

**A Researched Abuse, Diversion and Addiction-Related  
Surveillance (RADARS®) System Report:**

**RADARS® System Treatment Center Programs Combined  
Study of Naloxone Experiences and Attitudes**

**for**

**Submitted to Center for Substance Abuse Research,  
University of Maryland, College Park**

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# 1. Background and Introduction

From 1999 through 2019, more than 500,000 individuals died of a drug overdose involving an opioid. In 2019, over 70% of the 70,630 drug overdose deaths involved an opioid (1). Naloxone, an opioid antagonist approved by the Food and Drug Administration in 1971 to treat opioid overdose, can reverse an opioid overdose. Public health policy efforts have promoted increased access and carrying of naloxone, including among individuals who misuse opioids (2). Observational studies suggest communities that allow take-home naloxone observe fewer opioid fatalities with few naloxone-related adverse events (3, 4).

Despite evidence of take-home naloxone benefits, barriers exist in getting individuals who misuse opioids to own and carry naloxone (2). Tobin and colleagues (5) applied the “Cascade of Care” framework to naloxone carry to identify breakdowns among individuals who misuse opioids from awareness to actual carry. This framework has been applied to understand and improve outcomes with health conditions such as the human immunodeficiency virus (6). When applied to naloxone carry, the first step is to assess whether the degree the target population knows of naloxone, then determine the extent to which they know where to obtain naloxone, and finally calculate the number who are trained to use, who own, and who carry naloxone. In 2018, Belcher and her colleagues at the University of Maryland Drug Treatment Center in Baltimore piloted the Naloxone Perceptions and Attitudes Questionnaire developed by a National Drug Early Warning System (NDEWS) Naloxone Workgroup. Consistent with previous studies, Belcher and colleagues observed that individuals with opioid use disorder (OUD) were knowledgeable of naloxone, but few carried it with them. Additional findings from the NDEWS Naloxone Workgroup study raised concerns about possible increases in risk behaviors when individuals carried naloxone.

The success of the pilot led to a second National Institute on Drug Abuse NDEWS supplement. This award included two components, a detailed structured clinical interview to be administered on a OUD treatment-seeking sample in Baltimore, Maryland and a self-administered questionnaire completed by OUD treatment-seeking individuals across the United States. This report focuses on the results from the self-administered questionnaire. The questions were developed as part of a collaboration between the NDEWS Naloxone Workgroup and staff with the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System. These questions were designed to be included as part of a self-administered, anonymous survey of individuals enrolling in opioid treatment facilities across the United States. Survey items assessed stages of the Cascade of Care applied to naloxone. Additional items were intended to identify what may prevent this population from carrying naloxone. Respondents were asked about experience and barriers to carrying naloxone as well as other behaviors taken to prevent overdose.

The questionnaire was included as part of standard data collection in the RADARS System Treatment Center Programs Combined from April through September of 2020. The Treatment Center Programs Combined is comprised of participants recruited within the Opioid Treatment Program and the Survey of Key Informants’ Patients Program. The timeliness and catchment area of the program sample have made these data useful as an early indicator of changes in behaviors among individuals abusing opioids. These programs have identified changes in abuse of prescription opioids with tamper resistant formulations (7, 8), increases in co-abuse of methamphetamine (9), and changes in the types of opioids abused (10, 11).

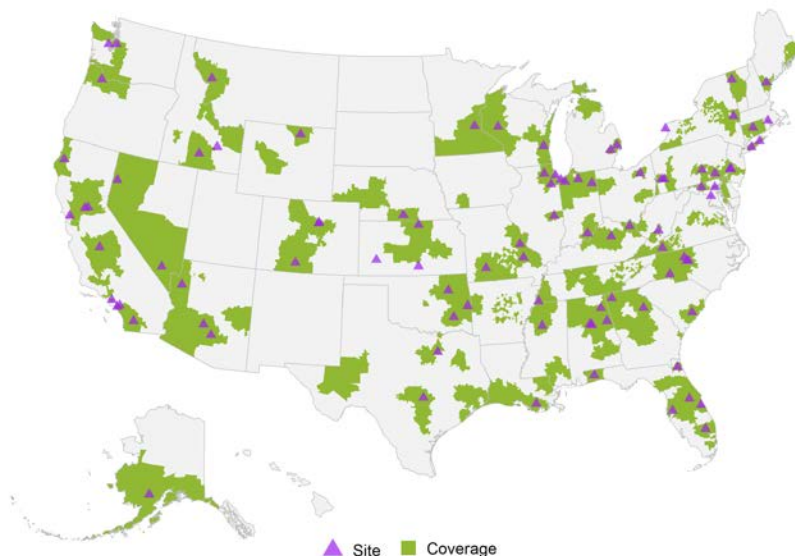
The objective of this report is to provide a summary of findings from this survey of naloxone-related questions among individuals entering treatment for opioid use disorders. This is an exploratory analysis focused on differences by demographic and substance use variables. Implications from the current findings and future directions for research are discussed.

## 2. Methods

### 2.1 Data Sources

The RADARS System Treatment Center Programs Combined provides data from two distinct RADARS System programs: Opioid Treatment Program and Survey of Key Informants' Patients Program. The Opioid Treatment Program survey's respondents were entering medication-assisted treatment facilities for opioid use disorders. The Survey of Key Informants' Patients Program survey's respondents come from a diverse network of public and private treatment facilities who are seeking treatment for an opioid use disorder and who report an opioid as their primary drug of abuse. These two programs use the same core data collection form, enabling data to be combined, and complement each other by providing information from patients entering both private and public opioid addiction treatment programs that are geographically diverse with representation from urban, suburban, and rural centers. Locations of centers that provided questionnaires and the three-digit ZIP codes where respondents resided are presented in figure 2.1.1. Descriptions of the data management and intentional review board considerations are provided in Appendix A.

