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Alcohol and Opioid Use, Co-Use, and Chronic Pain in the Context of the Opioid Epidemic: A Critical Review

Katie Witkiewitz, PhD and **Kevin E. Vowles, PhD**

University of New Mexico

Abstract

The dramatic increase in opioid misuse, opioid use disorder (OUD), and opioid-related overdose deaths in the United States has led to public outcry, policy statements, and funding initiatives. Meanwhile, alcohol misuse and alcohol use disorder is a highly prevalent public health problem associated with considerable individual and societal costs. This paper provides a critical review of alcohol and opioid misuse, including issues of prevalence, morbidity, and societal costs. We also review research on interactions between alcohol and opioid use, the influence of opioids and alcohol on alcohol use disorder (AUD) and OUD treatment outcomes, respectively, the role of pain in the co-use of alcohol and opioids, and treatment of comorbid OUD and AUD. Heavy drinking, opioid misuse, and chronic pain individually represent significant public health problems. Few studies have examined co-use of alcohol and opioids, but available data suggest that co-use is common and likely contributes to opioid overdose-related morbidity and mortality. Co-use of opioids and alcohol is related to worse outcomes in treatment for either substance. Finally, chronic pain frequently co-occurs with use (and co-use) of alcohol and opioids. Opioid use and alcohol use are also likely to complicate the treatment of chronic pain. Research on the interactions between alcohol and opioids, as well as treatment of the comorbid disorders is lacking. Currently most alcohol research excludes patients with OUD and there is lack of measurement in both AUD and OUD research in relation to pain-related functioning. Research in those with chronic pain often assesses opioid use, but rarely assesses alcohol use or AUD. New research to examine the nexus of alcohol, opioids, and pain, as well as their treatment is critically needed.

Keywords

Alcohol Misuse; Alcohol Use Disorder; Opioid Misuse; Opioid Use Disorder; Chronic Pain

Opioid misuse, opioid use disorder (OUD), and the rising rate of opioid overdose deaths in the United States (U.S.) has been described as an “opioid epidemic” (Clarke et al., 2016; Howe and Sullivan, 2014; Humphreys, 2017; Kertesz, 2017; Manchikanti et al., 2012). The rise in opioid-related problems can largely be attributed to three related factors. First, the prescription rates of opioid medications have increased dramatically over the past few decades (Compton and Volkow, 2006; McCabe et al., 2017; Okie, 2010). Second, the rise in

Corresponding Author: Katie Witkiewitz, PhD, Department of Psychology, University of New Mexico, MSC 03-2220, Albuquerque NM 87131, katiew@unm.edu, (505) 925-2334.

DR. KATIE WITKIEWITZ (Orcid ID : 0000-0002-1086-3067)

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prescription rates specifically for stronger opioids, such as oxycodone and fentanyl (Bedson et al., 2013), has provided greater availability of formulations that have higher potential for addiction (Kenan et al., 2012). Finally, there have been significant increases in the number of patients receiving long-term opioid therapy, typically defined as contiguous use of opioids for greater then three months (Chou et al., 2009; Højsted and Sjøgren, 2007; Portenoy, 1996). Thus, over the past few decades, there have been more opioids available, at greater strengths, and for longer durations. These changes have resulted in significant increases in prescription OUD. As seen in Figure 1, there has been an increase in prescription OUD in nationally representative epidemiological samples from 2002 to 2012, including the National Epidemiological Survey on Alcohol and Related Conditions (NESARC; Saha et al., 2016) and the National Survey on Drug Use and Health (NSDUH; Substance Abuse and Mental Health Services Administration (SAMHSA), 2013). The proportion of individuals who are seeking substance use disorder (SUD) treatment primarily for prescription opioids has also increased based on the Treatment Episode Dataset (TEDS; Jones et al., 2017; SAMHSA, 2014). The societal costs of prescription opioid misuse, abuse, and dependence were estimated at $55.7 billion in 2007 (Birnbaum et al., 2011) and the economic burden of opioid use was estimated at $78.5 billion in 2013 dollars (Florence et al., 2016).

