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## Harm reduction for young people who use prescription opioids extra-medically: Obstacles and opportunities

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### Abstract

Extra-medical prescription opioid (EMPO) use—intentional use without a prescription or outside of prescribed parameters—is a public health crisis in the United States and around the world. Epidemiological evidence suggests that the prevalence of EMPO use and adverse sequelae, including opioid overdose and hepatitis C infection, are elevated among people aged 18 to 25. Despite these preventable health risks, many harm reduction interventions are underutilized by, or inaccessible to, EMPO-using youth. In this commentary, we describe key harm reduction strategies for young people who use prescription opioids. We examine individual, social, and policy-level barriers to the implementation of evidence-based approaches that address EMPO use and related harms among young people. We highlight the need for expanded services and new interventions to engage this diverse and heterogeneous at-risk population. A combination of medical, social, and structural harm reduction interventions are recommended. Furthermore, research to inform strategies that mitigate particularly high-risk practices (e.g., polysubstance use) is warranted. Finally, we discuss how the meaningful involvement of youth in the implementation of harm reduction strategies is a critical component of the public health response to the prescription opioid epidemic.

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The authors have confirmed they have no potential conflicts of interest to declare.

## Keywords

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## Introduction

Concomitant with a dramatic rise in the prescribing and sale of opioid pain relievers, extra-medical prescription opioid (EMPO) use—defined as intentional opioid use without a prescription or use of one's own prescription outside of prescribed parameters—is one of the fastest growing forms of drug abuse in the United States (National Institutes on Drug Abuse, 2011). The prevalence of EMPO use is highest among young people aged 18 to 25, with an estimated 6 million (1 in 5) young adults reporting lifetime use and 2.7 million (1 in 12) reporting use in the past year (Center for Behavioral Health Statistics and Quality, 2015). High rates of EMPO use among young people have also been observed internationally (Brands, Paglia-Boak, Sproule, Leslie, & Adlaf, 2010; Ghandour, El Sayed, & Martins, 2012).

Increasing EMPO use has resulted in severe public health, social, and economic problems (Kolodny et al., 2015). The rate of EMPO-attributable fatal overdose has continued to climb over the past decade, and by 2011 was four times that observed in 1999 (Chen, Hedegaard, & Warner, 2014). Substantial increases in the number of emergency visits related to EMPO use have been observed, from 172,738 in 2004 to 488,004 in 2011 (Substance Abuse and Mental Health Services Administration, 2013a). Between 2002 and 2012, there was a 370% increase in the rate of individuals seeking publicly funded treatment for addiction to prescription opioids (Substance Abuse and Mental Health Services Administration, 2014).

Evidence also suggests that growth in the sale, use, and non-medical use of prescription opioids have contributed to a dramatic rise in heroin use in the United States. Analyses of data from the National Survey of Drug Use and Health (NSDUH) suggests that the risk of heroin initiation is approximately 20 times higher among persons who report extra-medical use of prescription opioids, with four out of five recent heroin initiates reporting prior EMPO use (Muhuri, Gfroerer, & Davies, 2013). Young adult populations are among those at greatest risk of heroin initiation: a recently published report from the Centers for Disease Control and Prevention found that heroin use is most common among persons 18 to 25 years, and has doubled since 2002, from 3.5 per 1,000 in 2002–2004 to 7.3 per 1,000 in 2011–2013 (C. M. Jones, Logan, Gladden, & Bohm, 2015). In a recently published retrospective analysis of NSDUH data, the peak hazard of heroin initiation among young EMPO users was 18 years old (Cerdá, Santaella, Marshall, Kim, & Martins, 2015). Notably, those reporting EMPO use initiation at ages 10–12 had the highest risk of transitioning to heroin use in young adulthood, compared to youth who initiated EMPO use later in adolescence. A recent longitudinal study of EMPO-using youth in Ohio also found that initiating prescription opioid use before age 15 increased the risk for transition to heroin use (Carlson, Nahhas, Martins, & Daniulaityte, 2016). These studies extend former work demonstrating that early onset non-medical prescription drug use is a risk factor for the development of opioid dependence (McCabe, West, Morales, Cranford, & Boyd, 2007).

With regards to injection drug use, early studies indicated that prescription opioid injecting among young adults was rare. For example, a US study of over 4,000 undergraduates found that injection drug use was reported by less than 0.5% of lifetime EMPO users (McCabe, Cranford, Boyd, & Teter, 2007). Another study of over 500 street-based EMPO users in New York City found that prescription opioid injection was reported by less than 5% (Davis & Johnson, 2008). More contemporary evidence suggests that injecting initiation is increasingly common in this population (Roy, Arruda, & Bourgois, 2011; Young, Havens, & Leukefeld, 2010). One study of rural Appalachian EMPO users found that the median time from first use of OxyContin® to injection was 3 years (Young & Havens, 2012). Although the majority of EMPO users do not transition to injection drug use, initiation rates are increasing, particularly among young people (Green, Black, Grimes Serrano, Budman, & Butler, 2011; Green, Bowman, Low, McHugh, & Friedmann, 2015). Qualitative research has identified several distinct typologies of substance use transitions among young EMPO users who progress to injecting. Many begin with snorting or sniffing prescription opioids, followed by non-injection heroin use and subsequent heroin injecting (Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2014), or direct progression to prescription opioid injecting (Lankenau et al., 2012a; Roy, et al., 2011).

There is significant concern that increasing rates of injecting among young people may offset declines in HIV incidence attributable to injection drug use observed in the US and other Western nations over the past decade (Hadland & Wood, 2012; Surratt, Kurtz, & Cicero, 2011). Moreover, the incidence of hepatitis C virus (HCV) among young persons in the US has risen dramatically since 2006, with the majority (77%) of new HCV cases reporting a history injection drug use, and 82% reporting sharing of other drug preparation equipment (Suryaprasad et al., 2014). One recent study involving young persons in Kentucky, Tennessee, Virginia, and West Virginia reported that 73% of acute HCV cases cited injection drug use as the principal risk factor (Zibbell et al., 2015). The study also found a concomitant increase in the percentage of admissions to publicly-funded substance abuse treatment centers for prescription opioid injection (from 6% to over 18%), further demonstrating a link between EMPO use, drug injecting, and HCV infection among young people. In another study of people who inject drugs (PWID), younger age and prescription opioid injection (compared to the injection of other drugs) were positively associated with HCV seropositivity (Zibbell, Hart-Malloy, Barry, Fan, & Flanigan, 2014). Prescription opioid injection was also identified as an independent risk factor for HCV acquisition in a street-based sample of drug users in Montréal (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012). Collectively, these findings demonstrate that youth who inject prescription opioids represent a population in need of improved access to evidence-based harm reduction and HIV/HCV prevention services.

