FACTORS ASSOCIATED WITH PREHOSPITAL NALOXONE USE

By

Benjamin W. Hatten

A THESIS

Presented to the Department of Public Health & Preventive Medicine
and the Oregon Health & Science University
School of Medicine
in partial fulfillment of
the requirements for the degree of

Master of Public Health

May 2013

Department of Public Health and Preventive Medicine

School of Medicine

Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's thesis of

Benjamin W Hatten

has been approved

Mentor/Advisor

Member

Member

Member

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To my wife Alyson and my daughter Clara for their support and patience

To my thesis committee for guidance and input

To N. Clay Mann and Mengtao Dai for their assistance with the dataset

ABSTRACT

Objectives: (1) Describe prehospital use of naloxone in the United States in 2010.

(2) Identify county level EMS and sociodemographic predictors of prehospital naloxone use.

(3) Generate profiles of low, medium, and high risk counties.

Methods: A 2010 national EMS database (NEMSIS) was joined to multiple sociodemographic databases. A negative binomial regression model was built to identify the most prominent predictors of prehospital naloxone use at the county level. Example risk profiles were produced for low, medium, and high risk counties.

Results: Naloxone was administered at a rate of 7.71 naloxone uses per 1000 scene calls for the year 2010. County level risk factors identified were lack of health insurance, median household income, receiving disability benefits, infant deaths, census division, EMS scene location at home, EMS complaint of cardiac arrest or death, median age of EMS patients, EMS patients transported, EMS use of antiemetics, EMS response time, and EMS scene time. Protective factors identified were EMS patients of black race, median patient age, and time from EMS call to dispatch of ambulance.

Conclusions: There is wide county level variation in the use of naloxone. County level EMS, sociodemographic, and geographic variables are important predictors of naloxone use.

Introduction

Poisoning is now the leading cause of injury death in the United States, largely driven by an increase in drug related death due to prescription opioid use(1-8). Obvious cases of respiratory arrest due to opioids and sedative/hypnotics are generally correctly identified as drug related by the medical examiner (ME), but the death may not be recorded as drug related in less clear cases(9). In addition, there is emerging evidence that opioids may increase the rate of sudden death due to dysrhythmia through direct effects on the heart and through worsened sleep apnea/hypopnea resulting in dysrhythmia(10-12). Furthermore, the role of opioids as contributing factors to respiratory failure in patients with co-morbid pulmonary disease or sleep apnea remains unclear(13-19). Finally, numerous studies have documented the large burden of substance use and abuse in cases of traumatic injury(20-28). For all of these reasons, the true contribution of opioids to sudden death is almost certainly underestimated with current epidemiologic methods.

Although the scope of the problem is large, little research has been conducted to describe the epidemiology of drug related death on a national scale. Factors associated with drug related death that have been identified include: demographics(1, 2), opioid dose(3, 4, 29, 30), specific opioids(11, 31), nonmedical use of opioids(5), use of multiple substances(32-34), use of powder cocaine(35), homelessness(31), overdose in abandoned building(35), recent participation in a drug rehabilitation program(31), treatment with oral naltrexone(36), and poor baseline state of health(37-40). However, these studies are limited by a focus on specific segments of the population, restriction of the analysis to certain substances, or examining a particular geographic study area. In addition, they have focused on patient level characteristics rather than social and community factors associated with death. This gap in knowledge is particularly important given that the primary cause of drug related death has shifted from street drugs to prescription opioids. Finally, there is no reliable and timely surveillance system that reflects rapidly shifting patterns of drug related death.

Opioids are substances that serve as agonists at specific opioid receptors in the human body. “The *sine qua non* of opioid intoxication is respiratory depression” due to the effects of mu opioid receptor agonism(41). Naloxone is a competitive mu opioid receptor antagonist that rapidly reverses opioid effects(41). It may be administered intravenously, intramuscularly, intranasally, subcutaneously, or through an inhaled route. Use of naloxone is indicated when respiratory depression occurs in the setting of opioid use(41). It is considered an essential medication in EMS organizations that have the capability to administer advanced therapies and has been routinely given for decades in most paramedic based EMS systems (42).

Naloxone use has been evaluated as a proxy for opioid overdose in epidemiologic and public health research. In the US, a single study from Rhode Island estimated opioid overdoses based on episodes of naloxone administration(43). However, additional research has occurred in Australia, where naloxone use has served as a marker for heroin overdose(44-48). Given that there are no physiologic difference between heroin and other opioid use, naloxone use by EMS could serve as a real time measure of opioids overdoses. It is unclear how the epidemiology of opioid overdose and naloxone use has changed as prescription opioid abuse has become widespread. To date, there are no studies examining patterns of prehospital naloxone use on a national level.

In this study, we describe the current distribution of naloxone use, identify county level sociodemographic and EMS system factors associated with prehospital naloxone use, and develop representative models of low, medium, and high-risk counties.

Methods

This is an ecological study analyzing a prospectively collected cohort to answer the question:

"What county-level factors are associated with prehospital naloxone use in the US?"

The National Emergency Medical Services Information System (NEMSIS) is a national registry of EMS calls supported by the National Highway Traffic Safety Administration (NHTSA). The goal of NEMSIS is to "standardize clinical information collected by EMS rescuers when responding to emergency calls and to develop an aggregate data set encompassing EMS data from every US state and territory" (49). It is the only national, comprehensive database of all US EMS calls. Medication administration is one of the standardized reporting fields in NEMSIS.

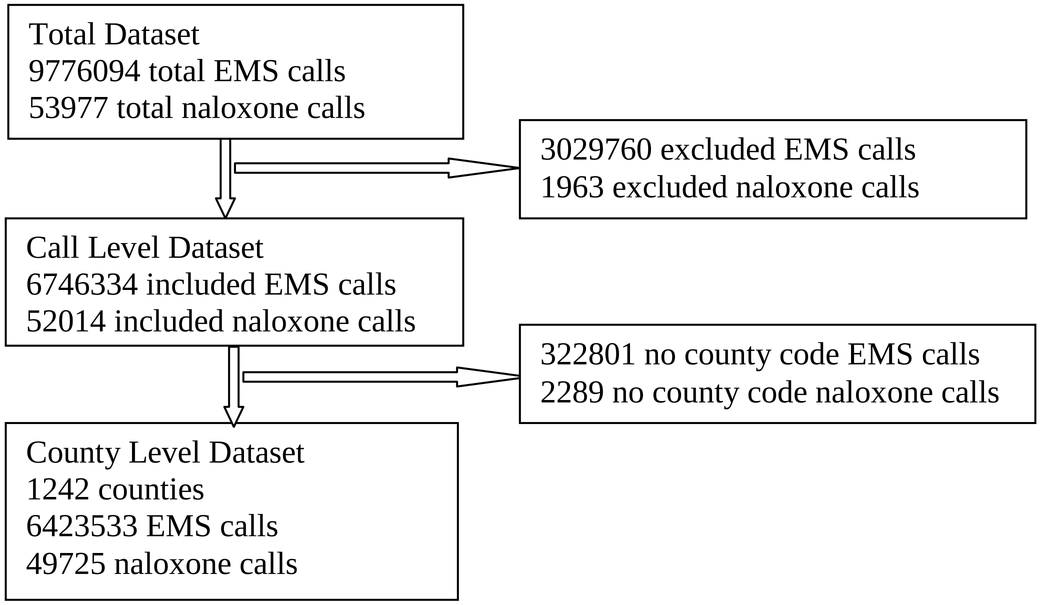
The NEMSIS dataset is a relatively unexplored resource for analysis of prehospital treatment. The cohort analyzed in this project is a customized version of the 2010 NEMSIS dataset. It is estimated that the 2010 dataset includes 25-40% of all US EMS calls (50-52). It contains call level data on 9,776,094 calls out of an estimated 17-28 million total EMS calls in the US in 2010. NEMSIS utilizes a standardized reporting system with participating EMS agencies in 29 states. These EMS agencies upload all calls received into the system. Medication administration is one of the required reporting fields in NEMSIS. In 2010, naloxone was administered during 53,977 calls. NEMSIS also provides details of the ambulance service that responds to the call, but does not provide county level or EMS system level data. Given that EMS jurisdiction in the US is often at the county level, we aggregated EMS calls in the 2010 database by county to allow for modeling of county level use of naloxone with sociodemographic variables and

EMS system characteristics. In addition, antiemetic use was examined as a proxy for the likelihood of medication administration by the EMS system because of the widespread use of antiemetics for a variety of indications.

In order to obtain county level sociodemographic data, publically available datasets were merged by the NEMSIS administration by EMS scene location to the county data. The public datasets included in the analysis were the US Census, American Community Survey, Bureau of Labor Statistics-Current Population Survey/Local Area Unemployment Statistics, Federal Bureau of Investigation Uniform Crime Reporting, Social Security Administration, National Center for Health Statistics, American Medical Association Physician Masterfile, Behavioral Risk Factor Surveillance System, Health Resources and Services Administration Area Resource File, and the North American Industry Classification System. When raw counts by county were reported, rates were generated using the Census 2010 county population as the denominator. Each factor was then divided into deciles, and the individual county level value was replaced with an ordinal value between 1 and 10. County predictor variables were then divided into deciles and matched to the NEMSIS ID and a random county identifier by the NEMSIS staff. In addition, a unique identifier was created for each unique county pattern in order to allow aggregation of EMS calls by county. Counties with less than 200 events were not assigned a county identifier. These steps were required so that the dataset released for analysis did not contain a pattern of identifiers that could identify a single subject or particular EMS system and remain in compliance with the state IRB restrictions covering the NEMSIS dataset.

Cases were defined as EMS calls where naloxone was administered. Cases were counted once even if naloxone is used more than once in a call. Only EMS scene calls where a patient encounter occurred were included. Calls where the call was for inter-facility transport, if the call was canceled, or no patient was found were excluded. For the county level analysis, calls without a location identifier recorded were excluded. The flowsheet of patient exclusions is represented in figure 1. Included and excluded calls for the county level analysis were compared on each predictor and outcome variable and both groups were similar.

Figure 1: Flowsheet of study cohort inclusion and exclusion



A large number of potential county level sociodemographic and EMS system predictors of prehospital naloxone use were considered. The county was the unit of analysis. A negative binomial regression model was built with naloxone use as the count and the number of EMS calls in the county as the population offset. Predictors were collapsed to the county level and analyzed in sequential univariate analyses. Univariate negative binomial regression was performed. Predictor variables with a $p<0.2$ were retained for the multivariate analysis. Variable selection occurred using the main effects technique with significance set at $p<0.05$. Regression modeling produced incidence rate ratios (IRR) for the negative binomial regression.

Sensitivity analyses examining EMS and sociodemographic variables separately, using poisson models, and examining decile variables as categorical were performed and were not superior to the final model using AIC and pseudo R squared to compare models. In addition, counties were divided into quartiles by the proportion of calls where naloxone is administered. The highest quartile was compared to the lower 3 quartiles. Binary recursive partitioning techniques using classification and regression tree (CART) software was performed in order to identify likely predictors. In addition, logistic regression models were built using the same binary outcome of highest quartile of naloxone use. None of the alternate models dramatically changed the identified predictors, so final negative binomial regression was retained as the primary model.

Finally, values for the lowest percentile (1st or 99th depending on whether the variable is a risk or protective factor), median percentile (50th), and the highest percentile (1st or 99th depending on whether the variable is a risk or protective factor) were entered into the model to provide concrete examples of various county profiles. All statistical analysis was performed in Stata v11.2.

Results

Naloxone was administered in 52014 of the 6746334 scene calls in 2010. This translates to a rate of 7.71 naloxone uses per 1000 scene calls for the year 2010. When dividing this dataset for the county analysis, the rate was not different between calls included and excluded. Antiemetics were administered in 88545 of the 6746334 scene calls kept for analysis. This translates to a rate of 13.12 antiemetic uses per 1000 scene calls for the year 2010. When examining the number of naloxone uses by county, we found a mean of 40 uses, median of 7 uses, and a range of 0-1796 uses. With regards to the proportion of EMS calls in a county where naloxone was administered, we found a mean of 5.83 per 1000 calls, median of 4.70 per 1000 calls, and a range of 0-24.48 per 1000 calls. Associations between predictor variables and naloxone use are presented in Table 1.

Table 1: Predictor variables and univariate p-values

Variable	Variable Type	Median	Range	Univariate p-value
EMS system factors				
EMS Region where county is located	Categorical	4 regions	-	<0.001
Mean degree of urbanicity for call locations in a county	Categorical	4 levels	-	<0.001
% patient White race	Proportion	91%	0%-100%	0.83
% patient Non-White	Proportion	9%	0%-100%	0.83
% patient American Indian and Alaska Native	Proportion	0%	0%-99%	0.58
% patient Asian	Proportion	0%	0%-37%	0.07
% patient Black and African-American	Proportion	2%	0%-89%	0.11
% patient Native Hawaiian and Pacific Islander	Proportion	0%	0%-23%	0.03
% patient nonidentified race	Proportion	1%	0%-90%	<0.001
% patient Hispanic ethnicity	Proportion	2%	0%-100%	<0.001
% scene home	Proportion	58%	0%-90%	<0.001
% scene outdoors	Proportion	15%	1%-76%	0.85
% scene non-home building	Proportion	6%	0%-67%	<0.001
% scene health care facility	Proportion	17%	0%-95%	<0.001
% patient with respiratory symptoms	Proportion	11%	0%-100%	<0.001
% patient with decreased level of consciousness or altered mental status	Proportion	14%	0%-100%	0.25
% patient with cardiac arrest, respiratory arrest, or death	Proportion	1%	0%-17%	0.01
Median age of patients in a county	Continuous	58	14-81	<0.001
% patient male	Proportion	47%	35%-70%	0.39
% patient treated	Proportion	87%	50%-100%	<0.001
% patient transported	Proportion	81%	0%-100%	0.001
% of calls where an antiemetic is administered	Proportion	1%	0%-20%	<0.001
Median time in seconds from call to dispatch	Continuous	8	0-26	0.003
Median time in minutes from dispatch to scene	Continuous	5	0-26	0.01
Median time in minutes on scene for calls in the county	Continuous	15	0-34	<0.001
Median time in minutes from scene to destination	Continuous	12	0-106	0.16
Median total time in minutes call time for calls in the county	Continuous	54	0-446	<0.001

County level sociodemographic factors		Median decile	Decile values	
Total Population (2010)	Deciles	6	25949-36743	<0.001
Median age years(2010)	Deciles	5	39-40	0.03
% of population under 18 years old (2010)	Deciles	6	23%-24%	0.48
% of population 65 years or older (2010)	Deciles	6	16%-17%	<0.001
% change population 2000 - 2010	Deciles	6	3%-5%	<0.001
Persons per square mile (2010)	Deciles	5	32-45	<0.001
% female population (2010)	Deciles	6	51%-51%	0.34
% White, including Hispanic/Latino (2010)	Deciles	5	85%-89%	<0.001
% White, excluding Hispanic/Latino (2010)	Deciles	5	80%-86%	<0.001
% Black or African American (2010)	Deciles	5	1%-2%	<0.001
% American Indian and Alaska Native (2010)	Deciles	6	0%-1%	<0.001
% Asian (2010)	Deciles	6	1%-1%	<0.001
% Native Hawaiian/Pacific Islander (2010)	Deciles	6	0%-0%	<0.001
% Hispanic or Latino (2010)	Deciles	6	3%-5%	<0.001
% children in single parent households (2006-2010)	Deciles	6	29%-32%	0.02
% >25 at least high school graduate (2005-2009)	Deciles	6	84%-86%	0.06
% >25 high school graduate only (2005-2009)	Deciles	5	35%-36%	0.001
% >25 some college (2005-2009)	Deciles	6	20%-21%	0.58
% >25 bachelors or higher (2005-2009)	Deciles	6	17%-18%	0.35
% >25 bachelors only (2005-2009)	Deciles	6	11%-13%	0.97
% >25 graduate degree (2005-2009)	Deciles	6	5%-6%	0.001
% < 65 without health insurance, (2009)	Deciles	6	18%-20%	<0.001
Median value of specified owner-occupied housing units in dollars (2005-2009)	Deciles	6	102600-116900	<0.001
% Vacant housing units (2010)	Deciles	6	13%-16%	0.69
% Renter-occupied housing units (2005-2009)	Deciles	5	20%-21%	0.72
Median household income in 2009 inflation-adjusted dollars (2005-2009)	Deciles	5	39383-41656	0.01

Median household income in dollars (2009)	Deciles	5	38887-41040	0.04
% Households with cash public assistance income (2005-2009)	Deciles	6	2%-2%	0.49
% Households with Food Stamp/SNAP benefits (2005-2009)	Deciles	6	9%-10%	0.54
Per capita income in 2009 inflation-adjusted dollars (2005-2009)	Deciles	5	20460-21502	0.18
% below poverty level (2009)	Deciles	6	15%-17%	0.31
% below poverty level (2005-2009)	Deciles	6	15%-16%	0.85
% foreign-born (2005-2009)	Deciles	6	2%-3%	<0.001
% not a U.S. citizen (2005-2009)	Deciles	6	1%-2%	<0.001
% over 18: Veterans (2005-2009)	Deciles	6	11%-12%	0.16
% unemployed (2010)	Deciles	5	8%-9%	<0.001
Violent crime rate per 100000 (2008)	Deciles	6	188-238	<0.001
Property crime rate per 100000 (2008)	Deciles	6	1860-2197	<0.001
% over 18: Social security recipients (2010)	Deciles	6	29%-30%	0.01
% over 18: Social security retirement recipients (2010)	Deciles	6	18%-19%	<0.001
% over 18: Social security disability recipients (2010)	Deciles	6	4%-5%	0.03
Births per 1,000 population (2007)	Deciles	6	13%-14%	0.32
Deaths per 1,000 population (2007)	Deciles	6	10%-11%	<0.001
Infant deaths per 1,000 live births (2007)	Deciles	6	6%-7%	<0.001
Motor vehicle crash death rate per 100,000 (2002-2008)	Deciles	6	23-36	0.45
Physicians per 100000 (2009)	Deciles	6	101-128	0.04
% adults obese: BMI>=30 (2009)	Deciles	6	31%-31%	<0.001
Liquor stores per 100000 (2006)	Deciles	5	6%-8%	0.004
Census Division where county is located	Categorical	9 divisions	-	<0.001

The final negative binomial regression model identified 13 predictors. 5 were county level sociodemographic factors and 8 were EMS system factors. Risk factors for naloxone administration included higher rates of uninsured, higher median household income, higher rates of disability benefits, higher infant mortality rate, specific regions of the country, higher proportion of calls where the scene was a home, higher proportion of calls where chief complaint was cardiac arrest or death, higher proportion of calls transported, higher rates of antiemetic administration, longer response time interval, and longer scene time. Protective factors were a higher proportion of patients of black race, higher patient median age, and a longer median time from initial call until an ambulance was dispatched. Table 2 is a detailed presentation of the final model results.

