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Behavioral Interventions to Prevent HIV Transmission and Acquisition for Transgender Women: A Critical Review

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Abstract: Worldwide, transgender women are at disproportionately higher risk of HIV infection, with the primary mode of infection being condomless anal intercourse. Although very few HIV prevention interventions have been developed and tested specifically for transgender women, growing evidence suggests that behavioral HIV risk reduction interventions for other marginalized groups are efficacious. We outline the current state of knowledge and areas in need of further development in this area.

Key Words: HIV, transgender, behavioral intervention, young adults

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INTRODUCTION

HIV Risk Among TW

Globally, the prevalence of HIV and other sexually transmitted infections (STIs) is disproportionately higher among transgender women (TW), particularly ethnic minority and younger TW. Because HIV-related surveillance data are not uniformly collected by gender identity, data on HIV infection among TW are lacking; however, data from local health departments, meta-analyses, and multi-city studies using convenience sampling methods demonstrate high levels of HIV infection among TW in the United States and other countries worldwide.1 A meta-analysis of the global burden of HIV infection in TW documented an HIV prevalence of 19% (95% CI: 17 to 21); TW had a 49-fold increased odds of HIV infection compared with all adults of reproductive age.2 In the United States, a meta-analysis of 29 studies with TW3 showed an HIV prevalence of 28% through laboratory-confirmed blood samples (4 studies) and 12% through self-report (18 studies). Data from local testing of over 500 TW with no known previous positive HIV test results in Miami, San Francisco, and Los Angeles found 12% HIV infection, suggesting a high percentage of undiagnosed HIV infection in this population.4 In an analysis of these newly diagnosed HIV infections by age, the highest number were detected among those ages 20–29 years (ie, 45% of all cases).4 Studies among young TW, in particular ages 16–29 years, have documented prevalence of HIV infection approaching those of adults.5–7 In addition, Garofalo et al found that much like in other high-risk populations (ie, men who have sex with men; MSM), racial/ethnic minority TW have higher prevalence of HIV and STIs but lower rates of sexual risk behavior, particularly among Black TW.5

Condomless anal intercourse (CAI) represents TW’s primary risk for HIV acquisition and transmission. In the review of 29 U.S. studies referred to above, the average prevalence of any receptive CAI was 44%; 32% of TW reported multiple sex partners (primarily nontransgender males) and 48.3% reported sex with casual partners (within varying recall periods).5 Among younger TW in Chicago, Garofalo et al5 found 59% reported any CAI in a cohort of younger TW in Boston. Although evidence among TW specifically is not available, recent findings among MSM suggest that inconsistent condom use during anal sex with HIV-infected partners offers little to no protection against HIV infection, and that consistent condom use over time is rare.9

There are specific structural, developmental, and interpersonal challenges to sexual safety faced by TW. Social structures and conditions include discrimination, mistreatment, and adversity in the form of rejection from friends, family, and others, which can become a central part of TW’s experience.5,7,10–13 Affecting the ability to secure housing, employment, social services, and health care beginning in early adulthood, this basic struggle for survival undermines TW’s ability to prioritize and practice safer sex.14,15 In addition, transactional sex is associated with CAI and HIV infection in
TW, and economic pressures often result in TW compromising safer sex practices for monetary incentives. Previous studies of TW suggest high prevalence of previous incarceration (~20%), largely related to arrest and conviction for commercial sex work. Evidence suggests that both history of sex work and incarceration are related to the psychosocial factors, which often drive HIV risk. Furthermore, the legal problems encountered by TW may serve as barriers to HIV-related services and access to health care.

The HIV prevention and care continuum is not well-characterized in TW, although evidence is of low prevalence of care initiation and engagement. Pre-exposure prophylaxis (PrEP) efficacy and demonstration projects provide evidence of safety, tolerability, and efficacy of PrEP to prevent HIV acquisition, with some evidence of effectiveness in TW. The limited studies conducted to date suggest that initiation and uptake of PrEP among TW is alarmingly low despite the complex profiles of HIV risk in this group. Analysis of data from an ongoing interventional study of younger TW found that only 5% of the sample had initiated PrEP, although 62% were indicated for PrEP based on Centers for Disease Control and Prevention (CDC) criteria; furthermore, only 31% of the sample had ever heard of PrEP, but 69% expressed interest once PrEP was described. This is echoed by 2 California-based studies: one study of TW in San Francisco, which demonstrated that fewer than 20% of TW had ever heard of PrEP; and a second qualitative study of 30 MSM and TW in 3 California metro areas suggesting that while awareness of PrEP was relatively low, expressed interest once PrEP was described was quite high (76%). Although very little research has been performed about TW within the HIV continuum of care, limited evidence suggests that HIV-infected TW are less likely than other groups to be on antiretroviral therapy (ART) and, if on ART, are less likely to be adherent. There is also some evidence suggesting that transgender-specific factors are related to ART adherence in adult TW, including gender affirmation and adherence to cross-sex hormone therapy.

