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Title

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Permalink

<https://escholarship.org/uc/item/33b995bn>

Journal

Archives of sexual behavior, 49(1)

ISSN

0004-0002

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Publication Date

2020

DOI

10.1007/s10508-019-01470-7

Peer reviewed



Syndemics and the PrEP Cascade: Results from a Sample of Young Latino Men Who Have Sex with Men

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Received: 30 August 2018 / Revised: 27 April 2019 / Accepted: 15 May 2019 / Published online: 7 October 2019
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Abstract

Young Latino men who have sex with men (MSM) are a highly vulnerable population for HIV infection. Pre-exposure prophylaxis (PrEP) is a novel biomedical HIV prevention tool that may aid in reducing the disparity in HIV incidence among Latino MSM. However, PrEP use is disproportionately low among Latino MSM and, therefore, identifying barriers along the PrEP continuum of care (the “PrEP cascade”) would provide insight into how to best deploy PrEP interventions. Syndemics theory is a prominent framework employed in HIV prevention; however, to date, no known studies have applied this theory to PrEP. Thus, the aim of the current study was to explore the association between syndemics and the PrEP cascade, including the degree to which psychosocial and structural syndemic constructs are related to the PrEP cascade. Participants were 151 young Latino MSM (M age = 24 years; $SD = 3$) residing in San Diego, California, who completed a battery of online self-report measures. Results indicated high levels of syndemic indicators and varying levels of engagement across the PrEP cascade. As syndemic indicators increased, the odds of engagement across the PrEP cascade were significantly lowered. Psychosocial and structural syndemic factors accounted for unique variance in the PrEP cascade. Results highlight the need for combination interventions that address both psychosocial and structural barriers to PrEP use and persistence among young Latino MSM.

Keywords PrEP · Latino · MSM · Syndemics · HIV prevention · Sexual orientation

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Introduction

Despite recent stabilization in the rate of new HIV diagnoses among men who have sex with men (MSM) in the United States, Latino MSM continue to be disproportionately affected by HIV compared to their White counterparts (CDC, 2018a). While MSM make up approximately 4% of the US adult male population (Purcell et al., 2012), they accounted for 82% of all HIV diagnoses in the U.S. in 2015 among males 13 and older (CDC, 2018b; Hess, Hu, Lanksy, Mermin, & Hall, 2017). In addition, while Latino MSM make up less than 1% of the total U.S. population, approximately 26% of new HIV diagnoses in 2015 were attributed to male-to-male sexual contact among Latino men (CDC, 2016). Among Latino MSM in the U.S., the lifetime risk of an HIV diagnosis is approximately 1 in 5, which is a rate three times higher than White MSM (Hess et al., 2017). In contrast to Black and White MSM, Latino MSM are also experiencing an increase in the rate of HIV diagnoses (CDC, 2018a); between 2010 and 2015, the incidence rate of HIV infection increased by 21.5% for Latino MSM, decreased by

13.4% for White MSM, and remained stable for Black MSM (CDC, 2018a). Age is also a factor in HIV diagnoses; new HIV diagnoses are most common among adolescents and young adults, particularly among men of color (CDC, 2016). In San Diego County, where participants for this study were recruited, rates of new HIV diagnoses for males and Hispanic/Latinos were higher in the county than national and state estimates in 2016 (HHS, 2017). In comparison with national and local data for modes of transmission, San Diego County also had a higher percentage of cases attributed to male-to-male sexual contact and lower percentages of cases attributed to heterosexual contact (HHS, 2017). Multiple factors likely contribute to the elevated rate of HIV infection among Latino MSM, including language barriers, social stigma associated with same-sex attraction among men, migration issues, and a lower average socioeconomic status (SES; CDC, 2018c). Innovative intervention approaches are needed to address the growing HIV epidemic among Latino MSM in the U.S.

One such novel intervention is pre-exposure prophylaxis (PrEP), which is an FDA-approved preventive medication for HIV-negative individuals at risk of HIV acquisition to reduce the risk of HIV infection. However, the efficacy of PrEP is highly dependent on adherence (Abbas, Glaubius, Mubayi, Hood, & Mellors, 2013; Celum, Hallett, & Baeten, 2013; Choopanya et al., 2013). When daily adherence is maintained, PrEP can decrease the risk of HIV transmission by 92–100% (Anderson et al., 2012; 2017; Grant et al., 2010). The Centers for Disease Control and Prevention (CDC) recommends daily adherence to PrEP (2018d) for maximum benefit; however, a study by Anderson et al. (2012) found a HIV risk reduction of 96% corresponded to drug levels consistent with four or more doses of PrEP per week in MSM (Riddell, Amico, & Mayer, 2018).