Historically, overdose fatalities have been most common among older adults (45 to 54); however, recent data suggests that mortality rates have been increasing among young people, at least 10% annually over the past decade (Hedegaard, Chen, & Warner, 2015). Similar trends have been observed in the rate of hospitalizations for prescription opioid overdose among young people (White, Hingson, Pan, & Yi, 2011). A growing literature has documented the contexts, experiences, and risk factors for overdose among EMPO-using young adults. For example, recent studies have revealed pervasive personal and/or social

experiences with overdose, primarily in the context of multiple pharmaceutical use—prescription opioids with benzodiazepines and other prescription medications—or combined use of opioid analgesics and heroin (Frank et al., 2015; Lankenau et al., 2012b). Polysubstance use significantly increases the risk of overdose among EMPO users, particularly when opioids are combined with other central nervous system-depressant drugs that result in respiratory depression (Webster et al., 2011). However, studies to date have shown young EMPO users have poor knowledge of opioid overdose avoidance and response strategies, and perceive prescription opioids as associated with a lower risk of overdose than illicit drugs such as crack, methamphetamine, and heroin (Daniulaityte, Falck, & Carlson, 2012; Frank, et al., 2015).

In sum, the collective body of evidence demonstrates substantial vulnerability to HCV infection, overdose, and other adverse health concerns among young people who use prescription opioids extra-medically. Although harm reduction approaches have a critical role to play in the prevention of morbidity and mortality among EMPO users, the uptake and effectiveness of evidence-based interventions (e.g., needle and syringe programs, naloxone distribution) among opioid-using young adults appears has been limited in some settings (Frank, et al., 2015; Mateu-Gelabert, Guarino, Jessell, & Teper, 2015). In this narrative commentary, we summarize key harm reduction strategies for EMPO users, focusing on young adult populations. We discuss established and emerging interventions to reduce harms associated with EMPO use among young people, and examine structural, programmatic, and logistical barriers to their implementation. Finally, we highlight promising new avenues for research and practice to address EMPO use and mitigate related harms.

## Harm reduction for extra-medical prescription opioid users

A number of evidence-based harm reduction interventions are available for EMPO users (European Monitoring Centre for Drugs and Drug Addiction, 2015a; Wermeling, 2010). For people who inject prescription opioids, engagement in needle and syringe programmes (NSPs) reduces injection-related risk behavior and can prevent HIV and HCV disease transmission (MacArthur et al., 2014). In addition to standalone NSPs, pharmacies are a common source of syringes for prescription opioid injectors (Zaller et al., 2012). Medication-assisted treatment (MAT) with opioid agonists (methadone and buprenorphine) and antagonists (short- or long-acting naltrexone) have been shown to be highly effective at diminishing opioid use (Mattick, Breen, Kimber, & Davoli, 2009), decreasing the risk of HIV infection (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011), improving adherence with HIV medications (Lappalainen et al., 2015), and reducing the risk of mortality (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010). Unfortunately, these medications are highly underutilized in the United States: of the 2.5 million persons with opioid dependence in 2012, fewer than one million received MAT (Volkow, Frieden, Hyde, & Cha, 2014). Supervised injecting facilities (SIFs) represent an additional, evidence-based harm reduction strategy to engage marginalized and street-based PWID. These facilities have been shown to enhance access to primary health care, increase uptake of addiction treatment, and reduce overdose mortality (Marshall, Milloy, Wood, Montaner, & Kerr, 2011; Potier, Laprevote, Dubois-Arber, Cottencin, & Rolland, 2014). Currently, the only public SIF in North America is located in Vancouver, Canada and offers services for young people who

inject drugs (Hadland et al., 2014). Implementation of SIFs in the US is currently prohibited by the Controlled Substances Act (Beletsky, Davis, Anderson, & Burris, 2008).

Naloxone is a safe and effective medication that is the standard treatment to reverse the effects of an opioid overdose (Boyer, 2012). Expanded access to naloxone is seen by many as critical to reduce overdose mortality in the United States (Kim, Irwin, & Khoshnood, 2009). Over the past two decades, community-based overdose education and naloxone distribution (OEND) programs have greatly expanded the reach and potential effectiveness of this intervention (Wheeler, Jones, Gilbert, & Davidson, 2015). Current evidence suggests that bystanders (including opioid users) trained through OEND programs can and will effectively use naloxone to reverse opioid overdoses (Clark, Wilder, & Winstanley, 2014; European Monitoring Centre for Drugs and Drug Addiction, 2015b; Green, Heimer, & Grau, 2008). However, few (if any) studies to date have evaluated OEND interventions specifically for young people who use prescription opioids extra-medically.

### **Obstacles to effective harm reduction for young adult EMPO users**

Young adults who use EMPO represent a diverse and fragmented population, often disconnected from drug-using networks traditionally reached by harm reduction services (Daniulaityte, Falck, Wang, & Carlson, 2009). For example, the past-year prevalence of EMPO use among young adults in the United States is similar across levels of educational attainment (13.2% among those without a high school education, 13.1% among those who have completed high school, and 11.3% among persons attending college) (Martins et al., 2015). Heroin use among frequent EMPO users is prevalent across all major racial/ethnic sub-groups (Martins, Santaella-Tenorio, Marshall, Maldonado, & Cerda, 2015). In the United States, the gaps between men and women in opioid-related emergency room visits, drug overdose, and heroin use US have narrowed over the past decade, with significant increases among women aged 18 to 24 (Centers for Disease Control and Prevention, 2013; C. M. Jones, et al., 2015). In part due to the sociodemographic diversity of the population and their dissimilarity with older, street-based drug users, EMPO-using young adults have proved difficult to reach with traditional harm reduction strategies (e.g., peer outreach, sterile syringe distribution). Ethno-epidemiological studies have demonstrated that young EMPO injectors frequently have no direct contact with NSPs or other harm reduction services, and are thus unfamiliar with safer injecting practices and techniques (Lankenau, et al., 2012a; Mars, et al., 2014; Roy, et al., 2011). One recent study in New York found that, since young EMPO injectors obtained syringes primarily from pharmacies or from friends rather than directly from harm reduction programs, they were largely unfamiliar with naloxone and other overdose prevention strategies (Frank, et al., 2015).

