A Longitudinal Study of Multiple Drug Use and Overdose Among Young People Who Inject Drugs

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Objectives. To determine the association between multiple drug use and nonfatal overdose among young people (younger than 30 years) who inject drugs.

Methods. We completed a longitudinal study of 173 injection drug users younger than 30 years living in San Francisco, California, between April 2012 and February 2014.

Results. The odds of nonfatal overdose increased significantly as heroin and benzodiazepine pill-taking days increased and when alcohol consumption exceeded 10 drinks per day compared with 0 drinks per day.

Conclusions. Heroin, benzodiazepine, and alcohol use were independently associated with nonfatal overdose over time among young people who inject drugs. Efforts to address multiple central nervous system depressant use remain an important component of a comprehensive approach to overdose, particularly among young people. (*Am J Public Health.* 2016;106:915–917. doi:10.2105/AJPH.2016.303084)

Deaths from drug overdose have been increasing for 2 decades,[1,2] and research indicates that prior nonfatal overdose is a strong predictor of future fatal overdose.[3] Correlates of overdose include young age,[3–5] non-White race/ethnicity,[6,7] female sex,[5,7,8] poverty,[9] homelessness,[4] reduced physiological tolerance[5] following incarceration, hospitalization and abstinence-based drug treatment,[4,8,10,11] frequency of use, and polysubstance use.[12] Years of potential life lost as a result of overdose are estimated at 18.3 in the United States,[13] making this an important topic for young people who inject drugs. However, overdose studies restricted to young people are rare and often cross-sectional.

We used follow-up data collected over 1.9 years to consider the effect of factors previously identified with overdose on nonfatal overdose risk estimated in longitudinal analyses among young people who inject drugs living in San Francisco, California.

METHODS

Between April 2010 and February 2014, individuals were recruited through street-based convenience sampling and screened for study participation in a young injection drug user's cohort study, known as the UFO ("U Find Out") Study. Eligibility criteria included being younger than 30 years, having injected drugs in the last 3 months, and having no immediate plans to leave San Francisco, California. Among 353 persons screened, 233 were enrolled into the cohort study.[14] Every 3 months, participants were reimbursed $25 for completing a 1- to 1.5-hour follow-up visit including an interviewer-administered questionnaire and HCV testing. Data for the current analysis were limited to interviews occurring after April 2012, a time during which detailed questions about the frequency of drug-using days were included in the study questionnaire (n = 173; Figure 1).

Self-reported nonfatal overdose in the past 3 months from opioids was defined as a loss of consciousness during which at least 1 intervention was attempted by a third party (e.g., naloxone or rescue breathing). We considered potential associations between overdose and several factors (Table 1). We used longitudinal logistic regression models fit by generalized estimating equations to estimate the effects of exposure variables on the population average of overdose. We deleted covariates from the full regression model if they did not contribute to its overall fit, resulting in a parsimonious model. We used Stata version 11.2[15] and SAS version 9.2[16] to perform statistical analyses.

RESULTS

Among the 173 study participants, 34% were female, 80% experienced recent homelessness, and the median age was 25 years (interquartile range = 23–27; Table A, available as a supplement to the online version of this article at http://www.ajph.org). During the 1.9-year study period, the median follow-up time was 9.3 months per participant, resulting in 674 study visits and 139.6 person-years of follow-up data; 81% of the participants completed at least 2 interviews.

The rate of nonfatal overdose was 19 per 100 person-years. In adjusted longitudinal analysis, the odds of nonfatal overdose during the prior 3 months increased 40% with every

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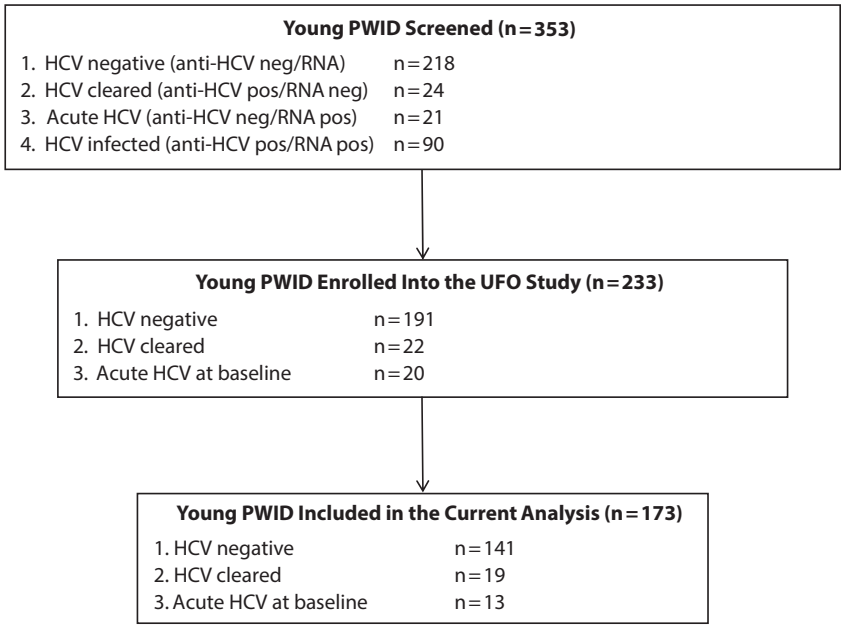

Note. PWID = people who inject drugs; UFO Study = "U Find Out" Study.

