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PREP-RELATED INTERACTIVE TOXICITY BELIEFS: ASSOCIATIONS WITH STIGMA, SUBSTANCE USE, AND PREP UPTAKE

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Despite documented efficacy in reducing HIV transmission, pre-exposure prophylaxis (PrEP) uptake among Black sexual minority men (BSMM) is limited. One understudied factor which may impede PrEP uptake is PrEP-related interactive toxicity beliefs (i.e., believing it is hazardous to use alcohol/drugs while taking PrEP). Data from $N = 169$ HIV negative BSMM over 4 months showed high rates of agreement with at least one alcohol (78%) or drug (84%) interactive toxicity belief. Univariate analyses showed increased alcohol or drug interactive toxicity beliefs predicted lower PrEP uptake. Multivariable regression suggested those with PrEP-related alcohol or drug interactive toxicity beliefs were more likely to report high PrEP stigma, more negative PrEP beliefs (e.g., concern that taking PrEP disrupts life), and were more likely to use alcohol/drugs (respectively) prior to/during sex. Findings warrant intervention work targeting interactive toxicity beliefs with tailored messaging to mitigate PrEP stigma and correct concerns around substance use and PrEP.

Keywords: PrEP uptake, Black sexual minority men, interactive toxicity beliefs, PrEP stigma, substance use, alcohol use

INTRODUCTION

High HIV transmissions rates in the U.S. South among Black sexual minority men (BSMM) have underscored the urgent need for continued advancement in

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biomedical HIV prevention techniques, such as pre-exposure prophylaxis (PrEP) use. As of 2020, these rates remain elevated in the Southeastern U.S., in particular in and around Atlanta, Georgia, which has demonstrated the highest rate of new HIV transmissions (28 per 100,000); two times higher than that of the national average (13 per 100,000), and one of the lowest PrEP-to-need ratios (2.27; i.e., the number of PrEP users divided by new HIV diagnoses, where a lower PrEP-to-need ratio reflects greater unmet need for PrEP) among Black men (AIDSVu, 2019; Georgia Department of Public Health, 2019). Further, BSMM account for 26% of new HIV diagnoses overall and 37% of new HIV diagnoses among sexual minority men (Johnson Lyons et al., 2021; Marano et al., 2018; Purcell et al., 2012). Further, BSMM from the metropolitan Atlanta area, defined in the CDC's Ending the HIV Epidemic priority jurisdictions as Cobb, DeKalb, Fulton, and Gwinnett counties, continue to be disproportionately affected by HIV, warranting targeted interventions to correct critical health disparities and reduce HIV transmission (George & Georgia Department of Public Health, 2021; Georgia Department of Public Health, 2019).

PrEP use is one of the most effective prevention methods for HIV negative individuals who are potentially at risk for HIV transmission. PrEP can reduce the risk of HIV transmission by up to 99% (Centers for Disease Control and Prevention [CDC], 2019, 2021). Yet, recent research suggests that when compared to the general population of sexual minority men, BSMM are both less likely to be aware of PrEP and only 19% have ever used PrEP (Okeke et al., 2021). Thus, despite the well-documented efficacy of PrEP as an HIV prevention tool, health disparities related to PrEP uptake remain (CDC, 2019; Quinn et al., 2020).

PrEP is most effective against HIV transmission when taken as instructed, highlighting the critical nature of consistent PrEP adherence. Interactive toxicity beliefs (i.e., believing that it is hazardous to use alcohol and/or drugs with certain medications like PrEP) have been shown to predict intentional nonadherence to antiretrovirals among people living with HIV and may also act as a barrier to PrEP uptake among those who are HIV negative (Kalichman et al., 2013, 2015, 2019, 2022; Kalichman & Eaton, 2017). While it can be hazardous to drink alcohol or take drugs with certain antiretrovirals for those with concurrent liver issues, there are no known risks for severe interactions among people with normal liver function (Fatch et al., 2017; Neuman et al., 2012; Price & Thio, 2010; Urbina & Faragon, 2014). Previous research suggests people who use stimulants have more concern that their substance use will interfere with PrEP (Oldenburg et al., 2016). Further, men who have stated they were not interested in taking PrEP were significantly more likely to binge drink and perpetuate interactive toxicity beliefs (Kalichman & Eaton, 2017). These findings align with the Interactive Toxicity Beliefs Process Model (Kalichman et al., 2019) used to guide the current study which suggests that alcohol and drug interactive toxicity beliefs act as a mechanism through which alcohol or drug use can lead to poor clinical outcomes such as low antiretroviral adherence among people living with HIV. It is possible this model may also extend to HIV negative men who are considering PrEP. If so, interactive toxicity beliefs may impede PrEP uptake among individuals at risk for HIV transmission, specifically those who engage in substance use. Therefore, along with the perception of intoxication leading to unintentional non-adherence to PrEP and increased sexual risk taking, endorsing PrEP-related interactive toxicity beliefs may also act as a predictor of intentional non-adherence or reduced likelihood of PrEP uptake (Kalichman et al., 2015, 2019, 2022; Kalichman & Eaton, 2017).