Awareness and use of PrEP among Latino MSM remain low (CDC, 2018e; Pulsipher et al., 2016). According to CDC (2018e) estimates based on current guidelines, approximately 300,000 people who are eligible for PrEP are Latino (roughly 25% of the total population of people who could benefit from PrEP). Yet, only 7600 Latinos out of a nearly 300,000 estimated Latinos who may have benefitted from PrEP (or 3%) filled a prescription for PrEP between September 2015 and August 2016 (Smith, 2018; Smith et al., 2015). This imbalance between Latino MSM who may benefit from PrEP and those that are currently on PrEP indicates that there are significant barriers preventing PrEP use in this population (Pulsipher et al., 2016). As a result, examination into the factors that predict PrEP use is necessary to determine the most effective PrEP intervention strategies among Latino MSM.

Based on analogous HIV continuum of care models, PrEP cascade models are used to examine factors associated with PrEP use at specific points along the PrEP cascade, from awareness to adherence (Gardner, McLees, Steiner, del Rio, & Burman, 2011; Kelley et al., 2015; McNairy & El-Sadr, 2014;

Parsons et al., 2017b). In order to maximize the efficacy of PrEP as a form of HIV prevention, a person must be aware of PrEP, willing to use it, able to use it, and able to successfully adhere to the treatment regimen. Understanding failures along the PrEP cascade may reveal potential points of intervention for Latino MSM. Existing studies show that Latino MSM are less aware of PrEP as a potential HIV intervention in comparison with Black and White MSM (Davey, Bustamente, Wang, Young, & Klausner, 2016; Strauss et al., 2017). In addition, while Latino MSM are less likely than White and Black MSM to use PrEP (Latino: 6.6%, White: 13.9%, Black: 9.8%), they report being most willing to use it (Latino: 63.4%, White: 49.3%, Black: 51.4%; Pulsipher et al., 2016). The disparity between PrEP willingness, or the degree to which someone is open to using PrEP, and PrEP use among Latino MSM suggests that specific barriers may exist that prevent its acquisition in this population. A syndemic theory framework may be useful in determining those factors associated with PrEP awareness, willingness, use, and adherence.

The term syndemic refers to a, “synergistic epidemic,” wherein multiple epidemics mutually reinforce and compound risk of disease within marginalized communities (Parsons et al., 2017a; Singer, 1994; Stall et al., 2003). The syndemic framework examines the intersection of interconnected social, cultural, and health factors that may exacerbate risk of disease, such as the compounding effects of living in poverty and experiencing stigma related to race, ethnicity, or sexual orientation (Parsons et al., 2017a; Singer, 2009). Applied frequently in epidemiological and anthropological studies, the syndemic framework has been used extensively to examine HIV transmission and antiretroviral therapy (ART) adherence among MSM (Blashill et al., 2014; Dyer et al., 2012; Friedman et al., 2015; Herrick et al., 2013; Mustanski, Garofalo, Herrick, & Donenberg, 2007; Parsons, Grov, & Golub, 2012; Parsons et al., 2017a). These studies show that multiple syndemic factors—including binge drinking, polysubstance use, intimate partner violence (IPV), childhood sexual abuse (CSA), and depression—have a cumulative effect on HIV transmission risk and poor ART adherence (Mustanski et al., 2007; Parsons et al., 2012; Stall et al., 2003). Longitudinal research found that syndemic factors may be predictive of negative outcomes among MSM, as increasing numbers of syndemic problems predicted higher odds of high-risk sexual behavior and seroconversion over time (Guadamuz et al., 2014; Mimiaga et al., 2015). A relatively small number of studies have examined the association between individual risk factors and failures along the PrEP cascade with mixed results (Bauermeister, Meanley, Pingel, Soler, & Harper, 2013; Davey et al., 2016; Grov, Rendina, Whitfield, Ventuneac, & Parsons, 2016; Hojilla et al., 2018; Jackson et al., 2012; Liu et al., 2016; Mehrotra et al., 2016; Pulsipher et al., 2016; Strauss et al., 2017; Taylor et al., 2014). To date, no known studies have examined how multiple

syndemic factors are related to PrEP awareness, willingness, use, and adherence.

The current study examined the occurrence of syndemic conditions and their associations with the stages of the PrEP cascade used in the current study (awareness, willingness, use, and adherence). This cascade is a simplified model that is informed by existing models and emphasizes direct antecedents of PrEP use and its efficacy (as measured through PrEP adherence; Gardner et al., 2011; Kelley et al., 2015; McNairy & El-Sadr, 2014; Parsons et al., 2017b). Consistent with syndemic theory, three structural syndemic factors (poverty, unstable housing, and incarceration) and six psychosocial syndemic factors (depression, binge drinking, marijuana use, illicit poly-substance use, childhood sexual abuse, and intimate partner violence) were calculated and examined for their associations with PrEP cascade steps. We hypothesize that a greater number of syndemic indicators will be associated with poorer engagement along each step of the PrEP cascade (i.e., lower awareness, lower willingness, lower use, and lower adherence). As the first known study to examine the PrEP cascade through a syndemic framework, the proportion of variance that psychosocial and structural syndemic conditions account for along each step of the PrEP cascade was also tested. However, due to the paucity of past research on structural versus psychosocial syndemic indicators, no directional hypotheses were generated.

