Naloxone

for opioid safety

A Nevada provider's guide

to prescribing naloxone to patients who use opioids

Overdose | is the leading cause of injury-related death in the U.S.

100 PEOPLE DIE FROM DRUG OVERDOSE EVERYDAY IN THE UNITED STATES.

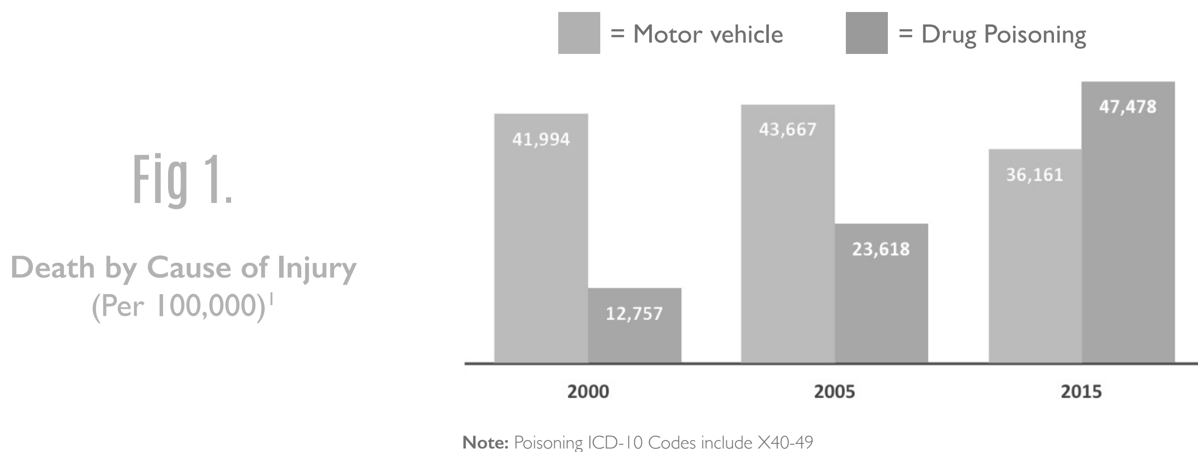


Fig 1.

Death by Cause of Injury (Per 100,000)[1]

Note: Poisoning ICD-10 Codes include X40-49

DRUG OVERDOSE DEATHS IN NEVADA ARE STATISTICALLY HIGHER THAN THE NATIONAL AVERAGE.

Fig 2.

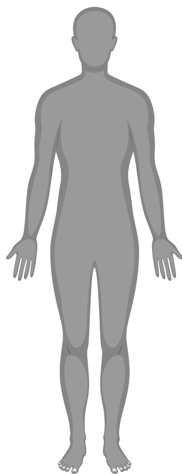
Drug Overdose Deaths[2]

Figure 2. Age-adjusted overdose death rates, by state: United States, 2015. Reprinted from Drug Overdose Deaths in the United States, 1999-2015, by H. Hedegaard, M. Warner, and A.M. Minino, 2017, NCHS data brief, no 273. Hyattsville, MD: National Center for Health Statistics. Reprinted with permission.

Accidental opioid overdose is preventable

The main risk of death from an opioid overdose is prior overdose.[3] In 2016, 1 in 10 patients hospitalized in Nevada for drug related overdoses died within the following year, with 17% of those deaths due to an accidental drug overdose.[4]

OTHER FACTORS THAT INCREASE RISK OF OVERDOSE:



Reduced Tolerance:

Period of abstinence, change in dose, release from prison

Genetic Predisposition

Concomitant Use of Substances:

