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Developing a Scale of Domains of Negative Consequences of Chronic Heroin Use

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Abstract

Background—Chronic use of heroin typically leads to numerous negative life consequences and serious clinical impairment. Increased negative consequences can result in poor treatment outcomes as well as adverse health effects and impaired social functioning. Certain risk factors, including early substance use initiation, concurrent use of other illicit substances, and injection drug use are associated with an increase in negative consequences. This study examined whether there are unique domains of heroin consequences and, if so, whether these domains are related to specific substance use characteristics.

Methods—Data regarding substance use characteristics were collected from 370 non-treatment seeking, heroin-using, 18 to 55 year-old participants from the Detroit metropolitan area. Principal component analysis (PCA) was used to analyze the factor structure of 21 negative heroin consequence items.

Results—PCA demonstrated that heroin consequences could be divided into 5 unique domains. These unique domains were related to specific substance use characteristics and heroin consequence domains. Injection heroin use was significantly associated with increased *Factor 1* consequences (primarily acute medical problems) but not with consequences in other domains. Certain substance use characteristics, such as injection status and earlier onset of marijuana use, were associated with increased consequences in specific domains.

Conclusions—These findings support the existence of unique domains of negative consequences, and indicate that some risk factors (e.g. injection use) may be specific to these

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domains. Potential tailored-treatment strategies aimed at improving treatment engagement and reducing harm for heroin use based on person-specific risks and negative consequences are discussed.

Keywords

Heroin; consequences; injection; harm reduction; scale development

1. Introduction

More than a half million Americans have a diagnosable heroin use disorder (Center for Behavioral Health Statistics and Quality, 2014). Adverse consequences from using heroin and other opioids include problems in health, legal, psychosocial and financial domains (Degenhardt & Hall, 2012; Kronenberg et al., 2014; Oviedo-Joekes et al., 2011; Stone et al., 2012). Increased negative consequences from substance use are associated with worse treatment outcomes (Arias et al., 2008; Schellekens et al., 2015; Simpson et al., 1999), making it important to understand factors associated with specific negative substance use consequences.

Previous studies have examined overall negative consequences of drug use (Gil et al., 2004; Kronenberg et al., 2014) and the impact of specific aspects of drug use (e.g. injection use) on a broad category of consequences (e.g., health) (Darke & Hall, 2003), but few have examined effects of drug use on specific areas of life functioning (Stein et al., 1987). We found no study establishing empirically distinct domains of substance use consequences (e.g. health, occupational, family) and their correlation with substance use characteristics. Nuanced understanding of an individual's specific impaired behavior may improve treatment planning and outcomes (Marsh et al., 2004; Marsh et al., 2009; Smith & Marsh, 2002).

The present study examined associations between heroin-use characteristics and consequences among a sample of community-recruited chronic heroin users. The Heroin Use Consequences scale (Woodcock et al., 2015a) was designed to assess heroin use-related sequelae within different domains (e.g., legal, health) and for specific events. We hypothesized that items on the scale could be empirically sorted into distinct domains and that unique substance-use characteristics would be associated with these domains. To test this hypothesis, we first used principal component analysis to determine empirically discrete areas of heroin consequences, and then we explored relationships between these domains and substance use characteristics previously associated with greater negative consequences of heroin use (e.g. injection use, polysubstance use, and early initiation into illicit substances).

2. Methods

2.1. Participant selection

Non-treatment seeking heroin users from the Detroit metropolitan region were recruited using newspaper advertisements and word-of-mouth for several behavioral pharmacology studies conducted from 2005 - 2015. All studies were approved by the local Institutional

Review Board and conducted in accordance with the Declaration of Helsinki (1964). Participants aged 18 to 55 who endorsed current heroin use during an initial phone screening were interviewed in-person. Participants were included in analyses if, at screening, they tested positive for opioid use (> 300 ng/ml), negative for alcohol (< .02%; Alco Sensor III Breathalyzer), and were cognitively intact as defined by a score > 80 on the Shipley Institute of Living Scale (Zachary, 1991).

