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RESEARCH ARTICLE

Syndemic violence victimization, alcohol and drug use, and HIV transmission risk behavior among HIV-negative transgender women in India: A cross-sectional, population-based study

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Abstract

Transgender women globally are disproportionately burdened by HIV. Co-occurring epidemics of adverse psychosocial exposures accelerate HIV sexual risk, including among transgender women; however, studies using additive models fail to examine synergies among psychosocial conditions that define a syndemic. We examined the impact of synergistic interactions among 4 psychosocial exposures on condomless anal sex (CAS) among transgender women in India. A national probability-based sample of 4,607 HIV-negative transgender women completed the Indian Integrated Biological and Behavioural Surveillance survey, 2014–2015. We used linear probability regression and logistic regression to assess 2-, 3-, and 4-way interactions among 4 psychosocial exposures (physical violence, sexual violence, drug use, and alcohol use) on CAS. Overall, 27.3% reported physical and 22.3% sexual violence victimization (39.2% either physical or sexual violence), one-third (33.9%) reported frequent alcohol use and 11.5% illicit drug use. Physical violence was associated with twofold higher odds of CAS in the main effects model. Statistically significant two- and three-way interactions were identified, on both the multiplicative and the additive scales, between physical violence and drug use; physical and sexual violence; physical violence, sexual violence, and alcohol use; and physical violence, alcohol use and drug use. Physical and sexual violence victimization, and alcohol and drug use are highly prevalent and synergistically interact to increase CAS among HIV-negative transgender women in India. Targeted and integrated multilevel initiatives to improve the assessment of psychosocial comorbidities, to combat systemic transphobic violence, and to provide tailored, trauma-informed alcohol and substance use treatment services may reduce HIV risk among transgender women.

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Introduction

Transgender women globally bear a disproportionate HIV burden [1] secondary to rampant stigma and discrimination in various domains of their lives [2]. India's National AIDS Control Organization (NACO) designates transgender women a 'high risk group' or 'key population', with official HIV prevalence estimates ranging from 9.5% (in 2015 [3]) to 3.1% (in 2017 [4])—up to 40 times higher than HIV prevalence in the general population (0.22%) [5]. Until 2006, NACO-supported HIV preventive interventions subsumed transgender women under "men who have sex with men"; but they are now reached through 41 interventions exclusively for transgender women and 152 'core-composite' targeted HIV interventions for transgender women with other at-risk populations [5]. These targeted interventions focus on HIV and STI education, condom promotion, free condom distribution, and HIV testing referrals. Transgender women in India have demonstrated a high (89%) awareness of the usefulness of condoms in preventing HIV infection; nevertheless, consistent condom use remains low, at 45% to 54% [3,6].

Syndemic theory has been applied to explain the clustering and concentration of diseases such as HIV in vulnerable populations [7], including transgender women [1,8]. In their classic paper, Stall et al. [9] highlighted the public health impacts of co-occurring psychosocial health problems or challenges among gay men in the U.S., advancing a life-course theory of syndemic production rooted in the cultural marginalization of a population that is heavily stigmatized and subjected to manifold human rights violations in the U.S. context [10]. In the Indian context, harmful social conditions such as societal stigma faced by transgender women may lead to clustering of psychosocial challenges, such as violence victimization [11–13], problematic alcohol use [14], depression [15], suicidal ideation and attempts [16], and HIV risk [17]; these may mutually reinforce one another and synergistically amplify the overall disease burden in this population. Transgender women in India have a high prevalence of psychosocial health challenges, including lifetime physical or sexual violence victimization (84%), alcohol use (37%) and depression (35%), all of which have demonstrated significant additive effects on HIV risk [14]. One study reported 18% past-year prevalence of sexual violence victimization, with higher risk for HIV among those who experienced sexual violence [18].

Exploring the presence of synergy among psychosocial health conditions requires the use of appropriate analytical strategies. A recommended analytical technique for testing synergy is by checking for statistical interaction (on the additive and/or multiplicative scale) between co-occurring conditions [19,20]. Most analyses in western literature that purportedly explored synergy used the number of psychosocial conditions or exposures as a cumulative count to predict HIV risk behavior, which does not address the interaction concept embedded in syndemic theory [19]. Two papers on syndemics among transgender women in India each used analytical strategies that did not involve testing for interactions between psychosocial conditions. One study used the number of psychosocial syndemic conditions as a cumulative count to predict HIV risk behavior [14]. Another study used latent class analysis to identify different 'syndemic classes' (combinations of depression, alcohol use, and/or violence victimization), which were associated with higher HIV risk compared to no syndemic class [6].

To address research gaps in the application of syndemic theory and support the design of tailored, evidence informed interventions, we assessed potential synergistic interactions between sexual and physical violence, alcohol use, and drug use on condomless anal sex (CAS) among transgender women.

Materials and methods

Ethics statement

The Integrated Biological and Behavioural Surveillance (IBBS) study was approved by the ethics committees of the National AIDS Control Organization (NACO) and participating Indian Council of Medical Research regional institutes. All participants provided written informed consent; for those 15–17 years-old, consent was also obtained from their parent/guardian. Monetary compensation of INR 200 (~3 USD) was provided. The present secondary analysis received administrative approval from NACO before accessing the IBBS data. Deidentified data are available on a case-by-case basis from NACO.

Study design and population

Data for these analyses were drawn from a population-based cross-sectional survey among transgender women recruited under India's NACO IBBS study, last conducted from 2014–2015. The IBBS aimed to generate evidence on risk behaviors among groups deemed to be at high risk of HIV acquisition (i.e., transgender women, female sex workers, men who have sex with men) to support planning and prioritization of HIV program efforts. Eligibility criteria were as follows: persons aged $\geq$15 years, whose self-identity does not conform unambiguously to conventional notions of male or female gender roles but combines or moves between them.

This paper presents findings from a secondary analysis of NACO population-based study data to examine the burden of adverse psychosocial exposures, co-occurrence of these exposures, and their potential independent and synergistic effects on CAS among transgender women.

Sampling and recruitment

The IBBS sample size was calculated with the primary objective to measure changes in consistent condom use with sexual partners and changes in HIV prevalence. The primary unit of survey was a 'domain': a geographical unit of either a single district or a group of four socio-culturally similar districts where a single district had an insufficient sample size. Sampling included both conventional cluster sampling (CCS) (at sites such as homes and brothels where transgender women could be found at any time of the day) and time-location cluster sampling (TLCS) (at sites such as parks and beaches where transgender women could be found on particular days and times to meet or socialize with other transgender people or potential male partners). The estimated sample size of transgender women for each domain was >700. However, considering feasibility based on sample availability in different domains, a target sample size of 400 per domain was chosen. In domains with sample sizes <400, a 'take all' approach was used. Overall, the target sample size was 5,588 transgender women in 15 domains across 11 states. A valid sample of 4,966 transgender women was achieved, with an 81% response rate. NACO's online report [21] provides further details on sampling and recruitment.

