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Global Epidemiology of HIV Infection and Related Syndemics Affecting Transgender People

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Introduction: Transgender populations have been underrepresented in HIV epidemiologic studies and consequently in HIV prevention, care, and treatment programs. Since 2012, there has been a dramatic increase in research focused on transgender people. Studies highlight the burden of HIV and risk determinants, including intersecting stigmas, as drivers of syndemics among transgender populations. This review synthesizes the most recent global epidemiology of HIV infection and describes current gaps in research and interventions to inform prioritization of HIV research for transgender populations.

Methods: A systematic review was conducted of the medical literature published between January 1, 2012 and November 30, 2015. The data focused on HIV prevalence, determinants of risk, and syndemics among transgender populations.

Results: Estimates varied dramatically by location and subpopulation. Transfeminine individuals have some of the highest concentrated HIV epidemics in the world with laboratory-confirmed prevalence up to 40%. Data were sparse among trans masculine individuals; however, they suggest potential increased risk for trans masculine men who have sex with men (MSM). No prevalence data were available for transgender people across Sub-Saharan Africa or Eastern Europe/Central Asia. Emerging data consistently support the association of syndemic conditions with HIV risk in transgender populations.

Discussion: Addressing syndemic conditions and gender-specific challenges is critical to ensure engagement and retention in HIV prevention by transgender populations. Future research should prioritize: filling knowledge gaps in HIV epidemiology; elucidating how stigma shapes syndemic factors to produce HIV and other deleterious effects on transgender health; and understanding how to effectively implement HIV interventions for transgender people.

Key Words: transgender, HIV epidemiology, HIV treatment, prevention, syndemics

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INTRODUCTION

The term “transgender” refers to a diverse population of people whose gender identities and/or expressions differ from the sex assigned to them at birth, typically via birth certificate. The variety of terms and ways of expressing gender preclude an exhaustive list of terms. Therefore, “trans feminine” refers to individuals who were assigned a male sex at birth and express their gender along a feminine spectrum—that is, as women, female, transgender women, male-to-female, and other diverse trans feminine gender identities and expressions. “Trans masculine” refers to people who were assigned female at birth and express their gender along a masculine spectrum, as men, male, transgender men, female-to-male, and other heterogeneous trans masculinities. Some transgender people do not identify within this binary of masculine and feminine. Unfortunately, at this time, there is still too little data to review among this nonbinary population; future research is needed to elucidate HIV-related risks and resiliencies in that group.

Reliable estimates of the size of the transgender population are sparse. Where they exist, data vary by location and study design. Data from gender clinics in Europe estimate that anywhere from 4.28 per 100,000¹ to 600 per 100,000² members of the population seek medical care for gender transition, and that 72%–80% of those seeking gender care identify along the trans feminine spectrum. However, recent population-based studies have found that 0.5%–0.9% of adults was identified with a gender different from their birth sex and the proportion is similar for birth-assigned males and females.³–⁵ The most recent population-based data from the United States estimate that 0.5% of the population was...
identified as transgender. This proportion is consistent with passport identity data from New Zealand, yet much lower than the 1.2% who identified as transgender in a recent nationally representative sample of New Zealand high school students.

Historically, HIV data have conflated gender with anatomy and subsumed trans feminine people under the category of men who have sex with men (MSM). Subsuming trans feminine individuals in the category of MSM is not only inaccurate, it also typically results in very small numbers of trans feminine people included in much larger samples of MSM and makes it difficult to distinguish their unique HIV vulnerabilities. Current HIV risk categories also make it difficult to identify HIV risk among trans masculine individuals. Where surveillance exists for this population, reported data have categorized trans masculine MSM under “heterosexual contact,” making their risks invisible.

