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Substance use over time among sexual and gender minority people: Differences at the intersection of sex and gender

Running Head: Substance use among SGM gender subgroups over time

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Abstract

Purpose: Sexual and gender minority (SGM) people are at greater risk for substance use than heterosexual and cisgender people, but most prior work is limited by cross sectional analyses or the examination of single substance use. This study examined substance use over time among SGM people to identify patterns of polysubstance use at the intersection of sex and gender.

Method: Data were collected annually over four years from SGM respondents *(n*=11,822) in The PRIDE Study. Differences in substance use patterns (any prior 30-day use of 15 substances) by gender subgroup were examined with latent class analysis, and multinomial regression models tested relationships between gender subgroup and substance use.

Results: Eight classes of substance use were observed. The three most common patterns were low substance use (49%), heavy episodic alcohol use (≥ 5 5 alcoholic drinks on one occasion) with some cannabis and tobacco use (14%), and cannabis use with some tobacco and declining heavy episodic alcohol use (13%). Differences observed included lower odds of patterns defined by heavy episodic alcohol use with some cannabis and tobacco use in all gender subgroups relative to cisgender men and persons with low substance use (odds ratios [ORs] 0.26-0.60). Gender expansive people assigned female at birth, gender expansive people assigned male at birth, and transgender men had greater odds of reporting cannabis use with small percentages of heavy episodic alcohol and tobacco use (ORs 1.41-1.60).

Conclusion: This study suggests there are unique patterns of polysubstance use over time among gender subgroups of SGM people.

Introduction

Sexual minority people (*i.e.,* individuals with a non-heterosexual sexual orientation) and gender minority people (*i.e.,* individuals whose gender identity and/or expression differ from or expand upon what society may have expected based on the sex assigned to them at birth), collectively abbreviated SGM, are at higher risk for substance use than heterosexual and cisgender people.[1–5] This disparity is attributed to greater sexual and gender minority stress (*e.g.*, discrimination and stigma)[6,7]. While research frequently examines substance use with methods that account for only one substance at a time, sexual minority people are more likely to use multiple substances (*i.e.,* polysubstance use) compared to heterosexual people (gender minority status was not measured in these studies).[8,9] Prior studies that have shown elevated risk for substance and polysubstance use have been done primarily with cisgender sexual minority people[10,11] and have examined sexual minority people *via* binary gender identity groups (*e.g.,* cisgender man, cisgender woman[12]). This approach of merging SGM subgroups can obscure differences in patterns of substance use among less commonly described SGM subgroups,[13] such as gender minority subgroups, and reduce the potential for identifying groups that may benefit from targeted prevention or treatment interventions.

Substance use over time among SGM people may be shaped by social experiences unique to SGM people[14] or gendered expectations or experiences. Reviews of studies among primarily presumed cisgender heterosexual people have found associations between both masculinity[15] and femininity[16] and substance use. These results are likely not directly applicable to SGM people but raise the possibility of unique pathways between gendered experiences and substance use. Further, substance use among SGM people is shaped by experiences of sexual and gender minority stress, which are an additional burden of identity-specific stress related to one's sexual minority or gender minority status.[17,18] Gender minority

stress is unique from sexual minority stress,[6] and SGM people may be subject to both sexual and/or gender minority stress. SGM narratives suggest that sexual and gender minority stress are both related to problematic substance use, with gender minority narratives describing a more complicated and entangled relationship between minority stress and substance use characterized by prolonged and/or multiple identity disclosure and more persistent minority stress.[14] Gender minority people are frequently also sexual minority and experience more minority stress burden than people who are solely sexual minority.[19,20] Further, qualitative work has suggested that socializing among SGM people often happens in the context of substance use or events where substance use is present.[14] This work highlights the potential for emphasis on different substances at these events among different gender groups. For example, cisgender men and transgender men have discussed pressure to use substances within social settings, such as a "gay bar"[14] where alcohol is likely to be a prominent substance.

Beyond social factors, sex differences in substance use have been well documented and correspond to substantial differences in side effects and potential for consequences related to different substances.[21] These studies do not account for whether the captured differences are due to sex assigned at birth, gender (as conflated with sex), or hormone exposures (*e.g.*, testosterone, estrogen). Hormonal changes are related to changes in substance use; for example, progesterone is related to reduced tobacco use, while estrogen may be associated with increased tobacco use.[22–25] Further, alcohol use may increase in the presence of more testosterone.[26] Hormonal changes are not independent of minority stress, however, as gender minority stress may be reduced among some gender minority people after accessing gender-affirming care and experiencing related gender presentation changes.[27] Examining substance use differences among SGM people by gender identity subgroups would direct us to conduct more precise research to understand the multiple factors that influence substance use among SGM people, including minority stress, social environments or expectations, and hormonal influences. This will improve the

generalizability of substance use research and uncover opportunities to intervene to reduce substance use risks, particularly among understudied SGM people (*e.g.*, gender expansive individuals, transgender men, transgender women).