Method

Participants

The current study was conducted online between April and June 2017. Participants were 151 Latino sexual minority men between 18 and 29 years old living in San Diego, California; mean participant age was 24 (SD 3) years. Study inclusion criteria were: (1) age 18–29 years old; (2) either English or Spanish-speaking; (3) reported negative HIV status, or unaware of current HIV status; (4) resided in the greater San Diego, California area (validated by zip code); and (5) identified as gay, bisexual, or as a man reporting same-sex attraction.

Procedure

Participants were recruited via advertisements on an MSM sexual networking app and website (i.e., Grindr and Squirr.org). All study advertisements and information were presented in both English and Spanish (discussed below). Potential participants were presented with a brief advertisement linked to a secure, digital form to provide a personal email for study staff to send the online survey link. This method of recruitment was utilized to encourage potential participants

to complete the survey on a non-mobile device in an attempt to reduce probable errors and completion fatigue and increase mindful responses from participants using mobile devices. All potential participants were provided with an online consent form detailing the nature of the study; all participants provided informed consent. Participants recruited from Facebook and Instagram from a previous online study who consented to be contacted about future studies and met the inclusion criteria for this study were sent an email notifying them of this study opportunity. Participants received a \$10 electronic gift card to a large, Internet-based retailer, delivered via personal email upon completion of the survey. All aspects of this study were approved of by the San Diego State University Institutional Review Board.

All study advertising and participation information was presented to potential participants in both English and Spanish. During the screening survey, potential participants selected their preferred language in which to complete the study. Subsequent informed consent documents, study measures, and study debriefings were provided in the participant's preferred language. One of the study co-authors, a bilingual HIV expert, and a bilingual research assistant, translated all measures, informed consent documents, and study debriefings, as well as all recruitment materials and advertisements. Measures which were previously published and translated from English to Spanish were utilized, when available (e.g., PHQ-8, HITS, etc.). Consistent with best practices in the adaptation and construction of culturally congruent data collection instruments (Formea et al., 2014; Rodríguez-Días et al., 2016; Sousa & Rojjanasirirat, 2010), the questionnaires developed for this study underwent a community-based validation process before beginning the data collection. All study materials were pilot-tested with local, bilingual men who met all inclusion criteria to ensure cultural and regional representativeness and comprehension of translated materials.

Measures

Depression

Participants completed the Personal Health Questionnaire Depression Scale (PHQ-8; Kroenke et al., 2009), an 8-item self-report measure of depression. Items are measured along a 4-point scale, ranging from 0 (*Not at all*) to 3 (*Nearly every-day*); scores range from 0 to 24, with higher scores indicating greater depressive symptoms. Consistent with recommendations for the general population (Kroenke et al., 2009), participants with a score of 10 or higher, indicating at least moderate depressive symptoms, were coded positive for depression. Internal consistency for this scale in the current sample was $\alpha = 0.76$.

Binge Drinking

Binge drinking was measured using a single item: “Over the past month, when you drank alcohol, what was the most number of drinks you drank on any one occasion?” Consistent with the definition of binge drinking for men used by the United States Substance Abuse and Mental Health Services Administration (2017), participants who reported five or more drinks on any drinking occasion in the past month were coded positive for binge drinking.

Marijuana Use

Use of marijuana was measured using a single item assessing the frequency in which marijuana, hash, or marinol was used in the past month. Participants who indicated using marijuana one or more times in the past month were coded positive for marijuana use.

Illicit Polysubstance Use

Illicit polysubstance use was measured by asking participants how frequently they used drugs (i.e., crack cocaine, cocaine, heroin, opiates, crystal meth, and hallucinogens [LSD, acid, and ecstasy]) in the past month; marijuana was not counted as an illicit substance, consistent with California state law. Participants who indicated using three or more drugs, at least once, over the past month were coded positive for illicit polysubstance use.

Childhood Sexual Abuse

Participants answered two questions pertaining to past childhood sexual abuse, consistent with the Finkelhor (1994) definition: “Before you turned 13 years old, did you have any sexual experiences with someone who was five or more years older than you?” and “Between the time you turned 13 and your 17th birthday, did you have any sexual experiences with someone who was ten or more years older than you?” Participants who indicated “yes” to either of these items were coded positive for a history of childhood sexual abuse.

