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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

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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. The most recent population-based data from the United States estimate that 0.5% of the population was

identified as transgender.⁶ This proportion is consistent with passport identity data from New Zealand⁷, yet much lower than the 1.2% who identified as transgender in a recent nationally representative sample of New Zealand high school students.⁸

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). 11,12 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. 13,14 Coinfection with perigenital or perianal STIs may also potentiate the acquisition and transmission of HIV. 15,16 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. 17 Network level risks include a high prevalence of HIV and limited awareness of HIV status within transgender-inclusive sexual networks. 18,19 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. 20–23

A systematic review and meta-analysis of the burden of HIV in trans feminine populations was published in 2012.²⁴ 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.²⁵ 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,²⁶ 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.²⁷ Stigma is a powerful social determinant of health²⁸ and a key driver of HIV disparities among transgender populations.¹¹ 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."29 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.³⁰ 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%).31 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

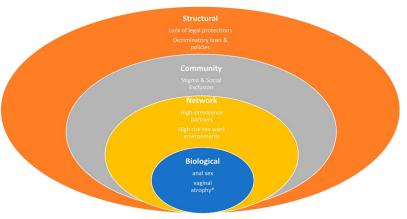


Figure 1. Multilevel drivers of HIV risk among transgender populations.

*Hormone mediated atrophy of vaginal tissue among trans masculine MSM taking testosterone

"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

TABLE 1. HIV Prevalence and Incidence Among Transgender People in the United States, 2012–2015

					Prevalence, % (n) (Incidence in	Method of HIV
Citation	City, State	Population	Sampling Method	Sample Size	Person-Yrs)	Ascertainment
Mixed Gender or Gender Spectrum Unspecified						
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 al ³⁷	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 al ³⁹	US, PR, UVI	All trans	HIV testing event* data	TF 13,154; TM 2364	2.7 new; 0.5 new	Laboratory
Leinung et al ⁴⁰	Upstate, NY	All trans	Gender clinic chart review	TF 192; TM 50	8.3 of TF (n = 16)	Laboratory
Reisner et al ⁴¹	Boston, MA	All trans	Clinic attendees	31	12.9 (n = 4)	Self-report
Reisner et al ⁴²	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 al ⁴³	Washington, DC	Trans unspecified	HIV testing campaign	85	10.6 (n = 9) overall	Laboratory
Trans Feminine						
Brennan et al ⁴⁴	Chicago and Los Angeles, CA	Youth 15-24 yrs	Clinic, venue based, peer referral	151	15.9 (n = 24)	Self-report
Garofalo et al ⁴⁵	Chicago, IL	Youth 16-24 yrs	Active and passive	51	5.9 (n = 3)	Self-report
Rowe et al ⁴⁶	San Francisco, CA	Youth 16-24 yrs	Peer referral, social network sites, trans events, CBOs	292	4.5 (n = 13)	Laboratory
Bowers et al ⁴⁷	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 al ³³	New York, NY	Adult	Purposive	591 (baseline); 230 (cohort)	40.1 2.9/100 p-y	Laboratory
Nemoto et al ¹³	San Francisco and Oakland, CA	Adult	Purposive, TW with sex work history	538	29.9	Laboratory
Rapues et al ⁴⁹	San Francisco, CA	Adult	RDS	314	35.0 (n = 110)	Lab
Reback and Fletcher ⁵⁰	Los Angeles	Adult	Street outreach	2136	13.6	Self-report
Reisner et al ⁵¹	San Francisco, CA	Adult	Purposive	191	18.3 (n = 35)	Self-report
Trans Masculine						
Peitzmeier et al52	Boston, MA	Adult	Clinic chart review	233	0.9 (n = 2)	Lab
Reisner et al ⁵³	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 study used respondent-driven sampling, whereas the rest drew upon convenience or clinic-based samples. Eight studies included prevalence estimates for very small samples (ie, n < 100), predominantly for trans masculine individuals. Four articles did not disaggregate prevalence data by trans feminine or trans masculine gender spectrum. 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 sample \$^{16}\$ to 29.9% 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 Francisco and New York, \$^{33}\$ 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 studies \$^{42,45,46}\$ and 15.9% in 1 study. \$^{44}\$