Alcohol misuse and alcohol use disorder (AUD) are even more prevalent public health problems associated with considerable individual and societal costs (Bouchery et al., 2011; Whiteford et al., 2013; World Health Organization (WHO), 2014). As seen in Figure 1, the prevalence of past 12-month AUD exceeds the rate of OUD in nationally representative epidemiological samples, including the NESARC (Grant et al., 2017) and NSDUH (SAMHSA, 2013), and the proportion of individuals who are seeking SUD treatment primarily for alcohol is also considerably higher than the proportion of individuals who are seeking treatment for prescription opioids based on the Treatment Episode Dataset (TEDS; SAMHSA, 2014). Alcohol causes over 3 million deaths worldwide each year and contributes to more than 5% of the global burden of disease (WHO, 2014). In the United States, alcohol use is the fourth leading cause of preventable death with approximately 88,000 people dying each year due to alcohol-related causes (Gonzales et al., 2014). It has been estimated that most countries spend approximately 1%–3% of the gross domestic product on alcohol (Rehm et al., 2009), however some countries spend far more (WHO, 2014). In Europe, estimates across studies suggest alcohol-attributable costs are roughly €26 to €1500 per person in 2014 dollars (Barrio et al., 2017), whereas prior estimates indicated approximately 125 billion euros were spent on alcohol in Europe in 2003 (Anderson and Baumberg, 2006). In the United States, the economic burden of alcohol was estimated at $249 billion in 2010 (Centers for Disease Control and Prevention (CDC), 2016).

There is increasing evidence that alcohol and opioids are commonly used together and that alcohol is a contributing factor in many opioid overdose deaths (Frank et al., 2015; Hickman et al., 2008). Co-use is problematic due to pharmacodynamic interactions (see Weathermon and Crabb, 1999), whereby both opioids and alcohol act as central nervous system depressants and use of both substances at the same time can produce significant respiratory depression contributing to overdose risk (White and Irvine, 1999). Further, use of alcohol may interfere with OUD treatment, particularly medication assisted treatment (el-Bassel et al., 1993; Häkkinen et al., 2012; Nolan et al., 2016; Senbanjo et al., 2007). Yet, research on

the association between alcohol and opioids is lacking, and there have been few studies examining the efficacy of interventions that may target both alcohol and opioid misuse (Crits-Christoph et al., 2015; Darker et al., 2016).

The concurrent use of alcohol and opioids may also interfere with treatment for chronic pain (defined as persistent pain lasting longer than 3 months; Landsman-Blumberg et al., 2017). Chronic pain affects more than 1 in 10 adults in the United States (Johannes et al., 2010; Nahin, 2015) and is often associated with clinically significant levels of distress and disability (Gatchel et al., 2007; Jensen and Turk, 2014). Alcohol and opioids activate many of the same neural circuits and may disrupt pain signaling in the brain (Egli et al., 2012). Further, the experience of pain is associated with greater risk of alcohol relapse during and following alcohol treatment (Jakubczyk et al., 2016; Witkiewitz et al., 2015). Importantly, most of the research on chronic pain has neglected the role of alcohol, and research on AUD rarely considers the impact of chronic pain or opioid misuse. An additional issue, with very little empirical data to inform a review of the topic, is the problem of benzodiazepine use concurrently with opioids and alcohol (Gudin et al., 2013), particularly among chronic pain patients (Nielsen et al., 2015). Thus, the purpose of the present review was to highlight the impact of opioid and alcohol misuse, particularly when they are used together, as well as consider this impact in relation to the presence of chronic pain and the use of benzodiazepines. We also examine numerous research gaps, particularly with respect to understanding the scope of the problem and treatment approaches.

Opioid and Alcohol Co-Use Prevalence, Morbidity, Mortality, and Costs

When examined separately, opioid and alcohol misuse are common, costly, and associated with increased risk of morbidity and mortality (Anderson and Baumberg, 2006; Barrio et al., 2017; Birnbaum et al., 2011; CDC, 2016; Florence et al., 2016; Okie, 2010; Rehm et al., 2009; Whiteford et al., 2013; WHO, 2014). There is, however, a general absence of research examining the co-use of alcohol and opioids, and we could not identify any studies of the economic or social costs of alcohol and opioid co-use. Population based samples in the U.S. have found that nonmedical prescription opioid use and OUD increases the risk of also having an AUD among adults (aged 18 and older) in the 2012–2013 NESARC III sample (Saha et al., 2016). Past year alcohol users (aged 12 and older) were more likely to have misused prescription drugs, including pain relievers, in the past year in the 2015 NSDUH (Hughes et al., 2016).