Several other factors contribute to the poor engagement of EMPO-using youth in harm reduction services. First, many EMPO users do not belong to larger networks of street-based drug users, and are thus poorly connected to harm reduction and HIV prevention programs in their communities (Bruneau, et al., 2012; Firestone & Fischer, 2008). Second, many harm reduction programs are located in urban centers, often far from neighborhoods in which many young EMPO users reside, socialize, and use drugs (Frank, et al., 2015; Heimer, Barbour, Palacios, Nichols, & Grau, 2014). Third, generational, class, and other socially

constructed boundaries (separating types of drug use and routes of administration), in addition to widespread stigmatization of older disadvantaged heroin users, contributes to EMPO-using youths' reluctance to access harm reduction services (Frank, et al., 2015). Fourth, traditional harm reduction strategies may not be youth-centered, and may be seen by young people as being targeted towards an older population (Merkinaitė, Grund, & Frimpong, 2010). Finally, young PWID experience a wide array of structural barriers to accessing harm reduction services, including stigma and social condemnation, fear of law enforcement, and lack of youth-friendly services (Krug, Hildebrand, & Sun, 2015; Merkinaitė, et al., 2010). Moreover, at least 18 countries have age restrictions on accessing NSPs (Harm Reduction International, 2012). As such, legal interventions may be needed to expand harm reduction interventions to minors. Research is warranted to determine the extent to which these same barriers exist for youth who use prescription opioids (rather than, or in addition to, those who use illicit drugs).

MAT is available for young opioid-dependent persons in the United States, although treatment is heavily underutilized and there exist manifold barriers to widespread uptake and implementation. Methadone maintenance is permitted for persons under age 18; however, federal US guidelines require at least two documented unsuccessful attempts at detoxification or drug-free treatment in the past 12 months (U.S. Government Publishing Office, 2013). An evaluation of one methadone program for young people found that staff generally believed methadone to be highly effective and should be made available as an initial treatment for opioid-dependent adolescents (Guarino et al., 2009). However, some clients noted that, since methadone is a long-term serious commitment, the treatment should only be used when other interventions have failed. Additional studies are needed to determine the feasibility and effectiveness of methadone therapy for young people, and to inform whether federal regulations should be changed.

Buprenorphine is FDA-approved for use in patient populations aged 16 and older (H. E. Jones, 2004). Two randomized controlled trials have shown efficacy of buprenorphine treatment for opioid-dependent youth (Marsch et al., 2005; Woody et al., 2008). Office-based buprenorphine therapy is effective for treating opioid addiction treatment among adults (Matson, Hobson, Abdel-Rasoul, & Bonny, 2014). Unfortunately, long-term retention in office-based buprenorphine treatment may be challenging with adolescents and young adults. One retrospective study found that emerging adults (aged 18 to 25) were significantly less likely to be retained in an office-based buprenorphine program than older adults (17% versus 45% at 12 months, respectively) (Schuman-Olivier, Weiss, Hoepfner, Borodovsky, & Albanese, 2014). Further research is needed to compare and combine abstinence-based residential treatment with outpatient care (including office-based buprenorphine therapy) for opioid-using young adults (Schuman-Olivier, Claire Greene, Bergman, & Kelly, 2014).

### **Towards youth-centered harm reduction for prescription opioid use**

Given that many EMPO-using youth do not access existing services (or experience barriers while attempting to do so), research is needed to identify innovative strategies and technologies that expand the reach of current harm reduction programs. Since health issues



vary across the EMPO-using youth population, research is also warranted to inform tailored, population-specific approaches.

To achieve these goals, community, institutional, and political support is vital. Furthermore, the meaningful involvement of young prescription opioid users in the planning and implementation of these services is critical to their sustainability and success. Although several different models of youth engagement exist, harm reduction interventions have successfully involved youth as peer educators, mentors, program designers, and evaluators (Poland, Tupker, & Breland, 2002). Positive outcomes related to youth involvement in the planning and implementation of these programs have been discussed in detail elsewhere (Paterson & Panessa, 2008), but include greater relevance of the material to the target population, the creation of pro-social relationships with peers, and a greater sense of social responsibility.

The expansion of harm reduction efforts to reach youth who use prescription opioids extra-medically requires re-assessment of the evolving “risk environment” within which EMPO use takes place (Mazumdar, McRae, & Islam, 2015). Specifically, recent research has begun to examine the specific social, economic, and political contexts that increase the risk of EMPO use and related harms. For example, an analysis of a nationally representative sample of US adolescents found that youth of lower socioeconomic status and those with greater residential instability were more likely to report lifetime non-medical use of prescription drugs (Stabler, Gurka, & Lander, 2015). A nationally representative study of Canadian adolescents found that recreational pain reliever use was highest among youth in low-income communities and those residing in rural areas in close proximity to urban centers (Pulver, Davison, & Pickett, 2014). These results suggest that street-based harm reduction efforts (e.g., mobile syringe distribution and peer outreach) should be expanded to semi-urban and rural communities.