For PrEP to have a significant positive impact on reducing higher levels of HIV incidence among populations at potentially elevated risk for HIV, efforts to

understand and address barriers to PrEP must be prioritized (Jenness et al., 2019). Guided by the Interactive Toxicity Beliefs Process Model (Kalichman et al., 2019), the current study explored whether PrEP-related alcohol and/or drug interactive toxicity beliefs impact PrEP uptake longitudinally among BSMM residing in and around the Atlanta metro area. Further as the Interactive Toxicity Beliefs Process Model aims to manage structural barriers and resolve sources of potential nonadherence/low uptake for medications like PrEP, multivariable regression analyses explored certain PrEP-related barriers (i.e., PrEP anticipated stigma and negative PrEP beliefs) as potential predictors of PrEP-related alcohol and drug interactive toxicity beliefs. These results will provide a foundation to better understand individuals who endorse PrEP-related interactive toxicity beliefs and can help to focus prevention efforts aimed at mitigating co-occurring barriers to increase PrEP uptake.

METHODS

PARTICIPANTS AND SETTING

The current study included $N = 169$ BSMM living within the greater Atlanta metro area of Georgia, including but not limited to, participants from four counties targeted as Ending the HIV Epidemic priorities (i.e., Cobb, DeKalb, Fulton, and Gwinnett, Georgia; George & Georgia Department of Public Health, 2021). Data from this study come from a larger behavioral intervention trial focused on testing a stigma counseling intervention. From the larger sample of 177, three participants identified as heterosexual, two identified at transgender women, and three participants had missing data relevant to the analyses, and thus were not included within the current sample. It should be noted that intervention counseling primarily focused on accessing medical care and not on interactive toxicity beliefs. Participants were recruited through online methods including social media advertisements (i.e., Facebook and Instagram) and participant driven referrals. Study inclusion criteria consisted of being 18 years of age or older, assigned male sex at birth, reporting condomless anal sex in the past year, reporting no current PrEP use, reporting HIV negative/unknown status, and reporting that their last HIV test was more than 3 months ago. Data were collected between 2019 and 2020. Study protocols received Institutional Review Board approval from the University of Connecticut.

STUDY PROCEDURES

Eligible participants were scheduled for an enrollment appointment to complete consenting activities. All study activities were delivered by a survey program (REDCap) or video chat with project staff (e.g., counseling and HIV testing). During the enrollment appointment, participants also took part in a guided video session to complete an oral HIV test using OraQuick HIV 1/2 antibody tests (OraSure Technologies, Bethlehem, PA). Participants testing HIV positive were immediately linked to HIV care providers and offered enrollment into other available studies at the research site. Participants testing HIV negative were eligible to continue with the study. Participants completed follow up surveys at 1, 2, and 4 months post-intervention. Data for the current study focused on baseline and, the most distal timepoint, 4-month follow-up. Participants received up to $220 for completing all study activities.

The analyses for the current study included initial descriptive statistics on relevant variables and substance use, stratified by PrEP uptake with appropriate chi-square or *T*-tests run to assess differences. Initial bivariate analyses were completed to assess the association of PrEP-related alcohol and drug interactive toxicity beliefs measured at baseline (prior to the intervention) on PrEP uptake (measured at 4 months post-intervention). Follow-up multivariable analyses were run to further explore whether potential predictors (measured at baseline) were associated with PrEP-related interactive toxicity beliefs (measured at 4 months post-intervention).

