



Published in final edited form as:

J Addict Dis. 2016 ; 35(1): 42–51. doi:10.1080/10550887.2016.1107264.

Risk factors for opioid overdose and awareness of overdose risk among veterans prescribed chronic opioids for addiction or pain

Christine M. Wilder, M.D.^{1,2,*}, Shannon C. Miller, M.D.^{1,2}, Elizabeth Tiffany, M.D.², Theresa Winhusen, Ph.D.², Erin L. Winstanley, Ph.D.³, and Michael D. Stein, M.D.⁴

¹Department of Veterans Affairs Medical Center, 3200 Vine Street, Cincinnati, OH 45220

²Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, 3131 Harvey Avenue, Cincinnati, OH 45229

³James L. Winkle College of Pharmacy, University of Cincinnati, PO Box 670004, Cincinnati, OH 45267-0004

⁴Department of Medicine, Alpert School of Medicine of Brown University, Butler Hospital, 345 Blackstone Blvd, Providence, RI 09206

Abstract

Background—Rising overdose fatalities among US veterans suggest veterans taking prescription opioids may be at risk for overdose. However, it is unclear whether veterans prescribed chronic opioids are aware of this risk.

Objectives—The objective of this study was to identify risk factors and determine awareness of risk for opioid overdose in veterans treated with opioids for chronic pain, using veterans treated with methadone or buprenorphine for opioid use disorder as a high-risk comparator group.

Methods—Ninety veterans on chronic opioid medication for either opioid use disorder or pain management completed a questionnaire assessing risk factors, knowledge, and self-estimate of risk for overdose.

Results—Nearly all veterans in both groups had multiple overdose risk factors although individuals in the pain management group had on average a significantly lower total number of risk factors than did individuals in the opioid use disorder group (5.9 v. 8.5, $p < 0.0001$). On average, participants treated for pain management scored slightly but significantly lower on knowledge of opioid overdose risk factors (12.1 v. 13.5, $p < 0.01$). About 70% of participants, regardless of group, believed their overdose risk was below that of the average American adult. There was no significant relationship between self-estimate of overdose risk and either number or knowledge of opioid overdose risk factors.

*Corresponding Author: Christine M. Wilder, MD; Christine.wilder@uc.edu.

Disclaimer

The contents do not represent the views of the Department of Veterans Affairs or the United States Government.

Contributors

All authors have reviewed and approved the manuscript. All authors contributed substantially to its content.

Conflict of Interest

The authors have no conflict of interest to declare.

Discussion—Our results suggest that veterans in both groups underestimated their risk for opioid overdose. Expansion of overdose education to include individuals on chronic opioids for pain management and a shift in educational approaches to overdose prevention may be indicated.

Keywords

overdose; veterans; opioids; chronic pain; medication assisted treatment; risk assessment

Introduction

Overdose is now a public health crisis in the United States¹. Deaths due to opioid overdose (OOD) have increased dramatically since the mid-1990's^{1, 2} such that unintentional poisoning is now the leading cause of injury-related death among Americans age 25–64³. Increased overdoses due to prescription opioid analgesics are responsible for most of this increase⁴. Opioid-using patients across a variety of health care settings, not just those identified as people who misuse substances, may be at risk for overdose.

It is unclear how frequently physicians warn patients about the risks of overdose when prescribing opioids⁵. Although researchers have identified factors associated with increased risk for OOD, patients taking prescribed opioids may or may not be aware of these specific risk factors. Even those who are aware of risk factors may not identify themselves as being at risk. Optimistic bias is present when an individual believes his or her personal risk for a particular outcome is lower than for others in a similar risk group^{6, 7}. This bias has been documented in studies of medical risks ranging from osteoporosis⁸ to HIV⁹ to heart disease¹⁰. Among people who misuse substances, several studies have noted that individuals with multiple HIV transmission risk factors tended to perceive their personal risk of contracting HIV as low^{11–13}. A recent qualitative study found that people who misuse opioids other than heroin often perceive these opioids as being safe from the risk of overdose, even though most of the interviewees had experienced one or more overdoses in the past¹⁴.

Studies of non-prescription use of opioids have identified risk factors associated with overdose. Some are not modifiable, such as a history of prior overdose^{15–17}, a history of incarceration or arrest^{18–20}, and male gender^{16, 17, 21}. Others are modifiable, such as injection drug use^{17, 22}, use of alcohol^{15, 20, 22, 23}, use of benzodiazepines/sedatives^{22, 23}, and use of cocaine^{15, 22}. Additionally, the period immediately following release from incarceration has been identified as a high risk period for drug-related death, primarily due to overdose²⁴. The risk of drug-related death is estimated to be 3 to 8 times as likely in the first 2 weeks of release as in the ensuing 10 weeks²⁵.

