Reduction and Cessation of Alcohol, Cannabis, and Stimulant Use: Prospective Associations With Changes in Depressive Symptoms Across Two Cohort Studies of Sexual and Gender Minorities

CHRISTINA DYAR, PH.D.,[a,*] HEATHER BRADLEY, PH.D.,[b,c] ETHAN MORGAN, PH.D.,[a] PATRICK S. SULLIVAN, D.V.M., PH.D.,[c] & BRIAN MUSTANSKI, PH.D.[a,d]

[a]*Institute for Sexual and Gender Minority Health and Wellbeing, Northwestern University, Chicago, Illinois*

[b]*School of Public Health, Georgia State University, Atlanta, Georgia*

[c]*Rollins School of Public Health, Emory University, Atlanta, Georgia*

[d]*Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois*

ABSTRACT. Objective: Sexual and gender minorities (SGM) are at increased risk for substance use and depression. However, little research has examined the directionality of associations between substance use and depression in this high-risk population, and we are not aware of any to parse associations between depression and changes in the frequency of substance use versus substance use cessation. Such research can help to inform the development of future interventions to address health disparities affecting SGM. **Method:** We used data from two longitudinal cohorts of SGM assigned male at birth (SGM-AMAB; N = 1,418) to examine associations between changes in frequency of alcohol, cannabis, and stimulant use and depressive symptoms. Multilevel models tested whether changes in substance use predicted changes in depressive symptoms and vice versa. **Results:** Results indicate that when SGM-AMAB decreased their alcohol use or ceased alcohol, cannabis, or stimulant use, they experienced concurrent decreases in depressive symptoms. Only reducing stimulant use (not alcohol or cannabis use) was associated with decreases in depressive symptoms over the subsequent 6 months. Depressive symptoms did not prospectively predict cessation or reduction in the use of any substance. **Conclusions:** These findings suggest that clinical interventions targeting substance use may simultaneously reduce depressive symptoms and that reductions in alcohol use (even in the absence of cessation) may simultaneously benefit mental health among SGM-AMAB. The limited evidence of prospective effects over 6 months suggests that studies with shorter lags may be better equipped to examine the directionality of the association between depressive symptoms and substance use/reduction. (*J. Stud. Alcohol Drugs, 81,* 790–797, 2020)

SEXUAL AND GENDER MINORITIES (SGM) are at increased risk for substance use, substance use disorders, and mood disorders compared with cisgender, heterosexual individuals (Bränström et al., 2016; Day et al., 2017; King et al., 2008; McCabe et al., 2009; Meyer et al., 2017). In addition, the incidence of comorbid mood and substance use disorders are further elevated among SGM (Pakula et al., 2016; Reisner et al., 2016). Most research on substance use and mental health among SGM has focused on identifying social determinants of health disparities, such as societal stigmatization (see Kidd et al., 2018). However, relatively little research has examined associations between substance use and depression or the effects of substance use reduction or cessation in this population. Given high rates of substance use and mental health disorders, further research is needed to understand the comorbidity of these disorders among sexual minorities and the effects of reduction and cessation of substance use on mental health. This research can inform future substance use and mental health interventions for SGM aiming to reduce these disparities.

Among the general adult population, substance use and depression are highly comorbid, with 41% of individuals with substance use disorders having comorbid mood disorders compared with only 19% of those without substance use disorders (Conway et al., 2006). However, determining the directionality of the association between substance use and depression is complex, and results are mixed. For example, depression has been associated with subsequent increases in illicit drug use (Wu et al., 2008), alcohol use and problems (Bell & Britton, 2014), and cannabis use (Feingold et al., 2015; Wittchen et al., 2007), as well as lower likelihood of ceasing substance use (Warner et al., 2004). On the other hand, prospective associations between substance use and subsequent changes in depressive symptoms have also been demonstrated (Conner et al., 2009; Delaney et al., 2018). For example, less frequent cannabis (Hser et al., 2017; Lev-Ran et al., 2014), alcohol (Boden & Fergusson, 2011; Sullivan

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*Correspondence may be sent to Christina Dyar at the Institute for Sexual and Gender Minority Health and Wellbeing, Northwestern University, 625 N. Michigan Ave, Office 14-049, Chicago, IL, 60611, or via email at: dyar.christina@northwestern.edu.

et al., 2011), and stimulant use (Glasner-Edwards et al., 2009; Gossop et al., 2000) have been linked to subsequent decreases in depressive symptoms. Although this suggests a bidirectional association between depressive symptoms and substance use, several studies have failed to find evidence of bidirectionality (Bell & Britton, 2014; Feingold et al., 2015; Wilkinson et al., 2016). Further research is needed to determine the directionality of associations between substance use and depressive symptoms.