MEASURES

Demographic characteristics including age, sexual orientation, and income were assessed. Substance use and sex were assessed with self-report questions providing examples of what our study considered alcohol and drug use. Alcohol use was assessed using the AUDIT-C (Bush et al., 1998) within the past month. Drug use within the past month spanned the substances: marijuana, crack, cocaine, poppers, injection drug use, opioids, and other drugs. Exemplars of substances considered were included within the items, for example "how often have you used poppers (nitrate inhalants) in the past month" and "how often have you used opioids (oxycodone, Oxycontin, Percocet, Vicodin, fentanyl, Dilaudid) in the past month?"

Alcohol Use Prior to or During Sex. Following the AUDIT-C, alcohol use prior to or during sex was assessed with one question asking participants to indicate the number of times in the past month they drank alcohol prior to or during sex. Responses were kept continuous.

Drug Use Prior to or During Sex. Following the self-report drug use questions outlined above, drug use prior to or during sex was assessed with one question asking participants to indicate the number of times in the past month they used drugs prior to or during sex. Responses were kept continuous.

PRIMARY OUTCOMES

PrEP Uptake. PrEP uptake was assessed by self-report measures. Participants answered either yes or no to the question: Are you currently taking PrEP? Results were then coded dichotomously to indicate any PrEP uptake across the 4-month follow-up time period.

PrEP-Related Interactive Toxicity Beliefs. PrEP-related interactive toxicity beliefs assessed toxicity concerns for using either alcohol or drugs while taking PrEP. Items were adapted from previous studies on antiretroviral use and substance use among individuals living with HIV (Kalichman et al., 2013, 2015). Ten items (i.e., 5 PrEP-related alcohol interactive toxicity beliefs and 5 PrEP-related drug interactive toxicity beliefs) consisted of similar wording for both alcohol and drug interactive toxicity beliefs: (1) Alcohol (Drugs) and PrEP should never be mixed; (2) A person should stop taking PrEP if they are drinking (using drugs); (3) Alcohol (Drugs) interfere(s) with PrEP so it will not work right; (4) Mixing alcohol (drugs) with PrEP is dangerous; and (5) Drinking alcohol (Taking drugs) while on PrEP is toxic to the body's system. Participants were asked to rate each item on a 6-point scale

from 1 (strongly disagree) to 6 (strongly agree) where a higher score corresponded with more concern for interactive toxicity beliefs. Both PrEP-related alcohol interactive toxicity belief scores (α = .92) and PrEP-related drug interactive toxicity belief scores (α = .95) were computed by taking the mean of responses at a given follow-up assessment relevant for each analysis.

PREDICTORS

PrEP Anticipated Stigma. Items were adapted from previous PrEP stigma scales tested among sexual minority men (Eaton et al., 2017; Watson et al., 2022). The three items include: (1) If I used PrEP, I would be worried that people would think I was gay; (2) If I used PrEP, I would keep it a secret; and (3) If I used PrEP, I would worry people would judge me. The mean of responses was taken which ranged from 1 (strongly disagree) to 6 (strongly agree) on a six-point scale and were coded such that higher scores reflect stronger PrEP anticipated stigma (α = .78).

Negative PrEP Beliefs. Four items were adapted from the beliefs about medications questionnaire to describe negative PrEP beliefs (Horne et al., 1999). Items included: (1) Taking PrEP would cause me concerns; (2) I worry about the long-term effects of PrEP; (3) Taking PrEP would disrupt my life; and (4) PrEP would give me unpleasant side effects. The final measure was calculated by taking the mean and responses ranged from 1 (strongly disagree) to 6 (strongly agree) on a six-point scale where higher scores indicate greater concern about taking PrEP (α = .80).

Trust in Health Care Providers. Trust in health care providers included three items that reflected broad medical trust in health care providers (Eaton et al., 2015; Pellowski et al., 2017). Items included: (1) I trust that health care providers are giving me the best treatment available; (2) I trust that health care providers have my best interest in mind when treating me; and (3) I trust that health care providers will tell me if a mistake is made regarding my medical treatment. The final measure was calculated by taking the mean and responses ranged from 1 (strongly disagree) to 6 (strongly agree) on a six-point scale where higher scores reflect more trust in health care providers (α = .90).