While there are well established risk factors for overdose from the non-prescription use of opioids, the potential for overdose from prescribed opioids, especially for treatment of chronic pain, is less well understood. Thus far, opioid dose, opioid type, and co-prescription of benzodiazepines have been identified as risk factors for overdose among individuals receiving prescribed opioids. Increasing dose of prescribed chronic opioid therapy, expressed in morphine-equivalents (ME), is directly associated with increasing risk of overdose^{23, 26, 27}. Methadone, when prescribed for pain, is disproportionately represented

among overdose related deaths²⁸, suggesting that individuals prescribed methadone as opposed to an alternative opioid for pain relief may also be at higher risk for fatal overdose. Finally, co-prescription of benzodiazepines and opioids is associated with a dose-dependent increased risk of overdose death²⁹ in US veterans.

The rise in OOD in the population of veterans seeking treatment through the Veterans Health Administration (VA) closely mirrors that of the US population. A recent study also demonstrated a population-level association between trends in VA opioid prescribing by state and overdose deaths in veterans by state³⁰. Risk factors for death from accidental overdose (including opioid overdose) among veterans include male sex, age between 30 and 59, and having a general psychiatric or substance use disorder³¹. Veterans may be at particular risk for OOD given that they have high rates of pain treated with prescription opioids³²: between FY 2004 and FY 2008, about 32% of individuals treated nationwide through the VA received at least one prescription for opioids for pain²⁷. Thus, veterans' hospitals are an important setting for studying the risk of prescription OOD.

Individuals treated for opioid use disorder with methadone or buprenorphine are likely to have easily identifiable risk factors for OOD, whereas determining risk level for veterans on chronic opioids for pain is more challenging. OOD prevention education is usually provided prior to prescription of either methadone or buprenorphine for opioid use disorder; in fact, this is a federally mandated component of patient orientation in methadone clinics³³. On the other hand, OOD education is not usually a focus for individuals on opioids for chronic pain, partly because it is not clear whether such education is needed. The purpose of this study was to identify the presence of risk factors and determine the risk awareness for OOD in veterans treated with opioids for chronic pain, using veterans treated with methadone or buprenorphine for opioid use disorder as a high-risk comparator group. Clarifying the risk factors and risk awareness for OOD in veterans treated with opioids for chronic pain could help determine whether and how OOD education should be administered to these veterans.

Material and Methods

Both outpatient clinics participating in this study are located in a VA hospital in a mid-sized mid-Western city. The Opioid Treatment Clinic (OTC) provides group and individual counseling as well as methadone or buprenorphine treatment for approximately 310 veterans with opioid use disorder. The Pain Management Clinic (PMC) provides comprehensive pain management, including counseling, physical therapy, acupuncture, chiropractic treatment, and pharmacologic treatment with opioid and other analgesic prescriptions, to about 150 veterans with chronic pain conditions. To be included in this study, veterans had to be receiving opioid medication prescribed by a VA medical provider for a minimum of 3 consecutive months and had to be receiving treatment from either the OTC or PMC, but not both, at the time of study entry. The study was approved by the requisite institutional review board and VHA research and development committees.

Veterans in both clinics were recruited from July 2013 to January 2014 through fliers posted in approved locations at each clinic. Fliers requested that interested patients who had been taking opioid medication for at least 3 months call a designated study number to participate

in a survey about veterans' perceptions of risk for overdose on opioid medications and interest in overdose treatment. Additionally, veterans in the OTC received a flier at the dosing window of the clinic, while veterans in the PMC received a flier from the clinic nurse at the beginning of their appointments. One hundred thirteen veterans were screened for participation and of these 106 met inclusion criteria. Veterans meeting inclusion criteria were scheduled for a face-to-face interview. Ninety veterans completed the study interview; 16 did not attend their interview sessions. Approximately 20% of the total estimated patient population of the two clinics participated in the survey.

All veterans completed the written informed consent process prior to beginning the 45 minute, verbally administered study interview. Prior to the study interview, research staff read the following definition of overdose to each participant: "When we use the term overdose, we mean when a toxic amount of drug or drugs overwhelms the body such that a person is no longer able to respond to others or breathe adequately. An overdose can occur with prescription or recreational drugs, or a combination of both, and can be deliberate or accidental." This definition, along with a list of common opioid and sedative medications, was provided in written form for the participant to refer to throughout the interview. During the first part of the interview, with permission from the participant, research staff recorded all active prescriptions in the VA electronic medical record for opioids and sedatives (benzodiazepines, barbiturates, and muscle relaxants), including the type of medication, the dose and frequency of the medication, and how long the medication had been prescribed. Veterans received a small monetary reimbursement for their participation.