Intimate Partner Violence

Intimate partner violence with main partner was measured using the HITS scale (Hurt, Insult, Threaten, Scream; Sherin, Sinacore, Li, Zitter, & Shakil, 1998). This is a 4-item self-report screen for intimate partner violence. Items are measured along a 5-point Likert frequency scale, ranging from 1 (*Never*) to 5 (*Frequently*), with possible scores ranging from 4 to 20; participants were given the option of “not applicable”

if they did not have a main partner. Per guidelines from Shakil, Donald, Sinacore, and Krepcho (2005) for males, a score of 11 or greater was coded positive for intimate partner violence. The internal consistency for this scale in the current sample was $\alpha = 0.92$.

Incarceration

Incarceration was measured using a single item: “Have you ever been in the correctional system? For example, convicted of a crime and sent to juvenile corrections, jail, prison, probation, or parole?” Participants were coded positive for a history of incarceration if they indicated “yes” to this item.

Unstable Housing

A single question was used to measure unstable housing: “Have you had unstable housing in the past 6 months?” Unstable housing means living in a hotel, boarding house group home, in the street, or having no fixed address in the past 6 months.” Participants were coded positive for having unstable housing if they indicated “yes” to this question.

Poverty

Participants were coded positive as living in poverty if they did not identify as a student and reported earning less than \$12,000 annually, which is in accordance with poverty guidelines set by the US Department of Health and Human Services (2018) for a single-person household in the contiguous U.S. and District of Columbia.

Syndemic Sum Variables

Three syndemic sum variables were computed. A total psychosocial syndemics variable was calculated by the number of positive psychosocial indicators (i.e., depression, binge drinking, marijuana use, illicit polysubstance use, childhood sexual abuse, and intimate partner violence) for each participant, with possible totals ranging 0–6. Additionally, a total structural syndemics variable was tabulated by the number of positive structural indicators (i.e., incarceration, unstable housing, and poverty) for each participant, with possible totals ranging 0–3. Finally, a total syndemics variable was calculated for each participant by summing the number of positive psychosocial and structural indicators, with possible syndemic total scores ranging 0–9.

PrEP Awareness

PrEP awareness was measured using a single question: “Before this study, had you ever heard of PrEP?”; participants were provided with three responses: “yes,” “no,” and “not sure.” Participants who responded “yes” were coded positive for PrEP awareness.

PrEP Willingness

PrEP willingness was measured with a single question: “How likely would you be to use PrEP?” Responses were measured along a 5-point Likert scale ranging from 1 (*Extremely Unlikely*) to 5 (*Extremely Likely*). Participants with a score of four or greater (corresponding to *Likely* or greater) were coded positive for PrEP willingness.

PrEP Use

PrEP use was captured by a single question: “Have you ever taken PrEP?” with possible responses of “yes” and “no”; participants who responded “yes” were coded positive for PrEP use. Participants who reported “yes” were subsequently asked about PrEP use over the previous month.

PrEP Adherence

Participants who reported PrEP use over the past month were subsequently asked about PrEP adherence: “Thinking about the past 30 days, what percent of the time did you take all of your PrEP medications as your doctor prescribed?”; on a scale of 0–100%, participants that indicated an adherence rate of 60% or greater were coded positive for PrEP adherence. This cut-score was chosen given that four + PrEP doses/week (or 57% adherence) provides a clinically protective effect from acquiring HIV (Anderson et al., 2012).

PrEP Stages

A mutually exclusive nominal PrEP stage variable was created from participants’ responses to PrEP awareness, willingness, use, and adherence. Five groups were created: (1) no awareness, willingness, or use; (2) awareness, but no willingness or use; (3) awareness and willingness, but no use; (4) use but low adherence; and (5) use and high adherence.

Demographics

Participants completed a demographic section, which assessed age, gender, race and ethnicity, sexual orientation,

relationship status, education level, income before taxes, employment status, healthcare insurance coverage, country of birth, and country of citizenship.

Statistical Analyses

The primary analyses employed two series of logistic regression models for each of the four PrEP cascade variables. In Model 1, the total syndemics count variable was entered as the sole predictor in each of the four models predicting a PrEP cascade variable, controlling for age, sexual orientation (exclusively gay vs. not), and relationship status (single vs. not). In Model 2, to examine the unique variance accounted for by psychosocial versus structural syndemics, the psychosocial syndemic count variable and the structural syndemic count variable were simultaneously entered as predictors in four additional models predicting each of the PrEP cascade variables (controlling for age, sexual orientation, and relationship status). Finally, supplemental multinomial logistic regressions were conducted with the PrEP stage variable as the outcome variable (with ‘PrEP use and high adherence’ set as the referent group). In Model 1, the total syndemics count variable was entered as the predictor; in Model 2, the psychosocial and structural syndemic count variables were simultaneously entered as predictors. In both Models, age, sexual orientation, and relationship status were controlled for. In all primary and supplemental analyses, adjusted odds ratios (AOR) and their 95% confidence intervals (95% CI) are reported.