Medical Mistrust. Medical mistrust included three items adapted from the Medical Mistrust Index (Pellowski et al., 2016). Items included: (1) Patients have sometimes been deceived or misled by health care providers; (2) When health care providers make mistakes, they usually cover it up; and (3) Health care providers have sometimes done harmful things to patients without their knowledge. The final measure was calculated by taking the mean and responses ranged from 1 (strongly disagree) to 6 (strongly agree) on a six-point scale where higher scores indicate more mistrust in medical professionals (α = .82).

RESULTS

DEMOGRAPHIC CHARACTERISTICS

Within the full sample, the majority of the 169 participants reported some college education or greater (77%) with an average income between $21,000 to $30,000 and an average age of 36 years. All participants identified as Black, 100% of whom

TABLE 1. Descriptive Statistics Stratified by PrEP Uptake

	PrEP Uptake (n = 54)	No PrEP Uptake (n = 115)	
	n (%)/Mean (SD), Range		t test/X^2
Age (years)	36.69 (11.76), 21.0–69.0	35.54 (10.99), 21.0–69.0	–0.44
Income	3.15 (2.03), 1.0–7.0	3.06 (1.93), 1.0–7.0	–0.36
Trust in providers	4.52 (1.63), 1.0–6.0	4.70 (1.31), 1.0–6.0	0.80
Medical mistrust	3.33 (1.49), 1.0–6.0	3.49 (1.48), 1.0–6.0	0.65
Alcohol use prior/during sex	2.23 (4.19), 0.0–20.0	1.24 (2.43), 0.0–20.0	–1.27
Drug use prior/during sex	1.83 (4.70), 0.0–20.0	1.05 (2.79), 0.0–20.0	–1.07
PrEP anticipated stigma	1.95 (1.32), 1.0–6.0	1.90 (1.15), 1.0–6.0	–0.22
Negative PrEP beliefs	2.95 (1.31), 1.0–6.0	3.07 (1.33), 1.0–6.0	0.54
Education, n (%)			
High school or less	15 (27.8%)	24 (20.9%)	4.00
Some college	15 (27.8%)	46 (40.0%)	—
College degree	14 (25.9%)	32 (27.8%)	—
Graduate school	10 (18.5%)	13 (11.3%)	—
Sexual orientation, n (%)			
Same gender loving	9 (16.7%)	21 (18.3%)	4.80
Gay/Homosexual	37 (68.5%)	62 (53.9%)	—
Bisexual	8 (14.8%)	32 (27.8%)	—
Gender identity, n (%)			
Male	53 (98.1%)	112 (97.4%)	4.69
Other	1 (1.9%)	3 (2.6%)	—

Note. N = 169. All descriptive statistics reflect baseline characteristics. t test/X^2 column reflects difference testing: chi-square or t test with significance: $^*p \leq .05$; $^{**}p \leq .01$; $^{***}p \leq .001$. Income is represented ordinally: (1) $0–$10,000; (2) $11,000–$20,000; (3) $21,000–$30,000; (4) $31,000–$40,000; (5) $41,000–$50,000; (6) $51,000–$60,000; (7) $61,000 or higher.

self-identified their gender as male or other, and 77% of whom identified their sexual orientation as gay/homosexual (59%) or same gender loving (18%). A further 24% of men identified as bisexual. Within the sample, 96% of BSMM reported they were aware of PrEP. Across the sample, 32% engaged in PrEP uptake in the 4-month follow-up period. Within Table 1, sample demographics are further divided by PrEP uptake (n = 54) and no PrEP uptake (n = 115). Difference testing including chi-square and t-tests suggested no significant differences in demographics and primary variables when stratified by PrEP uptake.

