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Earlier Sexual Debut as a Risk Factor for Substance Use Among Men Who Have Sex with Men (MSM) in Kazakhstan

Caitlin I. Laughney[1] · Yong Gun Lee[2] · Guakhar Mergenova[3] · Vitaliy Vinogradov[3] · Gulnara Zhakupova[3] · Emily Allen Paine[4] · Sholpan Primbetova[3] · Assel Terlikbayeva[3] · Elwin Wu[2,3]

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Abstract

Background Limited research have examined predictors of illicit use of drugs and binge drinking among gay, bisexual, and other men who have sex with men (MSM) in Kazakhstan and Central Asia. This study examines earlier sexual debut as a risk factor for lifetime and recent substance use behaviors among MSM in Kazakhstan.

Methods We conducted a secondary analysis of self-reported data from a NIDA-funded HIV prevention trial including 902 adult cisgender MSM in Kazakhstan who completed structured screening interviews. Logistic regression models were used to estimate associations between earlier sexual debut (ages 16 and older as the reference group) and lifetime and recent substance use, with covariance adjustment for sociodemographic characteristics.

Results The majority of MSM in our sample reported lifetime binge drinking behavior (73%) and illicit use of drugs (65%). Participants with an earlier sexual debut before 13 years old had significantly higher odds of lifetime binge drinking and any illicit use of drugs (*aOR* = 2.3, 95%CI: 1.2–4.5; *aOR* = 3.0, 95%CI: 1.6–5.8). MSM who reported an earlier sexual debut between 13–15 years old had significantly higher odds of lifetime binge drinking and illicit use of any drugs (*aOR* = 1.6, 95%CI: 1.1–2.3; *aOR* = 1.6, 95%CI: 1.1–2.3); as well as recent binge drinking behavior (*aOR* = 1.6, 95%CI: 1.2–2.3).

Conclusion Future research should examine pathways between earlier sexual experiences and substance use behaviors among sexually diverse populations. Earlier sexual experiences during childhood and adolescence may be relevant contextual information for interventions aimed at substance use risk prevention, treatment, and recovery among MSM populations.

Keywords Substance use · Binge drinking · Earlier sexual debut · Men who have sex with men · MSM · Kazakhstan

Introduction

Gay, bisexual, and other men who have sex with men (MSM) are a relatively understudied population in Kazakhstan and Central Asia, and limited research has examined how earlier sexual experiences during childhood and adolescence are related to HIV-risk factors, such as substance use, among MSM in Kazakhstan. MSM in Kazakhstan are navigating a recent rise in HIV incidence (UNAIDS, 2020), and substance use has been highlighted as a key possible driver of HIV disparities among MSM in Kazakhstan (ECOM, 2018; UNAIDS, 2020). Earlier age of first sexual activity, or earlier sexual debut, has been associated with substance use behaviors among sexually diverse populations globally, yet these factors have not been investigated among MSM in Kazakhstan (Cheung et al., 2014; Halkitis et al., 2021; Lowry et al., 2017).

Sexual Development and Sexual Debut Timing

Previous research have explored reports of heterosexual young people's sexual debut, but relatively fewer studies have examined sexual and gender diverse people's first

✉ Caitlin I. Laughney
cil2116@columbia.edu

1 Columbia School of Social Work, New York, NY 10027, USA

2 Social Intervention Group, Columbia School of Social Work, New York, NY 10027, USA

3 Global Health Research Center of Central Asia, Almaty, Kazakhstan

4 HIV Center for Clinical and Behavioral Studies, Division of Gender, Sexuality, and Health, Columbia University and New York State Psychiatric Institute, New York, NY 10032, USA