Results

Descriptive Analyses

Participants ($N = 151$) ranged in age between 18 and 29 years ($M = 24$, $SD = 3$). The sample endorsed substantial occurrence of syndemic indicators: depression (49%), intimate partner violence (42%), marijuana use (41%), unstable housing (40%), illicit polysubstance use (36%), binge drinking (31%), CSA (21%), poverty (13%), and incarceration (7%). Regarding the frequency of total syndemic indicators, only 17 (11%) participants reported none, while 18 (12%) reported 1, 30 (20%) reported 2, 31 (21%) reported 3, 26 (17%) reported 4, 21 (14%) reported 5, and 8 (5%) reported 6 or more indicators. Slightly less than half the sample was aware of PrEP (47%), 46% indicated willingness to use PrEP, 19% reported current/past use of PrEP, and 15% indicated current PrEP adherence at 60% or greater. Bivariate correlations between structural and psychosocial syndemics were $r = .22$ ($p = .007$); structural and total $r = .56$ ($p < .0001$); and psychosocial and total $r = .93$ ($p < .0001$). Phi bivariate correlations between binary syndemic

variables and PrEP cascade variables are also reported in Table 1.

Primary Analyses

In Model 1, which examined the effects of total syndemics as a count variable, each additional syndemic endorsed was significantly associated with lower odds of PrEP awareness (AOR 0.68, 95% CI 0.55, 0.85, $p = .001$, Nagelkerke $R^2 = 0.27$), PrEP willingness (AOR 0.79, 95% CI 0.64, 0.96, $p = .017$, Nagelkerke $R^2 = 0.08$), and PrEP use (AOR 0.71, 95% CI 0.54, 0.92, $p = .010$, Nagelkerke $R^2 = 0.19$), but not significantly associated with PrEP adherence (AOR 0.61, 95% CI 0.30, 1.23, $p = .17$, Nagelkerke $R^2 = 0.44$). See Table 2.

In Model 2, which examined the effects of psychosocial syndemics and structural syndemics as count variables, differential effects emerged. The structural syndemics count variable (AOR 0.27, 95% CI 0.14, 0.53, $p < .001$, Nagelkerke $R^2 = 0.34$), but not the psychosocial syndemics count variable (AOR 0.86, 95% CI 0.66, 1.12, $p = .253$), was significantly associated with lower odds of PrEP awareness. Conversely, neither the psychosocial syndemics count variable (AOR 0.80, 95% CI 0.63, 1.01, $p = .061$, Nagelkerke $R^2 = 0.08$) nor the structural syndemics count variable (AOR 0.75, 95% CI 0.43, 1.28, $p = .285$) were significantly associated with PrEP willingness. Similarly, neither the psychosocial syndemics (AOR 0.79, 95% CI 0.57, 1.08, $p = .142$, Nagelkerke $R^2 = 0.20$) nor the structural syndemics count variable was associated with lower odds of PrEP use (AOR 0.46, 95% CI 0.19, 1.10, $p = .080$). Finally, the psychosocial syndemics count variable was significantly associated with lower odds of PrEP adherence (AOR 0.27, 95% CI 0.08, 0.95, $p = .041$, Nagelkerke $R^2 = 0.57$); however, the structural syndemics count variable was not (AOR 5.21, 95% CI 0.35, 77.40, $p = .231$). See Table 3.

Supplemental Analyses

In Model 1, each additional syndemic endorsed was significantly associated with higher odds of being in the PrEP stage 1 (AOR 2.66, 95% CI 1.64, 4.33, $p < .001$), PrEP stage 2 (AOR 2.57, 95% CI 1.57, 4.20, $p < .001$), PrEP stage 3 (AOR 1.98, 95% CI 1.21, 3.23, $p = .006$), and PrEP stage 4 (AOR 3.38, 95% CI 1.80, 6.36, $p < .001$) compared to the referent

