

Who Overdoses on Opioids at a VA Emergency Department?

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This study examined the clinical characteristics of veterans admitted to a Veterans Affairs ED who were treated for opioid overdose.

Editor's Note: This article has been adapted from an article originally published in *Federal Practitioner* (Clement C, Stock C. Who overdoses at a VA emergency department? *Fed Prac.* 2016;33[11]:14-19. <http://www.fedprac.com>).

O verdose deaths remain epidemic throughout the United States. The rates of unintentional overdose deaths, increasing by 137% between 2000 and 2014, have been driven by a 4-fold increase in prescription opioid overdoses during that period.¹⁻³

Veterans died of accidental overdose at a rate of 19.85 deaths/100,000 people compared with a rate of 10.49 deaths in the general population, based on 2005 data.⁴ There is wide state-by-state variation, with the lowest age-adjusted opioid overdose death rate of 1.9 deaths/100,000 person-years among veterans in Mississippi and the highest rate in Utah of 33.9 deaths/100,000 person-years, using 2001 to 2009 data.⁵ These data can be compared with a crude general population overdose death rate of 10.6 deaths per 100,000 person-years in Mississippi and

18.4 deaths per 100,000 person-years in the general Utah population during that same period.⁶

Overdose deaths in the United States occur most often in persons aged 25 to 54 years.⁷ Older age has been associated with iatrogenic opioid overdose in hospitalized patients.⁸ Pulmonary disease, cardiovascular disease (CVD), and psychiatric disorders, including past or present substance use, have been associated with an increased risk of opioid overdose.⁹ However, veterans with substance use disorders are less likely to be prescribed opioids than are nonveterans with substance use disorders.¹⁰ Also, concomitant use of sedating medications, such as benzodiazepines (BZDs), can increase mortality from opioid overdose.¹¹ Patients prescribed opioids for chronic pain conditions often take BZDs for various reasons.¹² Veterans seem more likely to receive opioids to treat chronic pain but at lower average daily doses than doses prescribed to nonveterans.¹⁰

Emergency management of life-threatening opioid overdose includes prompt administration of naloxone.¹³ Naloxone is approved by the US Food and Drug Administration for

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Authors' Disclosure Statement: The authors report no actual or potential conflict of interest in relation to this article. The opinions expressed herein are those of the authors and do not necessarily reflect those of the US government or any of its agencies.

DOI: 10.12788/emed.2017.0018

complete or partial reversal of opioid-induced clinical effects, most critically respiratory depression.^{14,15} Naloxone administration in the ED may serve as a surrogate for an overdose event. During the study period, naloxone take-home kits were not available in the Veterans Affairs (VA) setting.

A 2010 ED study described demographic information and comorbidities in opioid overdose, but the study did not include veterans.¹⁶ The clinical characteristics of veterans treated for opioid overdose have not been published. Because identifying characteristics of veterans who overdose may help tailor overdose-prevention efforts, the objective of this study is to describe clinical characteristics of veterans treated for opioid overdose.

Methods

A retrospective chart review and archived data study was approved by the University of Utah and VA Institutional Review Boards, and conducted at the George E. Wahlen Veterans Affairs Medical Center (VAMC) in Salt Lake City, Utah. This chart review included veterans who were admitted to the ED and treated with naloxone between January 1, 2009 and January 1, 2013.

The authors used the Pharmacy Benefits Management Data Manager to extract data from the VA Data Warehouse and verified the data by open chart review (**Table**). The following data were collected: ED visit date (overdose date); demographic information, including age, gender, and race; evidence of next of kin or other contact at the same address as the veteran; diagnoses based on *International Classification of Diseases, 9th Revision (ICD-9)* codes, including sleep apnea, obesity, cardiac disease, pulmonary disease, mental health diagnoses (*ICD-9* codes 290-302 [wild card characters (*) included many subdiagnoses]), cancer, and substance use disorders and/or dependencies (SUDD); tobacco use; VA-issued prescription opioid and BZD availability, including dose, fill dates, quantities dispensed,

and day supplies; specialty of opioid prescriber; urine-drug screening (UDS) results; and outcome of the overdose.

