



# Wide Variation in Naloxone Dosing Recommendations for Acute Opioid Toxicity



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## Research Question

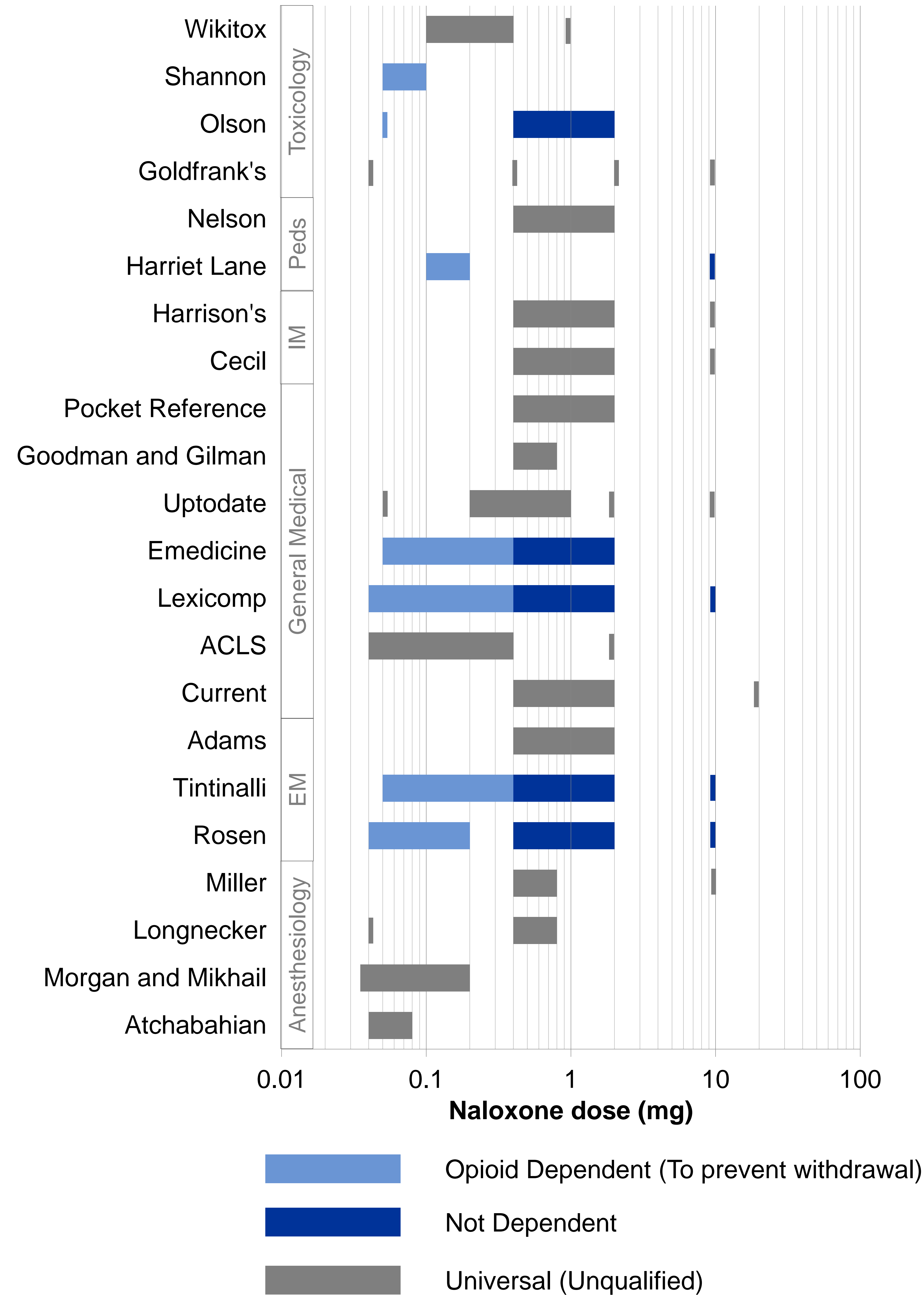
What naloxone dose do authoritative sources recommend to treat opioid-induced hypoventilation in a medical setting?

## Methods

- A convenience sample of textbooks, study guides, and internet resources published within the last ten years in several relevant medical disciplines were reviewed for:
  - Naloxone initial dosing
  - Maximum Dose
  - Titration protocol

## Results

- 22 resources identified that provided a naloxone dose recommendation.
  - Anesthesiology (4)
  - Emergency Medicine (EM) (4)
  - Internal Medicine (IM) (2)
  - Medical Toxicology (MT) (4)
  - General Medical (ACLS, pharmacology, online) (6)
  - Pediatrics (Peds) (2)
- Initial dose
  - 12/22 (55%) recommended an initial dose of 0.04 or 0.05 mg IV
  - 9/22 (41%) suggested 0.4 or 0.5 mg IV.
- Maximum dose by titration (number of sources)
  - 2 mg in 6
  - 10 mg in 8
  - 20 mg in 2
  - No maximum mentioned in 6
- No trend towards lower recommended dosage was noted based on year of publication.
- An initial dose less than 0.1 mg recommended by source was:
  - 3/4 Medical Toxicology
  - 3/4 Anesthesia
  - 4/6 General medical
  - 2/4 EM
  - 0/2 IM and 0/2 Pediatric sources recommended an initial dose less than 0.4 mg



