Published in final edited form as:

J Addict Med. 2017 ; 11(4): 266–272. doi:10.1097/ADM.0000000000000318.

Associations between physical pain, pain management, and frequency of non-medical prescription opioid use among young adults: A sex-specific analysis

Tristan I. Evans, ME¹, Elliott J. Liebling, BA¹, Traci C. Green, PhD, MSc^{1,2,3}, Scott E. Hadland, MD, MPH^{4,5,6}, Melissa A. Clark, PhD^{1,7}, and Brandon D.L. Marshall, PhD¹

¹Department of Epidemiology, Brown University School of Public Health, 121 South Main Street, Box G-S-121-2, Providence, RI, 02912, USA

²Boston University School of Medicine, Department of Emergency Medicine, 771 Albany Street, Room 1208, Boston, MA, 02118, USA

³Department of Emergency Medicine, The Warren Alpert School of Medicine of Brown University, Rhode Island Hospital, 55 Claverick Street, Providence, RI 02903, USA

⁴Division of General Pediatrics, Department of Pediatrics, Boston University School of Medicine, 88 East Newton Street, Vose Hall Room 322, Boston, MA, 02118, USA

⁵Division of Adolescent/Young Adult Medicine, Department of Medicine, Boston Children's Hospital, 333 Longwood Avenue, Boston, MA, 02115, USA

⁶Department of Pediatrics, Harvard Medical School, 25 Shattuck Street, Boston, MA, 02115, USA

⁷Department of Quantitative Health Sciences & Center for Health Policy and Research, University of Massachusetts Medical School, 55 Lake Ave North, Worcester, MA, 01605, USA

Abstract

Objectives—We sought to determine sex-specific associations between experiences of physical pain, pain management, and frequency of non-medical prescription opioid (NMPO) use among young adults.

Methods—Among participants enrolled in the Rhode Island Young Adult Prescription Drug Study (RAPiDS), we identified associations between physical pain in the past six months, pain history, pain management, polysubstance use, and weekly NMPO use. In sex-specific models, independent correlates of weekly NMPO use were identified via modified stepwise Poisson regression.

Results—Of 199 participants, the mean age was 24.6 and 65.3% were male. The racial composition was 16.6% black, 60.8% white, and 22.1% mixed or other race. A total of 119 (59.8%) participants reported weekly or greater NMPO use. The majority of male (86.2%) and female (84.1%) participants reported ever experiencing severe pain. A majority of males (72.3%)

and females (81.2%) reported that they engaged in NMPO use to treat their physical pain, and one-quarter (26.9%) of males and one-third (36.2%) of females had been denied a prescription from a doctor to treat severe pain. Among males, frequent NMPO use was independently associated with white race ($p<0.001$) and reporting greater physical pain ($p=0.002$). Among females, older age ($p=0.002$) and monthly or greater non-medical benzodiazepine use ($p=0.001$) were independently associated with weekly NMPO use.

Conclusions—Among young men in Rhode Island, physical pain may be related to frequent NMPO use. More research is needed to identify sex-specific, pain-related factors that are linked with NMPO use in order to improve harm reduction and pain management interventions.

Keywords

Non-medical prescription opioid use; Young adult; Pain management; Physical pain

Introduction

The United States is currently in the midst of an illicit and prescription opioid epidemic (Centers for Disease and Prevention, 2012). In 2015 alone, it is estimated that over 20,000 American overdose deaths were related to prescription opioid use, while approximately 13,000 were related to heroin use (Rudd et al., 2016). As a result, the use of opioid medications for the treatment of chronic non-cancer pain management is increasingly controversial (Rosenblum et al., 2008; Barry et al., 2010; Tobin et al., 2016). Various professional organizations, including the American Pain Society and the American Academy of Pain Medicine, cite concerns that some patients on chronic opioid therapy are at high risk for the development of an opioid use disorder (OUD), and/or misuse or diversion (either intentionally or unintentionally) of their opioid medications (Savage et al., 2008; Chou et al., 2009; Butler et al., 2010).

Although alternative pain management therapies (such as non-steroidal drugs, physiotherapy, and surgery) may be offered to patients for whom opioids are contraindicated, patients who display risk factors for OUD and suffer from chronic pain are frequently ineffectively treated (Rupp and Delaney, 2004; Alford et al., 2006; Ti et al., 2015; Voon et al., 2015a). Several recent reports suggest that misidentification of risk factors for and symptoms of OUD, as well as complexities associated with managing patients who are concurrently experiencing physical pain and receiving treatment for opioid addiction could increase some clinicians' reticence to prescribe opioid medications (Rupp and Delaney, 2004; Fibbi et al., 2012; Dowden, 2014; King, 2014; Rutkow et al., 2015; Voon et al., 2015a). The high prevalence of untreated physical pain among patients who display symptoms of OUD, which has been shown to range in samples of individuals seeking methadone treatment from 37% to 61%, may also be related to frequent co-occurrence of other substance use disorders and mental health disorders (Jamison et al., 2000; Rosenblum et al., 2003; Savage et al., 2008; Pettes et al., 2015; Voon et al., 2015b).