Benzodiazepines, alcohol, cocaine

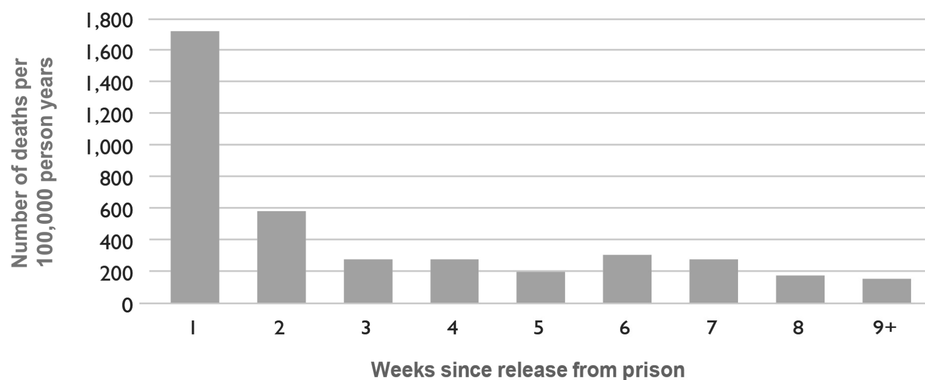
The majority of opioid overdose deaths involve at least one other drug, including benzodiazepines, cocaine or alcohol.[5]

WHEN A PATIENT REDUCES OR STOPS OPIOID USE, THERE IS AN INCREASED RISK OF OVERDOSE DEATH IF OPIOID USE INCREASES AGAIN.

An example of overdose risk if opioids are discontinued and restarted[6]

Fig 3.

Overdose Mortality Rate by week since prison release



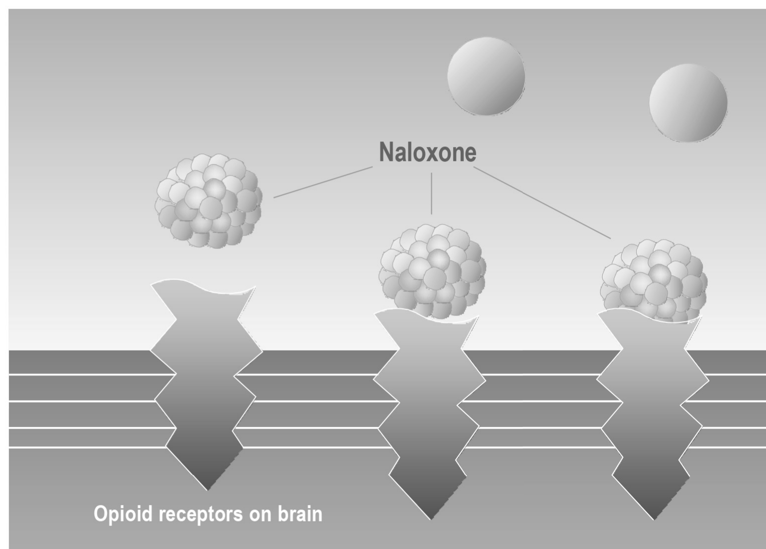
Naloxone also called 'Narcan'

- Highly specific, high-affinity opioid antagonist used to reverse the effects of opioids.
- Can be safely administered by laypersons via intramuscular or intranasal* routes, with virtually no side effects and no effect in the absence of opioids.
- Effects last 30-90 minutes; usually sufficient for short-acting opioids but help should always be sought. When naloxone wears off the overdose can come back and the person could stop breathing again.
- While high doses of intravenous naloxone by paramedics have been associated with withdrawal symptoms, lower lay-administered doses produce much more mild symptomatology.[7]

Fig 4.

Naloxone Mechanism of Action[8]

Naloxone has a higher affinity to the opioid receptors than opioids like heroin or oxycodone, so it knocks other opioids off the receptors for 30-90 minutes. This reverses the overdose and allows the person to breathe.



THE AMERICAN MEDICAL ASSOCIATION HAS ENDORSED THE DISTRIBUTION OF NALOXONE TO ANYONE AT RISK FOR HAVING OR WITNESSING AN OPIOID OVERDOSE.[9]