Table 2 Model 1 binary logistic regressions by PrEP cascade outcome

Syndemic	AOR	95% CI	Wald χ^2	<i>p</i>
PrEP awareness (<i>n</i> = 151)				
Total**	0.68	[0.55, 0.85]	11.54	.001
Age	0.98	[0.88, 1.11]	0.08	.78
Sexual orientation**	4.65	[2.04, 10.61]	13.37	< .001
Relationship status*	2.39	[1.09, 5.22]	4.72	.03
PrEP willingness (<i>n</i> = 151)				
Total*	0.79	[0.64, 0.96]	5.71	.02
Age	1.04	[0.93, 1.16]	0.42	.52
Sexual orientation	1.35	[0.66, 2.77]	0.67	.41
Relationship status	1.73	[0.84, 3.54]	2.24	.14
PrEP use (<i>n</i> = 151)				
Total*	0.71	[0.54, 0.92]	6.55	.01
Age	1.17	[1.00, 1.36]	3.98	.05
Sexual orientation	2.81	[0.88, 8.96]	3.07	.08
Relationship status	2.08	[0.79, 5.50]	2.18	.14
PrEP adherence (<i>n</i> = 28)				
Total	0.61	[0.30, 1.23]	1.88	.17
Age	1.41	[0.77, 2.59]	1.25	.26
Sexual orientation	0.64	[0.04, 11.62]	0.09	.77
Relationship status	11.27	[0.58, 219.77]	2.56	.11

* $p < .05$; ** $p \leq .001$

Table 1 Bivariate correlations of PrEP cascade variables with individual and composite syndemic variables

	Variable	PrEP awareness	PrEP willingness	PrEP use	PrEP adherence
1.	Depression	-.10	-.09	-.09	-.29
2.	IPV	-.40**	-.28**	-.14	-.63**
3.	CSA	.11	.05	-.03	.02
4.	Binge drink	.27**	.14	.05	-.16
5.	Polydrug	-.31**	-.34**	-.15	-.79**
6.	Marijuana	.05	-.02	-.17*	.10
7.	Poverty	-.04	.05	-.08	.15
8.	Housing	-.40**	-.22**	-.22**	-.44*
9.	Prison	-.09	.02	-.06	.10
10.	Psych	-.16*	-.17*	-.18*	-.46*
11.	Structural	-.36**	-.14*	-.23**	-.21
12.	Total	-.27**	-.19*	-.24**	-.43*

* $p < .05$; ** $p \leq .01$

group, PrEP stage 5 (use and high adherence). The pseudo- R^2 (Nagelkerke R^2) for the model was 0.34. See Table 4.

In Model 2, each additional psychosocial syndemic endorsed was significantly associated with higher odds of being in the PrEP stage 1 (AOR 2.34, 95% CI 1.32, 4.16, $p = .004$), PrEP stage 2 (AOR 2.38, 95% CI 1.33, 4.26, $p = .004$), PrEP stage 3 (AOR 2.09, 95% CI 1.17, 3.73, $p = .013$), and PrEP stage 4 (AOR 3.74, 95% CI 1.77, 7.91, $p = .001$) compared to the referent group, PrEP stage 5 (use and high adherence). Conversely, structural syndemics was not significantly associated with higher odds of being in the PrEP stage 1 (AOR 4.34, 95% CI 0.84, 22.52, $p = .081$), PrEP stage 2 (AOR 3.47, 95% CI 0.66, 18.30, $p = .143$), PrEP stage 3 (AOR 1.60, 95% CI 0.29, 8.80, $p = .593$), and PrEP stage 4 (AOR 2.44, 95% CI 0.37, 16.22, $p = .357$) compared to the referent group, PrEP stage 5 (use and high adherence). The pseudo- R^2 (Nagelkerke R^2) for the model was 0.36. See Table 5.

Table 3 Model 2 binary logistic regressions by PrEP cascade outcome

Syndemic	AOR	95% CI	Wald χ^2	p
PrEP awareness ($n = 151$)				
Psychosocial	0.86	[0.66, 1.12]	1.31	.25
Structural**	0.27	[0.14, 0.53]	14.90	< .001
Age	0.95	[0.84, 1.07]	0.81	.37
Sexual orientation**	4.69	[2.01, 10.99]	12.69	< .001
Relationship status	2.22	[0.99, 4.98]	3.77	.05
PrEP willingness ($n = 151$)				
Psychosocial	0.80	[0.63, 1.01]	3.52	.06
Structural	0.75	[0.43, 1.28]	1.14	.29
Age	1.03	[0.93, 1.15]	0.36	.55
Sexual orientation	1.34	[0.65, 2.76]	0.64	.42
Relationship status	1.72	[0.84, 3.52]	2.18	.14
PrEP use ($n = 151$)				
Psychosocial	0.79	[0.57, 1.08]	2.16	.14
Structural	0.46	[0.19, 1.10]	3.07	.08
Age	1.15	[0.99, 1.34]	3.14	.08
Sexual orientation	2.66	[0.83, 8.52]	2.71	.10
Relationship status	1.97	[0.74, 5.23]	1.83	.18
PrEP adherence ($n = 28$)				
Psychosocial*	0.27	[0.08, 0.95]	4.19	.04
Structural	5.21	[0.35, 77.40]	1.44	.23
Age	1.61	[0.76, 3.44]	1.54	.21
Sexual orientation	0.18	[0.01, 6.05]	0.92	.34
Relationship status	51.64	[0.52, 5168.25]	2.82	.09