Substance use research among SGM people is typically based on simple analyses: a specific group may be examined to assess the use prevalence of a specific substance compared to a different group. This has typically led to conclusions comparing the use of a single substance between two groups (*e.g.*, a conclusion that transmasculine people have higher rates of heavy episodic alcohol use than transfeminine people[28]). Despite the practical advantages of such research, these conclusions are limited because substance use is often dynamic over time and may involve the use of multiple substances (*e.g.,* heavy drinking may be higher in one group while cannabis use along with heavy drinking may be higher in a different group). Polysubstance use is more typical among people with substance use disorders than use of a single substance,[29] yet polysubstance use is not typically accounted for in analyses.

When polysubstance use has been accounted for among SGM people, there has been variability in how it has been defined, particularly with respect to substance use over time. Some research has queried lifetime prevalence of polysubstance use,[30] while other studies have reported past 1- to 12-month prevalence.[9,31,32] Some studies with sexual minority men and women (whether this referred to sex or gender was not specified) have defined polysubstance use as the use of two or more substances but did not describe the different combinations of substance use that may occur within the population.[33] This is a practical choice, as accounting for all the potential combinations of substance use that occur within the population becomes cumbersome; co-use of some substances may not be common and, thus, may not need to be considered. Most samples of SGM people are not large enough to consider the potential intersections of use of different substances. Precision healthcare models of substance use will require greater specificity and precision in accounting for substance use *(e.g.,* opioids are more lethal in the

presence of alcohol or other depressants[34,35]) than our current research models to effectively inform prevention and intervention efforts.

Substance use at a single point in time does not account for substance use over time or the associated health consequences of cumulative substance exposure. A longitudinal approach can help to advance our understanding of the health impact of longer-term substance use and the potential contributors to longer term substance use. While research models have begun to account for polysubstance use in a more complex manner among specific populations (*e.g.,* college students[36]), when these studies examine substance use over time, they typically include different waves of people and, thus, they cannot account for the clustering of different substances used over time. Understanding the use of substances within a cohort over time can allow us to study substance use more accurately without omitting substances that are commonly used by the same people. An accurate understanding of substance use among diverse SGM gender subgroups is essential to identify causes and potential opportunities for prevention or intervention to reduce substance use or related health risks among SGM people.

The purpose of this exploratory study was to identify if there were differences in patterns of substance use (*i.e.,* specific substance used over time) among SGM people at the intersection of sex and gender. We specifically examined substance use over time among cisgender sexual minority men, cisgender sexual minority women, gender expansive people assigned female at birth of any sexual orientation, gender expansive people assigned male at birth of any sexual orientation, transgender men of any sexual orientation, and transgender women of any sexual orientation (hereafter referred to by their gender subgroup irrespective of sexual minority status). We examined substance use annually among SGM people over four years and identified patterns of use (*i.e*., specific substances used) over time. We then examined if the SGM gender subgroups were related to these patterns of use. This study

will lay the groundwork to investigate the reasons for these differences, including social influences, minority stress, and/or hormonal exposures.

Methods

Data were collected within The Population Research in Identity and Disparities for Equality (PRIDE) Study (between May 2017-June 2021), a national, online, longitudinal cohort study of SGM adults within the United States (described in detail elsewhere[37]). This study used data collected *via* four Annual Questionnaires querying a wide variety of physical, mental, and social health constructs, which are made available to participants from approximately June of each year through the following May.

Inclusion criteria were that participants must: 1) identify as lesbian, gay, bisexual, transgender, queer, or another sexual and/or gender minority, 2) be age 18 or older, 3) reside in the United States or its territories, and 4) be comfortable reading and writing in English. After obtaining informed consent, The PRIDE Study notifies participants about available surveys through the method they prefer (*e.g.,* text messages, emails), but they are not required to complete surveys to remain in the study. Participants were included in this study if they provided data for one or more of the four Annual Questionnaires within the study period among the 21,749 people enrolled at the conclusion of data collection.

The PRIDE Study recruits participants through many methods. Primary among these is through PRIDEnet Community Partners, which are health clinics, community centers, and other LGBTQ+-serving and -supporting organizations within the United States. Additional recruitment is online through direct recruitment and advertising on social media and other venues and in-person at LGBTQ+-focused events. The PRIDE Study is a community-engaged research study where the primary motivator for participation is altruism, and the primary incentive is a return of research results directly to participants (though there are also drawings for prizes [*e.g.*, gift cards for survey completion or other completed activities]).