Further complicating our understanding of these associations, most existing studies have not distinguished the effects of reductions in substance use versus cessation on depressive symptoms. Although existing studies have examined the effects of cessation, initiation, or frequency of substance use (Conner et al., 2009; Lev-Ran et al., 2014; Rasic et al., 2013), they have rarely examined whether reductions in substance use (without cessation) are associated with subsequent decreases in depressive symptoms. In one exception, a longitudinal study of substance use among individuals living with HIV found that cessation or decreases in stimulant and cannabis use were associated with subsequent decreases in depressive symptoms (Delaney et al., 2018). Determining whether reduction in the frequency of substance use without cessation prospectively predicts reductions in depressive symptoms has important clinical implications. Cessation is often the main goal of substance use treatment. However, if reduction in substance use without cessation is prospectively linked to improvements in health, this may provide support for moderation and harm-reduction approaches to substance use treatment that focus on reducing hazardous substance use and do not require abstinence (Ritter et al., 2006; Witkiewitz & Marlatt, 2006). Such moderation-based approaches have demonstrated efficacy in reducing consequences of substance use (Carrico et al., 2014; Marlatt & Witkiewitz, 2002). Given the complicated nature of the relationship between substance use and depression and the limited research parsing the effects of reductions in substance use and cessation, more longitudinal work is needed. This work is particularly important among vulnerable populations at elevated risk for substance use and depression, such as SGM.

Current study

The goal of the current study was to examine associations between changes in alcohol, cannabis, and stimulant use and changes in depressive symptoms in a racially diverse sample of SGM individuals assigned male at birth (SGM-AMAB). Previous studies of SGM often have not had adequate power to examine these associations, particularly for stimulant use. To maximize power, we combined data from two large longitudinal cohorts of SGM-AMAB. We examined potential bi-directional associations between depressive symptoms and frequency of substance use and cessation. We hypothesized that both reductions in the frequency of use and cessation would be associated with concurrent decreases in depressive symptoms and that we would observe bi-directional prospective associations between reduction and cessation of substance use and depressive symptoms.

Method

Participants and procedures

Current analyses used data from two cohort studies of SGM-AMAB. Both studies were approved by the appropriate institutional review boards, and informed consent was obtained from all participants. See Table 1 for demographics.

RADAR is an ongoing longitudinal cohort study of multilevel influences on HIV and substance use among young SGM-AMAB in Chicago, Illinois. Data collection began in February 2015 and is ongoing. Current analyses used data through February 2019. To achieve a multiple cohort, accelerated longitudinal design (i.e., a method used to capture data across the age range of interest in a shorter period of time than would be possible in a single cohort longitudinal design; see Galbraith et al., 2017), SGM-AMAB from two previous cohort studies were invited to join the current study, and a new cohort of SGM-AMAB was recruited using venue-based recruitment, social media, and incentivized snowball sampling. At original cohort enrollment, participants were 16–20 years old, assigned male at birth, spoke English, and had a sexual encounter with a man in the previous year or identified as SGM. Cohort members could refer three peers and serious partners who met eligibility criteria. Participants completed study visits at 6-month intervals. At the time of current analyses, 1,119 participants had completed from one to seven visits and data from all completed visits were used.

EleMENt is a longitudinal cohort of young Black sexual minority cisgender men in Atlanta, Georgia, designed to evaluate the relationship between substance use and HIV/STI incidence. Eligible participants were non-Hispanic Black cisgender men ages 16–29 in the Atlanta Metropolitan Statistical Area who reported at least one male sexual partner in the 3 months before enrollment. A total of 299 HIV-negative participants were followed prospectively with six study visits over 24 months. Participants were recruited using venue-based recruitment, advertising on social media and public transportation, and peer referral. Data from baseline and from 6-, 12-, 18-, and 24-month follow-up visits were included in current analyses. The 3-month follow-up visit was dropped from analyses as there was not a 3-month follow-up visit for RADAR. Participants completed from one to five of the visits included in the current analytic sample.