HIV risk among transgender populations is driven by multilevel factors (Figure 1). At the biological level, transgender people with anatomically male partners face a high HIV transmission probability via condomless anal sex with serodiscordant and viremic partners. Coinfection with perigenital or perianal STIs may also potentiate the acquisition and transmission of HIV. Hormone-related determinants of HIV risk include testosterone use among trans masculine individuals, which may cause vaginal atrophy and increase the risk of HIV acquisition during vaginal intercourse. Network level risks include a high prevalence of HIV and limited awareness of HIV status within transgender-inclusive sexual networks. Community-level stigma and structural-level discriminatory laws also contribute to the high burden of HIV by limiting the provision and uptake of services as well as by driving transgender women, in particular to engage in sex work for economic survival and gender affirmation.

A systematic review and meta-analysis of the burden of HIV in trans feminine populations was published in 2012. In that analysis, Baral et al documented a worldwide HIV prevalence of 19% and a 49-fold increased odds of HIV infection compared with non-transgender adults of reproductive age. The review was limited to studies published between 2000 and 2011, with at least 50 participants, and laboratory-confirmed HIV-infection data. The most recent systematic review of HIV prevalence to include trans masculine individuals was published in 2008 and was limited to the United States. In that review, Herbst et al found only 5 studies among transgender men, and HIV prevalence ranged from 0% to 2%. Given the dramatic increase in research among transgender populations in recent years, an update and synthesis of HIV data among transgender populations is due.

Regardless of geographic location, transgender people exist within social contexts that stigmatize them. Stigma is a powerful social determinant of health and a key driver of HIV disparities among transgender populations. Therefore, transgender HIV data are best understood within the social context and consequences of widespread stigma. Moreover, HIV infection is only one of the multiple stigma-related health conditions that disproportionately impact transgender populations. Syndemics have been defined as “the concentration and deleterious interaction of 2 or more disease or other health conditions in a population, especially as a consequence of social inequity and the unjust exercise of power.” Syndemic psychosocial health problems, such as depression, substance use or abuse, violence or victimization, and internalized transphobia, may potentiate HIV risk and contribute to poor HIV treatment outcomes for transgender populations. A recent review of the use of syndemic theory in HIV research found that most studies focused on MSM, and the most frequently studied psychosocial problems included mental health (83%), substance abuse (90%), and violence (68%). The most frequently studied outcome variables were HIV risk behaviors (73%) or HIV infection (23%). No systematic review has yet examined the data on syndemic production of HIV among transgender populations.

METHODS

PubMed (MEDLINE), EMBASE, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched for English language articles. In addition, experts in HIV infection among transgender populations were contacted to request access to unpublished HIV prevalence data. Commonly used terms for transgender (including

Figure 1. Multilevel drivers of HIV risk among transgender populations.
“transsexual,” “cross dresser,” “transvestite,” and “travesti”) were cross-referenced with medical subject headings (MeSH) terms for HIV. Two reviewers independently conducted title and abstract reviews on unduplicated references for relevance, with subsequent full-text review for data abstraction.

The search was limited to data published between January 1, 2012 and November 30, 2015 to avoid overlap with Baral et al’s review.32 All studies with original quantitative HIV data that disaggregated transgender participants from other populations were included. Both self-reported and laboratory-tested HIV statuses and data on location of study, sampling strategies, sample size, and HIV prevalence and/or incidence were extracted. When present, data on syndemics among transgender populations were also abstracted. Where more than one manuscript reported on the same data set, the most recent publication is cited. Where a manuscript included both self-reported HIV status and HIV testing, the results of HIV tests were recorded. Where available, nonadjusted HIV-prevalence estimates were recorded for studies that used respondent-driven sampling.

### RESULTS

#### HIV Prevalence

##### United States

Twenty-one studies published between 2012 and 2015 described HIV prevalence among transgender people in the United States of which only one also measured incidence.33 (Table 1.) Four studies were national, regional, or state-level in scope, whereas the rest were single city or multicity. Three