Table 2: Final negative binomial regression model

Variable (deciles from county sociodemographic data)	IRR	95%CI	P value
<65 no health ins - % (2009)	1.03	1.01, 1.06	0.01
Median household income (2005-2009)	1.08	1.05, 1.10	<0.001
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.06	1.04, 1.09	<0.001
Infant deaths per 1,000 live births (2007)	1.03	1.02, 1.05	<0.001
Census Division			<0.001
0 – New England	-	-	-
1 - W North Central	1.26	0.95, 1.67	0.10
2 – E South Central	1.62	1.19, 2.22	0.002
3 – E North Central	1.65	1.22, 2.22	0.001
4 – W South Central	1.66	1.22, 2.27	0.001
5 – Middle Atlantic	2.11	1.42, 3.12	<0.001
6 – Pacific	2.32	1.63, 3.29	<0.001
7 – Mountain	2.36	1.73, 3.22	<0.001
8 – South Atlantic	2.44	1.82, 3.27	<0.001
Variable (EMS variables)			
Black - 10% of calls	0.93	0.90, 0.96	<0.001
Home scene location - 10% of calls	1.10	1.05, 1.15	<0.001
Complaint cardiac arrest or death - 1% of calls	1.11	1.06, 1.17	<0.001
Median age – years	0.98	0.97, 0.99	<0.001
Transported – 10% of calls	1.12	1.07, 1.17	<0.001
Antiemetic administered - 1% of calls	1.08	1.06, 1.10	<0.001
Median time from call to dispatch – seconds	0.91	0.88, 0.94	<0.001
Median call to scene time – minutes	1.06	1.03, 1.10	0.001
Median time on scene – minutes	1.04	1.02, 1.06	<0.001

Finally, profiles of hypothetical lowest risk, medium risk, and highest risk counties were developed. These were generated to provide a more interpretable picture of the county and EMS level factors. Values for the lowest percentile, median percentile, and highest percentile were inserted into the model in order to generate IRR's for each specific profile. We see that the IRR for the lowest risk county is 0.05, medium risk county is 7.78, and highest risk county is 907.88. This data is presented in detail in table 3.

Table 3: Low, medium, and high risk county profiles

	Low (1st percentile)		Medium (50th percentile)		High (99th percentile)	
Variable	IRR	Value	IRR	Value	IRR	Value
<65 no health ins - % (2009)	1.03	3%-11%	1.22	18%-20%	1.39	26%-43%
Median household income (2005-2009)	1.08	$18869-$31478	1.44	$39383-$41656	2.09	$57126-$113313
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.06	0%-2%	1.45	4%-5%	1.86	7%-17%
Infant deaths per 1,000 live births (2007)	1.03	0	1.22	6-7	1.39	15-333
Census Division	1.00	New England	1.66	W South Central	2.44	South Atlantic
Black – per 10% of EMS patients	0.57	78%	0.98	2%	1.00	0%
Home scene location – per 10% of calls	1.12	13%	1.69	58%	2.08	80%
Complaint cardiac arrest or death – per 1% of calls	1.00	0%	1.15	1%	1.66	5%
Median age – years	0.19	75	0.27	58	0.43	38
Transported – per 10% of calls	1.55	39%	2.50	81%	3.10	100%
Antiemetic administered – per 1% of calls	1.00	0%	1.06	1%	2.38	11%
Median time from call to dispatch – seconds	0.15	18 sec	0.43	8 sec	0.66	4 sec
Median call to scene time – minutes	1.15	2 min	1.42	5 min	2.90	15 min
Median time on scene – minutes	1.41	9 min	1.77	15 min	2.40	23 min
	IRR	95% CI	IRR	95% CI	IRR	95% CI
Total	0.05	0.02-0.13	7.78	3.43-17.63	907.88	304.20-2709.50

Discussion

This analysis provides an initial evaluation of the association between county level sociodemographic and EMS predictors of naloxone use. The negative binomial regression model provided the most informative analysis, and the consideration of multiple sensitivity analyses lends weight to this model. County sociodemographic, geographic, and EMS system factors all appear to be important predictors of naloxone use in this national dataset. Although IRRs are presented for models, it is unclear whether the magnitude of the point estimates are reliable given that this was an exploratory analysis without an a priori test of a predictor. However, the direction and relative importance is meaningful and should be considered when developing future studies. In addition, we recognize that neither EMS nor sociodemographic factors dominate, thus the analysis is valuable to inform both EMS systems and public health agencies with regards to policy.

The study has a number of strengths. First, it offers a novel analysis of prehospital naloxone use on a national scale. Given that substance abuse is enmeshed with social determinants of health, it is essential to include community factors in the analysis. In addition, the findings apply to both EMS system leaders and public health policy professionals. It may provide information for planned preventative EMS system or county level interventions. Finally, in the future, we plan to use this data set to develop multiple follow up projects, such as a multilevel model that integrates individual call level data, and a propensity score based effectiveness analysis.

There are also a number of potential limitations. Because NEMSIS relies on prehospital providers to enter data, there is always the possibility that the data points were incorrectly entered resulting in misclassification. However, there is no reason to think that this would result in a differential bias. In addition, the large number of cases and nationally representative sample increases confidence in the accuracy of our findings. Furthermore, the type of substance ingested is not recorded in the dataset, so there is no opportunity for providers to misclassify based on type of overdose. Finally, because the administration of naloxone is the only readily available opioid antidote in the field, its use is a valid record of opioid toxicity.

A second potential limitation is the use of county level sociodemographic data rather than more detailed data. Given that there is significant heterogeneity within some counties, we are unlikely to see a differential bias due to the use of county level statistics. In addition, the county level is frequently the smallest unit of analysis where detailed and valid measurements of certain sociodemographic factors are available. It is also the case that a single EMS agency has a single county as its coverage area. We believe that the ecological study design is important to examine community and EMS level factors that may influence prehospital naloxone administration.

A third limitation is the lack of an *a priori* primary predictor. However, this is the case because there is a lack of prior work in this area. As this project is the first national analysis of prehospital naloxone use and the first attempt to integrate county level factors on a national scale into a study of opioid overdoses, it is designed to identify the most prominent predictors through multiple methods. Fortunately, the large size of the dataset allows for a traditional analysis using regression models and a decision tree analysis using CART technique. We have a high degree of confidence in our findings identified through the combination of these methods.

Finally, the study period is limited to the 2010 calendar year. It is possible that naloxone use and opioid overdose patterns are not stable in each locale over time. However, given the national scale of the study, small regional variations should balance out. Nevertheless, ongoing surveillance and validation in a future time period will be necessary to ensure that the factors identified through the 2010 dataset are stable.

This project is both intrinsically valuable and offers a sound foundation for future projects. It is the first national study of prehospital naloxone use in the US. This study is important to assess current patterns of prehospital naloxone use. In addition, it is the first national US study of factors associated with opioid overdose. Given that naloxone use approximates the number of opioid overdoses, this type of analysis provides insight into community factors associated with opioid toxicity. Finally, examining factors associated with use serves as the first step in generating a multilevel model and an eventual propensity score to compare outcomes in future analysis of the dataset.

Conclusion

There is a wide degree of county to county variation in prehospital naloxone use. Both EMS and sociodemographic factors appear to serve as predictors of naloxone administration. Further research is required to assess the value of these observations with respect to county level prevention strategies.

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APPENDIX 1

Title

Factors associated with prehospital naloxone use

Investigators

Benjamin Hatten – Principal Investigator

<u>Thesis Committee</u>

Craig Newgard – Primary Mentor

Rochelle Fu – Biostatistics Mentor

Mohamud Daya – Content Mentor

Rob Hendrickson – Content Mentor, External Member

Abstract

<u>AIMS</u>

1. To examine the epidemiology, clinical features, and outcomes in cases of prehospital naloxone use

2. To examine county level predictors of high rates of prehospital naloxone use

<u>RATIONALE</u>

Poisonings have recently surpassed motor vehicle crashes as the leading cause of injury death. This epidemic has primarily been driven by an increase in prescription opioid related deaths. Little is known about the changing geographic distribution of drug related death, although the limited evidence available suggests that communities with a

history of few opioid related deaths are now seeing a dramatic increase. The antidote for opioid toxicity is the opioid receptor antagonist, naloxone. It is a standard medication used by Emergency Medical Services (EMS) systems in the United States (US). Given this, naloxone use has been suggested as a proxy for opioid overdose, but there are no large studies of prehospital naloxone use in the US.

DESIGN AND METHODS

This is an ecological study analyzing data from a prospectively collected cohort. A large number of potential predictors of prehospital naloxone use will be considered. The analysis will employ poisson and negative binomial regression models in order to identify predictors of naloxone use with county as the unit of analysis. The models will be built for EMS system factors, sociodemographic factors, and a combination of all factors.

SIGNIFICANCE

This study is the first large scale study of prehospital naloxone use in the US. It is important to assess in what circumstances naloxone is being administered in the field and identify predictors of its use. In addition, it is the first study of community and EMS factors associated with opioid overdose in the US. Given that naloxone use approximates the relative number of opioid overdoses, this type of analysis will provide insight into county level factors associated with opioid toxicity.

Lay Summary

This is a national study of the use of naloxone, the primary antidote for suspected or known opioid overdose, by providers outside of the hospital. It will describe the current patterns of use by county. In addition, it will identify the sociodemographic and EMS system factors associated with its use.

Specific Aims

Research Question: What are the county level factors associated with prehospital naloxone use in the US?

Background and Rationale:

Poisonings have recently surpassed motor vehicle crashes as the leading cause of injury death. This epidemic has primarily been driven by an increase in prescription opioid related deaths. The antidote for opioid toxicity is the opioid receptor antagonist, naloxone. It is a standard medication used across Emergency Medical Services (EMS) systems in the United States (US). Naloxone use has previously been identified as a proxy for opioid overdose.

The National Emergency Medical Services Information System (NEMSIS) is the first national registry of prehospital events. Participating EMS systems report clinical and demographic data in a standardized fashion. Over 9 million EMS calls from throughout the US were recorded in 2010. To date, we are not aware of large studies of prehospital naloxone use, reports describing the epidemiology of naloxone use in the US prehospital setting, or analyses of national county level factors associated with opioid overdose.

The aims of this study are:

1. To examine the epidemiology, clinical features, and outcomes in cases of prehospital naloxone use by:

a. Describing the distribution, clinical features and outcomes of calls where naloxone was administered.

b. Describing the county level sociodemographic factors and county level EMS factors in calls where naloxone was administered.

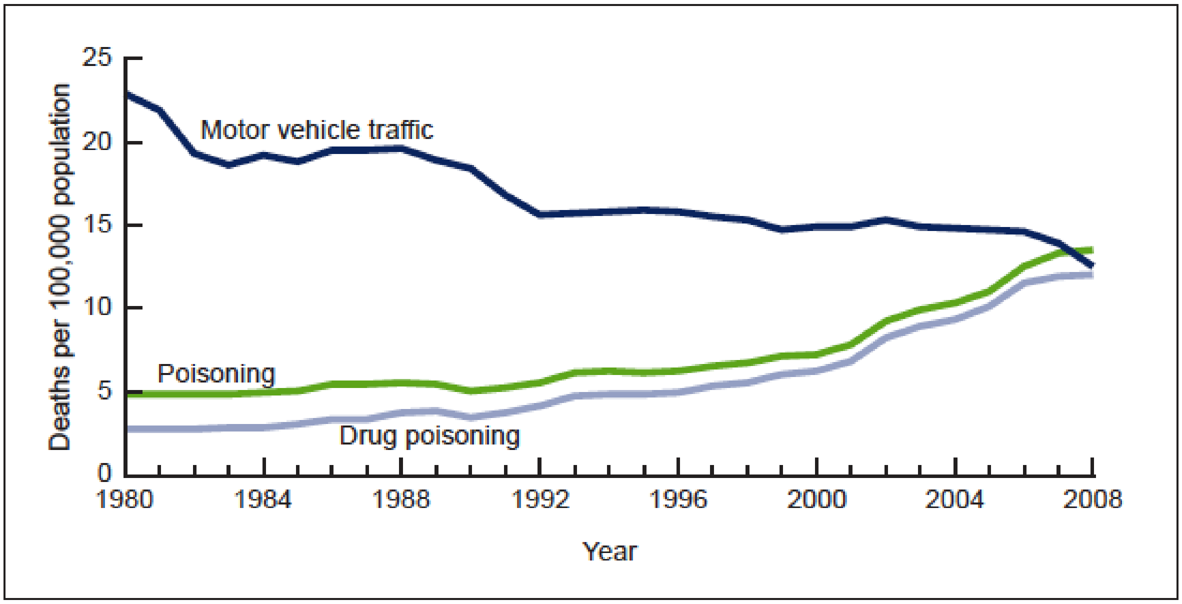
2. To examine county level sociodemographic and EMS system factors associated with prehospital naloxone use by:

a. Aggregating the NEMSIS dataset by county.

b. Generating count based models – both poisson and negative binomial regression models. Models will be built for county sociodemographic factors alone, EMS system factors alone, and combined analyses including both county sociodemographic and EMS system factors.

This study will examine the patterns of use, outcomes, and the epidemiology of prehospital naloxone use. It will also provide analysis of county level factors associated with opioid overdose throughout the US, with prehospital naloxone use serving as a proxy. Finally, the analysis of county level factors will be the first step in generating a multilevel model for prehospital naloxone use.

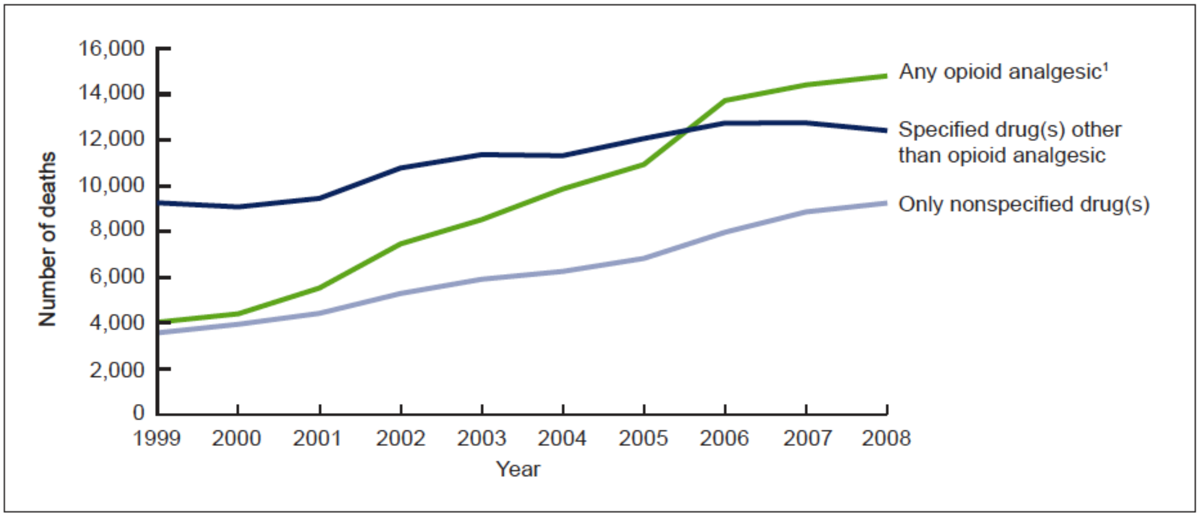
Background



NOTE: In 1999, the *International Classification of Diseases, Tenth Revision (ICD–10)* replaced the previous revision of the ICD (ICD–9). This resulted in approximately 5% fewer deaths being classified as motor-vehicle traffic–related deaths and 2% more deaths being classified as poisoning-related deaths. Therefore, death rates for 1998 and earlier are not directly comparable with those computed after 1998. Access data table for Figure 1 at http://www.cdc.gov/nchs/data/databriefs/db81_tables.pdf#1.
SOURCE: CDC/NCHS, National Vital Statistics System.

(1)

Poisoning is now the leading cause of injury death in the United States, largely driven by an increase in drug related death due to prescription opioid use(1-8). Obvious cases of respiratory arrest due to opioids and sedative/hypnotics are generally correctly identified as drug related by the medical examiner (ME), but the death may not be recorded as drug related in less clear cases(9). In addition, there is emerging evidence that opioids may increase the rate of sudden death due to dysrhythmia through direct effects on the heart and through worsened sleep apnea/hypopnea resulting in frequent arrhythmia(10-12). Furthermore, the role of opioids and sedative hypnotics as contributing factors to respiratory failure in patients with comorbid pulmonary disease or sleep apnea is unclear(13-19). Finally, numerous studies have documented the large burden of substance use and abuse in cases of traumatic injury(20-28). For all of these reasons, the true contribution of opioids to sudden death is almost certainly underestimated in current epidemiologic methods. Even with this uncertainty in the data, opioid toxicity is recognized as one of the most pressing public health problems facing the country.