Since 2014, 5 publications^{38,39,42,52,53} have described laboratory-confirmed HIV prevalence among trans masculine people in the United States, ranging from 0.9%⁵² to 4.3%.⁵³ 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 studies^{72,86} 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.⁸³

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 onequarter 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, laboratoryconfirmed prevalence was 6.4%-7.2% in 2 studies, 71,75 and 21.6% in a third.⁶⁹ 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 populations^{23,44,53,88–92} (Table 4). Only one study was conducted outside the United States.⁸⁸ Two studies were among trans masculine individuals^{23,53}; 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. 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.

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 al ⁸⁶	Vancouver, Canada	TMSM, RDS	14	0	Laboratory test
Bauer et al ⁷²	Ontario, Canada	TM, RDS	227	0.6 weighted; $n = 0$	Self-report
Reisner et al ⁸³	LAC, Spain, Portugal	TMSM, Internet	25	8.0 (n = 2)	Self-report
Patrascioiu et al85	Catalonia, Spain	TM, Clinic	92	2.2	Laboratory test
Scheim et al ⁸⁷	Global	TMSM, Internet	69	1.4 (n = 1)	Self-report

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

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 al ⁵⁸	Lima, Peru	Snowball	207	16.9 2.3/100p-y	Laboratory
Costa et al ⁵⁹	Multicity, Brazil	Gender clinic	284	25.0 (n = 71)	Laboratory
Carobene et al ⁵⁷	Multicity, Argentina	TSW	273	34.1 (n = 93)	Laboratory
Verre et al ⁶⁷	Multicity, Peru	Convenience: MSM & TF	709 (5148 total)	14.4 (n = 102)	Laboratory
Lipsitz et al ⁶¹	Lima, Peru	Mobile testing	208	30.8 (n = 64) 49-1st time testers	Laboratory
Aguayo et al54	Multicity, Paraguay	Not specified	311	27	Laboratory
Martins et al ⁶²	Fortaleza, Brazil	RDS	304	12	Self-report
Silva-Santisteban et al ⁶⁴	Lima, Peru	RDS	420	29.6	Laboratory
Barrington et al55	San Salvador, El Salvador	RDS	67	19	Laboratory
Zea et al ⁶⁸	Bogota, Columbia	RDS	58	13.8 (n = 8)	Laboratory
Solomon et al ⁶⁵	Guayaquil, Ecuador	iPrex screen	131	16.8	Laboratory
Pinheiro et al ⁶³	Fortaleza, Brazil	RDS	304 total; 208 ever tested	12 of those ever tested	Self-report
Fernandes et al ⁶⁰	Campo Grande, Brazil	Purposive	152	24.4 (n = 37)	Laboratory
Socias et al ⁸²	Multicity, Argentina	Snowball; quota	452	27.4 (n = 104)	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 al ⁶⁶	Tamil Nadu, India	Avahan eval	R1 = 404; R2 = 403	12.0; 9.8	Laboratory
Emmanuel et al ⁷⁵	Multicity, Pakistan	Peer referral MSM & TW	3714 HSW (16,642)	7.2	Laboratory
Yadegarfard et al ⁷⁹	Bangkok, Thailand	Purposive, youth	190	21 didn't report, 24 didn't know, no one said yes	Self-report
Nemoto et al ⁷⁷	Bangkok, Thailand	Venue based, Kathoey SW	112	0 (only half tested)	Self-report
Altaf et al ⁷¹	Multicity, Pakistan	Network sampling (HSW)	619	6.4	Laboratory
Sahastrabuddhe et al ⁷⁸	Multicity, India	Urban STI clinics	84	45.2	Laboratory
Akhtar et al ⁶⁹	Rawalpindi, Pakistan	Convenience (hijra)	306	21.6	Laboratory
Other					
Fernandez-Balbuena et al ⁷⁶	Multicity, Spain	Testing sites	101	5.0 (n = 5)	Laboratory
Dias et al ⁷³	Multicity, Portugal	SW CBOs and locations	59; 9	17.6; 22.2 (n = 2)	Self-report; Laboratory
Diez et al ⁷⁴	Multicity, Spain	STI clinics	529	24.5 1.2/100p-y	Laboratory
Almeida et al ⁷⁰	Lisbon, Portugal	Clinic-based, SW	20 (151)	80.0	Laboratory
Reisner et al ⁸³	Latin America, Spain, Portugal	Internet MSM	131 TF	6.9	Self-report
Bauer et al ⁷²	Ontario, Canada	RDS	205	3.0 weighted*	Self-report
Buchbinder et al ⁸⁴	Brazil, Ecuador, Peru, South Africa, Thailand, and USA	RCT, placebo arm	162	3.6/100 p-y	Laboratory
Manieri et al ⁸⁰	Torino, Italy	Gender clinic	TF 56; TM 27	5.3 of MTF (n = 3)	Laboratory
Patrascioiu et al ⁸⁵	Catalonia, Spain	Clinic	142	12.6	Laboratory test

