MedStar Health

Prevention of Fatalities from Opioid Overdose: Prescribing Naloxone in the Outpatient Setting

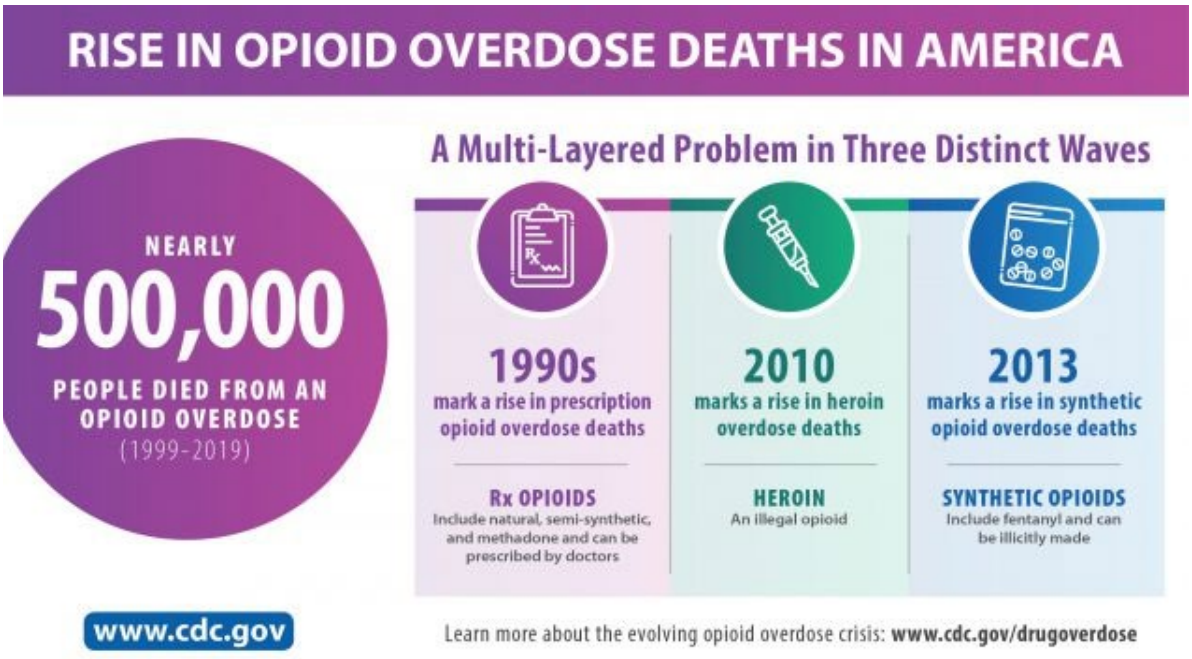
Clinical Practice Guideline

"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but should be used with the clear understanding that continued research may result in new knowledge and recommendations".

Background / General Principles

Opioid abuse and overdose are major public health problems locally and nationally. Rates of both abuse and overdose have skyrocketed. The death rate from opioid overdose in 2017 was 34.7 per 100,000 in Washington, D.C. and 32.2 per 100,000 in Maryland.[2] Nationally, the CDC reported that opioids were involved in more than 47,600 deaths in 2017.[15]

The CDC categorizes the rise in opioid related deaths as a multi-layer problem that occurred in three waves: first, an increase in prescription opioids, second an increase in heroin use, and finally an increase in synthetic opioid use (particularly fentanyl). This helps to explain the ongoing increase in opioid related deaths despite a decline in opioid prescribing by physicians of 19.2% between 2006 and 2017. [14]



Initial Approval Date and Reviews:	Most Recent Revision and Approval Date:	Next Scheduled Review Date:
October 2015, October 2017, October 2019, October 2021	October 2021	October 2023 Ambulatory Best Practice

As physicians, we are uniquely positioned to be able to intervene on a number of levels to prevent death from opioid overdose; this guideline focuses specifically on the use of prescription naloxone to treat opioid overdose.