| Citation | City, State | Population | Sampling Method | Sample Size | Prevalence, % (n) | Method of HIV Ascertainment |
|----------|-------------|------------|----------------|-------------|-------------------|----------------------------|
| Benotsch et al34 | Mid-Atlantic | All trans | Clinics, bars, events | TF 104; TM 51 | 22.6 (n = 35) overall | Self-report |
| Bradford et al35,36 | Virginia | All trans | Internet, peer referral | TF 229; TM 121 | 16 of TF (n = 28) | Self-report |
| Feldman et al37 | National | All trans | Internet | TF 697; TM 532 | 2.0 (n = 14); 0.4 (n = 2) | Self-report |
| Green et al38 | San Diego, CA | All trans | HTC program | TF 151; TM 30 | 2.0 (3); 3.3 (1) | Laboratory |
| Habarta et al39 | US, PR, UVI | All trans | HIV testing event* data | TF 13,154; TM 2364 | 2.7 new; 0.5 new | Laboratory |
| Leinung et al40 | Upstate, NY | All trans | Gender clinic chart review | TF 192; TM 50 | 8.3 of TF (n = 16) | Laboratory |
| Reisner et al41 | Boston, MA | All trans | Clinic attendees | TF 192; TM 50 | 12.9 (n = 4) | Self-report |
| Reisner et al42 | Boston, MA | Sexually active trans youth 14–29 | Retrospective EMR review | TF 63; TM 82 | 7.9 (n = 5); 2.4 (n = 2) | Laboratory |
| Castel et al43 | Washington, DC | Trans unspecified | HIV testing campaign | 85 | 10.6 (n = 9) overall | Laboratory |
| Brennan et al44 | Chicago and Los Angeles, CA | Youth 15–24 yrs | Clinic, venue based, peer referral | 151 | 15.9 (n = 24) | Self-report |
| Garofalo et al45 | Chicago, IL | Youth 16–24 yrs | Active and passive | 51 | 5.9 (n = 3) | Self-report |
| Rowe et al46 | San Francisco, CA | Youth 16–24 yrs | Peer referral, social network sites, trans events, CBOs | 292 | 4.5 (n = 13) | Laboratory |
| Bowers et al47 | Los Angeles, CA | Adult | HIV prevention program | 320 | 21.9 (n = 70) | Self-report |
| Fletcher et al48 | Los Angeles, CA | Adult | HIV prevention program | 517 | 24.2 (n = 125) | Self-report |
| Nuttbrock et al33 | New York, NY | Adult | Purposive | 591 (baseline); 230 (cohort) | 40.1 2.9/100 p-y | Laboratory |
| Nemoto et al13 | San Francisco and Oakland, CA | Adult | Purposive, TW with sex work history | 538 | 29.9 | Laboratory |
| Rapues et al49 | San Francisco, CA | Adult | RDS | 314 | 35.0 (n = 110) | Lab |
| Reback and Fletcher50 | Los Angeles | Adult | Street outreach | 2136 | 13.6 | Self-report |
| Reisner et al51 | San Francisco, CA | Adult | Purposive | 191 | 18.3 (n = 35) | Self-report |
| Peitzmeier et al52 | Boston, MA | Adult | Clinic chart review | 233 | 0.9 (n = 2) | Lab |
| Reisner et al53 | Boston, MA | Adult | Retrospective chart review + STD screen | 23 | 4.3 (n = 1) | Lab |

*Data are not deduplicated. Therefore, one person may have had multiple testing events.

TM, trans masculine; TF, trans feminine; RDS, respondent driven sampling; EMR, electronic medical record.
cities (San Francisco and Los Angeles, CA; Boston, MA) accounted for more than half (n = 12) of study sites. One study49 used respondent-driven sampling, whereas the rest drew upon convenience or clinic-based samples. Eight studies included prevalence estimates for very small samples (i.e., n < 100), predominantly for trans masculine individuals. Four articles did not disaggregate prevalence data by trans feminine or trans masculine gender spectrum.34,35,41,43 However, one of these articles used data from a previously published report that did disaggregate by gender spectrum.35,36

Self-reported HIV prevalence in trans feminine adults,13,37,40,47,48,50,51 ranged from 2.0% in a national internet-based sample16 to 29.9%18 in a sample of trans women with a history of sex work in San Francisco and Oakland, CA. Laboratory-confirmed HIV prevalence reached 35.0% and 40.1% in community samples in San Francisco39 and New York,40 respectively. Among trans feminine testing events at the US Centers for Disease Control sites nationally, 2.7% were positive.39 HIV prevalence among trans feminine youth was between 4.5% and 7.9% in 3 studies42,45,46 and 15.9% in 1 study.44

Since 2014, 5 publications38,39,42,52,53 have described laboratory-confirmed HIV prevalence among trans masculine people in the United States, ranging from 0.9%52 to 4.3%.73 Of trans masculine CDC testing events,39 0.5% were positive.

