

Trends in Paramedic Naloxone Administration and Patient Outcomes Throughout Increased Fentanyl Use

Key Findings and Considerations

- 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.
- This analysis does not provide evidence for decreased effectiveness or utility of current naloxone formulations in the context of increasing prevalence of highly potent opioids.
- Paramedics have extensive medical training which may contribute to these trends; increased community naloxone administration training may help maximize effectiveness of current formulations.

Introduction

Michigan's opioid overdose epidemic is a major public health crisis, with the drug landscape constantly evolving. That evolution has led to the concerning rise of fentanyl, a synthetic opioid that is 50 to 100 times more potent than morphine. Per the Michigan Department of Health and Human Services (MDHHS) dashboard on [Michigan.gov/OpioidsData](https://michigan.gov/OpioidsData), the percent of deaths involving synthetic opioids, such as fentanyl, increased from 39% in 2016 to 74% in 2022.¹ Naloxone, a life-saving medication that can reverse an opioid overdose, is critical in addressing the opioid epidemic. The increasing presence of fentanyl has raised concerns about the adequacy of the 4 milligram (mg) nasal spray, which until the approval of an 8 mg form (high dose naloxone formulations, or HDNF) in 2021, was the highest available nasal spray dose. Injectable naloxone can be titrated at smaller amounts while a nasal spray is only available in preset amounts.

This report examines trends in naloxone administration by paramedics and the percentage of probable opioid overdose patients who are treated and transported to the hospital in the context of the increasing prevalence of highly potent synthetic opioids such as fentanyl. If higher doses of naloxone are needed to rescue patients after overdoses involving fentanyl, it would be expected that either paramedics would begin administering higher average doses of naloxone over time, or that transport rates would change during consistent naloxone dosage administration.

This analysis focused on paramedic behavior since, compared to others responding to an opioid overdose (e.g., non-paramedic first responders, law enforcement, laypeople), paramedics have more EMS training, more experience treating opioid overdoses and the ability to titrate naloxone in precise doses, allowing them to make the most informed decisions regarding naloxone dosage. Further, since paramedics can titrate doses in small amounts, examining of paramedic practice provides information regarding exact amounts of naloxone needed by patients.

Patients who were treated and transported are the patient outcome of focus for this report since that is the goal of naloxone use by a first responder. Other potential response outcomes, including "dead on scene", are not examined here as an unknown subset of those patients may be dead prior to paramedic arrival and it would therefore be difficult to connect trends in that outcome with the effectiveness associated with trends in naloxone dosage.

Guidelines for Naloxone Use

Naloxone is available in formulations with two routes of administration, either via nasal spray or injection. Nasal spray naloxone can be administered by anyone, regardless of medical training or experience, and it comes in preset doses. While injectable naloxone is available by prescription, it is more commonly used by trained medical professionals and experienced laypeople; see Technical Notes for details. Injectable naloxone can be titrated into smaller doses. In cases of suspected opioid overdose, emergency responders administer naloxone if respiratory depression or arrest persists after providing ventilation and oxygen (specifically, 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.