In this clinical context, young adults with severe pain may engage in non-medical prescription opioid (NMPO) use, which is defined as using an opioid without a prescription, or in a manner inconsistent with one's own prescription, in attempts to self-medicate and

manage symptoms (Lessenger and Feinberg, 2008; Voon and Kerr, 2013). While all patterns of opioid use (e.g., prescribed, experimental, or attempts to self-medicate) can result in overdose and other harmful consequences, young adults who engage in frequent (i.e., weekly or greater) NMPO use are at especially high risk for overdose (Silva et al., 2013). Unmonitored frequent NMPO use could result also in professionally unmanaged opioid tolerance, recurrence of physical pain, and (subsequently) NMPO dose escalation and/or heroin initiation. One study of 150 young adult NMPO users in New York City and Los Angeles found that over half had self-medicated with an opioid to manage severe pain, and one-quarter had been denied prescription opioids for the treatment of pain (Fibbi et al., 2012; Voon et al., 2015a). Furthermore, self-medication frequently coincided with an escalation of more intensive drug use and new risk behavior (e.g., initiation of heroin use and sniffing, snorting, or injecting drugs). Additional research is needed to inform clinical practice and other interventions to prevent self-medication with prescription opioids, escalating NMPO use among youth denied prescription opioids, and other harms (e.g., injection drug use initiation) among young adults with severe physical pain.

It is also necessary to examine the influence of sex on the relationship between factors related to physical pain and pain management and the frequency of NMPO use among young adults (Green et al., 2013). This is especially true given the dynamic and complex nature of adolescence (both psychologically and physically), sex-specific differences in biological and perceptual pain processing mechanisms (Bartley and Fillingim, 2013), and documented gender-specific pain management experiences relevant to opioid use (Green et al., 2009). While recent studies have explored the potential relationship between under-treatment of physical pain among individuals who use prescription opioids non-medically or inject drugs (Fibbi et al., 2012; Voon et al., 2015a), there is a need for more sex and gender-specific analyses of the relationship between physical pain and NMPO use. Identification of sex-specific variables associated with self-medication and frequent non-medical use of prescription opioids could help improve screening tools used in clinical pain management practices, thereby decreasing unmitigated physical pain and escalating NMPO use (Green et al., 2009). The primary objective of this analysis was to determine sex-specific associations between variables related to pain and pain management with frequent (i.e., weekly or greater) NMPO use among 18- to 29-year-olds who engage in NMPO use in Rhode Island.

Methods

Data for this analysis were derived from the Rhode Island Young Adult Prescription Drug Study (RAPiDS). Individuals were eligible to participate if they were between 18–29 years of age, lived in Rhode Island, and had engaged in NMPO use in the last 30 days. Specifically, we defined NMPO use as using an opioid without a prescription, or in a manner inconsistent with one's own prescription (e.g., higher dose than prescribed, non-oral route of consumption). A total of 200 persons were recruited between January 2015 and February 2016 via online classifieds (e.g., Craigslist), bus advertisements, flyers, and word of mouth referrals. Participants were paid \$25 to complete the confidential survey. With the exception of questions concerning injection drug use, which were administered via computer-assisted personal interviewing (CAPI), surveys were administered in person with a study interviewer.

Participants provided informed consent, and study protocols were approved by the Brown University Human Research Subject Protections Office Institutional Review Board.

The primary outcome of this analysis was frequent NMPO use (defined as weekly or greater NMPO use in the past six months). Pearson's chi-square tests and Fisher's exact tests (for cell counts <5) were used to determine bivariate associations between factors listed in Table 1, which are related to physical pain and pain management, and/or are established risk factors for frequent NMPO use (Butler et al., 2004; Chou et al., 2009; Butler et al., 2010; Jones and Moore, 2013).

We assessed recent experiences with physical pain by asking participants to indicate the highest level of pain they had experienced in the last six months on a ten-point numeric scale (with 10 corresponding to the maximum level of severe pain). Welch's *t*-tests were used to assess the significance of differences in mean ages and average levels of pain reported on the numeric pain scale. We also assessed historical experiences with physical pain by asking participants (yes/no) whether they had "Ever experienced an injury or health condition that put them in severe pain?" Of participants who reported that they had experienced an injury or health condition, we asked, "Did you try to get medication from a doctor or health professional to treat this pain?" (yes/no) and "What kind of injury or health condition was it?" Participants could provide any text response. In order to assess young adult NMPO users' experiences accessing treatment for physical pain through both licensed medical providers and alternative illicit sources, we asked participants (all yes/no): "Do you engage in NMPO use to treat physical pain?"; "Of the two NMPOs you currently reported using most regularly, were you prescribed either opioid prior to using either opioid without a prescription or not as a doctor directed?"; "Have you ever been denied medication by a doctor or health professional to treat severe pain?"; and "The last time you used a prescription opioid non-medically, where did you obtain it?"