Measures

Depressive symptoms were assessed using the Patient-Reported Outcomes Measurement Information System

Table 1. Demographics and completion rates

	RADAR		eleMENt	
Variable	*n*	%	*n*	%
Gender identity				
Cisgender men	1,028	91.9%	299	100.0%
Transgender/nonbinary	91	8.1%	0	0.0%
Race/ethnicity				
Black	374	33.4%	299	100.0%
Latinx	335	29.9%	0	0.0%
White	284	25.4%	0	0.0%
Other	126	11.3%	0	0.0%
Sexual orientation				
Gay	775	69.3%	216	72.2%
Bisexual	237	21.2%	65	21.7%
Other	107	9.6%	18	6.0%
Age at Visit 1, *M* (*SD*)	21.39 (3.05); range: 16–30		24.33 (3.03); range: 18–29	
Substance use at baseline				
Alcohol	976	87.2%	263	88.0%
Cannabis	661	59.1%	196	65.6%
Stimulant	159	14.2%	39	13.0%

Notes: RADAR = an ongoing longitudinal cohort study of multilevel influences on HIV and substance use among young SGM-AMAB in Chicago, Illinois; eleMENt = a longitudinal cohort of young Black sexual minority cisgender men in Atlanta, Georgia, designed to evaluate the relationship between substance use and HIV/STI incidence.

(PROMIS) Depression Short Form 8a (Pilkonis et al., 2011) in RADAR. This measure includes eight items (e.g., "I felt worthless"; $\alpha = .93–.95$) measured on a scale of 1 (*never*) to 5 (*always*). In eleMENt, depressive symptoms were assessed using the Patient Health Questionnaire (PHQ) 8 (Kroenke et al., 2009), which includes eight items (e.g., "feeling down, depressed, or hopeless"; $\alpha = .70–.80$) measured on a scale of 0 (*not at all*) to 3 (*nearly every day*). Both measures asked about recent symptoms: past week for RADAR and past 2 weeks for eleMENt. To allow for merged cohort analyses, we used previously validated cross-walk score tables to transform PHQ scores into PROMIS *t* scores (Choi et al., 2014). Prior research has estimated and validated transformations of PHQ scores to PROMIS *t* scores via item response theory analyses of data from a large sample to which both measures were administered (Choi et al., 2014).

Alcohol use in the past 6 months was assessed using two items from the Alcohol Use Disorders Identification Test (AUDIT) in both samples (Saunders et al., 1993). The first question assessed the frequency of alcohol use ("how often do you have a drink containing alcohol?" on a scale of 0 [*never*] to 4 [*4 or more times a week*]), and the second assessed quantity of alcohol consumed ("how many drinks containing alcohol do you have on a typical day when you are drinking" on a scale of 0 [*1 or 2*] to 4 [*10 or more*]). Responses to these questions were multiplied to produce a quantity by frequency score.

Cannabis use in the past 30 days was assessed by asking participants to indicate how often they used cannabis. Item wording and response options differed slightly for the two samples. In RADAR, participants were asked, "on how many occasions have you used cannabis (also called 'Weed' or 'Pot') in the past 30 days?" and provided with response options ranging from 0 (*0*) to 7 (*40 or more*). In eleMENt, participants were asked to "please tell us how often you used cannabis" and provided with the response options 0 (*0 times*) to 8 (*more than once a day*). Scores were standardized within each sample to create harmonized scores.

Stimulant use was assessed using items that were parallel to those used to assess cannabis use. Items asking about the frequency of cocaine, crack, and methamphetamine use were summed to create a frequency of stimulant use score because sample sizes were too small to examine these three substances separately. Scores were standardized within each sample to create harmonized scores.