The interview included questions about demographics and medical/psychiatric conditions. It also contained multiple items about personal OOD risk factors. The AUDIT-C was used to assess alcohol use³⁴ and the DAST-10 was used to assess drug use³⁵. History of overdose, arrests, and intravenous drug use were assessed through additional interview questions. Opioid and sedative use were assessed through both the interview and a review of the participant's medical record; because participants were taking a variety of opioid medications, we converted their total daily opioid dose to the equianalgesic morphine equivalent (ME) dose, where 1 ME = 1 mg oral morphine per day³⁶. Participants were asked to assess their risk of OOD in two ways: 1) participants were asked, "Compared to the average American adult, what do you think is your risk of overdosing on opioids in the next year?" (higher versus the same or lower, referred to as "comparative risk self-estimate" in this paper); 2) participants were asked to estimate the percent chance that they would overdose on opioids in the next year using a visual analog scale (referred to as "absolute risk self-estimate" in this paper). Participant knowledge of OOD risk factors was assessed with an 18 question true/false test. Participants were instructed to consider whether each item was a risk factor for OOD in general, not whether it was a risk factor for them personally. Some items on the true/false test were modified from Domain A of the Opioid Overdose Knowledge Scale³⁷, a previously validated measure. However, we did not use the full OOKS for several reasons: it focused exclusively on heroin users, making some items (i.e., increase in heroin purity, switching from smoking to injecting heroin) inappropriate for participants who did not use heroin; it included multiple questions about symptoms and treatment of OOD which were not relevant to our study; and all answers in Domain A of OOKS were "true," which we thought might lead our participants to lose focus after

answering multiple items. Some false risk factors (such as, “Not getting enough sleep”) were therefore included to maintain participant engagement during the test. The risk factor knowledge test used in this study was piloted in a sample of 250 individuals in community treatment for substance use; validation of the test is ongoing.

All data analyses were completed using SAS, Version 9.3 (SAS Institute, Inc., Cary, North Carolina). Statistical tests were conducted at a 5% Type I error rate with Bonferroni correction for multiple comparisons. Baseline demographics and medication use were compared between the two clinics using Wilcoxon rank-sum, chi-square, or Fisher’s exact tests as appropriate. Percent of participants with each identified OOD risk factor and percent of participants correctly identifying each risk factor on the knowledge test was compared across clinics using Fisher’s exact tests. Mean number of participant risk factors and total score on the knowledge test were compared by clinic and by comparative risk self-estimate using the Wilcoxon rank-sum test. Pearson correlation coefficients were determined to compare number of risk factors with knowledge of risk factors, absolute risk self-estimate with knowledge of risk factors, and absolute risk self-estimate with number of risk factors.

Results

Ninety individuals completed the survey, 52 from the OTC and 38 from the PMC. Table 1 displays characteristics of respondents. The median VA-prescribed ME dose for PMC participants was 35 ME (interquartile range 70). The median total ME dose, based on self-reported use of all prescribed and illicit opioids, for PMC participants (excluding 2 individuals who used heroin, for which ME could not be calculated) was 56 ME (interquartile range 70). The median VA-prescribed ME dose for OTC participants was 430 ME (interquartile range 230); 77% of OTC participants were prescribed methadone and the remainder were taking buprenorphine. It was not possible to calculate the total ME dose (all prescribed plus all illicit) for OTC participants due to the inability to estimate ME for heroin. Seventy-nine percent of OTC and 58% of PMC participants ($p<0.05$) reported that they had “never” taken an extra dose of their VA-prescribed opioid medication, while 11% of OTC and 13% of PMC participants (NS) reported taking an extra dose at least once per week. Twenty-five percent of OTC and 29% of PMC (NS) participants reported opioid-related aberrant behaviors (defined as taking more than the prescribed amount of their VA-prescribed opioids, using opioids obtained from non-VA prescribers, or using illicit opioids) at least once in the last 3 months. Seventeen percent of OTC and 58% of PMC participants ($p<0.001$) were prescribed sedative medications (including benzodiazepines, other hypnotics such as zolpidem, and muscle relaxants such as carisoprodol); 6% OTC and 29% PMC ($p<0.01$) participants were prescribed benzodiazepines specifically. Six percent of OTC and 5% of PMC participants (NS) reported sedative-related aberrant behaviors (defined as taking more than the prescribed amount of their VA-prescribed sedatives, using sedatives obtained from non-VA prescribers, or using illicit sedatives) at least once in the last 3 months.

Table 2 displays all potential OOD risk factors assessed for participants. The average number of risk factors was significantly higher for participants in the OTC compared to participants in the PMC (8.5 v. 5.9, $p<0.0001$). There was no significant correlation between participants’ number of risk factors and their knowledge of OOD risk factors (Pearson’s

knowledge of OOD risk factors than did those being treated for opioid use disorder, suggesting individuals being treated for chronic pain might be less aware of their risk.

