Indiana State Epidemiological Outcomes Workgroup (SEOW)

Special Topics Research Report

ANALYSIS OF OPIOID OVERDOSE MORTALITY AND VULNERABILITY INDEX IN INDIANA

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SyraHealth

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Purpose of Special Topics Report

The purpose of SEOW Special Topic Reports (STRs) is to provide current information and data on issues related to substance use/misuse and mental and behavioral health in Indiana. STRs are intended to be utilized for strategic planning by addictions professionals, community stakeholders, community coalitions and workgroups, and grant writers, and should also be used to inform and develop public health policies at the local and state levels.

The purpose of this STR is to provide an analysis of the factors affecting the opioid overdose mortality and to provide a regional vulnerability index for opioid overdose using the latest available data.

What are opioids?

In the United States, there has been a rising concern regarding increasing opioid-related mortality in the past few years. Opioids are pharmaceutical drugs that are primarily prescribed for pain relief. Opioids also activate the reward regions of the brain and release endorphins, hormones that can cause an almost-euphoric feeling (Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies | NEJM, n.d.). However, an individual's tolerance to the effects of opioids increases with continued use (Death Rate Maps & Graphs | Drug Overdose | CDC Injury Center, 2022a). In other words, the more a person uses opioids, the more opioids they have to ingest to feel the euphoria. This behavior is what is commonly seen in opioid addiction (Death Rate Maps & Graphs | Drug Overdose | CDC Injury Center, 2022a).

According to the Centers for Disease Control, around 107,000 people in the United States died from a drug overdose in 2022 (Fighting Fentanyl, 2022). Almost two-thirds of those deaths involved a synthetic opioid, or an opioid that was made in a laboratory, the most common being fentanyl (Fighting Fentanyl, 2022). While this increased opioid overdose mortality has been seen across all demographics, however, overdose deaths in Black and Native communities disproportionately increased during the COVID-19 pandemic (Fighting Fentanyl, 2022). Another contributing factor to the rise of opioid overdose deaths has been increasing polysubstance use, or the use of multiple drugs at the same time. These factors are important to consider when thinking about opioid overdose mortality in the United States. The existing literature focuses on the rising mortality rate due to synthetic opioids, polysubstance use, the COVID-19 pandemic, and the disproportionate deaths among certain populations.

It has been suggested that the rise in opioid prescriptions for pain relief contributed to increased rates of opioid addiction (Salsitz, 2016). With opiates, physical dependence occurs quickly and can even occur within a few days. However, opioid dependence does not necessarily indicate opioid use disorder (Salsitz, 2016). If no adverse behavioral symptoms are present, individuals with physical opioid dependence do not meet the criteria for an opioid use disorder (i.e.. individuals who use opioids consistently to manage chronic pain) (Salsitz, 2016). There are further complications because opioids can cause relief from anxiety and depression, which causes further difficulties in identifying when an individual meets the criteria for opioid use disorder. It is possible that some patients currently taking opiates and are not exhibiting any psychological symptoms of opioid dependence may develop behavioral problems when withdrawal occurs (Salsitz, 2016). Individuals that experience opioid addiction can develop severe withdrawal symptoms including aches, bone pain, severe abdominal pain, agitation, and anxiety (Wang, 2019). The inability to curb withdrawal symptoms have been reported by individuals with opioid addiction as a reason for continued opioid use (Wang, 2019). Consistent use to avoid withdrawal symptoms is another method that could lead to higher opioid tolerance. The higher dosages needed to achieve the desired effects increases the risk of death from opioid overdose.

There are opioid receptors throughout the body, with opioid use affecting the central nervous system, gastrointestinal, cardiovascular, and pulmonary systems. A key reaction to opioids is respiratory depression, which can lead to prolonged apnea and even sudden death (Kyatkin, 2019). Furthermore, there are effects of chronic opioid use that contribute to higher risk of drug-related overdose deaths (Han et al., 2019). Autopsies of chronic opioid users have found that chronic opioid use may cause cardiac hypertrophy, cardiac fibrosis, and atherosclerosis (Han et al., 2019). Individuals with these medical conditions are at even higher risk of opioid-related cardiovascular events.

The latest rise in opioid-related deaths has stemmed from the introduction and mass circulation of synthetic opioids and illicit fentanyl. The most recent findings suggest that, from 2019 to 2020, there was a 53.1 percent increase in synthetic opioid-related deaths in the United States. The increases in deaths are experienced in all demographic characteristics and rurality (Althoff et al., 2020). These trends are a shift from data in 2014-2017 which found that fentanyls were primarily a problem in the Northeast and Midwest (Ciccarone, 2021). In 2016, estimates indicate that fentanyls contributed to nearly half of opioid overdose deaths in the United States (Han et al., 2019). A key characteristic of fentanyl is its high potency, which has been indicated to be 30-50 times more potent than heroin. With this high potency, there is a smaller volume needed to reach overdose levels (Han et al, 2019). Because of the potency of fentanyl, it has been discovered more street drugs may commonly be laced with it to increase the effects of the advertised drug. To illustrate this, in 2015, Amlani et al. conducted a survey in British Columbia in people who survived a fentanyl overdose; 73% of these individuals reported no knowledge of using fentanyl. Thus, it is likely that many fentanyl-related overdose deaths occur in individuals that have no knowledge that fentanyl is present in the drugs they are using (Amlani et al. 2015).