**Figure 2.1.1: Treatment Site Location and Respondent Residential ZIP Codes, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**

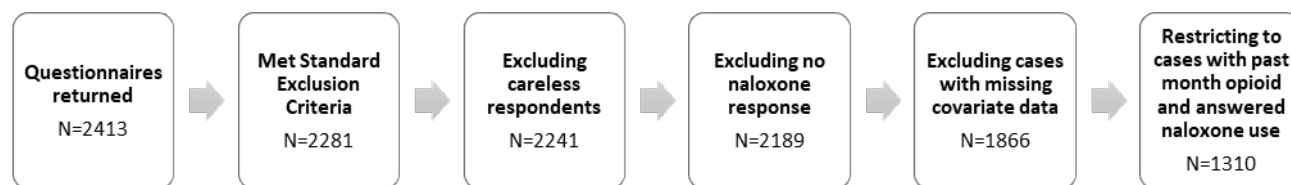


Patients enrolling in the study voluntarily completed a self-administered anonymous questionnaire within the first week of admission. From April 2020 through September 2020,

2,278 responses were completed. Participants meeting standard Treatment Center Programs Combined exclusion criteria were excluded. Standard criteria are missing or invalid residential ZIP codes or participants with missing ages or ages under 18 years. Questionnaires suggestive of careless or extreme response patterns were removed. Surveys with 24 or more opioid item endorsements or endorsements of nine or more consecutive items were determined to be suggestive of careless response and were excluded from the analysis. In addition, respondents who did not respond to any items in the naloxone questionnaire were excluded.

For this exploratory analysis, participants who did not endorse any past month drug abuse were excluded. This was done so that these analyses were focused on individuals who had recently abused drugs entering treatment facilities. We also excluded respondents with missing or invalid data on covariates of interest used in these analyses and who did not respond to the question asking, “Have you heard of naloxone (Narcan®, Evzio®, injection, or nasal spray)?”. This was done to ensure the number of respondents included in unadjusted and adjusted analyses were consistent. The final sample was of 1,310 respondents. Frequencies and proportions of endorsements among the entire sample after standard and careless exclusions were applied are presented in the previous report. Figure 2.1.2 is a flow chart outlining exclusion criteria and sample size from the number of completed questionnaires received to the sample included in this report.

**Figure 2.1.2: Flowchart of Respondent Included in Analyses, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**



## 2.2 Questionnaire Themes and Items

The standard Opioid Treatment Program and Survey of Key Informants’ Patients Program data collection instrument was amended with a list of items asking naloxone-related questions. The primary themes assessed were:

**Cascade of Care:** A series of questions intended to assess breakdowns from naloxone awareness to naloxone carry. Items assessed a respondent’s knowledge of naloxone, knowledge of where to get naloxone, training with naloxone, ownership of naloxone, and whether or not they carry naloxone.

**Harm Reduction:** Questions about opioid use practices the respondent uses in an effort to reduce the risk of an overdose.

**First person and Third person Barriers:** Assessments of knowledge of naloxone and fears about carrying naloxone. Respondents were asked about their perspective (first person) and asked about their peers’ perspective (third person).

**Access:** Respondents were asked about the ease of obtaining and affordability of naloxone.

**Experiences with naloxone:** Respondents were asked about their experiences with naloxone.

**Attitudes:** Respondents were asked about their changes in opioid use behaviors when naloxone was present.

Table 2.2.1 provides includes a summary of each theme assessed and associated items.

**Table 2.2.1 Naloxone Questionnaire and Themes, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**

Theme	Question Wording
Cascade of Care	19. Have you heard of naloxone (Narcan®, Evzio®, injection, or nasal spray)?
	20. What are all of the places where you can get naloxone in your area?
	36. Have you ever received training on how to give someone naloxone?
	24. Do you currently own naloxone?
	25. Do you carry naloxone with you?
Harm Reduction*	46. Do you use fentanyl test strips to prevent overdosing?
	47. Do you take a small test amount of drug before using the full amount to prevent overdosing?
	48. Do you take your drug slowly or in small doses ('go slow' with your injection) to prevent overdosing?
	49. Do you use smaller amounts of drugs (more small injections) to prevent overdosing?
	50. Do you use opioids only when you're with other people to prevent overdosing?
	51. Do you watch others with higher tolerance use drugs before you use to prevent overdosing?
First person/ Third Person Barriers*	Transportation
	27. Do you have transportation to get naloxone?
	52. Do other people have transportation to get naloxone?
	Embarrassment
	28. Are you embarrassed to ask for naloxone?
	53. Are other people embarrassed to ask for naloxone?
	Afraid of police
	29. Are you afraid of the police finding out that you have naloxone?
	54. Are other people afraid of the police finding out that they have naloxone?
	Afraid family and friends
	30. Are you /afraid of friends or family finding out that you have naloxone?
	55. Are other people afraid of friends or family finding out that they have naloxone?
	Afraid legal trouble
	35. Are you afraid of getting arrested or into legal trouble for giving someone else naloxone during an overdose?
56. Are other people afraid of getting arrested or into legal trouble for giving someone else naloxone?	
Know how to give	
37. Do you know how to give someone naloxone during an overdose?	
57. Do other people know how to give someone naloxone during an overdose?	
Know when to give	
38. Do you know when to give someone naloxone during an overdose?	
58. Do other people know when to give someone naloxone during an overdose?	
Afraid others reaction	
39. Are you afraid of someone's reaction by giving them naloxone during an overdose?	
59. Are other people afraid of someone's reaction by giving them naloxone during an overdose?	
Access*	21. Do you think naloxone is easy to get?
	22. Can you get naloxone for free?
	23. Do you think that naloxone is affordable?
Experiences*	26. Do you know other people who carry naloxone?
	33. Have you ever given someone naloxone during their overdose?
	34. Have you ever seen someone else give naloxone during an overdose?
	40. Have you ever been in a situation when naloxone was needed but was not available?
	42. Have you ever had naloxone available while using opioids?
Attitudes*	43. If naloxone is nearby, do you feel safer when you use opioids?
	44. If naloxone is nearby, do you feel more aware of high risks of opioid use?
	45. If naloxone is nearby, do you feel motivated to take additional harm reduction measures?

\*Analysis for these categories restricted to 1,001 respondents who reported having heard of naloxone.

## 2.3 Statistical Analyses

Exploratory analyses were conducted to examine the proportion of subjects who endorsed items related to naloxone awareness, attitudes, and behaviors and associated demographic and substance use variables.

**RADARS System Program:** This variable indicated whether the respondent was recruited through a treatment facility from the Opioid Treatment Program or the Survey of Key Informants' Patients Program.