## Discussion

- The increase in chronic opioid therapy for pain and addiction, and an increase prevalence of opioid abuse raises the likelihood of opioid withdrawal syndrome following naloxone.
- Low dose naloxone is highly effective in reversing ventilatory depression.
  - While onset is slower than higher doses, external ventilatory support is available
  - Opioid withdrawal is less likely and severe.
- Complications of precipitated opioid withdrawal include
  - Pulmonary edema
  - Agitation
  - Gastrointestinal Distress
- Many believe an initial naloxone dose of 0.04 mg IV is preferred

## Conclusion

- Wide variation in the naloxone dose recommended for acute opioid toxicity is noted in sources with the potential for patient harm due to Opioid Withdrawal Syndrome.
- Given that 0.04 may be a safer dose and can be titrated to effect, this should be considered as the initial dose for the opioid intoxicated patient.
- Clinical studies are needed to evaluate whether this results in greater safety without sacrificing efficacy.

### Sources:

2010 AHA Guidelines for CPR and ECC  
 Bardsley CH. Opioids. In: Marx JA, Hockberger RS, Walls RM, et al. Rosen's emergency medicine: concepts and clinical practice. Philadelphia: Mosby Elsevier; 2014. p 2055.  
 Butterworth JF IV, Mackey DC, Wasnick JD. (editors). Naloxone. In: Morgan & Mikhail's Clinical Anesthesiology. McGraw-Hill; 2013  
 Doyon S. Chapter 180. Opioids. In: Tintinalli JE, Stacpuzynski JS, Ma OJ, Cline DM, Cydulka RK, Meckler GD, eds. Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 7th ed. New York: McGraw-Hill; 2011.  
 Ford MD. Acute Poisoning. In: Goldman L, Schafer AI, editors. Goldman's Cecil medicine. Philadelphia: Elsevier/Saunders; 2012. pp. 670-84.  
 Fukuda K. Opioids. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller: Miller's Anesthesia. Churchill Livingstone; 2009. pp. 769-823.  
 Gomella LG, Haist SA (editors). Common Medical Emergencies. In: Clinicians Pocket Reference. McGraw-Hill; 2007  
 Greene S. General Management of Poisoned Patients. In: Tintinalli JE, Stacpuzynski JS, Ma OJ, Cline DM, Cydulka RK, Meckler GD, editors. Tintinalli's emergency medicine : a comprehensive study guide. New York: McGraw-Hill; 2014.  
 Hoffmann C, Tourtier JP. Antidotes. In: Atchabahian A, Gupta R (editors). The Anesthesia Guide. McGraw-Hill; 2013  
 Kosten TR. Opioid Drug Abuse and Dependence. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (editors). Harrison's Online. McGraw-Hill; 2012  
 Lank PM, Kusin S. Ethanol and Opioid Intoxication and Withdrawal. In: Adams JG, Barton ED, Collings J, DeBlieux PMC, Gisoni MA, Nadel ES. (editors) Emergency Medicine: Clinical Essentials. Philadelphia: Elsevier; 2013  
 Lee CKK, Tschudy MM, Arcara KM. Drug Doses. In: Tschudy MM, Arcara KM, editors. Johns Hopkins: The Harriet Lane Handbook. Mosby; 2011. pp. 661-988.

Nelson LS, Howland MA. Antidotes in Depth: Opioid Antagonists. In: Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE, editors. Goldfrank's toxicologic emergencies. New York: McGraw-Hill; 2011.  
 O'Donnell KA, Ewald MB. Poisonings. In: Kliegman RM, Stanton BF, Geme JW III, Schor NF, Behrman RW, editors. Nelson Textbook of Pediatrics. Philadelphia: Saunders; 2011.  
 Rosow C, Dershwitz M. Pharmacology of Opioid Analgesics. In: Longnecker DE, Brown DL, Newman MF, Zapol WM (editors). Anesthesiology. McGraw-Hill; 2012  
 Schonwald S. Medical Toxicology: A Synopsis and Study Guide. Philadelphia: Lippincott Williams & Wilkins; 2001.  
 Stephens E. Emedicine: Opioid intoxication in adults. Uptodate. Web MD; 2011. Accessed on 10/29/13  
 Stolbach A, Hoffman RS. Opioid intoxication in adults. Uptodate. April 2013. Accessed on 10/28/13  
 Stone CK, Humphries RL, editors. Poisoning. In: Current diagnosis & treatment emergency medicine. New York: McGraw-Hill; 2011.  
 Wong, J. Naloxone and Nalmefene. In: Olson KR. (editor) Poisoning & Drug Overdose. McGraw Hill; 2012  
 Yaksh TL, Wallace MS. Opioids, Analgesia, and Pain Management. In: Brunton LL, Blumenthal DK, Murri N, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's The Pharmacological Basis of Therapeutics. McGraw Hill; 2011  
 Yip L, Mégarbane B, Borron SW. Opioids. In: Shannon MW, Borron SW, Burns MJ, editors. Haddad and Winchester's clinical management of poisoning and drug overdose. Philadelphia: Saunders/Elsevier; 2007. pp. 635-58.  
 Wikitox: 2.1.1.3 Opioids. Wikitox. Accessed on 10/28/13

