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Alcohol and Drug Use and Aberrant Drug-Related Behavior Among Patients on Chronic Opioid Therapy

Cynthia I. Campbell^{a,b}, Andrea H. Kline-Simon^a, Michael Von Korff^c, Kathleen W. Saunders^c, and Constance Weisner^{a,b}

^aKaiser Permanente Northern California, Oakland, California, USA

^bDepartment of Psychiatry, University of California San Francisco, San Francisco, California, USA

^cKaiser Permanente Washington Health Research Institute, Seattle, Washington, USA

Abstract

Objective—To better identify individuals on chronic opioid therapy (COT) at high risk for aberrant-drug related behavior (ADRB). We examine whether patients with low level alcohol and drug use have similar characteristics to those with alcohol and drug disorders. We then examined the relationship of alcohol and drug use to ADRBs among COT patients.

Methods—The sample was 972 randomly selected COT patients (age 21–80 years old) from a large health system in Northern California, USA, and interviewed in 2009. Logistic regression models were used to model the dependent variables of: alcohol use, illicit drug use, alcohol disorders, illicit drug disorders, and ADRBs.

Results—The odds of daily/weekly alcohol use were lower for those with a high daily opioid dose (120 + mg/day vs. < 20 mg/day) (OR = 0.32, p < 0.010). Illicit drug disorders were associated with depression (OR = 2.31, *p* < .001) and being on a high daily opioid dose (OR = 5.51, *p* < .01). Participants with illicit drug use had higher odds of giving (OR = 2.57, *p* < 0.01) and receiving opioids from friends or family (OR = 3.25, *p* < 0.001), but disorder diagnoses were not associated with ADRBs.

Conclusions—Findings reinforce that illicit drug use should be of high concern to clinicians prescribing opioids, and suggest it should be considered separately from alcohol use and alcohol disorders in the evaluation of ADRBs. Frequent alcohol use is low, but not uncommon, and suggests a need to discuss specific issues regarding safe use of opioids among persons who use alcohol that may differ from their risk of drug use.

Keywords

Alcohol use; drug use; chronic opioid therapy; aberrant drug related behavior; alcohol disorder; drug disorder

Declaration of interest

Dr. Weisner and Ms. Kline-Simon have no conflicts to report.

CONTACT Cynthia I. Campbell, cynthia.i.campbell@kp.org, Division of Research, Kaiser Permanente Medical Care Program, 2000 Broadway, 3rd Floor, Oakland, CA 94612 USA.

Given the significant public health problem of prescription opioid abuse and overdose, there is considerable interest in better identifying individuals at risk of prescription opioid use problems (Boudreau et al., 2009; Braden et al., 2010; Dunn et al., 2010; Hall et al., 2008; Rudd, Aleshire, Zibbell, & Gladden, 2016). Aberrant-drug related behavior (ADRB) is defined variously as "patient practices that fall outside those usually expected in opioid treatment" (Larance, Degenhardt, Lintzeris, Winstock, & Mattick, 2011) and/or as behavior that raises the possibility of misuse (Argoff, Kahan, & Sellers, 2014; Cheatle et al., 2013), and is one way to identify patients with potential problems. ADRBs can reflect either poorly managed pain or problems with pain medication (e.g., misuse or diversion), and are typically recommended for inclusion in screening assessments as indicators of problems, given the difficulty of diagnosing opioid use disorder in those taking opioids for pain chronically using standard diagnostic criteria (Chou et al., 2009). No standard set of ADRBs exists in the literature, and they can range from requests for early refills to unauthorized dose escalation, borrowing or stealing medication from others, hoarding, aggressive complaining, and diversion (Chou et al., 2009; Hansen et al., 2011; Merlin et al., 2014).

Alcohol and drug use disorders are a major risk factor for predicting ADRBs (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008). A study of VA patients found substance use disorder to be related to borrowing opioid medication and requesting early refills compared to those without a substance use history (Morasco & Dobscha, 2008). In a community primary care sample, a history of substance use disorder was positively associated with physician identified aberrant behaviors (Cheatle et al., 2013). A study of primary care patients on daily opioid therapy found younger age, psychiatric severity, and four ADRBs associated with substance use problems (Fleming, Davis, & Passik, 2008).

Information about patients who use alcohol and drugs at lower levels is limited. Lower level alcohol use can put chronic opioid therapy (COT) patients at risk for adverse events (Saunders et al., 2012) and screening for unhealthy levels of alcohol use is recommended in primary care for even the general population (Jonas et al., 2012). Alcohol use, a central nervous system depressant, can exacerbate the depressant and sedation effects of prescription opioid use and places COT patients at higher risk of overdose and other adverse events (Hall et al., 2008; Saunders et al., 2012). There is no established 'healthy' level of illicit drug use, and screening for illicit drug use is recommended for patients on COT, given their higher risk profile (Chou et al., 2009). COT patients are more likely to have comorbid substance use and psychiatric problems, as well as poor health and functioning, thus even low levels of use may lead to worsened outcomes and adverse events (e.g. development of opioid use disorder or overdose) (Braden et al., 2009; Park et al., 2016; Ray et al., in press; Turner & Liang, 2015; Weisner et al., 2009). Our study objective was to examine whether characteristics of COT patients with lower levels of alcohol and drug *use* are similar to those of patients with alcohol and drug disorders, and whether the two groups exhibit similar ADRBs (Passik, Messina, Golsorkhi, & Xie, 2011).