partnered sexual experiences (Averett et al., 2014; Babin & Humphreys, 2021; Dion & Boislard, 2020). As young people sexually develop they often become curious about aspects of sexual activity—however, common forms of exploratory sexual behaviors can vary between developmental age groups (Wurtele & Kenny, 2011). For example, although partnered sexual intercourse is frequently reported among adolescents, these behaviors are rarely reported among children ages twelve and under (Hornor, 2004; Kellogg, 2010; Lindberg et al., 2021; Wurtele & Kenny, 2011); it is important to note that among pre-teenage children, reports of oral-genital, anal, and vaginal sex are often indicators of child sexual abuse (CSA) victimization as well as other forms of abuse and neglect (Hornor, 2004; Kellogg, 2010; Wurtele & Kenny, 2011). Although it is common for children and adolescents to develop curiosity about their own bodies, as well as other people's bodies, earlier age of sexual debut is associated with higher risk behaviors including substance use (Clark et al., 2020; Wurtele & Kenny, 2011).

Earlier Sexual Debut and Substance Use

Substance use behaviors associated with earlier sexual debut have been mainly explored among adolescent heterosexual people in the USA, and fewer studies have examined sexually diverse and global populations (Cavazos-Rehg et al., 2009; Halkitis et al., 2021; Lowry et al., 2017; Outlaw et al., 2011; Xu et al., 2016).

In the general population, earlier sexual debut has been associated with substance use behaviors. A longitudinal study of Mexican-origin youth found that earlier sexual debut was associated with increased risk of long-term trends in substance use throughout adolescence (Clark et al., 2020). A study of adolescents in eight African countries found that young people who began having sex before 15 years old were more likely to report alcohol, tobacco, and illicit use of drugs (Peltzer, 2010). Among a sample of adolescents from six Caribbean countries, earlier sexual debut was associated with male gender and substance use (e.g., smoking and alcohol use) (Peltzer & Pengpid, 2015).

Among sexually diverse young people in the USA, earlier sexual debut before the age of 13 has been linked to drug-related risk behaviors including recent cigarette, alcohol, and marijuana use as well as lifetime use of prescription drugs, cocaine, methamphetamine, heroin, and injected drugs (Lowry et al., 2017). Specifically among US MSM, sexual debut before the age of 16 has been associated with lifetime drug use, particularly marijuana use (Outlaw et al., 2011). A qualitative study of non-gay identified (NGI) Latino men who have sex with men and women found that those who experienced a sexual debut between 13 and 20 years of age were more likely to be recruited into sex work as teenagers by drug-involved NGI peers (Finlinson et al., 2006). A longitudinal study of MSM in the Netherlands found that MSM with a higher behavioral risk score for HIV seroconversion were more likely to report an earlier sexual debut and increased frequency of substance use over time (Basten et al., 2018).

Earlier Sexual Debut, Risky Sexual Behavior, and Substance Use in Kazakhstan

Limited research has investigated the role or potential implications of earlier sexual debut among people in Kazakhstan. A nationally representative survey of adolescents in Kazakhstan found that approximately a third of young people were sexually active by their 18th birthday, and that the average age of sexual debut among sexually active adolescents was 16 years old (UNFPA, 2018). Among a study sample of medical students in Semey, Kazakhstan, men reported an earlier median age of sexual debut (16 years old) compared to women (18 years old) (Hansson et al., 2008). The difference in reported sexual debut by gender in this region may be a result of sociocultural double standards that encourages men's heterosexual sexual behavior and stigmatizes women's sexual behavior (Hansson et al., 2008). Information about sexual debut or earlier sexual behavior among sexually diverse people in Kazakhstan is limited and may be a result of broader issues around stigma against LGBTQ people (Hansson et al., 2008; Latypov et al., 2013).