Given that many young people use prescription opioids in indoor locations and private social contexts, the dissemination of harm reduction interventions through EMPO users’ social networks is recommended. Pharmacy-based naloxone distribution is a promising method to prevent opioid-related overdose deaths, particularly in light of the fact that young people who inject prescription opioids often obtain syringes from pharmacies (Frank, et al., 2015; Zaller, et al., 2012). However, potential barriers that have been identified include: laws governing the distribution of naloxone; misconceptions about the formulation and use of naloxone; the need for training on behalf of both the recipient and the dispensing pharmacist; and cost of the intervention (Bailey & Wermeling, 2014; Zaller, Yokell, Green, Gaggin, & Case, 2013). Nonetheless, pilot programs have demonstrated an ability to overcome these barriers and have shown success (Bailey & Wermeling, 2014; Kan et al., 2014). Venue-based interventions (including for example the distribution of harm reduction materials in clubs, bars, music events, and other venues in which youth prescription opioid use may occur) also merit consideration. Venue-based interventions that combine social influence and structural components (e.g., peer-based education plus enhanced health services within alcohol-serving establishments) have shown promising results in decreasing hazardous alcohol use and HIV risk behavior among gay men and commercial sex workers (Kalichman, 2010). The extent to which venue-based programming could be adapted to

address extra-medical prescription opioid use among young people is unknown and in need of investigation. Finally, fear of arrest has been identified as a primary reason for young people's reluctance to contact emergency services in the event of an overdose (Davidson, Ochoa, Hahn, Evans, & Moss, 2002; Frank, et al., 2015); therefore, the continued expansion of Good Samaritan Laws is recommended.

Fostering an effective harm reduction approach to address the opioid epidemic among young people will necessitate shifts in school, family, and community norms regarding the public health response to adolescent substance use. Psychosocial developmental and educational initiatives have long been the mainstay of interventions to address youth substance use, despite the fact that many have limited evidence of effectiveness (Strang et al., 2012). However, a brief universal prevention program has been shown to result in long-term reductions in EMPO use, maintained 6 to 14 years after the intervention (Spath et al., 2013). In tandem with evidence-based primary prevention interventions, school-based approaches to reduce harms among youth who have initiated EMPO are recommended, particularly in communities heavily affected by prescription opioid misuse. Harm reduction education within health curricula, overdose prevention and response training for school nurses, distribution of harm reduction materials by nurses in school health clinics, and the provision of naloxone in high school are all potentially effective interventions and should be evaluated. Cluster randomized trials have shown harm minimization smoking interventions to be more effective than abstinence-based approaches (Hamilton, Cross, Resnicow, & Hall, 2005; Resnicow et al., 2008), suggesting that harm reduction approaches to address EMPO use among school-attending youth might be effective. Given the controversial nature of harm reduction in school environments, such interventions may require robust community and institutional support. Communities heavily affected by EMPO use among young adults could be most appropriate for piloting these interventions. Finally, the expansion of harm reduction programs in school environments may necessitate changes to local or state laws. For example, the requirement that public schools stock naloxone requires amendment to existing laws: as of 2015, only five states in the US had done so (Faust, 2015).

Rapidly evolving technologies offer new venues for the dissemination of services to youth who are geographically isolated and/or disconnected from traditional harm reduction services. For example, numerous websites (e.g., [www.BlueLight.org](http://www.BlueLight.org)) rely on user-contributed content to provide information regarding use experiences and harm reduction strategies. Although several studies have successfully employed internet-based recruitment to survey EMPO users (Chiauzzi, Dasmahapatra, Lobo, & Barratt, 2013; Katz, Fernandez, Chang, Benoit, & Butler, 2008), it remains unclear whether online venues are an effective medium with which to disseminate harm reduction information among youth. Despite the fact that three quarters of young adults in the US access social-networking websites, few studies have examined the use of social media venues (e.g., Facebook) to engage substance users (Ramo & Prochaska, 2012). However, the use of digital media to provide sexual health promotion and risk reduction has been shown to be effective at reaching diverse populations of youth (Guse et al., 2012). Similar interventions may be effective for reaching young adults who use prescription opioid extra-medically.



Social media venues also provide an opportunity to promote virtual “communities of intravention”, in which youth EMPO users (as persons with lived experience and expert knowledge) are active participants in their own harm reduction, health promotion, and community protection. Established cultures of intravention have been observed among older PWID to prevent HIV transmission (Friedman et al., 2004). Research is needed to identify how similar phenomena can be fostered and sustained among young adults who use prescription opioids extra-medically. Finally, telehealth technologies hold promise to improve access to specialized pediatric addiction treatment and care, particularly for youth living outside of urban areas and those with complex multi-morbidities. Telehealth models have been shown to increase access to subspecialty HCV treatment, psychiatric care, and opioid dependence management in underserved communities across the US (Arora et al., 2011; Norman, 2006; Ruetsch, Tkacz, McPherson, & Cacciola, 2012).

Ultimately, the inclusion of people who use drugs in the planning, staffing, and implementation of harm reduction interventions is critical to ensure effective intervention, particularly for youth (Buccieri, 2010; Henderson, 2014). Peer-based naloxone training and distribution (Piper et al., 2008), and drug user-led programs to provide safer injection education (Small et al., 2012), are two examples of effective drug user “intravention”. Since people who use drugs are active agents in their own self-protection and in those of the broader community (Friedman et al., 2007), youth-focused harm reduction interventions should seek to strengthen existing protective behaviors within young people’s drug-using networks. Many EMPO-using youth are engaged in harm minimization strategies, including limiting dose and avoiding polysubstance use or mixing with alcohol (Daniulaityte, et al., 2012). Further research is needed to identify how existing harm reduction behaviors in the community can be best supported.

## Conclusions

In sum, a growing body of evidence indicates young people who engage in extra-medical opioid use are at high risk of transition to heroin use, injection drug use initiation, overdose, HCV acquisition, and other harms. Medical, social, and structural interventions, grounded in a harm reduction framework, are necessary to respond effectively to this public health crisis. Community, statewide, and federal programs that address high-risk practices broadly (e.g., high-dose opioid prescribing, combined opioid and benzodiazepine use) are in need of continued development. The specific impact of these policies and programs on youth EMPO use needs to be evaluated. Finally, the diverse nature of the at-risk population and different motivations for use requires multiple interventions that address the full spectrum of opioid use, from recreational use to opioid dependence. Social media and other communication technologies warrant attention as potentially powerful media to expand the reach of current interventions. In moving towards a youth-centered harm reduction approach, the meaningful involvement of young people who use prescription opioids, both in the planning of new efforts and the support of existing minimization practices, is critical.