**Age:** Respondents were categorized into one of four groups, 18 to 25 years, 26 to 34 years, 35 to 49 years, or 50 years or older.

**Gender:** Respondents who indicated either male or female gender were included. Due to a low number of respondents, individuals who endorsed non-binary were excluded from the analysis. If a respondent endorsed multiple categories, the response was considered invalid and data were excluded from the analyses.

**Ethnicity:** The categories used for these analyses were White, Hispanic/Latino/a, African American, Native American, or Other. Respondents could endorse multiple ethnicities.

**Region:** Respondents were grouped into one of four US Census Regions (Northeast, South, Midwest, West) based on the three-digit ZIP code where they resided.

**Education:** Respondents were asked about the highest level of education obtained. We analyzed four education categories, less than high school, completion of the general educational development test (GED), completion of high school or technical or vocational school, and more than high school. More than high school included respondents who endorsed some college and those who completed bachelors or graduate degrees. If a respondent endorsed multiple categories, the response was considered invalid and data were excluded from the analyses.

**Living situation:** Respondents were asked where they had been living most of the time in the past month. Five living situation groupings were analyzed, temporarily with friend/family member, safe haven/shelter, rent/own, street dwelling, or other living situation. If a respondent endorsed multiple categories, the response was considered invalid and data were excluded from the analyses.

**Primary drug:** Respondents were asked to select the one drug substance (primary drug substance) that they used the most to get high with before coming to this program. Respondents could select buprenorphine, codeine, fentanyl, heroin, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, sufentanil, tramadol, or tapentadol. Primarily illicit drug use refers to respondents who selected either heroin or fentanyl. Fentanyl was included with heroin as many of these endorsements appear to be primarily illicitly manufactured. Primarily prescription drug use refers to respondents who selected other substances. A third group represents respondents who selected both a prescription and illicit opioid.

**Overdose:** All respondents were asked “*Have you ever overdosed on an opioid?*” Endorsements of yes were considered positive for a history of overdose. If the ‘yes’ box was not selected, then the response was considered to indicate no history of overdose.

Each survey item presented in Table 2.2.1 was categorized into a binary variable “yes” or “no” response. For third-person items “I don’t know” responses were grouped with “no”. If an item was missing a response it was excluded from the analysis. All respondents were included in the analysis of Cascade of Care theme items. For all other groupings, only the 1,001 respondents who responded “yes” to item 19 were included. Each multiple logistic regression analysis included all potential covariates. This allowed for an adjustment of potential confounding across demographic and drug use variables. To adjust for multiple comparisons we used the false discovery rate (12). This approach is standard with exploratory data analyses where several tests are conducted with the intent to identify associations for further investigation (13).

### 3. Results

Table 3.1 displays the demographic data from the final sample. Most respondents were from the Opioid Treatment Program (73.8%). The majority identified as male (56.0%), white (75.3%), and resided in the South Census Region (41.8%). Of the 1,310 respondents, 73.6% reported heroin or fentanyl as their primary drug used to get high prior to entering treatment.

**Table 3.1 Sample Demographics, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**

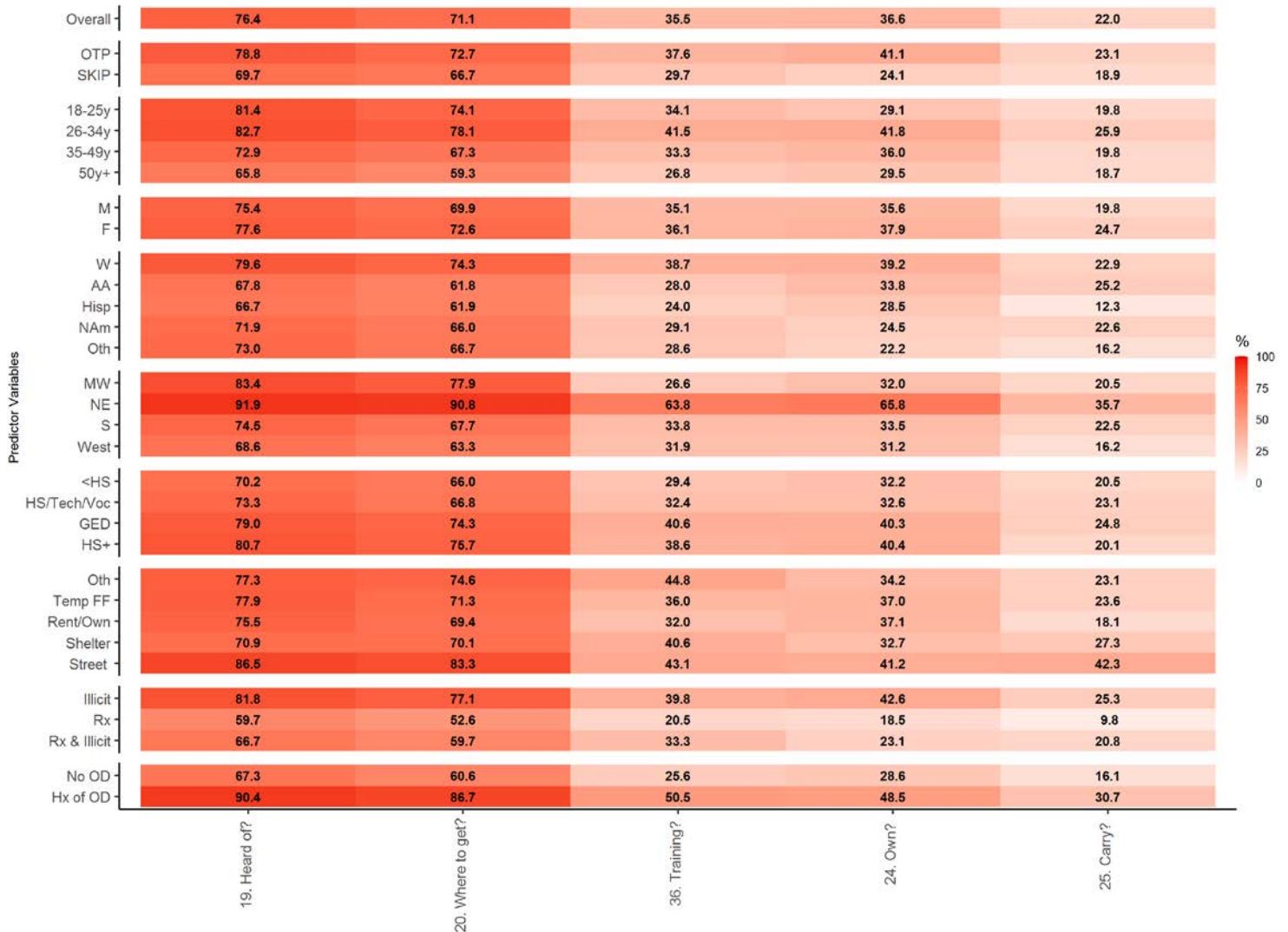
Variable	Value	N (%)
N	N	1,310
Data source	Opioid Treatment Program	967 (73.8)
	Survey of Key Informants' Patients Program	343 (26.2)
Age	18-25 years	129 (9.8)
	26-34 years	496 (37.9)
	35-49 years	498 (38.0)
	50+ years	187 (14.3)
Gender	Male	733 (56.0)
	Female	577 (44.0)
Race/Ethnicity*	White	986 (75.3)
	Hispanic/Latino/a	135 (10.3)
	African American	152 (11.6)
	Native American	57 (4.4)
	Other	27 (2.1)
Region	Midwest	223 (17.0)
	Northeast	160 (12.2)
	South	548 (41.8)
	West	379 (28.9)
Education	Less than high school	205 (15.6)
	GED	224 (17.1)
	High school, technical or vocational school	419 (32.0)
	More than high school	462 (35.3)
Living	Temporarily with friend/family member	385 (29.4)
	Safe Haven/shelter	110 (8.4)
	Rent/own	644 (49.2)
	Street dwelling	52 (4.0)
	Other	119 (9.1)
Primary Drug	Illicit Opioids Only	964 (73.6)
	Prescription Opioid Use Only	268 (20.5)
	Illicit and Other Prescription Opioid	78 (6.0)
Overdose	History of Opioid Overdose	519 (39.6)
	No Opioid Overdose	791 (60.4)