2.2. Outcome measures

A standardized self-report instrument (Drug History and Use Questionnaire (DHUQ); available on request) was used to assess substance use characteristics including: use of other substances (alcohol, tobacco, marijuana, sedatives, cocaine), age of initiation of use, and whether these substances were used regularly (i.e. at least weekly). Injection use was defined as a binary lifetime variable (ever used: yes/no). Lifetime heroin use-related negative consequences were assessed using a drug-specific checklist of 21 item Heroin Use Consequences scale (HUC, Table 1; Woodcock et al., 2015a). Participants indicated whether they had (never [0] or ever [1]) experienced each consequence (e.g. overdose, missed work, financial problems related to drug use) as a *direct result of their heroin use*.

2.3. Data analyses

First, we conducted an exploratory principal component analysis (PCA) to analyze factor structure of the 21 HUC items. Components with eigenvalues > 1.0 were retained (Hair et al., 1995). For this exploratory analysis, no assumptions were made for the number of factors. The covariance matrix was Varimax rotated with Kaiser normalization. Item factor loadings > 0.4 were considered significant and retained. Variables that loaded on multiple factors were assigned to the factor with the highest loading value.

Second, bivariate correlations were used to examine statistical dependence between *age at initial use* of alcohol, tobacco, marijuana, cocaine, sedatives and heroin, and number of heroin consequences endorsed in each domain. Follow-up linear regressions were performed with *duration of heroin use* entered as a covariate to confirm any significant correlations.

Lastly, independent *t*-tests were conducted between categorical substance use characteristics (injection status, regular use of an additional substance) and number of heroin consequences endorsed in each domain.

Descriptive data are presented as mean \pm one standard deviation. Threshold for rejecting the null hypothesis was p < .05 for all significance testing. Non-normally distributed variables were transformed (log10 or square root) or coded into binary variables and analyzed using chi-square tests.

3. Results

3.1. Participant characteristics

Data from 370 heroin-using participants were included in the analyses. The modal participant was a 42.0±10.1 year-old African American (54.9%) male (70%) who had completed 12.3±1.7 years of formal education, initiated heroin use aged 24.2±8.0 years and

began regular use approximately 2 years later, aged 26.5 ± 8.1 years. The mean duration of regular heroin use was 15.4 ± 11.2 years, ranging from <1 to 40 years of heroin use. Two-thirds of the sample (68.4%) used heroin intravenously at least once. The mean number of heroin consequences endorsed for the sample was 8.1 ± 4.7 . Table 2 shows the substance use characteristics for the sample.

3.2. Heroin consequence domains

Exploratory PCA of the 21-item HUC scale identified one item ("fight or quarrel") that did not load significantly on any factor (< 0.4); this was removed from further analyses. The second PCA (20 items) derived five factors (eigenvalues > 1.0) that accounted for 59.3% of the total variance. The KMO test for sampling adequacy was met (KMO=0.859) and Bartlett's test of sphericity indicated the model was appropriate (χ^2 =2495.1; df=190; p<001). Table 3 depicts item loadings on each of the five factors (item loadings < 0.4 were suppressed).

Six items (visited the emergency room, overdose, health problems, accident or injury, arrested or legal problems, unexpected reaction) loaded on *Factor 1* and accounted for 29.3% of the total variance. Four items (lost job, warning at work, missed work, high at work) loaded on *Factor 2* and accounted for 10.1% of the total variance. Three items (missed school, high at school, suspended or expelled from school) loaded on *Factor 3* and accounted for 8.7% of the total variance. Four items (financial problems, family problems, drove under the influence, couldn't stop using) loaded on *Factor 4* and accounted for 5.8% of the total variance. Three items (seizure and fits, shakes and tremors, and memory lapse or blackout) loaded on *Factor 5* and accounted for 5.4% of the total variance.

3.3. Substance use characteristics and consequence domains

Next, we examined relationships between substance use characteristics previously found to be related to negative heroin consequences (e.g. route of administration, age of initiation (Gil & Wagner, 2004; Trenz et al., 2012)), and each PCA-derived consequence domain. *Factor 3* (high at school, missed school, suspended/expelled due to heroin use) was excluded from subsequent analyses because: 1) nearly all participants (91.8%) reported initial heroin use after their final year of formal education, and 2) infrequent item endorsement relative to other domains.

Participant age, age of initial and regular heroin use, and duration of heroin use did no t significantly relate to number of consequences endorsed in any domain (ps>.05); however, total number of heroin consequences (across domains) negatively related to current age (r=-0.12; p=.02), age of initial heroin use (r=-.24; p<.001), and age of regular use (r=-.27; p<.001). Total number of heroin consequences (across domains) was unrelated to duration of heroin use (p>.05).