Measures

Information on participants' sociodemographic characteristics included age (in years), years of education, marital status, engagement in sex work (past year) and self-identified gender-affirmative surgical status (*ackwa*: pre- or non-operative, or *nirvan*: post-operative). Table 1 describes how the outcome, primary exposures, and other relevant covariates used in the analysis were measured—survey items, response range and scoring, and creation of binary and continuous measures. The binary outcome measure was CAS with any type (regular, paying, paid, and casual) of male sexual partner in the past month. The binary exposure variables of

Table 1. Summary of key measures: Outcome, primary exposures, and other relevant covariates.

Measures	Survey items		Range of responses, coding, and scores	Types of variables
	Number of items	Questions asked		
Outcome				
Condomless anal sex with male partners (past month)	4	In the last one month, how often have you used condoms when you had anal sex with your . . .? a. regular non-paying male partner b. paying male partner c. paid male partner d. casual non-paying male partners	0 for 'every time' and 1 for all other options (most of the time, sometimes, never) 'Condomless anal sex' was created by combining the condom use (= 1) responses from these four types of partners.	Binary
Primary exposures				
Physical violence (past year)	2	In the last 12 months, how many times would you say someone has beaten (hurt, hit, slapped, pushed, kicked, punched, choked or burned) you? In the last 12 months, who was the person (or people) who have beaten you?	0 for 'never' and 1 for other responses (Once, 2–5 times, 6–10 times, >10 times). Those who responded as "Do not remember" but reported the person who caused physical violence were also categorized as having experienced physical violence.	Binary
Sexual violence (past year)	1	In the last 12 months, were you physically forced to have sexual intercourse with someone even though you didn't want to?	Yes = 1, No = 0	Binary
Violence victimization (past year)	-	Recoding of the final coding of physical and sexual violence variables.	'Violence victimization' was created by considering the codes of physical violence (from never = 0, Once = 1, 2–5 times = 2, 6–10 times = 3, >10 times = 4) and sexual violence (Yes = 1, No = 0) as scores, and combining these scores. Score range: 0–5	Continuous
Alcohol use (past week)	1	How many days did you consume alcohol in the last one week?	Responses dichotomized at the upper quartile of consumption, ≤3 vs. >3 days/week. Score range: 0–7 (Number of days of alcohol use in the past week)	Binary Continuous
Drug use (past year)	2	Have you consumed drugs such as Ganja, Heroine for pleasure in the last 12 months? Have you injected drugs for nonmedical reasons in the last 12 months?	Yes = 1, No = 0 Consumption of any drug (injection or not) was considered as 'drug use'. Score range: 0–3	Binary Continuous
Relevant covariates				
Engagement in sex work (past year)	1	Have you received cash or gifts from men in exchange for sex in the last 12 months?	Yes = 1, No = 0	Binary
Knowledge of HIV transmission risk	5	Can a person get HIV/AIDS? a. by having unprotected sex with an infected person b. by sharing infected needles c. by infected blood transfusion d. through mosquito bites Can HIV be transmitted from an HIV infected mother to e. her unborn baby during pregnancy/delivery or to the new born child through breastfeeding?	Yes = 1, No = 0 For the analysis, each correct response was coded as 1, otherwise 'zero'. Score range: 0 to 5	Continuous
HIV risk perception	1	To what extent do you feel yourself at risk to being infected with HIV/AIDS?	High = 1, Moderate = 2, Low = 3, No risk = 4 Responses were dichotomized by combining response 1 and 2 as 'High risk', 3 and 4 as 'Low risk'	Binary
Forced sex experience during adolescence	2	How old were you when you had your first sex with a male? Were you forced to have sex during the first sexual encounter with a male?	Participants who reported first sex with a male when they were <18 years (age of consent for heterosexual intercourse in India), and of them who reported forced sex during the first sexual encounter with a male, were categorised as having experienced forced sex during adolescence.	Binary

(*Continued*)

Table 1. (Continued)

Measures	Survey items		Range of responses, coding, and scores	Types of variables
	Number of items	Questions asked		
HIV program exposure	8	Have you received following services from any NGO/program/individual/group during the last 12 months? a. Received information on STI/HIV/AIDS b. Received condoms c. Received lubricants d. Seen a demonstration on correct condom use e. Received check-up and counselling for STIs f. Received free medicine for STIs g. Visited drop in center h. Referred to other services (STI clinic, HIV testing, etc.)	Yes = 1, No = 0 Score range: 0 to 8	Continuous
Social support score	3	Have you received following services from any NGO/program/individual/group during the last 12 months? a. Received help and support when faced with physical or sexual violence b. Received help and support when faced with trouble from police Are you a member of . . .? c. a self-help group or transgender women collective	Yes = 1, No = 0 Score range: 0 to 3	Continuous

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interest included any physical violence [PV], sexual violence [SV], and drug use [D] (non-injection or injection drugs) in the past year, and frequent alcohol use [A] (>3 days) in the past week (Table 1). Other covariates included engagement in sex work, forced sex experience during adolescence (<18 years), HIV transmission knowledge (score), HIV risk perception (high vs. low), social support (score), and HIV program exposure (score).

Analysis

The present analysis was restricted to HIV-negative transgender women (n = 4,607). HIV-positive participants (n = 359; 7.2%) were excluded given the objective of identifying correlates of HIV risk behavior to inform primary prevention initiatives. All analyses were conducted in Stata (version 16; College Station, Texas, USA). Descriptive statistics were used to summarize participant characteristics. Independent associations between adverse psychosocial exposures (binary) and CAS (binary) were estimated using logistic regression. The extent to which the adverse psychosocial exposures synergistically interacted with each other in their associations with CAS was examined by assessing interactions on the additive scale using linear probability regression models, and on the multiplicative scale using logistic regression models [19,22]. All possible two-way (e.g., physical violence × drug use), three-way (e.g., sexual violence × drug use × alcohol use), and four-way interaction terms (e.g., physical violence × sexual violence × drug use × alcohol use) were included in the regression models. All regression models were adjusted for age (in years), education, marital status (single vs. heterosexually married), gender-affirmative surgical status (*ackwa* vs. *nirvan*), engagement in sex work, forced sex experience during adolescence, knowledge of HIV transmission risk, HIV risk perception, social support, and exposure to HIV interventions. To account for the complex survey design [23] involving cluster sampling, 'svyset' and 'svy' Stata commands were used to estimate all regression models [24].

On the additive scale in linear probability regression models, synergy is interpreted as a statistically significant relative excess risk due to interaction (RERI) greater than zero; and on the

multiplicative scale in logistic regression models, synergy is interpreted as a statistically significant positive coefficient on the product term [22,25]. Multiplicative interaction estimated on the odds scale using logistic regression was re-estimated as 'semi-elasticities' on the probability scale using the Stata 'margins' command. The estimated semi-elasticities can be interpreted as the proportional change in the probability of CAS that is associated with a one unit change in the covariate or with the interaction. For example, a semi-elasticity of .40 is interpreted as a 40% relative change in the expected probability of CAS associated with a one unit change in the covariate (e.g., age in years) or with the joint effect of two (PV × D) or more (PV × SV × D) exposures, above and beyond their independent associations with the outcome.

Sensitivity analysis for the model of synergistically interacting epidemics

To confirm the robustness of our findings, as part of the sensitivity analysis, we specified: 1) drug use (score range, 0–3) and alcohol use (range, 0–7) as continuous exposures; 2) physical and sexual violence (score range, 0–5) as a single continuous exposure, along with CAS (range, 0–4) as a continuous outcome in both sensitivity analyses.