Analytic plan

Analyses were conducted in Mplus 8.1. Less than 1% of data within completed visits was missing and was handled using full information maximum likelihood. Cross-lagged multilevel structural equation models (MSEM) with a Bayesian estimator and the default of diffuse (non-informative) priors were used. See next paragraph for a detailed description of cross-lagged models estimated. We used Markov Chain Monte Carlo (MCMC) algorithms to generate a series of 5,000 random draws from the multivariate posterior distribution of our sample for each model. Trace plots and the Gelman-Rubin potential scaling reduction (PSR) were used to determine whether convergence was achieved (Depaoli & Clifton, 2015; Muthén, 2010).

Separate multilevel models were used to examine each substance (alcohol, cannabis, and stimulants). Repeated assessments were clustered within individuals. Only participants who used the substance at baseline were included in the relevant model. To allow for the simultaneous modeling

of substance use cessation and frequency of use, we treated frequency of substance use variables as two-part variables. This separates the substance use frequency score into two variables: (a) a binary variable representing whether an individual is currently using (score of 0) or not using (score of 1) and (b) among those who are currently using, a continuous frequency of use score. In each cross-lagged model, three sets of associations were included at the within-person level: (a) autoregressive associations for each of the three central variables (cessation, frequency of use, and depressive symptoms; e.g., cessation at t predicts cessation at $t + 1$), (b) concurrent associations between depressive symptoms at time $t + 1$and cessation/frequency of use at time $t + 1$, and (c) prospective associations with depressive symptoms at time t predicting cessation/frequency of use at time $t + 1$ and vice versa. Within-persons, control variables included time since baseline assessment and the use of other substances. Between-persons, associations among depressive symptoms and cessation/frequency of use were modeled and adjusted for age at baseline, use of other substances, and cohort. To determine whether effects differed based on cohort, we conducted a set of follow-up analyses in which cohort (RADAR or eleMENt) was entered as a cross-level predictor of concurrent and prospective associations.

Results

Before conducting the primary analyses, we examined between-person differences across the two samples. Results indicated that on average, the eleMENt sample reported lower depressive symptoms (b = -0.52, $p < .001$), more alcohol use ($b = 0.72$, $p < .001$), and were less likely to use cannabis (odds ratio [OR] = 0.52, $p < .001$) compared with the RADAR sample. Participants did not differ significantly on likelihood of stimulant use (OR = 0.71, $p = .06$). Study was included as a control variable in subsequent analyses to control for these differences.

In the cross-lagged model of alcohol use (Table 2), more depressive symptoms were associated with more concurrent alcohol consumption and a lower likelihood of cessation. None of the prospective associations between alcohol use and depressive symptoms were significant. In the cannabis use model, more depressive symptoms were concurrently associated with a lower likelihood of cannabis cessation, but the concurrent association between frequency of cannabis use and depressive symptoms was not significant. In addition, none of the prospective associations between cannabis use and depressive symptoms were significant. In the stimulant use model, more depressive symptoms were associated with a lower concurrent likelihood of stimulant cessation, but the concurrent association between frequency of stimulant use and depressive symptoms was not significant. Only one prospective association was significant in the stimulant use model, with an increase in the frequency of stimulant use predicting subsequent increases in depressive symptoms. Follow-up analyses, in which cohort moderated concurrent and prospective associations in the cross-lagged models (results not present for brevity) indicated that these associations did not differ significantly between the two cohorts.

Discussion

The current study provides evidence that both substance use cessation and reductions in stimulant use without cessation were concurrently associated with decreases in depressive symptoms in a sample of racially and ethnically diverse SGM-AMAB. However, only reductions in stimulant use prospectively predicted decreases in depressive symptoms. These findings build on the results of one of the only existing studies to separately examine effects of substance use cessation and reduction on depressive symptoms (Delaney et al., 2018) in four ways: (a) by examining these associations in a different high-risk population (SGM), (b) by testing associations between alcohol use and depressive symptoms, (c) by examining concurrent and prospective associations, and (d) by integrating the size of changes in substance use by means of continuous frequency of use variables rather than categorizing change in use. Our findings indicated that when individuals reduced their alcohol use or ceased their use of stimulants, alcohol, or cannabis, they experienced decreases in depressive symptoms. These decreases either co-occurred with or closely followed changes in substance use. However, only reductions in stimulant use were associated with decreases in depressive symptoms over the subsequent 6 months. Changes in cannabis and alcohol use did not prospectively predict changes in depressive symptoms. These findings suggest that clinical interventions that target the use of some substances may simultaneously reduce depressive symptoms and that stimulant use reduction (even without cessation) has benefits to mental health among SGM-AMAB.