Routine prescribing of naloxone to patients at risk for opioid overdose is publically supported by:

- The AMA (American Medical Association)
- The ASAM (American Society of Addiction Medicine),
- AAPCC/AACT/ACMT (American Association of Poison Control Centers / American Academy of Clinical Toxicology / American College of Medical Toxicology)
- The National Guideline Clearinghouse--"strong" recommendation

Patients at risk for opioid overdose [1,3,4]

Please note that some of these characteristics would put patients in violation of the chronic narcotics contract; *always consider safely ceasing to prescribe narcotics to patients in violation of the contract.*

- Patients who have a history of IV drug use or misuse of prescription opioids
- Patients who are receiving opioids from multiple physicians
- Patients who are on a regimen of multiple different opioids
- Patients who use opioids in conjunction with antidepressants, benzodiazepines or alcohol
- Patients with a history of prior overdose
- Patients who are being treated for a substance abuse disorder
- Patients who are active substance abusers, not in treatment
- Patients who use opioids and have mental illness
- Patients who take opioids and have a major organ dysfunction (renal, hepatic, cardiac, or pulmonary)
- Patients receiving high dose opioids (see below)

While there is no absolute cutoff to define a daily dose that would indicate a need for naloxone prescription, the literature shows that patients taking 100 mg oral morphine equivalents (OME or MME) per day or higher are almost **9 times** as likely to overdose compared to a "standard" dose of 1-20 MME per day[5]. Patients taking 50-99 MME per day were almost **4 times** as likely to overdose compared to the standard dose[5].

Approximate **daily** doses equal to 50 mg and 100 mg oral morphine equivalents are below

Medication	**50 mg MME**	**100 mg MME**
Fentanyl TD (Duragesic)	20 mcg	40 mcg
Methadone	12 mg	20 mg
Hydromorphone (Dilaudid)	12.5 mg	25 mg
Oxymorphone (Opana, Numorphan)	16.5 mg	33 mg
Oxycodone (Oxycontin)	33.5 mg	67 mg
Hydrocodone (Vicodin, Norco)	50 mg	100 mg
Tramadol (Ultram)	250 mg	500 mg

Recommendations[1,3,4,5,8]

- ✓ **Physicians are strongly encouraged to prescribe naloxone for patients taking more than 50 mg MME daily or higher (see table above).**

- ✓ **Physicians are strongly encouraged to prescribe naloxone for any patient taking opioids at any dose who have one or more of the above risk factors, particularly COPD or other chronic respiratory conditions.**

- ✓ **ED physicians are strongly encouraged to prescribe naloxone for patients who present to the ED with opiate overdose.**

Naloxone Overview

- Opioid antagonist that competes for the opioid receptor with strongest affinity for the mu receptor.
- Has been used in emergency settings for over 40 years.
- Often used by EMT's and other emergency non-physician personnel.
- FDA approved formulations include IV and IM injections (including an auto-injector) and an intranasal formulation.
- Works quickly (within 1-2 minutes if given iv; 2-5 minutes if given IM or SC and 8-13 minutes if given intranasally) and lasts on average 30-90 minutes. **Note that repeated administration is often necessary, since the half life of naloxone is much shorter than that of most opioids**. [9] Consequently, EMS should be called immediately when naloxone is given.
- Adverse effects are rare[3]:
    - -Most common are acute opiate withdrawal (unpleasant but almost never fatal)
    - -Most serious include:
        - Seizures, occurring in 0.6% and causing death in 0.2% of cases
        - Pulmonary edema, occurring in 1.5% and causing death in 0.2% of cases

Pneumonia, occurring in 0.3% and causing death in 0.3% of cases
Cardiovascular arrest, occurring in 1.7% and causing death in 0.9% of cases

Note: general consensus is that the above fatal events may be due to the overdose rather than the naloxone. It is clear that naloxone markedly decreases fatalities from opioid overdose.

Naloxone Formulations

(adapted from the Medical Letter, June 5, 2017, Sept 20, 2021, and UpToDate Sept 2017)[10,13]

Drug	Formulations	Usual Dose	Cost (wholesale cost for a single dose)	How supplied
Parenteral generic Naloxone	0.4 mg/ml vials and syringes; 1 mg/ml syringes; 2 mg/2 ml prefilled syringes	0.4-2 mg IV, IM or SC Used with mucosal atomization device intranasally	$18.50 $20	1 ml vial 2 ml syringe
Narcan nasal spray; High dose Narcan nasal spray (Kloxxado)	4 or 8 mg/-0.1 ml nasal spray	4-8 mg intranasally	$75	2 nasal spray devices per carton

*Nasal spray has slower onset than IM or IV formulations

Insurance coverage

For both DC and Maryland Medicaid, generic naloxone and Narcan nasal spray are preferred.
For other insurers, preferred formulations and co-pays vary.