Completing surveys within The PRIDE Study requires multiple steps on The PRIDE Study platform, including consent, creation of an account, authentication of the account by logging in with their username and password, and navigating within the website after logging on to select and complete surveys. Participants have the option to enable two-factor authentication to access their account. Each participant has a unique participant ID number and each survey is given a unique survey ID number. To prevent internet bot responses, participants must log into their unique participant portal in The PRIDE Study platform to access and complete surveys, where the system checks that the participant is authorized to access the survey uniform resource locator (URL). Then, participants complete a survey hosted through a Qualtrics link that is unique to the survey and associated uniquely with the participant ID. Only valid participants assigned unique URLs are included in final data sets, which means that bot responses without a valid participant ID and matched survey URL would be excluded. Human participant procedures have been approved by the Institutional Review Boards (IRB) of the University of California, San Francisco, Stanford University, and WIRB-Copernicus Group (WCG).

Demographic Characteristics

Age was calculated by subtracting participant birth date from survey start date. In 2017, gender and sexual orientation were queried when participants signed up for the study; for that year, we used the information they had selected when the 2017 Annual Questionnaire closed. In subsequent years, gender and sexual orientation were queried within the Annual Questionnaires. Sexual orientation was queried with the item: “What is your current sexual orientation? (Check all that apply.)” with 10 answer choices: asexual, bisexual, gay, lesbian, pansexual, queer, questioning, same-gender loving, straight/heterosexual, another sexual orientation (with a write-in text response). This was expanded based on participant feedback to include two-spirit beginning in 2019. Race and ethnicity were queried when participants signed up for the study and again beginning in 2019 through the item: “Which categories describe you?

(Check all that apply.)" with answer choices: American Indian or Alaska Native; Asian; Black, African American, or African; Hispanic, Latino, or Spanish; Middle Eastern or North African (added beginning in 2018); Native Hawaiian or other Pacific Islander; White; or None of these fully describe me (with a write-in text response). All demographic characteristics are reported for participants at the first available time that these questions were answered for each participant.

Gender and Sex Assigned at Birth

Gender was queried with the item: "What is your current gender identity? (Check all that apply.)" In the 2017 data and 2018 Annual Questionnaire, this item had the answer choices: genderqueer, man, transgender man, transgender woman, woman, another gender identity (participants were asked to specify with a write-in text response). Based on participant feedback and the write-in responses received in 2018, the responses to this question expanded beginning in 2019 to: agender, cisgender man, cisgender woman, genderqueer, man, non-binary, questioning, transgender man, transgender woman, two-spirit, woman, and another gender identity (with a write-in text response). Sex assigned at birth (SAAB) was queried with the item: "What was your sex assigned at birth, for example on your original birth certificate?" with the options: male or female.

Using an automated algorithm (as in [38]) that takes into account both answer choice selections and strings that occur in write-in responses, the following 6 gender subgroups were created at the intersection of sex and gender: cisgender men (reporting a gender of cisgender man, man, or on the masculine spectrum and assigned male sex at birth), cisgender women (reporting a gender of cisgender woman, woman, or on the feminine spectrum and assigned female sex at birth), gender expansive individuals assigned female at birth (reporting a non-binary or expansive gender and/or both masculine and feminine genders and assigned female at birth), gender expansive individuals assigned male at birth (reporting a non-binary or expansive gender and/or both masculine and feminine genders and assigned

male at birth), transgender men (reporting a gender of cisgender man, man, transgender man, or on the masculine spectrum and assigned female at birth or reporting a gender of transgender man) and transgender women (reporting a gender of cisgender woman, transgender woman, woman, or on the feminine spectrum and assigned male at birth or reporting a gender of transgender woman). Endorsing cisgender man or cisgender woman and being categorized as a transgender man or transgender woman was a very infrequent pattern. Our validation research to categorize participants based on their gender has shown that, for transgender men and transgender women, our categorization method is concordant with their own selection from a reduced set of options (*e.g.*, transgender man, transgender woman) 97% or more of the time (A. Ceja, B.A *et al.*, unpublished data, 2023). A participant's gender was taken from the year that the participant first completed a survey and provided substance use data; thus, it coincided with the start of their recorded substance use.

Substance Use

Substance use was measured by past 30-day use (none *versus* any) for each year for each substance. Cannabis, cocaine, prescription stimulants, methamphetamine, inhalants (not including inhaled nitrates), inhaled nitrates (poppers), sedatives or sleeping pills, GHB (G, gamma-hydroxybutyric acid), hallucinogens, prescription opioids, street opioids, MDMA (ecstasy or Molly), and "other" drug use were captured by the first item of the modified National Institute on Drug Abuse Modified Alcohol, Smoking, and Substance Involvement Screening Test (NIDA-Modified ASSIST) with a follow-up item querying past 30-day use. Based on expert and community feedback, the ASSIST was modified to distinguish substances of use relevant to SGM communities including inhaled nitrates (poppers), MDMA, and GHB. When a substance was endorsed that could be prescribed by a physician, follow-up items queried if any of their use was prescribed and if all their use was exactly as prescribed.