Among a cohort of 5307 adult patients (18 or older) with OUD in an electronic health record database, the majority of which had a chronic pain diagnosis, 23.4% also had a diagnosis of AUD (Hser et al., 2017) based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes obtained from the health records (Centers for Disease Control, 2013). Those patients who had an OUD prior to the onset of pain were more likely to have an AUD (33.4% with AUD; Hser et al., 2017). Similarly, in an opioid treatment seeking sample recruited in the National Institute on Drug Abuse Clinical Trials Network (n=1397; Hartzler et al., 2010), 38% had a comorbid AUD diagnosis based on the Diagnostic and Statistical Manual for Mental Disorders – fourth edition (American Psychiatric Association, 1994). Among youth (ages 11–21) entering treatment for marijuana

or alcohol problems, approximately 7% were identified as also having problematic opioid use (Subramaniam et al., 2010), whereas among adults in treatment for alcohol or drug use disorder approximately 68% had used prescription opioids non-medically in the 30 days prior to intake (Price et al., 2011). The percent of individuals reporting any alcohol use and any prescription opioid use at the time of admission to SUD treatment in the SAMHSA Treatment Episode Dataset has increased by 181% in a 10 year period from 1.6% in 2002 to 4.5% in 2012.

Risk of morbidity and mortality increases greatly with co-use of alcohol and opioids. Castle and colleagues (2016) conducted a records review of the Drug Abuse Warning Network (DAWN), a U.S. surveillance system administered by SAMHSA reported an 84% increase in drug-related emergency department (ED) visits involving adverse drug effects from 2005 to 2011, with most of the increase attributable to increases in opioid visits. Among those who also had alcohol involvement at the time of the adverse drug reaction, the odds of a more serious outcome of the ED visit were significantly higher as compared to ED visits for adverse drug reactions without alcohol involvement (Castle et al., 2016). In another DAWN study, ED visits with benzodiazepines and co-use of opioids or alcohol resulted in more severe outcomes than visits with benzodiazepines alone (Center for Behavioral Health Statistics and Quality, 2014). Relatedly, out of the 3,883 opioid pain reliever deaths reported in the DAWN medical examiner data (across 13 of the U.S. states) in 2010, approximately 22.1% also involved alcohol, and out of the 1,512 benzodiazepine deaths, 21.4% involved alcohol (Jones et al., 2014). A smaller study of opioid overdose deaths in West Virginia during 2006 found 13.5% of decedents had alcohol in their bloodstream at the time of death (Hall et al., 2008). Similarly, among OUD patients in the United Kingdom, comorbid AUD significantly increased risk of all-cause mortality and also significantly increased risk of fatal overdose and liver related deaths (Bogdanowicz et al., 2015).

Among patients in the MarketScan medical claims database with chronic non-cancer pain on long-term opioid therapy (n=21,203), approximately 3.5% also had an AUD diagnosis (n = 742) based on ICD-9-CM codes. Importantly, AUD diagnosis predicted significantly higher risk of opioid overdose, accidents, and injuries, as compared to those without an AUD diagnosis (Landsman-Blumberg et al., 2017). More generally, both AUD and OUD increase disease burden. A medical record review of visits within the Kaiser Permanente Northern California Health System in the U.S. indicated that 21.6% of individuals with OUD also had an AUD diagnosis based on ICD-9 codes, and patients with an AUD and/or an OUD had significantly higher disease burden and higher rates of multiple medical comorbidities, compared to patients without any SUD (Bahorik et al., 2017). The risk of all-cause mortality from the combination of alcohol and opioids has not been studied and most research on opioid mortality has focused on opioid overdose risk, with few studies examining all-cause mortality (Sordo et al., 2017). Examining deaths that are alcohol and opioid-attributable, including overdose and all-cause mortality is an important area for future research.