Global

**Trans Masculine**

Table 2 summarizes the very few data available regarding HIV prevalence among trans masculine individuals outside the United States. Four of 5 studies had very small samples (n = 14–92). Two Canadian respondent-driven sampling studies72,86 found no prevalent known HIV infections. Among gender clinic patients in Catalonia, Spain, 2.2% of trans masculine individuals had laboratory-confirmed HIV infection.85 In 2 internet studies of trans masculine people who have sex with men, self-reported prevalence was 1.4% in a global sample,87 and 8.0% in a sample from Spanish-speaking and Portuguese-speaking countries.85

**Trans Feminine**

Thirty-three studies published between 2012 and 2015 described the HIV infection burden among trans feminine individuals globally.16,54–83, 3 included incidence data.58,74,84 (Table 3). All were from countries with male-predominant, concentrated epidemics. Seven studies used respondent-driven sampling and 1 abstract reported an unspecified probability-based sampling method. Three countries in Latin America (Peru, Brazil, and Argentina) and 3 in Asia (India, Pakistan, and Thailand) accounted for over half of reports. For Colombia, El Salvador, China, Vanuatu, Italy, and Portugal, all HIV burden data were based on samples with fewer than 100 participants. In Latin America and the Caribbean, laboratory-confirmed HIV prevalence ranged from 13.8% to 34.1%; in half of such studies, more than one-quarter of trans feminine persons were HIV-positive. Only self-reports were available from East and Southeast Asia, where data were limited by low levels of HIV testing.48,56,77,79 Laboratory-confirmed HIV prevalence in India varied by sampling design, but was 18.1% in a probability sampling study.81 Among hijra sex workers in Pakistan, laboratory-confirmed prevalence was 6.4%–7.2% in 2 studies,71,75 and 21.6% in a third.89 Laboratory-confirmed and self-reported HIV prevalence, and sampling approaches were highly variable in other countries, primarily in southern Europe.

**Syndemics**

Eight studies were identified that examined syndemics and HIV among transgender populations23,44,53,88–92 (Table 4). Only one study was conducted outside the United States.89 Two studies were among trans masculine individuals23,53; and both were conducted in Boston, MA. Half of all studies were conducted in California. One study did not specify trans feminine or trans masculine gender spectrum of transgender participants.89 All studies were cross-sectional and none used population-based sampling methods, limiting the ability to make causal inferences or generalize beyond the study population.

The most common syndemic factors studied included alcohol/substance use (n = 6), mental health (n = 5), and abuse/violence (n = 4). One study measured self-reported HIV status as an outcome; 7 studies measured sexual risk behaviors, including condomless intercourse, multiple partners, and history of STIs as primary outcomes. One study among people living with HIV examined only biomedical conditions (tuberculosis, viral hepatitis, and STIs) as syndemics with HIV infection.89 Antitransgender stigma, discrimination, or victimization factors were included in all studies of syndemics in trans feminine individuals (n = 5). These variables were modeled both as component conditions of syndemics (n = 3) and as potential determinants of syndemic production (n = 2). Stigma was not measured in any of the studies among trans masculine individuals.

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**TABLE 2. HIV Prevalence Among Trans Masculine Persons Outside the United States, 2012–2015**

| Citation          | Location          | Sample and Method | Sample Size | Prevalence, % | Method of HIV Ascertainment |
|-------------------|-------------------|-------------------|-------------|---------------|-----------------------------|
| Rich et al86      | Vancouver, Canada | TMSM, RDS         | 14          | 0             | Laboratory test             |
| Bauer et al72     | Ontario, Canada   | TM, RDS           | 227         | 0.6 weighted; n = 0 | Self-report                 |
| Reisner et al83   | LAC, Spain, Portugal | TMSM, Internet | 25          | 8.0 (n = 2)   | Self-report                 |
| Patrasciou et al85 | Catalonia, Spain | TM, Clinic        | 92          | 2.2           | Laboratory test             |
| Schein et al87    | Global            | TMSM, Internet   | 69          | 1.4 (n = 1)   | Self-report                 |

TMSM, trans masculine men who have sex with men; RDS, respondent driven sampling.