Exploratory analyses to check for rival theoretical models

In addition to the model of synergistically interacting epidemics, Tsai [26] described two other models of co-occurring epidemics—the serially causal epidemics model (exposures producing an outcome through mediators; or one epidemic leading to another epidemic, which in turn leads to another) and the mutually causal epidemics model (reciprocal relationships between exposures and outcomes, or between two epidemics) [27]; these have been used, variably, in the literature on syndemics. Although our analysis was focused specifically on testing a model of synergistically interacting epidemics, we also tested these other two models as they may suggest alternate or complementary mechanisms of risk. To test the model of serially causal epidemics, we conceptualized alcohol (score range, 0–7) and drug use (range, 0–3) as potential mediators of the association between sexual and physical violence victimization and CAS (range, 0–4). Similarly, we tested the model of mutually causal epidemics, in which we hypothesized that violence victimization (range, 0–5) and drug use (range, 0–3) were mutually reinforcing of one another, given that both were measured in the same time-period (past year). For assessing both of these models, we conducted path analysis (sem command) in Stata-16.

Results

Participant characteristics

Table 2 describes participant characteristics. Participants' mean age was 28.5 years (SD 7.4) and mean number of years of education was 8.4 (SD 4.0). A majority (86.1%) were currently single. Nearly one-third (31.1%) reported sex work as their main occupation, while over half (56.8%) reported engaging in sex work during the past month. About one-fifth (18.3%) reported having experienced forced sex during adolescence (<18 years of age). More than half (57.2%) self-identified as *ackwa*, 42.7% as *nirvan*. About three-fifths (61.6%) perceived themselves at high risk for HIV infection. Reported CAS with different types of male partners in the past month ranged from 35.0% to 46.0%; CAS with any type of male partner was 45.1%.

Co-occurrence of adverse psychosocial exposures

Among the 4,607 HIV-negative transgender women, irrespective of other exposures, more than one-fourth (27.3%) reported having been exposed to physical violence and 22.3% to sexual violence. More than one-third (39.2%) had been exposed to either physical or sexual

Table 2. Characteristics of HIV-negative transgender women who participated in the Integrated Biological and Behavioural Surveillance (IBBS) study, 2014–15 (N = 4,607).

Characteristics	Mean (SD)
Age (in years)	28.5 (7.4)
Education (years)	8.4 (4.0)
HIV transmission knowledge score	4.3 (1.2)
HIV program exposure score	4.7 (2.8)
Social support score	1.7 (1.0)
	N (%)
Engagement in sex work (past month)	2617 (56.8)
Gender-affirmative surgical status	
Ackwa (pre-operative/non-operative)	2636 (57.2)
Nirvan (post-operative)	1969 (42.7)
Current marital status	
Single (never married/widowed/divorced/separated)	3940 (86.1)
Married	637 (13.9)
HIV risk perception [a]	
Low	1594 (34.6)
High	2839 (61.6)
Forced sex experience during adolescence	837 (18.2)
Condomless anal sex (past month), with[b]:	
Regular non-paying male partner	935/2033 (46.0)
Paying male partners	884/2375 (37.2)
Paid male partners	310/885 (35.0)
Casual non-paying male partners	483/1146 (42.1)
Any type of male partner	1502/3328 (45.1)

[a] Percentages may not add to 100 due to missing values.

[b] Among those who had that type of partner(s) and reported anal sex during the past month.

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violence and 10.5% to both physical and sexual violence. Over one-third (33.9%) reported frequent alcohol use and 11.5% reported drug use. Table 3 reports the co-occurrence of physical violence, sexual violence, frequent alcohol use, and drug use. Overall, 16.5% (n = 698) reported two co-occurring psychosocial exposures, ranging from 1.8% (n = 76) co-occurrence of alcohol and drug use to 6.1% (n = 256) alcohol use and physical violence. Three exposures were reported by 5.8% (n = 243), and 2.7% (n = 113) reported all four exposures. About 43% of participants reported no adverse psychosocial exposures.

Perpetrators of physical or sexual violence

Among those who experienced sexual violence (n = 1,029), over one-third (35.9%; n = 369) reported more than one type of perpetrator. Perpetrators were identified as strangers (41.1%), hoodlums (or bullies; *goondas*) (23.9%), clients (23.2%), and family members (21.8%). Among those who experienced physical violence (n = 1,257), 32.5% (n = 409) reported more than one perpetrator type. Perpetrators were identified as strangers (33.0%), police (24.5%), hoodlums (21.2%), family members (20.0%), and clients (17.3%). The Hindi term '*goonda*' (i.e., hoodlum) used in the survey, refers to persons many of whom have a criminal history and extort money from transgender women (and others) in their neighborhood, as well as subject them to threats, and physical and sexual violence.

Table 3. Adverse psychosocial exposures among HIV-negative transgender women (N = 4,607): Physical violence, sexual violence, frequent alcohol use, drug use, and their co-occurrence.

Adverse psychosocial exposures and their co-occurrence	n (%)[a]
Each exposure including co-occurrence with other exposures	
Physical violence, past 12 months	1257 (27.3)
Sexual violence, past 12 months	1029 (22.3)
Drug use, past 12 months	488 (11.5)
Frequent alcohol use, past week (>3 days/week)	1563 (33.9)
Each exposure alone	
Physical violence	352 (8.3)
Sexual violence	264 (6.2)
Drug use	86 (2.0)
Frequent alcohol use	655 (15.5)
Co-occurrence of exposures	
Frequent alcohol use + Drug use	76 (1.8)
Frequent alcohol use + Physical violence	256 (6.1)
Frequent alcohol use + Sexual violence	124 (2.9)
Physical violence + Drug use	35 (0.8)
Sexual violence + Drug use	62 (1.5)
Physical violence + Sexual violence	145 (3.4)
Physical violence + Drug use + Frequent alcohol use	40 (1.0)
Sexual violence + Drug use + Frequent alcohol use	59 (1.4)
Physical violence + Sexual violence + Frequent alcohol use	127 (3.0)
Physical violence + Sexual violence + Drug use	17 (0.4)
Physical violence + Sexual violence + Frequent alcohol use + Drug use	113 (2.7)
No adverse psychosocial exposures	1814 (42.9)

[a] Percentages may not add to 100 due to missing values.

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Synergistic interactions between adverse psychosocial exposures

Using logistic regression to model CAS, without product terms, physical violence [PV] had a statistically significant association with CAS (aOR = 1.94, 95% CI: 1.47–2.56; $p < .001$), while frequent alcohol use [A] (aOR = 1.32, 95% CI: .98–1.77; p = .07), drug use [D] (aOR = .86, 95% CI: .60–1.22; p = .40) and sexual violence [SV] (aOR = .97, 95% CI: .73–1.29; p = .86) did not have statistically significant associations with CAS. Among the other covariates included in the multivariable logistic regression model of main effects without product terms, higher levels of education (aOR = .93, 95% CI: .90–.97; $p < .001$), being unmarried (aOR = .64, 95% CI: .45–.92; p = .016), and nirvan gender-affirmative surgical status (aOR = .68, 95% CI: .52–.88; p = .003) were associated with lower odds of CAS, and forced sex during adolescence with higher odds of CAS (aOR = 1.35, 95% CI: 1.02–1.78; p = .04).