[1]Opioid analgesics include natural and semi-synthetic opioid analgesics (for example, morphine, hydrocodone, and oxycodone) and synthetic opioid analgesics (for example, methadone and fentanyl). Some deaths in which the drug was poorly specified or unspecified may involve opioid analgesics.
NOTES: Drug categories are mutually exclusive. Access data table for Figure 3 at http://www.cdc.gov/nchs/data/databriefs/db81_tables.pdf#3.
SOURCE: CDC/NCHS, National Vital Statistics System.

(1)

Although the scope of the problem is large, little research has been conducted to describe the epidemiology of drug related death. Factors associated with drug related death that have been identified include: demographics(1, 2), opioid dose(3, 4, 29, 30), specific opioids(11, 31), nonmedical use of opioids(5), use of multiple substances(32-34), use of powder cocaine(35), homelessness(31), overdose in abandoned building(35), recent drug rehabilitation program(31), treatment with oral naltrexone(36), and poor baseline state of health(37-40). However, these studies are limited by a focus on specific segments of the population, restriction of the analysis to certain substances, or examining a particular geographic study area. In addition, they have tended to focus exclusively on patient level characteristics rather than social and community factors associated with death. This gap in knowledge is particularly important given that the primary cause of drug related death has shifted from street drugs to prescription opioids.

Finally, there is no reliable and timely surveillance system that reflects rapidly shifting patterns of drug related death.

Opioids are substances that serve as agonists at specific opioid receptors in the human body. “The *sine qua non* of opioid intoxication is respiratory depression” due to the effects of mu opioid receptor agonism(41). Naloxone is a competitive mu opioid receptor antagonist that reverses opioid effects(41). It is rapidly active when given intravenously, intramuscularly, intranasally, subcutaneously, or through an inhaled route. Use of naloxone is indicated when respiratory depression occurs in the setting of opioid use(41). It is considered an essential medication in EMS organizations that have the capability to administer advanced therapies and has been routinely given for decades in most paramedic based EMS systems (42).

Naloxone administration as a treatment in cardiac arrest is not recommended by current guidelines(43). Nevertheless, it is occasionally administered in both drug related and non-drug related arrest with mixed clinical effects(44-47). There are human and animal studies that suggest a potential increase in vascular tone and increase in return of spontaneous circulation when given, particularly in cases of opioid toxicity associated with cardiac arrest(45-47). The aforementioned beneficial effects are not consistent; thus, there is insufficient evidence to recommend the routine use of naloxone in cardiac arrest at this time(43, 44). National patterns of naloxone administration in cardiac arrest have not been described.

Finally, naloxone use has been employed as a proxy for opioid overdose in epidemiologic and public health research. In the US, there was a single study in Rhode

Island where opioid overdoses were estimated by naloxone administration(48). However, the bulk of this research occurred in Australia, with naloxone use serving as a marker for heroin overdose(49-53). There is no physiologic difference in heroin use and other opioid use, so naloxone use will be a good marker for all types of opioids. It is unclear how the epidemiology of opioid overdose and naloxone use has changed as prescription opioid abuse has become widespread. To date, there are no studies examining patterns of prehospital naloxone use on a national level.

The National Emergency Medical Services Information System (NEMSIS) is a national registry of EMS calls supported by the National Highway Traffic Safety Administration (NHTSA). The goal of NEMSIS is to “standardize clinical information collected by EMS rescuers when responding to emergency calls and to develop an aggregate data set encompassing EMS data from every US state and territory” (54). It is the only national, comprehensive database of all US EMS calls. The number of states reporting to NEMSIS has been expanding, with the majority of states contributing in 2010. Medication administration is one of the standardized reporting fields in NEMSIS.

Significance

This project is both intrinsically valuable and offers a sound foundation for future projects. It is the first national study of prehospital naloxone use in the US. This study is important to assess current patterns of prehospital naloxone use. In addition, it is the first national US study of factors associated with opioid overdose. Given that naloxone use approximates the number of opioid overdoses, this type of analysis will provide insight into community factors associated with opioid toxicity. Finally, examining factors associated with use will serve as the first step in generating a multilevel model and an eventual propensity score to compare outcomes in future analysis of the dataset.

Preliminary Studies

The NEMSIS dataset is a relatively unexplored resource for analysis of prehospital treatment. Articles discussing the design of NEMSIS and descriptions of the data have been published, with an estimated coverage of 25-40% of all US EMS calls included in the 2010 dataset(55, 56). A 2011 article examined prehospital airway management on a national scale using this database(57). One of the authors on these projects, N. Clay Mann, is the coordinator of NEMSIS. He is providing the custom version of the NEMSIS dataset for the proposed project.

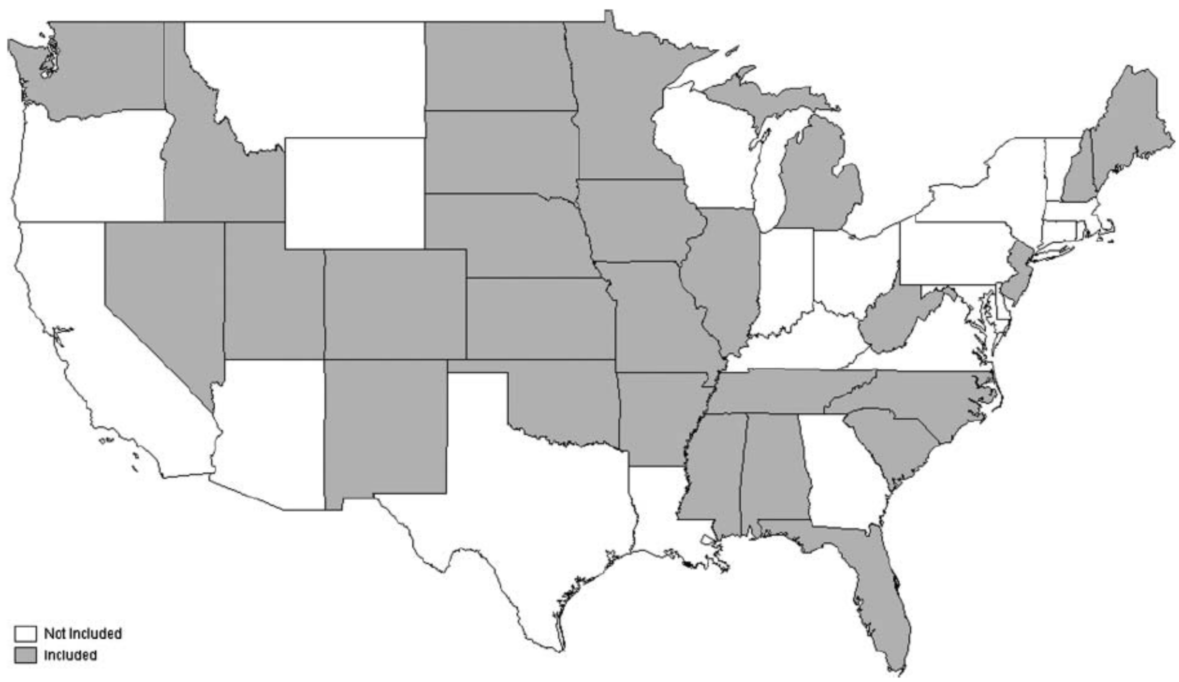


FIGURE 1. States contributing data to the National Emergency Medical Services Information System (NEMSIS) 2010 data set. Alaska and Hawaii also contributed data to NEMSIS. Boxes and borders indicate U.S. Census regions.

Methods

Overview

The proposed study is an ecological study derived from a prospectively collected cohort to answer the specific question:

"What county-level factors are associated with prehospital naloxone use in the US?"

It will utilize the National Emergency Medical Services Information System (NEMSIS) 2010 dataset. This is the first national registry of prehospital events and provides a national lens to examine this question. In this study, we will describe the current epidemiology of naloxone use and identify sociodemographic and EMS system factors associated with prehospital naloxone use.

Study subjects/selection criteria

A. NEMSIS

The cohort being analyzed in this project is the 2010 NEMSIS dataset. It is the only national, comprehensive database of US EMS calls. It contains call level data on 9,776,094 million calls out of an estimated 17-28 million total calls in US in 2010. NEMSIS utilizes a standardized reporting system with participating EMS agencies in 29 states. These EMS agencies upload all calls received into the system. Medication administration is one of the required reporting fields in NEMSIS. In 2010, naloxone was administered during 53,977 calls. NEMSIS also provides details of the ambulance service that responds to the call, but does not provide county level or EMS system level data. It also reports treatment provided prior to the EMS response. The majority of EMS systems cover an entire county. We will aggregate EMS calls by county to serve as a proxy for EMS system level variables. Complete information on NEMSIS reporting and the NEMSIS dataset is available at: http://www.nemsis.org/.

B. US Census

The US Constitution mandates that the government count each resident and that this enumeration will occur every 10 years. It is conducted by a federal government agency, the US Census Bureau. The US Census is widely considered the benchmark measure of population and demographics in the US. Data by county from the 2010 census was accessed through the American Factfinder website: http://factfinder2.census.gov and the USA Counties website: http://www.census.gov/support/USACdataDownloads.html#SPR. Additional background and detailed methodology regarding the US census are available at: http://2010.census.gov.

C. American Community Survey (ACS)

The ACS is conducted yearly by the US Census Bureau to provide information regarding the social and economic issues in the community. This survey provides well-accepted estimates for a variety of detailed community level factors. Data by county from 2006-2010 was accessed through the American Factfinder website: http://factfinder2.census.gov and the USA Counties website: http://www.census.gov/support/USACdataDownloads.html#SPR. Additional background and detailed methodology regarding the ACS are available at: http://www.census.gov/acs/www/.

D. Bureau of Labor Statistics-Current Population Survey/Local Area Unemployment Statistics (BLS-CPS/LAUS)

The BLS-CPS is a monthly survey conducted by the US Census Bureau for the BLS. Data from this survey is used by the BLS to generate periodic LAUS that estimate unemployment at various geographic subdivisions. Data by county from the 2010 annual LAUS were accessed at the BLS website: http://www.bls.gov/lau/data.htm. Additional background and detailed methodology regarding the BLS-CPS is available at: http://www.bls.gov/cps/. Additional background and detailed methodology regarding the LAUS are available at: http://www.bls.gov/lau/home.htm.

E. Uniform Crime Reporting (UCR)

The Federal Bureau of Investigation aggregates crime statistics from local agencies for the Department of Justice in a standardized fashion. These statistics are made publically available through the UCR program. The UCR program is the sole reliable source of national crime data. Data by county from the 2007-2009 UCR program was accessed at: http://bjs.ojp.usdoj.gov/ucrdata/Search/Crime/Crime.cfm. Additional background and detailed methodology regarding the UCR program are available at: http://bjs.ojp.usdoj.gov/ucrdata/.

F. Social Security Administration (SSA)

The US SSA administers both federal retirement and disability programs. It is the only payer for these programs. Data by county reporting the number of residents in December 2010 receiving SSA benefits was accessed at the USA Counties website: http://www.census.gov/support/USACdataDownloads.html#SPR.

G. National Center for Health Statistics (NCHS)

The NCHS is a branch of the Centers for Disease Control that is charged with compiling national health statistics. It is the repository for national birth and death data. Data by county reporting the number of births, deaths, and infant deaths in 2007 was accessed at the USA Counties website: http://www.census.gov/support/USACdataDownloads.html#SPR. Data by county reporting the years of potential life lost in 2006-2008 and the percent low birth weight births and motor vehicle crash death rate from 2002-2008 were accessed at the NCHS public-use data files website: http://www.cdc.gov/nchs/data_access/ftp_data.htm. Additional background and detailed methodology regarding the NCHS datasets are available at: http://www.cdc.gov/nchs/

H. American Medical Association (AMA)

The AMA maintains the Physician Masterfile. This is a database of all US physicians. Physician address is continuously updated through multiple methods. Data by county reporting the number of physicians with a practice address in that county in 2009 was accessed at the USA Counties website: http://www.census.gov/support/USACdataDownloads.html#SPR. Additional background and detailed methodology regarding the AMA Physician Masterfile are available at: http://www.ama-assn.org/ama/pub/about-ama/physician-data-resources/physician-masterfile.page?.

I. Behavioral Risk Factor Surveillance System (BRFSS)

BRFSS is a national telephone based health survey in existence since 1984. It is administered by the Centers for Disease Control and tracks multiple health conditions and risk behaviors. BRFSS is widely used to study risk factors in the US. Data by county for multiple risk factors from 2004-2010, except obesity (limited to 2009), was accessed at the BRFSS website: http://www.cdc.gov/brfss/technical_infodata/index.htm.

Additional background and detailed methodology regarding BRFSS are available at: http://www.cdc.gov/brfss/.

J. Area Resource File (ARF)

The Health Resources and Services Administration is a branch of the Department of Health and Human Services. It publishes yearly reports that provide county level data aggregated from multiple sources. These sources include the American Medical Association, the American Dental Association, the American Osteopathic Association, the US Census Bureau, the Centers for Medicare and Medicaid Services, Bureau of Labor Statistics, National Center for Health Statistics, and the Veteran's Administration. Data by county reporting the number of primary care physicians with a practice address in that county in 2009 was accessed at the ARF database website: http://arf.hrsa.gov/purchase.htm. Additional background and detailed methodology regarding ARFs are available at: http://arf.hrsa.gov/

K. North American Industry Classification System (NAICS)

NAICS is a database maintained by the US Census Bureau to track businesses in North America. A report is published every 5 years that includes the number of business by type in each county. Data by county reporting an estimate of the number of liquor stores per population using the 2007 NAICS and the 2008 US Census population estimate was accessed through the American Factfinder website: http://factfinder2.census.gov. Additional background and detailed methodology regarding NAICS is available at: http://www.census.gov/eos/www/naics/.

Predictor variables

Variable	Source	Variable Type	Proposed direction of effect: (+) is increased naloxone use and (–) is decreased naloxone use)
EMS system factors			
EMS Region where county is located	NEMSIS	Categorical	(+)/(-): location plays an unclear role
Mean degree of urbanicity for call locations in a county	NEMSIS	Continuous	(+): opioid abuse is traditionally concentrated in urban areas
Proportion of calls in a county where the patient race is White	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is Non-White	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is American Indian and Alaska Native	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is Asian	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is Black and African-American	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is Native Hawaiian and Pacific Islander	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is of another nonidentified race	NEMSIS	Proportion	(+)/(-): race plays an unclear role
Proportion of calls in a county where the patient race is of Hispanic ethnicity	NEMSIS	Proportion	(+)/(-): Hispanic ethnicity plays an unclear role
Proportion of calls in a county where the scene location is a home	NEMSIS	Proportion	(-): only location previously associated with overdose is abandoned building
Proportion of calls in a county where the	NEMSIS	Proportion	(-): only location

scene location is outdoors			previously associated with overdose is abandoned building
Proportion of calls in a county where the scene location is a non-home building	NEMSIS	Proportion	(+): only location previously associated with overdose is abandoned building
Proportion of calls in a county where the scene location is a health care facility	NEMSIS	Proportion	(-): only location previously associated with overdose is abandoned building
Proportion of calls in a county where the patient has respiratory symptoms	NEMSIS	Proportion	(+): respiratory depression is an indication for naloxone
Proportion of calls in a county where the patient has symptoms of a decreased level of consciousness or a altered mental status	NEMSIS	Proportion	(+): naloxone is often given for a decreased level of consciousness
Proportion of calls in a county where the patient has symptoms of cardiac arrest, respiratory arrest, or death	NEMSIS	Proportion	(+): naloxone is sometimes administered during cardiac arrest
Median age of patients in a county	NEMSIS	Continouous	(-): younger age is traditionally associated with opioid abuse
Proportion of calls in a county where the patient is male	NEMSIS	Proportion	(+): males have a higher rate of substance abuse
Proportion of calls in a county where an advanced life support (ALS) EMS unit responds	NEMSIS	Proportion	(+): ALS units will be more likely to use medication
Proportion of calls in a county where the reason is for an injury	NEMSIS	Proportion	(+)/(-): injury plays an unclear role
Proportion of calls in a county where the EMS primary or secondary diagnosis is a respiratory diagnosis	NEMSIS	Proportion	(+): respiratory depression is an indication for

			naloxone
Proportion of calls in a county where the EMS primary or secondary diagnosis is dysrhythmia or cardiac arrest	NEMSIS	Proportion	(+): opioid use is associated with both dysrhythmia and respiratory arrest
Proportion of calls in a county where the EMS primary or secondary diagnosis is drug overdose	NEMSIS	Proportion	(+): naloxone is the antidote for opioid overdose
Proportion of calls in a county where the EMS primary or secondary diagnosis is altered mental status or psychiatric	NEMSIS	Proportion	(+): opioid use results in altered mental status
Proportion of calls in a county where the EMS primary or secondary diagnosis is cardiac or respiratory arrest	NEMSIS	Proportion	(+): opioid use is associated with respiratory arrest
Proportion of calls in a county where the EMS considers the patient in cardiac arrest	NEMSIS	Proportion	(+): opioid use is associated with respiratory arrest
Proportion of calls in a county where the patient is treated	NEMSIS	Proportion	(+): naloxone is a treatment
Proportion of calls in a county where the patient is transported	NEMSIS	Proportion	(+): many patients who require naloxone are transported
Proportion of calls in a county where an antiemetic is administered	NEMSIS	Proportion	(+): antiemetic use is being treated as a surrogate for likelihood of IV medication use
Median time from call to dispatch for calls in the county	NEMSIS	Continouous	(+)/(-): call to dispatch time is likely a function of system efficiency
Median time from dispatch to scene for calls in the county	NEMSIS	Continouous	(+)/(-): dispatch to scene time is likely a function of geographic size and system resources
Median time on scene for calls in the county	NEMSIS	Continouous	(+): increased scene time likely represents increased use

			of interventions
Median time from scene to destination for calls in the county	NEMSIS	Continouous	(+)/(-): scene to destination time is likely a function of geographic size and system resources
Median total call time for calls in the county	NEMSIS	Continouous	(+)/(-): total call time is likely a function of geographic size and system resources. However, large scene times could drive this variable
Proportion of calls in a county where an advanced airway is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression, increasing the need for airway management
Proportion of calls in a county where positive pressure ventilation is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression, increasing the need for airway management
Proportion of calls in a county where an intermediate airway is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression, increasing the need for airway management
Proportion of calls in a county where a basic airway is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression, increasing the need for airway management
Proportion of calls in a county where an any invasive airway is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression,

			increasing the need for airway management
Proportion of calls in a county where an any airway maneuver is attempted	NEMSIS	Proportion	(+): Opioid abuse results in respiratory depression, increasing the need for airway management
Proportion of calls in a county where compressions are attempted	NEMSIS	Proportion	(+): Opioid abuse results can result in arrest
Proportion of calls in a county where defibrillation is attempted	NEMSIS	Proportion	(+): Opioid abuse results can result in arrest
Proportion of calls in a county where pacing is attempted	NEMSIS	Proportion	(+)/(-): Opioid abuse results can result in arrest, but pacing is unlikely to be indicated
Proportion of calls in a county where restraints are employed	NEMSIS	Proportion	(+): Restraints are often used for patients who are intoxicated
County level sociodemographic factors			
Total Population (2010)	US Census	Deciles	(+): More urban areas are traditionally associated with opioid abuse
Median age (2010)	US Census	Deciles	(-): younger age is traditionally associated with opioid abuse
Percent of population under 18 years old (2010)	US Census	Deciles	(+): younger age is traditionally associated with opioid abuse
Percent of population 65 years or older (2010)	US Census	Deciles	(-): younger age is traditionally associated with opioid abuse
Percent change population 2000 - 2010	US	Deciles	(+)/(-): unclear

