

FAST FACTS AND CONCEPTS #328
NALOXONE FOR OUTPATIENTS AT RISK OF OPIOID OVERDOSE
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Background: In the US, approximately 28,000 opioid overdose deaths occur annually, with at least half of these deaths involving prescription opioids (1). This *Fast Fact* discusses the use of naloxone in the outpatient setting for patients with an advanced illness on opioid therapy who may be at risk for opioid overdose. See *Fast Fact* #39 for further information on naloxone use for inpatient care settings.

Opioid Overdose in Palliative Care Patients: Previous studies have suggested that opioid overdoses are infrequent for patients receiving palliative care (2). In recent years, however, palliative care clinicians have been more routinely involved in the outpatient treatment of cancer pain and, in some instances, may also manage pain in long-term cancer survivors and/or non-cancer pain (2-4). Therefore, there is concern that many palliative care patients may be at risk for opioid overdose given their co-morbidities, relatively high doses of opioids needed to control symptoms, and, in some instances, a history of substance use disorders (see *Fast Facts* #127, 310 and 311) (5). There is also an emerging awareness of inappropriate or excessive use of opioids among patients with cancer-related pain (2).

Naloxone Co-prescribing: In the 1990s, public health and community organizations initiated naloxone distribution programs such as the Overdose Education and Naloxone Distribution (OEND) to prevent opioid overdose fatalities among heroin users (6). Between 1996 and 2010, naloxone was distributed to 50,000 persons, and more than 10,000 overdose reversals were documented (7). In many scenarios, bystanders were able to recognize an overdose from a prescribed opioid and administer naloxone effectively. Federal agencies from the US, Canada, Australia, and many European countries have endorsed the provision of outpatient naloxone as part of a larger strategy to reduce overdose fatalities from prescribed opioids (6). Co-prescribing of naloxone for patients on chronic opioids is currently being implemented through the US Veterans Affairs Medical System (8).

Pharmacology: Naloxone is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. A needle-free formulation which is FDA approved for the emergency treatment of an opioid overdose is available via a pre-filled, single dose intranasal spray. Intranasal administration of naloxone begins to reverse opioid-induced respiratory depression and sedation in 8-13 minutes; peak effect is 20-30 min; and the half-life is about 2 hours (9). The nasal spray is supplied in a box containing two, 4 mg single-use nasal spray devices. A dose can be repeated every 2-3 minutes in alternating nostrils, if necessary (8). In some states, it is available in pharmacies without a prescription. In a study of patients who received naloxone by paramedics, intranasal naloxone was found to be noninferior to intravenous naloxone regarding the reversal of sedation and respiratory rate (10).

Indications For Outpatient Naloxone Prescribing: Co-prescribing of naloxone with prescription opioid medications is still the exception rather than a rule, especially in the palliative care setting. There is a concern that bystanders may administer naloxone inappropriately in seriously ill patients when physiological changes related to disease progression are mistakenly thought to be related to an overdose. The final decision about co-prescribing naloxone should be individualized based on a patient's risk profile, prognosis, care preferences, and the availability of an informed caregiver. Establishing more rigorous evidence-based criteria for co-prescribing is needed, but the following patients may be at risk of an opioid-related fatality when death from their underlying illness is not imminently anticipated (6,11):

- Daily morphine equivalent doses of > 100 mg/day (12,13)
- Methadone as a prescribed analgesic (14)
- Benzodiazepines and/or antidepressants in combination with opioids (15)
- History of unintentional or intentional overdose (16)
- History of a substance use disorder including alcohol or tobacco (17)
- History of chronic pulmonary, renal, or hepatic disease (12)
- A recent history of incarceration (18)

Patient Information: Patients and their caregivers should be educated on how to properly identify an opioid overdose and how to administer naloxone. Informational handouts are available for patients and their family members (see reference #19). Patients and caregivers should also be advised to call 911 with any administration of naloxone (19). Naloxone should not be administered to patients who are imminently dying. This recommendation needs to be clearly communicated to caregivers of patients to avoid inappropriate use. The adverse effects of naloxone administration are primarily opioid-withdrawal related however precipitation of a pain crisis is of serious concern (20). Another concern is the relatively high and raising price of Naloxone. As of 2016, estimated costs were \$150 for two nasal-spray doses (21).