Number of *Factor 1* items endorsed (visited emergency room, overdose, health problems, accident/injury, arrested/legal problems, unexpected reaction) significantly differed by heroin injection status (t(249)=3.49; p<.001), ever/never regularly using marijuana (t(331)=-2.50; p=.013), and ever/never regularly using sedatives (t(212)=2.31; p=.02). Individuals who had ever injected heroin endorsed more *Factor 1* consequences (1.84±1.80;

n=252) than those who denied ever injecting (1.22 ± 1.43 ; n=107). Individuals who reported lifetime regular marijuana use reported fewer $Factor\ 1$ consequences (1.60 ± 1.70 ; n=267) than those who denied regular marijuana use (2.20 ± 1.90 ; n=66). Individuals who reported lifetime regular, recreational (non-prescribed) sedative use had more $Factor\ 1$ consequences (1.88 ± 1.81 ; n=112) than those who denied regular recreational sedative use (1.40 ± 1.50 ; n=149). $Factor\ 1$ consequences were not correlated with earlier first use of any substance. There were significant race differences in $Factor\ 1$ consequences (n=360; t(358)=2.31; p=.022): Caucasians reported significantly more consequences (n=1.88; SD=1.80; n=159) than African Americans (n=1.46; n=201) and were more likely to have reported injecting heroin than African Americans (n=201). Nearly all Caucasians (94.9%) reported a history of injection heroin use, compared to 50.7% of African Americans.

Factor 2 (lost job, warning at work, missed work, high at work) heroin use consequences were associated with earlier first age of marijuana use (r=-.097; p=.02) and lifetime regular marijuana use (t(331)=-2.17; p=.031 [log₁₀]). Individuals who began using marijuana earlier reported more Factor 2 consequences, while those who endorsed lifetime regular marijuana use had fewer Factor 2 consequences (M=1.79; SD=1.60; n=267) than those who denied regular marijuana use (M=2.36; SD=1.71; n=66).

Factor 4 (financial problems, family problems, drove under the influence, and couldn't stop using) consequences followed a similar pattern to Factor 2 consequences. Earlier age of first marijuana use was associated with more heroin use consequences (r=-.105; p=.02). To appropriately analyze the relationship between lifetime regular use of marijuana and Factor 4 heroin consequences, total consequences were re-coded as a binary variable (endorsing all 4 Factor 4 consequences versus endorsing 0-3 consequences). Lifetime regular marijuana use was associated with decreased endorsement of all Factor 4 consequences (χ^2 =5.20; p=.023). Individuals who reported lifetime regular marijuana use showed fewer Factor 4 consequences (M=3.19; D=1.15; D=1.15;

Factor 5 consequences (seizure and fits, shakes and tremors, memory lapse or blackout) were not correlated with any of substance use characteristic examined. None of the factor scores was significantly related to age of first alcohol, cocaine or heroin use, or regular use of alcohol or cocaine.

4. Discussion

Our previous work examined relationships between heroin use and total scores on the HUC scale (Woodcock et al. 2015a, 2015b). The present study empirically disaggregated the consequence scale by identifying five separate heroin use consequence domains (Table 3).

Factor 1 (6 items) explained the most variance. Five of these consequences are acute health problems. "Arrested or legal problems" is distinct as the only non-health item; we hypothesize a heroin user experiencing these acute health consequences may be more likely to interact with law enforcement officials, e.g., a participant who endorsed heroin-related "accident or injury" might also endorse arrest/legal problems if police discover s/he was

'high'. Legal problems may also relate to severity of use among individuals who endorsed more consequences. *Factor 1* (unlike other domain) scores were uniquely related to two substance use characteristics: injection drug use and regular sedative use. Neither finding is surprising considering established associations between injection drug use and negative health consequences (Darke & Hall, 2003; Trenz et al., 2012) and negative health outcomes (e.g. overdose, death) associated with concurrent use of opioids and sedatives (Overdyk et al., 2016; Park et al., 2015).

Factor 2 (four employment-related problems) explained the second largest share of variance. Factor 3 consequences included all school-related consequences. It is noteworthy that due to age of heroin use initiation of our participants, very few endorsed Factor 3 consequences, thus we are underpowered to make further conclusions about these consequences.

