

NALOXONE RESCUE

Naloxone HCl nasal spray (Narcan®)
Naloxone HCl autoinjector (Evzio®)

Recommendations for Issuing Naloxone Rescue for the VA Opioid Overdose Education and Naloxone Distribution (OEND) Program

August 2016

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives
in collaboration with the VA OEND National Support and Development Work Group

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. Local adjudication should be used until updated guidance and/or CFU are developed by the National PBM. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The drug Product Information should be consulted for detailed prescribing information. Also see Naloxone Autoinjector and Naloxone HCl Nasal Spray 4mg Abbreviated Reviews at www.pbm.va.gov

BACKGROUND¹⁻⁸

Naloxone is a safe and effective opioid antagonist that works predominantly at mu-opioid receptors and less so at kappa- and delta-opioid receptors. Its safety is due to its specificity; its only action is to reverse opioid mediated effects, which include respiratory depression, central nervous system depression and hypotension. Naloxone does not reverse the effects of alcohol, benzodiazepines or other central nervous system depressants. Naloxone is a highly effective intervention for reversing opioid overdoses and has been used for this purpose by emergency departments and emergency services personnel in the U.S. and abroad for decades.

In 1996, community-based programs such as syringe exchange and other harm reduction programs for injection drug users began to offer naloxone and other opioid overdose educational services to drug users, their families and friends, health care providers, substance use disorder treatment programs and other service providers (e.g., homeless shelters). Opioid overdose education and naloxone distribution (OEND) programs aim to ensure that individuals who are likely to require intervention are educated and trained about overdose prevention, recognition and naloxone administration. Many OEND programs target people most likely to be present during an opioid overdose (e.g., family and peers), thereby improving chances of immediate resuscitative intervention and naloxone administration.

As observations emerged that OEND programs might prevent numerous opioid-related overdose deaths, the support for OEND programs grew in the U.S. and abroad. The World Health Organization recommends naloxone as an essential intervention to prevent overdose. The Centers for Disease Control and the Global Fund to Fight AIDS, Tuberculosis, and Malaria both support naloxone distribution to drug users. The United Nations, American Medical Association (AMA), American Public Health Association (APHA), and the U.K. Advisory Council on the Misuse of Drugs (ACMD) support opioid overdose education and training and provision of naloxone to prevent opioid overdose, especially among high-risk populations such as illicit drug users. Moreover, in 2010, Scotland became the first country to implement a national naloxone program. In response to public health concerns about opioid overdose, in 2013 the Substance Abuse and Mental Health Services Administration (SAMHSA) released an Opioid Overdose Prevention Toolkit. This toolkit suggests that patients on long-term opioid therapy or who are at risk for overdose (e.g., completing abstinence programs) may benefit from education and access to naloxone rescue.

The VA has had an increasing concern about the risk for opioid-related adverse events among Veteran patients and fully endorses efforts designed to minimize risk. The **VA Opioid Overdose Education and Naloxone Distribution (OEND) Program** is a risk mitigation initiative that aims to decrease opioid-related overdose morbidity and mortality among VA patients. Educational, informational and implementation resources geared towards opioid overdose prevention, recognition of opioid overdose and rescue response are available via the OEND SharePoint (<https://vaww.portal2.va.gov/sites/mentalhealth/OEND/default.aspx>). Naloxone rescue medications have been made available via the VA National Formulary process. VA providers should consider providing OEND to Veterans who are at significant risk of opioid overdose. Decisions to provide OEND can be assisted through use of tools designed to identify such patients by estimating individual patient risk for overdose.

Naloxone rescue product utilization and rates of opioid overdose and mortality are tracked nationally in VA to evaluate the OEND program's performance. Clinicians are encouraged to document identified opioid overdoses in the medical record utilizing the standardized note template and ICD-10 codes described in this document. The PBM, MAP, and VPEs, in collaboration with the VA OEND National Support and Development Work Group, prepared the following recommendations to provide standardized guidance on the issuance of naloxone rescue under the VA OEND program.

RECOMMENDATIONS AND INFORMATION FOR OFFERING NALOXONE RESCUE

Assess the risk of opioid-related adverse events. **Discuss** the provision of naloxone rescue as an opioid risk mitigation option with patients and/or family/carers. **Offer** naloxone rescue to Veterans prescribed or using opioids who are at increased risk for opioid overdose or whose provider deems, based on their clinical judgment, that the Veteran has an indication for ready naloxone availability. **Educate** patients and carers on the proper use and storage of naloxone rescue medications. **Document** OEND-related discussions and opioid overdoses in patients' medical records and through appropriate diagnostic coding, including documenting any reversal events with VA naloxone rescue medications using a nationally recommended and standardized note template (see VA National OEND SharePoint for more information).

The Risk Index for Overdose or Serious Opioid-induced Respiratory Depression (RIOSORD) is a practical and relatively simple and brief risk assessment instrument that has been automated by VA to assess a patient's baseline risk. Another automated tool is the VA Stratification Tool for Opioid Risk Mitigation (STORM) which helps identify patients – including patients prescribed opioids – who are at risk for adverse events such as drug overdose or suicide. The Opioid Therapy Risk Report (OTRR) and the Current Opioid Misuse Measure (COMM)TM are also useful tools (see Overdose Risk Assessment and Opioid Risk Mitigation, pages 6-10).