Veterans in both clinics did fairly well overall on the test of overdose knowledge, consistent with prior studies done among non-veterans^{38, 39}. While it is encouraging that over 90% of veterans recognized a range of important OOD risk factors, there were certain risk factors neither group was apt to recognize. Many veterans in both groups did not identify liver disease or sleep apnea as potential risks for overdose in persons using opioids, even though these conditions are particularly prevalent in the veteran population. PMC participants were significantly less likely than OTC participants to recognize that using opioids after a week or more of not using was a risk factor for overdose. This risk is often emphasized in OOD education programs for people who inject drugs, where brief periods of enforced abstinence (due to detox, jail, or drug availability) are common. However, individuals in pain management programs can also experience brief periods of abstinence if they overuse their prescriptions and then run out of medication prior to scheduled refill. Increased education about OOD risks for individuals who are not identified as having substance use disorders may be needed, especially for those on high dose opioids.

Our study also revealed that about a quarter of the individuals in both the OTC and PMC samples were misusing their medications at least occasionally. Among PMC participants, the median ME of total opioids used was over 160% of the median ME dose prescribed through the VA, suggesting that some individuals were using substantially more opioids (either prescribed by non-VA physicians, obtained from family or acquaintances, or purchased illicitly) than prescribed by their VA providers. In two large studies^{26, 27}, one of which focused on veterans, opioid therapy doses of just 50–100mg ME per day were associated with significantly increased risk for unintentional overdose: the median total dose of PMC participants was 56 ME. Almost 30% of individuals in the PMC group were also prescribed benzodiazepines, further increasing their risk for overdose.

Although all of the veterans surveyed, regardless of treatment group, had risk factors for OOD, 70% of participants estimated their risk as lower than the average American. There was no correlation between a participant's total number of risk factors and his/her own estimate of risk as compared to the general population. We interpret this as an example of the optimistic bias that has already been demonstrated in multiple studies of health risk perception^{8–10}. Participants were somewhat better at recognizing their risk when asked to estimate the chance that they would overdose within the next year rather than when asked to make a comparison with the "average American." Although participants remained over-optimistic, with more than half estimating their chance as 0, the correlation between number of risk factors and estimate of absolute risk suggests that individuals had some awareness of the effects of personal risk factors on chance of OOD.

The difference between the two OOD risk estimates (one using comparative risk and one using absolute risk) might be explained by the "representative heuristic," one of the driving components of optimistic bias. The representative heuristic describes the tendency for individuals who are asked to judge something relative to a prototype ("the average American adult") to imagine instead a prototype that is stereotypical of the risk category ("someone

who might overdose on opioids”)⁴⁰. When an individual compares herself to this “risky” prototype, she then judges herself at lower risk than the stereotyped image. The representative heuristic may have been particularly likely in veterans in the OTC sample, who may associate with individuals at much higher risk for overdose than would be representative of the US population as a whole. When participants were asked to estimate their own absolute risk, without making a comparison to another group, the representative heuristic component of optimistic bias was no longer present, resulting in a more accurate self-assessment. Other aspects of optimistic bias, such as the tendency to focus on personal factors that decrease risk⁷ and to overestimate personal control⁶, remained in play, however; thus, even when asked about absolute risk, participants underestimated their risk.

Our findings suggest that OOD education efforts may be more salient if emphasis is placed on absolute risk rather than relative risk, for example, by identifying personal risk factors and discussing how these risk factors increase a particular individual’s risk of OOD. In a pain clinic setting, this might include highlighting personal medical and psychiatric problems that increase risk for OOD independent of a history of substance abuse. Because individuals tend to judge the risk of others as higher than their own risk⁴⁰, focusing on the benefits of OOD education for at-risk family and friends may also be more effective than focusing only on the individual receiving the education. Finally, eliciting and reflecting on personal experiences of OOD, if any, may help individuals better recognize their risk for OOD, making them more likely to be invested in education and prevention programs.