No standardized research criteria identify overdose in medical chart review.¹⁷ For each identified patient, the authors reviewed provider and nursing notes charted during an ED visit that included naloxone administration. The event was included as an opioid overdose when notes indicated that the veteran was unresponsive and given naloxone, which resulted in increased respirations or increased responsiveness. Cases were excluded if the reason for naloxone administration was anything other than opioid overdose.

Medical, mental health, and SUDD diagnoses were included only if the veteran had more than three patient-care encounters (PCE) with *ICD-9* codes for a specific diagnosis entered by providers. A PCE used in the electronic medical record (EMR) helps collect, manage, and display outpatient encounter data, including providers, procedure codes, and diagnostic codes. Tobacco use was extracted from health factors documented during primary care visit screenings. (Health factors help capture data entered in note templates in the EMR and can be used to query trends.) A diagnosis of obesity was based on a calculated body mass index of at or greater than 30 kg/m² on the day of the ED visit date or the most recently charted height and weight. The type of SUDD was stratified into opioids (*ICD-9* codes 304.0*), sedatives (*ICD-9* codes 304.1*), alcohol (*ICD-9* codes 303.*), and other (*ICD-9* codes 304.2-305.9).

The dosage of opioids and BZDs available to a veteran was determined by using methods similar to those described by Gomes et al¹⁸: the dose of opioids and BZDs available based on prescriptions dispensed during the 120 days prior to the ED visit date and the dose available on the day of the ED visit date if prescription instructions were being followed. Prescription opioids and

Table. Veteran Characteristics, Based on Prescription Availability on Day of Opioid Overdose (N = 92)

Characteristics	Opioid Only (n = 34)	Opioid and BZD (n = 19)	BZD only (n = 4)	No Opioid or BZD (n = 35)
Age, y (SD)	64.4 (11.6)	56.4 (9.1)	51 (16.9)	65.6 (14.6)
Next-of-kin or contact at same address, %	84	37	25	33
Documented Diagnoses^a				
Cardiovascular disease (%)	31 (91)	17 (89)	3 (75)	27 (77)
Mental health diagnosis (%)	25 (74)	17 (89)	4 (100)	26 (74)
Pulmonary disease (%)	22 (65)	10 (53)	2 (50)	16 (46)
Cancer (%)	19 (56)	8 (42)	1 (25)	16 (46)
Obesity (%)	13 (38)	11 (58)	2 (50)	13 (37)
Sleep apnea (%)	16 (47)	8 (42)	2 (50)	12 (34)
Tobacco use disorder (%)	7 (21)	5 (26)	2 (50)	4 (11)
SUDD				
Other (cocaine, marijuana, stimulants, etc) (%)	16 (47)	11 (58)	3 (75)	8 (23)
Alcohol (%)	9 (27)	2 (11)	0	4 (11)
Sedative (%)	0	0	0	1 (3)
Opioid (%)	0	0	0	0

Abbreviations: BZD, benzodiazepine; SD, standard deviation; SUDD, substance use disorders and/or dependencies.

^aEach veteran may have more than 1 diagnosis.

BZDs were converted to daily morphine equivalent dose (MED) and daily lorazepam equivalent dose (LED), using established methods.^{19,20}

Veterans were stratified into four groups based on prescribed medication availability: opioids only, BZDs only, opioids and BZDs, and neither opioids nor BZDs. The specialty of the opioid prescribers was categorized as primary care, pain specialist, surgeon, emergency specialist, or hospitalist (discharge prescription). Veteran EMRs contain a list of medications obtained out-

side the VA facility, referred to as non-VA prescriptions. These medications were not included in the analysis because accuracy could not be verified.

A study author reviewed the results of any UDS performed up to 120 days before the ED visit date to determine whether the result reflected the currently prescribed prescription medications. If the UDS was positive for the prescribed opioids and/or BZDs and for any nonprescribed drug, including alcohol, the UDS was classified as not reflective. If the prescribed BZD was

alprazolam, clonazepam, or lorazepam, a BZD-positive UDS was not required for the UDS to be considered reflective because of the sensitivity of the UDS BZD immunoassay used at the George E. Wahlen VAMC clinical laboratory.²¹

Outcomes of the overdose were categorized as discharged, hospitalized, or deceased. Descriptive statistical analyses were performed using Microsoft Excel. Group comparisons were performed using Pearson chi-square or Student *t* test.

