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Motivation to Change and Treatment Participation Among Syringe Service Program Utilizers in Rural Kentucky

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Abstract

Purpose: Kentucky experiences a disproportionate burden of substance use disorder (SUD), particularly in rural areas of the state. Multiple factors increase vulnerability to SUD and limit access to services in rural communities. However, the recent implementation and expansion of syringe service programs (SSPs) in rural Kentucky may provide a leverage point to reach at-risk people who inject drugs (PWID).

Methods: Data were collected as part of an ongoing NIDA-funded study designed to examine uptake of SSPs among PWID in Appalachian Kentucky. Using Respondent Driven Sampling (RDS), the study enrolled a sample of 186 PWID SSP attenders across 3 rural Appalachian Kentucky counties and conducted face-to-face interviews regarding health behaviors, injecting practices, SSP utilization, and treatment services. Using logistic regression analyses, we examined consistent SSP use, as well as importance and confidence to reduce substance use as predictors of current treatment participation.

Findings: For the prior 6 months, 44.6% of the sample reported consistent SSP use. Consistent use of SSPs was associated with treatment participation in the unadjusted logistic regression models. Significant predictors of treatment participation in the adjusted model included high confidence to reduce substance use, and not reporting primary methamphetamine injection.

Conclusions: Rurally located SSPs may play an important role in supporting confidence and motivation to change substance use behaviors among PWID impacted by SUD. SSPs may be critical venues for integration and expansion of prevention, health promotion, and treatment linkage services for this underserved population.

Keywords

injection drug use; motivation to change; rural; syringe service programs; treatment

Substance use disorder (SUD) is increasingly prevalent in the US, broadly affecting individuals, families and communities across the nation.¹ SUD results in significant threats to health and well-being, contributes to family distress, and creates major socioeconomic burdens.¹⁻⁴ Persistent substance use can result in significant clinical impairment, disability, and failure to meet responsibilities at school, work or home.⁵ Children exposed to parental substance use have a higher risk of abuse and neglect, which can negatively affect their physical and emotional well-being.⁶ In addition, parental substance use can lead to parent and child separation due to parental incarceration,⁷ long-term treatment, or removal of a child from an unsafe home environment to foster care or a residential home by child protective services.⁸ Substance misuse and SUD is estimated to cost the US approximately \$740 billion annually from medical care spending and loss of productivity.⁹

In 2017, an estimated 7.5 million people, or 2.8% of the US population ages 12 and older, reported past year SUD exclusive of alcohol,^{10,11} of which approximately 2.1 million indicated opioid use disorder (OUD).¹¹ OUD has reached epidemic proportions in the US, posing a serious public health threat.¹²⁻¹⁴ In Kentucky, SUD is estimated to impact more than 100,000 individuals ages 12 and older.¹⁰ Adverse health consequences of OUD including opioid-related overdose mortality increased markedly from 2006 to 2016,¹¹ with higher rates observed in rural areas¹⁵ and especially in states like Kentucky.¹⁶ Kentucky continues to experience a disproportionate burden of OUD, with higher rates of neonatal abstinence syndrome, overdose deaths, and injection-related hepatitis C compared to national averages.¹⁷⁻¹⁹ Kentucky reported approximately 1,150 opioid-related deaths in 2017, a rate of 27.9 deaths per 100,000 persons, compared to the national average of 14.6 deaths per 100,000 persons.²⁰ Though the impact of the opioid crisis in Kentucky is evident, adverse health outcomes appear to be tied to a range of substances and polysubstance use, with recent indicator data suggesting an increasing prevalence of methamphetamine in many areas of the state.²¹

Noted risk factors for SUD are multi-factorial, including socioeconomic factors such as poverty and unemployment,²² isolation, co-morbid psychiatric conditions,²³⁻²⁵ and social environments that encourage misuse.^{2,26} Rural individuals are often disproportionately impacted by multiple factors that increase vulnerability to SUD and deter uptake of services,²⁷ including risky social network attributes and characteristics.²⁸ Rural areas also experience critical disparities in resources for prevention, harm reduction, and treatment for substance use.²⁹ This combination of factors may adversely impact motivation for treatment, engagement in treatment seeking behaviors, and access to SUD recovery pathways in rural communities.