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Central to syndemics theory is that harmful social factors and health conditions are concentrated in affected populations and interact to enhance deleterious consequences, such as increased HIV risk. All of the identified studies found support for the concentration of harmful social factors and/or co-occurring health conditions among transgender people and

**TABLE 3. HIV Prevalence and Incidence Among Trans Feminine People Outside the United States, 2012–2015**

| Citation                  | Location                     | Sampling Method          | Sample Size | Prevalence, %, n (Incidence) | Method of HIV Ascertainment |
|---------------------------|------------------------------|--------------------------|-------------|------------------------------|------------------------------|
| **Latin America/Caribbean Region** |                              |                          |             |                              |                              |
| Castillo et al58          | Lima, Peru                   | Snowball                 | 207         | 16.9 2.3/100p-y              | Laboratory                   |
| Costa et al59             | Multicity, Brazil            | Gender clinic            | 284         | 25.0 (n = 71)                | Laboratory                   |
| Carobene et al77          | Multicity, Argentina         | TSW                      | 273         | 34.1 (n = 93)                | Laboratory                   |
| Verre et al57             | Multicity, Peru              | Convenience:             | 709 (5148 total) | 14.4 (n = 102) | Laboratory                  |
|                          |                              | MSM & TF                 |             |                              |                              |
| Lipsitz et al61           | Lima, Peru                   | Mobile testing           | 208         | 30.8 (n = 64) 49-1st time testers | Laboratory                   |
| Aguayo et al64            | Multicity, Paraguay          | Not specified            | 311         | 27                            | Laboratory                   |
| Martins et al62           | Fortaleza, Brazil            | RDS                      | 304         | 12                            | Self-report                  |
| Silva-Santisteban et al64 | Lima, Peru                   | RDS                      | 420         | 29.6                          | Laboratory                   |
| Barrington et al65        | San Salvador, El Salvador    | RDS                      | 67          | 19                            | Laboratory                   |
| Zea et al66               | Bogota, Columbia             | RDS                      | 58          | 13.8 (n = 8)                  | Laboratory                   |
| Solomon et al65           | Guayaquil, Ecuador           | iPrex screen             | 131         | 16.8                          | Laboratory                   |
| Pinheiro et al63          | Fortaleza, Brazil            | RDS                      | 304 total; 208 ever tested | 12 of those ever tested | Self-report                  |
|                          |                              |                          |             |                              |                              |
| **Asia/Pacific Islands**  |                              |                          |             |                              |                              |
| Best et al56              | Multicity, China             | LGBT websites            | 52          | 11.1                          | Self-report                  |
| Veronese et al16          | Port Vila, Vanuatu           | RDS                      | 23          | 0                             | Laboratory                   |
| Ramakrishnan et al81      | Tamil Nadu, India            | Probability              | 575         | 18.1 (n = 104)                | Laboratory                   |
| Subramanian et al86       | Tamil Nadu, India            | Avahan eval              | 120; 9.8    |                               | Laboratory                   |
| Emmanuel et al75          | Multicity, Pakistan          | Peer referral            | 3714 HSW (16,642) | 7.2 | Laboratory                   |
|                          |                              | MSM & TW                 |             |                              |                              |
| Yadegarfard et al79       | Bangkok, Thailand            | Purposive, youth         | 190         | 21 didn’t report, 24 didn’t know, no one said yes | Self-report                  |
|                          |                              |                          |             |                              |                              |
| Nemoto et al77            | Bangkok, Thailand            | Venue based, Kathoey SW  | 112         | 0 (only half tested)          | Self-report                  |
| Altaf et al71             | Multicity, Pakistan          | Network sampling (HSW)   | 619         | 6.4                           | Laboratory                   |
| Sahastrabuddhe et al78    | Multicity, India             | Urban STI clinics        | 84          | 45.2                          | Laboratory                   |
| Akhtar et al79            | Rawalpindi, Pakistan         | Convenience (hijra)      | 306         | 21.6                          | Laboratory                   |
| **Other**                 |                              |                          |             |                              |                              |
| Fernandez-Balbuena et al80| Multicity, Spain             | Testing sites            | 101         | 5.0 (n = 5)                   | Laboratory                   |
| Dias et al73              | Multicity, Portugal          | SW CBOs and locations    | 59; 9       | 17.6; 22.2 (n = 2)            | Self-report; Laboratory      |
| Diez et al84              | Multicity, Spain             | STI clinics              | 529         | 24.5 1.2/100p-y              | Laboratory                   |
| Almeida et al79           | Lisbon, Portugal             | Clinic-based, SW         | 20 (151)    | 80.0                          | Laboratory                   |
| Reisner et al83           | Latin America, Spain, Portugal | Internet MSM            | 131 TF      | 6.9                            | Self-report                  |
| Bauer et al82             | Ontario, Canada              | RDS                      | 205         | 3.0 weighted*                 | Self-report                  |
| Buchbinder et al84        | Brazil, Ecuador, Peru, South Africa, Thailand, and USA | RCT, placebo arm | 162 | 3.6/100 p-y | Laboratory                   |
| Manieri et al80           | Torino, Italy                | RCT                      | 142         | 5.3 of MTF (n = 3)            | Laboratory                   |
| Patrascioiu et al85       | Catalonia, Spain             | Gender clinic            | 56; TM 27   | 12.6                          | Laboratory                   |