\*Participants may endorse more than one race/ethnicity.

### 3.1 Cascade of Care

The percentage of respondents who reported having heard of naloxone was 76.4%. Among all respondents, the percentage who identified at least one location where they could obtain naloxone was slightly lower (71.1%). A large decrease was observed in the proportion of respondents who received training on administering naloxone (35.5%), who currently own naloxone (36.6%), and who reported carrying naloxone with them (22.0%) (Figure 3.1.1). Notable differences in naloxone awareness were observed by region, where 91.9% of respondents in the Northeast reporting having heard of naloxone. This was higher than the Midwest (83.4%), South (74.5%), and West (68.6%). Similar differences were observed for all items within the Cascade of Care theme. Individuals who reported illicit opioids as a primary drug indicated more knowledge of naloxone (81.8%) than those who primarily abused prescription opioids (59.7%) or those who abuse illicit and prescription opioids (66.7%). History of an opioid overdose was also associated with greater awareness of naloxone (90.4%) than those without history of opioid overdose (67.3%).

**Figure 3.1.1: Heatmap of Percentage of All Respondents Endorsing Cascade of Care Items, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**



OTP=Opioid Treatment Program, SKIP=Survey of Key Informants' Patients Program, Y=Years, M=Male, F=Female, AA=African American, Hisp=Hispanic/Latino/a, Nam=Native American, W=White, Oth=Other, MW=Midwest, NE=Northeast, S=South, <HS=Less than High School, HS/Tech/Voc=High School, Technical, or Vocational School, HS+=More than High School, Temp FF=Temporarily with Family and Friends, Rx=Prescription, Hx=History, OD=Overdose

## 3.2 Harm Reduction

The harm reduction theme included items assessing behaviors used to reduce the risk of opioid overdose among the 1,001 respondents who reported having heard of naloxone. Items that indicated some form of pacing, taking smaller amounts, test amounts, taking slower, were endorsed by about half of respondents (51.3%) (Figure 3.2.1). Behaviors related to using around others (using around others or watching others use first) were endorsed by about one-quarter of respondents or fewer. Using fentanyl strips were also less likely to be endorsed overall. Differences in these items appeared to be most apparent by primary drug of abuse, with those who primarily use heroin or fentanyl as more likely to endorse using some form of pacing (55.0%, 55.2%, and 52.8%) relative to prescription opioids (35.7%, 33.3%, 30.8%).

**Figure 3.2.1: Heatmap of Percentage of All Respondents Endorsing Harm Reduction Items, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**