Out of six logistic regression models that included main effects and two-way product terms, the following product terms were statistically significant: PV × D (Model 1) and PV × SV (Model 5) (Table 4). In the additional five logistic regression models that included main effects and two- and three-way product terms, the following were statistically significant: PV × D (Model 7), PV × A × D (Models 8, 9, 10, and 11), D × PV × SV (Model 10) and A × PV × SV (Models 11 and 12). In the final logistic regression model that included all possible product terms, including a four-way product term, only A × PV × SV was statistically significant. Assessment of interactions on the additive scale using linear probability regression models showed similar results (Table 5).

Table 4. Effect of adverse psychosocial exposures on condomless anal sex with male partners among HIV-negative transgender women: Measures of multiplicative Two-/Three-/Four-way interactions between physical violence, sexual violence, drug use, and frequent alcohol use (N = 4,607).

Adverse psychosocial exposures and product terms	Effects on condomless anal sex											
	Model 1:	Model 2:	Model 3:	Model 4:	Model 5:	Model 6:	Model 7:	Model 8:	Model 9:	Model 10:	Model 11:	Model 12:
	Models with one two-way product term at a time						All two-way product terms PV × D PV × A SV × D SV × A PV × SV A × D	All two-way + one three-way product term (PV × A × D)	All two-way + two three-way product terms (PV × A × D) (SV × A × D)	All two-way + three three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV)	All two-way + four three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV)	All two-way + All three-way + four-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV) (A × D × PV × SV)
	PV × D	PV × A	SV × D	SV × A	PV × SV	A × D						
	Estimated semi-elasticity (95% CI), p value											
PV × D	.48 (.27, .69)***						.47 (.23, .71)***	-.17 (-.83, .48)	-.14 (-.79, .52)	-.39 (-1.20, .42)	-.25 (-.99, .49)	-.11 (-.88, .65)
PV × A		.13 (-.16, .42)					-.03 (-.28, .31)	-.08 (-.43, .27)	-.09 (-.45, .26)	-.09 (-.44, .26)	-.38 (-.84, .08)	-.36 (-.83, .11)
SV × D			-.02 (-.39, .35)				-.12 (-.53, .29)	-.21 (-.64, .22)	-.02 (-.54, .58)	-.13 (-.77, .52)	-.12 (-.75, .52)	-.04 (-.69, .61)
SV × A				-.01 (-.33, .30)			-.10 (-.43, .24)	-.06 (-.39, .26)	-.01 (-.35, .33)	.01 (-.33, .34)	-.38 (-.91, .14)	-.36 (-.89, .18)
PV × SV					.29 (.04, .53)*		.23 (-.04, .49)	.21 (-.06, .48)	.22 (-.05, .48)	.13 (-.18, .44)	.31 (-.76, .14)	-.28 (-.75, .19)
A × D						.08 (-.27, .43)	-.06 (-.49, .36)	-.40 (-1.0, .19)	-.23 (-.90, .44)	-.17 (-.81, .47)	-.11 (-.73, .51)	-.05 (-.69, .59)
PV × A × D								.69 (.38, 1.0)***	.69 (.38, 1.01)***	.65 (.29, 1.01)***	.61 (.23, .99)**	.52 (-.04, 1.08)
SV × A × D									-.39 (-1.32, .54)	-.65 (-1.72, .43)	-.53 (-1.56, .49)	-.74 (-2.09, .61)
D × PV × SV										.51 (.06, .96)*	.34 (-.24, .93)	.06 (-1.13, 1.25)
A × PV × SV											.66 (.35, .97)***	.63 (.27, .99)***

(*Continued*)

Table 4. (Continued)

Adverse psychosocial exposures and product terms	Effects on condomless anal sex											
	Model 1:	Model 2:	Model 3:	Model 4:	Model 5:	Model 6:	Model 7:	Model 8:	Model 9:	Model 10:	Model 11:	Model 12:
	Models with one two-way product term at a time						All two-way product terms PV × D PV × A SV × D SV × A PV × SV A × D	All two-way + one three-way product term (PV × A × D)	All two-way + two three-way product terms (PV × A × D) (SV × A × D)	All two-way + three three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV)	All two-way + four three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV)	All two-way + All three-way + four-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV) (A × D × PV × SV)
	PV × D	PV × A	SV × D	SV × A	PV × SV	A × D						
	Estimated semi-elasticity (95% CI), p value											
A × D × PV × SV												.40 (-.64, 1.46)

PV, physical violence in the past year; SV, sexual violence in the past year; D, drug use in the past year; A: Frequent alcohol use in the past week.

All models adjusted for age, education, marital status, sexual identity, forced sex experience during adolescence, HIV risk perception, knowledge of HIV transmission risk, social support, and HIV program exposure.

The estimates of the main effects are not shown.

Interpretation of semi-elasticity: A semi-elasticity of .48, for example in Model 1, is interpreted as a 48% relative change in the probability of condomless anal sex that is associated with the joint effect of physical violence and drug use, above and beyond their independent associations with the outcome.

*p < .05

**p < .01

***p < .001.

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Sensitivity analysis for the model of synergistically interacting epidemics

The sensitivity analysis specifying drug use and alcohol use as continuous exposures, physical and sexual violence as a single continuous exposure (violence victimization), and CAS as a continuous outcome, showed a similar pattern of two- and three-way interactions (see S1 Table).

Rival theoretical models: Serially causal and mutually causal epidemics

In the model of serially causal epidemics, we estimated a statistically significant total indirect effect of sexual violence (estimate = .04, 95% CI: .003–07; p = .03) on CAS through drug use and alcohol use, but the indirect effect of physical violence was not statistically significant. In the model of mutually causal epidemics, we found that violence victimization had a statistically significant association with drug use (estimate = .18, 95% CI: .15–.22; p < .001) and drug use had a statistically significant association with violence victimization (estimate = 1.97, 95% CI: 1.38–2.56; p < .001). The model fit (SRMR < .02) and the stability index (.60) were good (see S2 Table).

Table 5. Effect of adverse psychosocial exposures on condomless anal sex with male partners among HIV-negative transgender women: Measures of additive Two-/Three-/Four-way interactions between physical violence, sexual violence, drug use, and frequent alcohol use (N = 4,607).