Higher risk sexual behaviors (e.g., condomless sex with a partner) and substance use have been more widely investigated in Kazakhstan as a key factor underlying rising HIV prevalence (Jiwatram-Negrón et al., 2018; Marotta et al., 2018). Couple-based and intimate partner focused HIV prevention research among people in Kazakhstan have frequently focused on the role of risky sexual behavior in conjunction with injection drug use and other forms of substance use (El-Bassel et al., 2014; Gilbert et al., 2010; Marotta et al., 2018; Shaw et al., 2017). HIV prevention microfinance interventions have been implemented for women in Kazakhstan who engage in substance use and sex work (McCrimmon et al., 2018; Mergenova et al., 2019). Although substance use research with MSM in Kazakhstan is limited, one study based in Almaty found that condomless anal intercourse was significantly associated with non-injection drug use (Berry et al., 2012). Given evidence of associations between HIV-risk and substance use among MSM in Kazakhstan, and connections between substance use and sexual risk in other contexts, further insight into earlier sexual debut experiences among MSM in Kazakhstan is needed.

Study Aims

This study seeks to advance our understanding of the experiences of sexually diverse populations in Kazakhstan by examining whether earlier sexual debut is associated with an increased likelihood of substance use in a sample of

MSM from three major cities. Specifically, we explore the prevalence of earlier sexual debut and whether earlier sexual debut is associated with recent and lifetime binge drinking behaviors and illicit use of drugs among MSM in this region.

Materials and Methods

Data Collection and Procedures

This study uses data obtained during the conduct of a NIDA-funded clinical trial of a behavioral intervention seeking to increase the engagement of MSM who use substances (i.e., binge drink, illicit use of drugs) in Kazakhstan in the HIV care continuum (see Paine et al., 2021). In the parent study, a stepped wedge design was used to test the intervention across three geographically disparate cities: Almaty, Nur-Sultan (formerly Astana), and Shymkent. The clinical trial commenced in 2018 with all cities in the "pre-implementation" phase. After pre-implementation, the "implementation" clinical trial phase was conducted in each city spaced six months apart. The data presented in this report utilized self-reported data collected during structured screening interviews conducted in Russian or Kazakh in Almaty, Nur-Sultan, and Shymkent that were completed between July 2018 and September 2021 ($N=902$). All study procedures were approved by the Institutional Review Board (IRB) at Columbia University (Protocol # IRB—AAAQ7251) and the Local Ethical Committee at Farabi Kazakh National University (Protocol # IRB—A052).

Participants

Screened individuals were considered eligible for these analyses if they were 18 years and older, self-identified as a cisgender man, and reported having had consensual sex with a man.

Measures

Earlier Sexual Debut

Participants self-reported how old they were when they first had sex, which was characterized as their age of sexual debut. Due to the cultural relativity and subjectivity of what may be socially considered a normal age of sexual debut, earlier sexual debut was determined by the two lowest reported interquartile age groups in our MSM sample. Sexual debut was divided into three categories—those with a sexual debut before the age of 13 years old, between 13 and 15 years old, and 16 years and older with the former two categories indicating earlier sexual debut. The purpose of having two distinct earlier sexual debut categories was to recognize a possible difference in health behavior risk for those who experienced earlier sexual behavior prior to being a teenager (Hall et al., 2020). Additionally, the age of consent in Kazakhstan is 16 years old which coincides with our reference group (UNFPA, n.d.).

Substance Use

Participants were asked about recent (past 90 days) and lifetime binge drinking behavior as well as illicit use of drugs which included marijuana, heroin, other opioids, stimulants, cocaine, hallucinogens, inhalants, and club drugs. Any recent or lifetime illicit substance use was calculated using Boolean OR operators among all of the reported illicit drugs. Binge drinking was defined as consuming five or more drinks within a two-hour period (Courtney & Polich, 2009).

Covariates

The following population characteristics as covariates were included in all multivariable models: age; city (Almaty, Nur-Sultan, and Shymkent); marital status (single, married, no longer with a spouse, or "other"); highest educational attainment level (9th grade or less, high school or vocational, bachelor's degree or more, or "other" category); employment (full time, part time, unemployed, or "other"); housing insecurity (past 6 months); self-reported HIV status (positive, negative, or unknown); self-reported sexual orientation (heterosexual, bisexual or gay, and other); and self-reported estimated income in Kazakhstan Tenge (KZT) per month for the prior 6 months. Income was transformed using log squared to reduce heteroscedasticity.