We also assessed other risk factors for potential OUD, including: history of childhood sexual abuse, history of common mental health diagnoses (e.g., attention deficit hyperactivity disorder, obsessive-compulsive disorder, bipolar, schizophrenia, depression, anxiety, or an eating disorder), and other substance use, including lifetime heroin use, weekly or greater drug use (i.e., marijuana, ketamine, ecstasy, mushrooms, gamma hydroxybutyrate (GHB), methamphetamine, lysergic acid diethylamide (LSD) and heroin use), and at least monthly non-medical prescription stimulant or benzodiazepine use. Finally, we examined responses to the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) (Bush et al., 1998). Scores ranged between 0 and 12; values 4 and 3 were considered a positive screen for hazardous alcohol use in men and women, respectively.

Next, we developed multivariate stepwise regression models for a common outcome (weekly or greater NMPO use) according to previously established protocols (Lima et al., 2008; Harrell, 2015). Specifically, variables listed in Table 1 with $p < 0.20$ in bivariate analysis were included in the initial multivariate models. The variable with the highest type III p -value was removed from subsequent rounds of regression in a stepwise fashion. The model with the lowest AIC value was selected as the final models. Race was dichotomized as white versus all aggregated non-white races in the multivariate models due to low numbers of aggregated

non-white participants. Modified robust Poisson regression (Zou, 2004) was used to estimate standard error in the coefficients and calculate 95% confidence intervals (CI) and adjusted prevalence ratios (APR). R version 3.2.3(C) 2015 was used for all statistical analysis, and all *p*-values were two-sided.

Results

Of the 199 participants eligible for this analysis, 65.3% (n=130) were male, and the mean age was 24.6 years (SD=3.27). The racial composition of the eligible sample was 16.6% black (i.e., African American or of African, Haitian, or Cape Verdean descent), 60.8% white, and 22.1% mixed or other race.

The majority (n=119, 59.8%) of participants reported frequent NMPO use (i.e., at least weekly). Among these participants, the source of the prescription opioid they last used non-medically was as follows: the majority (n=66, 55.5%) obtained the opioid from a drug dealer, approximately one-quarter (n=30, 25.2%) bought it from a friend or relative, 16.8% (n=20) received it for free from a friend or relative, and only 1.7% (n=2) received it from her/his doctor. Additionally, approximately one-third (n=41, 34.5%) of these participants reported ever having overdosed by accident. Most (85.4%) of the NMPO users had experienced an injury or health condition that put them in severe pain. Out of these 170 (85.4%) respondents, the following types of physical pain were most common: leg pain (21.7%), back pain (20.0%), dental (7.6%) and other head, neck and shoulder pain (7.6%). Abdominal, kidney, and lung pain were rarely reported.

Sex-specific factors related to frequent NMPO use, including experiences of physical pain and pain management, are shown in Table 1. Among males (n=130), 62.3% (n=81) reported frequent NMPO use and 45.4% (n=59) reported lifetime heroin use. The vast majority (n=112, 86.2%) of male NMPO users reported experiencing an injury or health condition that put them in severe pain, and nearly three-quarters (n=94, 72.3%) reported that they engaged in NMPO use to treat their physical pain. Just under two-thirds of male NMPO users (63.8%) reported trying to obtain a prescription medication from a doctor to treat pain and 26.9% (n=35) reported having ever been denied medication by a doctor or health professional to treat severe pain.

In bivariate analyses, frequent NMPO use among males was significantly associated with lifetime heroin use (see Table 1). Among males, frequent NMPO use was also significantly associated with higher average scores on the numeric ten-point physical pain scale. White race was also associated with frequent NMPO use among males.

Among the 69 females in the eligible sample, over half (n=38, 55.1%) reported current frequent NMPO use and over one-third (n=26, 37.7%) reported lifetime heroin use. Most of the female NMPO users (n=58, 84.1%) reported experiencing an injury or health condition that put them in severe pain. Notably, however, frequency of NMPO use was not significantly associated with reporting pain on the numeric pain scale or with having ever experienced an injury or health condition that caused extreme pain (see Table 1). Additionally, 81.2% (n=56) of female NMPO users reported engaging in NMPO use to treat

physical pain, 68.1% (n=47) of female NMPO users reported that they tried to get medication from a doctor to treat severe physical pain, and 24.6% (n=17) reported having ever been denied medication by a doctor to treat severe pain.