Results

The ED at the George E. Wahlen VAMC averages 64 visits per day, almost 94,000 visits within the study period. One hundred seventy ED visits between January 1, 2009 and January 1, 2013, involved naloxone administration. Ninety-two visits met the inclusion criteria of opioid overdose, representing about 0.002% of all ED visits at this facility (**Figure 1**). Six veterans had multiple ED visits within the study period, including four veterans who were in the opioid-only group.

The majority of veterans in this study were non-Hispanic white ($n = 83$, 90%), male ($n = 88$, 96%), with a mean age of 63 years. Less than 40% listed a next of kin or contact person living at their address.

Based on prescriptions available within 120 days before the overdose, 67 veterans (73%) possessed opioid and/or BZD prescriptions. In this group, the MED available on the day of the ED visit ranged from 7.5 mg to 830 mg. The MED was less than or equal to 200 mg in 71.6% and less than or equal to 50 mg in 34.3% of these cases. Veterans prescribed both opioids and BZDs had higher MED (average, 259 mg) available within 120 days of the ED visit than did those prescribed opioids only (average, 118 mg) ($P = .015$; standard deviation [SD], 132.9). The LED ranged from 1 mg to 12 mg for veterans with available BZDs.

Based on prescriptions available on the day of opioid overdose, 53 veterans (58%) had opioid prescriptions. The ranges of

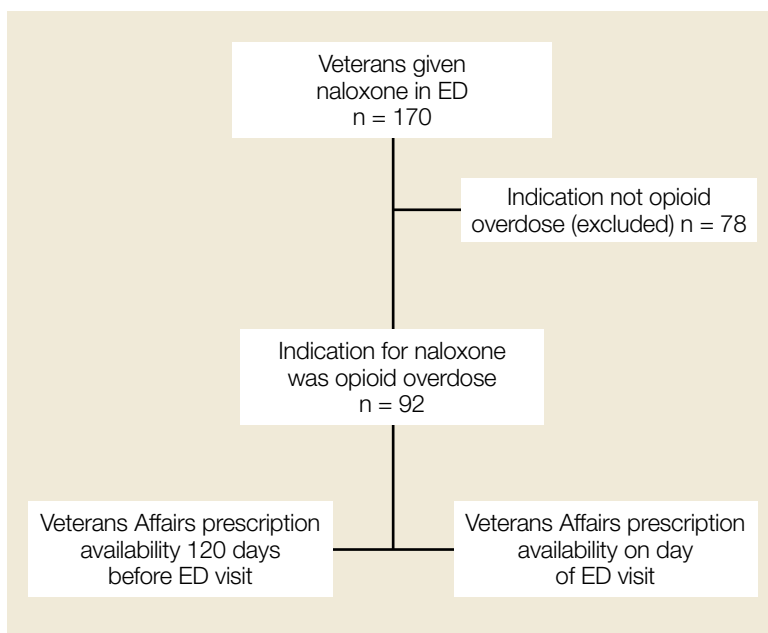


Figure 1. Patient flowchart.

MED and LED available on the day of overdose were the same as the 120-day availability period. The average MED was 183 mg in veterans prescribed both opioids and BZDs and 126 mg in those prescribed opioids only ($P = .283$; SD, 168.65; **Figure 2**). The time between the last opioid fill date and the overdose visit date averaged 20 days (range, 0 to 28 days) in veterans prescribed opioids.

All veterans had at least one diagnosis that in previous studies was associated with increased risk of overdose.^{9,15} The most common diagnoses included CVD, mental health disorders, pulmonary diseases, and cancer. Other SUDDs not including tobacco use were documented in at least half the veterans with prescribed opioids and/or BZDs. No veteran in the sample had a documented history of opioid SUDD.

Hydrocodone products were available in greater than 50% of cases. None of the veterans were prescribed buprenorphine products; other opioids, including tramadol, comprised the remainder (**Figure 3**). Primary care providers prescribed 72% of