Examples of Candidates for Naloxone Rescue include *but are not limited to*:

Veterans with:

- Opioid use disorder diagnosis (including individuals on Opioid Agonist Therapy; inpatient, residential, outpatient treatment; attending support groups)
- Prescription opioid misuse or injection opioid use
- History of previous opioid overdose
- Chronic hepatitis, cirrhosis, alcohol use disorder or other substance use disorder, sleep apnea or pulmonary disease and taking opioid

Veterans taking:

- An extended-release or long-acting prescription opioid
- ≥ 50 mg morphine equivalents per day
- A prescription benzodiazepine with an opioid

Veterans who receive VA or non-VA care in these situations:

- HIV education / prevention program (which may provide care to injection opioid users)
- Syringe access program
- Emergency departments (e.g., for opioid poisoning / overdose or intoxication)
- Primary health care (e.g., for follow-up of recent opioid poisoning / overdose or intoxication)
- Inpatient residential care or community-based treatment for homeless Veterans taking an opioid

Individuals in hospice/palliative care are likely NOT appropriate candidates for naloxone rescue. The signs and symptoms of life threatening opioid overdose overlaps with and may be mistaken for the common signs and symptoms of the dying process. A family member may erroneously administer naloxone to a Veteran approaching death, causing opioid reversal, withdrawal symptoms, pain and suffering. Family members of Veterans in hospice programs who receive OEND training should simultaneously receive education about the overlap in signs and symptoms with the dying process. OEND should be considered on a case by case basis and not routinely in hospice/palliative care patients.

VA STAFF EDUCATIONAL, INFORMATIONAL, AND IMPLEMENTATION RESOURCES (also see *Patient Education and Patient Education Resources*).

- Educational, informational and implementation resources are available to all VA staff via the **OEND SharePoint**. The link to the OEND SharePoint is: <https://vaww.portal2.va.gov/sites/mentalhealth/OEND/SitePages/Home.aspx> and for the PBM Academic Detailing Service (ADS) SharePoint is: <https://vaww.portal2.va.gov/sites/ad/SitePages/Home.aspx>
- **TMS training:**
 - **Opioid Overdose Education and Naloxone Distribution (OEND) Training** VA health professionals who work with patients on opioids or with patients at risk for opioid overdose may choose to take this course to integrate OEND into clinical practice. Target audience participants may include but are not limited to doctors, dentists, pharmacists, nurses, nursing assistants, social workers, counselors, psychologists, occupational therapists and healthcare executives. This is TMS item number 27440 (Pharmacists and other clinicians) and is accredited for ACCME, ACCME-NP, APA, ANCC, ADA, AOTA, ASWB, NBCC, and ACPE (for Pharmacy Technicians it is TMS item 27441, accredited for ACPE-T).
 - **Program Description:** This one hour advanced knowledge-based course is designed to train providers on opioid safety/overdose prevention and training patients to respond to an overdose with naloxone. The core curriculum will be presented in a web-based learning module with additional resources available for use after the training session. This course will increase provider awareness of the need for opioid safety/overdose prevention and describe national VA Naloxone rescue products and how to use them to respond to an opioid overdose. Emphasis will be placed on demonstrating how providers can integrate patient education on opioid safety/overdose prevention in clinical practice and in providing step-by-step instructions on how to respond to an opioid overdose with national VA Naloxone Rescue products. After successfully completing the course, learners will be able to use the information to integrate OEND into clinical practice.

PATIENT EDUCATION AND PATIENT EDUCATION RESOURCES

- Discuss naloxone rescue as an opioid harm reduction/risk mitigation option with patients and/or family/carers.
- Emphasize opioid overdose prevention and explain that naloxone combined with overdose education complement, but do not replace, safe and responsible opioid use.
- Educate and train the patient on the proper use, storage, administration and disposal of naloxone rescue products.
- Emphasize the importance of being familiar with naloxone administration technique before an emergency arises.
- Advise the patient about the importance of friends, family members, partners, and carers being educated and trained on the proper use, potential harms and limitations of naloxone treatment.
- Instruct the patient to inspect the naloxone solution for particulate matter or discoloration (autoinjector), and check the expiration date.
- Patient education resources also include the following (VA resources can be ordered through the VA National Repository):
 - VA OEND Patient Education Brochures (available on VA OEND SharePoint)
 - Opioid Overdose Prevention (patients with opioid use disorders): English and Spanish versions
 - Opioid Safety (patients prescribed opioids): English and Spanish versions
 - VA OEND Videos
 - Introduction to Naloxone for People with Opioid Use Disorders: <https://youtu.be/-qYXZDzo3cA>
 - Introduction to Naloxone for People Taking Prescribed Opioids: <https://youtu.be/NFzhz-PCzPc>
 - How to Use the VA Naloxone Nasal Spray: <https://youtu.be/0w-us7fQE3s>
 - How to Use the VA Auto-Injector Naloxone Kit: <https://youtu.be/-DQBCnrAPBY>
 - SAMHSA Opioid Overdose Prevention Toolkit: Contains safety advice for patients and resources for family members. <http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA13-4742>
 - Community-Based Overdose Prevention and Naloxone Distribution Program Locator: Identifies programs outside of the VA that distribute naloxone. <http://hopeandrecovery.org/locations/>
 - Prescribe to Prevent: Patient resources and videos demonstrating overdose recognition and response, including naloxone administration. • <http://prescribeprevent.org/video/>
- It is highly encouraged to also educate and train at least one patient-authorized acquaintance (i.e., one who is likely to witness an opioid overdose such as a friend, family member, partner or carer).