Although sexual abuse and lifetime history of mental health diagnosis were not significantly associated with frequency of NMPO use, nearly half of female NMPO users (n=31, 44.9%) had been sexually assaulted or abused before the age of 18, and nearly three-quarters (n=52, 75.4%) reported having ever been diagnosed with a mental health disorder. The rate of sexual assault and abuse was much higher among females than males in this sample (Table 1). Additionally, the rates of childhood sexual abuse and diagnoses of a mental health disorder among females were high for any frequency of NMPO use, resulting in low variability. In bivariate analyses, non-medical use of a prescription benzodiazepine medication more than once a month and lifetime heroin use were associated with frequent NMPO use among females (Table 1). Older age was the only sociodemographic factor associated with frequent NMPO use among females.

Among the NMPO users who had experienced an injury that put them in severe pain and who did not seek assistance from a health professional (n=40), half (n=20, 50.0%) stated that they did not seek medical care because they medicated with their own prescription painkillers, 47.5% (n=19) thought they could handle the pain themselves or medicate with over the counter drugs like acetaminophen or ibuprofen, 40% (n=16) stated that they did not like seeking medical help, 25% (n=10) reported that they thought they would be denied prescription painkillers by their doctor, and 25% (n=10) reported that they had no health insurance (see Table 2).

Among male NMPO users, the final explanatory multivariate model (with the lowest AIC) of factors associated with frequency NMPO use included the following covariates: race (APR=1.32, 95% CI: 1.14–1.49 for white versus all non-white races $p<0.001$), and reporting pain on the ten-point numeric pain scale (APR=1.08 per unit increase, CI: 1.02–1.14, $p=0.006$). Among women, age (APR=1.10 per year older, 95% CI: 1.04–1.17, $p=0.002$) and non-medical benzodiazepine use more than once a month (APR=2.33, 95% CI: 1.67–2.99, $p=0.001$) were independently associated with frequent NMPO use.

Discussion

Among young adults who engage in NMPO use in Rhode Island, physical pain—and self-medication with prescription opioids to treat physical pain—is commonplace. A majority of males (86.2%) and females (84.1%) reported experiencing an injury that put them in severe pain, and over half of both sexes reported engaging in NMPO use to treat their pain. These findings are generally consistent with previous literature, which demonstrate that among young adults, non-medical use of prescription drugs, and prescription opioids in particular, may be linked to attempts to address the conditions for which these drugs are medically indicated (i.e., pain) (Becker et al., 2008; Cranford et al., 2013). While engaging in NMPO use specifically to treat physical pain was not independently associated with frequent NMPO use among young adults of either sex in Rhode Island, our results suggest that sex-specific factors could be differentially associated with frequent NMPO use.

Among young male NMPO users in Rhode Island, white race and reporting numerically higher reported levels of pain on a ten-point scale were independently associated with weekly or greater NMPO use. In contrast, among female NMPO users, older age and non-medical prescription benzodiazepine use were independently associated with weekly or greater NMPO use. Sex-specific patterns of pain perception and experiences interacting with health professionals could conceivably impact the way male and females report pain to health care providers, and thus the way young adults with severe physical pain are treated. In our study, a similar percentage of male and female NMPO users tried to obtain medication from a doctor to treat severe pain. However, approximately one-third of females and one-quarter of males had ever been denied medication from a doctor. In addition to being denied medication to treat severe pain by a physician, a significant percentage (20%) of young NMPO users who reported experiencing a high level of pain did not try to obtain treatment from a doctor for reasons including the belief that they would be denied prescription painkillers and/or having no health insurance. Pervasive negative perceptions of health care providers (and/or the medical system in general), as well as issues related to accessing healthcare resources, may also underlie the high prevalence of professionally unmitigated physical pain in this population of young adults who use NMPOs in Rhode Island (Ahern et al., 2007; Sterling et al., 2010). In some cases, participants may have been experiencing pain that would have been more appropriately treated with non-opioid medications had they been seen and properly evaluated by medical provider (Dowell et al., 2016). Furthermore, current medical guidelines recommend that pain, particularly chronic pain, should primarily be treated with non-opioid therapy (Dowell et al., 2016). Individuals who self-medicate may not be aware of these developments and the risks associated with opioid use due to the widespread use of opioids for the treatment of pain. Future research should also assess the impact of purchasing NMPOs and the risks associated with engaging in illegal income-generating activities (e.g., drug dealing or sex work).

It is notable that nearly all established OUD risk factors (many of which are commonly used to screen patients for their potential to develop OUD in the clinic), such as a previous diagnosis of at least one mental health disorder, regular street drug use, sexual assault or abuse before the age of 18, non-medical prescription stimulant use, and hazardous alcohol use were not significantly associated with frequent NMPO use among males and females in our sample. However, we did not formally measure opioid use disorders or diagnosis of an OUD, which may have resulted in this null finding. Research is needed to better define the relationship between comorbid mental health conditions and substance use disorders to determine how to manage physical pain in populations with a diverse range of co-occurring psychiatric and substance use disorders (Twillman, 2007; Savage et al., 2008).