Statistical Analyses

For our descriptive analyses, we assessed the frequencies of population sociodemographic characteristics, and substance use, and age of sexual debut (see Tables 1, 2 and 3). For bivariate analyses, we used chi-square tests to evaluate any associations between earlier sexual debut and substance use behaviors. Finally, for the multivariable models, we used logistic regression to assess associations between earlier sexual debut and substance use while adjusting for age, city, marital status, education, employment, HIV-status, sexual orientation, and income (see Table 4).

Results

Sample Characteristics

Table 1 displays the population characteristics of the sample. Most of the men in our sample lived in Almaty (41%); about half had a college education or more (49%); and were 28 years

Table 1 Population characteristics of a sample of MSM in Kazakhstan, 2018–2021 ($N=902$)

Population characteristic	*n*	%
City		
Almaty	372	41.2%
Nur-Sultan	290	32.2%
Shymkent	240	26.6%
Marital Status		
Single	714	79.2%
Married	58	6.4%
No longer with spouse	74	8.2%
Other	56	6.2%
Highest educational attainment level		
9th grade or less	50	5.5%
High school or vocational	382	42.4%
Bachelor's Degree or More	440	48.8%
Other	30	3.3%
Employment		
Full time	473	52.4%
Part time	200	22.2%
Unemployed	99	11.0%
Other	130	14.4%
Housing insecurity in the past 6 months		
Yes	85	9.4%
No	817	90.6%
Self-reported HIV status		
HIV positive	65	7.2%
HIV negative	540	59.9%
Unknown	297	32.9%
Self-reported sexual orientation		
Gay, bisexual, or other	875	97.0%
Heterosexual	27	3.0%
Sexual debut[a]		
Ages less than 13	75	8.3%
Ages 13–15	226	25.1%
Ages 16 and older	600	66.5%

The present table represents the percentage (%) of a population characteristic within the total sample of MSM

[a]One participant response was coded as missing for sexual debut

old on average. The majority of participants worked full time (52%); were housing secure (91%); and had an average monthly income of approximately 140,000 KZT (about 300 USD) over the past 6 months. The majority of MSM in the sample reported being single (79%), HIV-negative (60%), and identified as gay, bisexual, or a sexual orientation other than heterosexual (97%). Approximately two-thirds (67%) of MSM participants were 16 years or older at the time of their sexual debut.

Substance Use

Table 2 displays descriptive statistics for substance use. The most frequently reported types of substance use were lifetime binge drinking (73%) and any use of illicit substances (65%), followed by lifetime marijuana use (48%) inhalants (34%). The same pattern occurred for reported substance use in the past 90 days, with the greatest reports of binge drinking (57%) and any illicit use of substances (28%), followed by marijuana (16%) and inhalant use (13%).

Table 2 Substance use within a sample of MSM in Kazakhstan, 2018–2021 ($N=902$)

Substance use	Ever		Past 90 Days	
	n	%	*n*	%
Binge drinking	654	72.5%	513	56.9%
Marijuana	437	48.4%	147	16.3%
Heroin	43	4.8%	17	1.9%
Other opioids	67	7.4%	25	2.8%
Stimulants	95	10.5%	40	4.4%
Cocaine	41	4.5%	2	0.2%
Hallucinogens	71	7.9%	7	0.8%
Inhalants	308	34.1%	119	13.2%
Club drugs	72	8.0%	20	2.2%
Any illicit substances	584	64.9%	256	28.4%

The present table represents the percentage (%) of substance use reported within the total sample of MSM

Associations Between Earlier Sexual Debut and Substance Use

Table 3 presents the distribution of the sample with respect to earlier sexual debut and substance use. Bivariate analyses indicated that earlier sexual debut was significantly associated with binge drinking and illicit drug use. Compared to participants reporting a sexual debut at age 16 or older, earlier sexual debut was associated with higher rates of ever binge drinking and using marijuana, heroin, opioids, stimulants, cocaine, club drugs, and any illicit drugs. Compared to sexual debut at 16 or older, earlier sexual debut was associated with higher rates of binge drinking and marijuana, heroin, opioid, stimulant, and any illicit drug use in the past 90 days.