Adverse psychosocial exposures and product terms	Effects on condomless anal sex											
	Model 1:	Model 2:	Model 3:	Model 4:	Model 5:	Model 6:	Model 7:	Model 8:	Model 9:	Model 10:	Model 11:	Model 12:
	Models with one two-way product term at a time						All two-way product terms PV × D PV × A SV × D SV × A PV × SV A × D	All two-way + one three-way product term (PV × A × D)	All two-way + two three-way product terms (PV × A × D) (SV × A × D)	All two-way + three three-way product terms (PV x A x D) (SV x A x D) (D x PV x SV)	All two-way + four three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV)	All two-way + All three-way + four-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV) (A × D × PV × SV)
	PV × D	PV × A	SV × D	SV × A	PV × SV	A × D						
	b (95% CI), p value											
PV × D	.24 (.11, .37)***						.23 (.08, .37)**	-.07 (-.31, .18)	-.05 (-.31, .19)	-.12 (-.39, .14)	-.07 (-.33, .19)	-.05 (-.34, .24)
PV × A		.05 (-.07, .19)					-.01 (-.12, .14)	-.03 (-.18, .11)	-.04 (-.18, .10)	-.04 (-.18, .11)	-.14 (-.31, .02)	-.14 (-.31, .03)
SV × D			-.01 (-.16, .14)				-.04 (-.19, .10)	-.07 (-.21, .08)	-.005 (-.22, .23)	-.04 (-.27, .20)	-.03 (-.26, .20)	-.02 (-.27, .23)
SV × A				-.005 (-.13, .12)			-.04 (-.17, .09)	-.02 (-.15, .11)	-.004 (-.15, .14)	-.002 (-.14, .14)	-.14 (-.32, .04)	-.13 (-.33, .05)
PV × SV					.13 (.01, .25)*		.10 (-.03, .22)	.09 (-.04, .21)	.09 (-.03, .22)	.05 (-.09, .20)	-.11 (-.28, .05)	-.11 (-.28, .06)
A × D						.03 (-.12, .18)	-.02 (-.18, .13)	-.13 (-.32, .05)	-.08 (-.31, .15)	-.06 (-.29, .18)	-.03 (-.26, .20)	-.02 (-.27, .22)
PV × A × D								.40 (.08, .71)*	.40 (.08, .71)*	.35 (-.02, .68)	.31 (-.01, .63)	.28 (-.12, .68)
SV × A × D									-.11 (-.40, .18)	-.17 (-.46, .13)	-.11 (-.41, .18)	-.13 (-.48, .21)
D × PV × SV										.20 (-.08, .48)	.08 (-.21, .37)	.02 (-.49, .54)
A × PV × SV											.36 (.10, .63)**	.35 (.06, .65)*

(*Continued*)

Table 5. (Continued)

Adverse psychosocial exposures and product terms	Effects on condomless anal sex											
	Model 1:	Model 2:	Model 3:	Model 4:	Model 5:	Model 6:	Model 7:	Model 8:	Model 9:	Model 10:	Model 11:	Model 12:
	Models with one two-way product term at a time						All two-way product terms PV × D PV × A SV × D SV × A PV × SV A × D	All two-way + one three-way product term (PV × A × D)	All two-way + two three-way product terms (PV × A × D) (SV × A × D)	All two-way + three three-way product terms (PV x A x D) (SV x A x D) (D x PV x SV)	All two-way + four three-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV)	All two-way + All three-way + four-way product terms (PV × A × D) (SV × A × D) (D × PV × SV) (A × PV × SV) (A × D × PV × SV)
	PV × D	PV × A	SV × D	SV × A	PV × SV	A × D						
	b (95% CI), p value											
A × D × PV × SV												.07 (-.54, .69)

PV, physical violence in the past year; SV, Sexual violence in the past year; D, drug use in the past year; A, frequent alcohol use in the past week.

All models adjusted for age, education, marital status, sexual identity, forced sex experience during adolescence, HIV risk perception, knowledge of HIV transmission risk, social support, and HIV program exposure.

The estimates of the main effects are not shown.

'*b*' represents the estimated regression coefficient on the product term which indicates the relative excess risk due to interaction (RERI) used to assess additive interaction.

*p < .05

**p < .01

***p < .001.

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Discussion

In this large, cross-sectional, probability-based analytical sample of HIV-negative transgender women in India, we tested a model of synergistically interacting epidemics, based on the joint effects of four psychosocial exposures—physical and sexual violence victimization, drug use, and alcohol use—on CAS. The high prevalence of these adverse psychosocial exposures, their frequent co-occurrence, and their synergistic interactions support the hypothesis that a syndemic is present in this population. On both the multiplicative and the additive scales, we found evidence of two-way synergistic interactions between physical violence victimization and sexual violence victimization, and between physical violence victimization and drug use. We found evidence of three-way synergistic interactions between physical violence victimization, sexual violence, and alcohol use; and between physical violence victimization, drug use and alcohol use. Our findings suggest that a harmful social-structural environment for transgender women in India contributes to clustering of psychosocial health challenges significantly associated with increased HIV risk, with ramifications for targeted HIV prevention initiatives.

The high levels of physical and sexual violence victimization faced by transgender women are corroborated by other studies from India [14,18,28]. A study from Karnataka reported past-year sexual violence prevalence of 18% in a combined sample of 543 men who have sex

with men and transgender women, but did not present estimates disaggregated by subpopulation [18]. In a study of 300 transgender women in four states, 84% reported having ever experienced physical and/or sexual violence [14]. Notably, in the present study, about one-third of those who experienced violence reported multiple perpetrators: family members/relatives, hoodlums, police, strangers, and sex work clients. Thus, not only do transgender women face violence on a large scale, but they experience violence across a myriad of settings in their social ecology—family, work, community settings, and in encounters with law enforcement officers, ostensibly positioned to offer protection from violence. A latent class analysis of patterns of violence victimization among transgender women in India (n = 299) indicated that the type (verbal, physical, or sexual) of violence victimization differentially influenced HIV risk; those who experienced police-perpetrated sexual assault vs. police-perpetrated physical violence had relatively higher risk of CAS [28]. However, that study did not assess synergistic effects, such as those identified in the present study between physical and sexual violence, nor their interactions with alcohol and drug use.

Studies among gender and sexual minority populations in other contexts [29,30] indicate that the presence of multiple types and domains of violence victimization is likely to substantially increase psychological distress. The present study further demonstrates that multiple forms of violence victimization against transgender women, and in conjunction with drug use and alcohol use, contribute to synergistically increasing HIV risk. In India, physical violence from family members has been shown to be a manifestation of non-acceptance of gender identity, with violence reportedly perpetrated as a form of discipline [31]. Physical and sexual violence from police and hoodlums in India have been identified as even more common among those transgender women who engage in sex work [11]. The multiple forms and domains of violence victimization can be seen as the manifestation of systemic stigma and discrimination, and economic marginalization, undergirded by lack of acceptance of transgender people in the family and society; and this is exacerbated by the lack of legal protections for those who engage in sex work [32].

The associations identified using models of synergistically interacting epidemics or mediation analyses have been demonstrated among transgender women in other countries. For example, studies among transgender women in North and South America indicate that life stressors [33], discrimination [34,35] and trauma [36] can lead to alcohol and/or substance use, possibly as maladaptive coping strategies. A longitudinal study among transgender women in the U.S. showed a causal association between sexual violence and drug use [37]. In several other studies with transgender women, alcohol use [38] and drug use [39], including sexualized drug use [40], were associated with increased HIV risk. As identified among other populations, such as gay and bisexual men, being under the influence of alcohol or drugs may increase the likelihood of engaging in sex and the risk of CAS [38,39]. Thus, experiences of sexual violence can precipitate drug or alcohol use as a coping mechanism, and alcohol and drug use (especially before or during sex) in turn may increase the likelihood of being targeted or otherwise exacerbate sexual or physical violence from male partners [40], which increases the risk of engaging in CAS. Given evidence that internalized transprejudice and depression may stem in part from discrimination and violence victimization [41,42], future studies should explore the potential mediating roles of internalized transprejudice and depression in the association between physical and sexual violence victimization and discrimination, and HIV transmission risk behavior.