Our study has several limitations and should be regarded as a starting point for more definitive studies of OOD risk factors and risk awareness. First, we recruited a relatively small convenience sample of veterans from two VA clinics at a single hospital. Our study sample cannot be assumed to be representative of these clinics, the larger VA population, or the U.S. population as a whole. Particularly in the PMC sample, individuals who had prior experience with OOD or for whom OOD was of personal relevance may have been more interested in and willing to participate in this survey, resulting in an over-estimate of the risk factors for the total PMC population receiving opioid treatment for chronic pain. Second, our study did not include a truly exhaustive assessment of OOD risk factors. Certain risk factors, such as alcohol use, were not assessed as effectively as they could have been (i.e., the AUDIT-C uses a time frame of the past year, which may not accurately reflect current use). Use of cocaine was not assessed at all due to concerns that this might affect responses focused specifically on opioid overdose, nor did we include any assessment or measure of pain in our survey. Additionally, it is difficult to assess the relative importance of various reported risk factors in contributing to overall risk of overdose. Therefore, the assessment of risk in this study is necessarily incomplete. Third, although the concept of equianalgesic doses of opioids allows comparison of opioids of varying potencies^{41, 42}, these calculations are over-simplifications which do not take into account the many factors that contribute to the potency of a given analgesic in a particular individual⁴². Conversion calculations often vary from publication to publication⁴³ and are particularly problematic for methadone and fentanyl^{44, 45}. There are limited data published on equianalgesic calculations for sublingual, rather than parenteral or transdermal, buprenorphine. Nonetheless, we believe the utility of comparing opioids of differing potencies outweighs the known problems of this method.

Despite these study limitations, we can draw tentative conclusions. Veterans receiving chronic prescription opioids, such as those in treatment for opioid use disorder or on opioids for chronic pain, may be at risk for OOD and not fully aware of this risk, making it critical for providers to raise awareness of OOD in these settings. Our study suggests that at least some veterans on chronic opioids for pain have similar risk factors for OOD as patients receiving opioid agonist treatment for addiction. These veterans are much more likely to be missed in education and prevention campaigns focused on OOD. It is critical that this group not be excluded from education efforts. We believe that all patients on chronic opioids above 50mg ME, including those without substance use diagnoses, should be considered for prevention programs focusing on OOD education and naloxone distribution.

Acknowledgments

This report is based upon work supported by the Department of Veterans Affairs and the Research in Addiction Medicine Scholars (RAMS) Program, National Institute on Drug Abuse Award Number R25DA033211. Dr. Stein is a recipient of a NIDA Mid-Career Investigator Award (K24 DA00512).

References

- Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *Morbidity & Mortality Weekly Report*. 2011; 60:1487–1492. [PubMed: 22048730]
- Centers for Disease Control and Prevention. Opioid overdoses in the United States. *Journal of Pain & Palliative Care Pharmacotherapy*. 2012; 26:44–47. [PubMed: 22448941]
- Centers for Disease Control and Prevention. National Center for Injury Prevention and Control. [Accessed Oct 20 2014] Data and Statistics Web-based Injury Statistics Query and Reporting System. 2005. <http://www.cdc.gov/injury/wisqars/LeadingCauses.html>
- Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiology & Drug Safety*. 2006; 15:618–627. [PubMed: 16862602]
- Beauchamp G, Winstanley E, Ryan S, Lyons M. Moving beyond misuse and diversion: the urgent need to consider the role of iatrogenic addiction in the current opioid epidemic. *American Journal of Public Health*. 2014; 104:2023–2029. [PubMed: 25211712]
- Shepperd JA, Klein WM, Waters EA, Weinstein ND. Taking stock of unrealistic optimism. *Perspectives on Psychological Science*. 2013; 8:395–411. [PubMed: 26045714]
- Weinstein ND. Unrealistic optimism about future life events. *Journal of Personality and Social Psychology*. 1980; 39:806–820.
- Giangregorio L, Dolovich L, Cranney A, et al. Osteoporosis risk perceptions among patients who have sustained a fragility fracture. *Patient Education & Counseling*. 2009; 74:213–220. [PubMed: 18977628]
- Brown EJ. College students' AIDS risk perception. *Journal of Psychosocial Nursing & Mental Health Services*. 1998; 36:25–30. [PubMed: 9760382]
- Green J, Grant M, Hill KL, Brizzolara J, Belmont B. Heart disease risk perception in college men and women. *Journal of American College Health*. 2003; 51:207–211. [PubMed: 12822712]
- Singer M, Dai H, Weeks MR, Malave D. AIDS risk perception among women drug users in Hartford, CT. *Women & Health*. 1998; 27:67–85. [PubMed: 9640635]
- Crisp BR, Barber JG, Ross MW, Wodak A, Gold J, Miller ME. Injecting drug users and HIV/AIDS: risk behaviours and risk perception. *Drug & Alcohol Dependence*. 1993; 33:73–80. [PubMed: 8370340]
- Johnston CL, Marshall BDL, Qi J, et al. HIV knowledge and perceptions of risk in a young, urban, drug-using population. *Public Health*. 2011; 125:791–794. [PubMed: 21996528]