Alcohol use was measured using a single item querying the consumption of five or more drinks on one occasion[38] in the past 30 days, hereafter referred to as heavy episodic alcohol use. The Alcohol Use Disorders Identification Test (AUDIT)[39] provided descriptive information about alcohol use but was not used in primary analyses. Tobacco use was measured through standardized items about cigarette smoking,[40] including: "When was the last time you smoked a cigarette, even one or two puffs?" with response options reflecting past 30-day use coded to indicate any cigarette use (reported as tobacco use hereafter).

Analysis

To account for the dynamic nature of substance use across the four timepoints, a latent class analysis was used to identify classes of participants reflecting different patterns of substance use. This analysis was done by entering substance use (dichotomized for each substance) for each participant at each available time point using M*plus* version 8.6.[41] Participants with incomplete data were included in analyses *via* maximum likelihood estimation.[42] The number of classes was determined with the Bayesian Information Criterion (BIC) calculated for each potential class solution, as BIC has been shown to perform well in simulations for selecting the number of latent classes empirically.[43] Final class selection considered the substantive interpretability of classes. Percentages of use of each substance were examined within each class at each time point (labeled here by the year the survey was released) and named based on percentages of observed data.

Differences in substance use by gender subgroup were determined using multinomial regression models fitted in SAS version 9.4[44] in relation to substance use class membership. The reference category used within the multinomial regression was selected to be cisgender men, as they are the most well-described in the prior literature. P-values were adjusted using simulated step-down adjustment for multiple comparisons.[45] Both unadjusted and adjusted models were run. Adjusted models covaried age,

race and ethnicity (indicator variables for each race and ethnicity category selected), and income (≤ $20K, $20K to $40K, $40K to $60K, and ≥$60K).

Results

Sample characteristics are reported in Table 1. Substance use items were completed by 11,822 participants. Mean participant age was 33.5 years (Median age 29). Gender, race or ethnicity, and sexual orientation do not consist of mutually exclusive categories as participants could endorse multiple categories. In our sample, 19.8% endorsed racial or ethnic minority identities. Among our sample, 88.6% endorsed White race (either alone or in conjunction with other race/ethnicity options) and 12.5% reported more than one (multiracial) race or ethnicity. The most commonly reported sexual orientations were queer (37.0%), gay (32.4%), and bisexual (29.2%). In addition, 72.6% had completed at least a 2- or 4- year college degree.

Latent Class Analysis of Substance Use

Based on the BIC and interpretability across 13 models, the 8-class solution had the best model fit (BIC=109375.67); additional fit statistics are reported in Table 2. Substance use class sizes, descriptions, and percentages of the 8-class solution can be found in Figure 1. The largest class (substance use class 8, *n*= 5,763, 48.7%) was one defined by very little (*i.e.*, less than 10% of participants reporting use of a particular substance) substance use at any time point. Closer examination of self-report alcohol use data identified that, among the very little use class (substance use class 8), 19.2-25.4% reported no past-year alcohol use across the time points, and among those who had consumed alcohol, 86.8-88.8% reported typical past year use of 1 or 2 drinks on a day when they had consumed alcohol (measured on the AUDIT through items 1-2). The two next largest classes consisted of people with heavy episodic alcohol use with some cannabis and tobacco use (class 6, *n* = 1,683,

14.2%) as well as cannabis use with some tobacco and declining heavy episodic alcohol use (class 5, *n* = 1,570, 13.2%).

Multinomial Logistic Regression of Gender Subgroup in Relation to Substance Use Class Membership.

Analyses of substance use class membership in relation to gender subgroup can be found in Table 3. For multinomial logistic regression models where gender subgroup was entered in relation to substance use class membership, substance use class 8 (very low substance use) was selected as the substance use reference group. All gender subgroups had lower odds of being in substance use class 6 (mostly heavy episodic alcohol use, some tobacco and cannabis use; odds ratios in adjusted models [aORs] 0.26-0.60, confidence intervals [CIs] in Table 3) than cisgender men.

Gender expansive people assigned female at birth, gender expansive people assigned male at birth, and transgender men had greater odds of being in substance use class 5 (mostly cannabis, small percentages of heavy episodic alcohol use and tobacco; aORs 1.41-1.60). Cisgender women, gender expansive people assigned female at birth, and transgender men had lower odds of being in substance use class 2 (mostly cannabis, heavy episodic alcohol, tobacco, and some polysubstance use; aORs 0.48-0.53). Gender expansive people assigned female at birth and gender expansive people assigned male at birth had greater odds of being in substance use class 3 (mostly prescription stimulant, some heavy episodic alcohol use, cannabis, and sedative or sleeping pills; aORs 1.60 and 1.97, respectively).