MedStar Pharmacies at MWHC, MGUH, MFSMC, MUMH, MGSH, MHH and Leisure World stock naloxone and will provide education to patients and care givers

Prescribing

Pharmacists in every state in the country may dispense naloxone to any person without a prescription and irrespective of training on use.

Narcan is available in every ward in the District of Columbia at the following sites:
https://dchealth.dc.gov/NarcanDC

Naloxone is available free of charge at multiple sites:
Text LiveLongDC to 888-111to Find No Cost Naloxone

The Maryland Department of Health Behavioral Health Administration maintains a calendar of free trainings which typically include a free dose of naloxone to take home.

https://bha.health.maryland.gov/NALOXONE/Pages/Training-Calendar.aspx

https://health.maryland.gov/pha/NALOXONE/Pages/Home.aspx

How to prescribe

Intramuscular:
Rx = Naloxone injection 0.4mg/1ml vial and 3cc, 23g, 1 inch syringes
Unit: 1 ml vial
Disp: two vials
Refill = PRN
Sig: For suspected opioid overdose, inject 1ml IM in deltoid or thigh, may repeat after 3 minutes if no or minimal response.

Intranasal:
Rx = Naloxone 1mg/ml needless syringe and intranasal mucosal atomizer device
Unit: 2 ml vial
Disp: two vials
Refill = PRN
Sig: For suspected opioid overdose, spray 1ml in each nostril, may repeat after 3 minutes if no or minimal response.

Intranasal:
Rx= Narcan nasal spray
Unit: 4 or 8 mg
Disp: one carton (2 devices)
Refill= PRN
Sig: For suspected opioid overdose, spray the contents of one device in either nostril, may repeat after 3 minutes if no or minimal response

Please note, the prescription may be written for the patient (and likely administered by a 3rd party) Or it may be prescribed directly to a significant other who will administer it to the patient