Our findings are similar to results from several studies that have shown a high prevalence of prescription analgesia denial among people who use drugs. In a recent study of 462 adults who injected drugs in British Columbia, nearly two-thirds of participants had been denied prescription opioids. In this study, many participants (44%) reported that prescription analgesia denial was commonly related to “being accused of drug seeking” (Voon et al., 2015a). Similarly, in a study of young adults who engaged in non-medical use of an opioid, tranquilizer and/or stimulant in the last 90 days, participants associated their experiences with being denied prescription analgesia with being identified as a drug user, a lack of health

insurance, and having medication withheld by a parent or authority figure (Fibbi et al., 2012). Approximately 40% of young adults in this sample who did not receive treatment escalated their NMPO use or self-medicated with heroin. The clinical practice of distinguishing “aberrant drug seekers” from individuals who present with “legitimate” unmanaged physical pain is valuable in ensuring patient safety and effective treatment of pain. However, given the documented consequences associated with escalating NMPO use as a result of pain self-management (Fibbi et al., 2012), improving clinical screening protocols for OUD and increasing access to treatment for individuals suffering from comorbid OUD (or other substance use disorders) and unmitigated physical pain is needed. Regardless, identification of factors specifically associated with the high risk transition to frequent NMPO use (e.g. a potential symptom of OUD progression associated with increased risk of fatal overdose) could aid more accurate identification of individuals who are in the process of developing increasingly dangerous patterns of opioid use, thereby potentially increasing the chance that education, harm reduction programs, and pain management interventions are timely and successful.

The results of this analysis should be considered in light of the limitations of this study, which include the potential for underreporting socially taboo behaviors (e.g. nonmedical use of prescription opioids, heroin use, etc.), which may result in socially desirable reporting biases. To minimize the potential for these biases to interfere with our results, computer-assisted self-interviewing (CASI) was used to collect particularly sensitive and/or stigmatizing information (e.g., injection drug use). In the context of this pilot study, we were only able to assess pain using a unidimensional pain score, which may not properly capture the functional impact of experiencing pain. Future research is needed to evaluate pain and pain experiences using validated multidimensional measures, including for example the PEG scale for assessing pain intensity and interference (Krebs et al., 2009). The study also used cross-sectional data, meaning that the results are only correlative and not causal. Specifically, we were unable to assess differences in NMPO use between acute and chronic pain conditions over time. Furthermore, since there are no prior studies of young adult NMPO use in Rhode Island, it is impossible to discern if the study population is representative of the larger NMPO using population. Finally, the small sample size may have limited our ability to detect clinically meaningful differences between men and women participating in the study. Larger studies are needed to definitely determine the sex-specific differences in pain experiences and pain management among young men and women who use prescription opioids non-medically.

Conclusions

This study demonstrated an independent association between higher reported levels of pain and weekly or greater NMPO use among young male NMPO users in Rhode Island. Among young adult NMPO users who did not seek medical care for an injury that put them in severe pain, the most commonly cited reasons were self-medication with prescription painkillers, a perceived ability to handle the pain by themselves or medicate with over the counter drugs, and not wanting to seek medical help. Improving access to treatment for individuals with comorbid opioid use and mental health disorders, as well as managing unmitigated physical pain, is a pressing task for providers. Harm reduction and pain management interventions, as

well as evidence-based clinical screening, may need to reflect sex-specific and pain-related factors associated with frequent NMPO use in order to successfully reach young adults.

Acknowledgments

We would like to thank the study participants, current and past RAPIIDS researchers and staff, as well as Jesse Yedinak and Beth Elston for their research and administrative assistance. The RAPIIDS project is supported by the US National Institute on Drug Abuse (R03-DA037770). Brandon Marshall is supported by a Henry Merrit Wriston Fellowship from Brown University.

Abbreviations

NMPO	Non-medical prescription opioid
NMPS	Non-medical prescription stimulant
OD	Opioid use disorder
APR	Adjusted prevalence ratio

