

Naloxone

for Overdose Prevention

Prescribing Guidance for Clinical Settings

Summary

Prescribe naloxone to your patients with these risk factors for opioid overdose:

1. High-dose opioid prescription (≥ 90 total morphine milligram equivalents/day)
2. Chronic opioid therapy (≥ 3 months)
3. Opioid* misuse/illicit use, including:
 - a. Current or past history
 - b. In treatment for opioid use disorder (e.g., methadone, buprenorphine, naltrexone, treatment without pharmacotherapy)
 - c. Opioid overdose history
4. Family member or friend of a person who meets the above criteria

**Refers to all opioid drug types (e.g., opioid analgesic prescription, heroin) and all routes of administration (e.g., injection drug use, oral, intranasal)*

For patients who meet any of criteria 1-3, additional risk can be conferred by:

Decreased tolerance after a period of abstinence (e.g., incarceration, hospitalization, detoxification).

Opioid use after periods of abstinence such as after incarceration, and the resulting loss of tolerance substantially increases risk for overdose. Overdose is a leading cause of death after incarceration.^{1,2} The period of abstinence and resulting loss of tolerance associated with incarceration, hospitalization and detoxification is likely the underlying reason for elevated overdose risk.¹

Concurrent use of central nervous system (CNS) depressants (e.g., benzodiazepines, alcohol):

Concurrent use of opioids and CNS depressants, such as benzodiazepines and alcohol, increase the risk for overdose.³⁻⁸

Background

Overdose deaths from opioid analgesics and heroin are a public health crisis in New York City (NYC). In 2013, the majority (77%) of overdose deaths involved an opioid. Between 2000 and 2013, opioid analgesic overdose deaths increased 256%, from 0.9 to 3.2 deaths per 100,000 New Yorkers. Between 2010 and 2013, heroin overdose deaths doubled from 3.1 to 6.2 deaths per 100,000 New Yorkers.⁹ These overdose deaths are preventable, using a comprehensive approach that includes prevention, treatment of opioid use disorder and raising public awareness. Because most overdoses

are witnessed by another person,¹⁰ a key strategy to prevent opioid overdose deaths is to increase access to naloxone — an antagonist medication that reverses an opioid overdose. In many states, including New York, legislation allows trained lay-people to carry and use naloxone as a first-aid response for an overdose. This strategy is effective. Nationally, since 1996, more than 150,000 individuals have received naloxone through community-based programs, and more than 26,000 overdose reversals have been reported.¹¹ A landmark Massachusetts study demonstrated reduced opioid

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overdose death rates in communities with naloxone distribution programs.¹²

In clinical settings (e.g., primary care practices, emergency departments), naloxone has not been routinely prescribed to patients for overdose prevention, but is more commonly administered by health care professionals for acute, on-site overdose reversals. Prescribing naloxone for overdose prevention to at-risk patients can have a two-fold benefit: the naloxone could be used to reverse an overdose experienced by the patient, or the patient

could use it to reverse an overdose that they witness. Prescribing naloxone to family members or friends of at-risk individuals can further expand the impact of this life-saving medication.

This guidance can help clinicians prescribe naloxone for overdose prevention; it includes the NYC Department of Health and Mental Hygiene's (DOHMH's) suggested criteria for determining which patients should be offered a naloxone prescription and the evidence for these criteria.

Guidance

DOHMH recommends offering naloxone to patients with the following risk factors for an opioid overdose. These criteria are based on review of the scientific literature, other published naloxone prescribing guidance and expert opinion.¹³⁻¹⁷