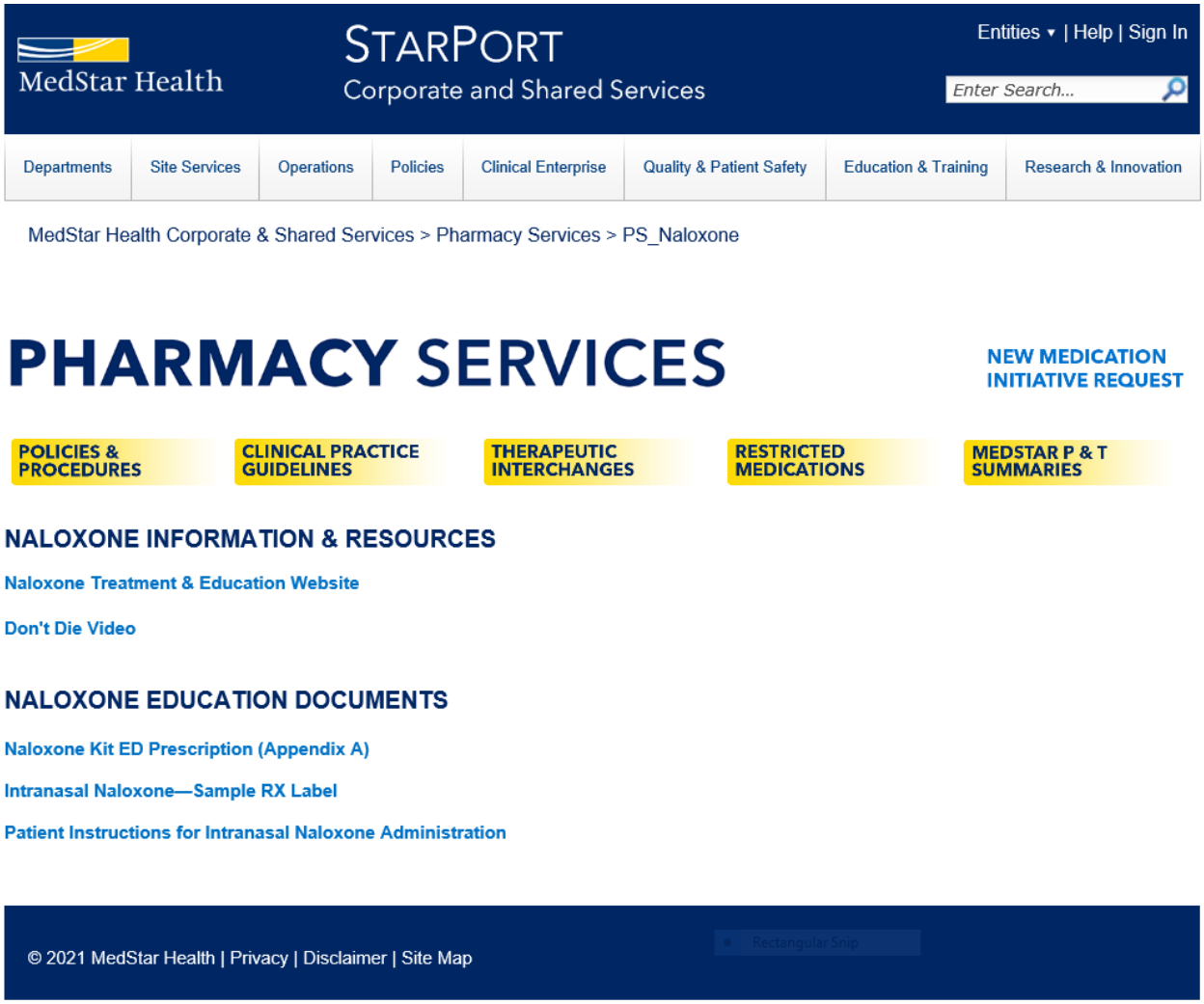
Training Resources

It is important to train the patient along with significant others and those likely to be in close proximity during a potential overdose. See below for some training options.

Please note that patients must present to the Emergency Department after using naloxone, as it is relatively short-acting; this point must be stressed during patient education.

For those providers with access to the MedStar Health intranet (StarPort), the following resources are available.

http://starport.medstar.net/msh/Pharmacy/Pages/PS_Naloxone.aspx

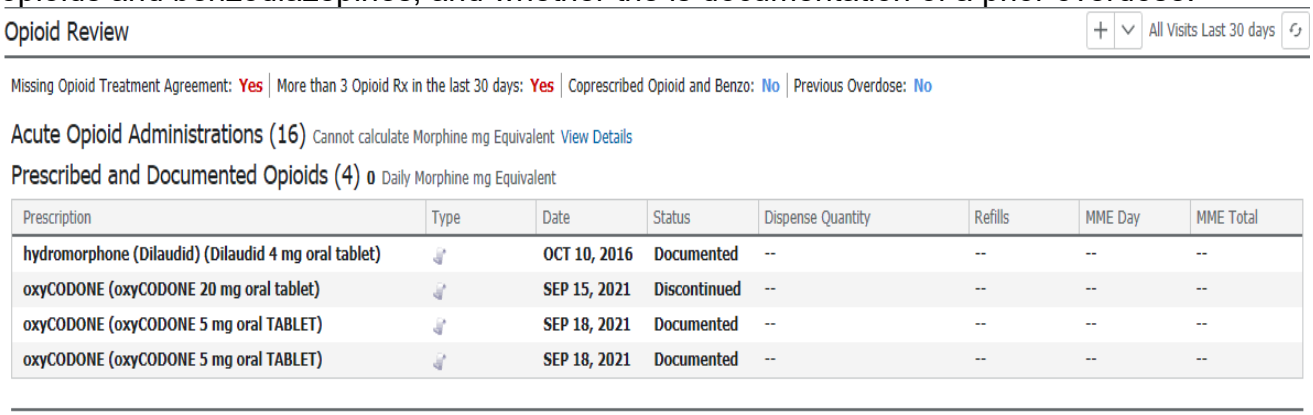


External resources include the following:

- NYC department of health training video: **https://vimeo.com/184043173**
- https://bha.health.maryland.gov/NALOXONE/Pages/Core-Curriculum.aspx
- https://www.getnaloxonenow.org/
- http://prescribetoprevent.org/
- https://bha.health.maryland.gov/NALOXONE/Pages/Naloxone.aspx

Point of care decision support within MedConnect

There is an opioid review component available in the primary care provider view noting whether an opioid treatment agreement is missing, whether more than 3 opioids have been prescribed in the past 30 days, whether there are concurrent prescriptions for opioids and benzodiazepines, and whether the is documentation of a prior overdose.