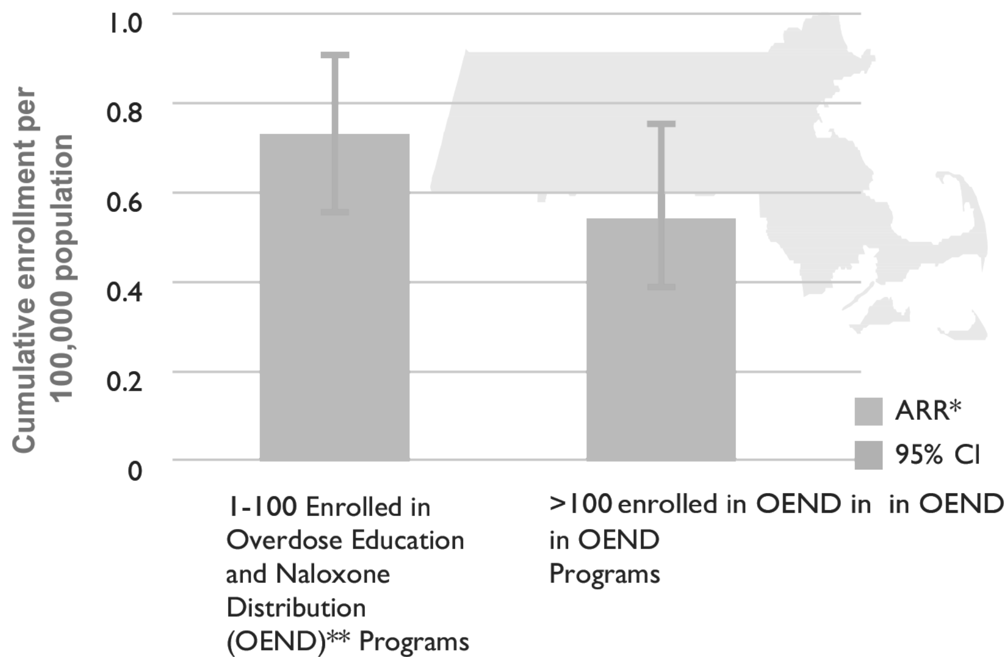
From 1996 through June 2014, naloxone has been distributed to over 152,000 people and more than 26,400 overdose reversals have been reported.[10]

* Intranasal is available in both FDA approved and off-label formulations. Both are supported by the American Medical Association and are the preferred route for many emergency responders.[11, 12, 13]

Naloxone is Effective

Fig 5.

Fatal Opioid Overdose Rates by Naloxone Implementation in Massachusetts[11]



* Adjusted Rate Ratios (ARR) adjusted for population age <18, male; race/ethnicity; below poverty level; medically supervised inpatient withdrawal, methadone and buprenorphine treatment; prescriptions to doctor shoppers, year

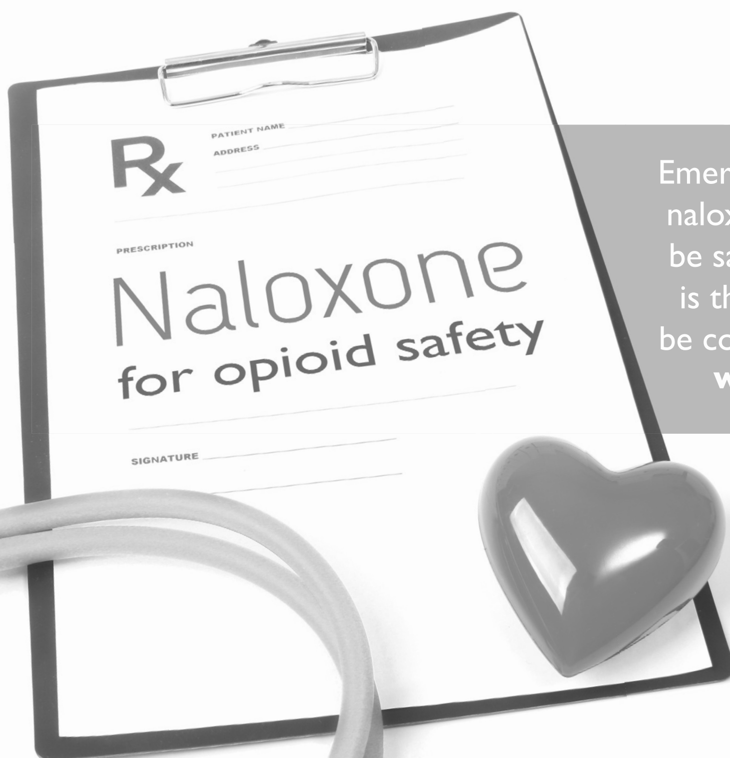
** OEND programs train opioid user and bystander enrollees on how to recognize the signs of an overdose, seek help, rescue breathe, and administer naloxone.