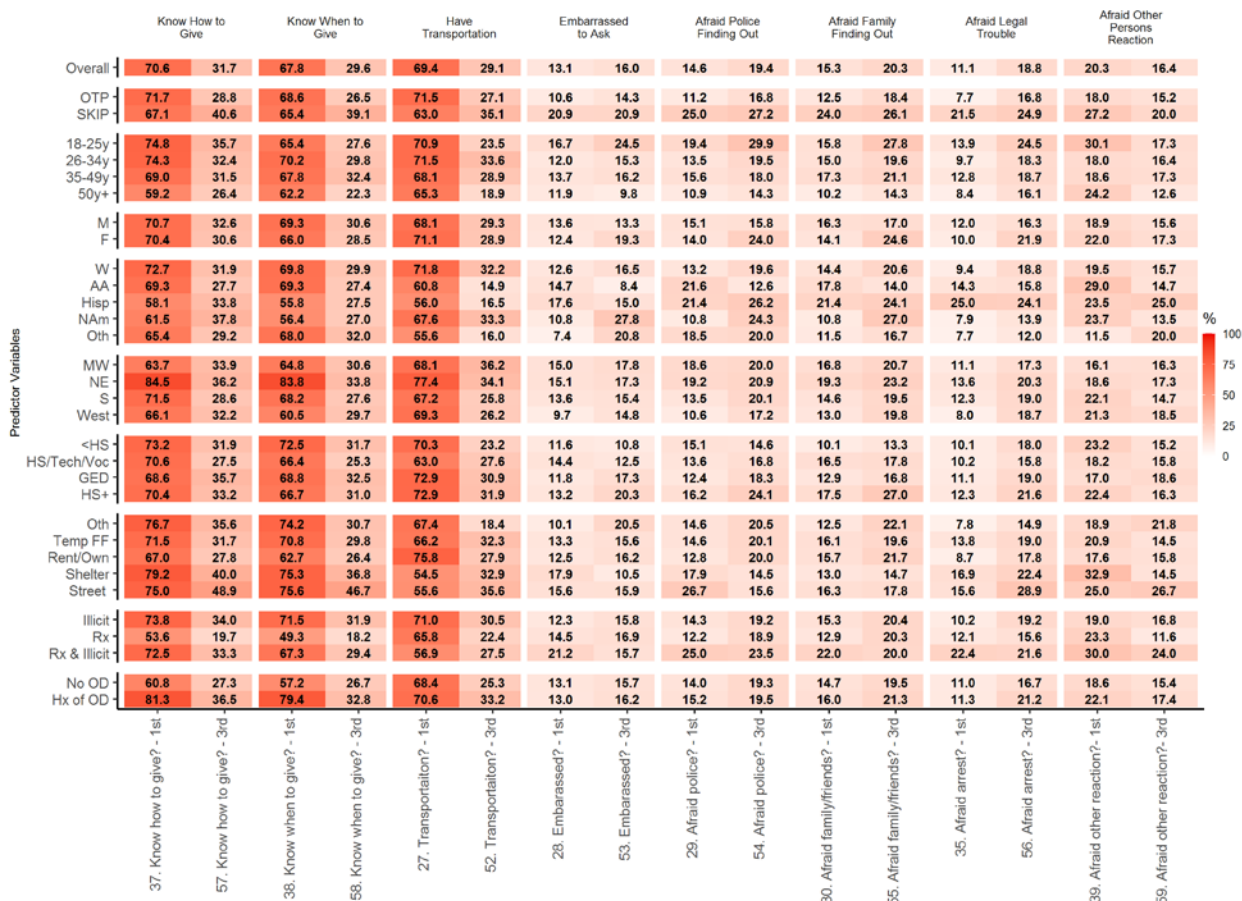


Analysis restricted to 1,001 respondents who reported having heard of naloxone. OTP=Opioid Treatment Program, SKIP=Survey of Key Informants' Patients Program, Y=Years, M=Male, F=Female, AA=African American, Hisp=Hispanic/Latino/a, Nam=Native American, W=White, Oth=Other, MW=Midwest, NE=Northeast, S=South, <HS=Less than High School, HS/Tech/Voc=High School, Technical, or Vocational School, HS+=More than High School, Temp FF=Temporarily with Family and Friends, Rx=Prescription, Hx=History, OD=Overdose

### 3.3 First and Third Person Barriers to Carrying Naloxone

Of the 1,001 respondents who had heard of naloxone, 70.6% of respondents reported knowing how to administer naloxone, and 67.8% reported knowing when to give naloxone. Only 31.7% reported that others knew how to give naloxone, and 29.6% reported others knowing when to give naloxone during an overdose (Figure 3.3.1). These differences were observed across all demographic and substance use history variables assessed. Also consistent across demographic and substance use history variables was transportation for naloxone. Most respondents (69.4%) reported having transportation to get naloxone, whereas only 29.1% said others had transportation for naloxone. Both responses may be due to many respondents who reported that they did not know about others access or barriers to obtaining naloxone. Among other items assessing barriers to obtaining naloxone, there were slightly higher percentages of respondents reporting that others were embarrassed to ask for naloxone, afraid of others finding out they had naloxone, and afraid of legal trouble. These percentages tended to be lower than 25% across demographic and drug use variables (Figure 3.3.1).

**Figure 3.3.1: Heatmap of Percentage of All Respondents Endorsing First-Person and Third-Person Barrier Items, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**



Analysis restricted to 1,001 respondents who reported having heard of naloxone. OTP=Opioid Treatment Program, SKIP=Survey of Key Informants' Patients Program, Y=Years, M=Male, F=Female, AA=African American, Hisp=Hispanic/Latino/a, Nam=Native American, W=White, Oth=Other, MW=Midwest, NE=Northeast, S=South, <HS=Less than High School, HS/Tech/Voc=High School, Technical, or Vocational School, HS+=More than High School, Temp FF=Temporarily with Family and Friends, Rx=Prescription, Hx=History, OD=Overdose

### 3.4 Naloxone Experiences and Proximity When Abusing Opioids

Of the 1,001 respondents who had heard of naloxone, 70.9% reported that naloxone was easy to get, 77.7% reported they could get naloxone for free, 73.3% reported that they thought naloxone was affordable, and 61.3% reported that they knew someone who carried naloxone (Figure 3.4.1). Only 35.5% of respondents reported having given naloxone, 48.1% reported having seen naloxone administered, and 45.9% reported having been in a situation where naloxone was needed but not available. Among respondents who had heard of naloxone, 67.1% reported having naloxone available when using opioids. Most respondents (69.8%) reported feeling safer when using opioids with naloxone nearby, 54.9% reported they were more aware of the risks of using opioids, and 46.6% reported taking more harm reduction measures. A greater percentage of respondents from the Northeast appeared to endorse access items than those from other regions, a greater percentage of respondents who reported a history of overdose endorsed experience items than those without a history of overdose, and a greater percentage of individuals whose primary drug was either heroin or fentanyl endorsed safety items than those whose primary drug was a prescription opioid (Figure 3.4.1).