We address gaps in the literature by examining lower levels of alcohol and drug use among COT patients, a topic which has received less attention and may represent a different patient risk profile. We first identify patient characteristics related to alcohol and drug use to determine if these patients represent a different population than one with disorder diagnoses

(abuse/dependence). We next examine the relationship of alcohol and drug use to ADRB measures, defined in this study as early refills, giving or receiving medication from others, and taking more than prescribed. We hypothesize that younger age, being male, having depression, and receiving a higher opioid dose will be related to greater risk of frequent alcohol use and illicit drug use (Braden et al., 2010; Edlund et al., 2010; Sullivan et al., 2010; Weisner et al., 2009). We expect alcohol and drug use to be associated with higher likelihood of engaging in ADRBs. Study findings will inform how to identify high-risk COT patients and how to manage their care, particularly before some patients advance to more significant substance use problems.

Methods

Study site

The CONsortium to Study Opioid Risks and Trends was a NIDA-funded study developed to improve understanding of COT for chronic non-cancer pain among adults in Group Health Cooperative (now Kaiser Permanente Washington Health Research Institute), and Kaiser Permanente of Northern California (KPNC) (Von Korff et al., 2008). The current study uses data from KPNC only (N = 972). KPNC is an integrated care delivery system with approximately 3.6 million members, covering 45% of the commercially insured population of the region. During the study period, 88% of members were commercially insured, 10% Medicare, and 2% Medicaid.

Survey

Eligible patients were between the ages of 21–80 and receiving COT at KPNC in 2009. Eligibility was determined using automated pharmacy and membership data: potential participants filled 10 prescriptions and/or received 120 days supply in a one-year period prior to the sample selection date, with at least 90 days between the first and last opioid dispensing. This threshold has been shown to predict high probability of sustained and frequent use of opioids (Von Korff et al., 2005). The study also required that patients were members of KPNC for at least one year prior to sampling. We excluded patients identified in the KPNC cancer registry (except for nonmelanoma skin cancer) or who had >2 cancer diagnoses in the electronic health record in the year prior to sampling.

Sample selection

Respondents were selected using stratified random sampling, with an equal number from three opioid dosage strata: Level 1 (1–49 milligrams per day morphine equivalents dose (MED)); Level 2 (50–99 milligrams per day MED); and Level 3 (100+ milligrams per day MED). The majority of COT opioid users receive relatively low dosage levels, thus oversampling higher dosage recipients ensured adequate numbers for analyses. Observations were then weighted by the inverse probability of selection within strata to be representative of the population of COT users from which they were drawn.

Recruitment and interview

Interviews were conducted between January through October 2009. Research staff sent invitational letters to eligible individuals explaining the study and a toll-free number to

contact the study for more information or to decline participation. A \$5 gift card was included. Experienced study interviewers obtained verbal consent from patients, and completed a 45-minute phone interview using Computer-Assisted Telephone Interview technology. Participants were compensated with a \$50 gift card. The total number of completed interviews was 972, with a response rate of 65%. All study protocols were approved by the KPNC Institutional Review Board. All study measures used the survey data, with the exception of prescription opioid use and the alcohol and drug disorder measures which were extracted from KPNC's electronic health record.

Electronic data

KPNC's electronic health record data includes pharmacy and medical encounter data, including encounters with external providers through claims. Pharmacy files contain generic drug name, strength, directions for use, date dispensed, quantity dispensed, days supply, prescriber identification number, and National Drug Code. Surveys at KPNC have consistently found that over 90% of patients obtain their prescription medications through health plan pharmacies (Selby et al., 2005).

Measures

Outcomes—The *frequency of alcohol use* was measured in the prior 3 months using the categories: never, 1 or 2 times, monthly, weekly, daily/almost daily. We were interested in frequent alcohol users since they may be more likely to experience problems with concurrent opioid use. We created a dichotomous measure representing "daily/weekly" use vs. less frequent use; daily/almost daily users comprised 40% of the frequent use group. *Illicit drug use* was measured with the NIDA Modified Assist 2.0 (National Institute on Drug Abuse, 2012) and indicated use in the 3 prior months of: cannabis, cocaine, stimulants, inhalants, tranquilizers, hallucinogens, opioids, and other drugs. Interviewers clarified to respondents that we were asking about non-medical use of prescribed medications.

Alcohol and drug disorder (abuse/dependence) ICD-9 diagnoses were extracted from the electronic health record. A participant was coded as having alcohol or drug disorder (abuse/ dependence) if they had received a diagnosis in the 3 years prior to the survey.

We also examined four dichotomous measures of ADRBs: "gave opioid to friend or relative in the last year", "was given opioids from friend or relative in the last year", "# of times asked for early refill in the last year", and "the frequency of taking more opioid medication than prescribed in last 2 weeks" (Fishbain et al., 2008; Passik et al., 2011). These measures were selected based on what was considered important in the literature, and what was available from the survey data.

Predictors: *Demographic* variables include gender, age (21–43; 44–64; 65+), and education (college vs. not). *Pain intensity* was measured by averaging responses to three pain intensity items: pain right now, usual pain and worst pain. Items range from 0–10, resulting in a combined and averaged 0–10 score. *Depression* was measured by the 8-item version of the Patient Health Questionnaire (PHQ), a validated and widely used self-report measure of depression (Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012). Scores greater than

or equal to 10 were classified as depression based on prior research (Kroenke et al., 2009). *Average daily opioid dose* was grouped into 4 categories: <20 mg/day, 20–50 mg/day, 50–120 mg/day, and 120+ mg/day, and were converted to morphine equivalents (Saunders et al., 2012; Von Korff et al., 2011).