Results from multivariable models are presented in Table 4. There was a significant relationship between earlier sexual debut and substance use. Compared to participants with a sexual debut of 16 years of age or older, those with sexual debuts before the age of 13 had significantly higher odds of ever reporting to binge drink, use marijuana, or any illicit drugs ($aOR=2.3$, 95%CI: 1.2–4.5; $aOR=3.0$, 95%CI: 1.7–5.4; $aOR=3.0$, 95%CI: 1.6–5.8). MSM with sexual debuts between the ages of 13 and 15 years old had significantly higher odds of ever binge drinking, using marijuana, heroin, other opioids, stimulants, cocaine, club drugs, or any illicit drugs ($aOR=1.6$, 95%CI: 1.1–2.3; $aOR=1.4$, 95%CI: 1.0–2.0; $aOR=3.8$, 95%CI: 1.8–8.2; $aOR=2.1$,

Table 3 Earlier sexual debut and substance use among MSM in Kazakhstan, 2018–2021 ($N=902$)

Substance type	Sexual debut less than 13 years old		Sexual debut 13–15 years old		Sexual debut 16 years or older	
	Ever	Past 90 days	Ever	Past 90 days	Ever	Past 90 days
	n(%)	*n(%)*	*n(%)*	*n(%)*	*n(%)*	*n(%)*
Binge drink alcohol	64(85.3%)	48(64.0%)	176(77.9%)	144(63.7%)	413(68.8%)	320(53.3%)
Marijuana	52(69.3%)	9(12.0%)	125(55.3%)	52(23.0%)	260(43.3%)	86(14.3%)
Heroin	5(6.75%)	2(2.7%)	23(10.2%)	9(4.0%)	15(2.5%)	6(1.0%)
Other opioids	8(10.7%)	4(5.3%)	28(12.4%)	10(4.4%)	31(5.2%)	11(1.8%)
Stimulants	8(10.7%)	3(4.0%)	39(17.3%)	22(9.7%)	48(8.0%)	15(2.5%)
Cocaine	5(6.7%)	0(0.0%)	20(8.8%)	1(0.4%)	16(2.7%)	1(0.2%)
Hallucinogens	9(12.0%)	1(1.3%)	23(10.2%)	1(0.4%)	39(6.5%)	5(0.8%)
Inhalants	32(42.7%)	12(16.0%)	85(37.6%)	33(14.6%)	191(31.8%)	74(12.3%)
Club drugs	7(9.3%)	2(2.7%)	29(12.8%)	8(3.5%)	37(6.2%)	11(1.8%)
Any illicit drugs	61(81.3%)	22(29.3%)	164(72.6%)	79(35.0%)	360(60.0%)	155(25.8%)

The present table represents the percentage (%) of participants within a sexual debut category who engaged in a substance use behavior

95%CI: 1.1–3.7; *aOR* = 2.4, 95%CI: 1.5–3.8; *aOR* = 2.7, 95%CI: 1.3–5.5; *aOR* = 2.0, 95%CI: 1.2–3.4; *aOR* = 1.6, 95%CI: 1.1–2.3), as well as binge drinking, use marijuana, or stimulants in the past 90 days (*aOR* = 1.6, 95%CI: 1.2–2.3; *aOR* = 1.5, 95%CI: 1.0–2.3; *aOR* = 4.3, 95%CI: 2.1–8.8).