References

- Ahern J, Stuber J, Galea S. Stigma discrimination the health of illicit drug users. *Drug Alcohol Depend.* 2007; 88:188–196. [PubMed: 17118578]
- Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med.* 2006; 144:127–134. [PubMed: 16418412]
- Barry DT, Irwin KS, Jones ES, et al. Opioids, chronic pain, and addiction in primary care. *J Pain.* 2010; 11:1442–1450. [PubMed: 20627817]
- Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth.* 2013; 111:52–58. [PubMed: 23794645]
- Becker WC, Sullivan LE, Tetrault JM, Desai RA, Fiellin DA. Non-medical use, abuse and dependence on prescription opioids among U.S. adults: psychiatric, medical and substance use correlates. *Drug Alcohol Depend.* 2008; 94:38–47. [PubMed: 18063321]
- Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP) Alcohol Use Disorders Identification Test. *Arch Intern Med.* 1998; 158:1789–1795. [PubMed: 9738608]
- Butler SF, Budman SH, Fanciullo GJ, Jamison RN. Cross validation of the current opioid misuse measure to monitor chronic pain patients on opioid therapy. *Clin J Pain.* 2010; 26:770–776. [PubMed: 20842012]
- Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. *Pain.* 2004; 112:65–75. [PubMed: 15494186]
- Centers for Disease C. and Prevention. CDC grand rounds: prescription drug overdoses - a U.S. epidemic. *MMWR Morb Mortal Wkly Rep.* 2012; 61:10–13. [PubMed: 22237030]
- Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *J Pain.* 2009; 10:131–146. [PubMed: 19187890]
- Cranford JA, McCabe SE, Boyd CJ. Adolescents' nonmedical use excessive medical use of prescription medications and the identification of substance use subgroups. *Addict Behav.* 2013; 38:2768–2771. [PubMed: 23954563]
- Dowden S. Considerations of non-medical use of prescription opioids (NMUPO) in pediatric pain management. *Pediatric Pain Letter.* 2014; 16:15–21.

- Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States 2016. *JAMA*. 2016; 315:1624–1645. [PubMed: 26977696]
- Fibbi M, Silva K, Johnson K, Langer D, Lankenau SE. Denial of prescription opioids among young adults with histories of opioid misuse. *Pain Med*. 2012; 13:1040–1048. [PubMed: 22882357]
- Green TC, Grimes Serrano JM, Licari A, Budman SH, Butler SF. Women who abuse prescription opioids: findings from the Addiction Severity Index-Multimedia Version Connect prescription opioid database. *Drug Alcohol Depend*. 2009; 103:65–73. [PubMed: 19409735]
- Green TC, Zaller N, Palacios WR, et al. Law enforcement attitudes toward overdose prevention and response. *Drug Alcohol Depend*. 2013; 133:677–684. [PubMed: 24051061]
- Harrell, FJ. Regression modeling strategies. Springer International Publishing; 2015.
- Jamison RN, Kauffman J, Katz NP. Characteristics of methadone maintenance patients with chronic pain. *J Pain Symptom Manage*. 2000; 19:53–62. [PubMed: 10687327]
- Jones T, Moore T. Preliminary data on a new opioid risk assessment measure: the Brief Risk Interview. *J Opioid Manag*. 2013; 9:19–27. [PubMed: 23709300]
- King SA. Iatrogenic opioid use disorder: an issue ignored. *Psychiatric Times*. 2014; 31:32G–32G.
- Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med*. 2009; 24:733–738. [PubMed: 19418100]
- Lessenger JE, Feinberg SD. Abuse of prescription and over-the-counter medications. *J Am Board Fam Med*. 2008; 21:45–54. [PubMed: 18178702]
- Lima VD, Harrigan R, Murray M, et al. Differential impact of adherence on long-term treatment response among naive HIV-infected individuals. *AIDS*. 2008; 22:2371–2380. [PubMed: 18981777]
- Pettes T, Kerr T, Voon P, Nguyen P, Wood E, Hayashi K. Depression and sexual risk behaviours among people who inject drugs: a gender-based analysis. *Sex Health*. 2015; 12:224–230. [PubMed: 25982173]
- Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. *JAMA*. 2003; 289:2370–2378. [PubMed: 12746360]
- Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. *Exp Clin Psychopharmacol*. 2008; 16:405–416. [PubMed: 18837637]
- Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths - United States, 2010–2015. *MMWR Morb Mortal Wkly Rep*. 2016; 65:1445–1452. [PubMed: 28033313]
- Rupp T, Delaney KA. Inadequate analgesia in emergency medicine. *Ann Emerg Med*. 2004; 43:494–503. [PubMed: 15039693]
- Rutkow L, Turner L, Lucas E, Hwang C, Alexander GC. Most primary care physicians are aware of prescription drug monitoring programs, but many find the data difficult to access. *Health Aff (Millwood)*. 2015; 34:484–492. [PubMed: 25732500]
- Savage SR, Kirsh KL, Passik SD. Challenges in using opioids to treat pain in persons with substance use disorders. *Addict Sci Clin Pract*. 2008; 4:4–25. [PubMed: 18497713]
- Silva K, Schrager SM, Kecojevic A, Lankenau SE. Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs. *Drug Alcohol Depend*. 2013; 128:104–110. [PubMed: 22974490]
- Sterling S, Weisner C, Hinman A, Parthasarathy S. Access to treatment for adolescents with substance use and co-occurring disorders: challenges and opportunities. *J Am Acad Child Adolesc Psychiatry*. 2010; 49:637–646. quiz 725–636. [PubMed: 20610133]
- Ti L, Voon P, Dobrer S, Montaner J, Wood E, Kerr T. Denial of pain medication by health care providers predicts in-hospital illicit drug use among individuals who use illicit drugs. *Pain Res Manag*. 2015; 20:84–88. [PubMed: 25562839]
- Tobin DG, Andrews R, Becker WC. Prescribing opioids in primary care: Safely starting monitoring and stopping. *Cleve Clin J Med*. 2016; 83:207–215. [PubMed: 26974992]