Data analysis

Pearson chi-square analyses were used to examine relationships between categorical predictors and outcomes of daily/weekly alcohol use, illicit drug use, alcohol and drug diagnoses, and the ADRB measures. ANOVA models were used to examine relationships between continuous predictors. We conducted multivariate logistic regression models to examine the associations between outcome measures (daily/weekly alcohol use, illicit drug use, alcohol disorder, drug disorder, and ADRBs) and patient characteristics: gender, age, education, average pain intensity, opioid dose category, and depression. Daily/weekly alcohol use was a covariate in the illicit drug use model; similarly, illicit drug use was a covariate in the illicit drug disorder was a covariate in the illicit drug disorder was a covariate in the illicit drug disorder was a covariate in the alcohol disorder model; similarly illicit drug disorder was a covariate in the alcohol disorder model. Alcohol and drug use were included in the models of ADRBs. Methods for stratified random samples were used to obtain unbiased estimates using the SAS SURVEY PROC procedures (SAS Institute Inc., 2011).

Results

Descriptive characteristics

The sample was predominately female (63%), college educated (60%), middle aged (56% aged 45–64) and consisted of Hispanics (11%), African Americans (10%), whites (76%), and other reported race/ethnicities (3%). The average pain intensity score was 7 (SD = 1.5) and 32% used <20 mg/day of opioid medication, 32% used 20-<50 mg/day, 19% used 50-<120 mg/day and 16% used 120+ mg/day and 45% met depression criteria. Fourteen percent of the sample had daily/weekly alcohol use in the prior 3 months; 16% used illicit drugs in the prior 3 months. The use and disorder groups were not mutually exclusive; 9% had an alcohol disorder diagnosis in the 3 years prior to the survey; 32% of those also drank daily/ weekly in the past 3 months. Fourteen percent of the sample had an illicit drug disorder diagnosis; 38% of those also reported illicit drug use in the past 3 months (data not shown).

Descriptive characteristics by outcome measures

There were fewer women (p < .001), and lower average reported pain intensity (p < .001) in the daily/weekly alcohol use group compared to the less frequent alcohol use group (Table 1). There were more low opioid dose patients and fewer high dose patients in the daily/ weekly alcohol use group compared to the less frequent use group (p < .001). Similar to alcohol use, fewer women than men reported using illicit drugs in the prior 3 months (p < .005). More middle age patients and fewer older patients had used illicit drugs, compared to those same age groups who had not used illicit drugs (p < .001). Fewer women than men had a documented alcohol disorder diagnosis (p < .05). Fewer older (65+) than younger patients had a documented drug disorder, (p < .001). More patients on a high (120+ mg) vs. lower

daily dose (p < .001) and more with depression than no depression (p < .001) had a drug disorder diagnosis.

Descriptive characteristics for ADRBs are reported in Table 2. More middle-aged patients (p < .05) and fewer college educated patients vs. college educated (p < .05) received opioids from friends or family. More whites gave and received more opioids than other race/ ethnicity groups (p < .01). More participants who were middle aged (p < .001), had depression (p < .001) and had a low (20– 50 mg) or high (120+mg/day) opioid dosage (p < .001) asked for early refills. Fewer women (p < .05) and fewer college educated patients asked for early refills (p < .05). More depressed patients (p < .01), younger patients (p < .001), and patients with higher average pain intensity scores (p < .001) took more opioids than prescribed.

Multivariate analyses of alcohol use and alcohol disorder

Multivariate models indicated that women (p < .05), those reporting greater pain severity (p < .001) and those on a high daily opioid dose (120+mg vs. <20 mg) (p < .01) had lower odds of *daily/weekly alcohol use*. Participants using illicit drugs had higher odds of daily/weekly alcohol use (p < .05). In the model of *alcohol disorder* diagnosis in the prior 3 years, women (p < .05) and participants aged 21–44 (p < .01) had lower odds of having an alcohol disorder diagnosis, while those with an illicit drug diagnosis had higher odds (p < .001) (Table 3).

Multivariate analyses of drug use and illicit drug disorder

Participants aged 45–64 had five times the odds of *using illicit drugs* compared to those aged 65 and older (p < 0.001). Women were less likely to report illicit drug use (p < 0.05). Those who used alcohol daily/weekly had almost 2 times the odds of illicit drug use in the past 30 days (p < .05). In the model of illicit *drug diagnosis*, college educated participants had lower odds of having a drug diagnosis (p < .05) while younger participants (p < .01) and those with: an alcohol disorder diagnosis (p < 0.001), depression (p < .001) and a higher daily opioid dose (p < .01) had higher odds of having a drug diagnosis (Table 4).

Aberrant drug-related behaviors

In bivariate analyses, two of the four *ADRBs* were significantly related to alcohol and drug use: receiving opioids from family/friends and giving opioids to family/friends (results not shown). These two measures were subsequently analyzed in the multivariate models. Participants who used illicit drugs had higher odds of *receiving opioids from friends or family* (p < .001), and of *giving opioids to friends or family* (p < .01) (Table 5). Younger participants, aged 21–44, had higher odds of *receiving opioids from friends or family* compared to those aged 65 and older (p < .05). However, those aged 45–64 had 37% lower odds of *receiving opioids from friends or family* (p < .001).

We also examined models of ADRBs substituting alcohol and drug disorders for alcohol and drug use; neither substance use disorder variable was significantly related to giving or receiving opioids (results not shown).

Discussion

Patients in this COT sample reported high enough levels of alcohol and/or illicit drug use to be a concern, with more patients using illicit drugs than engaging in frequent alcohol use. Women were less likely to use alcohol frequently or illicit drugs, as has been found in other studies. Among those using alcohol and/or drugs, polysubstance use was common, with frequent alcohol use associated with illicit drug use.