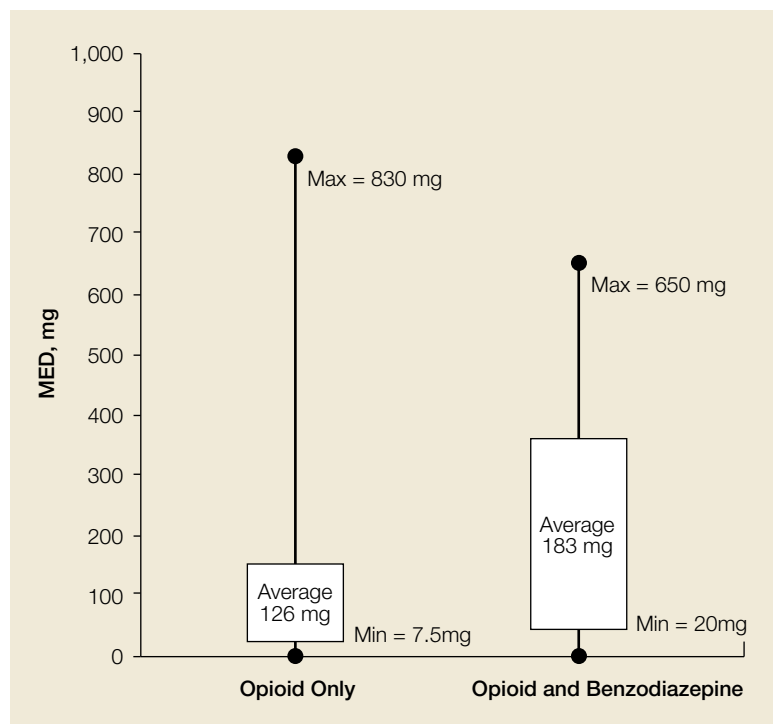


Figure 2. Morphine equivalent dose available on the day of ED visit.^a

Abbreviation: MED, morphine equivalent dose.

^aGroup data are displayed as the range (minimum and maximum dose in each group), and the average dose. The boxes represent the first (lower) and third (upper) quartiles of doses ($P = .283$; standard deviation, 168.55) between mean opioid doses of each group.

opioid prescriptions, with pain specialists, discharge physicians, ED providers, and surgeons prescribing the rest. When both opioids and BZDs were available, combinations of a hydrocodone product plus clonazepam or lorazepam were most common.

Overall, 64% of the sample had UDS results prior to the ED visit. Of veterans prescribed opioids and/or BZDs, 53% of UDSs reflected prescribed regimens.

On the day of the ED visit, 1 death occurred. Ninety-one veterans (99%) survived the overdose; 79 veterans (86%) were hospitalized, most for less than 24 hours.

Discussion

This retrospective review identified 92 veterans who were treated with naloxone in the ED for opioid overdose during a 4-year period at the George E. Wahlen VAMC. Seventy-eight cases were excluded

because the reason entered in charts for naloxone administration was itching, constipation, altered mental status, or unclear documentation.

Veterans in this study were, on average, older than the overdose fatalities in the United States. Opioid-overdose deaths in all US states and in Utah alone occur most frequently in non-Hispanic white men aged between 35 and 54 years.^{7,22,23} In the 2010 Nationwide Emergency Department Sample of 136,000 opioid overdoses, of which 98% survived, most were aged 18 to 54 years.¹⁶ The older age in this study most likely reflects the age range of veterans served in the Veterans Health Administration (VHA); however, as more young veterans enter the VHA, the age range of overdose victims may more closely resemble the age ranges found in previous studies. Post hoc analysis showed eight veterans (9%) with probable intentional opioid overdose based on chart review, whereas the incidence of intentional prescription drug overdose in the United States is 17.1%.²⁴

In Utah, almost 93% of fatal overdoses occur at a residential location.²² Less than half of the veterans in this study had a contact or next of kin listed as living at the same address. Although veterans may not have identified someone living with them, in many cases, it is likely another person witnessed the overdose. Relying on EMRs to identify who should receive prevention education in addition to the veteran, may result in missed opportunities to include another person likely to witness an overdose.²⁵ Prescribers should make a conscious effort to ask veterans to identify someone who may be able to assist with rescue efforts in the event of an overdose.

Diagnoses associated with increased risk of opioid-overdose death include sleep apnea, morbid obesity, pulmonary disease or CVD, and/or a history of psychiatric disorders and SUDD.^{8,9,16} In a large sample of older veterans, only 64% had at least one medical or psychiatric diagnosis.²⁶ Less than half of the 18,000 VA

primary care patients in five VA centers had any psychiatric condition, and less than 65% had CVD, pulmonary disease, or cancer.²⁷ All veterans in this study had medical and psychiatric comorbidity.