14. Frank D, Mateu-Gelabert P, Guarino H, et al. High risk and little knowledge: overdose experiences and knowledge among young adult nonmedical prescription opioid users. *International Journal of Drug Policy*. 2015; 26:84–91. [PubMed: 25151334]
15. Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S. Identifying injection drug users at risk of nonfatal overdose. *Academic Emergency Medicine*. 2007; 14:616–623. [PubMed: 17554010]
16. Stooze MA, Dietze PM, Jolley D. Overdose deaths following previous non-fatal heroin overdose: record linkage of ambulance attendance and death registry data. *Drug & Alcohol Review*. 2009; 28:347–352. [PubMed: 19594787]
17. Britton PC, Wines JD Jr, Conner KR. Non-fatal overdose in the 12 months following treatment for substance use disorders. *Drug and Alcohol Dependence*. 2010; 107:51–55. [PubMed: 19828263]
18. Jenkins LM, Banta-Green CJ, Maynard C, et al. Risk factors for nonfatal overdose at Seattle-area syringe exchanges. *Journal of Urban Health*. 2011; 88:118–128. [PubMed: 21246299]
19. Dietze P, Jolley D, Fry CL, Bammer G, Moore D. When is a little knowledge dangerous? Circumstances of recent heroin overdose and links to knowledge of overdose risk factors. *Drug and Alcohol Dependence*. 2006; 84:223–230. [PubMed: 16542798]
20. Seal KH, Kral AH, Gee L, et al. Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. *American Journal of Public Health*. 2001; 91:1842–1846. [PubMed: 11684613]
21. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008; 300:2613–2620. [PubMed: 19066381]
22. Brugal MT, Barrio G, De LFL, Regidor E, Royuela L, Suelves JM. Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration. *Addiction*. 2002; 97:319–327. [PubMed: 11964108]
23. Dietze P, Jolley D, Fry C, Bammer G. Transient changes in behaviour lead to heroin overdose: results from a case-crossover study of non-fatal overdose. *Addiction*. 2005; 100:636–642. [PubMed: 15847621]
24. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison—a high risk of death for former inmates. *N Engl J Med*. 2007; 356:157–165. [PubMed: 17215533]
25. Merrall ELC, Kariminia A, Binswanger IA, et al. Meta-analysis of drug-related deaths soon after release from prison. *Addiction*. 2010; 105:1545–1554. [PubMed: 20579009]
26. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Annals of Internal Medicine*. 2010; 152:85–92. [PubMed: 20083827]
27. Bohnert A, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011; 305:1315–1321. [PubMed: 21467284]
28. Centers for Disease Control and Prevention. Vital signs: risk for overdose from methadone used for pain relief - United States, 1999–2010. *Morbidity & Mortality Weekly Report*. 2012; 61:493–497. [PubMed: 22763888]
29. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert A. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *British Medical Journal*. 2015; 350:h2698. [PubMed: 26063215]
30. Bohnert A, Ilgen MA, Trafton JA, et al. Trends and regional variation in opioid overdose mortality among Veterans Health Administration patients, fiscal year 2001 to 2009. *Clin J Pain*. 2014; 30:605–612. [PubMed: 24281278]
31. Bohnert A, Ilgen MA, Ignacio RV, McCarthy JF, Valenstein M, Blow FC. Risk of death from accidental overdose associated with psychiatric and substance use disorders. *American Journal of Psychiatry*. 2012; 169:64–70. [PubMed: 21955932]
32. Bennett AS, Elliott L, Golub A. Veterans' health and opioid safety - contexts, risks, and outreach implications. *Federal Practitioner*. 2015; 32:4–7.
33. Substance Abuse and Mental Health Services Administration. *Federal Guidelines for Opioid Treatment Programs*. Rockville, MD: 2015. HHS Publication No. (SMA) PEP 15-FEDGUIDEOTP