*Forty-two percent never tested.

MSM, men who have sex with men; TM, trans masculine; TF, trans feminine.
most found that these factors/conditions were associated with HIV risk. However, few studies included methods to test for associations between the factors or synergistic (interactive) effects on health. Four studies report dose–response relationships between syndemic factors and HIV-related outcomes that suggest additive, rather than synergistic effects.52,53 Five studies23,44,88,89,91 operationalized syndemics by creating a composite index of scales to measure each included factor.

Two studies explored syndemic factors among trans masculine individuals. A small clinic sample (n = 23) of trans masculine individuals found that both alcohol use and psychosocial distress were associated with sexual risk behaviors.53 A larger study (n = 173) of trans masculine individuals found that both alcohol use and history of one or more suicide attempts associated with sexual risk behaviors53.

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The 2 studies that examined syndemics among trans feminine youth were both based in Los Angeles. Wilson et al found that an index including depression, trauma, bullying, stigma, and parental rejection was associated with both HIV risk behaviors and self-reported HIV (n = 282)44, and Brennan et al found associations between HIV risk and self-esteem, substance use, and victimization (n = 151).44

Among trans feminine adults, a San Francisco-based study developed a syndemic index of alcohol, drug use, and condomless anal intercourse and found that stigma was independently associated with this index (n = 151).40 However, no significant association was found between the index itself and self-reported HIV status. The study did identify significant correlations between the syndemic factors themselves. Zimmerman et al22 used structural equation modeling to test whether components of a syndemic of mental health problems, drug use, and alcohol use mediate the relationship between stigma and HIV risk behaviors among trans feminine people (n = 117) in Richmond and Washington, DC. This method was unique in allowing for multiple co-occurring HIV risk outcomes (eg, multiple partners, condomless sex, etc.) and multiple associated psychosocial risk factors. However, the model did not allow for correlations between the syndemic factors themselves.