- 1. High-dose opioid prescription (≥ 90 total morphine milligram equivalents/day):** Risk of opioid over-dose and overdose death increases with higher opioid analgesic dosages.¹⁸⁻²⁰ There is significantly increased risk for fatal overdose at ≥ 90 morphine milligram equivalents (MME) per day.¹⁸⁻²⁰ To quickly calculate MME for patients, use OpioidCalc, a free DOHMH app available through Apple and Google Play stores, specifically developed to assess overdose risk based on total daily MME. If dosing does reach ≥ 90 MME/day, thoroughly reassess the relative risks and harms versus pain and functional benefits, and consider reducing the dose if unfavorable. Offer naloxone for overdose prevention.²⁰
- 2. Chronic opioid therapy (≥ 3 months):** Chronic opioid therapy (≥ 3 months) for chronic non-cancer pain is associated with increased risk for overdose. Several factors might explain this observation. Individuals taking chronic opioid therapy might be taking higher dosages, and higher dosages are associated with increased overdose risk.^{18, 19} Additionally, these individuals might be more likely to take long-acting opioids, a formulation which confers a greater risk for overdose.²¹ Risks and benefits of pre-scribing chronic opioid therapy should be weighed carefully. The most recent reviews on the topic find insufficient evidence that chronic opioid therapy for chronic non-cancer pain improves pain or function.²²⁻²⁶ For patients on chronic opioid therapy, a naloxone prescription can be offered for overdose prevention.

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3. Opioid* misuse or illicit use, including:

a. Current or past history: Current and past history of illicit opioid use²⁷ and/or opioid analgesic misuse are risk factors for overdose.²⁸ All routes of opioid administration can confer overdose risk, although injection drug use is associated with the greatest risk.²⁹ One meta-analysis demonstrated that cohorts with higher injection prevalence had a higher overdose mortality rate (0.83 per 100 person-years) as compared to cohorts with low injection prevalence (0.33 per 100 person-years).³⁰

b. In treatment for opioid use disorder: Several modalities are used to treat opioid use disorder, including pharmacotherapy and treatment without pharmacotherapy. Pharmacotherapy with opioid agonists (methadone and buprenorphine) is the most effective form of treatment; in clinical trials, treatment with opioid agonist therapy is superior to treatment without.^{31, 32} Opioid agonist therapy decreases drug use and mortality.³¹⁻³⁴ Another pharmacotherapy option is the opioid antagonist naltrexone. For individuals who have a history of any treatment for opioid use disorder, periods out of treatment are associated with risk of relapse and overdose. In one study, the mortality rate was more than twice as high during out-of-treatment versus in-treatment periods; the risk of death was particularly pronounced in the first month after stopping treatment, with a mortality rate more than eight times higher during this period versus the mortality rate during the stable period of treatment.³³ Offering naloxone to patients receiving any treatment modality can reduce future overdose risk.

c. Opioid overdose history: Previous history of an opioid overdose is a strong predictor of risk for subsequent overdose.^{5, 35, 36} In one survey of drug users, history of previous overdose nearly doubled the risk of experiencing an overdose in the past year.³⁶

4. Family member or friend of an individual who meets criteria: Family members or friends of an individual who meets any of the above criteria can also be offered a naloxone prescription since they may witness an overdose. In a clinical setting, the family member or friend may be the patient or may be accompanying a patient to a visit. New York State Public Health Law provides liability protection for prescribing naloxone to non-patients when the institution or practice is registered as an opioid overdose prevention program. Any hospital or doctor's office can register.†

Naloxone is an important component of a comprehensive approach to reducing opioid overdose, along with effective treatment, judicious opioid prescribing, public awareness and community initiatives. By offering naloxone for overdose prevention to patients at risk of opioid overdose and their family and friends, New York City health care providers can help prevent overdose mortality. DOHMH offers technical assistance and educational materials on naloxone for patients and providers.

For more information, contact naloxone@health.nyc.gov.