Naloxone is Cost Effective[14]

A manuscript in the *Annals of Internal Medicine* indicated that providing naloxone to heroin users is robustly cost-effective and possibly cost-saving. Investigators believe similar results apply to other opioid users.

Cost: $421 per quality-adjusted life-year gained

Benefit: 164 Naloxone Scripts equals 1 prevented death



Emerging data suggests that providing naloxone may encourage patients to be safer with their opioid use. If this is the case, the intervention would be cost-saving and **36 prescriptions would prevent one death.**

Indications for Naloxone Prescription

CONSIDER OFFERING A NALOXONE PRESCRIPTION TO:

- All patients prescribed long-term opioids
- Anyone on >90mg morphine equivalents daily
- Anyone otherwise at risk of experiencing or witnessing an opioid overdose

Find a dose calculator online at:
https://www.oregonpaingu idance.org/opioidmedcalculator/
or in the CDC Opioid Guidelines App

WHY PRESCRIBE TO ALL PATIENTS USING OPIOIDS

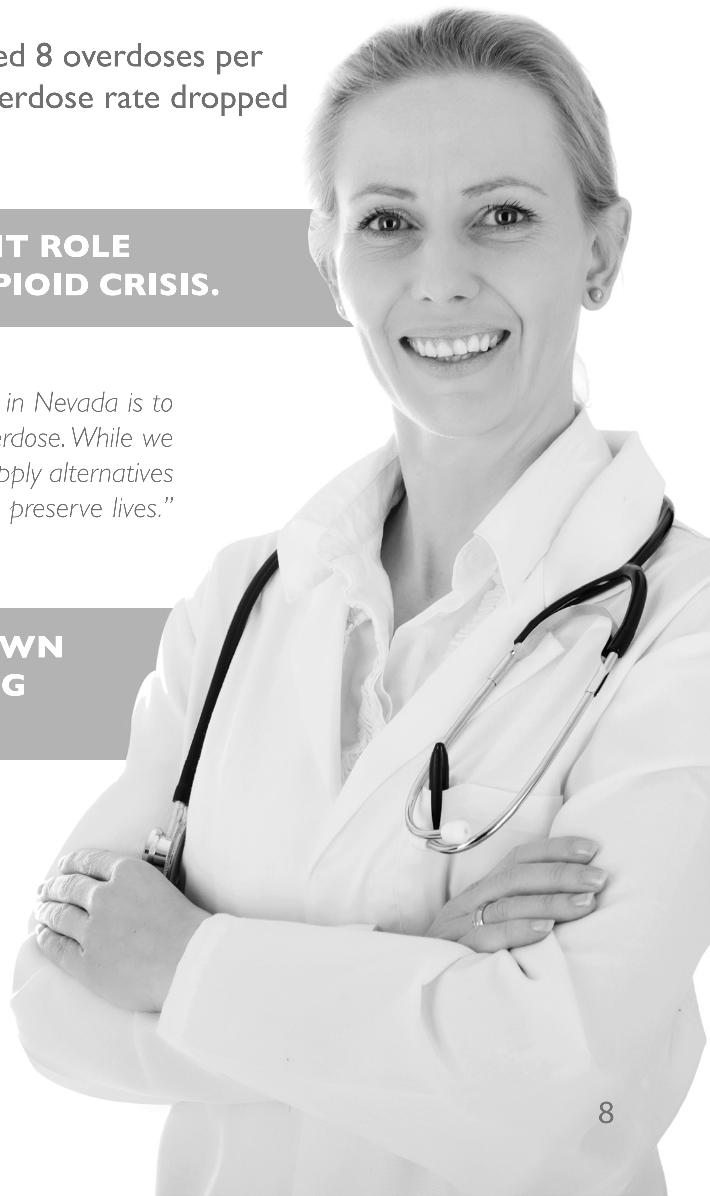
- It is difficult to predict which patients who take prescription opioids are at risk for overdose.
- Many patients do not feel they are at risk for overdose. Prescribing to all patients on opioids will help patients understand naloxone is being prescribed for risky drugs, not risky patients.
- About 40% of overdose deaths result from diverted medications.[15] Whether intentional or unintentional, diverted opioids are a serious risk. Co-prescribing naloxone increases the chance that the antidote will remain with the medication.