Within a syndemic framework, Chu et al examined coinfection with HIV and at least one other disease (including tuberculosis, viral hepatitis, and sexually transmitted infections) among over 15,000 people living with HIV in San Francisco, CA. They found that an index including depression, trauma, bullying, stigma, and parental rejection was associated with both HIV risk behaviors and coinfection (n = 15,056).49

### TABLE 4. Summary of Studies Examining Syndemic Production of HIV in Trans Populations, 2012–2015

| Citation | Location | Study Population | Sampling Method | Syndemic Production |
|----------|----------|-----------------|-----------------|---------------------|
| Reisner et al53 | Boston, MA | 23 adults | EMR review | Alcohol use and history of one or more suicide attempts associated with sexual risk behaviors |
| Reisner et al53 | Boston, MA | 173 TMSM | Convenience | Syndemic index (alcohol, substance use, depression, anxiety, childhood abuse, IPV) associated with multiple partners, lifetime STIs, and condomless anal or vaginal sex in TMSM who had socially affirmed their gender |
| Brennan et al44 | Los Angeles, CA | 151 youth | Outreach and referral | 3–4 syndemic factors (self-esteem, polysubstance use, victimization, IPV) associated with self-reported HIV, 2 or more syndemic factors associated with UAI |
| Wilson et al91 | Los Angeles, CA | 282 youth | Baseline cohort data | Test syndemic of depression, trauma, bullying, stigma, unstable housing, and parental rejection with HIV risk behaviors and self-reported HIV |
| Operario et al90 | San Francisco, CA | 191 adults | purposive | UAI, alcohol, and drug use intercorrelated = syndemic; Stigma independently associated with UAI, drug use, and composite syndemic index |
| Chakrapani et al88 | Multisite, India | 300 adults | Convenience | Higher number of psychosocial conditions (depression, alcohol, and victimization) associated with sexual risk |
| Zimmerman et al92 | Richmond, VA; Washington, DC | 117 adults | Various venues | SEM of syndemic theory and gender affirmation model testing (1) syndemic factors (mental health, drug use, alcohol use) as mediators between internalized homophobia/perceived discrimination and HIV risk behaviors versus (2) syndemic factors mediating HIV risk behaviors via exchange sex |

Chu et al49 | San Francisco, CA | 15,056 PLHIV | Registry monitoring | HIV and at least one co-infection (TB, viral hepatitis, and STDs) more common among transgender PLHIV

IPV, intimate partner violence; UAI, unprotected (condomless) anal intercourse; SEM, structural equation model; PLHIV, people living with HIV; TMSM, trans masculine men who have sex with men; EMR, electronic medical record.
Francisco and found that comorbidity was more common among transgender people than nontransgender people. They also found a significant positive correlation between the number of co-occurring infections and mean viral loads. The one study outside the United States recruited participants from 4 states in India. Chakrapani et al found that depression, alcohol, and victimization were associated with sexual risk for trans feminine participants (n = 300).

DISCUSSION

These data make it clear that trans feminine populations in the United States and around the world have a remarkably high prevalence and incidence of HIV infection. The discrepancy between self-reported HIV prevalence and laboratory-confirmed HIV suggests that many trans feminine individuals remain unaware of their HIV status and thus cannot benefit from early treatment and may be at risk of onward HIV transmission. While limited, data among trans masculine populations suggest low risk relative to trans feminine populations, with the potential exception of transgender men who have sex with nontransgender men. Public health agencies should increase HIV testing in these populations to identify those who are unaware of their HIV-positive status and effectively link them to HIV care and treatment programs.

The quality and quantity of HIV data on transgender populations are improving, but remain limited. HIV burden estimates from the reviewed studies should be cautiously interpreted in light of data limitations, particularly small sample sizes and convenience sampling from HIV prevention programs, sex work venues, and other settings that are likely to generate higher-risk samples. Globally, the lack of available HIV prevalence data among transgender people in sub-Saharan Africa and Eastern Europe/Central Asia represents a priority area for future epidemiologic research. In the United States, most recent HIV data in transgender populations have come from specialized centers in Massachusetts and California serving high numbers of lesbian, gay, bisexual, and transgender individuals in metropolitan urban areas. It will be important to identify the specific HIV-related needs of transgender people in rural areas of the United States, especially in the South where prevalence of HIV infection is highest.