PRESCRIBING AND AVAILABILITY OF NALOXONE RESCUE

- **A prescription is required to provide patients with naloxone rescue.**
- **Allow for individualized selection of the product and route of administration for naloxone.**
- **Each prescription order contains 2 dose units of naloxone.**
- **Prescriptions may be marked for one refill.**
- **Patient refusal of an offer for naloxone should be documented.**

Contraindications to intranasal naloxone can include nasal septal abnormalities, nasal trauma, epistaxis, excessive nasal mucus, and intranasal damage caused by the use of cocaine and other substances. Relative contraindications to intranasal naloxone: severe hypotension and the recent use of vasoconstrictors (which may prevent adequate absorption).¹⁴

Use requests to renew naloxone rescue prescriptions as opportunities to determine the circumstances (e.g., product was used for overdose, lost, confiscated, expired, etc.) and base decisions to renew any prescriptions for opioids on the discussion with the patient and re-assessment of risk-benefit.

Also use the discussion as an opportunity to engage the patient, re-assess risk-benefits, provide re-education about overdoses, review [Taking Opioids Responsibly](#) (as applicable), consider other opioid risk mitigation strategies (patient-centered risk mitigation strategies are included in the VA Stratification Tool for Opioid Risk Mitigation [STORM]), and modify treatment plans.

VA facility availability of naloxone rescue (similar to that of AEDs) may increase access and reduce opioid overdose response time, particularly at sites without crash cart availability.

Nonveterans requesting naloxone should be directed to community-based OEND programs and resources. National locators are available at <http://hopeandrecovery.org/locations/> and <http://harmreduction.org/connect-locally/>. Naloxone is increasingly becoming available through community pharmacies.

DOCUMENTATION OF OVERDOSE EVENTS

To aid in national tracking of OEND program performance, providers should document reversal events with VA naloxone rescue products in CPRS using a nationally recommended and standardized note template (see VA National OEND SharePoint for more information) and through use of recommended ICD-10-CM coding.

Recommended **ICD-10-CM coding** for opioid overdose events:

- Begin with **DIAGNOSTIC CATEGORY T40**, followed by a
- **3 digit EXTERNAL CAUSE** code, followed by a
- **7th character DESCRIBING ENCOUNTER**

Because **DIAGNOSTIC CATEGORY T40** denotes “*Poisoning by, adverse effect of and underdosing of narcotics and psychodysleptics (hallucinogens)*” broadly, it is important to use one of the opioid-related **3 digit EXTERNAL CAUSE** codes to allow documentation of the specific agent involved (if known) and whether the event was unintentional, intentional, an assault, undetermined, or due to an adverse effect. The **7th character DESCRIBING ENCOUNTER** are suffix letters A or D (initial or subsequent encounter, respectively) or S (sequela; a complication or condition arising from the overdose event). See the Table below for opioid-related 3 digit external cause codes to be tracked nationally.

Table 1. Three digit external cause codes (added to T40 Diagnostic category) for documentation/tracking of opioid poisonings/overdoses

Poisoning by:	Accidental (unintentional)	Intentional self-harm	Assault	Undetermined	Adverse effect
Opium	T40.0X1	T40.0X2	T40.0X3	T40.0X4	T40.0X5
Heroin	T40.1X1	T40.1X2	T40.1X3	T40.1X4	N/A
Other opioids	T40.2X1	T40.2X2	T40.2X3	T40.2X4	T40.2X5
Methadone	T40.3X1	T40.3X2	T40.3X3	T40.3X4	T40.3X5
Other synthetic narcotics	T40.4X1	T40.4X2	T40.4X3	T40.4X4	T40.4X5
Unspecified narcotics	T40.601	T40.602	T40.603	T40.604	T40.605
Other narcotics	T40.691	T40.692	T40.693	T40.694	T40.695

EFFICACY AND SAFETY OF NALOXONE⁹⁻¹⁶

Efficacy

Naloxone produces virtually no pharmacologic effects in patients not taking opioids.

Onset of action is less than 2 minutes when naloxone is administered IV to adults. IV has a faster onset than IN when time from dose administration to clinical response is measured, but there is no time difference when measuring the time from patient contact to clinical response due to the time required to establish an IV access. Time to clinical response is similar for IM and IN routes when a concentration of at least 2mg/ml is utilized for nasal administration.

Safety

Naloxone has a low risk of side effects; the most common stem from opioid withdrawal in persons who have a physical dependence.

Precipitated Opioid Withdrawal: In individuals with a physical dependence on opioids, precipitation of withdrawal occurs in a dose-related manner: the higher the dose of naloxone, the longer and more severe the withdrawal syndrome may be. Route of naloxone administration is an additional factor in incidence and severity of withdrawal symptoms; for example, IV push administration of naloxone can provide rapid and relatively higher exposure compared to routes that require drug absorption. Lastly, the dose of opioid taken and its affinity for the mu receptor will also influence potential for naloxone-precipitated withdrawal.

Withdrawal symptoms may start within minutes of naloxone administration but typically dissipate within an hour due to the metabolic clearance rate of naloxone relative to that of the offending opioid. Opioid withdrawal symptoms include: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, aggressiveness/agitation/combativeness, shivering, trembling, abdominal cramps, weakness and increased blood pressure. Withdrawal symptoms are often a necessary part of reversal of an opioid overdose; while they may be distressing to the patient and may complicate clinical management, they are generally not life threatening and represent a superior outcome to an overdose death.