- Twillman RK. Mental disorders in chronic pain patients. *J Pain Palliat Care Pharmacother*. 2007; 21:13–19. [PubMed: 18032311]
- Voon P, Callon C, Nguyen P, et al. Denial of prescription analgesia among people who inject drugs in a Canadian setting. *Drug Alcohol Rev*. 2015; 34:221–228. [PubMed: 25521168]
- Voon P, Hayashi K, Milloy MJ, et al. Pain Among High-Risk Patients on Methadone Maintenance Treatment. *J Pain*. 2015; 16:887–894. [PubMed: 26101814]
- Voon P, Kerr T. “Nonmedical” prescription opioid use in North America: a call for priority action. *Subst Abuse Treat Prev Policy*. 2013; 8:39. [PubMed: 24289260]
- Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004; 159:702–706. [PubMed: 15033648]

Table 1

Sex-specific associations between frequent non-medical prescription opioid (NMPO) use and variables related to physical pain and pain management among young adult NMPO users in Rhode Island (n=199)

Females (n=69) Males (n=130)	Males:		p - value	Male Total	Females: Frequent NMPO Use		p - value	Female Total	Male vs. Female p - value
	Frequent NMPO Use	Infrequent NMPO Use			Females: Frequent NMPO Use	Females: Infrequent NMPO Use			
Mean age (years, SD)	24.9 (3.2)	24.0 (3.3)	0.134	24.6 (3.3)	25.6 (2.8)	23.1 (3.2)	0.001	24.5 (3.2)	0.884
Current Gender Identity									
Male	80 (61.5)	47 (36.2)	0.466	127 (97.7)	1 (1.4)	2 (2.9)	0.309	3 (4.3)	
Female	0 (0.0)	1 (0.8)		1 (0.8)	37 (53.6)	26 (37.7)		63 (91.3)	
Transgender/Other	1 (0.8)	1 (0.8)		2 (1.5)	0 (0.0)	2 (2.9)		2 (2.9)	
Race									
White	62 (47.7)	23 (17.7)	0.002	85 (65.4)	20 (29.0)	16 (23.2)	0.989	36 (52.2)	
Black	8 (6.2)	14 (10.8)		22 (16.9)	6 (8.7)	5 (7.2)		11 (15.9)	
Mixed/Other Race	11 (8.5)	12 (9.2)		23 (17.7)	12 (17.4)	9 (13.0)		21 (30.4)	
Please indicate the worst your physical pain has been in the last six months on a scale of 1 – 10 (number, SD)									
	7.2 (2.5)	6.0 (2.7)	0.016	6.7 (2.6)	7.3 (2.3)	7.6 (2.2)	0.581	7.4 (2.3)	0.077
Have you ever been injured or experienced a health condition that put you in severe pain?									
Yes	72 (55.4)	40 (30.8)	0.369	112 (86.2)	32 (46.4)	26 (37.7)	0.721	58 (84.1)	0.936
No	9 (6.9)	9 (6.9)		18 (13.8)	6 (8.7)	3 (4.3)		9 (13.0)	
Did you try to get medication from a doctor or health professional to treat this pain? (of people who were ever injured or experienced a health condition that put them in severe pain)									
Yes	54 (41.5)	29 (22.3)	0.949	83 (63.8)	25 (36.2)	22 (31.9)	0.738	47 (68.1)	0.413
No	18 (13.8)	11 (8.5)		29 (22.3)	7 (10.1)	4 (5.8)		11 (15.9)	
Have you ever been denied medication by a doctor or health professional to treat severe pain?									
Yes	24 (18.5)	11 (8.5)	0.490	35 (26.9)	17 (24.6)	8 (11.6)	0.237	25 (36.2)	0.181
No	57 (43.8)	38 (29.2)		95 (73.1)	21 (30.4)	21 (30.4)		42 (60.9)	
Of the two NMPOs you currently reported using most regularly, were you prescribed either opioid prior to using either opioid without a prescription or not as a doctor directed?									
Yes	39 (30.0)	14 (10.8)	0.053	53 (40.8)	17 (24.6)	14 (20.3)	0.874	31 (44.9)	0.648
No	42 (32.3)	34 (26.2)		76 (58.5)	21 (30.4)	16 (23.2)		37 (53.6)	
Do you engage in NMPO use to treat physical pain?									
Yes	61 (46.9)	33 (25.4)	0.545	94 (72.3)	30 (43.5)	26 (37.7)	0.611	56 (81.2)	0.191
No	20 (15.4)	16 (12.3)		35 (26.9)	8 (11.6)	4 (5.8)		12 (17.4)	
Lifetime heroin use									