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## REFERENCES

- Arora S, Thornton K, Murata G, Deming P, Kalishman S, Dion D, Parish B, Burke T, Pak W, Dunkelberg J, Kistin M, Brown J, Jenkusky S, Komaromy M, Qualls C. Outcomes of treatment for hepatitis C virus infection by primary care providers. *New England Journal of Medicine*. 2011; 364(23):2199–2207. [PubMed: 21631316]
- Bailey AM, Wermeling DP. Naloxone for opioid overdose prevention: pharmacists' role in community-based practice settings. *Annals of Pharmacotherapy*. 2014; 48(5):601–606. [PubMed: 24523396]
- Beletsky L, Davis CS, Anderson E, Burris S. The law (and politics) of safe injection facilities in the United States. *American Journal of Public Health*. 2008; 98(2):231–237. [PubMed: 18172151]
- Boyer EW. Management of opioid analgesic overdose. *New England Journal of Medicine*. 2012; 367(2):146–155. [PubMed: 22784117]
- Brands B, Paglia-Boak A, Sproule BA, Leslie K, Adlaf EM. Nonmedical use of opioid analgesics among Ontario students. *Canadian Family Physician*. 2010; 56(3):256–262. [PubMed: 20228312]
- Bruneau J, Roy E, Arruda N, Zang G, Jutras-Aswad D. The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users. *Addiction*. 2012; 107(7):1318–1327. [PubMed: 22248184]
- Bucciari K. Harm reduction as practice: Perspectives from a community of street youth and social service providers. *Social Development Issues*. 2010; 32(3):1–15.
- Carlson RG, Nahhas RW, Martins SS, Daniulaityte R. Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study. *Drug and Alcohol Dependence*, ePub ahead of print. 2016
- Center for Behavioral Health Statistics and Quality. National Survey on Drug Use and Health: Detailed Tables. Substance Abuse and Mental Health Services Administration. , editor. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2015.
- Centers for Disease Control and Prevention. Vital Signs: Overdoses of prescription opioid pain relievers and other drugs among women — United States, 1999–2010. *MMWR: Morbidity and Mortality Weekly Report*. 2013; 62(26):537–542. [PubMed: 23820967]
- Cerdá M, Santaella J, Marshall BDL, Kim JH, Martins SS. Nonmedical prescription opioid use in childhood and early adolescence predicts transitions to heroin use in young adulthood: A national study. *Journal of Pediatrics*. 2015; 167(3):605–612. e602. [PubMed: 26054942]
- Chen, LH.; Hedegaard, H.; Warner, M. Drug-poisoning deaths involving opioid analgesics: United States, 1999–2011. N. C. f. H. Statistics (Ed.), (Vol. NCHS Data Brief, no. 166. Hyattsville, MD: 2014.
- Chiauzzi E, Dasmahapatra P, Lobo K, Barratt MJ. Participatory research with an online drug forum: a survey of user characteristics, information sharing, and harm reduction views. *Substance Use and Misuse*. 2013; 48(8):661–670. [PubMed: 23750771]
- Clark AK, Wilder CM, Winstanley EL. A systematic review of community opioid overdose prevention and naloxone distribution programs. *Journal of Addiction Medicine*. 2014; 8(3):153–163. [PubMed: 24874759]
- Cornish R, Macleod J, Strang J, Vickerman P, Hickman M. Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database. *BMJ*. 2010; 341:c5475. [PubMed: 20978062]
- Daniulaityte R, Falck R, Carlson RG. “I’m not afraid of those ones just ‘cause they’ve been prescribed”: perceptions of risk among illicit users of pharmaceutical opioids. *International Journal on Drug Policy*. 2012; 23(5):374–384. [PubMed: 22417823]
- Daniulaityte R, Falck RS, Wang J, Carlson RG. Illicit use of pharmaceutical opioids among young polydrug users in Ohio. *Addictive Behaviors*. 2009; 34(8):649–653. [PubMed: 19398164]
- Davidson PJ, Ochoa KC, Hahn JA, Evans JL, Moss AR. Witnessing heroin-related overdoses: the experiences of young injectors in San Francisco. *Addiction*. 2002; 97(12):1511–1516. [PubMed: 12472634]
- Davis WR, Johnson BD. Prescription opioid use, misuse, and diversion among street drug users in New York City. *Drug and Alcohol Dependence*. 2008; 92(1–3):267–276. [PubMed: 17913395]