Few studies have explicitly studied hazardous opioid and alcohol co-use in those with chronic pain, although the work in this area suggest it occurs in a clinically significant minority. In a sample of 11,848 patients enrolled in the Group Health Cooperative and Kaiser Permanente of Northern California health plans who consumed prescribed opioids

every day out of the previous two weeks, 12.4% reported concurrent use of alcohol, 31.9% reported concurrent use of sedative medication (including benzodiazepines, barbiturates, muscle relaxants, and other anxiolytics, hypnotics, and sedatives), and 3.1% reported concurrent use of all three substances via self-report assessed using computer-assisted telephone interview technology (Saunders et al., 2012). The primary care study of Saffier and colleagues (2007) assessed concurrent alcohol use in a sample of 908 individuals receiving prescribed opioids for chronic pain and found that 36% reported consumption of at least one alcoholic beverage in the past 30 days, 4.4% reported consumption of 6–10 drinks, and 5.8% reported consumption of >10 drinks. To our knowledge, only a single study in an Australian cohort has examined frequency and specific impact of alcohol misuse in patients on long-term opioid therapy diagnosed with chronic non-cancer pain (Larance et al., 2016). This study found that "risky drinkers" (i.e., consumption of five or more drinks on at least single occasion within the past year), reported higher levels of pain interference, as measured by the Brief Pain Inventory (Cleeland and Ryan, 1994), in comparison to "non-risky" drinkers. In the same Australian cohort of chronic non-cancer pain patients, Nielsen and colleagues (2015) found one-third of the sample reported benzodiazepine use in the past month and that benzodiazepine use was associated with greater pain severity, greater pain interference, and individuals with benzodiazepine use were more likely to meet criteria for an alcohol use disorder based on ICD-10 (WHO, 2011).

Chronic Pain as a "Third Variable" in Opioid and Alcohol Co-Use

It is possible that chronic pain is present in a noteworthy proportion of individuals who are using opioids and/or alcohol in a problematic manner. Recent estimates from the 2015 NSDUH, indicated 63.4% of individuals who misused opioids reported the primary motivation for misuse was to relieve physical pain (Han et al., 2017). In a review of 38 published studies assessing problematic opioid use among pain patients, the raw range of misuse and "addiction" (defined as harm resulting from opioid use) was very broad, ranging from <1% to 81% (Vowles et al., 2015). Studies were characterized by significant heterogeneity in methods, setting, and quality. When overall rates of misuse and addiction were calculated using averages weighted by sample size and study quality, rates of misuse ranged from 21% to 29% and rates of addiction ranged from 8% to12% (Vowles et al., 2015). These ranges are generally concordant with previous reviews regarding the prevalence of aberrant prescribed opioid use in those with chronic pain (Højsted and Sjøgren, 2007; Martell et al., 2007). Opioids have reasonable evidence for short term pain reduction, although evidence is less supportive in relation to effectiveness over the longer term (Chapman et al., 2010; Chou et al., 2009; Dowell et al., 2016; Shaheed et al., 2016). Within interdisciplinary chronic pain rehabilitation programs, those with opioid use resulting in considerable harm are at risk for poorer outcomes and earlier treatment dropout in comparison to those who do not meet this criterion (Vowles and Ashworth, 2011).

With respect to alcohol use, persistent and significant pain experiences appear to be common in those who are presenting for AUD treatment (Brennan et al., 2011). A recent review by Zale and colleagues (2015) indicated that the experience of moderate-to-severe pain has been documented in 43%–73% of individuals presenting for AUD treatment, and the prevalence of alcohol-related neuropathic pain has been estimated at 25%–66% among

individuals with AUD. A two year longitudinal study, which assessed pain every six months in treatment seeking problem drinkers, indicated that 24% of respondents noted the experience of moderate to severe pain at each assessment (Larson et al., 2007).