Gaps in Knowledge: The risks, benefits, safety, and best practices of co-prescribing in the palliative care setting, especially among patients with advanced illness and chronic cancer pain have not been closely examined and require further research.

References:

1. "Injury Prevention & Control: Opioid Overdose," Centers for Disease Control and Prevention, last updated March 16, 2016, <http://www.cdc.gov/drugoverdose/index.html>.
2. Bruera E, Paice JA. Cancer pain management: safe and effective use of opioids. *Am Soc Clin Oncol Educ Book*. 2015;35:e593-9. doi:10.14694/EdBook_AM.2015.35.e593.
3. Bohnert ASB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315-1321. doi:10.1001/jama.2011.370.
4. Chwistek M, Ewerth N. Opioids and Chronic Pain in Cancer Survivors : Evolving Practice for Palliative Care Clinics. *J Palliat Med*. 2016;19(3):19111. doi:10.1089/jpm.2015.0471.
5. Tan PD, Barclay JS, Blackhall LJ. Do Palliative Care Clinics Screen for Substance Abuse and Diversion? Results of a National Survey. *J Palliat Med*. 2015;18(9):752-757. doi:10.1089/jpm.2015.0098.
6. Mueller SR, et al. A Review of Opioid Overdose Prevention and Naloxone Prescribing: Implications for Translating Community Programming Into Clinical Practice. *Substance Abuse* 2016; 36(2):240-253.
7. Community-based opioid overdose prevention programs providing naloxone—United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2012;61:101–105
8. Oliva EM, Nevedal A, Lewis ET, et al. Patient perspectives on an opioid overdose education and naloxone distribution program in the U.S. Department of Veterans Affairs. *Subst Abuse*. 2016;37(1):118-126.
9. Naloxone (Narcan) nasal spray for opioid overdose. *Medical Letter on Drugs and Therapeutics* 2016; 58(1485):1-2.
10. Merlin MA, Saybolt M, Kapitanyan R, et al. Intranasal naloxone delivery is an alternative to intravenous naloxone for opioid overdoses. *Am J Emerg Med*. Mar 2010;28:296–303.
11. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *Jama*. 2016;315(15):1624-1645. doi:10.1001/jama.2016.1464.
12. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305:1315–1321
13. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152:85–92
14. Walley AY, Doe-Simkins M, Quinn E, Pierce C, Xuan Z, Ozonoff A. Opioid overdose prevention with intranasal naloxone among people who take methadone. *J Subst Abuse Treat*. 2013;44:241–247.
15. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008;300:2613–2620
16. 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;14:616–623.
17. Evans JL, Tsui JI, Hahn JA, Davidson PJ, Lum PJ, Page K. Mortality among young injection drug users in San Francisco: a 10-year follow-up of the UFO study. *Am J Epidemiol*. 2012;175:302–308.
18. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison—a high risk of death for former inmates. *N Engl J Med*. 2007;356:157–165.
19. Substance Abuse and Mental Health Services Administration - Opioid Overdose Toolkit. https://store.samhsa.gov/shin/content/SMA13-4742/Overdose_Toolkit_2014_Jan.pdf Accessed November 13, 2016

20. Buajordet I, Naess AC, Jacobsen D, Brors O. Adverse events after naloxone treatment of episodes of suspected acute opioid overdose. *Eur J Emerg Med.* 2004;11:19–23
21. Gupta, R., et al. (2016). The Rising Price of Naloxone — Risks to Efforts to Stem Overdose Deaths. *New England Journal of Medicine* 375(23): 2213-2215.

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