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65. Real-world examination of naloxone for drug overdose reversal (RENDOR) by bystanders, non-medical first responders, and EMS

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Background: The opioid crisis has driven widespread efforts to increase public access to naloxone. Naloxone administration by bystanders, non-medical first responders, and Emergency Medical Services (EMS) in the prehospital setting has become a key factor in preventing overdose deaths. We studied whether there are differences in how bystanders, non-medical first responders, and EMS deliver naloxone to reverse opioid overdose.

Methods: The Toxicology Investigators Consortium (ToxIC) Real-World Examination of Naloxone for Drug Overdose Reversal (RENDOR) study is an ongoing multi-site collaboration in Detroit, MI, Pittsburgh, PA, San Francisco, CA and Portland, OR, that leverages EMS personnel to collect granular details involving prehospital naloxone administrations by bystanders (family/friend/strangers), non-medical first responders (police and fire personnel), and EMS. Administration details include the administering provider, dose, and route of administration. Patients aged 13 years and older who were administered naloxone for a suspected opioid overdose in the prehospital setting were included. Commonly protected populations, such as pregnant women and prisoners, were also included. A waiver of consent was obtained, and Central/Site IRBs have approved this study.

Results: Of the 1,314 patients enrolled between July 2024 and April 2025, 1,012 with completed records were included in this analysis. Patients were categorized into three groups based on when naloxone was administered: pre-EMS-only, EMS-only, and pre-EMS + EMS. The pre-EMS group includes cases where naloxone was given by family members, friends, strangers, or non-medical first responders such as police or fire personnel; the EMS-only group includes cases where naloxone was administered solely by EMS personnel; and the pre-EMS + EMS group includes cases from both pre-EMS and EMS groups. Three hundred seventy-two cases (37%) received pre-EMS-only naloxone, 496 (49%) received EMS-only naloxone, and 144 (14.2%) received naloxone from both pre-EMS and EMS responders. Intranasal (IN) delivery was the most common route utilized in over 70% of total cases and was administered significantly more in the pre-EMS only group (n=358, 96%, $P < 0.01$). In contrast, EMS-only patients had more diversified routes of administration, with significantly more intramuscular use (IM; n=156, 31.5%, $P < 0.01$), intravenous (IV; n=103, 20.8%, $P < 0.01$), and intraosseous (IO; n=11, 2.2%, $P < 0.01$). The median number of doses in the pre-EMS and EMS-only groups was one (IQR: 1–2). The pre-EMS group had significantly higher doses of intranasal naloxone administration when compared to the EMS group (pre-EMS – median: 4.0mg, IQR: 2.0–8.0mg; EMS only – median: 2.0mg, IQR: 2.0–4.0mg; $P < 0.01$).

Conclusion: Findings from the RENDOR study highlight key differences in prehospital naloxone administration between pre-EMS and EMS responders. Pre-EMS much more commonly delivered naloxone intranasally and used a higher dose of intranasal naloxone than EMS.