^{*}Forty-two percent never tested.

MSM, men who have sex with men; TM, trans masculine; TF, trans feminine.

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

Citation	Location	Study Population	Sampling Method	Syndemic Production
Trans Masculine				
Reisner et al ⁵³	Boston, MA	23 adults	EMR review	Alcohol use and history of one or more suicide attempts associated with sexual risk behaviors
Reisner et al ²³	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
Trans Feminine				
Brennan et al ⁴⁴	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 al ⁹¹	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 al ⁹⁰	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 al ⁸⁸	Multisite, India	300 adults	Convenience	Higher number of psychosocial conditions (depression, alcohol, and victimization) associated with sexual risk
Zimmerman et al ⁹²	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
Gender Spectrum Unspecified				
Chu et al ⁸⁹	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.

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. 44,88,89,91 Five studies 23,44,88,90,91 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. A larger study (n = 173) of trans masculine adults who had sex with nontransgender men found an association between the number of negative psychosocial conditions (alcohol and substance use, depression, anxiety, childhood abuse, and intimate partner violence) and increased odds of sexual risk. This study also found a significant interaction between the number of psychosocial conditions and social gender transition; however, interactions between the psychosocial conditions themselves were not examined.

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)⁹¹, 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 = 191).90 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 al⁹² 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 and found that comorbidity was more common among transgender people than nontransgender people.⁸⁹ They also found a significant positive correlation between the number of co-occurring infections and mean viral loads. The one study from 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).⁸⁸

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 populations³⁹ 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.⁹³

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, 15,42 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. 21,93,95,96 Even within racial groups in close geographic proximity, access to care can vary widely by municipality.⁹⁷ 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. 98 For example, data from Spain and Portugal indicate that HIV infection disproportionately impacts trans feminine sex workers who have migrated from Latin America. 70,73,76,85 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 cooccurring psychosocial conditions and their interaction to produce synergistic deleterious effects.⁹⁹ As the importance of syndemics becomes increasingly clear, more sophisticated analytic methods are needed. 31,99 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. 100,101

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 destignatizing and include access to gender-affirming care. ^{102,103} 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 ¹⁰⁴ and are likely to be unacceptable to individuals who do not identify as men. ¹⁰⁵ 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. ^{15,87}

Although many of the syndemic conditions described for transgender populations are also well-known determinants of health for other groups,²⁹ transgender populations face additional challenges of gender-related stigma, unmet gender affirmation needs, and inadequately trained health care providers. 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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