* Refers to all opioid drug types (e.g., opioid analgesic prescription, heroin) and all routes of administration (e.g., injection drug use, oral, intranasal)

† Recent amendments to the State law provide expanded civil, criminal and administrative liability protection to institutions that are registered as overdose prevention programs.³⁷

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References

1. Lim S, Seligson AL, Parvez FM, et al. Risks of Drug-Related Death, Suicide, and Homicide During the Immediate Post-Release Period Among People Released from New York City Jails, 2001–2005. *Am J Epidemiol.* 2012; 175(6):519–26.
2. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison—a high risk of death for former inmates. *N Engl J Med.* 2007;356(5):536.
3. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ.* 2015;350:h2698.
4. Seal KH, Kral AH, Gee L, et al. Predictors and Prevention of Nonfatal Overdose Among Street-Recruited Injection Heroin Users in the San Francisco Bay Area, 1998–1999. *Am J Public Health.* 2001;91(11):1842–1846.
5. Coffin PO, Tracy M, Bucciarelli A, Ompad D, Vlahov D, Galea S. Identifying Injection Drug Users at Risk of Nonfatal Overdose. *Acad Emerg Med.* 2007. 14(7): 616–23.
6. Gudin JA, Mogali S, Jones JD, Comer SD. Risks, Management, and Monitoring of Combination Opioid, Benzodiazepines, and/or Alcohol use. *Postgrad Med.* 2013;125(4):115–130.
7. Pawasauskas, J, Stevens B, Youssef R, Kelley M. Predictors of Naloxone Use for Respiratory Depression and Oversedation in Hospitalized Adults. *Am J Health Syst Pharm.* 2014; 71(9): 746–50.
8. Merrall EL, Bird SM, Hutchinson SJ. Mortality of Those who Attended Drug Services in Scotland 1996–2006: record-linkage study. *Int J Drug Policy.* 2012;23(1):24–32.
9. Paone D, Tuazon E, O'Brien DB, Nolan M. Unintentional Drug Poisoning (Overdose) Deaths Involving Opioids in New York City, 2000–2013. *Epi Data Brief.* 2014;50:1–4. Available at: <http://www.nyc.gov/html/doh/downloads/pdf/epi/databrief50.pdf>. Accessed October 15, 2015.
10. Sporer K.A., Strategies for Preventing Heroin Overdose. *BMJ.* 2003; 326(7386): 442–444.
11. Opioid Overdose Prevention Programs Providing Naloxone to Laypersons – United States, 2014. *MMWR Morb Mortal Wkly Rep.* 2015;64(23):631–635.
12. Walley AY, Xuan Z, Hackman HH, et al. Opioid Overdose Rates and Implementation of Overdose Education and Nasal Naloxone Distribution in Massachusetts: Interrupted Time Series Analysis. *BMJ.* 2013;346:f174.
13. Albert S, Brason FW, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: Community-Based Overdose Prevention in Rural North Carolina. *Pain Med.* 2011;12 Suppl 2:S77–85.
14. Prescribe to Prevent. Instructions for Healthcare Professionals: Prescribing Naloxone. Available at: http://www.prescribeprevent.org/wp-content/uploads/2012/11/one-pager_12.pdf. Accessed October 15, 2015.
15. Substance Abuse and Mental Health Services Administration. OpioidOverdose Prevention Toolkit. Available at: http://store.samhsa.gov/shin/content//SMA14-4742/Overdose_Toolkit.pdf. Accessed October 15, 2015.
16. San Francisco Department of Public Health. Naloxone for Opioid Safety: A Provider's Guide to Prescribing Naloxone to Patients Who Use Opioids. Available at: <http://bayareaaetc.org/wp-content/uploads/2015/04/PDF-NaloxoneOpioidSafetyPatients.pdf>. Accessed October 15, 2015.
17. New Mexico Regulation and Licensing Department. Pharmacist Prescriptive Authority of Naloxone Rescue Kit Protocol. Available at: http://www.rld.state.nm.us/uploads/FileLinks/e3740e56e0fe428e991dca5bd25a7519/NRK_Protocol_BOP_Dale_Tinker.pdf. Accessed October 15, 2015.