- Degenhardt L, Charlson F, Mathers B, Hall WD, Flaxman AD, Johns N, Vos T. The global epidemiology and burden of opioid dependence: results from the global burden of disease 2010 study. *Addiction*. 2014; 109(8):1320–1333. [PubMed: 24661272]
- European Monitoring Centre for Drugs and Drug Addiction. Best Practice Portal: Harm reduction interventions for opioid injectors. Retrieved July 8 2015 from <http://www.emcdda.europa.eu/best-practice/harm-reduction/opioid-injectors>
- European Monitoring Centre for Drugs and Drug Addiction. Preventing fatal overdoses: A systematic review of the effectiveness of take-home naloxone. Luxembourg: EMCDDA Papers, Publications Office of the European Union; 2015b.
- Faust, M. School Nurses Stock Drug To Reverse Opioid Overdoses. Retrieved Jan 13 2016 from <http://www.npr.org/sections/health-shots/2015/09/16/440770695/school-nurses-stock-drug-to-reverse-opioid-overdoses>
- Firestone M, Fischer B. A qualitative exploration of prescription opioid injection among street-based drug users in Toronto: behaviours, preferences and drug availability. *Harm Reduct J*. 2008:530.
- Frank D, Mateu-Gelabert P, Guarino H, Bennett A, Wendel T, Jessell L, Teper A. High risk and little knowledge: overdose experiences and knowledge among young adult nonmedical prescription opioid users. *International Journal on Drug Policy*. 2015; 26(1):84–91. [PubMed: 25151334]
- Friedman SR, de Jong W, Rossi D, Touze G, Rockwell R, Des Jarlais DC, Elovich R. Harm reduction theory: users' culture, micro-social indigenous harm reduction, and the self-organization and outside-organizing of users' groups. *International Journal on Drug Policy*. 2007; 18(2):107–117. [PubMed: 17689353]
- Friedman SR, Maslow C, Bolyard M, Sandoval M, Mateu-Gelabert P, Neaigus A. Urging others to be healthy: "intravention" by injection drug users as a community prevention goal. *AIDS Education and Prevention*. 2004; 16(3):250–263. [PubMed: 15237054]
- Ghandour LA, El Sayed DS, Martins SS. Prevalence and patterns of commonly abused psychoactive prescription drugs in a sample of university students from Lebanon: an opportunity for cross-cultural comparisons. *Drug and Alcohol Dependence*. 2012; 121(1–2):110–117. [PubMed: 21924844]
- Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database of Systematic Reviews*. 2011:8.
- Green TC, Black R, Grimes Serrano JM, Budman SH, Butler SF. Typologies of prescription opioid use in a large sample of adults assessed for substance abuse treatment. *PLoS ONE*. 2011; 6(11):e27244. [PubMed: 22087270]
- Green TC, Bowman S, Low S, McHugh K, Friedmann P. Strategies to reduce prescription opioid abuse in the United States: How have they influenced the epidemic. *Drug and Alcohol Dependence*. 2015; 2015(146):e129–e130.
- Green TC, Heimer R, Grau LE. Distinguishing signs of opioid overdose and indication for naloxone: an evaluation of six overdose training and naloxone distribution programs in the United States. *Addiction*. 2008; 103(6):979–989. [PubMed: 18422830]
- Guarino HM, Marsch LA, Campbell WS 3rd, Gargano SP, Haller DL, Solhkhah R. Methadone maintenance treatment for youth: experiences of clients, staff, and parents. *Substance Use and Misuse*. 2009; 44(14):1979–1989. [PubMed: 20001689]
- Guse K, Levine D, Martins S, Lira A, Gaarde J, Westmorland W, Gilliam M. Interventions using new digital media to improve adolescent sexual health: a systematic review. *Journal of Adolescent Health*. 2012; 51(6):535–543. [PubMed: 23174462]
- Hadland SE, DeBeck K, Kerr T, Nguyen P, Simo A, Montaner JS, Wood E. Use of a medically supervised injection facility among street youth. *Journal of Adolescent Health*. 2014; 55(5):684–689. [PubMed: 24925493]
- Hadland SE, Wood E. Commentary on Bruneau et al. (2012): injection of prescription opioid pain relievers and infectious disease risk. *Addiction*. 2012; 107(7):1328–1329. [PubMed: 22672378]
- Hamilton G, Cross D, Resnicow K, Hall M. A school-based harm minimization smoking intervention trial: outcome results. *Addiction*. 2005; 100(5):689–700. [PubMed: 15847627]

- Harm Reduction International. The Global State of Harm Reduction 2012: Towards an integrated response. London, UK: Harm Reduction International; 2012. Excluding youth? A global review of harm reduction services for young people; p. 137-145.
- Hedegaard, H.; Chen, LH.; Warner, M. Vol. NCHS Data Brief, no 190. Hyattsville, MD: National Center for Health Statistics; 2015. Drug-poisoning deaths involving heroin: United States, 2000–2013.
- Heimer R, Barbour R, Palacios WR, Nichols LG, Grau LE. Associations between injection risk and community disadvantage among suburban injection drug users in southwestern Connecticut, USA. *AIDS and Behavior*. 2014; 18(3):452–463. [PubMed: 23921583]
- Henderson, M. On the ground: Programmes serving the needs of key populations. Retrieved July 15th 2015 from [http://apps.who.int/iris/bitstream/10665/145002/1/WHO\\_HIV\\_2014.50\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/145002/1/WHO_HIV_2014.50_eng.pdf?ua=1)
- Jann M, Kennedy WK, Lopez G. Benzodiazepines: a major component in unintentional prescription drug overdoses with opioid analgesics. *Journal of Pharmacy Practice*. 2014; 27(1):5–16. [PubMed: 24436437]
- Jones CM, Logan J, Gladden RM, Bohm MK. Vital Signs: Demographic and Substance Use Trends Among Heroin Users — United States, 2002–2013. *MMWR: Morbidity and Mortality Weekly Report*. 2015; 64:1–7. (Early Release). [PubMed: 25590678]
- Jones HE. Practical considerations for the clinical use of buprenorphine. *Sci Pract Perspect*. 2004; 2(2):4–20. [PubMed: 18552728]
- Kalichman SC. Social and Structural HIV Prevention in Alcohol-Serving Establishments Review of International Interventions Across Populations. *Alcohol Research & Health: The Journal of the National Institute on Alcohol Abuse and Alcoholism*. 2010; 33(3):184–194. [PubMed: 23584060]
- Kan M, Gall JA, Latypov A, Gray R, Bakpayev M, Alisheva D, Rakhmatova K, Sadieva AS. Effective use of naloxone among people who inject drugs in Kyrgyzstan and Tajikistan using pharmacy- and community-based distribution approaches. *International Journal on Drug Policy*. 2014; 25(6): 1221–1226. [PubMed: 24560486]
- Katz N, Fernandez K, Chang A, Benoit C, Butler SF. Internet-based survey of nonmedical prescription opioid use in the United States. *Clinical Journal of Pain*. 2008; 24(6):528–535. [PubMed: 18574362]
- Kim D, Irwin KS, Khoshnood K. Expanded access to naloxone: options for critical response to the epidemic of opioid overdose mortality. *American Journal of Public Health*. 2009; 99(3):402–407. [PubMed: 19150908]
- Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*. 2015; 36:559–574.
- Krug A, Hildebrand M, Sun N. “We don’t need services. We have no problems”: exploring the experiences of young people who inject drugs in accessing harm reduction services. *Journal of the International AIDS Society*. 2015; 18(2(Suppl 1)):19442. [PubMed: 25724510]
- Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. *International Journal on Drug Policy*. 2012a; 23(1): 37–44. [PubMed: 21689917]
- Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Patterns of Prescription Drug Misuse among Young Injection Drug Users. *Journal of Urban Health*. 2012b; 89(6):1004–1016. [PubMed: 22684424]
- Lappalainen L, Nolan S, Dobrer S, Puscas C, Montaner J, Ahamad K, Dong H, Kerr T, Wood E, Milloy MJ. Dose-response relationship between methadone dose and adherence to antiretroviral therapy among HIV-positive people who use illicit opioids. *Addiction*. 2015; 110(8):1330–1339. [PubMed: 25940906]
- MacArthur GJ, van Velzen E, Palmateer N, Kimber J, Pharris A, Hope V, Taylor A, Roy K, Aspinall E, Goldberg D, Rhodes T, Hedrich D, Salminen M, Hickman M, Hutchinson SJ. Interventions to prevent HIV and Hepatitis C in people who inject drugs: a review of reviews to assess evidence of effectiveness. *International Journal on Drug Policy*. 2014; 25(1):34–52. [PubMed: 23973009]