In contrast, a large ED sample described by Yokell et al¹⁶ found chronic mental conditions in 33.9%, circulatory disorders in 29.1%, and respiratory conditions in 25.6% of their sample. Bohnert et al⁹ found a significantly elevated hazard ratio (HR) for any psychiatric disorder in a sample of nearly 4,500 veterans. There was variation in the HR when individual psychiatric diagnoses were broken out, with bipolar disorder having the largest HR and schizophrenia having the lowest but still elevated HR.⁹ In this study, individual diagnoses were not broken out because the smaller sample size could diminish the clinical significance of any apparent differences.

Edlund et al¹⁰ found that less than 8% of veterans treated with opioids for chronic noncancer pain had nonopioid SUDD. Bohnert et al⁹ found an HR of 21.95 for overdose death among those with opioid-use disorders. The sample in this study had a much higher incidence of nonopioid SUDD compared with that of the study by Edlund et al,¹⁰ but none of the veterans in this study had a documented history of opioid-use disorder. The absence of opioid-use disorders in this sample is unexpected and points to a need for providers to screen for opioid-use disorder whenever opioids are prescribed or renewed. If prevention practices were directed only to those with opioid SUDDs, none of the veterans in this study would have been included in those efforts. Non-SUDD providers should address the risks of opioid overdose in veterans with sleep apnea, morbid obesity, pulmonary disease or CVD, and/or a history of psychiatric disorders.

Gomes et al¹⁸ found that greater than 100 mg MED available on the day of overdose doubled the risk of opioid-related mortality. The VA/Department of Defense Clinical Practice Guideline for Management of

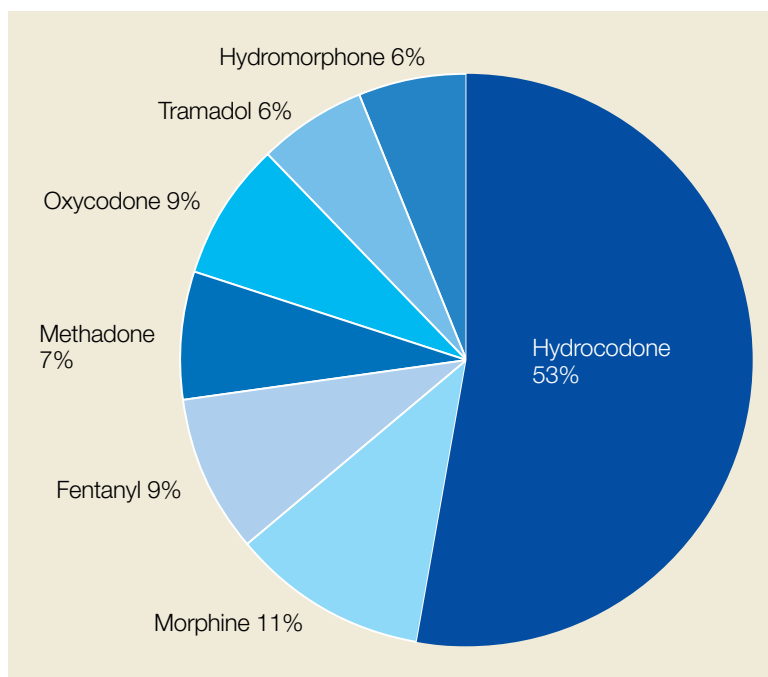


Figure 3. Type of prescribed opioid available on day of overdose (n = 53).

Opioid Therapy for Chronic Pain identifies 200 mg MED as a threshold to define high-dose opioid therapy.²⁸ Fulton-Kehoe et al²⁹ found that 28% of overdose victims were prescribed less than 50 mg MED. In this study, the average dose available to veterans was greater than 100 mg MED; however, one-third of all study veterans had less than 50 mg MED available. Using a threshold dose of 50 mg MED to target prevention efforts would capture only two-thirds of those who experienced overdose; a 200-mg MED threshold would exclude the majority, based on the average MED in each group in this study. Overdose education should be provided to veterans with access to opioids, regardless of dose.