Gender expansive people assigned female at birth had higher odds of being in substance use class 4 (mostly sedative or sleeping pill use, some cannabis and prescription opioid use, aOR 1.62). Cisgender women had lower odds of being in substance use class 7 (mostly tobacco use, some heavy episodic alcohol use, and polysubstance use; aOR 0.63). All gender subgroups had lower odds of being in substance use class 1 (mostly inhaled nitrates; aORs 0.01-0.35).

Discussion

Our study found that there were eight different patterns of substance use among six gender subgroups of SGM people over a four-year period when considering use of cannabis, cocaine, prescription stimulants, methamphetamine, inhalants, inhaled nitrate (poppers), sedatives or sleeping pills, GHB, hallucinogens, prescription opioids, street opioids, MDMA, "other" drug use, use of five or more alcoholic drinks in one setting (*i.e.*, heavy episodic alcohol use), and tobacco use. Notably, the substance use pattern evidenced by most SGM people (49%) was defined by little to no substance use over time. This indicates that the largest proportion of SGM people among our sample used very few substances over time, a reality that may be unwittingly overlooked by practitioners who may be considering problem substance use. Our results suggest that examining substance use by gender subgroups facilitates identification of SGM subgroups that may have distinctive patterns of substance use, and thus, may benefit from targeted intervention related to that use.

We found that all gender subgroups had lower odds of substance use patterns reflecting heavy episodic alcohol use, and some tobacco and cannabis use than cisgender sexual minority men. All gender subgroups were less likely to have substance use patterns reflecting inhaled nitrate (poppers) use than cisgender sexual minority men. Our results suggest that cisgender sexual minority men are, in general, more likely to have substance use defined by heavy episodic alcohol with some tobacco and cannabis use or use of inhaled nitrate (poppers) than other gender subgroups of SGM people. Consistent with our findings, prior literature has typically found that inhaled nitrate (poppers) use is higher among gay men individuals than other SM groups,[46,47] and interventions have been tested to reduce heavy episodic alcohol use among this population.[48,49] Cisgender sexual minority men experience high rates of sexual minority stress, [7,50] trauma exposure, and adverse childhood experiences (*e.g.,*[51–53]). Interventions to reduce sexual and intersectional minority stress as a pathway to reducing substance use and

improving mental health have been tested among sexual minority men[54–56] and may alleviate the high rates of substance use among cisgender sexual minority men.

There were two substance use classes defined by cannabis use among nearly all individuals over time. These two classes were distinctive because one was primarily just cannabis use, while the other was cannabis use paired with heavy episodic alcohol use, tobacco use, and polysubstance use. We found that three of the four gender subgroups reflecting gender minority identities – gender expansive people assigned female at birth, gender expansive people assigned male at birth, and transgender men – were more likely to have patterns of substance use reflecting primarily cannabis use with small percentages of people reporting heavy episodic alcohol use and tobacco use. The exact reasons for elevated rates of cannabis use among these groups are unknown. In this study, we examined any substance use, so this result reflects any cannabis use rather than solely problematic cannabis use. Future research should examine if a tendency toward cannabis use is socially driven, for example, related to increased exposure to specific types of gender minority stress where cannabis serves as a coping strategy,[57] as may have been the case among these three gender minority groups. Alternatively, there may be socialization to the acceptability of cannabis use or stigmatization of alternate substances within social groups. Further, exposure to stigma and a lack of economic and other opportunities (*e.g.,* social exclusion) may be related to greater cannabis use.[58]

There may be a biological reason for a tendency towards cannabis use (*e.g.*, greater reinforcement related to hormonal exposures). For example, people who receive certain types of gender-affirming care (*e.g.,* exogenous hormones, oophorectomy) may have a hormonal environment that may alter substance use reinforcement (*i.e.*, reward mechanisms of substance use). Evidence in animal models suggests that cannabinoid receptor density has been shown to be higher in the prefrontal cortex and amygdala of female animals that have had their ovaries removed than in males or females without

ovary removal.[59] Further, there are differences by sex in exposures to adversity and its interaction with cannabis use in animal models[60]. Importantly, these animal models of cannabis use have not yet been tested in ways that are directly applicable to gender minority people and their patterns of hormonal exposures.