IV naloxone may be titrated to minimize withdrawal symptoms; however, titration is not recommended when naloxone is administered via the IM or IN routes.

Recurrence of Respiratory Depression: Opioids with long durations due to formulation design (e.g., extended-release tablets, capsules or patches) or inherently slow systemic clearance (e.g., buprenorphine, levorphanol and methadone) may outlast the duration of effects of naloxone. Naloxone formulated for rescue use in the community has a half-life of 74 to 125 minutes (see Table 2). The duration of naloxone effect is dependent on the route of administration; being longer with IN or IM than IV. Duration of IN naloxone effect is not well described but plasma concentrations following 4mg IN have exceeded those obtained with 0.4mg IM at 1 hour and at 6 hours.

The maximum volume for effective nasal drug administration is 0.1 to 0.2 μ L per nares. Delivery of a greater volume results in pharyngeal pooling, swallowing, and inactivation of drug in the gastrointestinal tract.¹⁴ Non-response rates of between 9 and 26% have been reported in association with the 2mg dose of nasal naloxone (which were typically given in volumes that exceeded 1ml).¹⁵ While the exact incidence of recurrent respiratory depression after bystander administration of naloxone is unknown, in the Massachusetts community-based OEND program experience, 52% of bystanders used 2 or more doses of (nasal) naloxone.¹⁶

Rare, Life-Threatening Injuries Post-Naloxone Administration have been reported but these adverse effects (pulmonary edema, arrhythmias, hypertension, cardiac arrest) are more likely to be related to the excessive opioid dose, co-consumed drugs (e.g. cocaine), hypoxia, or pre-existing cardiac disease rather than to naloxone.

Table 2: COMPARISON OF NALOXONE NASAL SPRAY AND AUTOINJECTOR¹⁷⁻²¹

	Nasal Spray	Auto-injector
<i>Both products are FDA-approved for use in community settings, contain product labeling which includes instructions for layperson use, and are ready-to-use with no assembly required.</i>		
Trade name	Narcan	Evzio
Strength	4 mg/0.1ml	0.4 mg/0.4ml
Total volume of 2-unit package	8 mg/0.2ml	0.8 mg/0.8ml
Dosing ^a	Spray 0.1ml into one nostril; repeat with second device into other nostril after 2-3 minutes if no or minimal response	Inject into outer thigh as directed by voice-prompt system. Place black side firmly on outer thigh and depress and hold for 5 sec. Repeat with 2 nd device in 2-3 minutes if no or minimal response.
Pharmacokinetics		
<ul style="list-style-type: none"> ▪ Dose/route ▪ T_{1/2} (h) ▪ T_{max} (h) ▪ C_{max} (ng/ml) ▪ AUC_{0-inf} (ng·h/ml) ▪ Bioavailability (%) 	4mg IN ^b 2.08 0.50 4.83 7.95 46.7%	0.4mg autoinjector ^c 1.28 0.25 1.24 1.88 ~100%
Usability	90.5% successful use without training ^d	90.5% successful use without training; 100% successful use with training ^e
Storage requirements ^f	Store at 59-77 ^o F; excursions permitted from 39-104 ^o F	Store at 59-77 ^o F; excursions permitted from 39-104 ^o F
Disposal of Used or Expired Product	No defined requirements	Biohazard sharps container

^a Response = return of spontaneous respirations to rate \geq 10 breaths/minute. ^b All values listed for naloxone spray 4mg and IM syringe are geometric mean values. Relative bioavailability listed for IN naloxone is relative to IM-administered product. ^c All values listed for autoinjector are arithmetic mean values; doses administered by autoinjector were subcutaneous or IM, depending on the participant's subcutaneous fat thickness and underlying muscle depth. ^d Successful use = correct performance of two critical tasks 1) insertion of the nozzle of the spray applicator into the nostril and 2) correct use of the plunger to release dose of naloxone into the nose (ref 20) ^e Successful use = successful administration of a simulated dose of naloxone into a mannequin by a layperson during a simulated opioid emergency; training was performed by nurse and included participant demonstration of correct use (reference 21) ^f All naloxone products should be stored away from light and not subjected to freezing.

OVERDOSE RISK ASSESSMENT AND OPIOID RISK MITIGATION IN VETERANS

Opioid Overdose Education and Naloxone Distribution (OEND) is an important risk mitigation strategy for clinicians to incorporate into their practice to save Veteran lives. Risk assessment tools are available in VHA—and have been automated and integrated into VHA clinical decision support tools (e.g., dashboards, reports) available to clinical staff with appropriate permissions to aid the clinical care teams in identifying patients who may benefit from this life saving intervention. Risk assessment tools identified below along with the integrated data management risk tools such as OTTR and STORM will not identify every patient appropriate to offer OEND as a risk mitigation strategy, therefore it's critical that providers make an assessment at the point of care to consider OEND when overdose risk is identified as part of the clinical interview and assessment process in addition to population management approaches using the risk assessment tools.