Use of BZDs with opioids may result in greater central nervous system (CNS) depression, pharmacokinetic interactions, or pharmacodynamic interactions at the μ -opioid receptor.³⁰⁻³² About one-third of veterans in this study were prescribed opioids and BZDs concurrently, a combination noted in about 33% of opioid overdose deaths reported by the Centers for Disease

Control and Prevention.²⁴ Individuals taking methadone combined with BZDs have been found to have severe medical outcomes.³³ If preventive efforts are targeted to those receiving opioids and other CNS depressants, such as BZDs, about half (42%) of the veterans in this study would not receive a potentially life-saving message about preventing overdoses. All veterans with opioids should be educated about the additional risk of overdose posed by drug interactions with other CNS depressants.

The time since the last fill of an opioid prescription ranged from 0 to 28 days. This time frame indicates that some overdoses may have occurred on the day an opioid was filled but most occurred near the end of the expected days' supply. Because information about adherence or use of the opioid was not studied, it cannot be assumed that medication misuse is the primary reason for the overdose. Providing prevention efforts only at the time of medication dispensing would be insufficient. Clinicians should review local and remote prescription data, including via their states' prescription drug monitoring program, when discussing the risk of overdose with veterans.

Most veterans had at least one UDS result in the chart. Although half the UDSs obtained reflected prescribed medications, the possibility of aberrant behaviors, which increases the risk of overdose, cannot be ruled out with the methods used in this study.³⁴ Medication management agreements that require UDSs for veterans with chronic pain were not mandatory at the George E. Wahlen VAMC during the study period, and those used did not mandate discontinuation of opioid therapy if suspected aberrant behaviors were present.

A Utah study based on interviews of overdose victims' next of kin found that 76% were concerned about victims' aberrant behaviors, such as medication misuse, prior to the death.²² In contrast, a study of commercial and Medicaid recipients es-

timated medication misuse rates in at or less than 30% of the sample.³⁵ Urine-drug screening results not reflective of the prescribed regimens have been found in up to 50% of patients receiving chronic opioid therapy.

The UDS findings in this study were determined by the authors and did not capture clinical decisions or interpretations made after results were available or whether these decisions resulted in overdose-prevention strategies, such as targeted education or changes in prescription availability. Targeting preventive efforts toward veterans only with UDS results suggesting medication misuse would have missed more than half the veterans in this study. Urine-drug screening should be used as a clinical monitoring tool whenever opioids, BZDs, or other substances are used or prescribed.

The VA now has a nationwide program, Opioid Overdose Education and Naloxone Distribution (OEND), promoting overdose education and take-home naloxone distribution for providers and patients to prevent opioid-related overdose deaths. A national SharePoint site has been created within the VA that lists resources to support this effort.

Almost all veterans in this review survived the overdose and were hospitalized following the ED visit. Other investigators also have found that the majority (51% to 98%) of overdose victims reaching the ED survived, but fewer patients (3% to 51%) in those studies were hospitalized.^{16,36} It is unknown whether there are differences in risk factors associated with survived or fatal overdoses.

Limitations

Although Utah ranked third for drug-overdose death rates in 2008 and had the highest death rate among veterans from 2001 to 2009, this review captured only overdoses among veterans treated during the study period at the George E. Wahlen VAMC ED.^{5,6} The number and characteristics of

veterans during this same period who were treated for overdose in other community EDs or urgent care centers throughout Utah is unknown.

The definition of opioid and BZD dose available in this study may not represent actual use of opioids or BZDs because it was based on chart review of prescription dispensing information and UDS procedures at the George E. Wahlen VAMC, and medication misuse cannot be ruled out. This study did not evaluate specific aberrant behaviors.

Conclusion

Current overdose-prevention screening efforts primarily identify patients on high-dose opioids and those with SUDD. Many veterans in this study were older than the average US victims' age, did not have SUDD, were prescribed opioid doses not

considered high risk by current guidelines, were nearer the end of their medication supply, and had UDS reflective of prescribed medications. This study suggests that any veteran with access to opioids, whether prescribed or not, is at risk for an opioid overdose. Established risk factors may aid in developing overdose-prevention programs, but prevention should not be limited to veterans with prescribed opioids and known risk factors. Clinicians should screen patients for opioid-use disorder whenever opioids are prescribed and continue to screen them throughout therapy. Broader screening for overdose risk is needed to avoid missing important opportunities for overdose prevention.

Acknowledgments

Gale Anderson, VISN 19 PBM Data Manager, performed initial data query for the study.

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