Implications for practice and policy

Given that larger societal forces, including systemic stigma and discrimination, economic marginalization, and criminalization of sex work, contribute to violence victimization—as well as

indirectly leading to alcohol and drug use through internalized stigma and depression [17,32,43]—addressing these social and structural factors is crucial. Currently, 'crisis response' teams established in NACO-supported targeted HIV interventions act only *after* incidents of violence are reported; and we are aware of no societal-level campaigns in India designed to prevent discrimination and violence against transgender women in relation to their intersecting marginalized identities (e.g., gender minority *and* sex worker and/or HIV-positive status).

Syndemic approaches to prevention demand policies and programmatic initiatives to implement structural change, in addition to individual-level interventions [7,44]. To that end, important progress is evidenced in the passage of The Transgender Persons (Protection of Rights) Act, 2019 [45] and Rules, 2020 [44] in India, which explicitly state that transgender persons should not be discriminated against, and prescribe punishment for those who discriminate or perpetrate violence. Nevertheless, disparities in India's legal protections (e.g., punishments for sexual violence against transgender women are less severe than those for cisgender women) highlight ongoing challenges in protective policies and the systemic devaluation of transgender women's rights and lives. More recently, the Indian Ministry of Social Justice and Empowerment launched a social welfare program for transgender people, Support for Marginalised Individuals for Livelihood and Enterprise (SMILE) in 2022 [46], which includes scholarships for higher education and vocational training, shelter and food assistance, as well as state-level monitoring of discrimination and violence. This represents important advances in ameliorating structural vulnerability, such as housing instability, poverty, and violence victimization, which may improve physical and mental health outcomes among transgender people [47].

Our findings further indicate that physical violence victimization independently, and together with sexual violence, drug use and alcohol use synergistically increase CAS. That is, in the presence of physical violence victimization, relatively higher levels of CAS were observed with one or more combinations of sexual violence victimization, drug use and/or alcohol use. Thus, addressing all four exposures through integrated, multicomponent interventions may substantially reduce HIV risk [48]; however, in the context of synergistic interactions, single-component interventions (e.g., post-care support for survivors of sexual violence or treatment of alcohol or drug dependence) may still exert an incremental impact on reducing HIV transmission risk behavior.

Partial support for the model of serially causal epidemics—i.e., sexual violence victimization leading to alcohol and drug use, and possible mutually causal associations between violence victimization and drug use—suggest the utility of multilevel interventions: at the individual level, screening for and managing alcohol and drug use; and at the societal level, strengthening stigma and violence reduction or elimination programs. Although alcohol use and drug use were not independently statistically significant predictors of CAS (main effects model), in the presence of sexual and/or physical violence victimization, alcohol use and/or drug use substantially increased CAS. Nongovernmental (NGOs) and community-based organizations (CBOs) that implement targeted HIV preventive interventions for transgender women should establish or strengthen referral systems with public hospitals offering treatment for alcohol and drug dependence, post-violence (physical or sexual) support services, and post-sexual exposure prophylaxis (PEP). To this end, training and monitoring healthcare providers to ensure nondiscriminatory and gender-affirmative care is crucial. Similarly, support is required from police in duly filing complaints of sexual or physical violence, given that transgender persons are not covered in current sexual assault/rape laws (Indian Penal Code, Section 354)—a pernicious lapse in legal policy. Further, in addition to HIV and condom education and condom distribution, NGOs and CBOs should educate transgender women about the negative effects of alcohol and drug use on sexual decision-making and negotiation, and counsel and support them to reduce or avoid drug or alcohol use before or during sexual encounters.

Limitations and strengths

In addition to its strengths, this study has several limitations. First, the cross-sectional data preclude causal interpretations. However, theoretical frameworks and compatible recall periods for the adverse psychosocial exposures (physical and sexual violence victimization, one year; drug use, one year), support the plausibility of the three models tested. Second, our analysis was restricted to co-occurrence and interactions between exposures at the individual level, while the concept of a syndemic is a population-level phenomenon; multilevel analyses at the population level should be undertaken in future research. Nevertheless, this is among the largest probability-based studies of syndemics among transgender women [49], and had a high response rate (81%). Our use of appropriate statistical analyses (interactions on both additive and multiplicative scales) to assess synergy is another strength, given several studies that purportedly assessed syndemics and HIV risk among transgender women did not use such analytic techniques [49], among very few that did [50]. In line with current practice, we dichotomized the adverse psychosocial exposures in additive and multiplicative interactions [22]; however, sensitivity analyses revealed that similar findings were obtained if we used different ways of specifying exposures, strengthening the evidence for synergy among exposures.

Third, we conducted secondary analysis of data from a national Indian government survey of HIV-related risk behaviors among transgender women. As the original dataset did not include psychosocial variables such as depression and anxiety, which have been shown in other studies to be psychosocial syndemic conditions, we were unable to assess the synergistic effects of those variables. Nevertheless, we identified statistically significant effects of syndemic conditions on HIV risk among a uniquely large national sample of transgender women. Fourth, it is possible that some of the variables modelled as confounders could also be potential moderators; however, we did not explore the range of potential interactions among the confounders considering the stated focus of the analysis and standard procedures used in assessing the synergy of focal variables [19].

Finally, the relatively old data is another limitation; however, this was the last national level HIV-related risk behavior survey conducted among transgender women in India, and we modelled syndemic conditions among a uniquely large, national sample of transgender women. Further, while we anticipate positive changes in transgender people's health as a result of substantial improvements in the national policy environment initiated from 2019 through 2022 [44–46], institutional changes in response to these policies remain a work in progress and their salutary impacts are largely yet to be realized; thus, we do not believe the results would be substantially different if data had been collected in the five-year period since the last IBBS survey.

Conclusion

This study found evidence for synergistic (additive and multiplicative) interactions between sexual and physical violence victimization, drug use, and alcohol use on HIV transmission risk behavior among a large, population-based sample of transgender women. Our findings support the need to focus on preventing and eliminating violence victimization, as well as the importance of preventing or mitigating multiple co-occurring adverse psychosocial exposures, in order to reduce HIV risk among transgender women in India.