	Census		how population change is associated with opioid abuse
Population per square mile (2010)	US Census	Deciles	(+): population density is marker of urban area which is where opioid abuse is traditionally concentrated
Percent Urban population (2000)	US Census	Deciles	(+): urban areas are where opioid abuse is traditionally concentrated
Percent Rural population (2000)	US Census	Deciles	(-): urban areas are where opioid abuse is traditionally concentrated
Percent female population (2010)	US Census	Deciles	(-): substance abuse is traditionally associated with male gender
Percent White alone (2010)	US Census	Deciles	(+)/(-): race plays an unclear role
Percent White alone, not Hispanic or Latino (2010)	US Census	Deciles	(+)/(-): race plays an unclear role
Percent Black or African American alone (2010)	US Census	Deciles	(+)/(-): race plays an unclear role
Percent American Indian and Alaska Native alone (2010)	US Census	Deciles	(+)/(-): race plays an unclear role
Percent Asian alone (2010)	US Census	Deciles	(+)/(-): race plays an unclear role(+)/(-): race plays an unclear role
Percent Native Hawaiian and Other Pacific Islander alone (2010)	US Census	Deciles	(+)/(-): race plays an unclear role
Percent Hispanic or Latino population (2010)	US Census	Deciles	(+)/(-): ethnicity plays an unclear role

Percent children in single parent households (2006-2010)	US Census	Deciles	(+): single parent households are used as a surrogate for low SES
Percent >25 at least high school graduate (2005-2009)	ACS	Deciles	(-): higher educational attainment is thought to have inverse relationship to opioid abuse
Percent >25 high school graduate only (2005-2009)	ACS	Deciles	(+): higher educational attainment is thought to have inverse relationship to opioid abuse
Percent >25 some college (2005-2009)	ACS	Deciles	(-): higher educational attainment is thought to have inverse relationship to opioid abuse
Percent >25 bachelors or higher (2005-2009)	ACS	Deciles	(-): higher educational attainment is thought to have inverse relationship to opioid abuse
Percent >25 bachelors only (2005-2009)	ACS	Deciles	(-): higher educational attainment is thought to have inverse relationship to opioid abuse
Percent >25 graduate degree (2005-2009)	ACS	Deciles	(-): higher educational attainment is thought to have inverse relationship to opioid abuse
Persons under 65 years without health insurance, percent (2009)	ACS	Deciles	(+): uninsured may be a

			marker of low SES
Median value of specified owner-occupied housing units (2005-2009)	ACS	Deciles	(+)/(-): increased housing price could be associated with urban areas or could be a marker for increased SES
Percent Vacant housing units (2010)	ACS	Deciles	(+): drug overdoses have been associated with vacant builidings
Percent Renter-occupied housing units (2005-2009)	ACS	Deciles	(+): Renting is associated with lower SES which correlates with increased opioid abuse
Median household income (2005-2009)	ACS	Deciles	(-): Higher SES is thought to correlate with decreased opioid abuse
Median household income (2009)	ACS	Deciles	(-): Higher SES is thought to correlate with decreased opioid abuse
Percent Households with cash public assistance income (2005-2009)	ACS	Deciles	(+): Lower SES is thought to correlate with increased opoid abuse
Percent Households with Food Stamp/SNAP benefits (2005-2009)	ACS	Deciles	(+): Lower SES is thought to correlate with increased opoid abuse
Per capita income (2005-2009)	ACS	Deciles	(-): Higher SES is thought to correlate with decreased opioid abuse
Percent Population below poverty level (2009)	ACS	Deciles	(+): Poverty is thought to correlate with

			increased opioid abuse
Percent Population below poverty level (2005-2009)	ACS	Deciles	(+): Poverty is thought to correlate with increased opioid abuse
Place of birth, foreign-born, percent (2005-2009)	ACS	Deciles	(+)/(-): immigration has an unclear relationship with opioid abuse
Percent: Citizenship status in the United States - not a U.S. citizen (2005-2009)	ACS	Deciles	(+)/(-): immigration has an unclear relationship with opioid abuse
Percent Civilians over 18: Veterans (2005-2009)	ACS	Deciles	(+)/(-): there is emerging evidence that recent veterans have a high rate of substance abuse, but it is not clear how that translates to a population level
Income inequality (GINI) (2010)	ACS	Deciles	(+): increased income inequality is thought to correlate with increased opioid abuse
Unemployment rate (2010)	BLS-CPS/LAUS	Deciles	(+): increased unemployment is thought to correlate with opioid abuse
Violent crime rate (2008)	UCR	Deciles	(+): increased violent crime rate is thought to correlate with opioid abuse
Violent crime rate (2007-2009)	UCR	Deciles	(+): increased violent crime rate is thought to correlate with opioid abuse

Property crime rate (2008)	UCR	Deciles	(+): increased property crime rate is thought to correlate with opioid abuse
Percent Civilians over 18: Social security - benefit recipients (2010)	SSA	Deciles	(+)/(-): unclear relationship between social security benefits and opioid abuse
Percent Civilians over 18: Social security: retired workers - benefit recipients (2010)	SSA	Deciles	(-): retirees tend to be older and less likely to be in the highest opioid abuse group
Percent Civilians over 18: Social security: disabled workers - benefit recipients (2010)	SSA	Deciles	(+): disability status has been associated with increased opioid use
Births per 1,000 population (2007)	NCHS	Deciles	(+)/(-): births may be a marker of a younger population, but the relationship with opioid abuse is unclear
Deaths per 1,000 population (2007)	NCHS	Deciles	(+)/(-): deaths may be a marker of an older population, but the relationship with opioid abuse is unclear
Infant deaths per 1,000 live births (2007)	NCHS	Deciles	(+): infant deaths are often used as a surrogate for low SES and poor health
Premature Death (Years of Potential Life Lost) (2006-2008)	NCHS	Deciles	(+): Premature deaths would be expected to correlate with opioid abuse
Percent low birth weight births (<2500 grams)	NCHS	Deciles	(+): LBW is

(2002-2008)			often used as a surrogate for low SES and poor health
Motor vehicle crash death rate (2002-2008)	NCHS	Deciles	(+)/(-): MVC deaths may be a surrogate for substance abuse or for rural areas
Physicians per 100000 (2009)	AMA	Deciles	(+)/(-): increased physician coverage could result in i increased availability of opioids or increased treatment
Percent inadequate social support (2006-2010)	BRFSS	Deciles	(+): Poor social support would likely correlate with increased opioid use
Percent Fair or Poor health (2004-2010)	BRFSS	Deciles	(+): Poor health would likely correlate with increased opioid use
Average number of physically unhealthy days per month (2004-2010)	BRFSS	Deciles	(+): Poor health would likely correlate with increased opioid use
Average number of mentally unhealthy days per month (2004-2010)	BRFSS	Deciles	(+): Poor health would likely correlate with increased opioid use
Percent adult smoking (2004-2010)	BRFSS	Deciles	(+): Smoking would likely correlate with increased opioid use
Percent adult obesity (BMI>=30) (2009)	BRFSS	Deciles	(+): There is evidence that opioid use increases the severity of

			obstructive sleep apnea which is correlated with obesity
Percent excessive alcohol consumption (2004-2010)	BRFSS	Deciles	(+): Excessive alcohol use would likely correlate with increased opioid use
Primary Care Physician rate per 100000 (2009)	ARF	Deciles	(+)/(-): increased physician coverage could result in i increased availability of opioids or increased treatment
Liquor stores per 10000 (2006)	NAICS	Deciles	(+): liquor store density correlates with low SES and poor health
Census Division where county is located	NEMSIS	Categorical	(+)/(-): location plays an unclear role

When raw counts by county were reported, rates were generated using the Census 2010 county population as the denominator. County predictor variables have been divided into deciles and matched to the NEMSIS ID and a random county identifier by the NEMSIS staff.

<u>Outcome variables</u>

Outcome	Source	Variable Type	Use in which models
Primary			
Count of naloxone uses	NEMSIS	Count	County level Negative Binomial Regression
Highest quartile of proportion of naloxone use	NEMSIS	Binary	County level CART; Logistic Regression

Statistical Issues

Specific Aim 1

To describe the epidemiology, clinical features, and outcomes in cases of prehospital naloxone use.

A. Rationale

To date, the epidemiology of naloxone use in the US prehospital setting has not been reported. It is not known when naloxone is being used, what patients are receiving it, and the characteristics of communities where it is being used.

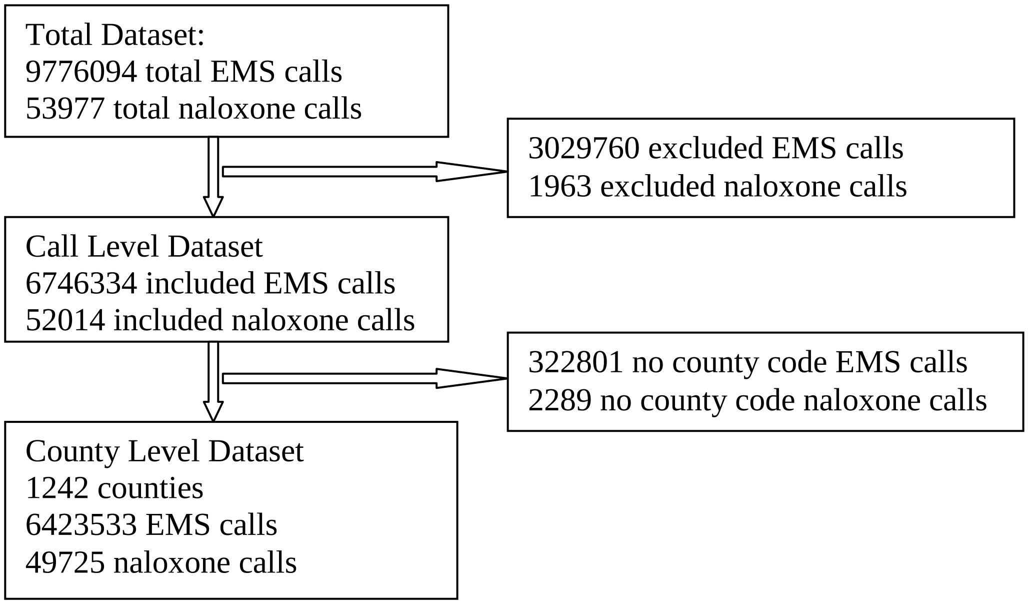
B. Case definition

Cases: EMS calls where naloxone was administered. Cases will only be counted once even if naloxone is used more than once in a call.

Control: All EMS calls in agencies reporting to NEMSIS where naloxone is not used.

C. Exclusion criteria

Only EMS scene calls where a patient encounter occurred will be included. Calls where the call was for inter-facility transport, if the call was canceled, or no patient was found will be excluded. For the county level analysis, calls without a location identifier recorded will be excluded. Included and excluded calls for the county level analysis will be compared on each predictor and outcome variable.



D. Descriptive statistics

Cases and controls will be described in detail. Each predictor variable will be summarized in relation to the outcome (case or control) using means and standard deviations for continuous variables and tabular data for categorical variables. Distributions will also be presented graphically. The proportion of cases in the cohort will be reported as the rate of naloxone use per 10000 prehospital patients. The correlation between decile of prehospital patient count and decile of total population will be reported. Outcomes in the case and control groups will also be reported.

Specific Aims 2

To examine county level sociodemographic and EMS system factors associated with prehospital naloxone use.

A. Statistical analysis plan

This is an ecological study analyzing data from a prospectively collected cohort. A large number of potential county level sociodemographic and EMS system predictors of prehospital naloxone use will be considered. The county will be the unit of analysis for Specific Aim 2. Predictors will be collapsed to the county level. Both a poisson and a negative binomial regression using naloxone use as the count and included EMS calls as the population will be created. The models for EMS system factors will be compared and predictors that are congruent across models will be presented. The process will be repeated for county level sociodemographic factors. Finally, all variables will be included in a final combined model. All 6 models will be presented.

B. Tests of hypotheses

H0: County level EMS and sociodemographic factors in counties with frequent naloxone use do not differ compared to counties with infrequent naloxone use.

H1: County level EMS and sociodemographic factors in counties with frequent naloxone use differ compared to counties with infrequent naloxone use.

ii. Regression models (Poisson and Negative Binomial)

-Univariate analysis: Predictors will be analyzed in sequential univariate analyses. TTests will be used for continuous variables and Chi-squared tests will be used for categorical variables. Predictor variables with a $p<0.2$ will be retained for the multivariate analysis.

-Multivariate analysis: Variable selection will occur using the main effects technique with significance set at $p<0.1$. Potential effect modifiers will be examined by generating interaction terms; those meeting statistical significance ($p<0.1$) will remain in the model and be interpreted. Regression modeling will produce incidence rate ratios for the negative binomial regression.

iii. Model comparison

Models will be compared using AIC and pseudo R Squared.

C. Sensitivity analysis

Counties will be divided into quartiles by the proportion of calls where naloxone is administered. The highest quartile will be compared to the lower 3 quartiles. The initial analysis will employ binary recursive partitioning techniques using classification and regression tree (CART) software in order to identify the most likely EMS system predictors. Simultaneously, a logistic regression model incorporating EMS system factors will be built using the same binary outcome of highest quartile of naloxone use.

Decision trees are classification algorithms, which specify cut points forming a “tree”. Highly specific nodes are then “pruned” in order to produce a more generalizable model. The final nodes represent relatively homogenous individual classes. CART is a specific type of decision tree analysis that produces probabilities for individual nodes. The predictors will be entered into the CART algorithm. A standard 10:1 partition will be performed with one 10% derivation subset and 9 equal validation subsets being formed. The model that best predicts correct classification will be generated in the derivation sample and revised in the validation subsets. Pruning algorithms impact the bias and generalizability of the model. The pruning algorithm will also be adjusted and refined to produce a coherent set of predictors. Both high sensitivity and high specificity models will be built. Such models have been used for analysis lung cancer mortality, smoking relapse, acute myocardial infarction mortality, and sexually transmitted diseases in pregnancy (58-61).

The CART model and regression models will be compared using percent correctly classified and AUC.

Sample size and power

There are 1242 counties and approximately 120 predictor variables. Using a 10:1 ratio of subjects to variables, an adequate sample size is suggested. In addition, given that this is an exploratory study rather than a test of various known predictors, we are primarily limited by the number of relevant predictors.

Quality control and data management

This is a secondary analysis of an existing dataset, so no interim analysis is necessary. Coding is standardized at the time of data entry into the registry. Each EMS call has a unique identifier associated, allowing various portions of the dataset to be merged. Data will be stored on a password protected OHSU network computer and analysis will be performed using Microsoft Excel, CART software, and Stata.

Human Subjects Protections

This project has been determined to be exempt by the OHSU IRB. This is a secondary analysis of publically available datasets. Therefore, it presents negligible risks to patients, as there is no active intervention. In addition, there are no identifiers that would allow subjects to be identified. NEMSIS operates with the approval of multiple state IRB's. Only the NEMSIS administration team has access to patient level data. In order to obtain county level sociodemographic data, publically available datasets were merged by the NEMSIS administration by EMS scene location to the county data. Each factor was then divided into deciles, and the individual county level value was replaced with an ordinal value between 1 and 10. In addition, a unique identifier was created for each unique county pattern in order to allow aggregation of EMS calls by county. Counties with less than 200 events were not assigned a county identifier. These steps were required so that the dataset released for analysis did not contain a pattern of identifiers that could identify a single subject and did not violate any of the state IRB restrictions.

