

**Critical Review Form
Prognosis**

PGY-1

[Vilke GM, Sloane C, Smith AM, Chan TC. Assessment for deaths in out-of-hospital heroin overdose patients treated with naloxone who refuse transport. Acad Emerg Med. 2003 Aug;10\(8\):893-6.](#)

Objectives: To test the hypothesis “that releasing patients AMA [prior to EMS transport] after reversing heroin overdose with naloxone would not result in subsequent death.” (893)

Methods: This retrospective chart review was conducted using the San Diego County Quality Assurance Network (QANet) database and the San Diego County Medical Examiner’s (ME) Office database. Protocols in San Diego County call for paramedics to administer 2 mg of naloxone intramuscularly (IM) or intravenously (IV) or 4 mg via endotracheal tube, and to repeat if no response is observed. If the patient responds to naloxone and wants to leave AMA without transport, the paramedic must answer the 6 following questions, and if the answer to all 6 questions is “yes,” the patient can be released AMA at the scene:

1. Is the patient oriented?
2. Is the patient not impaired by drugs or alcohol?
3. Is the patient competent to refuse care?
4. Have the risks and consequences been discussed?
5. Has the patient been advised that medics will return if called back?
6. Has AMA form been signed?

A list was compiled of all paramedic responses in San Diego County (population 2.8 million) over a 5-year period from January 1, 1996 to December 31, 2000 in which a patient received naloxone, had improved mental status, and signed out AMA prior to transport. A second list was compiled of all cases in the ME database in which a metabolite of morphine was noted as contributing to the cause of death. The two lists were reviewed and cross-referenced to identify any patients treated with naloxone by paramedics within 12 hours preceding the time of death documented by the ME’s office. A second independent reviewer evaluated any questionable cases.

Out of a total of 556,427 paramedic responses during the 5-year study period, 8,366 received naloxone. Of these, 998 patients received naloxone and were released AMA by the paramedics. The mean age was 37.7 years and 83.8% were male. Of these, 260 (26.1%) received a single dose of naloxone; 179 (68.8%) of these received the dose IV and 80 (30.8%) received the dose IM. Of the remaining patients, 714 (71.5%) received 2 doses of naloxone, and 24 (2.4%) received 3 doses. There were 601 deaths reported by the ME database in which morphine was listed as contributing to the cause of death. The mean age of these patients was 40.1 years and 83.6% were male.

Guide		Comments
I.	Are the results valid?	
A.	<p>Was the sample of patients representative? <i>In other words, how were subjects selected and did they pass through some sort of “filtering” system which could bias your results based on a non-representative sample. Also, were objective criteria used to diagnose the patients with the disorder?</i></p>	Yes. This was a sample of patients with opiate overdose for which EMS was called, and who received naloxone. Understandably, only those patients who responded to naloxone (regardless of the number of doses given) were eligible.
B.	<p>Were the patients sufficiently homogeneous with respect to prognostic risk? <i>In other words, did all patients share a similar risk from during the study period or was one group expected to begin with a higher morbidity or mortality risk?</i></p>	Yes. There was some heterogeneity with respect to risk, as naloxone was given by various routes (IV and IM) and received either 1, 2, or 3 doses. These factors could affect the likelihood of overdose recrudescence.
C.	<p>Was follow-up sufficiently complete? <i>In other words, were the investigators able to follow-up on subjects as planned or were a significant number lost to follow-up?</i></p>	Likely yes. Follow-up consisted of a review of the San Diego Medical Examiners records for any deaths in which morphine and its metabolites contributed to the cause of death. These records were cross-referenced with the EMS QANet database for any instances in which death occurred within 12 hours of treatment with naloxone. Any deaths that occurred outside of San Diego County risked not being included, though such a situation seems unlikely. Additionally, any death not considered suspicious or in which overdose was not suspected could also potentially be missed by the ME’s office, though this again seems unlikely in most cases.
D.	<p>Were objective and unbiased outcome criteria used? Investigators should clearly specify and define their target outcomes before the study and whenever possible they should base their criteria on objective measures.</p>	Yes. Death was the outcome, and is as objective and unbiased as you can get.
II.	What are the results?	
A.	<p>How likely are the outcome? In other words, how many patients had the outcome of interest?</p>	Of 998 patients treated with naloxone and released AMA at the scene, no deaths could be identified within 12 hours of treatment (0%, 95% CI 0% to 0.37%).
B.	How precise are the estimates of	See above. This database identified a relatively

	likelihood? <i>In other words, what are the confidence intervals for the given outcome likelihoods?</i>	large number of patients treated with naloxone and released AMA at the scene, the 95% CI is quite narrow, with an upper boundary of 0.37%).
III.	How can I apply the results to patient care?	
A.	Were the study patients and their management similar to those in my practice?	Mostly yes. The study was conducted in the late 1990s, and it would be interesting to know if any changes in the contents of heroin sold on the streets had occurred over this time (i.e. changes in the frequency with which heroin is laced with fentanyl or other confounding substances). Additionally, St. Louis EMS protocol now allows for the use of intranasal naloxone (see previous Journal Club), which was not used in any of the patients in this study.
B.	Was the follow-up sufficiently long?	Yes. It is extremely unlikely that overdose recrudescence would occur greater than 12 hours after a dose of naloxone, and any deaths after this time period would be more likely due to additional opiates ingested after release.
C.	Can I use the results in the management of patients in my practice?	Yes. This large retrospective study strongly suggests that overdose recrudescence is highly unlikely after a good response to naloxone given by EMS. It seems both safe and prudent to release patients who return completely to baseline after naloxone is given without transport to a medical facility.

Limitations:

- 1. Out of 8,366 subjects who received naloxone, only 998 were eligible for release and thus included. This therefore represents a small subset of patients treated with naloxone for opiate overdose.**
- 2. Evaluation of death limited to review of San Diego Medical Examiners records. Potentially, Any deaths that occurred outside of San Diego County risked not being included. Additionally, any death not considered suspicious or in which overdose was not suspected could also potentially be missed by the ME's office.**

Bottom Line:

In this large retrospective study of patients receiving naloxone by EMS for opiate overdose, there were no deaths attributable to opiates within 12 hours in patients released without transport (incidence of death 0%, 95% CI 0% to 0.37%). These

data strongly suggest that overdose recrudescence is highly unlikely after a good response to naloxone given by EMS. It seems both safe and prudent to release patients who return completely to baseline after naloxone is given without transport to a medical facility.