Multivariate models showed that alcohol use predicts illicit drug use and vice versa, but with the exception of gender, different characteristics predicted alcohol use and illicit drug use, suggesting different risk factors. Those with depression were no more likely than those without to use alcohol or illicit drugs, although they were more likely to have an illicit drug disorder. The hypothesis that depression would be correlated with alcohol or illicit drug use was largely not supported. Prior research has consistently supported a higher risk of depression among those with substance use disorders (Conway, Compton, Stinson, & Grant, 2006; Volkow, 2004), including those with opioid use misuse (Saha et al., 2016). The lack of a finding in our study could be due to our measures reflecting lower levels of use, although there was no relationship to alcohol disorder diagnosis either, only for drug disorders, reflecting greater complexity for those patients. The comorbid relationship of depression and alcohol or drug use may be different in COT patients who are often chronically ill with multiple conditions, and who may be conservative about using alcohol or illicit drugs, especially if using medications for other chronic conditions.

There is concern that patients may use alcohol as a self-medication strategy to control pain or to address other associated health problems such as insomnia (Jakubczyk et al., 2016; National Institute on Alcohol Abuse and Alcoholism, 2013; Witkiewitz et al., 2015; Woodrow & Eltherington, 1988). There is evidence to support this self-medication hypothesis (Brennan, Schutte, & Moos, 2005; Riley & King, 2009), although a recent study showed that men who reported pain at baseline experienced declining alcohol use over 10 years, compared to men who did not experience pain (Bobo, Greek, Klepinger, & Herting, 2013). Our own findings were consistent with this latter research, with those with more severe pain being less likely to drink daily/weekly, suggesting these patients were not selfmedicating for pain, at least in terms of frequent use which would be among the most risky behavior.

We also observed that those on high daily dosages of opioids were less likely to drink alcohol frequently, which is consistent with our finding. High dose patients may also be more aware and concerned about overdose risk and thus conservative in their alcohol use relative to patients on lower doses. There is also the possibility that risks of overdose may be underappreciated by lower dose patients. While frequent drinking is not typical, it remains an issue for some patients (Saunders et al., 2012), and often is not routinely addressed in medical encounters. Given the known risks of concurrent use with prescription opioids, such as overdose and addiction (Dunn et al., 2010; Saunders et al., 2012), regular screening for alcohol use is critical in this population (Chou et al., 2009).

The middle-age group remained at higher risk of using illicit drugs compared to older patients. Contrary to our hypothesis, the younger age group was not at higher risk for illicit drug use, although there was a greater risk for drug disorder, which is consistent with the literature. However, those in middle age were at higher risk for any use. Although younger patients are typically focused on as high risk, study findings suggest those in middle age may also benefit from education and monitoring.

Overall, we found modest overlap between the patient group who use and those with diagnosed disorders, reflecting that these may be different patient populations who need different management. We also observed modest differences in the models of disorders and models of alcohol and drug use, including that those with disorders are more likely to have a comorbid alcohol or drug use disorder. Those at lower but risky levels of alcohol use may benefit from a brief intervention in primary care, with continued monitoring. COT patients may need ongoing education around the risks of alcohol use. Patients with disorders should receive more specialized substance use services. Physicians and other providers may have opportunities to provide these services or motivate patients for referral given their regular contact around prescriptions.

While patients with disorders should be tapered from their opioids, it is perhaps less clear what the course of action is for patients with lower levels of use and providers will have to carefully weigh the risks and benefits for these patients (Dowell, Haegerich, & Chou, 2016). For example, some patients will use marijuana to manage pain, which can present a dilemma for providers since patients may feel it is helping and the use of marijuana is becoming more normalized. Patients who are identified as using illicit drugs may lose access to their opioids, particularly as the prescribing environment becomes more conservative.

Findings related to ADRBs suggest different relationships to alcohol and illicit drug use. Illicit drug use was associated with giving or receiving prescription opioids, but alcohol use was not, suggesting patients who use illicit drugs need a higher level of monitoring. Younger patients were more likely to receive opioids from family/friends, and those in middle age less likely, compared to older patients. Younger individuals may have a bigger network from which to obtain opioid medications, or may feel more willing to seek them from their social network. Middle-aged patients may be more aware of guidelines and/or less concerned about cost, relative to older patients. They may also be more likely to get them from their physician than older patients, who are likely taking other medications as well.

Overall, the disorder diagnoses were not associated with ADRBs. Although this is inconsistent with some of the literature, a previous study (Passik et al., 2011) found those with a history of substance abuse were less likely to display ADRBs than those without, similar to our findings for diagnosed disorders. Our survey measures represent more current use while the disorder diagnoses reflect a wider timeframe, and it could be that timing of use is a salient factor. Those with a history of substance abuse may be more cautious if they are in recovery. Our measures of ADRB may be imprecise in what they are measuring, for example they may reflect problems with pain control and not misuse, but findings also suggest different groups exhibit these behaviors for alcohol and drug use, as well as for diagnosed disorders.

Limitations

Findings should be viewed in the context of study limitations. The study was conducted in an integrated health care delivery system, and findings may not be generalizable to other populations (e.g., uninsured or publicly insured populations). It included measures of drinking frequency but not quantity of alcohol and drug use, thus the amount consumed cannot be measured or standardized. The response rate for the study was 65% and it is possible that responders and non-responders differed, although the age distribution was the same in both groups. The measures of ADRBs should be considered indicators of possible opioid misuse, and there is no consensus on what constitutes an ADRB. We selected measures examined in past research (Fishbain et al., 2008; Fleming et al., 2008). Finally, the pharmacy data represent opioid use dispensed, not actually consumed, although dispensation data are frequently used in the literature (Boudreau et al., 2009; Von Korff et al., 2008).