HIV Prevention Interventions for TW

Despite research documenting high prevalence of CAI and HIV infection among TW, there are no interventions developed specifically for TW in the CDC compendium of evidenced-based interventions. Only 5 U.S.-based HIV prevention interventions have been published in the peer-reviewed literature; all of which are early-phase non-randomized interventions (Table 1; see Poteat et al for a review of global interventions).

Four of these studies (Bockting, Nemoto, Taylor, and Garofalo) documented modest reductions in HIV risk and/or improvements in HIV knowledge and attitudes among TW, with some evidence that effects diminished over time (Bockting). Three of the studies (Bockting, Taylor, and Garofalo) reference a specific behavioral theory as part of their formative intervention development.

Theoretical Models for HIV Risk Reduction Interventions Among TW

Interventions designed to change behaviors such as reductions in the risky sexual activities that lead to the acquisition or transmission of HIV infection should be theory based. Using a theoretical framework to guide the contents of an HIV prevention intervention provides a means to empirically test the mechanisms of change (ie, the underlying theoretical constructs—hypothesized mediators—that produce a desired change in a behavioral health outcome). Whether implicitly or explicitly, nearly all HIV prevention interventions are informed or based on some element of behavioral theory. Most rely at least somewhat on the assumption that providing information and education about HIV transmission and prevention may lead to behavioral change. Yet research has proven time and time again that education alone is insufficient to induce effective behavioral change among most individuals. Thus, behavioral interventions were developed based on psychosocial and cognitive approaches that may, for example, educate individuals in practical skills and enhance their confidence in their ability (ie, self-efficacy) to reduce their risk for HIV. A number of behavioral change theories and models have demonstrated efficacy across diverse populations including the Health Belief Model, Social Cognitive Theory, Transtheoretical Stages of Change Model, the Theory of Reasoned Action, and the Information, Motivation, and Behavior (IMB) Model. None of these models are specific to TW, meaning that they do not by definition provide a conceptual target for the unique underlying mechanisms of HIV risk among this population. However, 2 have been explicitly applied in previously published HIV prevention interventions for TW: the Health Belief Model (Bockting) and the IMB Model (Taylor).

Researchers have increasingly come to realize that for TW, sexual risk behaviors occur in the context of complex socio-cultural factors and environmental determinants of risk, such stigma or discrimination based on transgender status, housing and/or economic instability, and/or transactional sex and that these factors must be considered when designing HIV prevention interventions for this group. As such, other developmental theories not specific to behavioral change have been used as heuristic models to inform the foci of interventions on transgender-specific social, cultural, and structural influence on sexual risk. For example, the LifeSkills intervention by Garofalo et al used a community-based participatory research approach and Bronfenbrenner’s Social Ecological Theory to guide intervention development for considering the potential impact of discrimination and stigma, as well as related socio-contextual challenges, such as securing housing, employment, and appropriate health care on HIV risk behaviors such as CAI for young TW. Much like the behavioral change models above, Bronfenbrenner’s theory is not specific to conditions affecting young TW but can be applied broadly in a holistic context grounded in this population’s social realities.

In recent years, at least 2 transgender-specific heuristic frameworks have been presented in the published literature that may hold promise for consideration in the design of future HIV prevention interventions for TW. Operario and Nemoto described the application of syndemic theory or the concept of multiple co-occurring psychosocial health problems specific to HIV risk among TW. This was followed by an empirical test by Brennan and colleagues
TABLE 1. Published Behavioral HIV Prevention Interventions Among TW

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention Description</th>
<th>Sample Size</th>
<th>Design</th>
<th>Theoretical Model</th>
<th>Effects</th>
<th>Funder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bockting et al</td>
<td>Prevention education workshop conducted over 3 afternoons</td>
<td>N = 59</td>
<td>Prepost</td>
<td>Health Belief Model</td>
<td>Increase in HIV-related knowledge and attitudes, diminished over time; no significant change in risk behavior</td>
<td>American Foundation for AIDS Research</td>
</tr>
<tr>
<td>Nemoto et al</td>
<td>18 workshops regarding: (1) sex, relationships, and health; (2) substance use, coping skills; and (3) life needs</td>
<td>N = 109 (completed at least 10 workshops)</td>
<td>Prepost</td>
<td>N/A</td>
<td>Significant reductions in level of sexual risk; no significant change in HIV knowledge</td>
<td>Substance Abuse and Mental Health Services Administration</td>
</tr>
<tr>
<td>DeSantis et al</td>
<td>A 1-day HIV prevention program based on Many Men, Many Voices (3MV) and a community needs assessment</td>
<td>N~50</td>
<td>Prepost</td>
<td>N/A</td>
<td>No formal outcomes evaluation</td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>Taylor et al</td>
<td>4 group sessions delivered over 4 days (stress, stigma, drugs/alcohol, growth/social support)</td>
<td>N = 55</td>
<td>Prepost</td>
<td>IMB</td>
<td>Significant reduction in sexual risk</td>
<td>CDC</td>
</tr>
<tr>
<td>Garofalo et al</td>
<td>6 group sessions delivered over a 3-wk period</td>
<td>N = 51 (ages 16–24)</td>
<td>Prepost</td>
<td>Social Ecological Theory</td>
<td>Significant reduction in sexual risk</td>
<td>CDC</td>
</tr>
</tbody>
</table>