The unmet need for SUD treatment is a critical public health concern,² particularly in underserved rural areas, and addressing SUD is essential for improving mental and physical well-being and quality of life. The recent implementation and expansion of syringe service programs (SSPs) in rural areas may provide an opportune leverage point to reach at-risk people who inject drugs (PWID) to reduce harms related to SUD. SSPs are anonymous public health programs designed to distribute sterile injection equipment to PWID at no cost, to reduce bloodborne infections and disease transmission associated with re-use and sharing of non-sterile injection equipment. Urban-located SSPs have been associated with large

reductions in HIV prevalence among PWID, as well as reductions in risk behaviors and improved linkages to substance use treatment.^{30–33} However, the utilization and impact of SSP participation among rural PWID has not been adequately studied,³⁴ and SSPs' potential for supporting and improving treatment and recovery processes among rural PWID is largely unknown.

Recovery from SUD can be influenced by improved abstinence self-efficacy and motivation to change.^{35–37} However, there is mixed evidence overall to support attitudes toward change as critical targets for intervention and drivers of intervention outcomes,³⁸ and the potential role of SSPs in supporting motivation and readiness for treatment in rural populations is understudied.³⁹ As an essential underpinning of the transtheoretical model of change,^{40,41} motivation is often assessed through examining readiness to change, importance of changing, and confidence in ability to change components of substance use behaviors.^{42–53} Motivation to change is a complex phenomenon; however, high confidence or self-efficacy to reduce substance use has been associated with favorable substance use outcomes in prior research.⁵¹ This paper examines consistent SSP use, and importance and confidence to reduce substance use among rural SSP attenders in Kentucky, and investigates their association with treatment participation, in order to inform the potential feasibility of integrating brief motivational interventions in rural SSP settings.

Methods

Sampling and Recruitment

Data were collected through an ongoing NIDA-funded study designed to examine uptake of SSPs among people who inject drugs (PWID) in Appalachian Kentucky. Eligible participants reported having injected substances non-medically in the month prior to interview and were at least 18 years of age. Participants were recruited using Respondent-Driven Sampling (RDS) techniques.⁵⁴ Consistent with RDS procedures, each participant-recruiter in this study was limited to 3 coupons to limit bias due to network size. The study enrolled a sample of 186 PWID from SSPs in 3 county health departments. The included counties were designated by the Health Resources and Services Administration (HRSA) as rural (Knox, Owsley) or having eligible rural census tracts (Clark).⁵⁵ The participating SSPs have varying operational and structural characteristics; however, each operates from a single, fixed location within the local health department setting. All had been operating for at least 9 months prior to the initiation of data collection for this study.

Study Procedures

Between February and October 2018, university-based project research staff enrolled, consented and interviewed PWID participants one-on-one on-site during SSP operating hours. SSP staff made clients aware of the opportunity to participate in the research interview after their exchange activities were completed, and interested clients were directed to a private office where the interviewer explained the study and conducted brief screening to ensure age and injection-related eligibility, followed by informed consent. These procedures allowed uninterested clients to leave the site without directly interacting with the study interviewer, which was important to reduce potential discomfort among PWID clients

who visit the SSP with the expectation of anonymity. Project interviewers completed human subjects training, as well as training in study protocols, interviewing techniques with substance using populations, and the administration of the interview instruments prior to the initiation of data collection. Across the 3 study locations, 7 interviewers participated in the data collection process, including the study PI. Interviews were completed during the client visit to the SSP, immediately post-exchange. The brief structured face-to-face interview used validated instruments and lasted approximately 35 to 40 minutes to reduce the time burden to participants. Participants received a \$20 gift card upon interview completion. All study protocols were reviewed and approved by the university IRB.

Study Measures

The interview instrument was primarily based on the Global Appraisal of Individual Needs (GAIN),^{56,57} and it included abbreviated segments of the core domains: demographics, substance use, physical health, sexual risk behaviors, mental health, and environment. To minimize the interview time burden to participants, we utilized single items to capture demographic and health information, and validated brief versions of scales for substance use, mental health, and social support. In this analysis, we examined need and enabling factors potentially associated with substance use treatment participation among this sample of SSP attenders.

Independent Variables

Demographics—We examined age, gender, race/ethnicity, insurance coverage status, and SSP site as potentially important demographic variables.