18. Bohnert, Amy SB, et al. "A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with chronic pain." *Medical care* 54.5 (2016): 435-441.
19. Garg, Renu K., Deborah Fulton-Kehoe, and Gary M. Franklin. "Patterns of opioid use and risk of opioid overdose death among Medicaid patients." *Medical care* 55.7 (2017): 661-668.
20. Dowell, Deborah, Tamara M. Haegerich, and Roger Chou. "CDC guideline for prescribing opioids for chronic pain—United States, 2016." *Jama* 315.15 (2016): 1624-1645.
21. Miller M, Barber CW, Leatherman S, et al. Prescription Opioid Duration of Action and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy. *JAMA Intern Med.* 2015;175(4):608–615.
22. Manchikanti L, Ailani H, Koyyalagunta D, et al. A systemic review of randomized trials of long-term opioid management for chronic non-cancer pain. *Pain Physician* 2011; 14: 91-121.
23. Noble M, Treadwell J R, Treager S J, et al. Long-Term Opioid Management for Chronic Noncancer Pain. *Cochrane Database Syst Rev.* 2010; 1: CD006605.
24. Furlan, AD, Sandoval JA, Malis-Gagnon A, Tunks E. Opioids for Chronic Noncancer Pain: A Meta-Analysis of Effectiveness and Side Effects. *CMAJ.* 2006; 174 (11):1589–1594.
25. Martell BA, O'Connor PG, Kerns RD, et al. Systematic Review: Opioid Treatment for Chronic Back Pain: Prevalence, Efficacy, and Association with Addiction. *Ann Intern Med.* 2007; 146(2):116–27.
26. Trescot AM, Glaser SE, Hansen H, Benyamin R, Patel S, Manchikanti L. Effectiveness of Opioids in the Treatment of Chronic Non-Cancer Pain. *Pain Physician.* 2008; 11(2 Suppl):S181–200.
27. Warner-Smith M, Darke S, Lynskey M, Hall W. Heroin Overdose: Causes and Consequences. *Addiction.* 2001; 96(8):1113–1125.
28. Gwira Baumbatt JA, Wiedeman C, Dunn JR, Schaffner W, Paulozzi LJ, Jones TF. High-Risk Use by Patients Prescribed Opioids for Pain and its Role in Overdose Deaths. *JAMA Intern Med.* 2014; 174(5):796–801.
29. Brugal MT, Barrio G, De LF, Regidor E, Royuela L, Suelves JM. Factors Associated with Non-Fatal Heroin Overdose: Assessing the Effect of Frequency and Route of Heroin Administration. *Addiction.* 2002; 97(3):319–27.
30. Degenhardt L, Bucello C, Mathers B, et al. Mortality among Regular or Dependent Users of Heroin and Other Opioids: A Systematic Review and Meta-Analysis of Cohort Studies. *Addiction.* 2011; 106(1): 32–51.
31. Mattick RP, Breen C, Kimber J, Davoli M. Methadone Maintenance Therapy Versus No Opioid Replacement Therapy for Opioid Dependence. *Cochrane Database Syst Rev.* 2009;3: CD002209.
32. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus Placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev.* 2014;2:CD002207.
33. Cornish R, Macleod J, Strang J, Vickerman P, Hickman M. Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database. *BMJ.* 2010;341:c5475.
34. Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT, O'Connor PG: Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial *JAMA Intern Med.* 2014;174(12):1947-1954.
35. Darke S, Williamson A, Ross J, Mills KL, Havard A, Teesson M. Patterns of Nonfatal Heroin Overdose Over a 3-Year Period: Findings from the Australian Treatment Outcome Study. *J Urban Health.* 2007; 84(2): 283–91.
36. Grau LE, Green TC, Torban M, et al. Psychosocial and Contextual Correlates of Opioid Overdose Risk Among Drug Users in St. Petersburg, Russia. *Harm Reduct J.* 2009; 6: 17.
37. New York State Public Health Law, Section 3309. Available at: <https://www.health.ny.gov/diseases/aids/consumers/prevention/opioidprevention/docs/regulations.pdf>. Accessed October 15, 2015.