Timeline

	Feb 2013	Mar 2013	Apr 2013	May 2013	Jun 2013	July 2013
Proposal	Committee meeting for approval	Proposal revisions and final submission by PI				
Data cleaning	PI to organize dataset for analysis	PI to perform descriptive analysis of variables and outcomes				
Initial CART analysis		Meet with Craig Newgard	PI to conduct analysis			
Initial regression model		Meet with Rochelle Fu and Craig Newgard	PI to conduct analysis			
Final CART and regression			Meet with Rochelle	PI to conduct analysis		

models			Fu and Craig Newgard to verify analysis plan			
Write manuscript				PI to skeleton manuscript	PI to complete draft manuscript	PI to integrate comments from defense into final draft
Thesis defense				Oral thesis defense		

Strengths and Limitations

The project offers a novel analysis of prehospital naloxone use on a national scale. Given that substance abuse is enmeshed with social determinants of health, it is essential to include community factors in the analysis. The EMS system analysis will be useful for EMS directors and the county sociodemographic factor analysis will be useful for both EMS system directors and the broader public health community. The combined county level analysis will be important to investigate the relative importance of EMS system factors and county sociodemographic factors. In addition, it may provide information for planned county level interventions. The thesis project will contribute to multiple follow up projects, such as a multilevel model and a propensity score based effectiveness analysis.

Because NEMSIS relies on prehospital providers to enter data, there is always the possibility that the data points were incorrectly entered resulting in misclassification. However, there is no reason to think that this would result in a differential bias. In addition, the large number of cases and nationally representative sample will increase confidence in the accuracy of the analysis. Furthermore, the type of substance ingested is not recorded, so there is no opportunity for providers to misclassify based on type of overdose. Because the administration of naloxone for opioids is the only readily available antidote in the field, and it is physiologically specific, response to naloxone is most likely a reliable record of opioid toxicity.

A second potential limitation is the use of county level sociodemographic data rather than more detailed data. Given that there is significant heterogeneity within some counties, we are unlikely to see a differential bias due to the use of county level statistics. In addition, the county level is frequently the smallest unit of analysis where detailed and valid measurements of certain sociodemographic factors are available. It is also the case that a single EMS agency has a single county as its coverage area. Moreover, the large sample size and individual case data allow a more detailed analysis than an ecological study using county level data.

A third limitation is the lack of an *a priori* primary predictor. However, this is the case because there is a lack of prior work in this area. As this project is the first national analysis of prehospital naloxone use and the first attempt to integrate county level factors on a national scale into a study of opioid overdoses, it is designed to identify the most prominent predictors through multiple methods. Fortunately, the large size of the dataset will allow for a traditional analysis using regression models and a decision tree analysis using CART technique. We will have a high degree of confidence in the relevance of factors identified through both methods.

Finally, the study period is limited to the 2010 calendar year. It is possible that naloxone use and opioid overdose patterns are not stable in each locale over time. However, given the national scale of the study, small regional variations should balance out.

Nevertheless, ongoing surveillance and validation in a future time period will be necessary to ensure that the factors identified through the 2010 dataset are stable.

Future Research

As stated in the background section, the current indications for naloxone use are respiratory insufficiency due to known or suspected opioid toxicity. However, naloxone is being administered empirically in cases of respiratory failure, altered mental status, and cardiac arrest with an unknown impact on clinical outcomes. The planned analysis will form the basis of both a multilevel analysis and a future propensity score for naloxone administration (70-72). Matching by propensity score will provide the ability to compare outcomes when naloxone is administered. This has the potential to change indications for naloxone use. Prospective analysis of EMS protocol changes could be tested by using a cluster randomized trial design. In addition, naloxone administration has been employed as a proxy for opioid overdose. This association will be verified by comparing high-risk patterns identified in this fashion with drug death rates identified by the Drug Abuse Warning Network area profiles of mortality and the NCHS death certificate based statistics. Harm reduction, treatment, and education efforts could target providers and community members in areas with high-risk patterns. These interventions could also be studied by cluster randomized prospective clinical trials. Finally, prehospital naloxone use has the potential to serve as a near real-time surveillance system identifying local increases in opioid poisoning. Utilizing GIS/Spatial analysis techniques to target interventions to areas, neighborhoods, or populations with high rates of naloxone will potentially offer a cost-effective approach to the opioid epidemic.

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APPENDIX 2

Univariate Analysis

EMS Variables

Variable	IRR (poisson)	p-value (poisson)	IRR (neg binomial)	p-value (neg binomial)
EMSreg	-	-	-	-
1	0.70	<0.001	0.72	<0.001
2	0.58	<0.001	0.80	0.004
3	0.46	<0.001	0.48	<0.001
Urban	1.17	<0.001	1.14	<0.001
White	1.00	0.87	0.97	0.83
Nonwhite	1.00	0.87	1.03	0.83
Nativeam	1.19	0.002	0.87	0.58
Asian	3.20	<0.001	16.23	0.07
Black	0.67	<0.001	0.79	0.11
hawaiipi	23.31	<0.001	376.67	0.034
Othrrace	2.88	<0.001	4.47	<0.001
Hispanic	2.12	<0.001	2.92	<0.001
Home	3.64	<0.001	4.26	<0.001
Outdoor	0.61	<0.001	1.07	0.85
Building	5.28	<0.001	14.55	<0.001
Hlthfac	0.16	<0.001	0.13	<0.001
Respsx	0.25	<0.001	0.09	<0.001
Lowloc	4.46	<0.001	1.69	0.25
Deathsx	5208.66	<0.001	2839.21	0.006
Ageyrmed	0.97	<0.001	0.97	<0.001
Male	2.35	<0.001	0.53	0.39
Als	1.35	<0.001	1.45	<0.001
Injury	0.95	0.06	0.78	0.05
Respdx	0.13	<0.001	0.37	0.04
Dyscadx	0.07	<0.001	0.36	0.31
Drugoddx	7.57	<0.001	447.19	<0.001
Amspsydx	2.61	<0.001	4.21	0.005
Arrestdx	0.29	<0.001	1.31	0.84
Caarrest	0.72	<0.001	0.70	0.005
Treated	0.49	<0.001	0.27	<0.001
Transp	0.38	<0.001	0.44	0.001
antiemet	88.45	<0.001	34810.7	<0.001
Sysremed	0.97	<0.001	0.97	0.003
Scenrmed	1.01	0.01	1.03	0.01
Scenemed	1.07	<0.001	1.06	<0.001
Trantmed	1.01	<0.001	1.00	0.16
Totcamed	1.00	<0.001	1.00	<0.001
Agegrmed	0.82	<0.001	0.74	<0.001
Airadvan	0.45	0.003	61.19	0.02
Airpress	1.40e-10	<0.001	0.60	0.88
Airinter	0.05	<0.001	0.27	0.22
Airbasic	0.71	<0.001	0.56	0.002
Airinvas	0.28	<0.001	1.13	0.90
Airany	0.67	<0.001	0.55	0.002

Cprcompr	0.002	<0.001	0.93	0.97
Defib	2.06e-09	<0.001	3.81e-09	<0.001
Pacing	0.88	0.91	184.94	0.39
Restrain	11900.55	<0.001	832.27	0.08

Sociodemographic Variables

Variable	iRR (poisson)	p-value (poisson)	IRR (neg binomial)	p-value (neg binomial)
Poptot	1.09	<0.001	1.08	<0.001
1	-	-	-	-
2	1.93	<0.001	1.73	0.02
3	1.67	0.003	1.60	0.04
4	1.87	<0.001	1.93	0.004
5	1.90	<0.001	1.80	0.01
6	1.87	<0.001	1.87	0.01
7	2.34	<0.001	2.25	<0.001
8	2.59	<0.001	2.55	<0.001
9	2.52	<0.001	2.50	<0.001
10	2.96	<0.001	2.77	<0.001
Agemed	0.97	<0.001	0.98	0.03
1	-	-	-	-
2	1.05	0.002	1.10	0.36
3	0.89	<0.001	1.04	0.74
4	0.77	<0.001	1.00	1.00
5	0.91	<0.001	0.99	0.92
6	0.80	<0.001	1.01	0.92
7	0.74	<0.001	0.95	0.65
8	0.78	<0.001	0.90	0.34
9	0.99	0.77	0.94	0.60
10	0.84	<0.001	0.86	0.22
Popped	1.03	<0.001	1.01	0.48
1	-	-	-	-
2	1.10	<0.001	1.07	0.54
3	1.00	0.99	1.04	0.73
4	0.92	0.001	0.89	0.32
5	0.89	<0.001	0.98	0.85
6	1.34	<0.001	1.10	0.39
7	1.04	0.10	1.06	0.59
8	1.21	<0.001	1.00	0.97
9	1.02	0.46	1.02	0.84
10	1.46	<0.001	1.12	0.34
Popsr	0.98	<0.001	0.96	<0.001
1	-	-	-	-
2	1.09	<0.001	0.96	0.74
3	0.81	<0.001	0.75	0.01
4	0.87	<0.001	0.87	0.19
5	0.83	<0.001	0.82	0.07
6	0.79	<0.001	0.79	0.03
7	0.79	<0.001	0.74	0.01
8	1.15	<0.001	0.80	0.05
9	0.80	<0.001	0.65	<0.001
10	0.89	<0.001	0.71	0.004

Popchang	1.07	<0.001	1.08	<0.001
1	-	-	-	-
2	0.91	0.03	1.33	0.03
3	1.06	0.14	1.61	<0.001
4	1.05	0.22	1.64	<0.001
5	1.03	0.43	1.64	<0.001
6	0.88	0.001	1.71	<0.001
7	1.18	<0.001	1.98	<0.001
8	1.47	<0.001	2.25	<0.001
9	1.40	<0.001	2.05	<0.001
10	1.56	<0.001	2.49	<0.001
Popdens	1.06	<0.001	1.05	<0.001
1	-	-	-	-
2	0.99	0.93	0.90	0.50
3	0.91	0.13	1.02	0.90
4	0.64	<0.001	0.76	0.05
5	0.88	0.04	0.98	0.91
6	0.92	0.18	1.03	0.82
7	0.93	0.23	1.00	0.98
8	1.06	0.33	1.29	0.08
9	1.09	0.12	1.30	0.06
10	1.20	0.001	1.38	0.03
Popurban	1.06	<0.001	1.04	<0.001
1	-	-	-	-
2	1.65	<0.001	1.45	0.05
3	1.92	<0.001	1.80	0.001
4	1.86	<0.001	1.54	0.02
5	1.77	<0.001	1.48	0.03
6	1.68	<0.001	1.40	0.06
7	2.02	<0.001	1.60	0.01
8	2.17	<0.001	1.99	<0.001
9	2.28	<0.001	1.69	0.004
10	2.45	<0.001	2.23	<0.001
Poprural	0.95	<0.001	0.97	<0.001
1	-	-	-	-
2	0.93	<0.001	0.76	0.01
3	0.89	<0.001	0.89	0.30
4	0.83	<0.001	0.73	0.004
5	0.68	<0.001	0.63	<0.001
6	0.72	<0.001	0.66	<0.001
7	0.76	<0.001	0.69	0.001
8	0.80	<0.001	0.80	0.06
9	0.44	<0.001	0.46	<0.001
10	0.72	<0.001	0.75	0.01
Femcnty	0.98	<0.001	0.99	0.34
1	-	-	-	-
2	0.95	0.24	0.87	0.25
3	1.56	<0.001	0.95	0.68
4	1.16	<0.001	0.93	0.55
5	1.01	0.74	0.85	0.17
6	1.05	0.18	0.96	0.71
7	1.21	<0.001	0.96	0.72
8	1.21	<0.001	0.89	0.32
9	1.08	0.01	0.95	0.64
10	1.01	0.77	0.81	0.07
whitcnty	0.97	<0.001	0.95	<0.001

1	-	-	-	-
2	1.13	<0.001	1.40	0.001
3	1.39	<0.001	1.67	<0.001
4	1.26	<0.001	1.59	<0.001
5	1.12	<0.001	1.34	0.01
6	1.11	<0.001	1.37	0.002
7	0.83	<0.001	1.06	0.60
8	0.72	<0.001	0.90	0.38
9	0.67	<0.001	0.85	0.14
10	0.76	<0.001	0.89	0.32
whixhisp	0.95	<0.001	0.94	<0.001
1	-	-	-	-
2	1.11	<0.001	1.16	0.16
3	1.18	<0.001	1.25	0.04
4	1.06	<0.001	1.19	0.10
5	1.07	<0.001	1.25	0.03
6	0.99	0.51	1.07	0.51
7	0.73	<0.001	0.92	0.44
8	0.64	<0.001	0.65	<0.001
9	0.59	<0.001	0.74	0.01
10	0.70	<0.001	0.73	0.02
blckcnty	1.01	<0.001	1.04	<0.001
1	-	-	-	-
2	1.17	<0.001	0.94	0.63
3	1.65	<0.001	1.31	0.03
4	1.43	<0.001	1.27	0.05
5	2.26	<0.001	1.81	<0.001
6	1.63	<0.001	1.45	0.003
7	1.74	<0.001	1.75	<0.001
8	1.83	<0.001	1.93	<0.001
9	1.86	<0.001	1.62	<0.001
10	1.45	<0.001	1.13	0.30
natvcnty	1.05	<0.001	1.05	<0.001
1	-	-	-	-
2	1.28	<0.001	1.32	0.04
3	1.29	<0.001	1.22	0.12
4	1.70	<0.001	1.83	<0.001
5	1.23	<0.001	1.37	0.01
6	1.90	<0.001	1.65	<0.001
7	1.58	<0.001	1.62	<0.001
8	1.50	<0.001	1.61	<0.001
9	1.67	<0.001	1.75	<0.001
10	2.16	<0.001	1.80	<0.001
asiacnty	1.06	<0.001	1.05	<0.001
1	-	-	-	-
2	1.00	0.95	1.07	0.63
3	0.95	0.33	1.01	0.96
4	0.98	0.71	1.07	0.62
5	0.99	0.80	1.02	0.88
6	1.18	0.001	1.20	0.15
7	1.10	0.04	1.29	0.04
8	1.31	<0.001	1.51	0.001
9	1.39	<0.001	1.30	0.04
10	1.45	<0.001	1.44	0.01
hwpicnty	1.09	<0.001	1.05	<0.001
1	-	-	-	-

2	0.79	<0.001	0.86	0.28
3	0.88	0.01	1.02	0.90
4	0.85	0.001	0.87	0.28
5	1.02	0.57	1.10	0.43
6	0.97	0.51	1.11	0.40
7	1.07	0.10	1.08	0.54
8	0.98	0.63	1.12	0.37
9	1.29	<0.001	1.35	0.01
10	1.56	<0.001	1.51	0.001
hispcnty	1.09	<0.001	1.07	<0.001
1	-	-	-	-
2	0.75	<0.001	0.85	0.17
3	0.79	<0.001	0.95	0.66
4	1.01	0.76	0.92	0.51
5	1.19	<0.001	1.23	0.07
6	1.14	<0.001	1.13	0.28
7	1.08	0.01	1.24	0.04
8	1.45	<0.001	1.42	0.001
9	1.58	<0.001	1.44	0.001
10	1.68	<0.001	1.83	<0.001
Singpar	1.00	0.03	1.02	0.02
1	-	-	-	-
2	1.09	0.01	0.90	0.42
3	0.91	0.001	1.13	0.31
4	1.07	0.01	1.08	0.55
5	0.98	0.60	1.29	0.04
6	0.95	0.06	1.25	0.07
7	0.99	0.79	1.29	0.04
8	1.11	<0.001	1.42	0.003
9	1.17	<0.001	1.43	0.003
10	0.79	<0.001	0.88	0.30
Hsmin	1.00	0.04	0.98	0.06
1	-	-	-	-
2	1.15	<0.001	1.25	0.08
3	1.22	<0.001	1.41	0.01
4	1.23	<0.001	1.34	0.02
5	1.43	<0.001	1.29	0.05
6	1.49	<0.001	1.28	0.06
7	1.25	<0.001	1.26	0.07
8	0.92	0.01	0.89	0.40
9	1.39	<0.001	1.09	0.47
10	1.09	0.01	1.16	0.23
Hsonly	0.96	<0.001	0.97	0.001
1	-	-	-	-
2	1.06	<0.001	0.97	0.77
3	0.87	<0.001	0.83	0.08
4	0.85	<0.001	0.88	0.23
5	0.86	<0.001	0.82	0.07
6	0.99	0.56	0.70	0.001
7	0.71	<0.001	0.62	<0.001
8	0.71	<0.001	0.71	0.002
9	0.86	<0.001	0.87	0.26
10	0.84	<0.001	0.86	0.25
Somecoll	1.03	<0.001	1.01	0.58
1	-	-	-	-
2	1.02	0.49	1.15	0.31

3	1.04	0.15	0.97	0.81
4	1.46	<0.001	1.01	0.93
5	0.90	<0.001	0.79	0.07
6	1.06	0.02	0.96	0.74
7	1.08	0.003	0.90	0.40
8	1.29	<0.001	1.00	0.99
9	1.17	<0.001	0.98	0.89
10	1.60	<0.001	1.19	0.19
Bachmin	1.02	<0.001	1.01	0.35
1	-	-	-	-
2	0.90	0.01	0.93	0.55
3	0.96	0.27	0.98	0.84
4	0.99	0.87	1.00	0.97
5	0.94	0.09	0.83	0.13
6	1.08	0.02	0.79	0.06
7	1.04	0.20	0.91	0.46
8	1.00	0.91	0.91	0.44
9	1.26	<0.001	1.09	0.45
10	1.01	0.75	1.04	0.76
Bachonly	1.02	<0.001	1.00	0.97
1	-	-	-	-
2	0.81	<0.001	0.87	0.29
3	1.04	0.25	1.05	0.71
4	0.97	0.41	1.05	0.68
5	0.91	0.004	0.83	0.13
6	1.07	0.03	0.85	0.18
7	0.94	0.06	0.78	0.04
8	1.02	0.55	0.88	0.29
9	1.17	<0.001	1.01	0.90
10	1.04	0.22	1.03	0.78
Graddeg	1.02	<0.001	1.03	0.001
1	-	-	-	-
2	1.00	0.93	0.89	0.35
3	0.95	0.23	0.96	0.76
4	1.11	0.01	1.02	0.90
5	1.00	0.98	1.01	0.93
6	1.32	<0.001	1.03	0.82
7	1.01	0.81	1.16	0.24
8	1.13	<0.001	1.10	0.44
9	1.43	<0.001	1.16	0.22
10	1.09	0.01	1.24	0.07
Noins	1.06	<0.001	1.07	<0.001
1	-	-	-	-
2	0.88	<0.001	1.12	0.34
3	1.16	<0.001	1.50	<0.001
4	0.94	0.02	1.52	<0.001
5	1.40	<0.001	1.78	<0.001
6	1.30	<0.001	1.74	<0.001
7	1.67	<0.001	1.82	<0.001
8	1.81	<0.001	1.54	<0.001
9	1.32	<0.001	1.91	<0.001
10	1.17	<0.001	1.95	<0.001
Medhome	1.05	<0.001	1.06	<0.001
1	-	-	-	-
2	1.59	<0.001	1.70	<0.001
3	1.42	<0.001	1.60	0.001