34. Bush K, Kivlahan D, McDonell M, Fihn S, Bradley K. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. *Archives of Internal Medicine*. 1998; 158:1789–1795. [PubMed: 9738608]
35. Yudko E, Lozhkina O, Fouts A. A comprehensive review of the psychometric properties of the Drug Abuse Screening Test. *Journal of Substance Abuse Treatment*. 2007; 32:189–198. [PubMed: 17306727]
36. Svendsen K, Borchgrevink P, Fredheim O, Hamunen K, Mellbye A, Dale O. Choosing the unit of measurement counts: the use of oral morphine equivalents in studies of opioid consumption is a useful addition to defined daily doses. *Palliative Medicine*. 2011; 25:725–732. [PubMed: 21378066]
37. Williams A, Strang J, Marsden J. Development of Opioid Overdose Knowledge (OOKS) and Attitudes (OOAS) Scales for take-home naloxone training evaluation. *Drug & Alcohol Dependence*. 2013; 132:383–386. [PubMed: 23453260]
38. Strang J, Manning V, Mayet S, et al. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction*. 2008; 103:1648–1657. [PubMed: 18821875]
39. Tobin KE, Sherman SG, Beilenson P, Welsh C, Latkin CA. Evaluation of the Staying Alive programme: Training injection drug users to properly administer naloxone and save lives. *International Journal of Drug Policy*. 2009; 20:131–136. [PubMed: 18434126]
40. Shepperd JA, Carroll P, Grace J, Terry M. Exploring the causes of comparative optimism. *Psychological Belgica*. 2002; 42:65–98.
41. Berdine HJ, Nesbit SA. Equianalgesic dosing of opioids. *Journal of Pain & Palliative Care Pharmacotherapy*. 2006; 20:79–84. [PubMed: 17182514]
42. Knotkova H, Fine PG, Portenoy RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *Journal of Pain and Symptom Management*. 2009; 38:426–439. [PubMed: 19735903]
43. Shaheen PE, Walsh D, Lasheen W, Davis MP, Lagman RL. Opioid equianalgesic tables: are they all equally dangerous? *Journal of Pain and Symptom Management*. 2009; 38:409–417. [PubMed: 19735901]
44. O'Bryant CL, Linnebur SA, Yamashita TE, Kutner JS. Inconsistencies in opioid equianalgesic ratios: clinical and research implications. *Journal of Pain & Palliative Care Pharmacotherapy*. 2008; 22:282–290. [PubMed: 21923312]
45. Pereira J, Lawlor P, Vigano A, Dorgan M, Bruera E. Equianalgesic dose ratios for opioids a critical review and proposals for long-term dosing. *Journal of Pain and Symptom Management*. 2001; 22:672–687. [PubMed: 11495714]

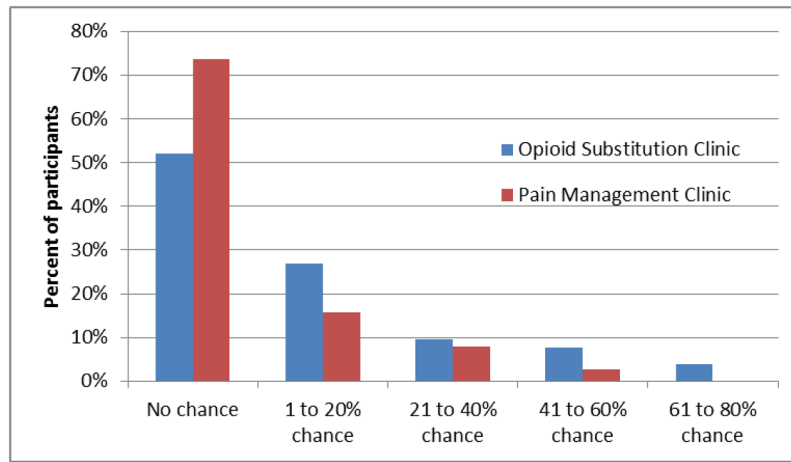


Figure 1. Participant estimate of risk for overdose on opioids in the next year, using visual analog scale graded from 0–100%

Table 1

Characteristics of participating veterans in the PMC and OTC

	Pain Management Clinic n=38 Mean (standard deviation) OR Percent (n)	Opioid Treatment Clinic n=52 Mean (standard deviation) OR Percent (n)
Age	55.2 (10.9)	46.2 (12.7)
Male	94.7% (36)	92.3% (48)
Race		
Caucasian	68.4% (26)	86.5% (45)
African American	18.5% (7)	3.9% (2)
Other	13.2% (5)	9.6% (5)
Hispanic ethnicity	2.6% (1)	7.7% (4)
High school graduate or GED	89.5% (34)	98.1% (51)
Married	55.3% (21) ^A	19.2% (10) ^A
Housing		
Lives alone	26.3% (10) ^A	32.7% (17) ^A
Lives with family	68.4% (26) ^A	32.7% (17) ^A
Lives with non-family	5.3% (2) ^A	34.6% (18) ^A
Lives with another opioid user	21.1% (8)	35.3% (18)
Homeless	0.0% (0)	11.5% (6)
OIF/OEF status*	15.8% (6)	26.9% (14)
Combat experience	50.0% (19)	38.5% (20)
Service connected disability	50.0% (19)	48.1% (225)
Medical conditions		
COPD or asthma	23.7% (9)	17.3% (9)
Liver disease	23.7% (9)	40.4% (21)
Kidney disease	10.5% (4)	3.9% (2)
Sleep apnea	31.6% (12)	25.0% (13)
Heart Disease	29.0% (11)	13.5% (7)
Psychiatric conditions		
Depression	47.4% (18)	80.8% (42)
Severe mental illness**	15.8% (6)	17.3% (9)
PTSD	36.8% (14)	57.7% (30)
PHQ-2	1.7 (2.0)	2.4 (2.1)
Substance use		
Daily Tobacco user	50.0% (19)	73.1% (38)
Used IVD in life	18.4% (7) ^C	71.2% (37) ^C
AUDIT-C	1.8 (2.6)	1.3 (2.2)
DAST-10	2.6 (3.3) ^B	8.6 (1.2) ^B