We did not find a concurrent effect of reducing the frequency of cannabis use (without cessation) on depressive symptoms or prospective effects of reducing or ceasing cannabis use on subsequent depressive symptoms. Evidence of concurrent and prospective associations between changes in cannabis use and depressive symptoms is somewhat mixed, with some studies finding that decreases in cannabis use are associated with decreases in depressive symptoms (Delaney et al., 2018; Hser et al., 2017) and others finding no association (Wilkinson et al., 2016). The current study may help to shed light on this mixed evidence by suggesting that cannabis cessation may be a stronger driver of concurrent decreases in depressive symptoms than reductions without cessation.

Our results differ from those of Delaney and colleagues (2018), who found that both reduction and cessation of cannabis use were associated with decreases in depressive symptoms. These divergent findings may be attributable to

TABLE 2. Cross-lagged models

Model	Effect	Estimate	*p*	[95% CI]
Alcohol (*n* = 1,239)				
Autoregressions				
	$Depression_t \rightarrow Depression_{t+1}$	.27	<.001	[.20, .33]
	$Q\times F\ Alcohol_t \rightarrow Q\times F\ Alcohol_{t+1}$	.29	<.001	[.24, .34]
	$Cessation_t \rightarrow Cessation_{t+1}$	.34	.002	[.12, .52]
Concurrent associations				
	$Depression_{t+1} \rightarrow Q\times F\ Alcohol_{t+1}$	.02	.049	[.001, .03]
	$Depression_{t+1} \rightarrow Cessation_{t+1}$	-.19	<.001	[-.28, -.09]
Prospective associations				
	$Q\times F\ Alcohol_t \rightarrow Depression_{t+1}$	.01	.64	[-.05, .08]
	$Cessation_t \rightarrow Depression_{t+1}$	-.01	.76	[-.09, .08]
	$Depression_t \rightarrow Q\times F\ Alcohol_{t+1}$	.01	.68	[-.02, .03]
	$Depression_t \rightarrow Cessation_{t+1}$	.07	.14	[-.03, .16]
Cannabis (*n* = 857)				
Autoregressions				
	$Depression_t \rightarrow Depression_{t+1}$	.35	<.001	[.28, .43]
	$Freq.\ cannabis_t \rightarrow Freq.\ cannabis_{t+1}$	.35	<.001	[.32, .40]
	$Cessation_t \rightarrow Cessation_{t+1}$	.68	<.001	[.55, .89]
Concurrent associations				
	$Depression_{t+1} \rightarrow Freq.\ cannabis_{t+1}$	.003	.78	[-.02, .03]
	$Depression_{t+1} \rightarrow Cessation_{t+1}$	-.13	.004	[-.23, -.04]
Prospective associations				
	$Freq.\ cannabis_t \rightarrow Depression_{t+1}$	.01	.74	[-.04, .06]
	$Cessation_t \rightarrow Depression_{t+1}$	-.07	.10	[-.16, .02]
	$Depression_t \rightarrow Freq.\ cannabis_{t+1}$	.07	.06	[-.01, .16]
	$Depression_t \rightarrow Cessation_{t+1}$	.01	.66	[-.03, .05]
Stimulants (*n* = 198)				
Autoregressions				
	$Depression_t \rightarrow Depression_{t+1}$	.29	<.001	[.16, .45]
	$Freq.\ stimulants_t \rightarrow Freq.\ stimulants_{t+1}$	.32	<.001	[.11, .51]
	$Cessation_t \rightarrow Cessation_{t+1}$	.91	<.001	[0.60, 1.27]
Concurrent associations				
	$Depression_{t+1} \rightarrow Freq.\ stimulants_{t+1}$	.01	.88	[-.12, .14]
	$Depression_{t+1} \rightarrow Cessation_{t+1}$	-.28	.01	[-.49, -.07]
Prospective associations				
	$Freq.\ stimulants_t \rightarrow Depression_{t+1}$	.11	.01	[.03, .19]
	$Cessation_t \rightarrow Depression_{t+1}$	-.11	.20	[-.31, .07]
	$Depression_t \rightarrow Freq.\ stimulants_{t+1}$	.05	.66	[-.17, .29]
	$Depression_t \rightarrow Cessation_{t+1}$	-.01	.92	[-.21, .20]