- 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 on Drug Policy*. 2014; 25(2): 257–266. [PubMed: 24238956]
- Marsch LA, Bickel WK, Badger GJ, Stothart ME, Quesnel KJ, Stanger C, Brooklyn J. Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. *Archives of General Psychiatry*. 2005; 62(10):1157–1164. [PubMed: 16203961]
- Marshall BDL, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet*. 2011; 377(9775):1429–1437. [PubMed: 21497898]
- Martins SS, Kim JH, Chen LY, Levin D, Keyes KM, Cerda M, Storr CL. Nonmedical prescription drug use among US young adults by educational attainment. *Social Psychiatry and Psychiatric Epidemiology*. 2015; 50(5):713–724. [PubMed: 25427665]
- Martins SS, Santaella-Tenorio J, Marshall BD, Maldonado A, Cerda M. Racial/ethnic differences in trends in heroin use and heroin-related risk behaviors among nonmedical prescription opioid users. *Drug and Alcohol Dependence*. 2015; 151:278–283. [PubMed: 25869542]
- Mateu-Gelabert P, Guarino H, Jessell L, Teper A. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. *Journal of Substance Abuse Treatment*. 2015; 48(1):13–20. [PubMed: 25124258]
- Matson SC, Hobson G, Abdel-Rasoul M, Bonny AE. A retrospective study of retention of opioid-dependent adolescents and young adults in an outpatient buprenorphine/naloxone clinic. *Journal of Addiction Medicine*. 2014; 8(3):176–182. [PubMed: 24695018]
- Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews*. 2009; (3)
- Mazumdar S, McRae IS, Islam MM. How Can Geographical Information Systems and Spatial Analysis Inform a Response to Prescription Opioid Misuse? A Discussion in the Context of Existing Literature. *Curr Drug Abuse Rev*. 2015; 8(2):104–110. [PubMed: 26452451]
- McCabe SE, Cranford JA, Boyd CJ, Teter CJ. Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. *Addictive Behaviors*. 2007; 32(3):562–575. [PubMed: 16843611]
- McCabe SE, West BT, Morales M, Cranford JA, Boyd CJ. Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction*. 2007; 102(12):1920–1930. [PubMed: 17916222]
- Merkinaite S, Grund JP, Frimpong A. Young people and drugs: next generation of harm reduction. *International Journal on Drug Policy*. 2010; 21(2):112–114. [PubMed: 20036526]
- Muhuri, PK.; Gfroerer, JC.; Davies, MC. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. Retrieved July 7th 2015 from <http://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm>
- National Institutes on Drug Abuse. Prescription Drug Abuse: December 2011. Retrieved July 11 2013 from [http://www.drugabuse.gov/sites/default/files/prescription\\_1.pdf](http://www.drugabuse.gov/sites/default/files/prescription_1.pdf)
- Norman S. The use of telemedicine in psychiatry. *Journal of Psychiatric and Mental Health Nursing*. 2006; 13(6):771–777. [PubMed: 17087682]
- Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ*. 2015; 350:h2698. [PubMed: 26063215]
- Paterson BL, Panessa C. Engagement as an ethical imperative in harm reduction involving at-risk youth. *International Journal on Drug Policy*. 2008; 19(1):24–32. [PubMed: 18164609]
- Paulozzi LJ, Weisler RH, Patkar AA. A national epidemic of unintentional prescription opioid overdose deaths: how physicians can help control it. *Journal of Clinical Psychiatry*. 2011; 72(5): 589–592. [PubMed: 21536000]
- Piper TM, Stancliff S, Rudenstine S, Sherman S, Nandi V, Clear A, Galea S. Evaluation of a naloxone distribution and administration program in New York City. *Substance Use and Misuse*. 2008; 43(7):858–870. [PubMed: 18570021]



- Poland BD, Tupker E, Breland K. Involving street youth in peer harm reduction education. The challenges of evaluation. *Canadian Journal of Public Health*. 2002; 93(5):344–348. [PubMed: 12353454]
- Potier C, Laprevote V, Dubois-Arber F, Cottencin O, Rolland B. Supervised injection services: what has been demonstrated? A systematic literature review. *Drug and Alcohol Dependence*. 2014; 145:48–68. [PubMed: 25456324]
- Pulver A, Davison C, Pickett W. Recreational use of prescription medications among Canadian young people: identifying disparities. *Canadian Journal of Public Health*. 2014; 105(2):e121–e126. [PubMed: 24886847]
- Ramo DE, Prochaska JJ. Broad reach and targeted recruitment using Facebook for an online survey of young adult substance use. *Journal of Medical Internet Research*. 2012; 14(1):e28. [PubMed: 22360969]
- Resnicow K, Reddy SP, James S, Gabebedeen O, Ouardien R, Kambaran NS, Langner HG, Vaughan RD, Cross D, Hamilton G, Nichols T. Comparison of two school-based smoking prevention programs among South African high school students: results of a randomized trial. *Annals of Behavioral Medicine*. 2008; 36(3):231–243. [PubMed: 19067098]
- Roy E, Arruda N, Bourgois P. The growing popularity of prescription opioid injection in downtown Montreal: new challenges for harm reduction. *Substance Use and Misuse*. 2011; 46(9):1142–1150. [PubMed: 21370963]
- Ruetsch C, Tkacz J, McPherson TL, Cacciola J. The effect of telephonic patient support on treatment for opioid dependence: outcomes at one year follow-up. *Addictive Behaviors*. 2012; 37(5):686–689. [PubMed: 22348921]
- Schuman-Olivier Z, Claire Greene M, Bergman BG, Kelly JF. Is residential treatment effective for opioid use disorders? A longitudinal comparison of treatment outcomes among opioid dependent, opioid misusing, and non-opioid using emerging adults with substance use disorder. *Drug and Alcohol Dependence*. 2014; 144:178–185. [PubMed: 25267606]
- Schuman-Olivier Z, Weiss RD, Hoepfner BB, Borodovsky J, Albanese MJ. Emerging adult age status predicts poor buprenorphine treatment retention. *Journal of Substance Abuse Treatment*. 2014; 47(3):202–212. [PubMed: 24953168]
- Small W, Wood E, Tobin D, Rikley J, Lapushinsky D, Kerr T. The Injection Support Team: a peer-driven program to address unsafe injecting in a Canadian setting. *Substance Use and Misuse*. 2012; 47(5):491–501. [PubMed: 22428817]
- Spoth R, Trudeau L, Shin C, Ralston E, Redmond C, Greenberg M, Feinberg M. Longitudinal effects of universal preventive intervention on prescription drug misuse: three randomized controlled trials with late adolescents and young adults. *American Journal of Public Health*. 2013; 103(4):665–672. [PubMed: 23409883]
- Stabler ME, Gurka KK, Lander LR. Association Between Childhood Residential Mobility and Non-medical Use of Prescription Drugs Among American Youth. *Matern Child Health J*. 2015; 19(12):2646–2653. [PubMed: 26156823]
- Strang J, Babor T, Caulkins J, Fischer B, Foxcroft D, Humphreys K. Drug policy and the public good: evidence for effective interventions. *Lancet*. 2012; 379(9810):71–83. [PubMed: 22225672]
- Substance Abuse and Mental Health Services Administration. Vol. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013a. Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits.
- Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. In: Office of Applied Studies. , editor. Vol. NSDUH Series H-48, HHS Publication No. (SMA)14-4863. Rockville, MD: SAMHSA; 2013b.
- Substance Abuse and Mental Health Services Administration. Treatment Episode Data Set (TEDS): 2002–2012: National Admissions to Substance Abuse Treatment Services. In: C. f. B. H. S. a. Quality. , editor. Vol. BHSIS Series S-71, HHS Publication No. (SMA) 14-4850. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.



