

# Fentanyl and Naloxone: What You Need to Know

Technical Notes and Methodology Details Can be Found in Full Report here – [Trends in Paramedic Naloxone Administration and Patient Outcomes Throughout Increased Fentanyl Use](#)

## The Issue

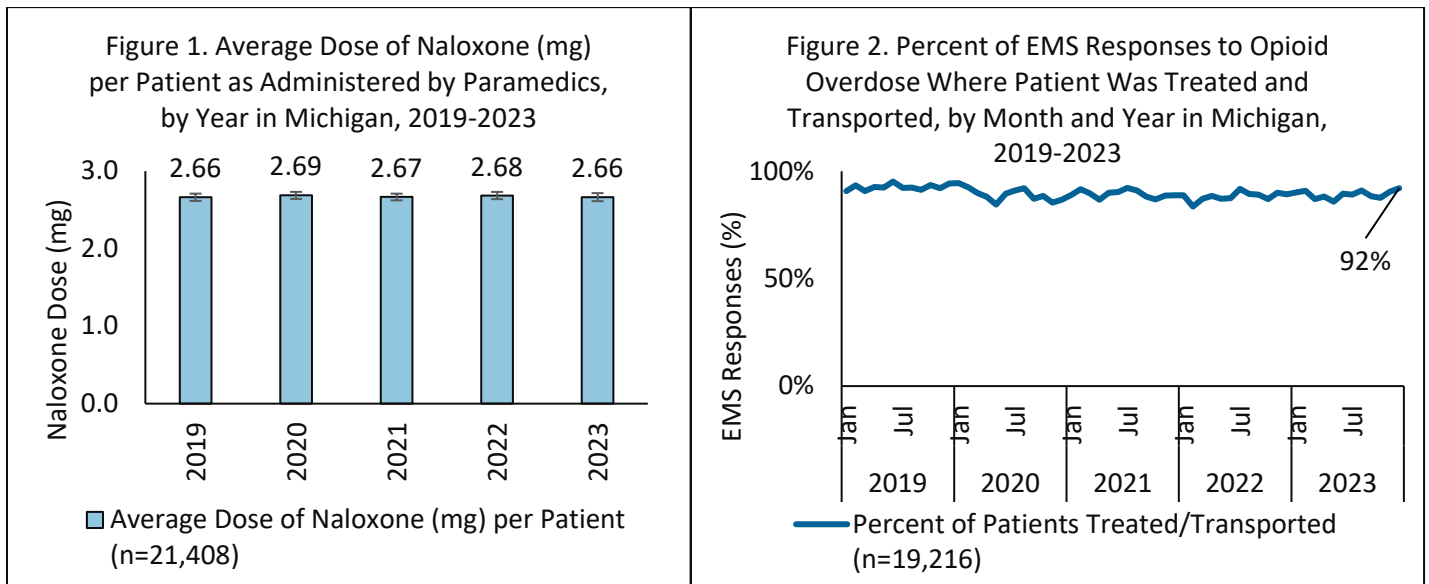
The increase in fentanyl use raises concerns about the efficacy of current 4 mg formulations of naloxone and the potential need for higher-dose formulations (above the standard 4 mg nasal spray) for reversing opioid overdoses.

## Guidelines for Naloxone Use

In cases of suspected opioid overdose, naloxone should be administered if respiratory depression or arrest persists after providing ventilation and oxygen. Paramedic treatment protocol calls for administration of naloxone up to 2mg intravenously (via injection) slowly, titrating to improvement in respiratory status and repeating as needed every three to five minutes. If patients are breathing adequately, regardless of responsiveness, naloxone is not administered, and ventilation support continues during transport to the emergency department.

## Insights from Michigan Data

In a recently published report by the Michigan Department of Health and Human Services (MDHHS), an analysis of paramedic responses to probable opioid overdoses in Michigan (2019-2023) showed that throughout the increase in fentanyl-related fatal overdoses (from 39% in 2016 to 74% in 2022), the average dose of naloxone (2.7 mg) administered by paramedics did not increase (Figure 1). The percent of patients who were treated and transported did not change (Figure 2). Paramedic responses were studied as they can titrate doses in smaller amounts via injection (compared to nasal spray which comes in preset amounts), providing information regarding exact amounts of naloxone needed by patients.



## Other Considerations

The NYSDOH released a data brief – [Post-Naloxone Symptoms Among People Administered 8mg --](#) in September 2023 and a report – [Comparison of Administration of 8-Milligram and 4-Milligram Intranasal Naloxone by Law Enforcement During Response to Suspected Opioid Overdose — New York, March 2022–August 2023](#) – explaining the findings from an assessment where a subset of law enforcement troops used 8 mg naloxone while the rest used 4 mg naloxone. NYSDOH found no significant difference in survival outcomes between the group who administered 4 mg vs. 8 mg naloxone; however, patients who received the 8 mg naloxone were more than twice as likely to experience opioid withdrawal symptoms compared to those who received the 4 mg naloxone. The Tennessee Harm Reduction’s report, [High-Dose Naloxone Formulations Are Not as Essential as We Thought](#), raised concerns about the cost, risks and limited evidence associated with high-dose naloxone formulations.

Although this report focuses on high-dose naloxone formulations, there are now non-naloxone opioid overdose reversal agents, like nalmafene (Opvee), that are also raising concerns about potential harms like prolonged withdrawal. These concerns are detailed in [Stronger, longer, better opioid antagonists? Nalmefene is NOT a naloxone replacement](#) and a [joint position statement](#) from the American College of Medical Toxicology (ACMT) and the American Academy of Clinical Toxicology (AACT) asserting that “nalmafene should not replace naloxone as the primary opioid antidote at this time”.

In 2022, 197,316 naloxone kits were ordered through MDHHS NARCAN Direct, with the 4 mg dose costing \$47.50. The retail of an 8 mg naloxone box is around \$141. Even if 8 mg naloxone were purchased at a discount, such as \$60, an amount reported by the One Ohio Foundation as the state pharmacy price, an additional \$2,470,212 would have been spent by MDHHS in 2022. If MDHHS offered 8 mg naloxone statewide, as is currently done for 4mg doses, this significant cost increase might negatively impact existing prevention, harm reduction and treatment programs.

## Conclusion

Throughout the increase in fentanyl use since 2019, paramedics in Michigan have continued to administer an average of 2.7 mg of naloxone per patient. There has not been a change in patients being treated and transported to the hospital at this average dosage. There is no evidence for the decreasing effectiveness or utility of current naloxone formulations in the context of increasing prevalence of highly potent opioids.

These results, in combination with other evaluations and potential costs, suggest high-dose naloxone formulations may not be needed for the continued effective reversal of opioid overdose in Michigan. Paramedics have extensive medical training which may contribute to the observed trends; increased community naloxone administration training may help maximize effectiveness of current formulations.