Factor 4 encompasses a broader category of impulse control and psychosocial function. Interestingly, financial problems did not load on employment-related consequences but instead on this factor, suggesting poor self-control (i.e., inability to stop using). Possibly these financial problems are tied to impulsivity—e.g., heroin overspending (Roddy & Greenwald, 2009; Roddy et al., 2011)—than to losing employment income due to heroin use. Similarly, driving under the influence of heroin did not load on the same factor as legal problems or accident/injury, again suggesting relatedness to impulse control. Furthermore, all four Factor 4 items were the most commonly endorsed items. Higher Factor 2 and Factor 4 heroin-consequence scores were both related to earlier marijuana onset, consistent with findings that early onset of marijuana use is an indicator for problem behaviors including substance use disorders in adulthood (Grant et al., 2010). Research also suggests early substance use initiation (e.g. marijuana) may be related to deficient inhibitory control (De Bellis et al., 2013; Smith et al., 2014; Zulauf et al., 2014). This deficit may explain increased consequences specifically in these behavioral domains.

Contrary to expectations, lifetime regular marijuana use correlated with fewer heroin consequences (a seemingly protective effect) on *Factors 1, 2*, and *4*. Although interpretation of this finding is unclear, some alternative hypotheses for future testing are that regular marijuana use (1) is a proxy for self-medication of comorbidities (psychiatric problems, pain) that could buffer heroin use and its sequelae, and (2) alleviates heroin withdrawal and may reduce heroin use that leads to overdose or other consequences.

Factor 5 consequences explained the least variance. These items are health-related and reflect longer-term neurological problems. These items were independent from the acute health consequences in Factor 1. Notably, these three Factor 5 consequences were among the least-frequently endorsed items.

Factor 1 but not other domain scores showed racial (Caucasian vs. African American) differences. One explanation is the distribution of injection drug use between the two races: 94.9% of Caucasians reported a history of injection use, but only 50.7% of African Americans did. We found no other significant gender, age, or education-based differences in consequences endorsed in any domains. These preliminary findings suggest these consequence domains are consistent across gender, age, and educational background. Yet,

due to the confounding of race and injection status in our sample, further studies are needed to disentangle the relationship between race and *Factor 1* scores.

Duration of heroin use was not correlated with any factor scores, indicating there may not be consequence domains specific to prolonged heroin use. On the other hand, most participants were long-term heroin users; thus, a range restriction problem may prevent our detection of associations of consequences with duration of use. Although no relationships were found between earlier onset of heroin use (initial or regular) and any of the individual domain scores, an association was found between earlier heroin onset and total heroin-use consequences, consistent with Woodcock et al. (2015b). It is possible that our sample was underpowered to sufficiently examine this at the individual domain level.

Next, we provide suggestions for incorporating this brief self-report screening measure into clinical practice, and for tailoring treatment plans and harm-reduction strategies specific to an individual's heroin-use consequence profile. The value of these findings lies in the ability to generate profiles of individual dysfunction such that resources can be focused to maximize likelihood of treatment success. The HUC scale could be used to guide development of personalized treatment plans targeted at specific domains of dysfunctional behavior.

Factor 1 scores reflect the extent of immediate health consequences from heroin use. The substance use characteristic most strongly related to these consequences was injection heroin use. Prior research has demonstrated that intravenous heroin use is associated with bloodborne infections, collapsed veins, and abscesses (Cooper et al., 2005; Hall & Henry, 2007; Rhodes et al., 2007). Targeted therapeutic interventions could focus on needle exchange programs and supervised injection rooms that can reduce health-related risks of injection drug use and drug-related crime (Kerr et al., 2005; Vlahov et al., 1997; Watters et al., 1994; Wood et al., 2006). Notably, supervised injection facilities generally attract higher-risk injection drug users, which may significantly reduce the healthcare burden these users face (Wood et al., 2005). In theory, harm reduction education could focus on changing the route of administration from intravenous to non-parenteral; however, studies have found these interventions have limited efficacy (Darke & Hall, 2003; Swift et al., 1999). Findings of the present study concur with previous studies that a history of injection (v s. non-injection) drug use results in greater negative health consequences (Bonar & Bohnert, 2016; Fuller et al., 2002; Hakansson et al., 2008; Trenz et al., 2012). Despite this, injection heroin use was not associated with higher scores in other consequence domains. These findings are supported by treatment studies that found injection (vs other routes of) heroin use is not related to negative outcomes of methadone maintenance treatment (Fischer et al., 2008; Ledgerwood et al., 2017). This finding also supports theories underlying harm reduction efforts such as syringe exchange and naloxone distribution programs, as it suggests injection heroin use risks are related to injection specifically (putting individuals at increased risk of overdose and infection) rather than other aspects of heroin use.