Methods

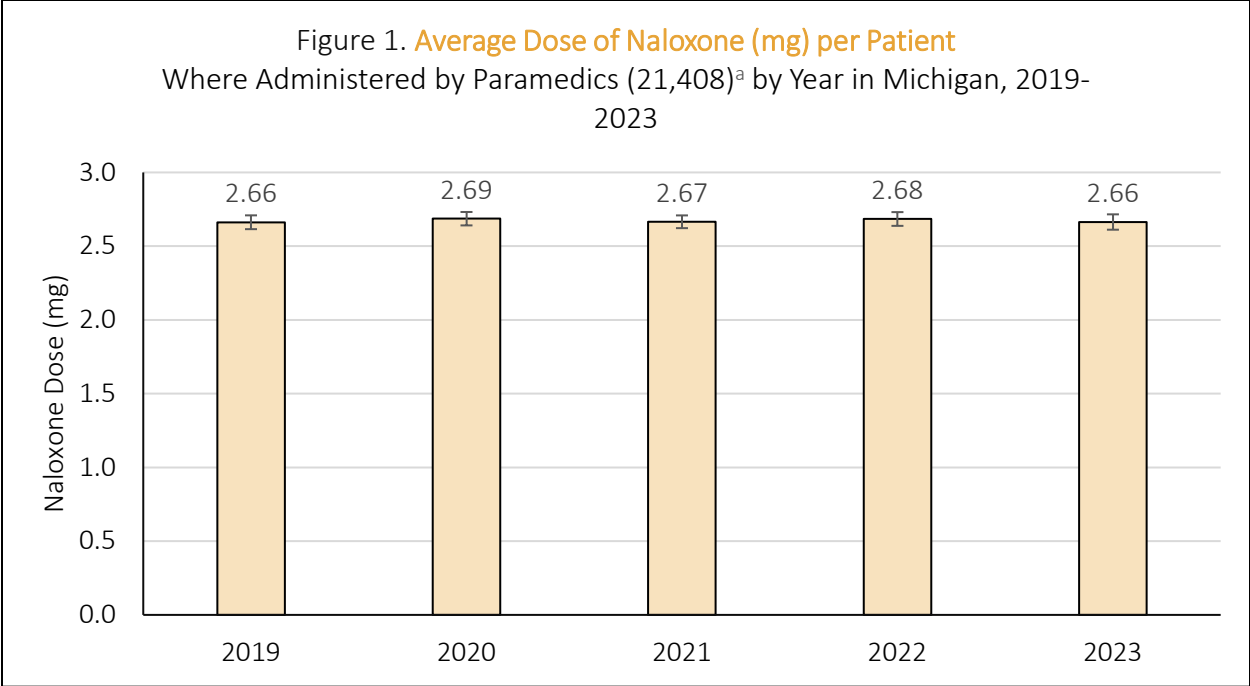
Opioid overdoses were estimated using data from the Michigan Emergency Medical Services Information System (MiEMSIS) which collects data on all Emergency Medical Service (EMS) responses in Michigan. EMS responses are designated as probable opioid overdoses based on vital signs, provider impressions, initial complaint, medications administered, procedures performed and information in the patient care narrative. The Michigan case definition is available online: [Michigan Emergency Medical Services Case Definition of Probable Opioid Overdose](#).²

Records are limited to those with naloxone dosage information available and where that naloxone was administered by paramedics. Total dose of naloxone (mg) per patient was calculated and then averaged across patients, stratified by year. As much as is possible with a deidentified data source, records were deduplicated. See Technical Notes for more details, case definitions and limitations.

Results

Naloxone dosage

To assess trends in naloxone administration dosage, EMS responses to probable opioid overdose that took place in Michigan between January 1, 2019, and December 31, 2023, were analyzed (n=63,995). Naloxone dosage information was available in 62% of records (n=39,733); of those, paramedics administered the naloxone in 54% of records (n=21,408). From January 2019 to December 2023 the percent of EMS responses to probable opioid overdose that did not require naloxone ranged from 9% to 11% per year. Paramedics administered an average dose of 2.7 mg of naloxone per patient consistently every year (Figure 1).



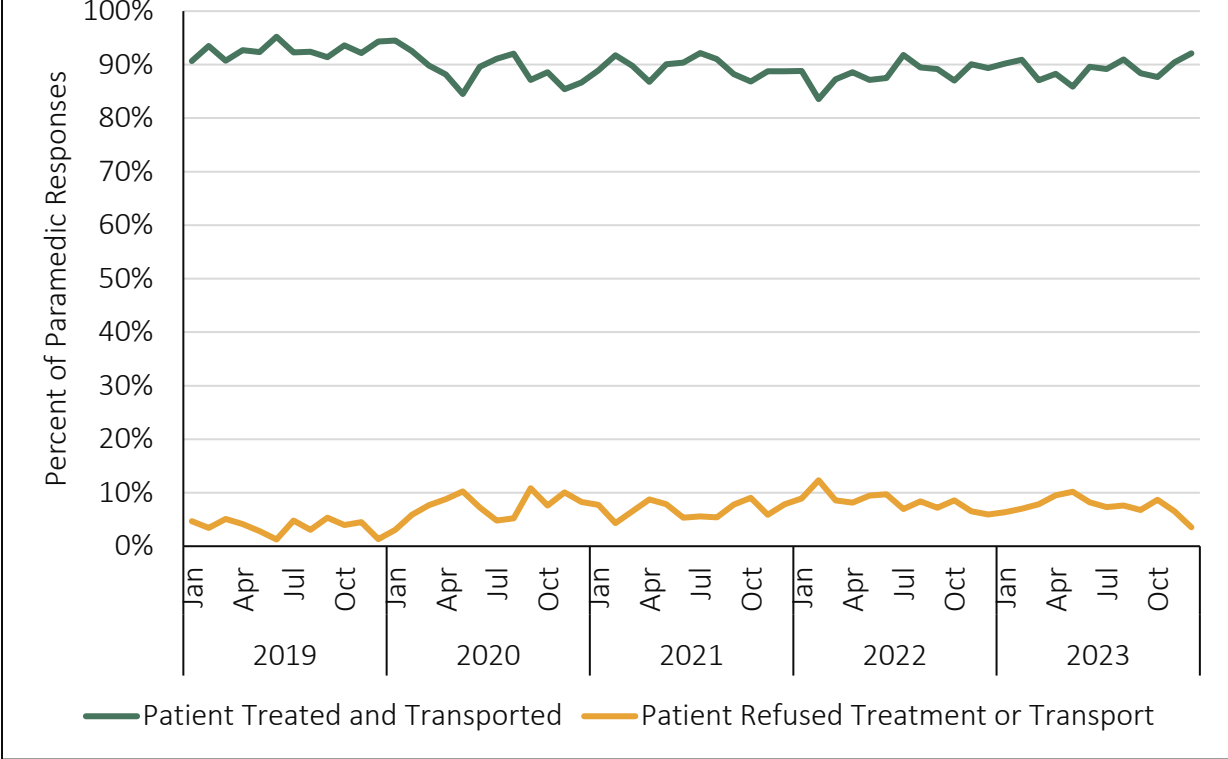
Source: Michigan Emergency Medical Services Information System (MiEMSIS), Bureau of Bureau of Emergency Preparedness, EMS and Systems of Care (BEPESOC).