RIOSORD – Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression²²

Zedler et al. (2015) performed a retrospective, case-controlled analysis of health care information drawn from a VHA database which included 1,877,841 patients that had received an opioid between Oct 1, 2010 and Sept 30, 2012. Of these, 817 patients were determined to have had an overdose or episode of serious opioid-induced respiratory depression (OSORD). Ten controls (total n = 8,170) were selected for each case of OSORD. Items for the risk index were selected from model variables that were statistically significantly associated with OSORD. Each item was assigned a point value and point values were totaled to give scores. Modeling of risk index scores produced risk classes that predicted probabilities of OSORD. The intent was to develop a practical and relatively simple and brief risk assessment instrument that could be utilized in a busy community health care setting before prescribing opioids to assess a patient's baseline risk of OSORD.

Fifteen items most highly associated with OSORD were retained for calculation of the risk index (table 3). Table 4 (next page) can be utilized to determine predicted probability of an OSORD event based upon risk index score.

Table 3: RIOSORD questions.

RIOSORD (Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression) Questions	Points for 'Yes' Response
In the past 6 months, has the patient had a healthcare visit (outpatient, inpatient or ED) involving any of the following health conditions?	
Opioid dependence?	15
Chronic hepatitis or cirrhosis?	9
Bipolar disorder or schizophrenia?	7
Chronic pulmonary disease (e.g. emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)?	5
Chronic kidney disease with clinically significant renal impairment?	5
An active traumatic injury, excluding burns (e.g., fracture, dislocation, contusion, laceration, wound)?	4
Sleep apnea?	3
Does the patient consume	
An extended-release or long-acting (ER/LA) formulation of any prescription opioid? (e.g., OxyContin, Oramorph-SR, methadone, fentanyl patch)	9
Methadone? (Methadone is a long-acting formulation so also check "ER/LA formulation" [9 points])	9
Oxycodone? If it has an ER/LA formulation [e.g., OxyContin] also check "ER/LA formulation" [9 points]	3
A prescription antidepressant? (e.g. fluoxetine, citalopram, venlafaxine, amitriptyline)	7
A prescription benzodiazepine? (e.g., diazepam, alprazolam)	4
Is the patients current maximum prescribed opioid dose:	
≥ 100 mg morphine equivalents per day?	16
50 to < 100 mg morphine equivalents per day?	9
20 to < 50 mg morphine equivalents per day?	5
In the past 6 months, has the patient:	
Had one or more emergency department (ED) visits?	11
Been hospitalized for one or more days?	8
Total Point score (maximum 115)	

Adapted from Zedler et al. Pain Medicine 2015; 16: 1566-79

The RIOSORD risk index has been validated in both US Veterans and in the general population.²³ As of March 9, 2016, at least one network has embedded a RIOSORD score calculator into the Computerized Patient Record System with ability to

produce clinical reports sortable by facility, PACT team, and provider. RIOSORD scoring has been automated by VHA and integrated into clinical decision support tools that are available to VHA staff with appropriate permissions.

The research that resulted in development of RIOSORD was funded by kaléo, Inc., Richmond, VA, manufacturer of the Evzio® naloxone HCL autoinjector; that company also reviewed and commented on the study methods utilized.

Table 4: RIOSORD: Risk classes and predicted probabilities

				Overdose or Serious Opioid-Induced Respiratory Depression (All patients, n = 8,987)	
Risk class	Risk Index score (Points)	All Patients (n = 8,987), n (%)	Average Predicted Probability (95% CI)	Observed Incidence	
1	0-24	7,133 (79.4)	0.03 (0.03, 0.03)	0.03	
2	25-32	780 (8.7)	0.14 (0.14, 0.15)	0.14	
3	33-37	306 (4.5)	0.24 (0.25, 0.24)	0.23	
4	38-42	238 (2.7)	0.34 (0.34, 0.35)	0.37	
5	43-46	133 (1.5)	0.46 (0.45, 0.46)	0.51	
6	47-49	77 (0.9)	0.55 (0.54, 0.55)	0.55	
7	50-54	101 (1.1)	0.64 (0.64, 0.65)	0.60	
8	55-59	87 (1.0)	0.76 (0.75, 0.76)	0.79	
9	60-66	73 (0.8)	0.85 (0.84, 0.85)	0.75	
10	≥ 67	59 (0.7)	0.94 (0.93, 0.95)	0.86	
Model performance: C-statistic = 0.88		Hosmer-Lemeshow goodness-of-fit statistic = 10.8 (p > 0.05)			

Adapted from Zedler et al. *Pain Medicine* 2015; 16: 1566-79

VHA NOTE: Average predicted probabilities are not population-based (based on case-control study matching 817 cases with OSORD to 10 controls).

Academic Detailing Service (ADS) OEND Data Resources

The ADS provides OEND data resources that identify overdose risk factors and calculate the RIOSORD score for patients at risk for opioid overdose. These resources are available to VA staff Nationally. All VA employees have access to view the summary level data presented on the OEND Patient Risk Dashboard; patient-level data are available to staff with PHI/PII access granted at the facility level.

The OEND Patient Risk Dashboard provides summary data available at the National, VISN, Facility, and Provider levels and has the ability to drill down to the OEND at Risk Patient report. The patient report displays the RIOSORD Score, OIRD % Risk, STORM Risk (see below), diagnoses relevant to increased risk, upcoming appointments and other related information. The report allows an authorized user to identify and filter a group of patients by risk factor(s), Provider(s), RIOSORD Risk Class, and upcoming appointment. It also gives the ability to drill down into additional information about the patient, including a list of upcoming appointments, details for the RIOSORD calculation, and benzodiazepine and opioid fill and dose history over the previous year.