SSP Uptake—A new series of items was developed to capture critical components of SSP uptake, in terms of both duration and frequency of SSP visits. SSP visits in our study settings are typically brief interactions, organized around return of used injection equipment and distribution of new sterile equipment in accordance with program policies. As harm reduction programs focused on disease prevention, SUD treatment is addressed only in the event of client request. A single item measured duration of use (“How long have you been coming to this SSP?”) and frequency of use (“How many times have you visited this SSP in the past 6 months?”). For analysis, consistent use was defined as at least 6 SSP visits over the prior 6 months.

Health—*Mental Health* distress was measured by the 6-item (GAIN) Internalizing Disorder Screener that incorporates somatic complaints, depression, anxiety, trauma, psychosis, and suicide. Response choices let the participant report whether they had each problem more than a year ago, 4 to 12 months ago, 2 to 3 months ago, during the past month, or never. We examined problems reported in the past 90 days. Low (0) scores indicate that services are likely not needed; moderate (1 or 2) to severe (3+) scores suggest possible diagnosis and need for mental health services.

Physical Health was assessed by one item from the GAIN related to functional interference resulting from health problems: “During the past 90 days, on how many days have medical problems interfered with your daily activities?”

Recent Violence was also assessed with a single item from the GAIN, in which participants were asked to indicate the last time they experienced physical, sexual or emotional abuse/violence.

Social Support—Social support was measured using the 8-item Medical Outcomes Study (MOS) Social Support Survey,⁵⁸ which includes the domains of emotional and instrumental support. Scores were calculated according to the scale’s authors’ guidelines, and they were transformed to a 0–100 scale and categorized as low, medium, and high.

Substance Use and Related Problems—Primary drug of injection was captured by an item that queried past month injection: “*In the past 30 days, which drug have you injected most often?*”

Substance Use Disorder (SUD) was measured by the 11-item GAIN Substance Use Disorder scale that examines symptoms of substance abuse, dependence, and craving in alignment with the DSM-V, and it is time-framed to capture symptoms in the past month, past 3 months, past year, and lifetime. Participants endorsing 4 to 5 symptoms in a particular time period are categorized with moderate SUD, and those with 6 or more symptoms as severe. *Overdose* was measured with a single lifetime item querying history of overdose.

Motivation to Change was measured along 2 dimensions: “importance to cut down or stop substance use” and “confidence to cut down or stop substance use” in line with use by the World Health Organization.^{52,59} Participants were asked to rate how important it is for them and how confident they are in cutting down or stopping substance use on a scale of 0 to 10, whereby 0 = “not important/confident,” and 10 = “extremely important/confident.” For analysis, both variables were re-coded into low (0–4), medium (5–7), and high (8–10), in line with prior research.⁴⁹

Dependent Variable

Treatment Participation for SUDs was measured by the GAIN item, “*when is the last time you received counseling, treatment, medication, case management or aftercare for your drug or alcohol use?*” Response choices included never, more than 12 months ago, 4 to 12 months ago, 1 to 3 months ago, 1–4 weeks ago, and within the past week. Because this item included multiple types of programs, modalities and intensities, we examined treatment within the past four weeks as indicating “current” treatment participation of any kind. For analysis, the dependent variable was recoded into a binary measure whereby 1 = current treatment and 0 = never or past treatment.

Data Analysis

This paper reports on the SSP utilizer sample (n=186) enrolled across the three participating county health department SSPs. Descriptive statistics were calculated on demographics, SSP utilization characteristics, health, substance use and related problems, and motivation to change substance use behaviors. Separate unadjusted and adjusted logistic regression models examined factors associated with substance use treatment participation in the prior month. Adjusted models controlled for demographics, as well as structural factors of insurance

coverage and county location as influencers of treatment availability and access, and included all factors significant at $p < .05$ level in the unadjusted models. Data were analyzed using SPSS version 23.⁶⁰

Results

Descriptive statistics were used to summarize sample characteristics of SSP attenders (see table 1). The sample was balanced by gender, with 46.8% being female, and had a mean age of approximately 38 years (SD 9.4). The large majority were non-Hispanic white, reflecting the demographic makeup of Kentucky's Appalachian region.

Uptake of the SSPs was moderate, with 44.6% of the sample reporting at least six visits to their local program over the past six months. Although more than one-third had initiated SSP attendance within the month prior to interview, 28.5% had been utilizing the program for at least six months, and some for as long as two years.