4	1.84	<0.001	1.88	<0.001
5	1.55	<0.001	1.66	<0.001
6	1.93	<0.001	1.98	<0.001
7	2.20	<0.001	1.99	<0.001
8	1.94	<0.001	1.87	<0.001
9	2.47	<0.001	2.26	<0.001
10	1.98	<0.001	2.44	<0.001
Vacant	0.99	<0.001	1.00	0.69
1	-	-	-	-
2	0.89	<0.001	0.92	0.48
3	1.09	<0.001	0.98	0.82
4	0.86	<0.001	1.05	0.63
5	1.16	<0.001	0.94	0.58
6	1.06	0.002	0.94	0.60
7	0.75	<0.001	0.97	0.82
8	1.05	0.01	1.04	0.73
9	0.90	<0.001	0.89	0.31
10	0.82	<0.001	1.08	0.50
Renter	1.02	<0.001	1.00	0.72
1	-	-	-	-
2	1.08	0.01	0.99	0.95
3	1.29	<0.001	1.02	0.88
4	1.41	<0.001	1.12	0.32
5	1.04	0.21	1.00	0.97
6	1.32	<0.001	1.07	0.58
7	1.11	<0.001	0.99	0.94
8	1.05	0.08	0.88	0.26
9	1.23	<0.001	1.03	0.78
10	1.46	<0.001	1.01	0.90
Medinc	1.03	<0.001	1.03	0.005
1	-	-	-	-
2	1.11	0.003	1.11	0.34
3	1.17	<0.001	1.22	0.08
4	1.28	<0.001	1.20	0.10
5	1.26	<0.001	1.17	0.17
6	1.41	<0.001	1.09	0.46
7	1.63	<0.001	1.09	0.44
8	1.54	<0.001	1.09	0.48
9	1.49	<0.001	1.38	0.004
10	1.28	<0.001	1.49	0.001
Medinc09	1.02	<0.001	1.02	0.04
1	-	-	-	-
2	1.28	<0.001	1.33	0.01
3	1.37	<0.001	1.34	0.01
4	1.37	<0.001	1.36	0.01
5	1.39	<0.001	1.27	0.04
6	1.71	<0.001	1.16	0.20
7	1.63	<0.001	1.15	0.22
8	1.56	<0.001	1.06	0.64
9	1.59	<0.001	1.45	0.001
10	1.47	<0.001	1.62	<0.001
Welfare	1.00	0.01	0.99	0.49
1	-	-	-	-
2	1.37	<0.001	1.47	0.004
3	1.62	<0.001	1.48	0.003
4	1.24	<0.001	1.18	0.21

5	1.84	<0.001	1.38	0.01
6	1.34	<0.001	1.17	0.24
7	1.38	<0.001	1.27	0.07
8	1.17	<0.001	1.24	0.10
9	1.52	<0.001	1.23	0.12
10	1.31	<0.001	1.31	0.04
Fdstamp	0.98	<0.001	0.99	0.54
1	-	-	-	-
2	1.25	<0.001	0.99	0.91
3	1.10	<0.001	1.03	0.80
4	1.41	<0.001	0.99	0.95
5	1.38	<0.001	1.20	0.14
6	1.04	0.05	1.11	0.38
7	1.15	<0.001	1.04	073
8	0.89	<0.001	1.08	0.54
9	1.05	0.02	1.12	0.34
10	0.72	<0.001	0.68	0.003
Pcinc	1.02	<0.001	1.01	0.18
1	-	-	-	-
2	1.04	0.25	1.01	0.94
3	1.18	<0.001	1.10	0.39
4	1.23	<0.001	1.23	0.08
5	1.17	<0.001	1.09	0.49
6	1.36	<0.001	1.01	0.92
7	1.05	0.13	0.87	0.23
8	1.40	<0.001	1.01	0.93
9	1.50	<0.001	1.16	0.21
10	1.15	<0.001	1.30	0.03
Poverty9	1.00	0.38	1.01	0.31
1	-	-	-	-
2	1.11	<0.001	0.78	0.03
3	1.22	<0.001	0.84	0.15
4	1.03	0.16	0.99	0.92
5	1.45	<0.001	1.10	0.40
6	1.27	<0.001	1.10	0.42
7	1.23	<0.001	1.15	0.20
8	1.09	<0.001	1.12	0.33
9	1.05	0.03	0.95	0.66
10	0.90	<0.001	0.82	0.09
Poverty	0.99	<0.001	1.00	0.85
1	-	-	-	-
2	1.35	<0.001	0.96	0.73
3	1.08	<0.001	0.91	0.43
4	1.03	0.13	0.99	0.90
5	1.49	<0.001	1.04	0.72
6	1.23	<0.001	1.18	0.15
7	1.26	<0.001	1.15	0.22
8	1.10	<0.001	1.17	0.18
9	0.96	0.09	0.99	0.91
10	0.97	0.19	0.80	0.06
Forbirth	1.09	<0.001	1.06	<0.001
1	-	-	-	-
2	0.98	0.67	1.17	0.22
3	0.92	0.08	0.94	0.65
4	0.91	0.02	0.99	0.96
5	1.11	0.02	1.11	0.41

6	1.11	0.01	1.17	0.17
7	1.22	<0.001	1.37	0.01
8	1.20	<0.001	1.54	<0.001
9	1.60	<0.001	1.50	0.001
10	1.64	<0.001	1.67	<0.001
Alien	1.08	<0.001	1.06	<0.001
1	-	-	-	-
2	1.00	0.93	1.14	0.32
3	1.00	0.92	1.09	0.48
4	0.93	0.12	1.06	0.62
5	0.99	0.75	1.02	0.90
6	1.10	0.02	1.20	0.13
7	1.18	<0.001	1.35	0.01
8	1.30	<0.001	1.36	0.01
9	1.61	<0.001	1.63	<0.001
10	1.58	<0.001	1.63	<0.001
Veterans	1.01	<0.001	1.01	0.16
1	-	-	-	-
2	0.96	0.04	0.90	0.40
3	1.17	<0.001	1.12	0.34
4	1.12	<0.001	1.04	0.77
5	1.26	<0.001	0.95	0.66
6	0.98	0.28	1.13	0.34
7	1.27	<0.001	1.06	0.62
8	0.99	0.68	1.08	0.54
9	0.98	0.41	1.13	0.31
10	1.12	<0.001	1.06	0.61
GINI	1.00	0.46	1.01	0.44
1	-	-	-	-
2	1.16	<0.001	1.19	0.15
3	1.15	<0.001	1.02	0.89
4	1.41	<0.001	1.26	0.05
5	1.28	<0.001	1.21	0.11
6	1.15	<0.001	1.28	0.03
7	1.06	0.02	1.23	0.07
8	1.13	<0.001	1.19	0.15
9	1.26	<0.001	1.14	0.28
10	1.15	<0.001	1.09	0.46
Unemp	1.02	<0.001	1.05	<0.001
1	-	-	-	-
2	2.66	<0.001	1.81	<0.001
3	2.99	<0.001	2.23	<0.001
4	2.78	<0.001	2.39	<0.001
5	2.63	<0.001	2.63	<0.001
6	2.56	<0.001	2.56	<0.001
7	2.40	<0.001	2.56	<0.001
8	3.05	<0.001	2.53	<0.001
9	3.26	<0.001	2.34	<0.001
10	2.81	<0.001	2.32	<0.001
Vcrime08	1.06	<0.001	1.06	<0.001
1	-	-	-	-
2	0.94	0.42	0.99	0.96
3	1.48	<0.001	1.27	0.13
4	1.26	<0.001	1.42	0.02
5	1.31	<0.001	1.49	0.01
6	1.52	<0.001	1.72	<0.001

7	1.82	<0.001	1.59	0.002
8	1.81	<0.001	1.62	0.001
9	1.54	<0.001	1.64	0.001
10	1.91	<0.001	1.76	<0.001
Vcrime	1.06	<0.001	1.06	<0.001
1	-	-	-	-
3	1.92	<0.001	1.54	0.003
4	1.49	<0.001	1.58	0.001
5	1.85	<0.001	2.04	<0.001
6	1.99	<0.001	1.81	<0.001
7	2.42	<0.001	2.11	<0.001
8	2.44	<0.001	1.95	<0.001
9	1.96	<0.001	1.90	<0.001
10	2.54	<0.001	2.32	<0.001
Pcrime08	1.07	<0.001	1.06	<0.001
1	-	-	-	-
2	1.09	0.24	1.09	0.59
3	1.05	0.50	1.03	0.84
4	1.14	0.05	1.18	0.27
5	1.37	<0.001	1.45	0.01
6	1.24	0.001	1.42	0.01
7	1.41	<0.001	1.42	0.01
8	1.64	<0.001	1.62	0.001
9	1.61	<0.001	1.64	<0.001
10	1.75	<0.001	1.57	0.001
Socsec	0.98	<0.001	0.98	0.01
1	-	-	-	-
2	1.03	0.02	0.81	0.06
3	0.83	<0.001	0.80	0.05
4	0.94	0.001	0.61	<0.001
5	0.83	<0.001	0.76	0.02
6	0.76	<0.001	0.67	<0.001
7	1.03	0.14	0.73	0.01
8	0.91	<0.001	0.77	0.02
9	0.66	<0.001	0.65	<0.001
10	0.94	0.004	0.78	0.03
Retired	0.98	<0.001	0.97	<0.001
1	-	-	-	-
2	0.83	<0.001	0.85	0.17
3	0.74	<0.001	0.79	0.05
4	0.69	<0.001	0.67	0.001
5	0.75	<0.001	0.80	0.05
6	0.75	<0.001	0.71	0.003
7	0.75	<0.001	0.68	0.001
8	0.94	0.004	0.76	0.02
9	0.81	<0.001	0.67	0.001
10	0.73	<0.001	0.70	0.004
Disabled	0.98	<0.001	1.02	0.03
1	-	-	-	-
2	0.71	<0.001	0.78	0.04
3	0.79	<0.001	0.89	0.34
4	0.84	<0.001	0.89	0.37
5	0.94	0.001	1.06	0.67
6	0.89	<0.001	1.04	0.75
7	0.92	<0.001	1.20	0.15
8	0.78	<0.001	1.15	0.23

9	0.66	<0.001	099	0.95
10	0.68	<0.001	0.94	0.62
Births	1.04	<0.001	1.01	0.32
1	-	-	-	-
2	1.15	<0.001	1.10	0.47
3	1.15	<0.001	1.04	0.74
4	1.16	<0.001	1.07	0.6
5	1.19	<0.001	1.20	0.16
6	0.92	0.02	0.98	0.86
7	0.90	0.001	1.04	0.77
8	1.24	<0.001	1.06	0.64
9	1.33	<0.001	1.20	0.15
10	1.54	<0.001	1.14	0.32
Deaths	0.96	<0.001	0.96	<0.001
1	-	-	-	-
2	0.94	<0.001	0.88	0.28
3	0.76	<0.001	0.82	0.08
4	0.97	0.03	0.91	0.40
5	0.82	<0.001	0.72	0.004
6	0.85	<0.001	0.83	0.09
7	0.68	<0.001	0.69	0.002
8	0.68	<0.001	0.64	<0.001
9	0.75	<0.001	0.74	0.01
10	0.77	<0.001	0.72	0.01
Infntdth	1.03	<0.001	1.04	<0.001
1	-	-	-	-
2	1.23	0.01	1.08	0.61
3	1.64	<0.001	1.44	0.01
4	1.76	<0.001	1.51	0.002
5	1.86	<0.001	1.57	<0.001
6	2.08	<0.001	1.72	<0.001
7	2.40	<0.001	1.63	<0.001
8	1.92	<0.001	1.56	0.001
9	1.81	<0.001	1.63	<0.001
10	1.61	<0.001	1.64	<0.001
Ypll	1.01	<0.001	1.04	<0.001
1	-	-	-	-
2	1.03	0.42	0.84	0.42
3	1.21	<0.001	0.99	0.96
4	1.27	<0.001	1.07	0.74
5	1.30	<0.001	1.17	0.46
6	1.43	<0.001	1.27	0.27
7	1.49	<0.001	1.52	0.05
8	1.46	<0.001	1.41	0.10
9	1.13	0.001	1.16	0.48
10	0.97	0.48	1.05	0.82
LBW	1.02	<0.001	1.04	<0.001
1	-	-	-	-
2	1.55	<0.001	1.22	0.25
3	1.22	0.02	1.36	0.08
4	1.91	<0.001	1.65	0.004
5	1.97	<0.001	1.95	<0.001
6	2.03	<0.001	1.99	<0.001
7	2.55	<0.001	2.11	<0.001
8	2.24	<0.001	2.15	<0.001
9	2.02	<0.001	1.97	<0.001

10	1.38	<0.001	1.42	0.04
Mvcdeath	0.99	<0.001	0.99	0.45
1	-	-	-	-
2	0.99	0.61	0.86	0.21
3	1.11	<0.001	0.85	0.15
4	0.97	0.04	0.93	0.58
5	0.96	0.04	0.96	0.71
6	0.91	<0.001	0.91	0.44
7	1.16	<0.001	0.96	0.74
8	0.87	<0.001	0.84	0.15
9	0.89	<0.001	0.94	0.61
10	0.81	<0.001	0.78	0.05
Drrate	1.03	<0.001	1.02	0.04
1	-	-	-	-
2	1.18	0.003	1.11	0.45
3	1.18	0.002	1.09	0.55
4	1.07	0.24	0.94	0.64
5	1.08	0.15	1.01	0.93
6	1.18	0.001	1.02	0.90
7	1.26	<0.001	1.12	0.40
8	1.39	<0.001	1.19	0.19
9	1.22	<0.001	1.10	0.46
10	1.44	<0.001	1.27	0.07
Nosocemo	1.01	<0.001	1.03	0.01
1	-	-	-	-
4	0.86	<0.001	1.10	0.42
5	0.99	0.69	1.23	0.06
6	1.13	<0.001	1.23	0.07
7	1.09	<0.001	1.34	0.01
8	1.31	<0.001	1.47	0.001
9	0.96	0.10	1.38	0.003
10	1.03	0.18	1.19	0.11
Poorhlth	1.03	<0.001	1.05	<0.001
1	-	-	-	-
2	-	-	-	-
3	1.19	<0.001	1.24	0.08
4	1.55	<0.001	1.32	0.03
5	1.28	<0.001	1.53	0.001
6	1.56	<0.001	1.74	<0.001
7	1.60	<0.001	1.66	<0.001
8	1.64	<0.001	1.66	<0.001
9	1.37	<0.001	1.76	<0.001
10	1.16	<0.001	1.60	<0.001
punhlth	1.03	<0.001	1.07	<0.001
1	-	-	-	-
2	3.17	<0.001	1.52	0.05
3	2.98	<0.001	1.88	0.002
4	3.54	<0.001	2.32	<0.001
5	3.45	<0.001	2.39	<0.001
6	4.07	<0.001	2.56	<0.001
7	4.51	<0.001	2.64	<0.001
8	3.48	<0.001	2.44	<0.001
9	3.47	<0.001	2.76	<0.001
10	3.29	<0.001	2.66	<0.001
Munhlth	1.04	<0.001	1.08	<0.001
1	-	-	-	-

2	2.97	<0.001	2.36	<0.001
3	4.21	<0.001	3.13	<0.001
4	5.15	<0.001	4.44	<0.001
5	5.27	<0.001	4.17	<0.001
6	4.88	<0.001	4.62	<0.001
7	5.15	<0.001	4.53	<0.001
8	7.00	<0.001	4.54	<0.001
9	5.17	<0.001	5.23	<0.001
10	4.15	<0.001	4.21	<0.001
Smoking	1.00	0.18	1.04	<0.001
1	-	-	-	-
4	0..85	<0.001	0.98	0.86
5	0.75	<0.001	0.90	0.37
6	0.88	<0.001	1.11	0.38
7	1.04	0.03	1.15	0.20
8	0.96	0.05	1.18	0.15
9	0.77	<0.001	1.18	0.14
10	0.85	<0.001	1.26	0.05
Obesity	0.97	<0.001	0.98	<0.001
1	-	-	-	-
2	0.87	<0.001	0.70	0.001
3	0.87	<0.001	0.70	0.001
4	0.91	<0.001	0.63	<0.001
5	0.73	<0.001	0.51	<0.001
6	0.74	<0.001	0.63	<0.001
7	0.77	<0.001	0.73	0.01
8	0.86	<0.001	0.73	0.004
9	0.84	<0.001	0.83	0.07
10	0.64	<0.001	0.58	<0.001
Etohabus	0.98	<0.001	0.96	<0.001
1	-	-	-	-
3	0.69	<0.001	1.24	0.33
4	0.61	<0.001	1.13	0.60
5	0.74	<0.001	1.12	0.59
6	0.75	<0.001	1.36	0.16
7	0.71	<0.001	1.19	0.42
8	0.72	<0.001	1.12	0.62
9	0.64	<0.001	1.02	0.91
10	0.49	<0.001	0.74	0.17
Pcprate	1.00	0.08	0.98	0.04
1	-	-	-	-
2	1.08	0.19	0.94	0.71
3	1.08	0.21	1.01	0.96
4	1.16	0.01	1.07	0.69
5	1.46	<0.001	1.03	0.84
6	1.18	0.004	1.03	0.84
7	0.98	0.70	0.90	0.52
8	1.30	<0.001	0.87	0.37
9	1.34	<0.001	0.93	0.67
10	1.08	0.18	0.83	0.25
Liqstore	0.96	<0.001	0.97	0.004
1	-	-	-	-
2	1.12	0.25	1.29	0.13
3	1.69	<0.001	1.53	0.01
4	1.58	<0.001	1.44	0.02
5	1.68	<0.001	1.49	0.02