* $p < .05$; ** $p \leq .001$

Discussion

Young Latino MSM are a highly vulnerable group for acquiring HIV and are less likely to use PrEP compared to other MSM, despite higher PrEP willingness (Pulsipher et al., 2016). The current study sought to explore potential barriers in the PrEP cascade among this at-risk group. It was the first known study to apply syndemics theory to PrEP. Consistent with extant literature on syndemics and HIV transmission risk and ART adherence (e.g., Blashill et al., 2014; Dyer et al., 2012; Friedman et al., 2015; Herrick et al., 2013; Mustanski et al., 2007; Parsons et al., 2012, 2017a), greater endorsement of syndemic indicators was associated with lower odds of engagement across the PrEP cascade.

Although the total syndemics count variable was significantly associated with PrEP variables across the cascade (with the exception of adherence), slight variations were revealed when this omnibus variable was disaggregated into psychosocial versus structural syndemic counts. For example, only psychosocial syndemics were significantly predictive of lower odds of PrEP adherence. Similarly, supplemental multinomial logistic regressions revealed that psychosocial, but not structural, syndemics were associated with greater odds of being placed in an early PrEP stage versus the last stage (use and high

Table 4 Model 1 supplemental multinomial logistic regressions

Syndemic	AOR	95% CI	Wald χ^2	p
PrEP Stage 1^a				
Total**	2.66	[1.64, 4.33]	15.53	< .001
Age*	0.77	[0.60, 0.99]	4.21	.04
Sexual orientation*	10.90	[1.19, 99.59]	4.48	.03
Relationship status*	4.72	[1.09, 20.46]	4.29	.04
PrEP Stage 2^a				
Total**	2.57	[1.57, 4.20]	14.01	< .001
Age*	0.75	[0.58, 0.96]	5.30	.02
Sexual orientation	5.69	[0.59, 54.43]	2.28	.13
Relationship status	2.97	[0.66, 13.49]	1.99	.16
PrEP Stage 3^a				
Total*	1.98	[1.21, 3.23]	7.50	.01
Age*	0.72	[0.56, 0.93]	6.37	.01
Sexual orientation	4.15	[0.42, 41.03]	1.48	.22
Relationship status	2.33	[0.51, 10.68]	1.19	.28
PrEP Stage 4^a				
Total**	3.38	[1.80, 6.36]	14.34	< .001
Age	0.73	[0.53, 1.00]	3.76	.05
Sexual orientation	6.08	[0.47, 79.34]	1.90	.17
Relationship status	4.58	[0.64, 33.01]	2.28	.13

* $p < .05$; ** $p \leq .001$

^aCalculations for each PrEP stage were made in comparison with the referent group, PrEP stage 5 (use and high adherence)

Table 5 Model 2 supplemental multinomial logistic regressions

Syndemic	AOR	95% CI	Wald χ^2	<i>p</i>
PrEP Stage 1 ^a				
Psychosocial*	2.34	[1.32, 4.16]	8.43	.004
Structural	4.34	[0.84, 22.52]	3.05	.08
Age	0.79	[0.61, 1.02]	3.40	.07
Sexual orientation*	10.17	[1.09, 94.72]	4.15	.04
Relationship status	4.47	[1.02, 19.62]	3.93	.05
PrEP Stage 2 ^a				
Psychosocial*	2.38	[1.33, 4.26]	8.50	.004
Structural	3.47	[0.66, 18.30]	2.14	.14
Age*	0.76	[0.59, 0.98]	4.59	.03
Sexual orientation	5.40	[0.55, 52.50]	2.11	.15
Relationship status	2.86	[0.62, 13.08]	1.83	.18
PrEP Stage 3 ^a				
Psychosocial*	2.09	[1.17, 3.73]	6.19	.01
Structural	1.60	[0.29, 8.80]	0.29	.59
Age*	0.72	[0.55, 0.93]	6.47	.01
Sexual orientation	4.07	[0.40, 41.01]	1.42	.23
Relationship status	2.38	[0.51, 11.00]	1.22	.27
PrEP Stage 4 ^a				
Psychosocial**	3.74	[1.77, 7.91]	11.97	.001
Structural	2.44	[0.37, 16.22]	0.85	.36
Age	0.73	[0.53, 1.01]	3.64	.06
Sexual orientation	5.58	[0.42, 74.82]	1.68	.20
Relationship status	4.50	[0.63, 32.45]	2.23	.14

p* < .05; *p* ≤ .001

^aCalculations for each PrEP stage were made in comparison with the referent group, PrEP stage 5 (use and high adherence)

adherence). Conversely, only structural syndemics were predictive of PrEP awareness. These findings suggest that structural barriers (e.g., unstable housing) serve as greater impediments to being aware of PrEP, whereas once PrEP has been started, psychosocial indicators (e.g., IPV, polysubstance use) account for greater variance in adherence to PrEP.