As shown in Table 1, health problems, both physical and psychological, were quite common in this SSP-recruited sample of PWID. The large majority reported symptoms of severe mental distress in the prior three months, as well as physical health problems that interfered with daily functioning.

In terms of substance use, methamphetamine was most often reported as the primary substance of injection (45.2%), followed by non-prescribed buprenorphine (25.8%), and heroin (16.1%). Polysubstance injection was common; some 63.3% of primary heroin injectors also injected methamphetamine (data not shown).

Regardless of primary substance, a full two-thirds of the sample (66.1%) met DSM-V (Diagnostic and Statistical Manual of Mental Disorders) criteria for severe substance use disorder (SUD) in the past 3 months. Examination of motivation to reduce substance use revealed that the majority of SSP attenders (69.9%) perceived high importance of quitting or cutting down. Confidence to reduce substance use was lower in comparison to importance, with some 48.4% reporting high confidence to quit or cut down, and sizeable proportions reporting medium and low confidence. Past month treatment participation was reported by 21.0% ($n=39$) of the sample overall.

Table 2 presents the results of logistic regression models examining past month substance use treatment participation among SSP attenders. In the unadjusted models, location at Site C was significantly associated with higher odds of past month treatment participation, relative to Site A (OR 2.808; 95% CI 1.153, 6.834). Consistent SSP uptake, in terms of number of attended visits, was linked to significantly greater odds of current treatment participation (OR 2.121; 95% CI 1.022, 4.403). In terms of substance use, primary methamphetamine injectors reported significantly lower odds of current treatment participation (OR 0.398; 95% CI .185, .859).

Motivation to reduce substance use, both perceived importance and confidence, were examined for association with substance use treatment participation. Participants reporting high confidence for decreasing substance use had significantly higher odds of treatment

participation (OR 2.562; 95% CI 1.221, 5.380). In the adjusted model, controlling for demographics, site, and insurance coverage, primary methamphetamine injection was significantly associated with substance treatment participation, with lower odds of treatment among this group (OR 0.341; 95% CI .146, .798). Confidence to reduce substance use was also significant in the adjusted model (OR 2.241; 95% CI 1.002, 5.009), with high confidence associated with greater odds of current treatment participation.

Discussion

This study is among the first to systematically explore patterns of syringe service program utilization in rural Kentucky and characteristics of SSP attenders in these underserved areas. Prior research has documented the relative dearth of rurally located harm reduction and treatment programs,^{34,61,62} indicating a tremendous need for data to inform our understanding of service gaps and to examine potential for creatively leveraging SSPs to integrate and extend health services provision.

We examined frequency and duration of SSP use among a sample of SSP attenders in 3 county health departments. Our findings indicate that consistent utilization of the SSPs was moderate: 44.6% of the enrolled sample reported at least 6 visits to their local SSP over the past 6 months. More than one-third of the sample had initiated SSP attendance within the month prior to interview; however, 28.5% had been utilizing the program for at least 6 months. Although published data on this topic are scarce, our findings indicate a higher proportion of *new* SSP participants than reflected in earlier urban-located SSP studies,⁶³ possibly signaling the relatively new establishment of these rural programs and a lower level of community awareness. Nevertheless, our findings also document that a very high proportion of the non-first-time clients in our rural settings indicated repeat SSP use (97%), compared to several studies in large metro areas indicating that a considerable proportion of PWID visited the SSP only once,^{63,64} or had only one return visit in a 12-month follow-up period.⁶⁵ These findings indicate that rurally located SSPs are being utilized by high-risk PWID and represent a critical venue for the delivery of harm reduction services in rural areas. Attention to strengthening and resourcing these programs to further increase access (operating with extended hours or in mobile capacities) would appear to be warranted.

Consistent with prior research documenting a more severe clinical profile of SSP users relative to non-SSP PWID,^{39,66} we found that the SSPs in our rural catchment areas serve a PWID population with chronic longstanding SUD, and significant physical and mental health comorbidities. Of our sample, 66% met criteria for past 90-day severe SUD and 78% reported severe mental distress in the same time period, indicating that this is an important population to reach with expanded services. Of note, our sample was 47% female, which departs somewhat from early urban studies indicating higher proportions of males utilizing SSPs, often as high as 70% or greater.^{63,65}

An important synthesis paper of SSP research found that SSP participants infrequently engage in treatment, despite high levels of problematic drug use and high treatment need.³⁹ In the present study, we measured both treatment participation and specific aspects of motivation to change substance use behaviors. Although past month treatment participation

was modest among our sample (21%), we found that the majority of SSP attenders (69.9%) perceived high importance of quitting or reducing substance use. Confidence to reduce substance use was somewhat lower overall, but nevertheless substantial, with 48.4% reporting high confidence. Importantly, this sample of rural PWID displayed high levels of substance-related problem recognition, and moderate levels of confidence to change, which are key indicators of motivation and readiness.