SUBSTANCE USE

Substances including alcohol and drug use are represented by frequency from most frequently used within the past month to least frequently used (Table 2). The most used substance was alcohol, at 81% for those with PrEP uptake and 79% among those without PrEP uptake. Marijuana use was also frequently reported among both those engaging in PrEP (43%) and those not engaging in PrEP use (50%), followed by poppers among 11% of the PrEP uptake group and 11% of those who did not uptake PrEP. The remaining drugs including other drugs used without a prescription, cocaine, opioids, methamphetamine, crack, and injection drug use were reported by

TABLE 2. Substance Use Frequencies by PrEP Uptake

	PrEP Uptake (*n* = 54)	No PrEP Uptake (*n* = 115)	
Substance use	***n*** **(%)**	***n*** **(%)**	X^2
Alcohol	44 (81.4)	91 (79.1)	2.29
Marijuana	23 (42.6)	58 (50.4)	7.24
Poppers	6 (11.1)	13 (11.3)	4.97
Other drugs	6 (11.1)	7 (6.1)	5.96
Cocaine	5 (9.3)	6 (5.2)	4.65
Opioids	4 (7.4)	2 (1.7)	4.97
Methamphetamine	3 (5.6)	4 (3.5)	5.98
Crack	2 (3.7)	2 (1.7)	2.89
Injection drug use	2 (3.7)	0 (0.0)	4.31

Note. *N* = 169. Substance use reflects self-reported, baseline characteristics within the past month. Substances in order from most used to least used. $^*p \le .05$. $^{**}p \le .01$. $^{***}p \le .001$.

a small percentage of the sample. Chi-square analyses indicated no significant differences in any substance use between those who engaged in PrEP uptake versus those who did not.

PREP-RELATED INTERACTIVE TOXICITY BELIEFS

The majority of the sample agreed with certain interactive toxicity beliefs for both alcohol and drugs. Across the whole sample, 78% agreed with at least one PrEP-related alcohol interactive toxicity belief and 84% agreed with at least one PrEP-related drug interactive toxicity belief.

Individual item frequencies ranged from 46% to 80% agreement across alcohol and drug interactive toxicity beliefs. The strongest item for both alcohol and drug interactive toxicity beliefs was the first question where BSMM believed alcohol or drugs and PrEP should *never* be mixed. Among the interactive toxicity beliefs for alcohol, 71% agreed (46% strongly agreed) that alcohol and PrEP should never be mixed, 46% agreed (22% strongly agreed) one should stop taking PrEP if drinking, 51% agreed (18% strongly agreed) alcohol interferes with PrEP, 59% agreed (26% strongly agreed) mixing alcohol and PrEP is dangerous, and 60% agreed (26% strongly agreed) mixing alcohol and PrEP is toxic. Interactive toxicity beliefs for drugs were endorsed at higher rates, 80% agreed (59% strongly agreed) that drugs and PrEP should never be mixed, 61% agreed (40% strongly agreed) one should stop taking PrEP if using, 63% agreed (32% strongly agreed) drugs interfere with PrEP, 77% agreed (43% strongly agreed) mixing drugs and PrEP is dangerous, and 75% agreed (37% strongly agreed) mixing drugs and PrEP is toxic.

Within the univariate logistic regression models (Table 3), having either alcohol or drug interactive toxicity beliefs at baseline predicted lower PrEP uptake at 4 months post-intervention, while controlling for the appropriate intervention condition. Thus, a one unit increase in PrEP-related alcohol interactive toxicity beliefs was associated with a lower likelihood of initiating PrEP (B = -.291, Exp(B) = .803, p = .025). Similarly, a one unit increase in PrEP-related drug interactive toxicity

TABLE 3. Univariate Logistic Regression Results Predicting PrEP Uptake

						95% CI		
	M	*SD*	*B*	*B SE*	Exp(*B*)	LL	UL	*p*
Alcohol Interactive Toxicity Beliefs Baseline	**3.803**	**1.618**	**–.219**	**.100**	**.803**	**.660**	**.979**	**.025**
Drug Interactive Toxicity Beliefs Baseline	**4.323**	**1.678**	**–.283**	**.100**	**.753**	**.619**	**.917**	**.005**

Note. $N = 169$. Unstandardized results shown. *M* = mean; *SD* = standard deviation; *B* = unstandardized coefficient; *B SE* = standard error for the unstandardized coefficient; Exp = exponentiated; CI = confidence interval; LL = lower limit; UL = upper limit (significant effects bolded). Randomized intervention condition was included as a control variable. Interactive toxicity beliefs were measured at baseline. PrEP uptake was measured at 4 months post-intervention. Bold indicates significant associations. $^{*}p \leq .05$. $^{**}p \leq .01$. $^{***}p \leq .001$.

beliefs at baseline was also associated with a lower likelihood of initiating PrEP ($B = -.283$, Exp(B) = .753, $p = .005$).