Conclusions

Illicit drug use was associated with higher opioid dose and sharing prescription opioids with others, whereas frequent alcohol use or an alcohol use disorder was not. Results suggest that illicit drug use should be considered separately from level of alcohol use and alcohol disorders in the evaluation of risks of aberrant behavior. Although frequent alcohol use was low, it was not uncommon, and there is a need to discuss specific issues regarding safe use of opioids among persons who use alcohol that may differ from their risk of drug abuse.

Patients with alcohol and drug disorders have been found to be more likely to be on COT and at higher dosages (Weisner et al., 2009). The high risk for adverse events, combined with weak evidence for the benefits of long-term opioid use, has resulted in closer screening and monitoring, and initiatives directed at more appropriate prescribing (Trescott, Beck, Seelig, & Von Korff, 2011; Von Korff & Dunn, 2008). Risk assessment falls largely to primary care physicians who prescribe the majority of prescription opioids, and face challenges in managing this often complex patient population. The reclassification of hydrocodone products to Schedule II (Drug Enforcement Administration & Department of Justice, August 22, 2014) and more restrictive prescribing policies may lead to the use of other substances such as heroin (Hedegaard, Chen, & Warner, 2015; Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2014; Unick, Rosenblum, Mars, & Ciccarone, 2013), making research in this area critical. Patients with alcohol and drug use problems continue to need pain relief. Additional research on strategies for monitoring high risk use (Trescott et al., 2011) is important to further inform how to provide appropriate and compassionate pain management to high risk patients.

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References

- Argoff CE, Kahan M, Sellers EM. Preventing and managing aberrant drug-related behavior in primary care: Systematic review of outcomes evidence. Journal of Opioid Management. 2014; 10(2):119–134. [PubMed: 24715667]
- Bobo JK, Greek AA, Klepinger DH, Herting JR. Predicting 10-source alcohol use trajectories among men age 50 sources and older. American Journal of Geriatric Psychiatry. 2013; 21(2):204–213. [PubMed: 23343494]
- Boudreau D, Von Korff M, Rutter CM, Saunders K, Ray GT, Sullivan MD, Weisner C. Trends in longterm opioid therapy for chronic non-cancer pain. Pharmacoepidemiology and Drug Safety. 2009; 18(12):1166–1175. [PubMed: 19718704]
- Braden JB, Russo J, Fan MY, Edlund MJ, Martin BC, DeVries A, Sullivan MD. Emergency department visits among recipients of chronic opioid therapy. Archives of Internal Medicine. 2010; 170(16):1425–1432. [PubMed: 20837827]
- Braden JB, Sullivan MD, Ray GT, Saunders K, Merrill J, Silverberg MJ, Von Korff M. Trends in longterm opioid therapy for noncancer pain among persons with a history of depression. General Hospital Psychiatry. 2009; 31(6):564–570. [PubMed: 19892215]
- Brennan PL, Schutte KK, Moos RH. Pain and use of alcohol to manage pain: Prevalence and 3-source outcomes among older problem and non-problem drinkers. Addiction. 2005; 100(6):777–786. [PubMed: 15918808]
- Cheatle MD, O'Brien CP, Mathai K, Hansen M, Grasso M, Yi P. Aberrant behaviors in a primary carebased cohort of patients with chronic pain identified as misusing prescription opioids. Journal of Opioid Management. 2013; 9(5):315–324. [PubMed: 24353044]
- Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: Prediction and identification of aberrant drug-related behaviors: A review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. Journal of Pain. 2009; 10(2):131–146. [PubMed: 19187890]
- Conway KP, Compton W, Stinson FS, Grant BF. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of Clinical Psychiatry. 2006; 67(2):247–257. [PubMed: 16566620]
- Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain–United States, 2016. Journal of the American Medical Association. 2016; 315(15):1624–1645. [PubMed: 26977696]
- Drug Enforcement Administration, & Department of Justice. Schedules of controlled substances: Rescheduling of hydrocodone combination products from Schedule III to Schedule II. Federal Register. 2014 Aug 22; 79(163):49661–49662. Retrieved from: http://www.gpo.gov/fdsys/pkg/ FR-2014-08-22/pdf/2014-19922.pdf. [PubMed: 25167591]
- Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Von Korff M. Opioid prescriptions for chronic pain and overdose: A cohort study. Annals of Internal Medicine. 2010; 152(2):85–92. [PubMed: 20083827]
- Edlund MJ, Martin BC, Fan MY, Devries A, Braden JB, Sullivan MD. Risks for opioid abuse and dependence among recipients of chronic opioid therapy: Results from the TROUP study. Drug and Alcohol Dependence. 2010; 112(1–2):90–98. [PubMed: 20634006]
- Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. Pain Medicine. 2008; 9(4):444–459. [PubMed: 18489635]
- Fleming MF, Davis J, Passik SD. Reported lifetime aberrant drug-taking behaviors are predictive of current substance use and mental health problems in primary care patients. Pain Medicine. 2008; 9(8):1098–1106. [PubMed: 18721174]
- Grattan A, Sullivan MD, Saunders KW, Campbell CI, Von Korff MR. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. Annals of Family Medicine. 2012; 10(4):304–311. [PubMed: 22778118]

- Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Paulozzi LJ. Patterns of abuse among unintentional pharmaceutical overdose fatalities. Journal of the American Medical Association. 2008; 300(22):2613–2620. [PubMed: 19066381]
- Hansen L, Penko J, Guzman D, Bangsberg DR, Miaskowski C, Kushel MB. Aberrant behaviors with prescription opioids and problem drug use history in a community-based cohort of HIV-infected individuals. Journal of Pain and Symptom Management. 2011; 42(6):893–902. [PubMed: 21802896]
- Hedegaard H, Chen LH, Warner M. Drug-poisoning deaths involving heroin: United States, 2000– 2013. NCHS Data Brief. 2015; (190):1–8.
- Jakubczyk A, Ilgen MA, Kopera M, Krasowska A, Klimkiewicz A, Bohnert A, Wojnar M. Reductions in physical pain predict lower risk of relapse following alcohol treatment. Drug and Alcohol Dependence. 2016; 158:167–171. [PubMed: 26653340]
- Jonas DE, Garbutt JC, Amick HR, Brown JM, Brownley KA, Council CL, Harris RP. Behavioral counseling after screening for alcohol misuse in primary care: A systematic review and metaanalysis for the U.S. Preventive Services Task Force. Annals of Internal Medicine. 2012; 157(9): 645–654. [PubMed: 23007881]
- Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. Journal of Affective Disorders. 2009; 114(1–3):163– 173. [PubMed: 18752852]
- Larance B, Degenhardt L, Lintzeris N, Winstock A, Mattick R. Definitions related to the use of pharmaceutical opioids: Extramedical use, diversion, non-adherence and aberrant medicationrelated behaviours. Drug and Alcohol Review. 2011; 30(3):236–245. [PubMed: 21545553]
- Mars SG, Bourgois P, Karandinos G, Montero F, Ciccarone D. "Every 'never' I ever said came true": Transitions from opioid pills to heroin injecting. International Journal of Drug Policy. 2014; 25(2): 257–266. [PubMed: 24238956]
- Merlin JS, Turan JM, Herbey I, Westfall AO, Starrels JL, Kertesz SG, Ritchie CS. Aberrant drugrelated behaviors: A qualitative analysis of medical record documentation in patients referred to an HIV/chronic pain clinic. Pain Medicine. 2014; 15(10):1724–1733. [PubMed: 25138608]
- Morasco BJ, Dobscha SK. Prescription medication misuse and substance use disorder in VA primary care patients with chronic pain. General Hospital Psychiatry. 2008; 30(2):93–99. [PubMed: 18291290]
- National Institute on Alcohol Abuse and Alcoholism. Using alcohol to relieve your pain: What are the risks? 2013 Jul. Retrieved from http://pubs.niaaa.nih.gov/publications/PainFactsheet/ Pain_Alcohol.pdf
- National Institute on Drug Abuse. The NIDA quick screen. Resource guide: Screening for drug use in general medical settings. 2012 Mar. Retrieved from https://www.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings/nida-quick-screen
- Park TW, Lin LA, Hosanagar A, Kogowski A, Paige K, Bohnert AS. Understanding risk factors for opioid overdose in clinical populations to inform treatment and policy. Journal of Addiction Medicine. 2016; 10(6):369–381. [PubMed: 27525471]
- Passik SD, Messina J, Golsorkhi A, Xie F. Aberrant drug-related behavior observed during clinical studies involving patients taking chronic opioid therapy for persistent pain and fentanyl buccal tablet for breakthrough pain. Journal of Pain and Symptom Management. 2011; 41(1):116–125. [PubMed: 20580202]
- Ray GT, Bahorik A, Van Heldhuisen P, Weisner C, Rubinstein AL, Campbell CI. Protocol of a prescription opioid registry in an integrated health system: Population characteristics of prescription opioid use. American Journal of Managed Care. (in press).
- Riley JL 3rd, King C. Self-report of alcohol use for pain in a multi-ethnic community sample. Journal of Pain. 2009; 10(9):944–952. [PubMed: 19712901]
- Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths— United States, 2000–2014. Morbidity and Mortality Weekly Report. 2016; 64(50–51):1378–1382. [PubMed: 26720857]