**Figure 3.4.1 Heatmap of Percentage of All Respondents Endorsing Access, Experience, and Safety Items, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**

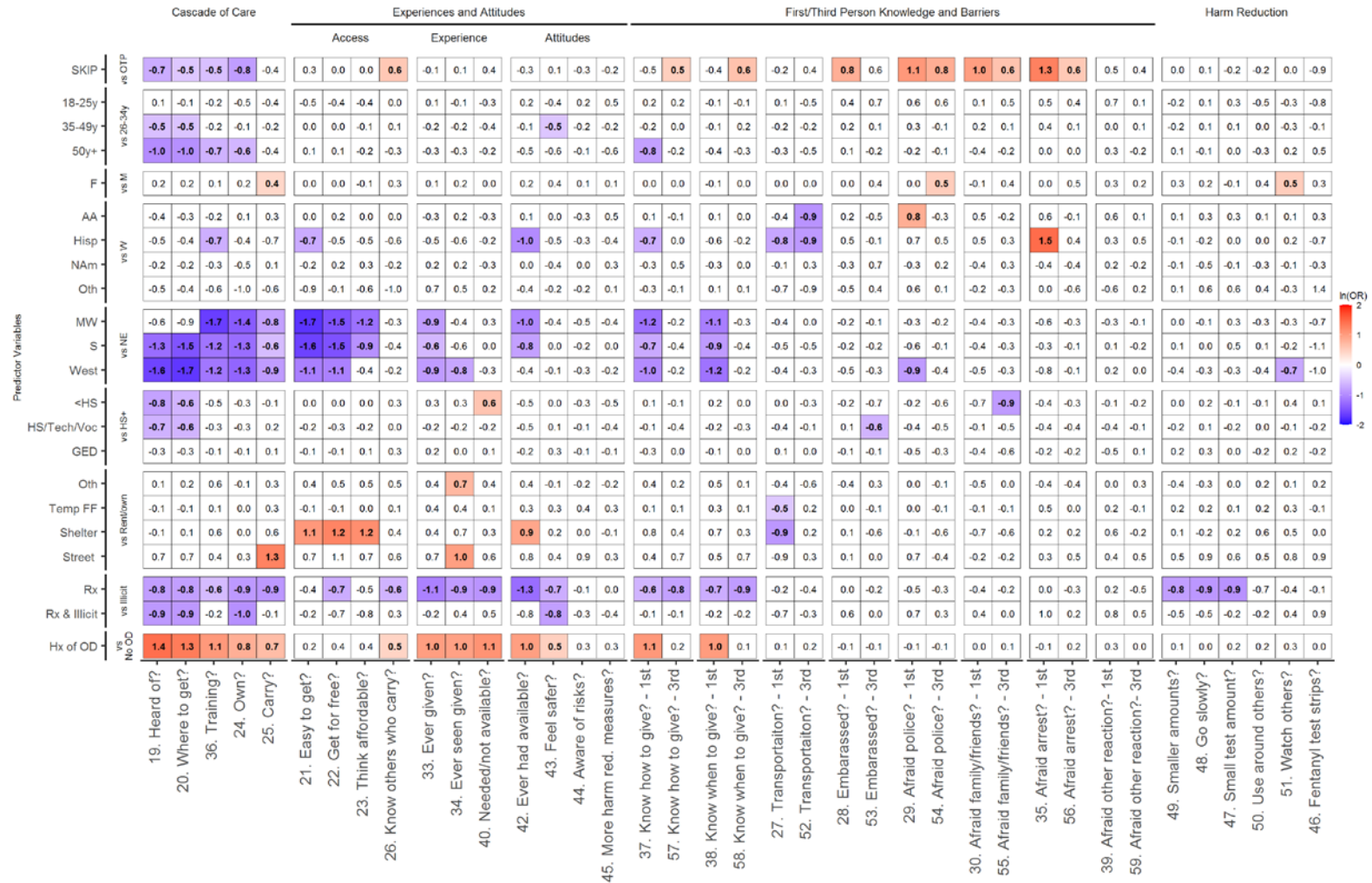


Analysis restricted to 1,001 respondents who reported having heard of naloxone. OTP=Opioid Treatment Program, SKIP=Survey of Key Informants' Patients Program, Y=Years, M=Male, F=Female, AA=African American, Hisp=Hispanic/Latino/a, Nam=Native American, W=White, Oth=Other, MW=Midwest, NE=Northeast, S=South, <HS=Less than High School, HS/Tech/Voc=High School, Technical, or Vocational School, HS+=More than High School, Temp FF=Temporarily with Family and Friends, Rx=Prescription, Hx=History, OD=Overdose

### 3.5 Logistic Regression Results

Multiple logistic regression analysis was used to test for associations between questionnaire items and each demographic and substance while simultaneously controlling for associations between predictor variables. All comparisons and beta coefficients (natural log of the odds ratios) are presented in Figure 3.5.1. Each column represents a questionnaire item, and questionnaire items are grouped by theme. Each row represents a demographic or substance use value included in the logistic regression model. The reference category for each variable is noted in the x-axis. Red shading indicates a finding where the variable is significantly greater than the reference, purple shading indicates a finding where the variable is significantly less than the reference category.

**Figure 3.5.1. Adjusted Beta Coefficients (Natural Log Odds Ratio) from Multiple Logistic Regression Model of each Questionnaire Item on each Predictor Variable, RADARS® System Treatment Center Programs Combined, April 2020 through September 2020**



Analysis of items other than Cascade of Care restricted to 1,001 respondents who reported having heard of naloxone. Red shading indicates a finding where the variable is significantly greater than the reference, purple shading indicates a finding where the variable is significantly less than the reference category. OTP=Opioid Treatment Program, SKIP=Survey of Key Informants' Patients Program, Y=Years, M=Male, F=Female, AA=African American, Hisp=Hispanic/Latino/a, NAm=Native American, W=White, Oth=Other, MW=Midwest, NE=Northeast, S=South, <HS=Less than High School, HS/Tech/Voc=High School, Technical, or Vocational School, HS+=More than High School, Temp FF=Temporarily with Family and Friends, Rx=Prescription, Hx=History, OD=Overdose

Survey of Key Informants' Patients Program respondents were less likely to endorse Cascade of Care items such as knowledge of naloxone ( $\beta=-0.7$ ,  $p=0.001$ ), knowing where to get naloxone ( $\beta=-0.5$ ,  $p=0.044$ ), training with naloxone ( $\beta=-0.5$ ,  $p=0.012$ ), and ownership of naloxone ( $\beta=-0.8$ ,  $p<0.001$ ) than respondents recruited through the Opioid Treatment Program. By contrast, respondents from Survey of Key Informants' Patients Program were more likely to indicate others knew how and when to get naloxone ( $\beta=0.6$ ,  $p=0.017$ ). Respondents from Survey of Key Informants' Patients Program were more likely to report being embarrassed to ask for naloxone ( $\beta=0.8$ ,  $p<0.001$ ), more afraid of the police ( $\beta=1.1$ ,  $p<0.001$ ) or family members ( $\beta=1.0$ ,  $p<0.001$ ) finding out about naloxone carrying. They also reported others were more concerned of these behaviors than respondents recruited through the Opioid Treatment Program.