* Served in Operation Iraqi Freedom/Operation Enduring Freedom

** Bipolar disorder, schizophrenia, or schizoaffective disorder

^A Group differences significant at $p < 0.05$ with Bonferroni correction for multiple comparisons

^B Group differences significant at $p < 0.01$ with Bonferroni correction for multiple comparisons

^C Group differences significant at $p < 0.001$ with Bonferroni correction for multiple comparisons

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Risk factors for opioid overdose identified in participating veterans in the PMC and OTC

Risk factor for opioid overdose	Percent with this risk factor for opioid overdose	
	Pain Management Clinic n=38 Percent (n)	Opioid Treatment Clinic n=52 Percent (n)
Male	94.7% (36)	92.3% (48)
Caucasian	68.4% (26)	86.5% (45)
Mental illness	57.9% (22)	86.5% (45)
Arrested more than 3 times in life	47.4% (18)	67.3% (35)
Divorced	34.2% (13)	53.9% (28)
Daily prescribed opioid dose >50 ME but 100 ME	31.6% (12) ^B	1.9% (1) ^B
Sleep apnea	31.6% (12)	25.0% (13)
Using benzodiazepines	29.0% (11)	11.5% (6)
DAST positive score	23.7% (9) ^C	98.1% (51) ^C
AUDIT-C positive score	23.7% (9)	23.1% (12)
Liver disease	23.7% (9)	40.4% (21)
COPD or asthma	23.7% (9)	17.3% (9)
Daily prescribed opioid dose >100 ME	21.1% (8) ^C	98.1% (51) ^C
Past overdose	21.1% (8)	53.9% (27)
Past intravenous drug use	18.4% (7) ^C	71.2% (37) ^C
Never married	10.5% (4)	19.2% (10)
Kidney disease	10.5% (4)	3.9% (2)
Did not finish high school	10.5% (4)	1.9% (1)
Taking opioids prescribed by more than one doctor	7.9% (3)	1.9% (1)
Average number of potential risk factors	5.9 (STD=2.6, median=6)	8.5 (STD= 1.7, median=9)

^A Group differences significant at p<0.05 with Bonferroni correction for multiple comparisons

^B Group differences significant at p<0.01 with Bonferroni correction for multiple comparisons

^C Group differences significant at p<0.001 with Bonferroni correction for multiple comparisons

Table 3

Performance of veterans in the PMC and OTC on a knowledge-based test of opioid overdose risk factors. Test was true-false; correct answer in parenthesis.

Is this a risk factor for opioid overdose?	Percent identifying item as a risk factor for opioid overdose	
	Pain Management Clinic n=38 Percent (n)	Opioid Treatment Clinic n=52 Percent (n)
Taking opioids from more than one doctor (T)	100.0% (38)	94.2% (49)
Taking larger than usual doses of opioids (T)	97.4% (37)	98.1% (51)
Injecting opioids (T)	97.4% (37)	92.3% (48)
Taking opioids and recreational drugs at the same time (T)	94.7% (36)	98.1% (51)
Drinking alcohol while taking opioids (T)	94.7% (36)	96.2% (50)
Taking opioids and sedatives at the same time (T)	89.5% (34)	98.1% (51)
Taking opioids again soon after release from jail or prison (T)	68.4% (26)	90.4% (47)
Not getting enough sleep (F)	60.5% (23)	65.4% (34)
Taking opioids with no one else around (T)	52.6% (20)	78.9% (41)
Taking opioids after a week or more of not using any (T)	50.0% (19) ^C	88.5% (46) ^C
Having liver or kidney disease (T)	50.0% (19)	69.2% (36)
Having breathing problems like asthma, emphysema, or COPD (T)	44.7% (17)	73.1% (38)
Having sleep apnea (T)	34.2% (13)	53.9% (27)
Being a tobacco smoker (F)	29.0% (11)	17.3% (9)
Not drinking enough water (F)	21.1% (8)	17.3% (9)
Being overweight (F)	15.8% (6)	42.3% (22)
Being female (F)	15.8% (6)	7.7% (4)
Having acid reflux (GERD) (F)	13.2% (5)	7.7% (4)

^A Group differences significant at $p < 0.05$ with Bonferroni correction for multiple comparisons

^B Group differences significant at $p < 0.01$ with Bonferroni correction for multiple comparisons

^C Group differences significant at $p < 0.001$ with Bonferroni correction for multiple comparisons