- Surratt H, Kurtz SP, Cicero TJ. Alternate routes of administration and risk for HIV among prescription opioid abusers. *Journal of Addictive Diseases*. 2011; 30(4):334–341. [PubMed: 22026525]
- Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, Hamdounia SB, Church DR, Barton K, Fisher C, Macomber K, Stanley M, Guilfoyle SM, Sweet K, Liu S, Iqbal K, Tohme R, Sharapov U, Kupronis BA, Ward JW, Holmberg SD. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006–2012. *Clinical Infectious Diseases*. 2014; 59(10):1411–1419. [PubMed: 25114031]
- U.S. Government Publishing Office. §8.12 (e) (2) Federal Opioid Treatment Standards. Retrieved July 9th 2015 from [http://www.ecfr.gov/cgi-bin/text-idx?SID=5cee631783378fd66f458439a24016e3&mc=true&node=se42.1.8\\_112&rgn=div8](http://www.ecfr.gov/cgi-bin/text-idx?SID=5cee631783378fd66f458439a24016e3&mc=true&node=se42.1.8_112&rgn=div8)
- Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies — tackling the opioid-overdose epidemic. *New England Journal of Medicine*. 2014; 370(22):2063–2066. [PubMed: 24758595]
- Webster LR, Cochella S, Dasgupta N, Fakata KL, Fine PG, Fishman SM, Grey T, Johnson EM, Lee LK, Passik SD, Peppin J, Porucznik CA, Ray A, Schnoll SH, Stieg RL, Wakeland W. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Medicine*. 2011; 12(Suppl 2):S26–S35. [PubMed: 21668754]
- Wermeling DP. Opioid harm reduction strategies: focus on expanded access to intranasal naloxone. *Pharmacotherapy*. 2010; 30(7):627–631. [PubMed: 20575626]
- Wheeler E, Jones TS, Gilbert MK, Davidson PJ. Opioid Overdose Prevention Programs Providing Naloxone to Laypersons - United States, 2014. *MMWR: Morbidity and Mortality Weekly Report*. 2015; 64(23):631–635. [PubMed: 26086633]
- White AM, Hingson RW, Pan IJ, Yi HY. Hospitalizations for alcohol and drug overdoses in young adults ages 18–24 in the United States, 1999–2008: results from the Nationwide Inpatient Sample. *Journal of Studies on Alcohol and Drugs*. 2011; 72(5):774–786. [PubMed: 21906505]
- Woody GE, Poole SA, Subramaniam G, Dugosh K, Bogenschutz M, Abbott P, Patkar A, Publicker M, McCain K, Potter JS, Forman R, Vetter V, McNicholas L, Blaine J, Lynch KG, Fudala PP. Extended vs Short-term Buprenorphine-Naloxone for Treatment of Opioid-Addicted Youth: A Randomized Trial. *JAMA*. 2008; 300(17):2003–2011. [PubMed: 18984887]
- Young AM, Havens JR. Transition from first illicit drug use to first injection drug use among rural Appalachian drug users: a cross-sectional comparison and retrospective survival analysis. *Addiction*. 2012; 107(3):587–596. [PubMed: 21883604]
- Young AM, Havens JR, Leukefeld CG. Route of administration for illicit prescription opioids: a comparison of rural and urban drug users. *Harm Reduct J*. 2010; 7:24. [PubMed: 20950455]
- Zaller ND, Yokell MA, Green TC, Gaggin J, Case P. The feasibility of pharmacy-based naloxone distribution interventions: a qualitative study with injection drug users and pharmacy staff in Rhode Island. *Substance Use and Misuse*. 2013; 48(8):590–599. [PubMed: 23750660]
- Zaller ND, Yokell MA, Nayak SM, Fu JJ, Bazazi AR, Rich JD. Syringe acquisition experiences and attitudes among injection drug users undergoing short-term opioid detoxification in Massachusetts and Rhode Island. *Journal of Urban Health*. 2012; 89(4):659–670. [PubMed: 22427232]
- Zibbell JE, Hart-Malloy R, Barry J, Fan L, Flanigan C. Risk factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. *American Journal of Public Health*. 2014; 104(11):2226–2232. [PubMed: 25211717]
- Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, Serrecchia J, Blankenship S, Ward JW, Holtzman D. Centers for Disease, C., & Prevention. Increases in hepatitis C virus infection related to injection drug use among persons aged <=30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012. *MMWR: Morbidity and Mortality Weekly Report*. 2015; 64(17):453–458. [PubMed: 25950251]