Supporting information

S1 Table. PV, physical violence in the past year; SV, sexual violence in the past year; VV, violence victimization (physical and/or sexual violence); D, drug use in the past year; A,

frequent alcohol use in the past week. All models adjusted for age, education, marital status, sexual identity, forced sex experience during adolescence, HIV risk perception, knowledge of HIV transmission risk, social support, and HIV program exposure. $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$. [a] Drug use score– 0 to 3. [b] Alcohol use score– 0 to 7 (consumption in number of days/ week). [c] Violence victimization score– 0 to 5. [#] Models 1–12: Model 1 –Two-way product term PV x D; Model 2 –Two-way product term PV x A; Model 3 –Two-way product term SV x D; Model 4 –Two-way product term SV x D; Model 5 –Two-way product term PV x SV; Model 6 –Two-way product term A x D; Model 7 –All two-way product terms; Model 8 –All two-way product terms + One three-way product term PV x A x D; Model 9 –All two-way product terms + Two three-way product terms PV x A x D and SV x A x D; Model 10 –All two-way product terms + Three three-way product terms PV x A x D, SV x A x D, and D x PV x SV; Model 11 –All two-way product terms + Three three-way product terms PV x A x D, SV x A x D, and D x PV x SV; Model 12 –All two-way product terms + Three three-way product terms PV x A x D, SV x A x D, D x PV x SV, and A x PV x SV + Four-way product term PV x SV x A x D. [$] Models 1–5: Model 1 –Two-way product term VV x D; Model 2 –Two-way product term VV x A; Model 3 –Two-way product term A x D; Model 4 –All two-way product terms; Model 5 –All two-way product terms + Three-way product term VV x A x D.
(DOCX)

S2 Table. Unstandardized estimates are presented. CI: Confidence interval. Adjusted for control variables: Age, education, marital status, sexual identity, forced sex experience during adolescence, HIV risk perception, knowledge of HIV transmission risk, social support, and HIV program exposure. $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.
(DOCX)

S1 Text. Inclusivity in global research.
(DOCX)

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References

1. Poteat T, Scheim A, Xavier J, Reisner S, Baral S. Global epidemiology of HIV infection and related syndemics affecting transgender people. J Acquir Immune Defic Syndr. 2016; 72(Suppl 3):S210–219. https://doi.org/10.1097/QAI.0000000000001087 PMID: 27429185
2. Hatzenbuehler ML, Pachankis JE. Stigma and minority stress as social determinants of health among lesbian, gay, bisexual, and transgender youth: Research evidence and clinical implications. Pediatr Clin North Am. 2016; 63(6):985–997. https://doi.org/10.1016/j.pcl.2016.07.003 PMID: 27865340
3. Rajan S, Kumar P, Sangal B, Kumar A, Ramanathan S, Ammassari S. HIV/AIDS-Related risk behaviors, HIV prevalence, and determinants for HIV prevalence among hijra/transgender people in India: Findings from the 2014–2015 integrated biological and behavioural surveillance. Indian J Public Health. 2020; 64(Supplement):S53–S60. https://doi.org/10.4103/ijph.IJPH_55_20 PMID: 32295957
4. NACO. HIV Sentinel Surveillance: Technical Brief, India 2016–17. New Delhi: National AIDS Control Organisation, Ministry of Health and Family Welfare, Government of India.; 2017.
5. National AIDS Control Organization (NACO). Sankalak: Status of National AIDS Response. NACO. 2020. Available from: http://naco.gov.in/nacoevents/release-sankalak-status-national-aids-response.
6. Chakrapani V, Willie TC, Shunmugam M, Kershaw TS. Syndemic classes, stigma, and sexual risk among transgender women in India. AIDS Behav. 2019; 23(6):1518–1529. https://doi.org/10.1007/s10461-018-2373-1 PMID: 30565093
7. Singer M. A dose of drugs, a touch of violence, a case of AIDS: Conceptualizing the SAVA syndemic. Free Inquiry Creative Sociol. 1996; 24:99–110.
8. Parsons JT, Antebi-Gruszka N, Millar BM, Cain D, Gurung S. Syndemic conditions, HIV transmission risk behavior, and transactional sex among transgender women. AIDS Behav. 2018; 22(7):2056–2067. https://doi.org/10.1007/s10461-018-2100-y PMID: 29589136
9. Stall R, Mills TC, Williamson J, Hart T, Greenwood G, Paul J, et al. Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. Am J Public Health. 2003; 93(6):939–942. https://doi.org/10.2105/ajph.93.6.939 PMID: 12773359
10. Stall R, Friedman M, Catania JA. Interacting epidemics and gay men's health: A theory of syndemic production among urban gay men. In: Wolitski RJ, Stall R, Valdiserri RO, editors. Unequal opportunity: health disparities affecting gay and bisexual men in the United States. New York: Oxford University Press; 2008. pp. 251–274.
11. Ganju D, Saggurti N. Stigma, violence and HIV vulnerability among transgender persons in sex work in Maharashtra, India. Cult Health Sex. 2017; 19(8):903–917. https://doi.org/10.1080/13691058.2016.1271141 PMID: 28132601
12. Shaw SY, Lorway R, Bhattacharjee P, Reza-Paul S, du Plessis E, McKinnon L, et al. Descriptive epidemiology of factors associated with hiv infections among men and transgender women who have sex with men in South India. LGBT Health. 2016; 3(4):292–9. https://doi.org/10.1089/lgbt.2015.0023 PMID: 27058882
13. Dutta S, Khan S, Lorway R. Following the divine: An ethnographic study of structural violence among transgender jogappas in South India. Cult Health Sex. 2019; 21(11):1240–56. https://doi.org/10.1080/13691058.2018.1555718 PMID: 30632909
14. Chakrapani V, Newman PA, Shunmugam M, Logie CH, Samuel M. Syndemics of depression, alcohol use, and victimisation, and their association with HIV-related sexual risk among men who have sex with men and transgender women in India. Glob Public Health. 2017; 12(2):250–265. https://doi.org/10.1080/17441692.2015.1091024 PMID: 26457339
15. Chakrapani V, Vijin PP, Logie CH, Newman PA, Shunmugam M, Sivasubramanian M, et al. Understanding how sexual and gender minority stigmas influence depression among trans women and men who have sex with men in India. LGBT Health. 2017; 4(3):217–226. https://doi.org/10.1089/lgbt.2016.0082 PMID: 28422615
16. Gomes de Jesus J, Belden CM, Huynh HV, Malta M, LeGrand S, Kaza VGK, et al. Mental health and challenges of transgender women: A qualitative study in Brazil and India. Int J Transgend Health. 2020; 21(4):418–30.
17. Chakrapani V, Newman PA, Shunmugam M. Stigma toward and mental health of hijras/trans women and self-identified men who have sex with men in India. In: Nakamura N, Logie CH, editors. LGBTQ Mental Health: International perspectives and experiences. Washington: American Psychological Association; 2020. pp. 103–119.
18. Shaw SY, Lorway RR, Deering KN, Avery L, Mohan HL, Bhattacharjee P, et al. Factors associated with sexual violence against men who have sex with men and transgendered individuals in Karnataka, India. PLoS One. 2012; 7(3):e31705. https://doi.org/10.1371/journal.pone.0031705 PMID: 22448214

19. Tsai AC, Venkataramani AS. Syndemics and health disparities: A methodological note. AIDS Behav. 2016; 20(2):423–30. https://doi.org/10.1007/s10461-015-1260-2 PMID: 26662266

20. VanderWeele TJ, Knol MJ. A tutorial on interaction. Epidemiol Methods. 2014; 3:33–72.

21. National AIDS Control Organization (NACO). National Integrated Biological and Behavioural Surveillance (IBBS), Hijras/Transgender People, India 2014–15. NACO. 2016. Available from: http://naco.gov.in/sites/default/files/TG-IBBS%20ReportPrint%20text_Edited.pdf.

22. VanderWeele TJ. Explanation in causal inference: Methods for mediation and interaction. New York: Oxford University Press; 2015.