^an = number of total EMS responses to probable opioid overdose and excludes responses where naloxone was given by role other than paramedic (n=18,325), responses where naloxone dosage was not recorded (n=13,333), responses where naloxone was not administered (n=6,263), responses where more than one type of role gave naloxone to one patient (n=3,305) and responses with suspected erroneous values (see data notes for detail) for mg of naloxone (n=1,361).

Trends in Patient Treatment and Transport

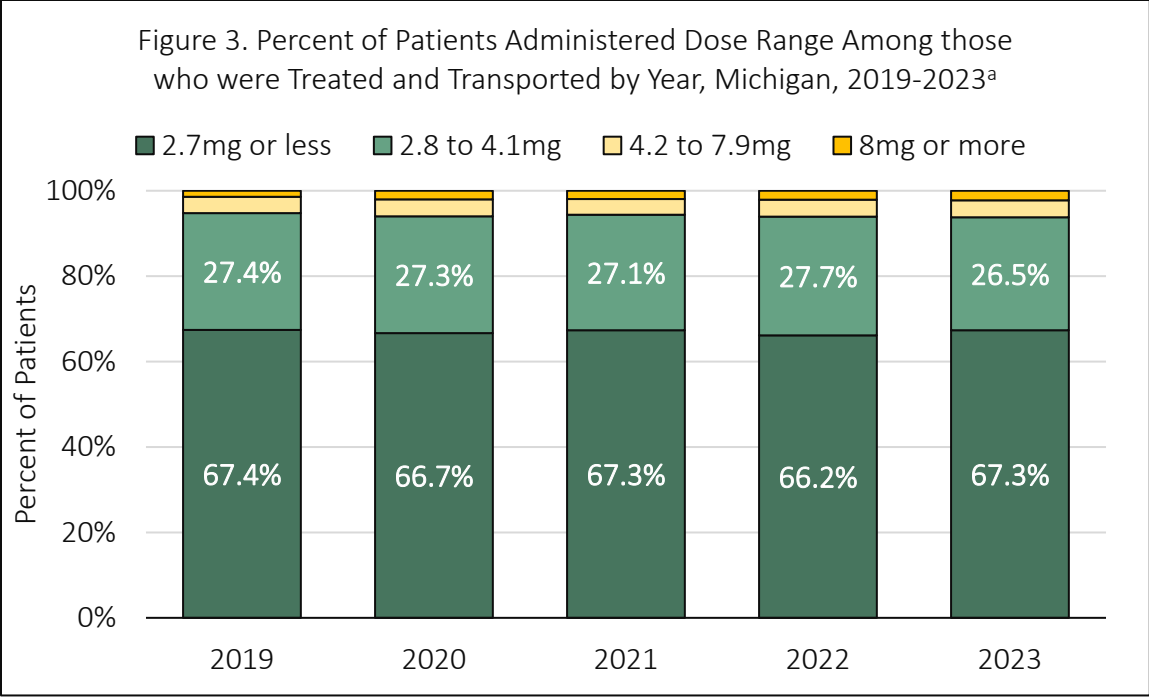
Temporal trends in the percent of patients who were treated and transported to the hospital or refused transport (Figure 2) were analyzed. Figure 2 shows that over 80% of patients have been and continue to be treated and transported to the hospital. After the onset of COVID-19 in March 2020, there were some slight increases in the percent of patients refusing transport to the hospital, a pattern likely due to the pandemic. Among those who were treated and transported each year, about 67% consistently received under 2.7mg of naloxone, followed by about 27% receiving 2.8-4.1mg (Figure 3).