Discussion

In our final models of earlier sexual debut and substance use among MSM in Kazakhstan, we found significant associations between earlier sexual debut and binge drinking as well as illicit use of drugs. Although earlier sexual debut has been found to be a significant risk factor for other sexual risk behaviors among MSM in China, sexual debut has rarely been assessed as a risk factor for substance use among this minority population in Central Asia or Eastern Europe, limiting our knowledge of the broader connections between sexual behavior and substance use (Tang et al., 2020; Wirtz et al., 2013; Xu et al., 2016; Zou et al., 2016). Our present study suggests that earlier age of sexual onset is a relevant risk factor for a variety of substance use behaviors among MSM in Kazakhstan, warranting incorporation of age of sexual debut in future substance use research among sexually diverse populations.

Table 4 Associations between earlier sexual debut and substance use among MSM in Kazakhstan, 2018–2021

Substance type	Sexual debut less than 13 years old		Sexual debut between 13–15 years old	
	Ever	Past 90 days	Ever	Past 90 days
	a0R (95% CI)	*a0R (95% CI)*	*a0R (95% CI)*	*a0R (95% CI)*
Binge drink alcohol	2.3* (1.2–4.5)	1.4 (0.8–2.3)	1.6* (1.1–2.3)	1.6** (1.2–2.3)
Marijuana	3.0*** (1.7–5.4)	0.7 (0.3–1.4)	1.4* (1.0–2.0)	1.5* (1.0–2.3)
Heroin	2.4 (0.8–7.3)	1.8 (0.3–11.2)	3.8*** (1.8–8.2)	2.9 (0.8–11.3)
Other opioids	1.7 (0.7–4.0)	1.7 (0.4–6.6)	2.1* (1.1–3.7)	1.3 (0.5–3.8)
Stimulants	1.2 (0.5–2.8)	1.7 (0.5–6.2)	2.4*** (1.5–3.8)	4.3*** (2.1–8.8)
Cocaine	2.0 (0.7–6.0)	a	2.7** (1.3–5.5)	a
Hallucinogens	1.8 (0.8–4.2)	1.4 (0.1–13.9)	1.4 (0.8–2.5)	0.3 (0.0–3.4)
Inhalants	1.5 (0.9–2.5)	1.1 (0.5–2.2)	1.2 (0.9–1.7)	1.2 (0.7–1.9)
Club drugs	1.4 (0.6–3.4)	1.2 (0.3–5.8)	2.0* (1.2–3.4)	1.9 (0.7–4.9)
Any illicit drugs	3.0*** (1.6–5.8)	0.9 (0.5–1.7)	1.6* (1.1–2.3)	1.4 (1.0–2.0)

The reference group is sexual debut 16 years and older. aOR: Odds ratio adjusted for age, income log2(*n*), city, marital status, education, employment, housing insecurity, HIV-status, and sexual orientation

CI Confidence interval

p-values: *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$

[a]Analyses not run due to insufficient cell size for the outcome: cocaine use in the past 90 days

Our findings make an important contribution to the current sexuality and substance use literature. Earlier sexual debut is often measured using one discrete age marker; however, we examined associations between average age of sexual debut (ages 16 and over) and two distinct age ranges of earlier sexual debut to account for variability between pre- and post-teenage sexual debuts and substance use risk (Lowry et al., 2017; Sawyer et al., 2018). Our findings support differentiating between earlier sexual debut groups. Although in our final models both earlier sexual debut categories were significantly associated with substance use risk compared to a sexual debut 16 years or older, MSM in the earliest sexual debut category (ages 12 and under) reported greater adjusted odd ratios of lifetime binge drinking, marijuana use, or any illicit substance. Due to concerns that sexual debut before 13 years old may be a result of CSA, future research should screen for CSA as a potential risk factor for substance use behaviors among MSM in Kazakhstan. These results suggest that age of sexual onset during earlier adolescence or childhood may be a particularly vulnerable time for sexual decision-making and identity formation that may result in higher-risk behaviors in the form of substance use.