Higher scores on *Factor 2* demonstrate greater instability with employment that, in turn, can lead to poor physical and mental health, as well as financial and housing instability (Benach et al., 2014; Vives et al., 2013; Desmond et al., 2016). Housing instability and

unemployment are known barriers to substance use treatment initiation and completion, especially for minority populations (Linton et al., 2013; Lister et al., 2017; Saloner & Lê Cook, 2013). It follows that individuals with financial consequences (from unemployment or increased spending on heroin) may benefit from non-abstinence-based housing programs, which have demonstrated efficacy for reducing substance use and retaining clients in stable housing (Collins et al., 2012; Padgett et al., 2011). One specific harm reduction program (*Housing First*) was associated with individual and societal and economic benefits by decreasing incarceration, shelter use, and emergency medical services (Larimer et al., 2009). Comprehensive case management may also prove effective for overcoming barriers by connecting financially-burdened people with services (e.g. housing and job training); use of case management during treatment has been shown to improve retention (Center for Substance Abuse Treatment, 2000; Laken & Ager, 2009).

Heroin users scoring higher on *Factor 4* will likely have inadequate social and financial support that is exacerbated (if not caused) by their drug use. They display less behavioral control through an inability to stop using heroin despite a potential desire to stop. Previous research indicates residential treatment reduced dangerous behaviors, decreased incarceration, and improved general functioning (Drake et al., 2008; Moggi et al., 1999; Sacks et al., 2004). Chronic heroin users have been found to have reduced impulse control (Pau et al., 2002), thus harm reduction efforts for those who experience demonstrable life problems associated with impulse control should focus on providing cognitive tools to help overcome potential behavioral disinhibition. Although treatments centered on social support systems benefit some populations (Latimer, 2003), those with social dysfunction may be unable to call on family/friends for effective support. Inadequate social support has been associated with shorter treatment retention (Chan et al., 2004), less drug abstinence (Salmon et al., 2000), and worse psychological well-being (Dodge & Potocky, 2000). Residential treatment may benefit individuals with poor social functioning and limited access to social support.

Factor 5 items reflect long-term neurological problems and deficits due to heroin use. Complications associated with neurological problems should be accounted for during treatment planning. Such symptoms may compromise an individual's ability to secure future employment and follow a treatment plan. Memory problems may compromise one's ability to participate in psychosocial treatment; in this population, treatment might focus more on behavioral than cognitive changes. Mitigating and managing these neurological symptoms should be a focus of treatment. Harm reduction efforts should focus on helping manage symptoms in daily life and on providing resources and support (i.e. case management) to help access available resources and adhere to the treatment plan.

Several limitations of this study should be considered. First, using self-report measures introduces potential recall bias for age of substance use, previous negative consequences, and substance abuse/dependence symptoms. Second, the data represent a cross-section of the non-treatment seeking heroin using population, prohibiting causal inferences. Third, these domains were created using one battery of items. While the DHUQ has been used in previous studies (Lister et al., 2015; Woodcock et al., 2015a, 2015b), future studies should confirm replicability of these consequence factors and clarify semantic definitions of these

factors. Finally, as noted, all heroin use consequence domains were positively correlated. Individuals who experienced heroin use consequences in one domain were more likely to experience consequences in other domains, which complicates interpretation of our analyses.

In summary, this initial study explored the validity of empirically derived subscales of some consequences of heroin use. Refinement of these domains may improve understanding of which drug-use characteristics and other factors (e.g., psychiatric diagnoses) exacerbate specific consequences, enabling us to predict challenges a person is most likely to experience that, in turn, could enable treatment providers to direct the patient to the most appropriate support and care (e.g., case manager to help manage housing difficulties). The Addiction Severity Index (ASI) is also an important measure to consider in further analyses of consequence domains. Although the ASI provides a more general context for domains of consequences it is not heroin specific, whereas the goal of this study was to focus on what can be isolated in terms of heroin consequences. Future studies should examine both ASI and consequence domains together.