among 151 young TW ages 16–24 years in Chicago and Los Angeles. They report evidence that multiple health-related psychosocial factors form a syndemic index (eg, low self-esteem, polysubstance use, intimate partner violence, victimization related to transgender identity) among younger TW, which was positively and additively related to sexual risk behaviors and prevalent HIV infection. In addition, the syndemic index was related to 2 indicators of social marginalization: transactional sex and incarceration. Sevelius collected data from 22 qualitative interviews with TW of color from the San Francisco Bay Area used an intersectional approach integrating prominent theories from stigma, body objectification, and HIV-related research to propose a gender affirmation framework for HIV risk among this population. Gender affirmation refers to an interpersonal, interactive process whereby a person receives social recognition and support for their gender identity. This framework conceptualizes that the need for gender affirmation among TW is related to engagement in high-risk behaviors and negative health outcomes, such as the acquisition of HIV infection. Overall, the evolution of behavioral models for understanding HIV risk behaviors among TW is a relatively nascent field and more work needs to be performed to better define and elucidate pathways of risk and resilience.

**Case Study/Lessons Learned: LifeSkills**

In 2011, after a successful pilot funded by the CDC, LifeSkills became the first full-scale, randomized controlled trial (RCT) examining the efficacy of a group-based, empowerment-focused behavioral intervention for HIV prevention among TW funded by the National Institutes of Health. Given the importance of behavioral theory for HIV prevention interventions as discussed above, we reviewed the LifeSkills intervention content for both behavioral change and transgender-specific theoretical approaches and proposed measurement and analysis of these factors (eg, IMB change; empowerment; transgender adaptation and integration) as potential mediators of the intervention effect, ie, beyond the original broad and heuristic framework that informed intervention development. We recruited 300 young TW ages 16–29 years, in 2 U.S. cities (Chicago and Boston) who were randomly assigned 2:2:1 in a 3-arm trial (LifeSkills, standard-of-care, and time-matched attention control). In this ongoing trial, participants are followed for 1 year with major assessment visits at baseline, 4, 8, and 12-months postrandomization. Participants were recruited and enrolled between 2012 and 2015, with follow-up visits ongoing through September 2016. Participants were racially/ethnically diverse: 49% Black, 12% Latina, 25% White, and 14% other. At enrollment, 22% of participants were HIV infected (3% previously undiagnosed). Proposed outcome measures included condomless sex acts (eg, both anal and vaginal), as well as the collection of biological specimens for urogenital STIs (eg, gonorrhea and chlamydia) and HIV-antibody screening. In this study, we present 6 lessons learned from this trial for consideration in the design of future HIV prevention efforts focused for TW:

- Ethics of the RCT: RCTs for behavioral HIV prevention research can pose a number of fundamental ethical issues to which researchers and study staff working with TW must give careful consideration. Although a RCT may be the preferred method of demonstrating efficacy of a behavioral intervention, the community may not understand or accept the randomization process particularly in the context of an “epidemic” of HIV infection among TW. In particular in Chicago, where a within person, preposttest design was used during the pilot study, the change to the RCT design as part of the current full-scale efficacy trial created, at times,
a lack of buy-in from community partners and participants. Alternative methods such as crossover or waitlist-controlled designs should be considered, or whenever possible the use of historical controls or another observational method, to be maximally responsive to the needs of the community.

- The 3-Arm Design: We found that there were a number of disadvantages to a 3-arm design and few benefits. The disadvantages included additional recruitment burden of a relatively rare population and the loss of sample size for the primary outcomes comparison. In addition, some participants provided feedback that the time-matched attention control did not address relevant psychosocial concerns and was an unnecessary time burden.

- Involving the Community: LifeSkills was developed using a community-participatory design. We involved key members of the target population in all aspects of the curriculum development, as well as the study design and procedures. This proved to critically important to our successful recruitment and retention efforts throughout the project period.