Potential Behavioral Impact

In a nonrandomized study among primary care clinics, patients receiving long-term opioid therapy for pain who received a naloxone prescription had: [16]

47%	fewer opioid-related ED visits per month after 6 months
63%	fewer opioid-related ED visits per month after 1 year

U.S. army base Fort Bragg in North Carolina averaged 8 overdoses per month. After initiating naloxone distribution, the overdose rate dropped to zero—with no reported naloxone use.[17]



PROVIDERS RECOGNIZE THE IMPORTANT ROLE NALOXONE HAS IN COMBATING THE OPIOID CRISIS.

"One way to reduce the harm created by the opioid epidemic in Nevada is to recommend and prescribe naloxone for persons at risk for overdose. While we create better ways of curtailing supply, treating addiction, and apply alternatives for patients in pain, we can immediately use naloxone to help preserve lives."
- Trudy Larson, MD[18]

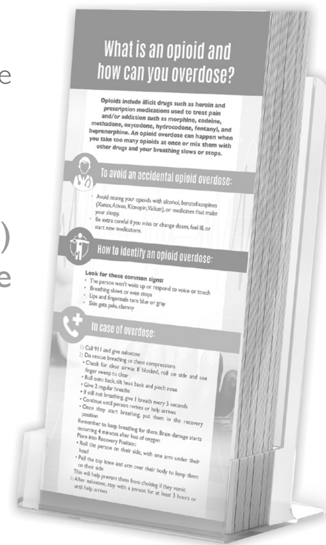
PROVIDERS HAVE DECIDED ON THEIR OWN TO INTEGRATE NALOXONE PRESCRIBING INTO THEIR PRACTICE.

"I started thinking about prescribing naloxone when it was too late. It was only after I had a patient die, likely of an accidental overdose, that I realized the importance of prescribing naloxone. While I had been aggressively treating his pain, I wasn't as aggressive in making sure his family had what they needed if he took too much of his meds. I don't want to see this happen again." - Andy Pasternak, MD, MS[19]

Naloxone patient Education

Clinic staff can educate patients about naloxone. Education generally includes:

- When to administer naloxone
- How to administer naloxone (including demonstration)
- Informing patients to alert others about the medication, how to use it and where it's kept, as it is generally not self-administered



Data suggest that brief educational encounters (5-10 minutes) are sufficient to increase patients' comfort with overdose recognition and response and naloxone administration.[20]

Brochures remind patients and caregivers how to manage an overdose. Downloadable brochures can be found at: prescribe365.nv.gov

OPIOID SAFETY LANGUAGE

The word "overdose" has negative connotations and prescription opioid users may not relate to it.

Instead of using the word "overdose," consider using language like "accidental overdose," "bad reaction" or "opioid safety." You may also consider saying:

"Opioids can sometimes slow or even stop your breathing."
"Naloxone is the antidote to opioids—to be [sprayed in the nose/injected] if there is a bad reaction where you can't be woken up."
"Naloxone is for opioid medications like an epinephrine pen is for someone with an allergy."

0 1 2 3 4 5 6 7 8 9 10

Patients prescribed opioids (including high-risk persons with a history of overdose) reported their risk of "overdose" was 2 out of 10.[21]

Nevada Law Encourages Naloxone Prescribing

Naloxone is NOT a controlled substance. **Any licensed healthcare provider can prescribe naloxone.** Nevada State law provides additional protections to encourage naloxone prescribing and distribution.

PROVIDER AND PATIENT PROTECTIONS (NV SB459 effective 10/1/15)

- **Naloxone prescriptions can be written directly to people at risk and to third party individuals** (caregivers, family members, friends, etc.) who are in a position to assist a person at risk of an opioid overdose.
- **A licensed healthcare prescriber can issue a standing order** for the dispensing of naloxone by healthcare or community workers to individuals at risk of experiencing or witnessing an overdose.
- **Lay persons can possess and administer naloxone** to others during an overdose situation.
- **Pharmacists may furnish naloxone without a prescription** under pharmacy implemented standardized procedures or a physician established written protocol. (effective 9/9/16)

GOOD SAMARITAN PROTECTION (NV SB459, effective 10/1/15)

- **Witnesses of an overdose who seek medical help are provided legal protection** from arrest and prosecution for controlled substances, a restraining order and violation of parole or probation.