In chronic pain treatment settings, problematic alcohol use appears relatively common, with between 16% and 25% patients noting a history of current or past alcohol dependence or heavy drinking (Hoffman et al., 1995; Kim et al., 2013; Lawton and Simpson, 2009). Finally, alcohol has analgesic properties in studies of acute pain (Thompson et al., 2016; Woodrow and Eltherington, 1988), and thus it is plausible that alcohol is sometimes used for analgesic purposes in those with chronic pain. Importantly, alcohol consumption may have greater analgesic effects among individuals with alcohol dependence (Cutter et al., 1979, 1976). Consistent with these early findings, analyses of the 2015 NSDUH data indicated that individuals with past 30 day binge alcohol use (defined as five or more drinks per occasion) were twice as likely to misuse prescription opioids for relieving pain symptoms. Zale et al. (2015) identified evidence across psychosocial and biological literatures indicating significant correlations between excessive alcohol consumption and greater pain intensity and interference. While this conclusion was based on correlational findings, thus causality cannot be inferred, it is interesting that a concordant pattern of findings is present for opioids and benzodiazepines – higher doses of opioids and taking benzodiazepines are associated with greater pain intensity and interference among pain patients (Kobus et al., 2012; Morasco et al., 2017, 2011; Seal et al., 2012). Importantly, tolerance to the analgesic effects of alcohol can occur under certain learning conditions (Egli et al., 2012), and chronic alcohol use can also increases pain sensitivity (Jochum et al., 2010).

Treatment of OUD and Impacts of Alcohol and Pain on OUD Treatment Outcomes

Medication-assisted treatments such as methadone, buprenorphine, and extended-release naltrexone are the most established evidence-based treatments for OUD (Brady et al., 2016). Importantly, medication assisted treatment has been most widely studied as a treatment for OUD among heroin users, and only a few studies have been conducted with patients who are presenting with OUD due to prescription opioid medications (Brady et al., 2016). The Prescription Opioid Addiction Treatment Study (POATS) and the Starting Treatment with Agonist Replacement Therapies (START) study, found that methadone (START) and buprenorphine (POATS and START) are effective medications for individuals with prescription OUD (Saxon et al., 2013; Weiss et al., 2011). Individuals with prescription OUD may have better outcomes than individuals with heroin and injection drug OUD (Potter et al., 2013).

With regard to psychosocial treatment that is adjunctive to medications, the evidence is mixed. One recent review indicated that psychosocial interventions tended to improve outcomes in methadone maintenance therapy (Dugosh et al., 2016). Specifically, beneficial effects on treatment attendance and/or opioid use were indicated in nine of fourteen studies reviewed. The most frequently studied intervention was contingency management. A more recent review on individuals prescribed buprenorphine for prescription OUD indicated that

psychosocial support does not seem to reliably improve outcomes, although some evidence of beneficial effect was present for specific intervention modalities, primarily contingency management (Carroll and Weiss, 2017). Thus, there is a degree of support for psychosocial interventions, but the evidence is not strong and both of these recent reviews highlighted significant gaps within these literatures. Furthermore, no studies have compared the efficacy of medication assisted treatment with or without psychosocial intervention to contingency management only. Furthermore, there have been no studies of contingency management for individuals with prescription OUD.

Individuals with OUD and alcohol use, misuse, or AUD may be at risk of worse treatment outcomes in OUD treatment. Among OUD patients who are treatment seeking, those with AUD tend to have a greater history of psychiatric problems and greater dysfunction in family/social domain (Hartzler et al., 2010), thus individuals who are using alcohol may present with a more complicated clinical picture for OUD treatment. While some studies do show that individuals with AUD in OUD treatment may reduce their alcohol use over time (see Caputo et al., 2002), more studies have found that alcohol use either increases or remains unchanged during medication assisted treatment (Soyka, 2015; Srivastava et al., 2008). History of alcohol intoxication in the 30 days prior to OUD treatment with extended release naltrexone predicted worse OUD treatment response, including a higher rate of opioid use relapse (Friedmann et al., 2017). Very little is known about the role of alcohol use in substitution treatment for individuals with prescription OUD. The START and POATS trials both excluded individuals with AUD that may require additional medical attention and no other studies have examined the role of alcohol in treatment for prescription OUD.