Service needs that may be relevant for MSM in Kazakhstan could include additional clinical attention towards assessing and addressing potential CSA as well as voluntary or consensual sexual activity during earlier adolescence and childhood. Within Kazakhstan, adolescents have limited access to sexual and reproductive health information, particularly in the native Kazakh language, and sexual education among young people remains a taboo social topic (WHO, 2020). Our findings warrant an increase of sexual health resources for a wide range of young people—including children and adolescents—and reducing barriers to care for youth and MSM. Overall, further research is needed to better elucidate causal pathways between earlier sexual experiences among sexually diverse people and risky substance use behaviors.

Clinicians who provide HIV prevention services for MSM who use substances in Kazakhstan should consider incorporating sexual history screening questions that inquire about childhood and adolescent sexual experiences, particularly non-consensual sexual experiences during this developmental period. Within the broader literature, trauma-informed HIV prevention and treatment among MSM has been recognized as an important aspect of holistic care for MSM at high co-occurring risk of HIV and trauma (Brezing et al., 2015; Brown & Adeagbo, 2022; Sales et al., 2016). MSM at elevated risk of HIV-infection who use substances and have a history of CSA-victimization may need comprehensive healthcare services, such as HIV prevention resources (e.g., HIV testing, pre-exposure prophylaxis), substance use harm reduction services, and trauma-informed mental health resources. MSM who use substances and are at elevated risk of HIV infection may require a multipronged approach to clinical care that addresses complex co-occurring issues, such as substance use, HIV risk, and history of CSA victimization.

Limitations

This study had several limitations. Some of our models were limited by small proportions of participants using certain illicit substances, particularly recent illicit use of drugs. This study is not necessarily representative of MSM in Kazakhstan, and all participants were recruited from major cities in the region which does not capture rural MSM experiences. The earlier sexual debut question used was a relatively broad single question about age of first sexual activity that did not assess information about the sexual partner (e.g., the partner's gender or age) and whether this experience was consensual or non-consensual. Additionally, the small number of participants reporting an earlier sexual debut before 13 years old ($n=75$) may have limited our ability to capture associations between substance use risks and earlier sexual debut among the sample size of MSM. Although sexual debut presumably predates the majority of substance use behaviors reported by adults, our study is cross-sectional and is unable to assess temporal sequences. Lastly, social desirability bias may have influenced how participants self-reported socially sensitive behaviors, such as substance use and sexual behaviors during childhood or adolescence.

Conclusion

Sexual experiences during childhood and early adolescence are a potential risk factor for current and lifetime substance use among MSM in Kazakhstan. Earlier onset of sexual activity was significantly associated with lifetime marijuana, heroin, opioid, stimulant, cocaine, and club drug use as well as binge drinking and any illicit use of drugs. Earlier sexual debut also was significantly associated with recent binge drinking, marijuana, and stimulant use. Further research is needed to examine how consensual and non-consensual sexual experiences during childhood and adolescence are linked to risky substance use behaviors among men who have sex with men.

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Author Contribution CIL conceptualized the study, conducted the data analysis, and drafted the manuscript. EW, YGL, and EAP edited and reviewed the manuscript prior to submission. YGL, GM, VV, and GZ were responsible for the oversite of data collection. SP, AT, and EW collaborated on the design and oversite of the parent study. All authors had full access to the data, reviewed and edited the manuscript, and take responsibility for its integrity as well as the accuracy of the analysis.

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Availability of Data and Material The dataset generated and/or analyzed during the current study is not publicly available.

Declarations

Ethics Approval and Consent to Participate The original trial was approved by both the institutional review board of Columbia University and The Local Ethical Committee et al.-Farabi Kazakh National University. Verbal informed consent was obtained from all participants; a waiver of written documentation of consent was obtained from the IRB because the research presented no more than minimal risk of harm to subjects. All procedures performed in studies involving human participants were in accordance with the ethical standards of the intuitional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The current data analysis for this manuscript was performed on completely de-identified data.

Consent for Publication Not applicable.

Competing Interests The authors declare no competing interests.

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