Notes: CI = confidence interval; Q×F = quantity × frequency; freq. = frequency. All estimates adjusted for use of other substances (alcohol, cannabis, stimulants, other illicit substances); linear change in depressive symptoms, likelihood of cessation, and frequency of use; age at baseline; and cohort. Number of individuals in each analysis depended on the number of participants who used each substance at baseline.

the relatively small reductions in cannabis use detected in the current study, with 71% of reductions being changes of 1–2 points on a 7-point scale. It is possible that reductions of this magnitude may not have had measurable concurrent effects on depressive symptoms. The lack of prospective associations between changes in cannabis use and depressive symptoms may also be attributable to the high proportion of individuals who increased cannabis use following a decrease or temporary cessation of use. For example, 50% of reductions in cannabis use were followed by an increase at the subsequent wave, and 25% of those who ceased cannabis use at time *t* had resumed using by *t* + 1. These relatively high proportions of reversals are likely to have affected depressive symptoms reported at *t* + 1 and may have obscured effects of sustained cessation or reduction in cannabis use. Future research should examine prospective effects of sustained reductions or cessation of cannabis use.

The current study did not find evidence of the directionality of the association between cannabis use or alcohol use and depressive symptoms. Research on the directionality of these associations has been mixed, with some studies finding evidence of bidirectionality (Conner et al., 2009; McGee et al., 2000) and others that cannabis or alcohol use prospectively predicts depressive symptoms (Boden & Fergusson, 2011; Lev-Ran et al., 2014) or vice versa (Bell & Britton, 2014; Feingold et al., 2015). It is possible that these prospective associations were not significant in the current sample because of the relatively high variance in depressive symptoms within-persons over time (51.1% among cannabis users). Given this variability, it is possible that increases in depressive symptoms may have been relatively short lived. According to self-medication theory, individuals who are experiencing elevations in depressive symptoms would be expected to increase their substance

use. For some, these increases in substance use may persist, whereas substance use may return to usual levels for others, resulting in a weakening of the effect of depressive symptoms on substance use (or vice versa) as the temporal distance from the event increases. Thus, self-medication theory may not predict that elevations in depressive symptoms at one time would predict sustained increases in substance use 6 months later, particularly if increases in depressive symptoms are acute rather than chronic. Alternatively, our use of a community sample, with its associated lower levels of substance use severity compared with the more commonly used clinical samples, may have contributed to the lack of prospective effects.

Two theories have been proposed to explain the prospective association between substance use and subsequent depressive symptoms, and both apply predominantly to heavy users. The first posits that substance use increases the number of stressful life events experienced, which in turn lead to increases in depressive symptoms (Marmorstein & Iacono, 2011; Sullivan et al., 2011), whereas the second holds that the pharmacological effects of heavy alcohol and cannabis use lead to depressive symptoms during use and/or withdrawal (Hill et al., 2006; Schuckit & Irwin, 1995). As a result, prospective associations between substance use and subsequent depressive symptoms may have been attenuated in our community sample, given its moderate use. Further research is needed to clarify the duration and direction of prospective effects of depressive symptoms on cannabis and alcohol use and vice versa among community samples of individuals with moderate use.

Results indicate that cessation of stimulant use was concurrently associated with decreases in depressive symptoms, whereas reductions in stimulant use predicted subsequent decreases in depressive symptoms. Existing evidence of the directionality of the association between stimulant use and depressive symptoms is somewhat mixed and may depend on the length of time since cessation. Stimulant cessation has been linked to heightened depressive symptoms during withdrawal (Newton et al., 2004; Wang et al., 2013), the result of neurological changes arising from chronic overstimulation of the brain's reward circuitry by stimulant use (Chang et al., 2007). However, this initial increase in depressive symptoms appears to abate over time, and studies of changes in depressive symptoms during stimulant use treatment suggest that there is a net decrease in depressive symptoms during treatment (Glasner-Edwards et al., 2009; Gossop et al., 2000). Given that at least 6 months had elapsed since stimulant cessation when depressive symptoms were assessed (longer than the withdrawal period), our prospective findings are consistent with the existing research. Because our study used a community sample in an area of research predominated by clinical samples, our findings also suggest that the results from previous clinical samples generalize to community samples with less severe use.