Following these results, multivariable linear regression was used to describe those who held PrEP-related alcohol or drug interactive toxicity beliefs (Table 4). Results were the same for both alcohol and drug interactive toxicity beliefs. Stronger PrEP anticipated stigma ($B = .275$, $p = .023$), more negative PrEP beliefs such as taking PrEP would disrupt my life ($B = .337$, $p = .008$), and more alcohol use prior to or during sex within the past month ($B = .191$, $p = .001$) predicted having stronger PrEP-related alcohol interactive toxicity beliefs. Similarly, stronger PrEP anticipated stigma ($B = .200$, $p = .025$), more negative PrEP beliefs ($B = .264$, $p = .045$), and more drug use prior to or during sex within the past month ($B = .106$, $p = .010$) predicted having stronger PrEP-related drug interactive toxicity beliefs. No significant effects were found for trust in health care providers, medical mistrust, or among the covariates age, income, and sexual orientation.

DISCUSSION

Findings from the current study warrant the further examination of PrEP-related interactive toxicity beliefs and highlight the utility of mitigating interactive toxicity beliefs to improve PrEP uptake among BSMM at elevated risk for HIV. Results demonstrate a high frequency of agreement with both alcohol and drug interactive toxicity beliefs among BSMM ranging from 46% to 80% (e.g., 80% of BSMM agreed that drugs and PrEP should never be mixed) along with high rates of alcohol use (80%) and marijuana use (48%). Univariate logistic regression findings suggest both alcohol and drug interactive toxicity beliefs may be predictive of lower PrEP uptake. This finding confirms similar research among people who are HIV negative and people living with HIV, suggesting future interventions targeting and correcting interactive toxicity beliefs and co-occurring barriers may help to bolster PrEP uptake or ART adherence and, in turn, reduce HIV transmission (Fatch et al., 2017; Kalichman et al., 2013, 2015, 2019; Kalichman & Eaton, 2017). Further, this data points to the need for clearer messaging to BSMM regarding drug interactions with PrEP and may lead to leverage points in the patient-provider conversations about PrEP. After adjusting for covariates, additional multivariable regression models revealed a group of co-occurring barriers in which those who held greater PrEP-related alcohol and drug interactive toxicity beliefs demonstrated high PrEP stigma (e.g., worry

TABLE 4. Multivariable Linear Regression Results Predicting PrEP-Related Interactive Toxicity Beliefs

			95% CI		
	B	*B SE*	LL	UL	*p*
Alcohol Interactive Toxicity Beliefs					
PrEP anticipated stigma*	**.275**	**.120**	**.038**	**.588**	**.023**
Negative PrEP beliefs**	**.337**	**.125**	**.089**	**.585**	**.008**
Trust in health care providers	.186	.108	–.029	.400	.090
Medical mistrust	–.047	.111	–.267	.172	.444
Alcohol use prior/during sex***	**.191**	**.053**	**.086**	**.296**	**.001**
Age	.016	.014	–.012	.045	.197
Income	–.168	.097	–.359	.023	.092
Sexual orientation	.259	.222	–.182	.700	.247
Drug Interactive Toxicity Beliefs					
PrEP anticipated stigma*	**.200**	**.091**	**.023**	**.380**	**.025**
Negative PrEP beliefs*	**.264**	**.130**	**.061**	**.522**	**.045**
Trust in health care providers	.208	.119	–.021	.436	.099
Medical mistrust	–.047	.124	–.292	.199	.375
Drug use prior/during sex**	**.106**	**.043**	**.021**	**.191**	**.010**
Age	.014	.015	–.017	.044	.376
Income	–.019	.085	–.187	.149	.824
Sexual orientation	.106	.242	–.374	.586	.660

Note. $N = 169$. Unstandardized results shown. *B* = unstandardized coefficient; *B SE* = standard error for the unstandardized coefficient; CI = confidence interval; LL = lower limit; UL = upper limit. Predictors measured at baseline. PrEP-related interactive toxicity beliefs measured at 4 months post-intervention. *$p \leq .05$. **$p \leq .01$. ***$p \leq .001$ (significant effects bolded).

others may judge PrEP use), more negative PrEP beliefs such as worrying that PrEP use would disrupt one's life, and demonstrated a higher likelihood of using corresponding alcohol or drug use prior to or during sex within the past month. These findings highlight the potentially cyclical and contradictory process in which HIV risk assessments prioritize substance use as a critical determining factor for PrEP intervention, yet that very substance use may act as a critical barrier preventing PrEP uptake among those who are of an increased risk for transmission.