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Highlights

- Negative consequences of heroin use can be empirically divided into 5 factors
- These 5 domains of heroin consequences have unique substance use profiles
- Injection heroin use was only associated with one domain of consequences
- Early onset of marijuana use was associated with two domains of consequences

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Table 1
21-Item Heroin Consequence List and Participant Item Endorsement (N=370)

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| Canacanana Itama | Samuela En dangament y (0/) |
|----------------------------|-----------------------------|
| Consequence Items | Sample Endorsement n (%) |
| Financial Problems | 331 (89.5%) |
| Drove Under Influence | 290 (78.4%) |
| Family Problems | 290 (78.4%) |
| Couldn't Stop Using | 278 (75.1%) |
| High at Work | 222 (60.0%) |
| Missed Work | 196 (53.0%) |
| Lost Job | 152 (41.1%) |
| Arrested or Legal Problems | 144 (38.9%) |
| Unexpected Reaction | 131 (35.4%) |
| Warning at Work | 119 (32.2%) |
| Overdose | 110 (29.7%) |
| Memory Lapse/Blackout | 109 (29.5%) |
| Fight or Quarrel | 109 (29.5%) |
| Visited Emergency Room | 103 (27.8%) |
| Shakes and Tremors | 92 (24.9%) |
| Health Problem | 80 (21.6%) |
| High at School | 73 (19.7%) |
| Missed School | 68 (18.4%) |
| Accident or Injury | 41 (11.1%) |
| Suspended or Expelled | 27 (7.3%) |
| Seizure or Fits | 21 (5.7%) |

Table 2 Substance Use Characteristics for Sample of 370 (means and standard deviation shown unless otherwise specified)

| | Tobacco | Alcohol | Marijuana | Cocaine | Heroin |
|-----------------------|-------------|-------------|--------------------------------------------------------------------|-------------|------------|
| Ever Used % (n) | 97.6% (361) | 94.1% (348) | 97.6% (361) 94.1% (348) 91.1% (337) 90.3% (334) 100% (370) | 90.3% (334) | 100% (370) |
| Regular Use % (n) | 93.2% (345) | 67.6% (250) | 93.2% (345) 67.6% (250) 72.4% (268) 49.5% (183) 100% (370) | 49.5% (183) | 100% (370) |
| Current Use % (n) | 81.4% (301) | 44.1% (163) | 81.4% (301) 44.1% (163) 38.9% (144) 53.0% (196) 100% (370) | 53.0% (196) | 100% (370) |
| Age of First Use | 15.6±4.9 | 14.6±4.5 | 15.0±3.5 | 24.4±7.8 | 24.2±8.0 |
| Age of Regular Use | 17.6±5.1 | 18.6±5.0 | 16.2±3.6 | 27.4±8.7 | 26.5±8.2 |
| Lifetime Consequences | 5.0±4.6 | 2.8±4.3 | 3.0±4.1 | 3.1±3.8 | 8.1±4.7 |
| Ouit Attempts | 3.4±8.5 | 1.4 ± 3.5 | 1.5 ± 6.2 | 5.6±14.3 | 9.4±17.2 |

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Rotated Components Matrix from Principal Component Analysis of 20 Heroin Consequences

| | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 |
|----------------------------|----------|----------|----------|----------|----------|
| Visited Emergency Room | 0.750 | | | | |
| Overdose | 0.701 | | | | |
| Health Problem | 0.645 | | | | |
| Accident or Injury | 0.642 | | | | |
| Arrested or Legal Problems | 0.527 | | | | |
| Unexpected Reaction | 0.467 | | | | |
| Lost Job | | 0.828 | | | |
| Warning at Work | | 0.773 | | | |
| Missed Work | | 0.742 | | | |
| High at Work | | 0.615 | | 0.444 | |
| Missed School | | | 0.890 | | |
| High at School | | | 0.877 | | |
| Suspended or Expelled | | | 0.754 | | |
| Financial Problems | | | | 0.791 | |
| Family Problems | | | | 0.676 | |
| Drove Under the Influence | | | | 0.613 | |
| Couldn't Stop Using | | | | 0.578 | |
| Seizure or Fits | | | | | 0.683 |
| Shakes or Tremors | | | | | 0.625 |
| Memory Lapse or Blackout | | | | | 0.531 |

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