- Saha TD, Kerridge BT, Goldstein RB, Chou SP, Zhang H, Jung J, Grant BF. Nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder in the United States. Journal of Clinical Psychiatry. 2016; 77(6):772–780. [PubMed: 27337416]
- SAS Institute Inc. SAS 9.3. Cary, NC: Author; 2011.
- Saunders KW, Von Korff M, Campbell CI, Banta-Green CJ, Sullivan MD, Merrill JO, Weisner C. Concurrent use of alcohol and sedatives among persons prescribed chronic opioid therapy: Prevalence and risk factors. Journal of Pain. 2012; 13(3):266–275. [PubMed: 22285611]
- Selby, JV., Smith, DH., Johnson, ES., Raebel, MA., Fried-man, GD., McFarland, BH. Kaiser permanente medical care program. In: Strom, BL., editor. Pharmacoepidemiology. 4th. New York, NY: Wiley; 2005. p. 241-259.
- Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and medicaid insurance plans: The TROUP Study. Pain. 2010; 150(2):332–339. [PubMed: 20554392]
- Trescott CE, Beck RM, Seelig MD, Von Korff MR. Group Health's initiative to avert opioid misuse and overdose among patients with chronic noncancer pain. Health Affairs (Millwood). 2011; 30(8):1420–1424.
- Turner BJ, Liang Y. Drug overdose in a retrospective cohort with non-cancer pain treated with opioids, antidepressants, and/or sedative-hypnotics: Interactions with mental health disorders. Journal of General Internal Medicine. 2015; 30(8):1081–1096. [PubMed: 25650263]
- Unick GJ, Rosenblum D, Mars S, Ciccarone D. Intertwined epidemics: National demographic trends in hospitalizations for heroin-and opioid-related overdoses, 1993–2009. PLoS One. 2013; 8(2):e54496. [PubMed: 23405084]
- Volkow ND. The reality of comorbidity: depression and drug abuse. Biological Psychology. 2004; 56(10):714–717.
- Von Korff M, Crane P, Lane M, Miglioretti DL, Simon G, Saunders K, Kessler R. Chronic spinal pain and physical-mental comorbidity in the United States: results from the national comorbidity survey replication. Pain. 2005; 113(3):331–339. [PubMed: 15661441]
- Von Korff M, Dunn KM. Chronic pain reconsidered. Pain. 2008; 138(2):267–276. [PubMed: 18226858]
- Von Korff M, Merrill JO, Rutter CM, Sullivan M, Campbell CI, Weisner C. Time-scheduled versus pain-contingent opioid dosing in chronic opioid therapy. Pain. 2011; 152(6):1256–1262. [PubMed: 21296498]
- Von Korff M, Saunders K, Thomas Ray G, Boudreau D, Campbell C, Merrill J, Weisner C. De facto long-term opioid therapy for noncancer pain. Clinical Journal of Pain. 2008; 24(6):521–527. [PubMed: 18574361]
- Weisner CM, Campbell CI, Ray GT, Saunders K, Merrill JO, Banta-Green C, Von Korff M. Trends in prescribed opioid therapy for non-cancer pain for individuals with prior substance use disorders. Pain. 2009; 145(3):287–293. [PubMed: 19581051]
- Witkiewitz K, Vowles KE, McCallion E, Frohe T, Kirouac M, Maisto SA. Pain as a predictor of heavy drinking and any drinking lapses in the COMBINE study and the UK Alcohol Treatment Trial. Addiction. 2015; 110(8):1262–1271. [PubMed: 25919978]
- Woodrow KM, Eltherington LG. Feeling no pain: alcohol as an analgesic. Pain. 1988; 32(2):159–163. [PubMed: 3362554]

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Table 1

Study sample descriptives by alcohol and illicit drug use and disorders.

	Daily/weekly al	Daily/weekly alcohol use in prior 3 months	3 months	Illicit drug u	Illicit drug use in prior 3 months	months	Alcohol dise	Alcohol disorder in prior 3 years	3 years	Drug disod	Drug disoder in prior 3 years	years
	Yes $(n = 134)$	\mathbf{No} ($n = 838$)	> d	Yes $(n = 157)$	No $(n = 815)$	> d	Yes $(n = 90)$	$\mathbf{No} (n = 882)$	> d	Yes $(n = 138)$	$\begin{array}{l} \mathbf{No}\\ (n=834) \end{array}$	p_{\leq}
Age (%)												
21-44	23.7	20.3		22.9	20.4		15.2	21.4		30.8	19.6	
45-64	54.2	56.1		68.8	53.0		59.2	55.4		57.9	55.5	
65+	22.1	23.7	su	8.3	26.5	.001	25.6	23.2	su	11.2	25.0	.001
College (%)	57.8	59.4	su	48.7	61.3	.05	55.6	59.4	su	50.2	60.3	su
Ethnicity (%)												
Hispanic	9.0	11.5		11.0	11.1		14.8	10.7		14.1	10.7	
White	81.1	75.5		78.6	76.0		76.9	76.4		74.2	76.7	
Black	6.7	10.0		7.8	9.7		4.8	9.8		8.4	9.5	
Other	3.3	3.1	ns	2.6	3.2	su	3.5	3.1	su	3.4	3.1	su
Female (%)	46.0	66.4	.001	51.0	65.4	.05	44.2	64.7	.05	57.0	63.7	su
Opioid dose (%)												
<20 mg/day	48.4	28.8		24.8	33.4		20.8	33.2		7.2	35.3	
20-50 mg/day	29.5	32.5		38.1	30.8		38.0	31.4		38.9	31.1	
50-120 mg/day	14.6	20.5		16.8	20.0		18.8	19.5		22.4	19.1	
120+ mg/day	7.5	18.3	.001	20.3	15.7	su	22.4	15.9	su	31.4	14.5	.001
Depression (%)	41.8	47.0	ns	56.1	44.3	su	53.3	44.4	su	67.2	42.3	.001
Average pain intensity (mean, std)	5.9 (0.2)	6.6 (1.7)	.001	6.5(0.07)	6.5 (1.5)	su	6.5(1.6)	6.6(1.2)	su	6.6(1.3)	6.5(1.6)	ns

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Table 2

Study sample descriptives by aberrant drug related behaviors.