When examining factors associated with past month substance use treatment participation among SSP attenders in the unadjusted models, we found that those with consistent SSP uptake, and those reporting high confidence to decrease substance use, had significantly higher odds of current treatment participation, while primary methamphetamine injectors reported significantly lower odds of current treatment participation. The precise interpretation of the documented association of consistent use of the SSP, confidence to change, and treatment participation is unknown, given the limitations of our cross-sectional data and the breadth of data collected. It is plausible that the association is a result of active, intentional treatment referrals from the SSP, an indirect effect of general social and recovery support available at the SSPs, or increased agency for behavior change that accrues from ongoing successful participation in the SSP. These findings are nevertheless promising and warrant additional investigation.

A finding of primary importance in the adjusted model was the significant association of confidence to reduce substance use and treatment participation. Although we cannot examine causality based on the cross-sectional nature of our data, these findings support the notion that providing brief motivational and targeted goal setting interventions may improve treatment seeking and enrollment.³⁹ Overall, motivation to change substance use behaviors in SSP clients is an understudied area that warrants further research, as an early study in Baltimore found no differences between SSP and non-SSP users in motivation to reduce or stop drug use using a validated measure reflecting intention to quit.⁶⁷ Nevertheless, SSPs have demonstrated success in linking clients to treatment through active intervention initiatives,⁶⁸ and most SSPs nationally engage in referrals to treatment.³⁴ Our findings suggest that rurally located SSPs can play a role in supporting motivation to change substance use behaviors among PWID impacted by SUD.

In the adjusted model, controlling for demographics, insurance coverage, and site, primary methamphetamine injection was significantly inversely associated with substance treatment participation. In the midst of the opioid crisis, methamphetamine was the most common primary drug injected by PWID using SSPs in our sites. These emerging data resonate with Kentucky overdose and inpatient hospitalization data for 2017, which demonstrate large increases in methamphetamine use.²¹ The low prevalence of non-prescribed opioids as a primary drug suggests supply reduction interventions and stewardship programs are having success. The high proportion using methamphetamine, and the overlapping use of opioids, highlight the complexities of responding appropriately to the drug crisis with single-substance focused approaches. Our finding that primary methamphetamine users have lower odds of treatment participation likely reflects a lack of treatment services designed for methamphetamine users, inadequate treatment capacity, as well as the lack of effective medication assisted treatment for methamphetamine use disorder. Improving formal access

to opioid-focused MAT, and emphasizing combination behavioral and psychosocial therapies and adjuvants to address methamphetamine and other substance use, appears critical in these settings.

Limitations

Our findings should be interpreted with caution, given the limitations in our study design and data collection methods. As mentioned above, we conducted study interviews with SSP clients at a single time point, and therefore our findings are limited by the inherent constraints of cross-sectional data in unpacking the temporal relationships between SSP use, confidence to change substance use, and treatment participation. We relied on client self-report to collect information on SSP utilization, substance use behaviors, and treatment participation, which has well-known limitations, including potential recall issues and social desirability biases. Nevertheless, due to the high levels of severe SUD, physical and mental health problems reported, we are confident that our use of trained research staff and confidentiality protections mitigated under-reporting of behaviors potentially perceived as undesirable.

Taken together, our findings provide an important picture of SSP utilization patterns among rural PWID in our 3-county area. Consistent use of the SSPs was evident among a substantial proportion of PWID interviewed as part of this study, speaking to the need for and viability of these programs in underserved communities. Given the multiple health and social vulnerabilities among this sample of PWID and the relative lack of access to health services for rural substance users, SSPs appear to be critical venues for the integration and expansion of prevention and health promotion services for this underserved population.⁶⁹ SSPs also appear well-positioned and viable as effective sites to deliver motivational enhancement and treatment linkage interventions.

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Table 1.