Each of the OEND data resources is available from the ADS SharePoint Site:

ADS Dashboards and Reports Site - <https://vaww.portal2.va.gov/sites/ad/Dashboards/Site%20Pages/Home.aspx>

OEND Patient Risk Dashboard - https://spsites.cdw.va.gov/sites/PBM_AD/AnalyticsReports/OEND/OENDDashboard.rdl

OEND at Risk Patient Report - https://spsites.cdw.va.gov/sites/PBM_AD/AnalyticsReports/OEND/OENDPatientReport.rdl

OEND Patient Details Report - https://spsites.cdw.va.gov/sites/PBM_AD/AnalyticsReports/OEND/OSIOENDPatientDetail.rdl

STORM – Stratification Tool for Opioid Risk Mitigation

STORM is a clinical decision support tool that utilizes a VA-developed predictive model that estimates the likelihood of drug overdose or suicide-related events in patients receiving opioid prescriptions from VA. A description of the development and applications of STORM has been peer-reviewed and is available through *Psychological Services* (title, *Development and applications of the Veterans Health Administration's Stratification Tool for Opioid Risk Mitigation (STORM) to improve opioid safety and prevent overdose and suicide*).

A multivariate mixed effects logistic regression model was formulated to predict the occurrence of an overdose- or suicide-related event (overdose/suicide) using secondary data from VA national administrative databases. Each model participant had at least one outpatient opioid analgesic prescription during FY2010; participants were followed for one year (FY2011) to identify any overdose/suicide-related events. The predictor variables were derived from FY2010 data and addressed the following domains: (a) Demographics; (b) Previous Overdose/Suicide and Treatment Risk Indicators; (c) Prescriptions; (d) Substance Use and Mental Health Disorder diagnoses; and (e) Medical Co-morbidities. The outcome variable of overdose/suicide related events came from FY2011 data. This predictive model greatly improves identification of patients receiving opioid prescriptions at risk of adverse events; once identified, STORM provides a tailored list of risk mitigation strategies, including non-pharmacological pain modalities, for providers to consider that could help to reduce risk and address risk factors.

Variables included in the risk model were selected based on published literature, the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain (2010), and recommendations from the VA National Pain Workgroup. STORM, including definitions for the predictor variables, may be viewed in detail at this link:

https://spsites.cdw.va.gov/sites/OMHO_PsychPharm/Pages/Real-Time-STORM-Dashboard.aspx

There are two risk models: **Specific Risk**, defined as risk for suicide-related event or opioid, sedative, or acetaminophen poisoning or overdose and **Overall Risk**, which is the same as specific risk plus accidents, falls, or drug-induced condition (e.g., psychosis). Risk groups are defined by magnitude of risk scores in the specific and overall risk categories (Table 5).

Table 5: Risk group stratification based upon specific or overall risk scores (see text for definitions); percentage of VA population with an active opioid analgesic prescription estimated to be in each risk group. Patients with opioid-use disorder (OUD) without an active opioid prescription are categorized as very high risk.

Risk Group	Specific Risk	Overall Risk	% of Population
Very High	Risk score over 12.4% or OUD diagnosis	Risk score over 30.0% or OUD diagnosis	Roughly 2.5% of the population
High	Risk score between 6.3% and 12.4%	Risk score between 10.0% and 30.0%	Roughly 2.5-10% of the population
Medium	Risk score between 1.5% and 6.3%	Risk score between 9.5% and 10.0%	Roughly 10-33% of the population
Low	Risk score below 1.5%	Risk score below 9.5%	Roughly 66% of the population

In addition to providing an estimate of specific or overall risk score, STORM also:

- Provides patient-specific information on key clinical factors that elevate risk per the model
- Provides a tailored list of risk mitigation strategies for consideration, with tracking of current use of the strategy
- Provides information on key providers and appointments to facilitate communication and care coordination between mental health and primary care teams, and the opioid prescriber
- Provides tracking of non-pharmacological treatments for pain

STORM provides risk scores and risk mitigation strategies for patients with an active outpatient prescription order for any opioid analgesic; data utilized in STORM is updated nightly. RIOSORD risk classes and scores have been integrated into STORM and the predictive risk model will be updated annually and/or as data become available.

STORM is available to VA staff nationally. All VA employees have access to view the summary level data presented on the STORM dashboard; STORM patient-level data are available to staff with SSN access granted at the facility level. Link to STORM homepage: https://spsites.cdw.va.gov/sites/OMHO_PsychPharm/Pages/Real-Time-STORM-Dashboard.aspx

Figure 1: STORM patient report showing estimated risk score, RIOSORD risk class and score, diagnoses and medications relevant to increased risk, risk mitigation strategies and other related information. The report allows an authorized user to identify and filter a group of patients by risk mitigation strategies, opioid prescriber, and risk score.

