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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.
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 (Merkinaite, 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; Merkinaite, 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, Hoeppner, 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 (Spoth 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) 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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Conflict of interest statement

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