	Received opic	Received opioids from others year	in past	Gave opioids	Gave opioids to other in past year	st year	Asked for an	Asked for an early refill in past year	past year	Taking more op	Taking more opioids than prescribed in past two weeks	d in past
	$\mathbf{Yes} \\ (n = 121)$	$\begin{array}{l} \mathrm{No}\\ (n=849) \end{array}$	> <i>d</i>	Yes (<i>n</i> = 163)	$\begin{array}{c} \mathrm{No}\\ (n=808) \end{array}$	≥d	Yes (n = 359)	$\begin{array}{l} \mathrm{No}\\ (n=610) \end{array}$	×d	Sometimes/ Always (n = 186)	Never/Rarely $(n = 775)$	Þ
Age (%)												
21-44	33.0	19.1		27.8	19.4		29.0	16.4		31.7	17.9	
45-64	43.9	57.3		51.1	56.6		53.0	57.2		50.9	57.2	
65+	23.2	23.6	.05	21.0	24.0	su	18.0	26.4	0.001	17.4	24.9	.001
College (%)	46.8	60.8	.05	58.8	59.0	su	54.1	61.3	0.05	54.7	59.7	su
Ethnicity (%)												
Hispanic	3.5	12.3		6.3	12.2		11.0	11.2		5.1	12.4	
White	87.6	75.1		85.8	74.7		71.3	79.2		76.7	76.6	
Black	8.0	9.5		7.2	9.9		15.6	6.4		13.0	8.7	
Other	1.0	3.1	.001	0.7	3.2	.01	2.0	3.2	0.001	5.1	2.3	.01
Female (%)	57.6	64.1	su	58.6	64.2	su	58.8	65.6	0.05	63.0	63.9	su
Opioid dose category (%)												
<20 mg/day	33.5	31.7		24.7	33.4		21.8	36.6		24.5	32.9	
20–50 mg/day	33.0	31.9		41.8	30.0		38.6	29.0		38.9	30.7	
50–120 mg/day	19.5	19.6		20.8	19.3		19.6	19.5		19.2	19.9	
120+ mg/day	14.0	16.9	su	12.8	17.3	su	20.0	14.9	0.001	17.4	16.5	su
Depression (%)	53.8	43.6	su	48.4	44.2	su	56.8	41.9	0.001	58.8	41.7	.001
Average pain intensity (mean. std)	6.6(1.5)	6.5(1.5)	us	6.5(1.4)	6.5(1.6)	su	6.6(1.4)	6.5(1.6)	us	7.0(1.4)	6.4(1.5)	.001

Table 3

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ession of alcohol
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Logistic

	Daily/wee	Daily/weekly alcohol use in prior 3 months	use in prio	r 3 months	Alcohe	ol disorde	Alcohol disorder in prior 3 years	3 years
	OR	95%	95% CI	$b^{<}$	OR	95%	95% CI	>d
Female	0.53	0.32	0.88	.05	0.44	0.22	0.87	0.05
College education	06.0	0.54	1.51	su	0.81	0.41	1.58	su
Age 21-44 (vs. 65+)	0.98	0.44	2.20	su	0.23	0.08	0.64	.01
Age 45–65 (vs. 65+)	1.03	0.52	2.02	su	0.48	0.20	1.18	su
Pain severity	0.74	0.63	0.89	.001	1.08	0.85	1.39	su
Daily opioid dose (20-50 mg) (vs. < 20 mg)	0.65	0.34	1.25	ns	1.53	0.46	5.13	su
Daily opioid dose (50-120 mg) (vs. < 20 mg)	0.60	0.34	1.07	su	1.50	0.47	4.79	su
Daily opioid dose $(120+mg)$ (vs. $< 20 mg$)	0.32	0.16	0.63	.01	1.56	0.49	4.93	su
Illicit drug use	1.87	1.02	3.44	.05		I		
Illicit drug <i>disorder</i>		I			9.75	4.61	20.61	.001
Depression	0.88	0.51	1.49	su	1.07	0.50	2.29	ns

Logistic regression of illicit drug use and illicit drug use disorder.

	Illicit d	lrug use	Illicit drug use in prior 3 months	months	Drug (<u>disorder</u> j	Drug disorder in prior 3 years	s years
	OR	95%	95% CI	$b^{<}$	OR	95%	95% CI	>d
Female	0.57	0.35	0.93	0.05	0.75	0.42	1.35	us
College education	0.66	0.40	1.09	su	0.55	0.31	0.98	.05
Age 21–44 (vs. 65+)	3.74	1.44	9.68	su	4.42	1.58	12.42	.01
Age 45–65 (vs. 65+)	5.05	2.10	12.14	0.001	2.11	0.79	5.63	su
Pain severity	0.99	0.81	1.21	su	0.87	0.75	1.02	su
Daily opioid dose (20-50 mg) (vs. < 20 mg)	2.06	1.03	4.11	su	3.20	1.07	9.57	su
Daily opioid dose (50-120 mg) (vs. < 20 mg)	1.39	0.73	2.64	su	2.87	1.08	7.63	su
Daily opioid dose $(120+mg)$ (vs. $< 20 mg)$	1.91	1.01	3.63	su	5.54	2.10	14.61	.001
Daily/weekly alcohol use	1.92	1.03	3.57	0.05				
Alcohol disorder					8.69	4.04	18.70	.001
Depression	1.21	0.70	2.09	su	2.31	1.27	4.19	.00

Table 5

Logistic regression models of aberrant drug related behavior.

	Received	Received opioids from others in past year	m others in	past year	Gave op	ioids to ot	Gave opioids to others in past year	ıst year
	OR	95%	95% CI	<i>b</i> <	OR	95% CI	cI	>d
Female	0.81	0.47	1.40	su	0.88	0.53	1.48	su
College education	0.63	0.36	1.09	su	1.01	0.62	1.65	su
Age 21–44	1.74	0.71	4.30	.05	1.30	0.61	2.78	su
Age 45-65	0.63	0.27	1.43	.01	0.82	0.42	1.59	su
Pain severity	66.0	0.82	1.19	su	1.00	0.86	1.17	su
Daily/weekly alcohol use	1.49	0.76	2.91	su	1.21	0.65	2.24	su
Illicit drug use	3.25	1.76	6.02	.001	2.57	1.44	4.61	.01
Depression	1.64	0.92	2.95	su	1.30	0.79	2.14	su