There has been a surprising lack of studies examining the effect of chronic pain on treatment response among patients in OUD treatment (Dennis et al., 2016). The handful of studies that have been conducted have found that patients in OUD treatment with pain may be more likely to use illicit drugs and alcohol to treat their pain symptoms (Rosenblum et al., 2003) and pain may be associated with greater medical and psychiatric problems among OUD patients (Trafton et al., 2004). Experience of chronic pain during medication assisted treatment is associated with increased craving for opioids (Tsui et al., 2016) and increased risk of relapse to opioids following treatment (Griffin et al., 2016).

Treatment of AUD and Impacts of Opioids and Pain on AUD Treatment Outcomes

There are currently four medications that are approved by the U.S. Food and Drug Administration (FDA) for the treatment of AUD: disulfiram, acamprosate, and naltrexone (oral and injectable extended release versions). The European Medicines Agency has approved disulfiram, acamprosate, naltrexone, and nalmefene. Baclofen is an approved medication in France. Numerous other medications are used off-label and some of these medications, particularly topiramate, varenicline, and gabapentin, have data supporting their use in the treatment of AUD (Litten et al., 2012; Soyka and Müller, 2017). The available medications are modestly effective in the treatment of AUD (Jonas et al., 2014) and generally no more effective than behavioral interventions without medication (Anton et al.,

2006). With respect to behavioral interventions for AUD, effective options include cognitive-behavioral and coping skills treatments (Magill and Ray, 2009; Powers et al., 2008), motivational interviewing and related brief interventions (Miller and Wilbourne, 2002), twelve-step facilitation (Project MATCH Research Group, 1997), community reinforcement approaches (Manuel et al., 2012), and mindfulness-based interventions (Witkiewitz et al., 2014a).

Unlike the treatment of OUD, the treatment of AUD rarely involves medication-assisted treatment and behavioral interventions are far more widely utilized. Specifically, prescribing rates of medications for AUD are low (typically fewer than 15% of patients, Harris et al., 2012; Mark et al., 2003), and prescribing to patients with AUD is atypically low as compared to the medications prescribed to the same patients for other mental health disorders (Rubinsky et al., 2015). Recent estimates indicate that approximately 9% of the population with AUD have ever received a single prescription for an AUD medication (Mark et al., 2009). Reasons for low rates of prescribing include compliance issues, affordability of medications, and lack of knowledge about the availability of medications for AUD (Mark et al., 2003). The low rate of alcohol medications is unfortunate given the modest effectiveness of these medications, particularly in helping individuals reduce their heavy drinking (van Amsterdam and van den Brink, 2013) and reductions in health care utilization and costs associated with medication assisted treatment for AUD (Baser et al., 2011).

Most large randomized clinical trials for AUD have excluded individuals with comorbid OUD (Anton et al., 2006; Mann et al., 2013; O'Malley et al., 1996; Project MATCH Research Group, 1997), thus there is very little data on the effect of comorbid opioid use on AUD treatment outcomes in large clinical trials. A recent analysis of individuals enrolled in two clinical trials (n = 2126; COMBINE Study in the United States (Anton et al., 2006) and United Kingdom Alcohol Treatment Trial (UKATT) in the United Kingdom (UKATT Research Team, 2005)) found that individuals with any opioid use at baseline (7.7% of the combined sample) had significantly worse drinking outcomes at 1 year follow-up, including greater percentage of heavy drinking days (Cohen's d = .27) and more drinks per drinking day (Cohen's d = .32), as compared to those without baseline opioid use (Witkiewitz et al., under review). In multivariate analyses, opioid use at baseline remained a significant predictor of drinking outcomes in the COMBINE study after controlling for other predictors of AUD treatment outcome (Witkiewitz et al., under review). More generally, research on the effects of illicit drugs on AUD treatment outcomes has found that illicit drug use may increase risk of relapse to alcohol (Tonigan and Beatty, 2011) and frequency of alcohol and other drug use is significantly correlated among individuals with AUD (Staines et al., 2001).

Recent studies have started to consider the effect of pain on alcohol treatment outcomes. Jakubczyk and colleagues (2016) found reductions in physical pain during alcohol treatment predicted lower risk of alcohol relapse during the 4 weeks following treatment. Similarly, Witkiewitz and colleagues (2015) found pain interference and pain intensity at the end of treatment significantly predicted heavy drinking and time to first heavy drinking day during and following treatment. Additional research has found that pain may be associated with worse alcohol use outcomes following liver transplant (Rustad et al., 2014).