6	1.44	<0.001	1.33	0.09
7	1.33	0.002	1.36	0.07
8	1.28	0.01	1.33	0.10
9	1.27	0.01	1.12	0.50
10	1.10	0.32	0.97	0.85
Cendiv		<0.001		<0.001
0	Ref	ref	ref	ref
1	1.11	<0.001	0.97	0.86
2	0.80	<0.001	0.68	0.01
3	0.46	<0.001	0.56	<0.001
4	0.77	<0.001	0.88	0.38
5	0.51	<0.001	0.72	0.12
6	0.39	<0.001	0.43	<0.001
7	0.66	<0.001	0.69	0.03
8	0.37	<0.001	0.40	<0.001

APPENDIX 3

<u>Final main effects model w/ threshold of 0.05</u>

. xi: nbreg naloxcnt disabled i.cendiv noins medinc infntdth black home deathsx ageyrmed transp an

> tiemet sysremed scenrmed scenemed, exposure(numcalls) irr

i.cendiv   _Icendiv_0-8   (naturally coded; _Icendiv_0 omitted)

Fitting Poisson model:

Iteration 0:   log likelihood = -9362.4662

Iteration 1:   log likelihood = -8372.577

Iteration 2:   log likelihood = -8370.0684

Iteration 3:   log likelihood = -8370.0676

Fitting constant-only model:

Iteration 0:   log likelihood = -4269.0628

Iteration 1:   log likelihood = -4241.8843

Iteration 2:   log likelihood = -4211.9199

Iteration 3:   log likelihood = -4211.6559

Iteration 4:   log likelihood = -4211.6559

Fitting full model:

Iteration 0:   log likelihood = -4058.1654

Iteration 1:   log likelihood = -3969.2068

Iteration 2:   log likelihood = -3967.5549

Iteration 3: log likelihood = -3967.5522

Iteration 4: log likelihood = -3967.5522

Negative binomial regression Number of obs = 1242

LR chi2(21) = 488.21

Dispersion = mean Prob > chi2 = 0.0000

Log likelihood = -3967.5522 Pseudo R2 = 0.0580

naloxcnt	IRR	Std. Err.	z	P>|z|	[95% Conf. Interval]	
disabled	1.063993	.0139333	4.74	0.000	1.037031	1.091655
_Icendiv_1	1.018612	.1422518	0.13	0.895	.7747049	1.33931
_Icendiv_2	.7170326	.1071943	-2.23	0.026	.5349174	.9611498
_Icendiv_3	.6998127	.106291	-2.35	0.019	.5196334	.9424678
_Icendiv_4	1.051852	.1428103	0.37	0.710	.8060955	1.372532
_Icendiv_5	.9093588	.1721492	-0.50	0.616	.6274739	1.317877
_Icendiv_6	.4310882	.077043	-4.71	0.000	.3036978	.6119145
_Icendiv_7	.709647	.1055779	-2.31	0.021	.5301573	.9499047
_Icendiv_8	.5449542	.0734007	-4.51	0.000	.4185144	.7095934
noins	1.033129	.0129365	2.60	0.009	1.008083	1.058798
medinc	1.076396	.0137632	5.76	0.000	1.049756	1.103712
infntdth	1.033274	.0091793	3.68	0.000	1.015438	1.051422
black	.4818902	.0740715	-4.75	0.000	.3565411	.6513082
home	2.494554	.5696943	4.00	0.000	1.594408	3.902889
deathsx	44041.95	112645.5	4.18	0.000	292.927	6621763

```
    ageyrmed |   .9779824   .0039052    -5.58   0.000     .9703582    .9856666
      transp |   3.107444   .6732554     5.23   0.000     2.032277    4.751423
    antiemet |   1969.067   2146.268     6.96   0.000     232.5184    16674.92
    sysremed |   .8999693   .0132749    -7.15   0.000     .8743235    .9263673
    scenrmed |   1.073442   .0189258     4.02   0.000     1.036982    1.111185
    scenemed |   1.038792    .009816     4.03   0.000      1.01973    1.058211
    numcalls | (exposure)
-------------+----------------------------------------------------------------
    /lnalpha |  -.9399077     .05983                     -1.057172    -.822643
-------------+----------------------------------------------------------------
       alpha |   .3906639   .0233734                      .3474368    .4392691
------------------------------------------------------------------------------
Likelihood-ratio test of alpha=0:  chibar2(01) = 8805.03 Prob>=chibar2 = 0.000
```

Check for overdispersion

Written as a glm

. xi: glm naloxcnt disabled i.cendiv noins medinc infntdth black home deathsx ageyrmed transp anti

> emet sysremed scenrmed scenemed, exposure(numcalls) family(nb ml) link(log)

i.cendiv   _Icendiv_0-8   (naturally coded; _Icendiv_0 omitted)

Iteration 0:   log likelihood = -4648.2579

Iteration 1:   log likelihood = -4003.0867

Iteration 2:   log likelihood = -3967.5887

Iteration 3:   log likelihood = -3967.5522

Iteration 4:   log likelihood = -3967.5522

Generalized linear models   No. of obs   =   1242

Optimization   : ML   Residual df   =   1220

Scale parameter =   1

Deviance   =   1439.71884   (1/df) Deviance = 1.180097

Pearson   = 1354.450663   (1/df) Pearson = 1.110205

Variance function: V(u) = u+(.3907)u^2   [Neg. Binomial]

Link function   : g(u) = ln(u)   [Log]

AIC   =   6.4244

Log likelihood   = -3967.552193   BIC   = -7252.145

| OIM

naloxcnt	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
disabled	.0620284	.0130797	4.74	0.000	.0363927	.0876642
_Icendiv_1	.0184409	.1396518	0.13	0.895	-.2552716	.2921533
_Icendiv_2	-.332634	.1494737	-2.23	0.026	-.6255971	-.0396709
_Icendiv_3	-.3569426	.1518849	-2.35	0.019	-.6546316	-.0592536
_Icendiv_4	.0505519	.1357703	0.37	0.710	-.2155529	.3166568
_Icendiv_5	-.0950156	.1892765	-0.50	0.616	-.4659907	.2759595
_Icendiv_6	-.8414425	.1787061	-4.71	0.000	-1.1917	-.4911849
_Icendiv_7	-.3429876	.1487743	-2.31	0.021	-.6345798	-.0513953
_Icendiv_8	-.6070536	.1346864	-4.51	0.000	-.8710341	-.343073
noins	.0325923	.0125212	2.60	0.009	.0080511	.0571334
medinc	.0736184	.0127863	5.76	0.000	.0485576	.0986791
infntdth	.0327322	.0088836	3.68	0.000	.0153207	.0501437
black	-.7300391	.1536844	-4.75	0.000	-1.031255	-.4288231
home	.9141099	.228348	4.00	0.000	.4665561	1.361664
deathsx	10.6929	2.556941	4.18	0.000	5.681385	15.70441
ageyrmed	-.0222636	.003992	-5.58	0.000	-.0300878	-.0144394
transp	1.133801	.2165476	5.24	0.000	.7093752	1.558226
antiemet	7.585315	1.089113	6.96	0.000	5.450693	9.719938
sysremed	-.1053946	.0147438	-7.15	0.000	-.1342919	-.0764974
scenrmed	.0708708	.0176291	4.02	0.000	.0363183	.1054232
scenemed	.0380588	.0094407	4.03	0.000	.0195553	.0565623
_cons	-6.533045	.4068751	-16.06	0.000	-7.330506	-5.735585
numcalls	(exposure)					

Note: Negative binomial parameter estimated via ML and treated as fixed once estimated.

Model Diagnostics

Pseudo r2

```
. predict ppred
(option mu assumed; predicted mean naloxcnt)
. . pwcorr naloxcnt ppred
             | naloxcnt    ppred
-------------+------------------
    naloxcnt |   1.0000
       ppred |   0.8875   1.0000
. . display 0.8875^2
.78765625
```

```
. fitstat
Measures of Fit for nbreg of naloxcnt
Log-Lik Intercept Only:    -4211.656     Log-Lik Full Model:       -3967.552
D(1219):                    7935.104     LR(21):                     488.207
                                         Prob > LR:                    0.000
McFadden's R2:                 0.058     McFadden's Adj R2:            0.052
Maximum Likelihood R2:         0.325     Cragg & Uhler's R2:           0.325
AIC:                           6.426     AIC*n:                     7981.104
BIC:                        -749.635     BIC':                      -338.593
```

```
. estat ic

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |   1242   -4211.656   -3967.552     23     7981.104    8098.967
-----------------------------------------------------------------------------
               Note:  N=Obs used in calculating BIC; see [R] BIC note
```

1. AIC: 7981.10

2. ML R2 (from fitstat): 0.33

pseudo r2 (from ppred covariance): 0.79

Residual analysis

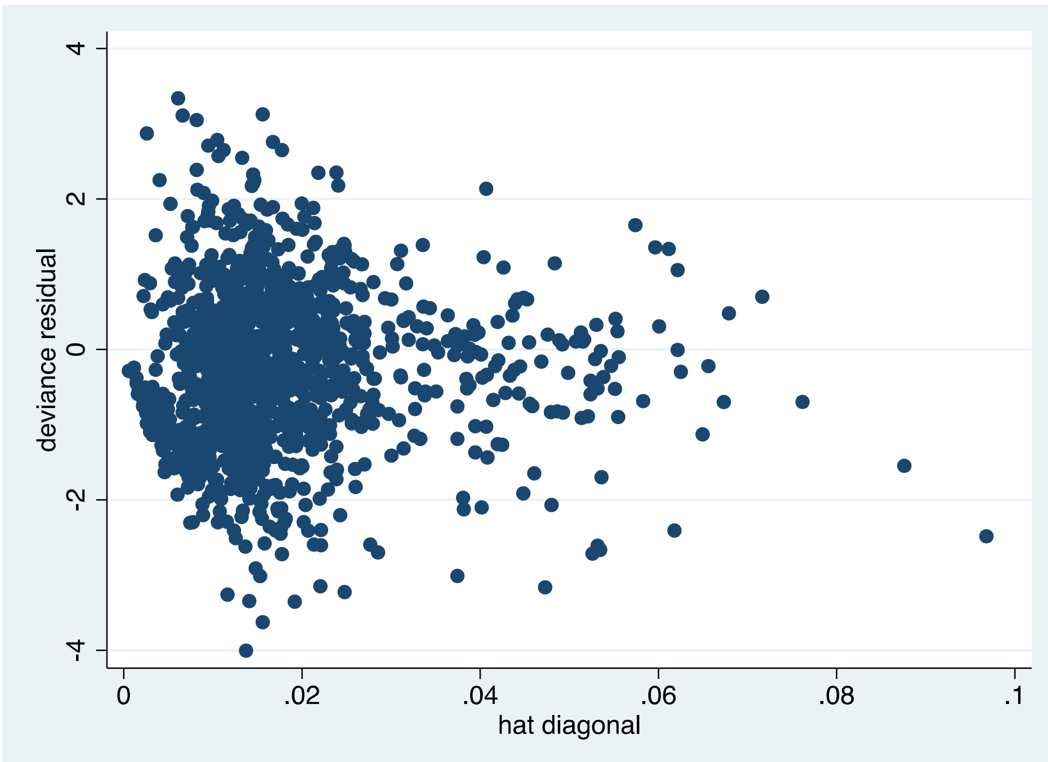
. predict x2, pearson

. . predict deviance, dev

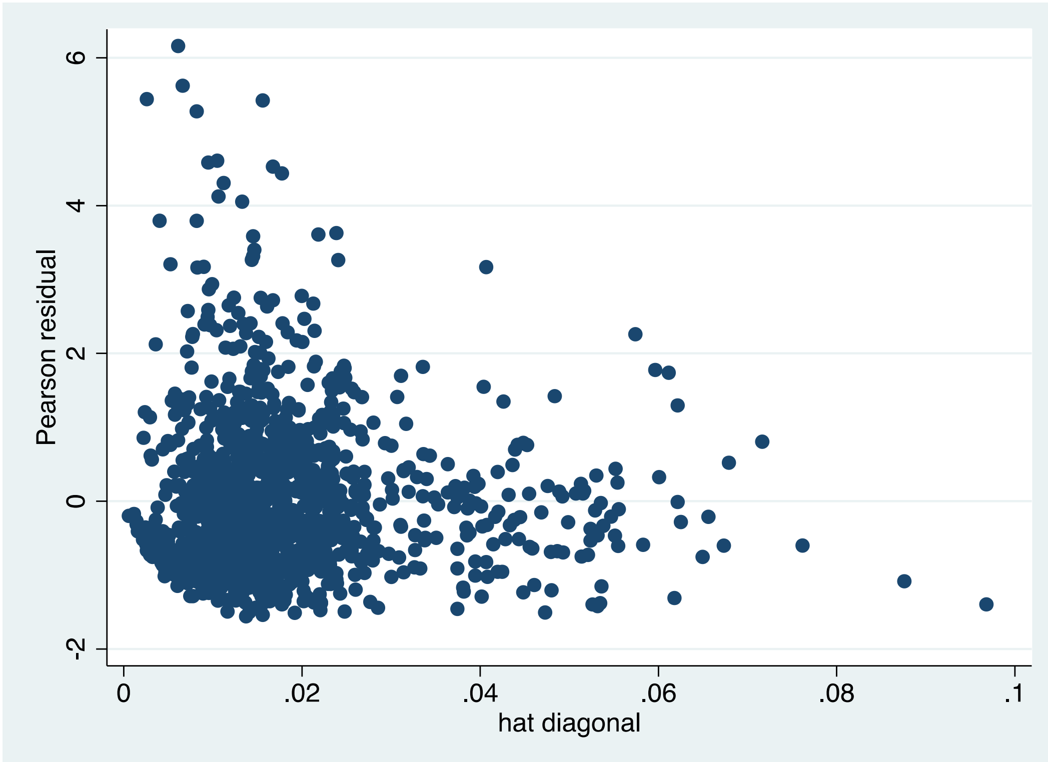
. . predict leverage, hat

. . predict cooksd, cooksd

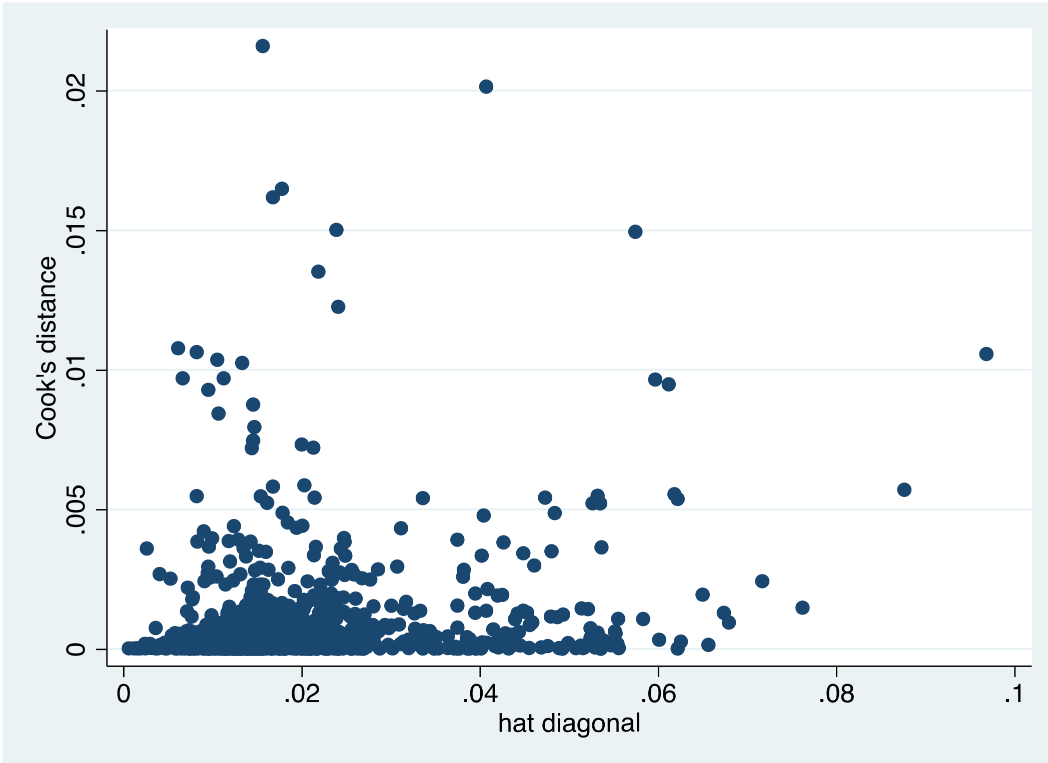
. twoway (scatter dev leverage)



twoway (scatter x2 leverage)



. twoway (scatter cooksd leverage)



Rescaling

. summarize disabled cendiv noins medinc infntdth black home deathsx ageyrmed transp antiemet sysremed scenrmed scenemed

Variable	Obs	Mean	Std. Dev.	Min	Max
disabled	1242	5.878422	2.97595	1	10
cendiv	1242	4.578905	2.678106	0	8
noins	1242	5.313205	2.766958	1	10
medinc	1242	5.310789	2.857626	1	10
infntdth	1242	5.669887	2.790373	1	10
black	1242	.1226176	.1919296	0	.8852459
home	1242	.5569896	.1282023	0	.9
deathsx	1242	.0138669	.0109969	0	.1666667
ageyrmed	1242	58.18599	7.482132	14	81
transp	1242	.8010482	.1214238	.0043668	1
antiemet	1242	.0167101	.0232302	0	.2
sysremed	1242	8.084138	2.915194	0	25.5
scenrmed	1242	5.735105	2.654926	0	25.5
scenemed	1242	14.57206	2.927584	0	34

highlighted need to be rescaled

0 – Pacific

1 - Mountain

2 – W South Central

3 – E South Central

4 – South Atlantic

5 – Middle Atlantic

6 – New England

7 – E North Central

8 – W North Central

Replacing reference cendiv with lowest level

. gen cendivrecode=.