Opioid Review

All Visits Last 30 days

Missing Opioid Treatment Agreement: Yes | More than 3 Opioid Rx in the last 30 days: Yes | Coprescribed Opioid and Benzo: No | Previous Overdose: No

Acute Opioid Administrations (16) Cannot calculate Morphine mg Equivalent View Details

Prescribed and Documented Opioids (4) 0 Daily Morphine mg Equivalent

Prescription	Type	Date	Status	Dispense Quantity	Refills	MME Day	MME Total
hydromorphone (Dilaudid) (Dilaudid 4 mg oral tablet)		OCT 10, 2016	Documented	--	--	--	--
oxyCODONE (oxyCODONE 20 mg oral tablet)		SEP 15, 2021	Discontinued	--	--	--	--
oxyCODONE (oxyCODONE 5 mg oral TABLET)		SEP 18, 2021	Documented	--	--	--	--
oxyCODONE (oxyCODONE 5 mg oral TABLET)		SEP 18, 2021	Documented	--	--	--	--

When prescriptions are entered or renewed for patients at risk for overdose, prescribers receive a prompt suggesting that a prescription for naloxone be provided as well.

These risks include:

- Prescribing an extended-release opioid when the patient is opioid naïve
- Daily MME > 50
- 3 or more narcotic analgesic prescriptions in the past 30 days
- More than 50% of prescribed narcotic remaining (looking at the last 120 days)
- Concurrent opioid and benzodiazepine prescriptions
- Active Problems documented: Alcoholism, Misuses drugs, Opioid abuse, Breathing-related sleep disorder, Depressive disorder, Disorder of liver, Illicit drug use, Mental disorder, Mood disorder, Overdose of drug groups primarily affecting the central nervous system, Renal impairment, Severe depression, Sleep apnea
- History of the following diagnoses: Poisoning by opioids/heroin/opium/benzodiazepines/synthetic narcotics/unspecified narcotics
- 2 or more ED visits with narcotic administration in the past 30 days

Morphine milligram equivalents calculators:

https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

Legal considerations

- Naloxone is FDA-approved for treatment of opioid overdose; physicians need not worry about legal risks.[8]
- Studies have not shown an increase in abuse or in overdose with naloxone prescriptions.[8,9]
- Good Samaritan laws cover lay people who intervene and administer naloxone.
- Legal precedent of 3rd party emergency administration—epinephrine injection pens for anaphylaxis.

References

1. Wen, Leana S., MD. Letter to Physician Colleagues. 26 June 2015. Baltimore City Health Department.
2. https://www.cdc.gov/drugoverdose/data/analysis.html Review of naloxone safety for opioid overdose: practical considerations for new technology and expanded public access. Therapeutic Advances in Drug Safety. 2015, Vol. 6(1) 20-31. Doi: 10.1177/-2042098614564776
3. http://www.mhaonline.org/resources/opioid-resources-for-hospitals
4. Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, et al. Opioid Prescriptions for Chronic Pain and Overdose: A Cohort Study. Ann Intern Med. 2010;152:85-92. doi:10.7326/0003-4819-152-2-201001190-00006
5. prescribetoprevent.org.
6. http://www.guideline.gov/
7. Beletsky, Leo et al. Prevention of Fatal Opioid Overdose. JAMA. 2012 November 14; 308(18): 1863–1864. doi:10.1001/jama.2012.14205.
8. Burris S, Castagna C, et al. Stopping an invisible epidemic: legal issues in the provision of naloxone to prevent opioid overdose. Drexel Law Rev. 2009; 1(2):273-340.
9. Naloxone (Narcan) Nasal Spray for Opioid Overdose. Med Lett Drugs Ther. 2016 Jan 4; 58 (1485): 1-2.
10. Drugs for Opioid Use Disorder. Med Lett Drugs Ther. 2017 Jun 5; 59 (1522): 89-96.
11. https://bha.health.maryland.gov/OVERDOSE_PREVENTION/Documents/Maryland%202016%20Overdose%20Annual%20report.pdf
12. https://bha.health.maryland.gov/NALOXONE/Documents/Statewide%20Naloxone%20Standing%20Order%20Pharmacy%20Guidance%205.31.17.pdf
13. https://www.uptodate.com/contents/naloxone-drug-information?source=search_result&search=naloxone&selectedTitle=1~150
14. https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf
15. https://www.cdc.gov/mmwr/volumes/67/wr/mm675152e1.htm?s_cid=mm675152e1_w