23. Solon G, Haider SJ, Wooldridge JM. What are we weighting for? J Hum Resour. 2015; 50(2):301–316.

24. Heeringa SG, West BT, Berglund PA. Applied survey data analysis. New York: Chapman and Hall/CRC; 2010.

25. Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. Int J Epidemiol. 2012; 41(2):514–520. https://doi.org/10.1093/ije/dyr218 PMID: 22253321

26. Tsai AC. Syndemics: A theory in search of data or data in search of a theory? Soc Sci Med. 2018; 206:117–122. https://doi.org/10.1016/j.socscimed.2018.03.040 PMID: 29628175

27. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. J Epidemiol Community Health. 2003; 57(10):778–783.

28. Willie T, Chakrapani V, White Hughto J S, Kershaw T. Victimization and human immunodeficiency virus-related risk among transgender women in India: A latent profile analysis. Violence Gend. 2017; 4 (4):121–9. https://doi.org/10.1089/vio.2017.0030 PMID: 29279854

29. Newman PA, Fantus S, Woodford MR, Rwigema M-J. "Pray that God will change you": The religious social ecology of bias-based bullying targeting sexual and gender minority youth—A qualitative study of service providers and educators. J Adolesc Res. 2017; 33(5):523–548.

30. Sterzing PR, Ratliff GA, Gartner RE, McGeough BL, Johnson KC. Social ecological correlates of polyvictimization among a national sample of transgender, genderqueer, and cisgender sexual minority adolescents. Child Abuse Negl. 2017; 67:1–12. https://doi.org/10.1016/j.chiabu.2017.02.017 PMID: 28226283

31. Chakrapani V, Dhall P. Family acceptance among self-identified men who have sex with men (MSM) and transgender people in India. Mumbai: Family Planning Association of India; 2011.

32. Chakrapani V, Newman AP, Noronha E. Hijras/Transgender women and sex work in India: From marginalization to social protection. In: Nuttbrock LA, editor. Transgender sex work & society. New York: Harrington Park Press; 2018. pp. 214–235.

33. Hotton AL, Garofalo R, Kuhns LM, Johnson AK. Substance use as a mediator of the relationship between life stress and sexual risk among young transgender women. AIDS Educ Prev. 2013; 25 (1):62–71. https://doi.org/10.1521/aeap.2013.25.1.62 PMID: 23387952

34. Ehlinger PP, Folger A, Cronce JM. A qualitative analysis of transgender and gender nonconforming college students' experiences of gender-based discrimination and intersections with alcohol use. Psychol Addict Behav. 2021. https://doi.org/10.1037/adb0000752 PMID: 34081485

35. Kcomt L, Evans-Polce RJ, Boyd CJ, McCabe SE. Association of transphobic discrimination and alcohol misuse among transgender adults: Results from the U.S. Transgender Survey. Drug Alcohol Depend. 2020; 215:108223. https://doi.org/10.1016/j.drugalcdep.2020.108223 PMID: 32777693

36. Johnson EEH, Wilder SMJ, Andersen CVS, Horvath SA, Kolp HM, Gidycz CA, et al. Trauma and alcohol use among transgender and gender diverse women: An examination of the stress-buffering hypothesis of social support. J Prim Prev. 2021; 42(6):567–581. https://doi.org/10.1007/s10935-021-00646-z PMID: 34546505

37. Smith LR, Yore J, Triplett DP, Urada L, Nemoto T, Raj A, et al. Impact of sexual violence across the lifespan on HIV risk behaviors among transgender women and cisgender people living with HIV. J Acquir Immune Defic Syndr. 2017; 75(4):408–416. https://doi.org/10.1097/QAI.0000000000001423 PMID: 28653970

38. Hearld KR, Milner AN, Budhwani H, Abreau N, Rodriguez-Lauzurique RM, Charow R, et al. Alcohol use, high risk behaviors, and experiences of discrimination among transgender women in the Dominican Republic. Subst Use Misuse. 2019; 54(10):1725–1733. https://doi.org/10.1080/10826084.2019.1608253 PMID: 31046549

39. Avila MM, Dos Ramos Farias MS, Fazzi L, Romero M, Reynaga E, Marone R, et al. High Frequency of illegal drug use influences condom use among female transgender sex workers in Argentina: Impact on HIV and syphilis infections. AIDS Behav. 2017; 21(7):2059–2068. https://doi.org/10.1007/s10461-017-1766-x PMID: 28424971

40. Fan X, Lau JTF, Cai Y, Li J, Ma T, Gu J, et al. Prevalence and associated factors of sexualized drug use in sex work among transgender women sex workers in China. AIDS Care. 2021; 33(8):1098–1106. https://doi.org/10.1080/09540121.2020.1851017 PMID: 33258694

41. Kaighobadi F, Collier KL, Reddy V, Lane T, Sandfort TGM. Sexual violence experiences among black gay, bisexual, and other men who have sex with men and transgender women in South African townships: Contributing factors and implications for health. S Afr J Psychol. 2020; 50(2):170–182. https://doi.org/10.1177/0081246319859449 PMID: 33583966

42. Logie CH, Lacombe-Duncan A, Poteat T, Wagner AC. Syndemic factors mediate the relationship between sexual stigma and depression among sexual minority women and gender minorities. Womens Health Issues. 2017; 27(5):592–599. https://doi.org/10.1016/j.whi.2017.05.003 PMID: 28645707

43. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: Conceptual issues and research evidence. Psychol Bull. 2003; 129(5):674–697. https://doi.org/10.1037/0033-2909.129.5.674 PMID: 12956539

44. Dean HD, Fenton KA. Integrating a social determinants of health approach into public health practice: A five-year perspective of actions implemented by CDC's national center for HIV/AIDS, viral hepatitis, STD, and TB prevention. Public Health Rep. 2013;128 Suppl 3:5–11.

45. Government of India. The Transgender Persons (Protection of Rights) Act, 2019. No. 40. December 5, 2019. https://www.indiacode.nic.in/bitstream/123456789/13091/1/a2019-40.pdf.

46. Ministry of Social Justice and Empowerment, Government of India (MJSE). Social Justice & Empowerment Department launches 'SMILE' for the Welfare of Transgender community and the Beggars tomorrow New Delhi: MJSE, Government of India; 2022. Available from: https://pib.gov.in/PressReleasePage.aspx?PRID=1797628.

47. King WM, Jadwin-Cakmak L, Trammell R, Gamarel KE. Structural vulnerability as a conceptual framework for transgender health research: Findings from a community needs assessment of transgender women of colour in Detroit. Cult Health Sex. 2022:1–17. https://doi.org/10.1080/13691058.2022.2086709 PMID: 35736653

48. Operario D, Nemoto T. HIV in transgender communities: Syndemic dynamics and a need for multicomponent interventions. J Acquir Immune Defic Syndr. 2010; 55(Suppl 2):S91–S93. https://doi.org/10.1097/QAI.0b013e3181fbc9ec PMID: 21406995

49. Tsai AC, Burns BF. Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept. Soc Sci Med. 2015; 139:26–35. https://doi.org/10.1016/j.socscimed.2015.06.024 PMID: 26150065

50. Alvarado B, Mueses HF, Galindo J, Martínez-Cajas JL. Application of the "syndemics" theory to explain unprotected sex and transactional sex: A cross-sectional study in men who have sex with men (MSM), transgender women, and non-MSM in Colombia. Biomedica. 2020; 40(2):391–403.