(1242 missing values generated)

cendivrecode=0 for New England

. replace cendivrecode=0 if cendiv==6

(31 real changes made)

cendivrecode=1 for W North Central

. replace cendivrecode=1 if cendiv==8

(357 real changes made)

cendivrecode=2 for E South Central

. replace cendivrecode=2 if cendiv==3

(142 real changes made)

cendivrecode=3 for E North Central

. replace cendivrecode=3 if cendiv==7

(82 real changes made)

cendivrecode=4 for W South Central

. replace cendivrecode=4 if cendiv==2

(130 real changes made)

cendivrecode=5 for Middle Atlantic

. replace cendivrecode=5 if cendiv==5

(22 real changes made)

cendivrecode=6 for Pacific

. replace cendivrecode=6 if cendiv==0

(37 real changes made)

cendivrecode=7 for Mountain

. replace cendivrecode=7 if cendiv==1

(163 real changes made)

cendivrecode=8 for South Atlantic

. replace cendivrecode=8 if cendiv==4

(278 real changes made)

Rescaling proportion of calls black race to calls with black race per 10%

. gen black10=black*10

. summarize black10

```
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+---------------------------------------------------------
     black10 |      1242    1.226176    1.919296          0   8.852459
```

Rescaling proportion of calls scene location home to calls with scene location home per 10%

. gen home10=home*10

. summarize home10

```
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+---------------------------------------------------------
      home10 |      1242    5.569896    1.282023          0          9
```

Rescaling proportion of calls with cardiac arrest or death to percent of calls with cardiac arrest or death.

gen deathsx100=deathsx*100

```
. summarize deathsx100

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
  deathsx100 |      1242    1.386687    1.099686          0   16.66667
```

Rescaling proportion of calls transported to calls transported per 10%

```
. gen transp10=transp*10

. summarize transp10

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
    transp10 |      1242    8.010482    1.214238   .0436681         10
```

Rescaling proportion of calls with cardiac arrest or death to percent of calls with cardiac arrest or death.

```
. gen antiemet100=antiemet*100

. summarize antiemet100

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
 antiemet100 |      1242    1.671006     2.32302          0         20
```

Rerunning final effects model with variables rescaled

. xi: nbreg naloxcnt disabled i.cendivrecode noins medinc infntdth black10 home10 deathsx100 ageyrmed transp10 antiemet100 sysremed scenrmed scenemed, exposure(numcalls) irr

i.cendivrecode _Icendivrec_0-8 (naturally coded; _Icendivrec_0 omitted)

Fitting Poisson model:

Iteration 0: log likelihood = -9362.4662

Iteration 1: log likelihood = -8372.577

Iteration 2: log likelihood = -8370.0684

Iteration 3: log likelihood = -8370.0675

Fitting constant-only model:

Iteration 0: log likelihood = -4269.0628

Iteration 1: log likelihood = -4241.8843

Iteration 2: log likelihood = -4211.9199

Iteration 3: log likelihood = -4211.6559

Iteration 4: log likelihood = -4211.6559

Fitting full model:

Iteration 0: log likelihood = -4058.1654

Iteration 1: log likelihood = -3969.2068

Iteration 2: log likelihood = -3967.5549

Iteration 3: log likelihood = -3967.5522

Iteration 4: log likelihood = -3967.5522

Negative binomial regression Number of obs = 1242

LR chi2(21) = 488.21

Dispersion = mean Prob > chi2 = 0.0000

Log likelihood = -3967.5522 Pseudo R2 = 0.0580

naloxcnt	IRR	Std. Err.	z	P>|z|	[95% Conf.	Interval]
disabled	1.063993	.0139333	4.74	0.000	1.037031	1.091655
_Icendivre~1	1.264136	.1812884	1.63	0.102	.9543857	1.674417
_Icendivre~2	1.623363	.2577023	3.05	0.002	1.189298	2.21585
_Icendivre~3	1.646176	.2531655	3.24	0.001	1.217783	2.225269
_Icendivre~4	1.663308	.2623739	3.23	0.001	1.220962	2.265913
_Icendivre~5	2.109449	.4225332	3.73	0.000	1.424522	3.123698
_Icendivre~6	2.319711	.4145727	4.71	0.000	1.634215	3.292747
_Icendivre~7	2.362885	.3731565	5.44	0.000	1.733873	3.220089
_Icendivre~8	2.439991	.3626444	6.00	0.000	1.823384	3.265114
noins	1.033129	.0129365	2.60	0.009	1.008083	1.058798
medinc	1.076396	.0137632	5.76	0.000	1.049756	1.103712
infntdth	1.033274	.0091793	3.68	0.000	1.015438	1.051422
black10	.9295972	.0142889	-4.75	0.000	.9020092	.958029
home10	1.095719	.0250235	4.00	0.000	1.047756	1.145879
deathsx100	1.112855	.0284634	4.18	0.000	1.058443	1.170064
ageyrmed	.9779824	.0039052	-5.58	0.000	.9703582	.9856666
transp10	1.120058	.024267	5.23	0.000	1.073491	1.168644
antiemet100	1.078804	.0117589	6.96	0.000	1.056002	1.102099
sysremed	.8999693	.0132749	-7.15	0.000	.8743235	.9263673

```
    scenrmed |   1.073442   .0189258     4.02   0.000     1.036982    1.111185
    scenemed |   1.038792    .009816     4.03   0.000      1.01973    1.058211
    numcalls | (exposure)
-------------+----------------------------------------------------------------
    /lnalpha |  -.9399077     .05983                     -1.057172    -.822643
-------------+----------------------------------------------------------------
       alpha |   .3906639   .0233734                      .3474368    .4392691
------------------------------------------------------------------------------
Likelihood-ratio test of alpha=0:  chibar2(01) = 8805.03 Prob>=chibar2 = 0.000
```

Negative binomial regression model – combined variables 1. AIC: = 7981.10 2. ML R2 (from fitstat) = 0.33 Pseudo R2 (calculated from ppred covariance) = 0.79			
Variable (deciles from county sociodemographic data)	IRR	95%CI	P value
<65 no health ins - % (2009)	1.03	1.01, 1.06	0.01
Median household income (2005-2009)	1.08	1.05, 1.10	<0.001
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.06	1.04, 1.09	<0.001
Infant deaths per 1,000 live births (2007)	1.03	1.02, 1.05	<0.001
Census Division 0 – New England 1 - W North Central 2 – E South Central 3 – E North Central 4 – W South Central 5 – Middle Atlantic 6 – Pacific 7 – Mountain 8 – South Atlantic	 - 1.26 1.62 1.65 1.66 2.11 2.32 2.36 2.44	 - 0.95, 1.67 1.19, 2.22 1.22, 2.22 1.22, 2.27 1.42, 3.12 1.63, 3.29 1.73, 3.22 1.82, 3.27	<0.001 - 0.10 0.002 0.001 0.001 <0.001 <0.001 <0.001 <0.001
Variable (EMS variables)			
Black - 10% of calls	0.93	0.90, 0.96	<0.001
Home scene location - 10% of calls	1.10	1.05, 1.15	<0.001
Complaint cardiac arrest or death - 1% of calls	1.11	1.06, 1.17	<0.001
Median age – years	0.98	0.97, 0.99	<0.001
Transported – 10% of calls	1.12	1.07, 1.17	<0.001
Antiemetic administered - 1% of calls	1.08	1.06, 1.10	<0.001
Median time from call to dispatch – seconds	0.91	0.88, 0.94	<0.001
Median call to scene time –	1.06	1.03, 1.10	0.001

minutes			
Median time on scene – minutes	1.04	1.02, 1.06	<0.001

APPENDIX 4

Negative Binomial Models

EMS variables

Negative binomial model – EMS variables 1. AIC: 8076.07 2. ML R2 (from fitstat): 0.265 pseudo r2 (from ppred covariance): 0.770			
Variable	IRR	95%CI	P value
EMS Region 0 (West) 1 (South Central) 2 (East) 3 (North Central)	 - 0.89 0.94 0.55	 - 0.75, 1.06 0.79, 1.11 0.47, 0.64	<0.001 - 0.19 0.45 <0.001
Urbanicity 0 (Wilderness) 1 (Rural) 2 (Suburban) 3 (Urban)	 - 0.93 1.08 1.12	 - 0.80, 1.09 0.90, 1.29 0.96, 1.31	<0.001 - 0.37 0.41 0.15
Black - % of calls	0.54	0.40, 0.72	<0.001
Home call location - %	3.44	2.22, 5.34	<0.001
Complaint respiratory symptoms - %	0.40	0.14, 1.10	0.08
Complaint cardiac arrest or death - %	22184.14	133.73, 3680049.00	<0.001
Median age – years	0.98	0.97, 0.99	<0.001
Transported calls - %	2.53	1.63, 3.93	<0.001
Antiemetic administered - %	2681.02	285.66, 25162.36	<0.001
Median time from call to dispatch – seconds	0.90	0.87, 0.92	<0.001
Median call to scene time – minutes	1.09	1.05, 1.13	<0.001
Median time on scene – minutes	1.04	1.02, 1.06	<0.001

Sociodemographic variables

Negative binomial regression model – County sociodemographic variables 1. AIC: = 8173.542 2. ML R2 (from fitstat) = 0.208 Pseudo R2 (calculated from ppred covariance) = 0.787			
Variable (deciles)	IRR	95%CI	P value
Total population (2010)	1.01	0.97, 1.05	0.69
65 or over - % (2010)	1.05	1.01, 1.10	0.02
Persons per square mile (2010)	1.03	0.99, 1.07	0.14
Percent population change (2000 – 2010)	1.03	1.00, 1.05	0.03
Native American - % (2010)	1.03	1.01, 1.05	0.01
<65 no health ins - % (2009)	1.03	1.01, 1.06	0.02
Median household income (2005-2009)	1.09	1.05, 1.12	<0.001
Civilians over 18: Social security: Retired workers - benefit recipients - % (2010)	0.94	0.90, 0.98	0.004
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.10	1.07, 1.13	<0.001
Infant deaths per 1,000 live births (2007)	1.03	1.01, 1.05	0.003
Census Division 0 – Pacific 1 - Mountain 2 – W South Central 3 – E South Central 4 – South Atlantic 5 – Middle Atlantic 6 – New England 7 – E North Central 8 – W North Central	 - 1.08 0.58 0.54 0.80 0.71 0.42 0.74 0.54	 - 0.81, 1.45 0.42, 0.79 0.39, 0.74 0.59, 1.09 0.47, 1.07 0.29, 0.62 0.54, 1.03 0.41, 0.73	<0.001 - 0.60 0.001 <0.001 0.16 0.10 <0.001 0.07 <0.001

APPENDIX 5

Poisson models

EMS variables

Poisson regression model – EMS variables 1. AIC: 17882.20 2. Pseudo R2 Pseudo R2 (from poisson model) = 0.2714 Pseudo R2 (calculated from ppred covariance) = 0.8499			
Variable	IRR	95%CI	P value
EMS Region 0 (West) 1 (South Central) 2 (East) 3 (North Central)	 - 0.98 0.82 0.54	 - 0.86, 1.10 0.71, 0.93 0.48, 0.61	<0.001 - 0.69 0.003 <0.001
Urbanicity 0 (Wilderness) 1 (Rural) 2 (Suburban) 3 (Urban)	 - 0.89 1.11 1.18	 - 0.71, 1.11 0.89, 1.39 0.96, 1.45	<0.001 - 0.29 0.34 0.12
Asian - % of calls	0.22	0.08, 0.62	0.004
Black - % of calls	0.66	0.52, 0.83	<0.001
Hawaiian/PI - % of calls	19.02	2.72, 133.18	0.003
Other race - % of calls	1.68	1.10, 2.57	0.02
Home call location - %	2.32	1.50, 3.60	<0.001
Outdoor call location - %	0.21	0.11, 0.41	<0.001
Complaint respiratory symptoms - %	0.37	0.13, 1.06	0.07
Complaint decreased level of consciousness - %	2.88	1.29, 6.44	0.01
Complaint cardiac arrest or death - %	139832.00	1497.78, 13100000.00	<0.001
Median age – years	0.98	0.97, 0.99	<0.001
Antiemetic administered - %	123.65	20.08, 761.44	<0.001
Median time from call to dispatch – seconds	0.92	0.89, 0.96	<0.001
Median call to scene time – minutes	1.07	1.03, 1.12	0.001
Median time on	1.05	1.04, 1.07	<0.001

scene – minutes			

Sociodemographic variables

Poisson regression model – County sociodemographic variables 1. AIC: 17421.16 2. Pseudo R2 Pseudo R2 (from poisson model) = 0.291 Pseudo R2 (calculated from ppred covariance) = 0.857			
Variable (deciles)	IRR	95%CI	P value
Under 18 - % (2010)	1.03	1.01, 1.05	0.009
Persons per square mile (2010)	1.06	1.03, 1.08	<0.001
Females - % (2010)	0.98	0.97, 1.00	0.07
White, non Hispanic - % (2010)	1.04	1.01, 1.07	0.01
Asian - % (2010)	1.03	1.00, 1.06	0.09
Children in single parent households - % (2006-2010)	0.97	0.95, 1.00	0.03
>25 some college - % (2005-2009)	0.97	0.95, 0.98	<0.001
>25 bachelors only - % (2005-2009)	0.97	0.94, 1.00	0.07
>25 graduate degree - % (2005-2009)	1.03	1.00, 1.06	0.03
<65 no health ins - % (2009)	1.04	1.02, 1.06	<0.001
Median household income (2005-2009)	1.04	1.01, 1.07	0.008
Households with cash public assistance income - % (2005-2009)	1.08	1.05, 1.10	<0.001
Households with Food Stamp/SNAP benefits - % (2005-2009)	0.97	0.94, 1.00	0.05
Place of birth, foreign-born - % (2005-2009)	1.07	1.04, 1.10	<0.001
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.06	1.03, 1.08	<0.001
Births per 1,000 population (2007)	0.98	0.96, 1.00	0.06
Infant deaths per 1,000 live births (2007)	1.03	1.01, 1.05	0.001

Census Division			<0.001
0 – Pacific	-	-	-
1 - Mountain	1.38	1.12, 1.70	0.003
2 – W South Central	0.95	0.74, 1.21	0.65
3 – E South Central	0.75	0.57, 0.98	0.04
4 – South Atlantic	0.98	0.77, 1.24	0.84
5 – Middle Atlantic	0.45	0.36, 0.57	<0.001
6 – New England	0.32	0.23, 0.44	<0.001
7 – E North Central	0.68	0.54, 0.84	<0.001
8 – W North Central	0.48	0.38, 0.60	<0.001

Combined EMS and Sociodemographic variables

Poisson regression model – combined variables 1. AIC: 15499.29 2. Pseudo R2 Pseudo R2 (from poisson model) = 0.291 Pseudo R2 (calculated from ppred covariance) = 0.857			
Variable (deciles from county sociodemographic data)	IRR	95%CI	P value
Persons per square mile (2010)	1.04	1.01, 1.06	0.001
Children in single parent households - % (2006-2010)	0.97	0.96, 0.99	0.01
>25 some college - % (2005-2009)	0.97	0.95, 0.98	<0.001
<65 no health ins - % (2009)	1.03	1.01, 1.05	0.01
Median household income (2005-2009)	1.03	1.00, 1.06	0.02
Households with cash public assistance income - % (2005-2009)	1.05	1.03, 1.07	<0.001
Households with Food Stamp/SNAP benefits - % (2005-2009)	0.98	0.95, 1.00	0.10
Place of birth, foreign-born - % (2005-2009)	1.06	1.03, 1.08	<0.001
Civilians over 18: Social security: disabled workers - benefit recipients - % (2010)	1.04	1.02, 1.06	<0.001
Infant deaths per 1,000 live births (2007)	1.02	1.01, 1.04	0.01
Census Division 0 – Pacific 1 - Mountain 2 – W South Central 3 – E South Central 4 – South Atlantic 5 – Middle Atlantic 6 – New England 7 – E North Central	 - 1.42 1.10 1.00 1.34 0.68 0.49 0.79	 - 1.09, 1.84 0.83, 1.46 0.73, 1.38 1.00, 1.79 0.50, 0.93 0.35, 0.68 0.61, 1.04	<0.001 - 0.009 0.52 0.98 0.05 0.01 <0.001 0.09

8 – W North Central	0.59	0.45, 0.78	<0.001
Variable (EMS Variables)			
Asian - %	0.16	0.06, 0.41	<0.001
Black - %	0.57	0.43, 0.76	<0.001
Hawaiian/PI - %	22.92	3.00, 174.95	0.003
Home call location - %	2.15	1.40, 3.31	<0.001
Outdoor call location - %	0.30	0.16, 0.56	<0.001
Complaint decreased level of consciousness - %	4.28	2.17, 8.45	<0.001
Complaint cardiac arrest or death - %	377648.10	5114.39, 27900000.00	<0.001
Median age – years	0.98	0.98, 0.99	<0.001
Antiemetic administered - %	78.71	13.83, 447.91	<0.001
Median time from call to dispatch – seconds	0.94	0.91, 0.97	0.001
Median call to scene time – minutes	1.03	1.00, 1.08	0.09
Median time on scene – minutes	1.04	1.02, 1.05	<0.001