Accurate data capture of HIV risk in transgender populations requires gender-affirmative sexual and behavioral risk assessments that assess anatomical structures in a sensitive way while being socially affirming of individual gender identities. Although condomless receptive anal sex appears the most predominant proximal risk behavior for trans feminine people globally, trans feminine people may also have condomless insertive anal sex. Similarly, trans masculine people may have receptive vaginal sex with nontransgender male partners, and condomless vaginal sex may be more common than condomless anal sex for this population. Additionally, the types of sex transgender people have, and levels of risk behaviors they engage in, may differ by partner type (eg, transactional sex partners, casual partners, main/primary partners).

The variability in HIV prevalence estimates within and across geographic locations indicates the importance of context. In the United States, trans feminine people of color have the highest prevalence of HIV in every study that included an analysis by race. Trans feminine people of color face unique social and economic vulnerabilities created by the intersection of gender identity stigma and the systemic racism that potentiates a higher prevalence of HIV among people of color in the general US population. Even within racial groups in close geographic proximity, access to care can vary widely by municipality. Similar dynamics impact racial/ethnic minorities and migrants in Europe and elsewhere, who face additional barriers to health care and social inclusion if they are undocumented. For example, data from Spain and Portugal indicate that HIV infection disproportionately impacts trans feminine sex workers who have migrated from Latin America. Lower access to healthcare, increased levels of poverty and housing instabilities, treatable STIs, lower levels of health literacy, higher HIV prevalence in social networks, and higher network or community viral load are all potential explanatory factors producing and maintaining inequities in HIV infection for trans feminine people of color and migrants. The combination of high burden of HIV, systemic disadvantage, and unmet need for gender affirming services make trans feminine people of color an underserved and priority population for HIV testing, prevention, and treatment.

Existing data on syndemics suggest difficulty in successfully treating and preventing HIV infection in isolation from the other social, behavioral, and medical conditions that co-occur and interact to limit successful and sustained engagement in health care. However, research on syndemic production of HIV among transgender populations is nascent. Studies that aim to examine syndemics often do not use methods that capture both the concentration of co-occurring psychosocial conditions and their interaction to produce synergistic deleterious effects. As the importance of syndemics becomes increasingly clear, more sophisticated analytic methods are needed. This includes examining the developmental trajectories of syndemics, such as timing, onset, and antecedents, to inform early prevention efforts and identifying appropriate multimodal interventions that address syndemics and the barriers they present to effective engagement in HIV prevention and treatment programs, including initiation of and adherence to oral pre-exposure prophylaxis (PrEP) and antiretroviral medications (ART) for those living with HIV.

ART and PrEP have emerged as powerful tools in the HIV response. However, unless HIV services are acceptable and accessible to transgender people, coverage and ultimate effectiveness of these interventions will be limited. Emerging data suggest that HIV services are more acceptable to transgender people when they are destigmatizing and include access to gender-affirming care. Although there are specialized centers in a few urban settings that provide primary care and HIV wrap-around services, the clearly identified and urgent need for transgender-competent HIV services has largely gone unmet globally. Programs designed for MSM are inappropriate for trans feminine populations and are likely to be unacceptable to individuals who do not identify as men. At the same
time, MSM programs may be unwelcoming to trans masculine individuals who have sex with men who may desire and benefit from MSM services.\textsuperscript{15,87}

Although many of the syndemic conditions described for transgender populations are also well-known determinants of health for other groups,\textsuperscript{29} transgender populations face additional challenges of gender-related stigma, unmet gender affirmation needs, and inadequately trained health care providers.\textsuperscript{106} In combination, these factors form significant challenges to engagement in HIV prevention and treatment. The enormous burden of HIV, especially among trans feminine individuals, suggest a growing epidemic that requires us to address these challenges to engage transgender people and meet global objectives for HIV prevention and care. Future research should prioritize filling critical gaps in HIV epidemiology among transgender people in sub-Saharan Africa and Eastern Europe and rural areas globally. Studies are needed to clarify how stigma shapes syndemic factors to produce HIV and other deleterious effects on transgender health and ultimately to understand how best to implement acceptable, accessible, and effective HIV interventions for transgender people.

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