Figure 2. Percent of Paramedic Responses to Probable Opioid Overdose Where Patient Was **Treated and Transported (n=19,216)^a** or **Refused Treatment or Transport (n=1,452)^a**, by Month and Year, Michigan, 2019-2023



Source: Michigan Emergency Medical Services Information System (MiEMSIS), Bureau of Bureau of Emergency Preparedness, EMS and Systems of Care (BEPESOC).

^an = number of total EMS responses to probable opioid overdose and excludes responses where naloxone was given by role other than paramedic (n=18,325), responses where naloxone dosage was not recorded (n=13,333), responses where naloxone was not administered (n=6,263), responses where more than one type of role gave naloxone to one patient (n=3,305) and responses with suspected erroneous values (see data notes for detail) for mg of naloxone (n=1,361).



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Discussion

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 during this time. This analysis does not provide 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. Further investigation and monitoring is ongoing.

Effective reversal of an opioid overdose requires naloxone to be administered correctly, while ensuring adequate ventilation, which may include CPR. Paramedics are trained to do so, which may contribute to their effective use of lower doses of naloxone. Increased community naloxone administration training may be the most cost-effective approach toward ensuring efficacious naloxone administration with current dosing protocols and naloxone formulations.

This report is a retrospective analysis that does not include data on use of 8 mg naloxone formulations. In a direct comparison between naloxone formulations, the New York State Department of Health (NYSDOH) collected information from two subsets of law enforcement troops: one that used 8mg nasal spray naloxone and one that used 4mg nasal spray naloxone. NYSDOH found no significant difference in hospital transportation or survival between groups; however, those who received 8 mg of naloxone had more than double the likelihood of experiencing opioid withdrawal symptoms compared to those who received 4 mg. NYSDOH has released the findings of this assessment via a data brief, [Post-Naloxone Symptoms Among People Administered 8mg](#)³, and a formal paper, [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](#)⁴.

It is important to note that this report does not include the perspectives of those with lived experience. While the perspectives of staff of Michigan Syringe Service Programs (SSPs) may not be representative of all those with lived and/or living experience, they do represent a critical subset. Informal feedback communicated by SSP staff communicates some concerns over High-Dose Naloxone Formulations (HDNF) such as the 8 mg dose. Those concerns include:

- A long duration of withdrawal.
- A potential distraction from addressing systemic issues.
- The limited additional impact of new naloxone formulations amid rapidly increasing stimulant use.
- The “more is better” mentality distracting from rescue breaths and ensuring ventilation.

Tennessee Harm Reduction did a more robust assessment of the perspectives of those with lived and living experience in the paper [High-Dose Naloxone Formulations Are Not as Essential as We Thought](#)⁵ that examined the need for HDNF. The authors did not recommend HDNF in comparison to the use of standard naloxone due to concerns regarding cost, risk of precipitated withdrawal, and limited evidence of its benefits. The authors also emphasized the need to consider and include the perspectives of, and consent from, those with lived experience when it comes to decisions around the use of HDNF.

As described by the Tennessee Harm Reduction paper, the cost of naloxone is a key consideration of those looking to potentially purchase 8 mg naloxone. In 2022, through MDHHS NARCAN Direct, 197,316 naloxone kits were ordered. NARCAN Direct is funded by Substance Abuse and Mental Health Services Administration (SAMHSA) dollars, with kits going to a wide range of prevention, harm reduction and treatment programs. The cost of 4 mg naloxone was \$47.50 in 2022, which would bring the total cost to \$9,386,807. The retail price of a box of 8 mg naloxone is about \$141. If the 2022 naloxone orders through MDHHS NARCAN Direct had been for the 8 mg formulation, an additional \$18,477,189 would have been spent. These funds would need to come from existing efforts, such as prevention, harm reduction and treatment programs. Even if 8 mg naloxone were purchased at a severe 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 in 2022.

