

**Washington University Emergency Medicine Journal Club**  
**Treat and Release After Naloxone Following Opiate Overdose**

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**Vignette**

It's a typical TCC shift when you hear yelling coming from the ambulance bay. You run over to find an apneic patient has just been pushed out of a car that then sped off. As you place him on a gurney and move him into the emergency department (ED), you notice fresh track marks, a recently used syringe on the ground, and drug paraphernalia sticking out of his pockets. You begin to bag him and notice that he has pinpoint pupils and no other signs of trauma. You administer an atomized dose of intranasal naloxone and continue bagging him until he begins to breathe adequately. A few minutes later, the nurse comes to get you to let you know that the patient is now awake and wants to go. You go back to the room and tell him that he needs to stay since you are worried that he will stop breathing once the naloxone wears off. You offer him a turkey sandwich as a compromise to get him to stay and go to see the new patient with respiratory distress.

You have just finished intubating the patient with respiratory distress and are getting ready to place a central line in a patient with severe sepsis when the nurse comes to let you know that your overdose patient is getting belligerent and that you need to do something. Before you even have a chance to calm him down, he tells you that he is leaving now and angrily asks who gave you permission to bring him here, wants to know who is going to give him money to get home, and wants to know why someone filled his pants with ice. You tell him he cannot go yet, and if he doesn't calm down, you will have to call security. After going through this 2 more times, he has now been in the ED for approximately an hour. You offer him chemical dependency information and discharge him. After he leaves, you realize that neither you, the patient, the nursing staff, or the patient sharing a trauma room with him enjoyed this experience and wonder if it was really necessary to go through all that or if you could have just let him go much earlier.

**PICO Question**

**Population:** Patients with acute opioid overdose requiring naloxone administration with return to baseline.

**Intervention:** Transport to the hospital by EMS or ED observation.

**Comparison:** Immediate release by paramedics or from the ED

**Outcome:** Rebound opioid toxicity resulting in death or anoxic brain injury, or requiring additional administration of naloxone.

## Search Strategy

PubMed was searched using the following strategy: “naloxone AND overdose AND (release OR transport OR recurrence)” (<http://tinyurl.com/n937tns>). The 57 resulting citations were searched for observational or randomized controlled trials evaluating the safety and efficacy of immediate release for patients responding to naloxone after opiate overdose. The following 4 articles were selected for review.

**Article 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. \[Answer Key.\]\(#\)](#)

**Article 2:** [Wampler DA, Molina DK, McManus J, Laws P, Manifold CA. No deaths associated with patient refusal of transport after naloxone-reversed opioid overdose. Prehosp Emerg Care. 2011 Jul-Sep;15\(3\):320-4. \[Answer Key.\]\(#\)](#)

**Article 3:** [Watson WA, Steele MT, Muelleman RL, Rush MD. Opioid toxicity recurrence after an initial response to naloxone. J Toxicol Clin Toxicol. 1998;36\(1-2\):11-7. \[Answer Key.\]\(#\)](#)

**Article 4:** [Rudolph SS, Jehu G, Nielsen SL, Nielsen K, Siersma V, Rasmussen LS. Prehospital treatment of opioid overdose in Copenhagen--is it safe to discharge on-scene? Resuscitation. 2011 Nov;82\(11\):1414-8. \[Answer Key.\]\(#\)](#)

## Bottom Line

Opioid overdose remains an increasing problem in the United States, resulting from the [high prevalence of heroin abuse and the increasing abuse of prescription opioids](#). Death due to opioid overdose has been [increasing in recent years](#), prompting some communities (such as [Boston, MA](#)) to institute programs for bystander administration of naloxone to reverse toxicity. Whether administered by a bystander or EMS, naloxone typically results in adequate reversal of toxicity. In most EMS systems, such patients are then transported to an ED for observation, given the theoretically short-lived action of naloxone and concerns for recurrent toxicity. Some have proposed that such observation is unnecessary, and that such patients can be released at the scene as long as they return to their baseline. We sought to evaluate the evidence for such a proposed “treat and release” protocol, and to assess the incidence of recurrent toxicity following naloxone administration.

In those studies involving the treatment and release of patients by EMS, without transport to the hospital, the risk of death from recurrent opioid toxicity was low, ranging from 0% ([Vilke 2003, Wampler 2011](#)) to 0.13% ([Rudolph 2011](#)). The 3rd of these studies was conducted in Denmark, where a physician is present in the field to assess the patient and make transport decisions. This makes it difficult to extrapolate the study’s results to our EMS system. A strength of this study was Denmark’s centralized database inclusive of all citizens, allowing the authors to

easily find anyone that died after being released. In addition, the authors were able to obtain all forensic data surrounding the deaths to determine which were from rebound opioid intoxication and which were from other causes. The former two studies, on the other hand, were conducted in large US cities (San Diego, CA and San Antonio, TX respectively) with more familiar EMS systems, and demonstrated similarly low rates of death due to recurrent toxicity. While no deaths were found in the US studies, it is possible if people died in different counties that they could have been missed, as the US does not have a central database. A fourth study based in Helsinki showed similar results; the authors found no cases of patients dying from recurrent opioid toxicity ([Boyd 2006](#)).

A single ED-based study evaluated the risk of toxicity recurrence based on a retrospective chart review ([Watson 1998](#)). A [Delphi Panel](#) was employed to determine whether rebound occurred following a response to naloxone administration in the ED. In this small study (42 total cases), recurrence of toxicity was identified as either definite or probable in 13 cases (31%, 95% CI 17-45%). Interestingly of the 13 cases, only 2 were noted to have recurrent respiratory depression. The other 11 patients had decreased mental status without any respiratory compromise. The authors later state that neither of the patients with respiratory depression received any specific treatment. As such, it is difficult to determine the significance of their respiratory depression. These results are confounded by differences in baseline patient characteristics from those in our practice as well as the use of a highly subjective outcome. Specifically, nearly 50% of patients in this study presented following suicide attempt, and 81% of cases involved an oral ingestion of opiates. Anecdotally, the large majority of opiate overdoses seen in our setting involve the recreational use of IV heroin, and recurrence rates may therefore be different. Additionally, in those patients receiving naloxone initially, only 27% were noted to have respiratory depression, and thus the indication for naloxone is suspect. Recurrence of toxicity, the primary outcome, was highly subjective and thus determined by a Delphi panel. Only 18 of the 42 cases considered to have had recurrence were deemed “definite,” with the remaining only “probable.” Even in those cases with definite recurrence of toxicity, the exact indication for repeated doses of naloxone remain unclear, and there is no evidence that more serious patient-centered outcomes were prevented in any of these cases.

The bulk of this data supports the “treat and release” strategy adopted by many EMS systems, with the caveat that such a strategy be employed in select patients who have returned to baseline with stable vital signs and are capable of understanding the risks associated with discharge in the field. If patients want to go to the ED, this should still be encouraged as patients could be evaluated for drug related infectious diseases, as well as receive information about addiction treatment and other social services. Transporting the patient against their will, and holding them in the ED, is probably unnecessary and does not seem to be supported by available evidence. However if the patient took a longer-acting opioid such as methadone, it may be prudent to specifically warn them of possible risks associated with these agents as studies did not specifically look at the safety of a “treat and release” strategy in patients exposed to long-acting opioids.