- Selection of Biological Specimens: Baseline prevalence and incidence of urogenital STIs was very low hampering the use of these data when interpreting the potential impact of the behavioral intervention on surrogate makers of HIV infection. We know from the published literature that rectal STIs and syphilis are indicators of risk for HIV infection in Black MSM; however, to date, there are no similar studies focused on the link between STI diagnosis and HIV risk in TW. As the National Institutes of Health has increasingly prioritized biological outcomes within the context of behavioral HIV prevention research, it will be important to broaden the collection of specimens to include both rectal STIs and syphilis whenever possible.

- High Seroprevalence of HIV Infection at Baseline: As mentioned above, the baseline HIV seroprevalence for our sample was 22% (3% previously undiagnosed). This seroprevalence is considerably higher than our team’s previous experience conducting HIV prevention interventions with MSM and young MSM, but consistent with other community-based, convenience samples of HIV prevalence among young TW. The high seroprevalence is particularly concerning given the relatively young age of our study population (eg, ages 16–29 years). Lessons learned from this finding include the need for interventions to be developed and implemented at young ages, as well as to develop interventions or to include elements of secondary prevention that target not just sexual risk behaviors but all outcomes across the HIV care continuum.

- Intervention Delivery and the Small Group–Based Format: In both our pilot work and RCT, the LifeSkills intervention was delivered in 2-hour small-group sessions twice per week for 3 consecutive weeks. In the RCT, the overall attendance rate was 79%. Lessons learned regarding the format and session attendance included (1) safety concerns for travel to study sites; (2) difficulty with attendance for participants engaged in sex work because of competing economic needs; (3) some eligible participants were unable to attend sessions at a specific date and time because of competing work or school schedules; (4) because of a high rate of incarceration history in the sample (29%), participants on house arrest were unable to attend sessions because of restricted movement; and (5) while the group-based sessions were empowering for many participants (ie, meeting other young TW), staff reported problems with the group-based dynamic, including mistrust among participants (eg, fear of personal disclosure) and failure to share vulnerabilities. As such, consideration for future interventions may be more individualized approaches, a hybrid design with individual- and group-based components, or the use of mobile platform, to increase the reach, accessibility, and privacy of the intervention.

### Other Future Directions and Priority Research Areas

One of the current limitations of the published behavioral interventions designed to prevent transmission and acquisition of HIV among TW is that each was designed and implemented before the advent of PrEP. PrEP is a once-daily fixed combination of tenofovir disoproxil fumarate and emtricitabine that has been shown to reduce the risk of HIV transmission. Studies of PrEP specifically in TW have not been conducted. The iPrEx study of PrEP in MSM and TW found a 44% risk reduction using an intention-to-treat analysis. A sub analysis of only the TW in the iPrEx sample found evidence of protection in the context of medication adherence, despite the lack of efficacy using an intention-to-treat analysis. Furthermore, in this analysis, there was evidence of both greater sexual risk for HIV acquisition among TW (versus MSM; more frequent reports of transactional sex, condomless receptive anal intercourse, and multiple partners) and lower medication adherence (per drug concentrations regardless of use of feminizing hormones). In our LifeSkills sample, PrEP seemed to be being underused as an HIV prevention strategy among the young TW. Despite 2014, clinical guidelines recommending that PrEP be considered for people who are HIV negative and at substantial risk for the acquisition of HIV infection, including anyone who is in an ongoing sexual relationship with an HIV-infected partner, in the LifeSkills sample 62% had a clinical indication for PrEP, yet only 5% had ever taken PrEP. Clearly, further prioritization and study of PrEP in TW, particularly in context and in concert with behavioral interventions are warranted, as combination biobehavioral approaches may hold the greatest promise for reducing HIV transmission in this high-risk population.

As the next generation of behavioral and biobehavioral approaches to reduce HIV risk and transmission among TW are developed it will be important to move beyond group-level interventions, which have been the mainstay of efforts to date. Approaches that have shown promise in other populations like MSM such as couples-based approaches or the use of social networks also warrant consideration among TW. In addition, the use of mobile technology may offer convenient access and privacy to interventions, and present an opportunity to test a method amenable for widespread dissemination, which is especially important for a relatively rare, often isolated, and highly stigmatized population such as TW who can be difficult to reach and engage. Finally, given the
profound socioeconomic instability—which far-too-often is a social reality for TW—and its influence on the initiation and engagement in high-risk behaviors such as transactional sex, the development of structural approaches such as employment and vocational interventions and initiatives should be strongly considered and prioritized because they may offer the greatest promise at holistically improving the lives of TW, including holding promise for the reduction of HIV transmission.

In conclusion, few theory-based behavioral interventions designed to reduce HIV risk or HIV incidence currently exist in the published literature for TW. Given the epidemic that currently exists of HIV infection among this population, there is a critical and urgent need for additional behavioral, biobehavioral, and structural approaches, which target the unique mechanisms of HIV risk for TW and those are grounded in both behavioral theory and the often harsh social realities facing this population.

REFERENCES