How to **Prescribe** Naloxone

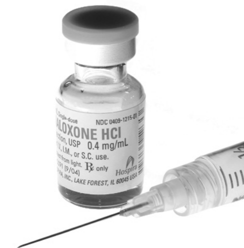
MOST COMMON ROUTES OF NALOXONE ADMINISTRATION IN NEVADA

INTRANASAL (FDA APPROVED)

- Naloxone HCl Nasal Spray 4mg for suspected overdose. Administer as a single spray into one nostril. Call 911. Repeat with second device into other nostril every 2-3 minutes after if no or minimal response.

INJECTABLE

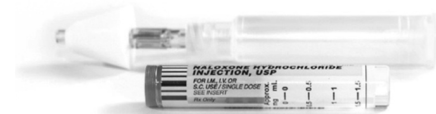
- Naloxone 0.4mg/1ml IM if overdose. Call 911. Repeat if necessary. #2
    - IM syringes (3ml 25g 1" syringes are recommended)
    - Dispense two syringes



OTHER ROUTES OF NALOXONE ADMINISTRATION

INTRANASAL (OFF-LABEL)

- Naloxone 2mg/2ml prefilled syringe, spray ½ into each nostril if overdose. Call 911. Repeat if necessary. #2
- MAD (Mucosal Atomization Device) nasal adapter



Atomizer access is complicated. Pharmacies may need to purchase them directly from a manufacturer.

AUTO-INJECTOR

- Naloxone auto-injector 0.4mg. Dispense one (two pack), use as needed for suspected opioid overdose. Call 911.

SIDE EFFECTS: Anxiety, sweating, nausea/vomiting, dizziness or shaking.

Pharmacy Access

All pharmacies can fill naloxone prescriptions, but naloxone is new for many pharmacists so some may not know how. If a pharmacist is unsure how to fill a naloxone prescription, the information outlined on this page may be helpful.

ORDERING:

- Intranasal (FDA Approved): NDC#69547-353-02
- Injectable: **Pfizer** NDC#00409-1215-01; **Mylan** NDC#67457-292-02; **West-Ward** NDC#0641-6132-25
- Intranasal (Off-label): NDC#76329-3369-01
- MAD (atomizer) nasal devices produced by Teleflex
- Auto-injector: NDC#60842-030-01 and 60842-051-01

BILLING:

- The table below displays which forms of naloxone are covered and associated restrictions for each of the four different Nevada Medicaid healthcare plans

Drug	Healthcare Plans			
	Fee for Service	Health Plan of Nevada	Amerigroup	Silver Summit Health
Intranasal (FDA Approved)	X	X (NP)	X	X
Injectable	X	X	X (QL)	X (QL)
Auto-injector	X	X (NP)	X (NP; QL; PA)	X (NP; PA)

*NP: Nonpreferred

**QL: Quantity Limits. The quantity limit for Silver Summit is 2ml per 90 days.

***PA: Prior Authorization

- The MAD does not have an NDC, therefore cannot be billed through usual pharmacy billing routes. Pharmacies may be willing to cover the cost of the MAD or patients may be requested to pay for the cost of the MAD, which is around $5 per atomizer.

COUNSELING:

- Instruct patients to administer if non-responsive from opioid use and how to assemble for administration.
- Include family/caregivers in patient counseling or instruct patients to train others.

NEVADA MEDICAID SBIRT CODES	COVERING TRAINING/COUNSELING
99408	15 to 30 minutes
99409	Greater than 30 minutes

Resources

Prescribe to Prevent:
Clinic-based prescribing information and guidelines:

www.prescribetoprevent.org

Know your Pain Meds:
Information about prescription drug abuse and awareness in Nevada:

www.knowyourpainmeds.com

Division of Health and Human Services (DHHS)
Naloxone resources for providers, naloxone legal status, trainings and contact information:

prescribe365.nv.gov

Contact DHHS for additional questions at 775-784-8090 or 800-273-8255
or opioidstrgrant@health.nv.gov.