The findings from the current study may impart implications for clinical practice. Given that both psychosocial and structural syndemic indicators account for unique variance across the PrEP cascade, combination interventions may be needed to maximize PrEP use and adherence. For example, while traditional interventions focused on psychoeducation and treatment of psychosocial problems (e.g., depression, substance use) may yield benefits to PrEP adherence (Blashill, Ehlinger, Mayer, & Safren, 2015; Mayer et al., 2017), they do not directly address structural barriers. One potential strategy to address both psychosocial and structural barriers to the PrEP cascade is patient navigation. Patient navigators can be laypersons, peers, or clinical staff (e.g., social workers, nurses), who connect with patients and determine their specific needs in accessing healthcare, direct patients to resources, and counsel them in

overcoming barriers. Although there is no known current efficacy data on PrEP patient navigation programs, such interventions have recently been initiated by the California Department of Public Health (2017, among other states: <https://aidsinfo.nih.gov/contentfiles/HIVPrEPNav.pdf>), and qualitative work suggests patients may find these services acceptable (Mutchler et al., 2015). A navigator could assist a patient in applying for health insurance, housing assistance, and other governmental aid programs. In addition, a navigator may also provide psychoeducation on PrEP, connect, and schedule PrEP consultation sessions; offer phone, text, and/or in-person reminders of medical appointments; problem-solve around barriers to PrEP adherence; and provide referrals and connection to mental health and substance use treatment. Future research would benefit from testing the efficacy and effectiveness of these programs along the PrEP cascade.

Limitations

The current study is not without limitations. Of note, the design was cross-sectional, limiting inferences regarding temporal ordering. Although theoretically one would not expect PrEP variables to cause changes in syndemic indicators, prospective designs may address the issue of ordering. Additionally, multiplicative analyses (i.e., interaction effects) with syndemic indicators were not employed within the current study. Instead, additive models were tested. Statistical power limited the ability to test higher-order interaction terms, and future research in this area would be enhanced via testing synergetic models (Tsai & Burns, 2015; Tsai & Venkataramani, 2016). The sample composition also precludes generalizability to non-Latinos, or MSM living outside of urban Southern California. Also, the current study tested one form of a PrEP cascade model, although variations exist (e.g., Parsons et al., 2017b) which include other salient constructs, such as PrEP intentions. Indeed, recent research has underscored the importance of assessing hypothetical willingness in addition to behavioral intentions for PrEP use (Rendina, Whitfield, Grov, Starks, & Parsons, 2017). Finally, measures assessing the PrEP cascade have yet to be fully psychometrically examined. For instance, the measure of PrEP adherence was adapted from validated self-report measures of ART adherence; however, it is unclear if this is a valid measure of adherence for PrEP.

As the first known study to examine the PrEP cascade in a syndemics framework, future research could build on these results by examining other measures of PrEP adherence, complementary stages of the PrEP cascade, and whether results could generalize to other demographic groups. Although future studies could benefit from biological measures of PrEP adherence, additional research is needed to develop and test self-report markers of PrEP adherence validated with biological values of PrEP use (e.g., hair and dried blood spots, plasma, and peripheral blood mononuclear cells; Abaasa et al., 2018;

Haberer, 2016; Haberer et al., 2015). Future studies could also examine whether or not results from this study could generalize to other sociodemographic groups, such as Latino MSM outside of San Diego County or to people outside the 18–29 age range. Although there are no prior data on how findings from PrEP syndemics may generalize, comparable studies on syndemics among MSM have found behavioral health effects across age and race (e.g., Friedman et al., 2015). In addition, although this study was fully translated to Spanish, only two participants responded in Spanish. Future studies could focus on recruitment for Spanish-speaking participants, as language could have differential effects on navigating the PrEP cascade.

Conclusions

In summary, the current study explored the association with syndemics and the PrEP cascade. Findings revealed that greater syndemics were associated with lower engagement across the PrEP cascade. Psychosocial and structural syndemic variables appear to account for unique variance in PrEP behaviors and suggest the potential utility of combination interventions in addressing multiple aspects of the PrEP cascade. To increase the awareness, willingness, use, and adherence to biomedical HIV prevention efforts, such as PrEP, researchers and clinicians should consider the role of psychosocial and structural level factors that may serve as substantial barriers to vulnerable populations at risk of HIV acquisition.

Acknowledgements Research reported in this publication was supported by the Department of Psychology at San Diego State University. Additionally, some of the author time was funded by K23MH096647 (Blashill) and 9K24DA040489 (Safren). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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