Adjusting for other variables, respondents age 35 to 49 years were less likely to know about naloxone ( $\beta=-0.5$ ,  $p<0.001$ ) and where to get naloxone ( $\beta=-0.5$ ,  $p=0.023$ ) than those 26 to 34 years. Respondents 50 years and older were less likely to report knowing about naloxone ( $\beta=-1.0$ ,  $p<0.001$ ), knowing where to obtain naloxone ( $\beta=-1.0$ ,  $p<0.001$ ), to have received training on how to administer naloxone ( $\beta=-0.7$ ,  $p=0.020$ ) or owning naloxone ( $\beta=-0.6$ ,  $p=0.026$ ) than individuals aged 26 to 34 years. Respondents aged 50 years and older were less likely to report knowing how to give naloxone ( $\beta=-0.8$ ,  $p=0.011$ ).

Respondents who identified as African American were less likely than those who only identified as White to say others had transportation to obtain naloxone ( $\beta=-0.9$ ,  $p=0.027$ ). Respondents who identified as African American were more likely to report being afraid of the police finding out they had naloxone ( $\beta=0.8$ ,  $p=0.034$ ). Individuals who identified as Hispanic were less likely than respondents who only identified as white to say naloxone was easy to get ( $\beta=-0.7$ ,  $p=0.041$ ). Individuals who identified as Hispanic were less likely to report that they ( $\beta=-0.8$ ,  $p=0.018$ ) or others had transportation to receive naloxone ( $\beta=-0.9$ ,  $p=0.048$ ). Individuals who identified as Hispanic were more afraid of getting into legal trouble if someone found out they had naloxone ( $\beta=1.5$ ,  $p<0.001$ ) and were less likely to have reported having naloxone available when using opioids than those who only identified as White ( $\beta=-1.0$ ,  $p=0.002$ ).

Knowledge of where to obtain naloxone, ease of obtaining naloxone, use of naloxone, and carrying naloxone were significantly lower in every US region relative to the Northeast. Knowledge of how and when to give was significantly lower in every US region relative to the Northeast. History of having given someone naloxone was lower in every US region relative to the Northeast.

Respondents who reported their primary drug was a prescription opioid were significantly less likely to have heard of naloxone ( $\beta=-0.8$ ,  $p<0.001$ ), to know where to obtain naloxone ( $\beta=-0.8$ ,  $p<0.001$ ), have received training on use of naloxone ( $\beta=-0.6$ ,  $p=0.016$ ), to own ( $\beta=-0.9$ ,  $p<0.001$ ), or to carry naloxone ( $\beta=-0.9$ ,  $p=0.003$ ) than those who primarily abused illicit opioids. Respondents whose primary drug was a prescription opioid were less likely to take measures to reduce the risk of overdose, were less likely to know how ( $\beta=-0.6$ ,  $p=0.014$ ) and when to give naloxone ( $\beta=-0.7$ ,  $p=0.006$ ), and to know others who carried naloxone ( $\beta=-0.6$ ,  $p=0.013$ ) than those whose primary drug were illicit opioids. Finally, individuals who had a history of opioid overdose were more likely to know of naloxone ( $\beta=1.4$ ,  $p<0.001$ ) and to carry it ( $\beta=0.7$ ,  $p<0.001$ ). They were more likely to report that they knew when ( $\beta=1.0$ ,  $p<0.001$ ) and how ( $\beta=1.1$ ,  $p<0.001$ ) to administer naloxone. They also reported feeling safer with naloxone nearby when using opioids ( $\beta=0.5$ ,  $p=0.016$ ) and know others who carried naloxone ( $\beta=0.5$ ,  $p=0.017$ ).

## 4. Discussion and Conclusions

This report provides a detailed assessment of naloxone experiences, attitudes, and behaviors among current opioid users entering treatment for opioid use disorders. Our findings are consistent with other studies evaluating the Cascade of Care from naloxone awareness to naloxone carry: we also observed a large drop off from awareness and access to training, ownership, and carry.

A notable finding was that these results identified large disparities in naloxone awareness, access, ownership, and carry by US Census region. Specifically, over 90% of respondents in the Northeast had heard of naloxone. This value is consistent with those observed by other researchers sampling participants in Baltimore (5) and with those of Belcher and colleagues as part of this collaboration. Prevalence of naloxone access, training, ownership, and carry was significantly lower in the Midwest, South, and West after controlling for other demographic and substance use variables. Within the Northeast, while these variables were higher than other regions, there was a notable drop off from 66% of respondents owning naloxone to only about 35% carrying naloxone with them. These findings highlight the need for different interventions to increase naloxone carry in different areas of the country.

Respondents recruited through the Survey of Key Informants' Patients Program reported less knowledge, were less likely to know places to obtain naloxone, and had less training and ownership than those recruited through the Opioid Treatment Program. Interestingly they reported knowing more individuals who carried naloxone and greater levels of first and third person barriers to carrying naloxone, including embarrassment, fear of legal trouble, and fear of family finding out that they had naloxone. The reasons for these differences after adjusting for demographic variables could reflect the location of these programs. Opioid Treatment Program respondents may be more likely to reside in urban areas with more experience with harm reduction efforts whereas Survey of Key Informants' Patients Program respondents may reside in rural or micropolitan areas with less history and different strategies in addressing opioid abuse.

Significant differences in naloxone carry were observed by respondents' primary drug of abuse. Respondents who reported primarily abusing prescription opioids prior to entering treatment reported less knowledge, access, ownership, carry, and experience with naloxone than those who primarily abused illicit opioids. In addition, respondents who reported primarily abusing prescription opioid prior to entering treatment were less likely to use measures to reduce overdose risk. It is noteworthy that this is adjusting for history of opioid overdose. These findings reflect concerns that individuals who abuse prescription opioids may view them as less dangerous to abuse which may increase risks among these individuals.

Finally, history of an opioid overdose was strongly associated with knowledge, experience, access, ownership, and carry of naloxone. Interestingly, individuals with a history of overdose showed no difference in engaging in other efforts to reduce overdose. These findings suggest that overdose experience increases likelihood to carry naloxone without changing other behaviors intended to avoid overdose.

