 248–254. doi: 10.1089/apc.2012.0419. [PubMed: 23565928]

Gomez GB, Borquez A, Caceres CF, Segura ER, Grant RM, Garnett GP, Hallett TB. The potential impact of pre-exposure prophylaxis for HIV prevention among men who have sex with men and transwomen in Lima, Peru: a mathematical modelling study. PLoS Med. 2012; 9(10):e1001323. doi: 10.1371/journal.pmed.1001323PMEDICINE-D-11-01724. [PubMed: 23055836]

Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, Glidden DV. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010; 363(27):2587–2599. doi: 10.1056/NEJMoa1011205. [PubMed: 21091279]

Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N, Team, H. A. P. R. S. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. AIDS Behav. 2008; 12(1):1–17. Review. doi: 10.1007/s10461-007-9299-3. [PubMed: 17694429]

Hoffman B. An Overview of Depression among Transgender Women. Depress Res Treat. 2014; 2014:394283. Review. doi: 10.1155/2014/394283. [PubMed: 24744918]

Marcus JL, Glidden DV, Mayer KH, Liu AY, Buchbinder SP, Amico KR, Grant RM. No evidence of sexual risk compensation in the iPrEx trial of daily oral HIV preexposure prophylaxis. PLoS One. 2013; 8(12):e81997. doi: 10.1371/journal.pone.0081997. [PubMed: 24367497]

Melendez RM, Exner TA, Ehrhardt AA, Dodge B, Remien RH, Rotheram-Borus MJ, Hong D. Health and health care among male-to-female transgender persons who are HIV positive. Am J Public Health. 2006; 96(6):1034–1037. doi: 10.2105/AJPH.2004.042010. [PubMed: 16131645]

Microbicides Trials Network. MTN Statement on Decision to Discontinue Use of Oral Tenofovir Tablets in VOICE, a Major HIV Prevention Study in Women. 2011. Retrieved from http://www.mtnstopshiv.org/node/3619

Molina JM, Pintado C, Gatey C, Ponscarme D, Charbonneau P, Loze B, Delaugerre C. Challenges and opportunities for oral pre-exposure prophylaxis in the prevention of HIV infection: where are we in Europe? BMC Med. 2013; 11:186. doi: 10.1186/1741-7015-11-186. [PubMed: 23972284]

Olyslager, F.; Conway, F. On the Calculation of the Prevalence of Transsexualism; Paper presented at WPATH 20th International Symposium; Chicago, IL. Sep. 2007

Peterson L, Taylor D, Roddy R, Belai G, Phillips P, Nanda K, Cates W. Tenofovir disoproxil fumarate for prevention of HIV infection in women: a phase 2, double-blind, randomized, placebo-controlled trial. PLoS Clin Trials. 2007; 2(5):e27. doi:10.1371/journal.pctr.0020027. [PubMed: 17525796]

San Francisco Department of Health. HIV/AIDS Epidemiology Annual Report: 2012. 2013. Retrieved from http://www.sfdph.org/dph/files/reports/RptsHIVAIDS/AnnualReport2012.pdf

Santos GM, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. Sex Transm Infect. 2014 doi: 10.1136/sextrans-2013-051342.

Sevelius JM, Carrico A, Johnson MO. Antiretroviral therapy adherence among transgender women living with HIV. J Assoc Nurses AIDS Care. 2010; 21(3):256–264. doi: 10.1016/j.jana.2010.01.005. [PubMed: 20347342]

Sevelius JM, Patouhas E, Keatley JG, Johnson MO. Barriers and facilitators to engagement and retention in care among transgender women living with human immunodeficiency virus. Ann Behav Med. 2014; 47(1):5–16. doi: 10.1007/s12160-013-9565-8. [PubMed: 24317955]

Sevelius JM, Saberi P, Johnson MO. Correlates of antiretroviral adherence and viral load among transgender women living with HIV. AIDS Care. 2014 doi: 10.1080/09540121.2014.896451.

Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, Brooks JT. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med. 2012; 367(5):423–434. doi: 10.1056/NEJMoa1110711. [PubMed: 22784038]

Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, Taylor D. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012; 367(5):411–422. doi: 10.1056/NEJMoa1202614. [PubMed: 22784040]

van der Straten A, Van Damme L, Haberer JE, Bangsberg DR. Unraveling the divergent results of pre-exposure prophylaxis trials for HIV prevention. AIDS. 2012; 26(7):F13–19. doi: 10.1097/QAD.0b013e3283522272. [PubMed: 22333749]

Yang D, Chariyalertsak C, Wongthanee A, Kawichai S, Yotruean K, Saokhieo P, Chariyalertsak S. Acceptability of pre-exposure prophylaxis among men who have sex with men and transgender women in Northern Thailand. PLoS One. 2013; 8(10):e76650. doi: 10.1371/journal.pone.0076650. [PubMed: 24116132]

World Health Organization. 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. 2012. Retrieved from WHO website: http://www.who.int/hiv/pub/guidance_prep/en/

Table 1

Oral PrEP Efficacy Trial Characteristics, Including Transgender Enrollment

Trial	Primary Population	Setting(s)	Enrollment	Trans Women Enrollment (%)
TFV Phase II[*]	Women	Cameroon, Ghana, Nigeria	936	0 (0%)
iPrEx	MSM and TGW	Ecuador, Brazil, Peru, South Africa, Thailand, USA	2,499	29 (1.2%)
FEM-PrEP[*]	Women	Kenya, South Africa, Tanzania	1,951	0 (0%)
TDF2	HSM and HSW	Botswana	1,200	0 (0%)
PartnersPrEP	SDC	Kenya, Uganda	4,747 (Couples)	0 (0%)
VOICE[*]	Women	South Africa, Uganda, Zimbabwe	5,029	0 (0%)
Bangkok Tenofovir Study	PWID	Thailand	2,413	0 (0%)
Total			18,775	29 (0.2%)

Abbreviations: Men who have sex with men (MSM), transgender women (TGW), heterosexual men (HSM), heterosexual women (HSW), serodiscordant couples (SDC), people who inject drugs (PWID)

[*] Enrolled only cisgender women