The current study furthers our understanding of PrEP-related alcohol and drug interactive toxicity beliefs and is the first to assess these beliefs in association with PrEP uptake over time. Results suggest that PrEP-related alcohol and drug interactive toxicity beliefs may co-occur alongside other barriers including PrEP anticipated stigma and negative concerns about taking PrEP, potentially compounding the negative effects. Thus, BSMM who were already worried about the stigmatizing impact of taking PrEP and hold negative beliefs about using PrEP may also be more likely to hold stronger PrEP-related interactive toxicity beliefs about alcohol and drugs. If left unaddressed, these negative notions about the hurdles of taking PrEP may forgo its use. Further, findings help to bolster the Interactive Toxicity Beliefs Process Model (Kalichman et al., 2019) by extending it to HIV negative BSMM who are candidates for PrEP. As suggested by the model, alcohol and drug interactive toxicity beliefs may act as a mechanism through which substance use can lead to poor clinical and health outcomes. While more research is needed to extend this model to PrEP candidates,

the current results form a foundation for such a process by suggesting people who believe in the adverse interactive toxicity effects of mixing alcohol or drugs while on PrEP medication, may choose to intentionally forgo PrEP due to co-occurring barriers and prioritize substance use (Kalichman et al., 2015, 2019, 2022). Likewise, participants who held greater PrEP-related alcohol and drug interactive toxicity beliefs also engaged in more corresponding alcohol or drug use prior to sex (Kalichman & Eaton, 2017), potentially leading to sex without the protection of PrEP. Applying the Interactive Toxicity Beliefs Process Model to our results suggests that target populations of BSMM may not fully understand the implications of forgoing PrEP in favor of substance use. Possible interventions may include opening up communication between trusted medical professionals and patients to describe how PrEP can be used effectively with substances, or interventions aimed at promoting intermittent PrEP use or Post-exposure Prophylaxis (PEP) depending on the individual's needs.

Current findings should be considered in light of study limitations. The sample consisted of BSMM from the Atlanta metropolitan area. Although it is critical to study barriers to PrEP in Atlanta given PrEP disparities in the Atlanta metro area, more research is needed to extend generalizability of results to outside the sample location. Further research is also needed to explore PrEP-related interactive toxicity beliefs among sexual minority men across races/ethnicities. Likewise, all men within the sample self-identified as male when asked about their gender. Future research among other sexual and gender diverse groups vulnerable to HIV, including individuals who identify as transgender, is warranted. Multiple psychosocial measures and PrEP uptake counts relied on self-report. Despite the confidential nature of the survey, bias may have been introduced when reporting socially sensitive behaviors. Further, the sample was one of convenience among those who were willing to take part in a PrEP-related study.

Interventions to increase PrEP uptake hold great potential to reduce the high number of new HIV transmission rates among the US South. According to the current results, it may be necessary to tailor messaging surrounding interactive toxicity beliefs and the potentially compounding impacts of PrEP anticipated stigma and negative PrEP beliefs within a single intervention aimed at addressing concerns about taking PrEP. Interventions that target misperceptions about taking PrEP that involve interactive toxicity beliefs within the context of engaging in alcohol or substance use (Kalichman et al., 2013) are needed, as it is generally not advised to cease using substances while taking PrEP. Addressing these beliefs may be especially important among groups of people who engage in frequent alcohol or drug use such as people living with substance use disorders, as the opportunity to skip PrEP doses due to misconceptions about interactive toxicity beliefs may be more salient (Kalichman et al., 2013, 2015). Further research is needed to guide future interventions aimed at addressing PrEP-related interactive toxicity beliefs within the context of substance use and PrEP stigma.

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