Treatment of Comorbid OUD and AUD

To date, there have been few large-scale studies examining combination treatments for OUD and AUD. Early work with patients with AUD and OUD on methadone maintenance found that making receipt of methadone contingent on taking disulfiram was an effective method for reducing alcohol consumption and increasing engagement with treatment (Bickel et al., 1988), however adding disulfiram to methadone maintenance without contingencies was not more effective than placebo (Ling et al., 1983). One of the more promising medications for treating both OUD and AUD is extended release naltrexone, which has been approved for both indications by the FDA and has shown positive results for treating patients with either OUD or AUD (Gastfriend, 2011; Hartung et al., 2014). A small pilot study found extended release naltrexone to be safe and feasible in the treatment of OUD and AUD among individuals in an HIV clinic setting (Korthuis et al., 2017), however only 8 individuals met criteria for both OUD and AUD in the pilot trial.

One of the largest studies conducted, to date, targeting OUD and/or AUD examined the efficacy of a collaborative care intervention among 377 primary care patients with AUD (54%), or OUD with or without AUD (46%; Watkins et al., 2017). The collaborative care intervention included facilitated care coordination by a clinical psychologist with addiction expertise and incorporated six sessions of brief psychotherapy using a motivational interviewing approach and/or referral to medication-assisted treatment using buprenorphine/naloxone or extended release naltrexone. Participants were randomized to receive collaborative care or treatment as usual in primary care, where usual care consisted of receiving information that the clinic provided OUD/AUD treatment and receiving a list of community referrals. Results at a 6-month follow-up indicated that individuals who received collaborative care were significantly more likely to receive treatment for OUD/AUD (39% in collaborative care and 17% in usual care) and had significantly greater rates of self-reported abstinence from opioids or alcohol (33% in collaborative care and 22% in usual care). Yet, as noted by the authors, rates of treatment seeking and abstinence were still low in both conditions (Watkins et al., 2017). Unfortunately, the authors failed to report the number of individuals with both OUD and AUD, as well as any subgroup differences with respect to AUD, OUD, or OUD+AUD outcomes.

Given the intersection of pain with OUD and AUD, behavioral interventions that have been shown to be effective for OUD, AUD, and chronic pain are particularly appealing. For example, mindfulness-based interventions have been shown to be effective in the treatment of polysubstance use (Bowen et al., 2014; Witkiewitz et al., 2014b), opioid treated chronic pain (Garland et al., 2017), chronic pain (Veehof et al., 2016), and can be feasibly combined with methadone maintenance treatment (Bowen et al., 2017). Cognitive behavioral treatment (CBT) has long been supported as efficacious in the treatment of alcohol and SUDs (Magill and Ray, 2009) and while CBT has mixed evidence for chronic pain (Williams et al., 2012) and OUD (Fiellin et al., 2013; Moore et al., 2016), there may be advantages to offering integrated CBT treatment for pain and AUD/OUD. Future research on the topic is worth pursuing, particularly as a non-medication option for patients with chronic pain and AUD and/or OUD.

In addition to the potential of integrated treatment, the available data suggest overlapping patterns of problematic alcohol and opioid use behavior and high rates of pain in the general population. One future direction for research is to assess the degree to which both alcohol and opioid use reflect pain avoidance strategies among individuals with chronic pain. Identifying the function of alcohol and opioid use behavior is critical for developing treatment strategies that might address the nexus of AUD, OUD, and pain (Murphy et al., 2015; Zale et al., 2015).

Conclusions

As highlighted throughout this review, heavy drinking and AUD, opioid misuse and OUD, and chronic pain are each significant public health problems. Yet, heavy drinking and AUD far surpasses opioid misuse and OUD with respect to prevalence (see Figure 1) and societal costs (approximately $78.5 billion due to opioids versus $249 billion due to alcohol in the U.S.; CDC, 2016; Florence et al., 2016). The opioid epidemic has garnered attention in North America and Australia, but there is growing evidence that opioid misuse could become a global problem (Birke et al., 2016; Helmerhorst et al., 2017; Humphreys, 2017; Morley et al., 2017) and alcohol use is a leading cause of morbidity and mortality worldwide (Whiteford et al., 2013; World Health Organization, 2011).