Sample Characteristics of SSP Attenders

		Total
		N (%)
		186 (100.0%)
Demographics		
Age:	<i>mean(SD)</i>	37.5 (9.41)
Gender:	Female	87 (46.8%)
Race/ethnicity:	non-Hispanic White	172 (92.5%)
Current Medicaid coverage:	Yes	146 (78.5%)
Site:	Site A	86 (46.2%)
	Site B	61 (32.8%)
	Site C	39 (21.0%)
SSP Uptake		
SSP visits (past 6 months): 1–5		98 (52.7%)
	6 or more	83 (44.6%)
Duration of SSP participation:	Less than 1 month	71 (38.2%)
	1–5 months	62 (33.3%)
	6 or more months	53 (28.5%)
Health		
Health problem interference (past 90 days)		114 (61.3%)
Severe mental distress (past 90 days)		146 (78.5%)
Violent victimization (past 90 days)		44 (23.7%)
Social support:	low	45 (24.2%)
	medium	50 (26.9%)
	high	91 (48.9%)
Substance Use		
Primary drug of injection:	heroin	30 (16.1%)
	methamphetamine	84 (45.2%)
	non-prescribed buprenorphine	48 (25.8%)
	non-prescribed opioids	21 (11.3%)
Substance Related Problems		
.Severe substance use disorder (past 90 days)		123 (66.1%)
Drug overdose (lifetime)		70 (37.6%)
Motivation to Change Substance Use		
Importance of Reducing Substance use:	low	23 (12.4%)
	medium	33 (17.7%)
	high	130 (69.9%)
Confidence in Reducing Substance use:	low	42 (22.6%)
	medium	53 (28.5%)

	high	90 (48.4%)
Substance Use Treatment		
Treatment participation (past month)		39 (21.0%)

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Table 2.

Logistic Regression Models Examining Current Substance Use Treatment Participation among SSP Attenders, Kentucky, 2018

Current Substance Use Treatment (N=186)		Unadjusted OR (95%CI)	Adjusted OR (95%CI)
Demographics			
Age		1.002 (0.965–1.040)	1.002 (0.958–1.048)
Gender ^a		1.104 (0.544–2.237)	1.249 (0.554–2.817)
Race/ethnicity ^b		0.766 (0.197–2.981)	.867 (0.190–3.956)
Current Medicaid coverage ^c		3.055 (0.876–10.648)	2.980 (0.788–11.264)
Site ^d :	Site B	1.521 (0.650–3.561)	1.246 (0.433–3.584)
	Site C	2.808 (1.153–6.834)*	2.676 (0.895–8.004)
SSP Uptake			
SSP visits (past 6 months) ^e	6+	2.121 (1.022–4.403)*	1.368 (0.557–3.362)
Duration of SSP participation ^f :	1–5 months	1.779 (0.727–4.355)	-----
	6 or more months	2.408 (0.982–5.904)	-----
Health			
Health problem interference (past 90 days) ^c		1.164 (0.559–2.422)	-----
Severe mental distress (past 90 days) ^c		0.529 (0.239–1.172)	-----
Violent victimization (past 90 days) ^c		0.650 (0.265–1.597)	-----
Social support ^g :	medium	0.881 (0.301–2.581)	-----
	high	1.564 (0.637–3.842)	-----
Substance Use			
Primary drug of injection ^c :	heroin	1.179 (0.465–2.992)	-----
	methamphetamine	0.398 (0.185–0.859)*	0.341 (0.146–0.798)*
	non-prescribed buprenorphine	1.660 (0.744–3.443)	-----
	non-prescribed opioids	2.078 (0.775–5.570)	-----
Substance Related Problems			
Severe substance use disorder (past 90 days) ^h		1.393 (0.642–3.024)	-----
Drug overdose (lifetime) ^c		1.045 (0.506–2.162)	-----
Motivation to Change Substance Use			
High Importance of Reducing Substance use ⁱ		2.286 (0.942–5.548)	-----
High Confidence in Reducing Substance use ⁱ		2.562 (1.221–5.380)*	2.241 (1.002–5.009)*

^a ref group is male/other;

^b ref group is non-white;

^c ref group is no;

^d ref group is site A;

^e ref group is <6;

^f ref group is < 1 month;

^g ref group is low;

^h ref group is none/minimal/moderate;

ⁱ ref group is low/medium;

* $P < .05$.

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