Integrated Opioid Treatment and Recovery Centers

Center for Behavioral Health
3050 E Desert Inn #116 Las Vegas, NV 89121 • 702.796.0660
2290 McDaniel Street, Suite 1C North Las Vegas, NV 89030 • 702.399.1600
3470 W Cheyenne Road, Suite 400 North Las Vegas, NV 89032 • 702.636.0085
1311 South Casino Center Blvd Las Vegas, NV 89104 • 702.382.6262
160 Hubbard Way, Suite A Reno, NV 89502 • 775.829.4472

Life Change Center
1201 N. Steward St, Carson City, NV 89701 • 775.350.7250
1755 Sullivan Lane Sparks, NV 89431 • 775.355.7734

Vitality Unlimited
3740 Idaho St Elko, NV 89801 • 800.242.8327

References

(1) Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2015 on CDC WONDER Online Database, released December, 2016. Data are from the Multiple Cause of Death Files, 1999-2015, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/ucd-icd10.html on Nov 29, 2017. **(2)** Hedegaard H, Warner M, Minino AM. Drug Overdose Deaths in the United States, 1999-2015. NCHS data brief, no 273. Hyattsville, MD: National Center for Health Statistics. 2017. **(3)** Darke S, Williamson A, Ross J, Teesson M. Non-fatal heroin overdose, treatment exposure and client characteristics: findings from the Australian treatment outcome study (ATOS). Drug Alcohol Rev. 2005;24(5):425-32. **(4)** Thompson, J. Drug overdose among Nevada residents: associations between hospital encounters and mortality. Poster presented at: 2017 Nevada Public Health Association Conference, September, 2010; Reno, NV. **(5)** Policy Impact: Prescription Painkiller Overdoses. Center for Disease Control and Prevention website. www.cdc.gov/homeandrecreationalsafety/rxbrief/. Updated Jul 2013. Accessed Dec 2014. **(6)** Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med. 2013;159(9):592-600. **(7)** Enteen L, Bauer J, McLean R, Wheeler E, Huriaux E, Kral AH, et al. Overdose prevention and naloxone prescription for opioid users in San Francisco. J Urban Health. 2010;87(6):931-41. **(8)** Understanding Naloxone. Harm Reduction Coalition website. www.harmreduction.org/issues/overdose-prevention/ overview/overdose-basics/understanding-naloxone/. Accessed Dec 2014. **(9)** AMA adopts new policies at annual meeting: promoting prevention of fatal opioid overdose. American Medical Association website. www.ama-assn.org/ama/pub/news/news/2012-06-19-amaadopts-new-policies.page. Jun 2012. Accessed Dec 2014. **(10)** Opioid Overdose Prevention Programs Providing Naloxone to Laypersons – United States, 2014. MMWR 2015; 64(23): 625-635. **(11)** Walley AY, Xuan Z, Hackman HH, Quinn E, Doe-Simkins M, Sorensen-Alawad A, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013;346. **(12)** Barton ED, Colwell CB, Wolfe T, Fosnocht D, Gravitz C, Bryan T, et al. Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting. J. Emerg. Med. 2005;29(3):265-71. **(13)** Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. Addiction. 2009;104(12):2067-74. **(14)** Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. Ann Intern Med. 2013;158(1):1-9. **(15)** Hirsch A, Proescholdbell SK, Bronson W, Dasgupta N. Prescription histories and dose strengths associated with overdose deaths. Pain Med. 2014;15(7):1187-95. **(16)** Coffin PO, Behar E, Rowe C, et al. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. Ann Intern Med. 2016; 165:245-252. **(17)** Role of Naloxone in Opioid Overdose Fatality Prevention. Food and Drug Administration website. www.fda.gov/downloads/Drugs/NewsEvents/UCM304621.pdf. 2012;339-340. Accessed Dec 2014. **(18)** Trudy Larson, MD, email communication, November 20, 2017. **(19)** Andy Pasternak, MD, MS, email communication, November 18, 2017. **(20)** Behar E, Santos G, Wheeler E, Rowe C, Coffin PO. Brief overdose education is sufficient for naloxone distribution to opioid users. Drug Alcohol Depend. 2015; 145: 209-212. **(21)** Patient Interviews. Naloxone for Opioid Safety Evaluation. San Francisco Department of Public Health. Oct 2013—Dec 2014.

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The recommendations contained in this brochure are general and informational only; specific clinical decisions should be made by providers on an individual case basis.