Females (n=69) Males (n=130)	Males: Frequent NMPO Use	Males: Infrequent NMPO Use	Males: Infrequent NMPO Use	<i>p</i> - value	Male Total	Females: Frequent NMPO Use	Females: Infrequent NMPO Use	<i>p</i> - value	Female Total	Male vs. Female <i>p</i> - value
Yes	46 (35.4)	13 (10.0)	13 (10.0)	0.001	59 (45.4)	21 (30.4)	5 (7.2)	0.003	26 (37.7)	0.416
No	35 (26.9)	36 (27.7)	36 (27.7)		71 (54.6)	17 (24.6)	25 (36.2)		42 (60.9)	
Do you use any of these drugs (marijuana, ketamine, MDMA, mushrooms, GHB, methamphetamine, cocaine, LSD, or heroin) more than once a week?										
Yes	70 (53.8)	36 (27.7)	36 (27.7)	0.075	106 (81.5)	29 (42.0)	20 (29.0)	0.693	49 (71.0)	0.197
No	10 (7.7)	13 (10.0)	13 (10.0)		23 (17.7)	9 (13.0)	9 (13.0)		18 (26.1)	
At least monthly non-medical use of a benzodiazepine medication?										
Yes	57 (43.8)	26 (20.0)	26 (20.0)	0.071	83 (63.8)	31 (44.9)	12 (17.4)	0.001	43 (62.3)	0.932
No	24 (18.5)	23 (17.7)	23 (17.7)		47 (36.2)	7 (10.1)	18 (26.1)		25 (36.2)	
At least monthly non-medical use of a stimulant medication?										
Yes	38 (29.2)	21 (16.2)	21 (16.2)	0.788	59 (45.4)	21 (30.4)	16 (23.2)	0.874	37 (53.6)	0.290
No	43 (33.1)	28 (21.5)	28 (21.5)		71 (54.6)	17 (24.6)	14 (20.3)		31 (44.9)	
Before the age of 18, were you ever sexually assaulted or abused?										
Yes	15 (11.5)	9 (6.9)	9 (6.9)	0.954	24 (18.5)	20 (29.0)	11 (15.9)	0.343	31 (44.9)	0.003
No	60 (46.2)	37 (28.5)	37 (28.5)		97 (74.6)	18 (26.1)	18 (26.1)		36 (52.2)	
While you were growing up, was anyone who lived with you using street drugs?										
Yes	42 (32.3)	27 (20.8)	27 (20.8)	0.937	69 (53.1)	20 (29.0)	11 (15.9)	0.353	31 (44.9)	0.439
No	36 (27.7)	21 (16.2)	21 (16.2)		57 (43.8)	17 (24.6)	17 (24.6)		34 (49.3)	
Ever been diagnosed with any of the following psychiatric disorders (ADHD, OCD, bipolar, schizophrenia, depression, anxiety, or an eating disorder)?										
Yes	58 (44.6)	34 (26.2)	34 (26.2)	0.858	92 (70.8)	29 (42.0)	23 (33.3)	0.867	52 (75.4)	0.438
No	22 (16.9)	15 (11.5)	15 (11.5)		37 (28.5)	8 (11.6)	7 (10.1)		15 (21.7)	
Hazardous alcohol use *										
Yes	51 (39.2)	35 (26.9)	35 (26.9)	0.425	86 (66.2)	19 (27.5)	16 (23.2)	0.977	35 (50.7)	0.063
No	30 (23.1)	14 (10.8)	14 (10.8)		44 (33.8)	19 (27.5)	14 (20.3)		33 (47.8)	

[§]Not all columns add to 100% due to missing values

* Defined based on responses to the AUDIT-C

Table 2 Reasons that young adult NMPO users did not go to the doctor to be treated for severe pain (n=40^{§§})

	Total n (%)[§]	Males n (%)[§]	Females n (%)[§]
I thought I could handle the pain myself or medicate with over the counter drugs like acetaminophen and ibuprofen			
Yes	19 (47.5)	15 (57.7)	4 (40.0)
No	17 (42.5)	11 (42.3)	6 (60.0)
I medicated with my own prescription painkillers			
Yes	20 (50.0)	15 (57.7)	5 (50.0)
No	16 (40.0)	11 (42.3)	5 (50.0)
I thought I would be denied prescription painkiller by my doctor			
Yes	10 (25.0)	8 (30.8)	2 (20.0)
No	26 (65.0)	18 (69.2)	8 (80.0)
I don't like seeking medical help			
Yes	16 (40.0)	13 (50.0)	3 (30.0)
No	20 (50.0)	13 (50.0)	7 (70.0)
I have no health insurance			
Yes	10 (25.0)	7 (26.9)	3 (30.0)
No	26 (65.0)	19 (73.1)	7 (70.0)

[§]Not all columns add to 100% due to missing values^{§§}Of those who experienced an injury that put them in severe pain and did not seek assistance from a health professional