Further, we found that three SGM groups – cisgender sexual minority women, gender expansive people assigned female at birth, and transgender men – were less likely to have substance use defined by cannabis use in concert with high rates of episodic drinking and polysubstance use. All of these three gender subgroups were assigned female at birth. Among these three gender subgroups that had lower likelihood of cannabis use in concert with other substances, gender expansive people assigned female at birth and transgender men were *more* likely to use cannabis *without* other substances (as discussed above). Specific hormonal environments may make other non-cannabis use more aversive (*e.g.,* alcohol use may induce greater discomfort). We did not test the specific hormone exposures (*e.g.,* oophorectomy, use of gender-affirming hormones) as they relate to substance use, but that should be a focus of future work and has implications regarding the way gender-affirming care (*e.g.,* exogenous hormone administration and/or surgery) may influence substance use patterns. Alternatively, people who were assigned female sex at birth may have been socialized to gender norms about alcohol use that have carried forward into adulthood. This is supported by work demonstrating that alcohol use among women (gender minority status was not measured) is shaped by birth cohort.[61] A greater understanding of the biology and social contributors to cannabis and alcohol use at the intersection of sex and gender is needed to be able to provide more clear clinical guidance about use of these substances.

Gender expansive people assigned female at birth and gender expansive people assigned male at birth had higher odds of reporting a less common substance use pattern defined by mostly prescription stimulant use with some heavy episodic alcohol use, cannabis, and sedative or sleeping pill use.

Importantly, most participants who endorsed prescription stimulant use also noted that most-to-all of their prescription stimulant use was exactly as prescribed by their doctor. Prior literature has indicated that sexual minority people are more likely to use stimulants than heterosexual people,[62] and both sexual and gender minority people have relatively high rates of stimulant use.[63] However, given that these patterns of substance use reflect primarily prescription stimulant use and some co-occurring sleeping pill or sedative use, these results may suggest underlying patterns of health needs (*e.g.,* attention deficit hyperactivity disorder [ADHD] diagnoses, insomnia) and health access for these health needs. More research is needed to identify the underlying causes of these differences among gender expansive people.

Prescription stimulant use may have a distinct purpose among people within these subgroups. For instance, there may be a relationship between stimulant use, trauma history, and posttraumatic stress disorder (PTSD) symptoms.[64–70] Notably, research among veterans has found that prescription stimulant use was significantly related to increased risk of PTSD diagnoses, even after controlling for attention deficit disorder and ADHD diagnoses and other participant characteristics.[71] In future intervention studies addressing trauma, victimization, and minority stress among these subgroups of SGM populations, the presence of and motivation for prescription stimulant use may be an important consideration. Ultimately, the investigation of biological, social, and environmental factors driving motivations behind these distinct patterns of substance use will be essential for the design of interventions that effectively support subgroups of SGM populations.

Limitations

This study was limited by self-report measures of substance use within the prior 30 days to survey item completion; thus, it does not reflect substance use across the entire prior year. Here, we examined any use of a substance rather than frequency of use. Tobacco use was defined as cigarette use

and did not incorporate vaping; thus, it likely underestimated total tobacco and nicotine use. The PRIDE Study is a volunteer sample, not a population-based sample. However, these data represent some of the best longitudinal data of substance use among SGM populations with a large sample representing a diversity of gender identities and sexual orientations. The sample reflected a high level of education with 72.6% of the sample reporting having at least a 2-year college degree, around 10% more than the U.S. population.[72] The sample was predominantly white (88.6%), though some of these individuals also reported other races and ethnicities in addition to white race.

In this study, we did not test differences between people who explicitly self-identified as transgender (*e.g.* identifying as a transgender man) *versus* those we categorized as transgender because they reported a gender that does not align with traditional expectations based on sex (*e.g.,* reporting a gender of man and an assigned sex at birth of female). Further, we did not remove participant data from this study due to inconsistent response patterns, as we abide by a core principle within The PRIDE Study that participants know best—which means that infrequently occurring human experiences are taken at face value as real experiences for our participants. This approach may allow for responses to be included from inaccurate responders (*e.g.,* someone who meant to pick another choice or was carelessly selecting items), as we have no way to ascertain if the response was inaccurate versus an infrequently occurring human experience. While this may mean that our sample could have included inaccurate responses, the size of the sample and the general robustness of our results to adjusted models suggests that the impacts of any fraudulent or careless responders are likely to be minimal.

In this study, we included a minimal list of covariates (race and ethnicity, age, and income) as well-established covariates related to substance use that remain relatively untested in SGM people and may function differently among SGM communities and among specific gender subgroups. For example, marital status or parenthood status, which have been well-studied among presumed non-SGM samples,

may have different relationships with substance use in SGM populations. Identification of these differences is an area for future research. Further, SGM subgroups may differ in stigma related to their SGM-status or other individual characteristics (*e.g.,* race, ethnicity, income), which may, in turn, be related to differences in substance use. We did not control for stigma in these analyses but did control for race, ethnicity, and income, and we plan to identify how stigma is related to differences in substance use in future research.