FIGURE 1—Study Flow Diagram of Young People Who Inject Drugs: San Francisco, CA, April 2010–February 2014

5 additional heroin injection days (adjusted odds ratio [AOR] = 1.40; 95% confidence interval [CI] = 1.22, 1.61), 22% with every 5 additional benzodiazepine pill-taking days (AOR = 1.22; 95% CI = 1.04, 1.43), and 4.5-fold when alcohol consumption exceeded 10 drinks per drinking day compared with 0 (AOR = 4.50; 95% CI = 1.77, 11.45; Table 1).

DISCUSSION

Nonfatal overdose increased as the ingestion of multiple central nervous system depressants (benzodiazepines and alcohol) increased. Factors associated with overdose in previous studies not restricted to young people, including race, sex, and methadone use, did not significantly predict nonfatal overdose in longitudinal analyses within this population of young people who inject drugs.

Consistent with findings presented here, nearly 30% of overdose deaths from a recent analysis of National Vital Statistics also involved benzodiazepines.[17] The phenomenon whereby benzodiazepines are rarely ascribed as the cause of death, but widely recognized as a potentiating substance identified at autopsy, has been noted since the early 1990s.[18,19] Taken together, results indicate that benzodiazepines continue to be an important contributor to overdose 2 decades later.

The continued increase in rates of illicit drug use and deaths from overdose are a public health problem,[1] particularly among young people who inject drugs.[12] Longitudinal findings regarding nonfatal overdose among community-recruited young people who inject drugs presented here support efforts to address use of multiple central nervous

TABLE 1—Longitudinal Associations Between Number of Drug Use Days and Nonfatal Overdose Among Young People Who Inject Drugs: San Francisco, CA, April 2012–February 2014

	Prevalence at Baseline, % (No) or Median (IQR)	Unadjusted OR[a] (95% CI)	Parsimonious Model,[b] AOR[a] (95% CI)
Alcoholic drinks on drinking days			
0	24 (41)	1 (Ref)	1 (Ref)
1–4	37 (64)	0.65 (0.28, 1.49)	0.63 (0.26, 1.52)
5–9	26 (45)	0.57 (0.19, 1.73)	0.75 (0.25, 2.26)
≥ 10	12 (21)	4.39 (1.84, 10.51)	4.50 (1.77, 11.45)
Drug-taking days			
Opioid pill-taking days[c]	0.5 (0–7)	1.15 (1.01, 1.32)	
Benzodiazepine pill-taking days[c]	0 (0–5)	1.23 (1.07, 1.43)	1.22 (1.04, 1.43)
Heroin-only (not mixed) injection days[c]	5 (0–20)	1.46 (1.28, 1.67)	1.40 (1.22, 1.61)
Amphetamine/speed-only (not mixed) injection days[c]	3 (0–10)	1.08 (0.90, 1.29)	
Cocaine-only (not mixed) injection days[c]	0 (0–0)	1.18 (0.52, 2.69)	
Crack only (not mixed) injection days[c]	0 (0–0)	1.10 (0.59, 2.04)	
Heroin + cocaine ("speedballs") injection days[c]	0 (0–0)	1.32 (0.86, 2.02)	
Methamphetamine + heroin ("goofballs") injection days[c]	0 (0–0)	1.47 (1.18, 1.84)	
No. of injections on an average day	3 (2–4)	1.18 (1.07, 1.30)	

Note. AOR = adjusted odds ratio; CI = confidence interval; IQR = interquartile range; OR = odds ratio. The sample size was n = 173.

[a]ORs obtained using generalized estimating equations.

[b]Only variables significantly contributing to the fit of the model are retained in the adjusted parsimonious model.

[c]Per 5 days.

system depressants as one arm of a comprehensive approach to overdose. AJPH

CONTRIBUTORS

E. D. Riley designed the analysis plan and led writing efforts. J. L. Evans contributed to the analysis plan, conducted all analyses, and contributed to multiple versions of this brief. J. A. Hahn and P. J. Lum contributed to the analysis plan, assisted with the interpretation of findings, and contributed to multiple versions of this brief. A. Briceno supervised all field operations and contributed to multiple versions of this brief. P. J. Davidson assisted with the interpretation of findings and contributed to multiple versions of this brief. K. Page was the study Principal Investigator, assisted with the interpretation of findings, and contributed to multiple versions of this brief.

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HUMAN PARTICIPANT PROTECTION

All research and informed consent protocols were approved by the institutional review board at the University of California, San Francisco.

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