Why did we find that reductions in stimulant use predicted subsequent decreases in depressive symptoms whereas cessation did not? One potential reason for this initially counterintuitive finding lies in the operationalization of stimulant cessation (binary) and frequency (continuous) in the current study. As the effect of cessation was averaged across heavy and infrequent users, the larger effect of cessation on depressive symptoms for heavy regular users (14%—more than weekly use) was likely attenuated by the smaller effects of cessation for infrequent users (86%—less than weekly use). On the other hand, the continuous treatment of frequency incorporated the size of the change in frequency, which allows for the estimation of a larger reduction in depressive symptoms for those who reduced their use more dramatically. These findings highlight the importance of using continuous measures of stimulant use frequency to capture the severity of use and the size of changes over time.

Findings have a number of implications for clinical treatment of substance use and depression among SGM-AMAB clients. There is current debate regarding the best approach to treating individuals with comorbid depression and substance use disorders. Some evidence supports separate, concurrent treatment of substance use and depression, whereas other studies indicate that integrated treatment may lead to better outcomes (Hesse, 2009; Kelly & Daley, 2013; Torrens et al., 2012). Findings from the current study could be interpreted as supporting either approach. Results indicate that interventions addressing substance use may have simultaneous effects on depressive symptoms. For individuals with less severe depressive symptoms, changes in depression that co-occur with reductions or cessation of substance use may be sufficient to make formal treatment of depression unnecessary. However, given limited evidence of the directionality of the association between depression and substance use, findings may also support the integrated treatment of depression and substance use. Existing research indicates that depression is a risk factor for future substance use relapse (e.g., Hasin et al., 2002), highlighting the need for attention to depressive symptoms in the context of substance use treatment. As reductions in alcohol and stimulant use without cessation were associated with decreases in depressive symptoms, findings support the use of harm-reduction approaches to the treatment of substance use problems. Together, these findings suggest that interventions, such as ESTEEM (Pachankis et al., 2015), that take a transdiagnostic approach to simultaneously treat problems with substance use and depressive symptoms alongside the unique risk factors for SGM (e.g., stigma-related stressors), may be most effective for SGM-AMAB clients with co-occurring substance use problems and depressive symptomology.

Study findings should be considered in light of study limitations. First, there were some differences in the measures used by the two cohort samples that may have affected results. We took several steps to harmonize measures across

studies, including standardizing cannabis and stimulant use frequency within samples and using validated cross-walk tables to harmonize scores for depressive symptoms across samples. However, these differences may still have affected our results. Second, we did not have a large enough sample of individuals who used specific substances to separately examine cocaine and methamphetamines or to examine other illicit substances, such as heroin or club drugs. Third, this combined sample included only individuals assigned male at birth. Future research should test whether findings extend to SGM assigned female at birth and to other noncannabis illicit substances. Fourth, it is likely that there are potential confounding variables that were not assessed and thus could not be accounted for in analyses. Therefore, we cannot assume that even prospective associations are indicative of causality. Last, participants who did not report substance use at baseline were not included in analyses. This was necessary for the binary portion of the two-part variable to be interpreted as cessation of substance use (rather than more generally as abstinence from substance use).

Despite these limitations, the current study has a number of strengths. It combined two large cohort studies of SGM-AMAB individuals to conduct analyses that would have been underpowered in either sample alone. This combined sample was large, racially and ethnically diverse, and included SGM-AMAB individuals from two large metropolitan areas. Although the samples were recruited using convenience techniques, the racial and ethnic diversity of this sample increases the likelihood that results will generalize to diverse SGM-AMAB in metropolitan areas of the United States. In addition, we were able to use strong analytic and methodological approaches to test the directionality of the association between changes in substance use and depressive symptoms, including testing lagged effects, incorporating autocorrelations, and testing for bi-directionality.

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