Finally, although this report focuses on naloxone dose, there are now non-naloxone opioid overdose reversal agents, like nalmafene (Opvee)⁶, that are also raising concerns about potential harms like prolonged withdrawal (see commentary in the [International Journal of Drug Policy February 2024 Issue](#)⁷ and a [joint position statement](#)⁸ from the American College of Medical Toxicology (ACMT) and the

excluded because of erroneous dosages (ex: dosages above what currently exists, such as 15mg for a single dose or 20mg for two doses).

- Among EMS responses to probable opioid overdose in Michigan from January 1, 2019 – December 31, 2023, where naloxone dosage was recorded, there was a high percentage of responses where the person administering naloxone to the patient was not recorded (ranging from 24.7% to 39.2% of EMS responses where naloxone dosage was recorded).
- EMS records only include patient outcomes about what occurred while patient was in EMS care.

Naloxone Details

Nasal spray naloxone:

- **Form:** Comes in a prefilled device that sprays medication into the nose.
- **Dose:** Available in 2 and 4 mg doses, until recent FDA approval of the 8 mg dose in June 2023.
- **Action of onset:** The action of onset, or time it takes for drug's effects to occur after administration, is three to four minutes.
- **Who Can Administer:** Anyone, regardless of medical training or experience, can easily administer the nasal spray form.

Injectable naloxone:

- **Form:** The injectable form needs to be administered into a muscle (intramuscular or IM), under the skin (subcutaneous or SC), or into a vein (intravenous or IV).
- **Dose:** 2 mg, if administered IV, can be administered in smaller amounts and is usually given in 0.4 mg increments. Administering smaller doses provides a way to restore breathing while avoiding precipitated withdrawal, which is the occurrence of sudden and severe withdrawal symptoms. Precipitated withdrawal can be harmful to patients causing extreme nausea, vomiting, tremors, and, in severe cases, seizures.
- **Action of onset:** one to two minutes (IV); three to four minutes (IM).
- **Who Can Administer:** Available by prescription, requires more training to administer compared to nasal spray; in Michigan, all Advanced Life Support EMS responders may use the intranasal or injectable naloxone route.

Regardless of route, once a dose of naloxone is given, rescue breathing (which is advised immediately if a patient's breathing is unstable) must be continued to allow naloxone to be absorbed into the patient's system to restore respiratory effort.

Michigan EMS Protocol for Treating Opioid Overdose

In cases of decreased level of consciousness associated with respiratory depression from opioid overdose, signs of opioid use, and/or scenes with indications of opioid use:

- If patient has respiratory depression, provide oxygenation and support ventilations. Treatment goal is to restore effective respirations; the patient need not be completely awakened.
- If respiratory depression or respiratory arrest continues, for adults, administer:
 - Narcan® Nasal Spray 4 mg in one nostril. May repeat one time in three to five minutes in opposite nostril if effective respirations are not restored OR
 - Naloxone prefilled 2 mg/2 mL IN via Atomizer. Half dose in each nostril. May repeat one time in three to five minutes if effective respirations are not restored OR

Naloxone 2 mg IM or slow IV push titrating to improvement in respiratory status. IV naloxone may be repeated as needed every three to five minutes.

Contact Information

With naloxone being available for over-the-counter purchase, training can help people identify an opioid overdose and administer naloxone safely and effectively. Training programs are available through a variety of organizations, including community health centers, harm reduction programs and EMS.

- For anyone who is interested in naloxone administration and/or CPR training, courses are available through the American Heart Association: cpr.heart.org/opioid-education¹¹
- For larger groups, or any public safety agency such as law enforcement, fire department and EMS wanting tailored training, please contact Anthony Pantaleo, EMS Opioid Outreach Coordinator, Division of EMS and Systems of Care, Bureau of Emergency Preparedness, EMS, and Systems of Care, MDHHS, at pantaleoa@michigan.gov.

MDHHS Non-Discrimination Policy: The Michigan Department of Health and Human Services (MDHHS) does not discriminate against any individual or group on the basis of race, national origin, color, sex, disability, religion, age, height, weight, familial status, partisan considerations, or genetic information. Sex-based discrimination includes, but is not limited to, discrimination based on sexual orientation, gender identity, gender expression, sex characteristics, and pregnancy.

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https://www.health.ny.gov/diseases/aids/general/opioid_overdose_prevention/docs/naloxone_data_brief.pdf

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