VA STORM: Patient Detail Dashboard Stratification Tool for Opioid Risk Mitigation											
Home Definitions Contact Us Facility-level Summary Report											
Total Patients: 686 Last Update: 08/09/16											
Patient Information	What is my patient's risk level? (Click + for details)			What factors contribute to my patient's risk?		How can I reduce my patient's risk?			How can I follow-up with this patient?		
	Suicide-related event, overdose, falls or accident 3 yr	Suicide-related event or overdose 1 yr	Overdose or opioid-induced respiratory depression	Relevant Diagnoses	Relevant Medications	Risk Mitigation Strategies	Non-pharmacological Pain Treatment	Recent Appointments	Upcoming Appointments	Care Providers	
John Doe Last Four: 0000 Gender: F Station: Facility A	Very High 56% risk of suicide-related event, overdose, falls or accidents in the next three years	Very High 40% risk of suicide-related event or overdose in the next year	Risk Class: 10 RIOSORD Score: 87	SUD Dx: OUD AUD Nicotine Dep. Mental Health Dx: PTSD Depression Bipolar Other MH Medical Dx: Chronic Pulm Dis. Electrolyte Disorder Deficiency Anemia Recent Adverse Events: Suicide Attempt	Active Opioids: Methadone (Dr. ABC) Sedating Evidence-based Pain Meds: Gabapentin (Dr. ABC) Duloxetine (Dr. ABC) Topiramate (Dr. ABC)	MEDD <= 100** <input checked="" type="checkbox"/> MEDD: 90 Naloxone Kit <input type="checkbox"/> Opioid Signed Informed Consent <input checked="" type="checkbox"/> 6/22/15 Timely Follow-up <input checked="" type="checkbox"/> 10/31/15 Timely UDS <input checked="" type="checkbox"/> 10/23/15 Psychosocial Assessment <input checked="" type="checkbox"/> 10/22/15 Psychosocial Tx <input checked="" type="checkbox"/> 10/22/15 Active SUD Tx <input type="checkbox"/> Opioid Agonist Tx <input type="checkbox"/> Bowel Regimen <input checked="" type="checkbox"/> 10/22/15 Med. Reconciliation <input checked="" type="checkbox"/> 10/23/15 PDMP <input checked="" type="checkbox"/> 6/22/16	Active Therapies <input checked="" type="checkbox"/> 1/16/16 Comp & Integ Medicine <input type="checkbox"/> Chiropractic Care <input type="checkbox"/> Occupational Therapy <input type="checkbox"/> Pain Clinic <input checked="" type="checkbox"/> 1/15/16 Physical Therapy <input checked="" type="checkbox"/> 1/16/16 Specialty Therapy <input type="checkbox"/>	Primary Care 10/23/2015 Mental Health 10/31/15 Mental Health Clinic - Ind 10/23/15 Pain Clinic 7/12/2015 Other 10/23/2015 Telephone Triage	Primary Care 10/21/16 Mental Health 1/18/2016 11:00 AM Substance Use Disorder - Ind Pain Clinic 10/21/16 Other None	Recent Opioid Prescriber Dr. ABC Primary Care Provider Dr. DEF MH Tx Coordinator Jane Doe BHIP Team Team A	

OTRR- Opioid Therapy Risk Report

The Opioid Therapy Risk Report (OTRR) is a patient-focused, actionable and provider-specific report that is available to Primary Care Providers (PCP), Primary Care Managers, Primary Care Administrators and Chiefs of Staff, PAC Teams, Clinical Pharmacists, Pain Clinic and Specialty Care clinicians caring for patients on opioid therapy and Behavioral Health Interdisciplinary Program (BHIP) Team Members. Users must have real SSN authorization to view.

Data are gathered across VA and updated daily (data freshness is indicated by the 'As of' date) so that the most recent information is available, regardless of where care was delivered. Data presented includes documented diagnoses that influence patient risk, such as PTSD, Substance Use Disorder (SUD) and Obstructive Sleep Apnea (OSA) as well as the most recent patient interaction with health

providers such as Last PCP visit date, Last Pain Clinic visit date and last Mental Health visit date. Dates and status of the signed iMedConsent™ for Opioid Therapy are included. The Patient Details page contains results from the latest Urine Drug Test (UDT), Patient Pain Scores as well as patient Opioid and Benzodiazepine medication history tables listing the prescriber, dispensing location, strength, number of days supply and Morphine Equivalents.

OTRR can be accessed through several avenues; a commonly used route by Primary care practitioners is via CPRS → Tools → Primary Care Almanac → Opioid Therapy Risk Report → Patient List. Another method to access: <http://vssc.med.va.gov/> then click "Primary Care" under "Clinical Care", then "Primary Care management" then "Opioid Therapy Risk Report".

Page 10 contains an example of an OTRR Patient Detail Report. The upper right corner contains several links to useful sites or resources; including: Data Definitions, VA OEND, VHA Pain Management, and a link to the 2010 VA/DoD Clinical Practice Guidelines for Chronic Opioid Therapy.

Figure 2: Example of OTRR Patient Detail Report. A detailed description of the information contained can be found in the following text.



Long-Term Use Opioid Therapy Patient Details

[VA OEND Site](#)
[Data Definitions](#)
[Clin Practice Guide](#)
[VSSC Help Desk](#)
[VHA Pain Mgt Site](#)
[GoTo Excel-Friendly Multi-select Pt List](#)

Current As Of: 1/22/2016 **Double Asterisk** identifies values evaluated for the past two years.