Conclusions

In sum, this study found eight distinct patterns of substance use over a period of four years among SGM people. The most common pattern of substance use was very low substance use. Further, we found that the intersection of gender and sex assigned at birth was related to distinct patterns of substance use over time.

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Author Contributions

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Gowri Sunder: Formal analysis, data curation, project administration, writing-original draft, writing - review and editing, visualization.

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Table 1. Sample characteristics of participants within The PRIDE Study who provided information about their substance use in one or more years of the four-year study period (*N* =11,822).

Variable	
Personal characteristics	
Age, in years (Mean, Median, SD)[a]	33.52, 29, 13.40
Race or ethnicity[b] (*n, %*)	
American Indian or Alaska Native	386 (3.38)
Asian	531 (4.64)
Black, African American, or African	428 (3.74)
Hispanic, Latino, or Spanish	855 (7.48)
Middle Eastern or North African	76 (.66)
Native Hawaiian or other Pacific Islander	49 (.43)
White	10126 (88.58)
None of these fully describe me	292 (2.55)
Reported more than one race or ethnicity	1421 (12.45)
Sexual Orientation[b] (*n, %*)	
Asexual	1151 (10.42)
Bisexual	3250 (29.23)
Gay	3598 (32.38)
Lesbian	2549 (22.97)
Pansexual	1888 (17.02)
Queer	4111 (36.95)
Questioning	183 (1.66)
Same-gender loving	288 (2.61)
Straight/heterosexual	246 (2.23)
Two-spirit	34 (.41)
Another sexual orientation	416 (3.77)
Reported more than one sexual orientation	4565 (40.22)
Gender Subgroup (*n, %*)	
Cisgender woman	4094 (35.34)
Cisgender man	2943 (25.40)
Gender expansive assigned female sex at birth	2617 (22.59)
Gender expansive assigned male sex at birth	426 (3.68)
Transgender women	523 (4.51)
Transgender men	982 (8.48)
Sex Assigned at Birth (*n, %*)	
Female	7490 (66.21)
Male	3823 (33.79)

Socioeconomic status	
Annual individual income (*n, %*)[a]	
≤ $20,000	4468 (41.88)
$20,000 to $40,000	2272 (21.30)
$40,000 to $60,000	1482 (13.89)
≥$60,000	2446 (22.93)
Educational level (*n, %*)[a]	
No high school diploma	65 (.73)
High school/GED graduate or some college[c]	2378 (26.67)
College degree (2-year)	408 (4.58)
College degree (4-year)	3063 (34.35)
Graduate degree[d]	3004 (33.68)

Notes: The number of participants who endorsed a given option (n) and percent (%). Available data for each variable presented, percentage reflects available data for that variable.
[a]These are reported as the highest value or level reported (SD, standard deviation).
[b]Race and ethnicity and sexual orientation categories are not mutually exclusive as participants could have selected more than one option.
[c]Also includes participants with trade, technical, or vocational training.
[d]Graduate degree = Master's, doctoral, or professional (*e.g.,* MD, JD, MBA) degrees.

Table 2. Class solution fit statistics for latent class analyses of substance use over 4 years

Class Solution	Smallest Class *n*	BIC	Entropy	LMRT (*p*)	AIC	ABIC
1	11822	122529.955	-	-	122057.781	122326.570
2	4012	114448.813	0.628	0.000	113497.087	114038.866
3	1450	112845.399	0.61	0	111414.122	112228.890
4	807	111581.859	0.662	0.2549	109671.031	110758.787
5	617	110605.64	0.645	0.1079	108215.26	109576.005
6	413	109946.894	0.675	0.0003	107076.962	108710.697
7	399	109503.388	0.682	0	106153.904	108060.628
8	**398**	**109375.670**	**0.695**	**0.0123**	**105546.634**	**107726.348**
9	289	109435.221	0.676	0.1465	105126.634	107579.337
10	202	109715.942	0.681	0.2655	104927.803	107653.495
11	65	109889.641	0.688	0.3464	104621.95	107620.631
12	124	110385.295	0.691	0.7159	104638.053	107909.723
13	68	110587.766	0.703	0.4372	104360.972	107905.631

Note: Bolded row is the class solution with the smallest BIC and was chosen as the preferred solution.
BIC = Bayesian Information Criterion
LMRT = Lo-Mendell-Rubin Adjusted Likelihood Ratio Test p-value
AIC = Akaike Information Criterion
ABIC = Sample-Size Adjusted Bayesian Information Criterion

Table 3. Results of adjusted and unadjusted multinomial regression of gender subgroup in relation to substance use class membership (N=11,585 in unadjusted models, 10,628 in adjusted models)