### 4.1 Limitations

A limitation of this study is that the information is based on self-reported data. This has the potential to effect response patterns. Respondents may over-endorse favorable behaviors of

themselves and under-estimate the prevalence of these behaviors among peers. Fatigue may also affect participant responses. Finally, this sample reflects individuals who are using opioids and seeking treatment and is done through convenience sampling. Attitudes and behaviors from individuals who abuse opioids not seeking treatment may be different, and this population may be at greater risk.

## 4.2 Strengths

An offsetting strength is the large catchment area for the Treatment Center Programs Combined. Cases arise from both large metropolitan areas as well as rural areas across multiple states. This provides results that are more broadly applicable than those from a smaller geographic region. Though the self-report nature of the survey makes responses vulnerable to biases associated with self-report data, the anonymity of the survey may increase the comfort respondents have in reporting illegal or high-risk behaviors or those that may result in exclusion from a treatment facility.

## 4.3 Future Directions

This exploratory analysis identified disparities in naloxone awareness, but further studies can be performed using the data collected. This study assessed *a priori item* groupings. Latent variable analyses such as factor analysis may be effective in identifying clusters in responses or redundancy in questions. Further investigations into the associations between variables may aid in informing patient education about naloxone use. For example, understanding the extent to which barriers versus access are associated lower levels of naloxone carry.

A notable finding was that individuals who endorsed primarily abusing both illicit opioids and prescription opioids prior to enrolling in treatment tended to report levels of naloxone knowledge and access significantly lower than those who used illicit opioids alone and similar to those who primarily abused prescription opioids. Further investigation into whether this group represents a high-risk group to due heavy polysubstance abuse or a group transitioning from prescription to illicit opioids is warranted.

Finally, less than half of respondents reported engaging in harm reduction behaviors involving others. Though not directly assessed, this suggests that many individuals may use primarily alone. This could be an important focus of future research in understanding the impact of carrying naloxone. Finally, responses to items such as where respondents reported they could get naloxone (e.g. a pharmacy, needle exchange program) and preferences for method of administration (injection versus nasal) were not analyzed as part of this report. These could be explored further in future studies, particularly in efforts to understand regional differences.

## 5. References

1. CDC NCHS. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA2020. Available from: <http://wonder.cdc.gov>.
2. McDonald R, Campbell ND, Strang J. Twenty years of take-home naloxone for the prevention of overdose deaths from heroin and other opioids-Conception and maturation. *Drug and alcohol dependence*. 2017;178:176-87.
3. McDonald R, Strang J. Are take-home naloxone programmes effective? Systematic review utilizing application of the Bradford Hill criteria. *Addiction*. 2016;111(7):1177-87.
4. Giglio RE, Li G, DiMaggio CJ. Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis. *Injury epidemiology*. 2015;2(1):10.
5. Tobin K, Clyde C, Davey-Rothwell M, Latkin C. Awareness and access to naloxone necessary but not sufficient: Examining gaps in the naloxone cascade. *The International journal on drug policy*. 2018;59:94-7.
6. Zandoni BC, Mayer KH. The adolescent and young adult HIV cascade of care in the United States: exaggerated health disparities. *AIDS patient care and STDs*. 2014;28(3):128-35.
7. Cicero TJ, Ellis MS. Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States: Lessons Learned From OxyContin. *JAMA psychiatry*. 2015;72(5):424-30.
8. Cicero TJ, Ellis MS, Kasper ZA. A tale of 2 ADFs: differences in the effectiveness of abuse-deterrent formulations of oxycodone and oxycodone extended-release drugs. *Pain*. 2016;157(6):1232-8.
9. Ellis MS, Kasper ZA, Cicero TJ. Twin epidemics: The surging rise of methamphetamine use in chronic opioid users. *Drug and alcohol dependence*. 2018;193:14-20.
10. Cicero TJ, Ellis MS, Kasper ZA. Increases in self-reported fentanyl use among a population entering drug treatment: The need for systematic surveillance of illicitly manufactured opioids. *Drug and alcohol dependence*. 2017;177:101-3.
11. Iwanicki JL, Severtson SG, McDaniel H, Rosenblum A, Fong C, Cicero TJ, et al. Abuse and Diversion of Immediate Release Opioid Analgesics as Compared to Extended Release Formulations in the United States. *PloS one*. 2016;11(12):e0167499.
12. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological)*. 1995;57(1):289-300.
13. Glickman ME, Rao SR, Schultz MR. False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *Journal of clinical epidemiology*. 2014;67(8):850-7.

# Appendix A

## Data Management

**Opioid Treatment Program:** The American Association for the Treatment of Opioid Dependence and Rocky Mountain Poison & Drug Safety work collaboratively to manage data collection from patients admitted to opioid treatment programs nationwide. The opioid treatment programs submit completed surveys to the project coordinator at Washington University at St. Louis (WUSTL). Incoming surveys are manually logged to represent the number of surveys received from each study site, each week. To protect subject confidentiality, all information is housed in a locked office that is limited to access by study personnel. Data entry occurs at WUSTL. All data are entered using dual data entry and are audited for accuracy. A random sample of surveys undergoes an audit each quarter by RMPDS staff to ensure accurate data entry.

**Survey of Key Informants' Patients Program:** The Survey of Key Informants' Patients Program is conducted by WUSTL. The project manager or designee at WUSTL mails hard copies of questionnaires to the Key Informants who have opted to enlist their patients to complete the questionnaire. WUSTL maintains completed questionnaires. Upon receipt of completed questionnaires, each questionnaire is logged in the Key Informants' binder, indicating date received. Data are then entered into the database using dual data entry and verified for accuracy using similar procedures as for the Opioid Treatment Program.

## Institutional Review Board Approval

**Opioid Treatment Program:** The protocol was originally approved on 11 May 2004 by the Institutional Review Board at the National Development & Research Institute with the most recent authorization provided on 10 March 2021 by Colorado Multiple Institutional Review Board.

**Survey of Key Informants' Patients Program:** The protocol was originally approved on 28 September 2006 by the WUSTL Human Research Protection Office, with the most recent authorization provided on 12 April 2021.