To Print: Use toolbar located just above report title, click the Export icon select PDF, then Print

Almanac, Patient1026

SSN: 000701013 DOB: 8/16/1966 Age: 50 Gender: M

BHIP Team Location	BHIP Team
(V13) (777) Paradise, TX	MH BHIP TEAM 2

Location	Team	PCP Name	Next PC Appt	Next PC Appt Clinic
(V13) (777XX) Dwight D. Eisenhower CBOC	PC TEAM 1	Primary Care Provider Name	1/26/2016 2:30:00 PM	PC CLINIC 1

Last 30 days Avg Morph Equiv	Urine Drug Test Screen Date**	Last Visit w/PCP**	Pain Clinic**	Mental Health**	Last Visit SUD Tx**	Palliative Care**	DEP Dx**	SMI Dx**	OMD Dx**	PTSD Dx**	SUD Dx**	OSA Dx**	PalCare Dx**	CA Pain Dx**	Active Opioid Rx	Active Benzo Rx
318	12/28/2015	7/24/2015	11/30/2015	11/30/2015	11/29/2015		✓	✓	✓	✓	✓	✓			!	✓

Agonist Tx	Last Op Sub Visit	Dispense Date	Naloxone Product Dispensed	OT Consent Date	IMed User	IMedConsent Location
✓	1/19/2016	11/19/2015	NALOXONE RESCUE KIT INTRANASAL	8/23/2015	✓	(V13) (777) Paradise, TX

Most Recent Urine Drug Test: 12/28/2015

Sta6a	AMPHET	BARB	BENZO	CANNAB	COCAINE	CODEINE	ETHANOL	HYDROCODO	HYDROMORPH	METHADONE	MORPHINE	OPIATE	OXY
777XX	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE		NEG mg/dl			POSITIVE		NEGATIVE	

Daily Average Morphine Equivalents Per Month - Past Twelve Months

Pain Score - Past Twelve Months

Opioid History Past Twelve Months

Release Date	VA Product	Strength	Days Supply	Daily Morphine Equivalent
Prescriber: Primary Care Provider Name (V13) (777) Paradise, TX				
1/7/2016	METHADONE HCL 10MG TAB	10.00	30	360
Prescriber: Not my Primary Care Provider (V13) (777) Paradise, TX				
12/10/2015	HYDROCODONE 8MG/ACETAMINOPHEN 325MG TAB	5.00	30	10

Benzodiazepine History Past Twelve Months

Release Date	VA Product	Strength	Days Supply

Upper banner: Patient name, SSN, date of birth, age, gender, BHIP team assignment. Also see DATA DEFINITIONS
1st line: Clinic location, PC Team assignment, PCP name, date of next PC appointment, name of next PC appointment clinic
2nd line: Last 30 days average morphine equivalents, urine drug screen test screen date, date of last visit with PCP, last Pain Clinic visit date, last Mental Health visit date, last Visit in SUD Treatment date, last Palliative Care Visit date, (documented diagnoses

Updated versions may be found at <http://www.pbm.va.gov> or <http://vaww.pbm.va.gov> 9

that increase patient risk following): depression (DEP), serious mental illness (SMI), other mental disorder (OMD), post-traumatic stress disorder (PTSD), substance use disorder (SUD), obstructive sleep apnea (OSA), palliative care (PalCare), cancer pain (CA), active opioid prescription (Rx), active benzodiazepine (Benzo) Rx.

3rd line: Opioid agonist treatment, last opioid substitution visit, ***last naloxone dispensed***, last opioid treatment consent date, location of iMed consent

4th line: urine drug test (UDT) date and results for amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, codeine, ethanol, hydrocodone, hydromorphone, methadone, morphine, opiates, oxycodone

5th line graphs: average morphine equivalent daily dose, by month for past 12 months; pain scores past 12 months

6th line tables: opioid history past 12 months; benzodiazepine history past 12 months.

COMM™ - Current Opioid Misuse Measure²⁴

The Current Opioid Misuse Measure (COMM)™ is a validated, 17-question easy-to-administer patient self-assessment that can be completed in less than 10 minutes. Completion of the COMM™ helps clinicians identify whether and to what extent a patient currently on long-term opioid therapy may be exhibiting aberrant behaviors associated with misuse of opioid medications; in addition, it can be utilized to develop or justify treatment strategies such as the level of monitoring planned for a patient or referral to a specialty pain clinic.

The assessment questions can be viewed at: <http://www.opioidprescribing.com/documents/09-comm-inflexion.pdf> . Questions focus on six key issues:

- Signs and symptoms of intoxication
- Emotional volatility
- Evidence of poor response to medications
- Addiction
- Healthcare use patterns
- Problematic medication behavior

Each question asks the relative frequency of a thought or behavior over the last 30 days. Responses are recorded from 0 = “never” to 4 = “very often”. A score ≥ 9 is considered a positive indicator that misuse of medication is likely occurring.

COMM™ was developed with a grant from the National Institutes of Health and an educational grant from Endo Pharmaceuticals.

REGULATION OF NALOXONE AND COMMUNITY MEDICO-LEGAL RISK

Naloxone remains a medication obtainable only by prescription in most states in the U.S.

In general, the risk of civil liability for a layperson who administers naloxone in an overdose is very low; a recent review found no case where a layperson was sued for using naloxone in an emergency.²⁵ Almost every state provides laypeople who provide medical assistance to another person in an emergency with some civil liability protection. In addition, most states have enacted laws that provide specific immunity to people who administer naloxone in the event of an overdose. The particulars of this protection vary between states.

For additional information and to review state specific legislation surrounding naloxone, including Good Samaritan laws, refer to the following links: <http://prescribetoprevent.org/>

<http://lawatlas.org/query?dataset=laws-regulating-administration-of-naloxone> .

<http://phlr.org/product/naloxone-community-opioid-overdose-reversal>

https://www.networkforphl.org/_asset/qz5pvn/naloxone- FINAL.pdf

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