Substance Use Class Descriptions (Class Number) ordered by class size from largest to smallest	Cisgender men	Cisgender women OR [95%CI]		Gender expansive people assigned female at birth OR [95% CI]		Gender expansive people assigned male at birth OR [95% CI]		Transgender men OR [95% CI]		Transgender women OR [95% CI]	
		Unadj.	Adj.	Unadj.	Adj.	Unadj.	Adj.	Unadj.	Adj.	Unadj.	Adj.
Little substance use (class 8).	REF	REF		REF		REF		REF		REF	
Heavy episodic alcohol use. Some tobacco and cannabis use (class 6).	REF	**0.57 [0.49, 0.65] *** **	**0.44 [0.38, 0.51]*** **	**0.36 [0.30, 0.42] *** **	**0.26 [0.22, 0.32]*** **	**0.70 [0.52, 0.95] * **	**0.60 [0.44, 0.84]** **	**0.44 [0.35, 0.55] *** **	**0.32 [0.25, 0.42]*** **	**0.38 [0.28, 0.51] *** **	**0.38 [0.27, 0.52]*** **
Cannabis. Some tobacco and heavy episodic alcohol use declining (class 5).	REF	1.13 [0.96, 1.34]	1.06 [0.89, 1.27]	**1.59 [1.34, 1.88] *** **	**1.41 [1.16, 1.71]** **	**1.70 [1.24, 2.33] ** **	**1.60 [1.15, 2.23]* **	**1.65 [1.33, 2.06] *** **	**1.49 [1.17, 1.89]** **	1.10 [0.82, 1.48]	1.04 [0.76, 1.42]
Cannabis, heavy episodic alcohol, and tobacco use. Some polysubstance use (class 2).	REF	**0.61 [0.49, 0.76] *** **	**0.48 [0.38, 0.60]*** **	**0.67 [0.53, 0.85] ** **	**0.46 [0.35, 0.60]*** **	1.42 [0.97, 2.08]	1.14 [0.75, 1.72]	0.73 [0.52, 1.00]	0.**53 [0.37, 0.75]** **	0.68 [0.45, 1.03]	0.69 [0.45, 1.06]
Prescription stimulant increasing. Some heavy episodic alcohol use, cannabis, sedatives or sleeping pill use (class 3).	REF	**1.42 [1.11, 1.82]* **	1.28 [0.98, 1.67]	**1.88 [1.45, 2.42] *** **	**1.60 [1.21, 2.13]** **	**2.11 [1.36, 3.27] ** **	**1.97 [1.24, 3.13]* **	1.24 [0.86, 1.78]	1.08 [0.74, 1.59]	0.71 [0.41, 1.22]	0.74 [0.43, 1.28]
Sedative use increasing. Some cannabis, prescription opioids use (class 4).	REF	0.87 [0.69, 1.09]	1.28 [1.00, 1.64]	0.87 [0.67, 1.11]	**1.62 [1.21, 2.17]** **	0.84 [0.50, 1.43]	1.14 [0.65, 1.98]	0.78 [0.55, 1.12]	1.28 [0.86, 1.89]	1.06 [0.71, 1.58]	0.95 [0.62, 1.44]
Tobacco use. Some	REF	**0.64 [0.51,**	**0.63 [0.48,**	0.85 [0.66,	0.73 [0.54,	0.99 [0.60,	0.98 [0.59,	1.05 [0.76,	0.95 [0.66,	1.11 [0.76,	1.04 [0.70,

polysubstance use (class 7)**.**		**0.82] ****	**0.82]****	1.09]	0.97]	1.62]	1.64]	1.45]	1.36]	1.64]	1.55]
Inhaled nitrates (poppers) use. Some polysubstance use (class 1).	REF	**0.01 [0.00, 0.02] *****	**0.01 [0.00, 0.02]*****	**0.03 [0.01, 0.05] *****	**0.03 [0.02, 0.06]*****	**0.32 [0.19, 0.54] *****	**0.35 [0.20, 0.61]*****	**0.12 [0.07, 0.19] *****	**0.13 [0.08, 0.23]*****	**0.05 [0.02, 0.14] *****	**0.05 [0.02, 0.15]*****

* p <.05 ** p<.01 ***p<.001, bolding indicates p<.05 for ease of identification in the table

Notes: REF = reference category. P-value thresholds and odds ratios (OR) are based on simulated step-down adjustment for multiple comparisons. Confidence intervals (CI) are reported without simulated step-down adjustment. Substance use class descriptions are based on predominant substances within classes, declining indicates a decline over time, increasing indicates an increase over time. Unadjusted (Unadj.); Adjusted (Adj.).

Figure 1. Percentages of people reporting past 30-day use of each substance among each of the substance use classes across each of the four survey years, ordered by class size from largest to smallest *(N=11,822)*

Notes: MDMA=3,4-methylenedioxy-methamphetamine (*e.g.*, ecstasy or molly). GHB= Gamma-hydroxybutyrate.