Despite the clear public health relevance and problems associated with alcohol and opioid co-use, as well as the growing concern about chronic pain management, there is very little attention paid to co-use in the research literature. Many studies of OUD exclude individuals with severe AUD and most alcohol clinical trials exclude individuals with OUD. Pain researchers do not typically assess rates of heavy drinking or AUD, and SUD researchers do not include standardized measures of pain or pain functioning. There are currently few evidence-based treatments available to target co-use and a further lack of treatments to address chronic pain among individuals with comorbid OUD and AUD. The role of benzodiazepine use has also been understudied, and given at least 30% of pain patients might receive opioid and benzodiazepine prescriptions, it is imperative to address the risks of using opioids, alcohol, and benzodiazepines, particularly in the context of managing chronic pain (Gudin et al., 2013). Behavioral interventions to manage chronic pain are available and may prevent the risks of morbidity and mortality associated with opioids and benzodiazepines, particularly when individuals are also using alcohol. We hope this review stimulates discussion and encourages future research, as well as funding opportunities, examining issues at the intersection of alcohol, opioids, and pain.

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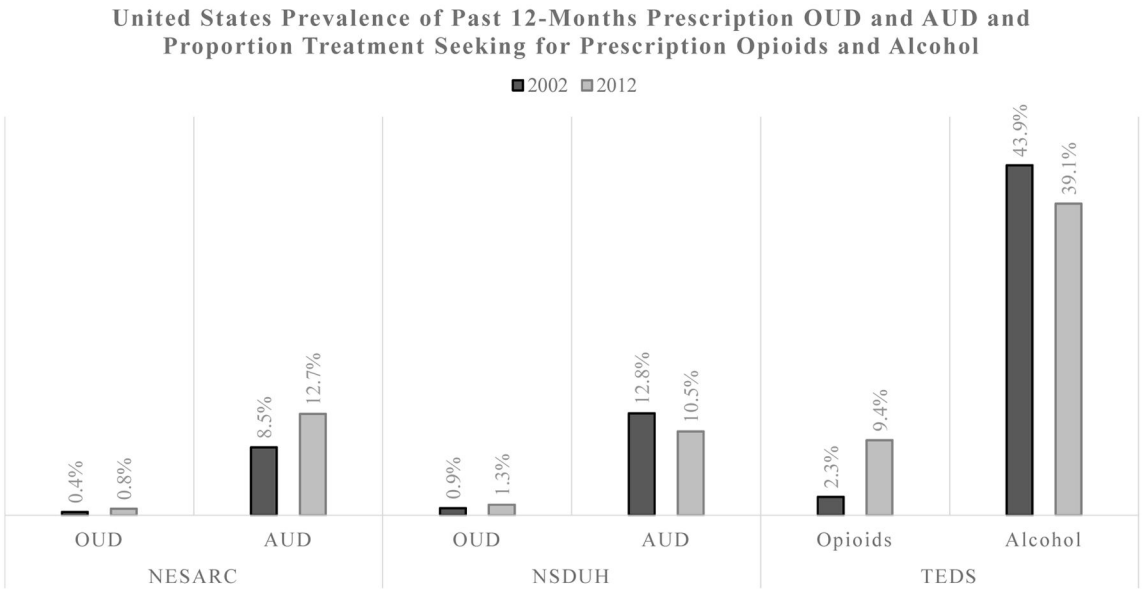

Figure 1.

Prevalence of alcohol use disorder (AUD) and prescription opioid use disorder (OUD) in the 2001–2002 and 2012–2013 National Epidemiological Survey on Alcohol and Related Conditions (NESARC; Grant et al., 2017; Saha et al., 2016) and 2002 and 2012 National Survey on Drug Use and Health (NSDUH; Han et al., 2017), and proportion of individuals seeking treatment primarily for prescription opioids or alcohol in the 2002 and 2012 Treatment Episode Dataset (TEDS; SAMHSA, 2014).