Regarding polysubstance use, it can be difficult to identify if users intentionally ingest or inject opioids because synthetic opioids are being increasingly found in heroin, methamphetamine, cocaine, and counterfeit pills (LaRue et al., 2019). One study assessed 1 million unique urine drug tests to assess rates of fentanyl positivity when screening for cocaine or methamphetamine (LaRue et al., 2019). The report indicated that between 2013 and 2018, rates of fentanyl positivity increased by 1850% in individuals that tested positive for cocaine and by 798% in individuals that tested positive for methamphetamine (LaRue et al., 2019). Some individuals report using stimulants to help balance out the effects of opiates to allow them to function "normally" (Volkow 2020). These combinations can enhance lethality because both stimulants and opiates affect the cardiovascular and pulmonary systems (Volkow 2020).

Another important trend has been a greater increase in rates of synthetic opioid related deaths amongst urban Black and Hispanic populations, partially explained by low socio-economic status and related stressors (Ciccarone, 2021). In conjunction, increased use of multiple substances in opioid-related deaths has also contributed to recent increases in overdose mortality. Data from 2019 found that around 40 percent of opioid-related deaths also involved a stimulant (O'Donnell, 2021). Recently, a significant rise of methamphetamine use was observed within individuals with opioid use disorder. These individuals reported that methamphetamines were used as an alternative to opioids due to similar psychoactive effects and increasingly limited access to prescriptions opioids, and individuals reported that opioids were even used in conjunction with methamphetamine or cocaine to elicit a synergistic high (Ellis et al., 2018). A study focused on youth populations found in 2018 that polysubstance-involved opioid overdose deaths surpassed the prevalence of opioid only deaths, with the rate of stimulant-opioid related deaths increased by 351 percent since 2010 (Lim et al., 2021) Around this time, the Midwest saw the largest increases in deaths involving psychostimulants (Mattson, 2021).

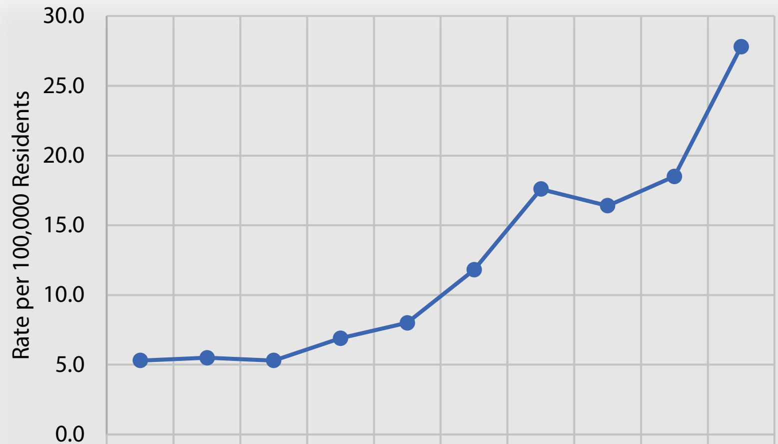
Current data also found that national opioid overdose mortality was affected by the COVID-19 pandemic. An article published in the American Journal for Emergency Medicine found that, while the COVID-19 pandemic slowed the rate of increase of opioid overdose admittances to emergency departments, there was no decrease in opioid-related overdoses (Rosenbaum et al., 2021). In fact, there was a 30 percent increase of drug overdose deaths in 2020, with rates spiking starting in March (Tanz et al., n.d.). It was estimated that drug overdose deaths increased by 17% from 2020 to 2021 (Joint Economic Committee Democrats, 2022). This increase is likely due to increased social isolation and similar stressors related to mental health and well-being, economic stress, and postponed medical care due to the pandemic (Tanz et al., n.d.). Furthermore, the limited access to healthcare and treatment services during the pandemic has been reported to be a potential contributor to higher relapse rates (Joint Economic Committee Democrats, 2022).

While the Indiana state government has enacted several laws trying to mitigate rising deaths from opioid overdoses, deaths continue to increase at an alarming rate, particularly in vulnerable communities. The Indiana state government has passed Naloxone access laws, Good Samaritan laws, and Naloxone with Rx laws. Despite continued government interventions overdose mortality rates are still increasing within the state (Adams et al., 2020). Opioid-related mortality in Indiana has increased in recent years. In 2020, 2,321 people in Indiana died from an opioid-related overdose (Death Rate Maps & Graphs | Drug Overdose | CDC Injury Center, 2022). Around 70 percent of those deaths involved synthetic opioids (Death Rate Maps & Graphs | Drug Overdose | CDC Injury Center, 2022). However, there are certain vulnerable communities that have been affected more than others. National trends of disproportionate mortality rates amongst Black communities are similar to those in the Midwest (Le et al., 2022). This study found that rural communities with higher proportions of minority populations and urban communities with higher rates of unemployment were correlated with higher overdose rates (Zhu et al., 2022). In Indiana, a 2019 report indicated that Black communities experienced the largest increase in opioid-related overdose deaths from 2015-2017 (Indiana State Department of Health, 2019). Both Black communities and Hispanic communities experienced greater increases in rates of opioid-related overdose deaths as compared to Caucasian communities at an estimated 103% and 57% vs. 25%, respectively (Lippold et al., 2019). It is important for future legislation to focus on prescriber education in conjunction with interventions in these vulnerable communities in order to reduce opioid-related mortality in Indiana (Adams et al., 2020).

Overall statistics and trends in Indiana

Figure 1: Deaths from drug poisoning involving any opioid in Indiana per 100,000 Residents, 2011-2020

Indiana Department of Health Stats Explorer provides data on drug poisoning deaths involving any opioid in Indiana per 100,000 residents. The rate remained relatively similar from 2011 (5.3) to 2012 (5.5) to 2013 (5.3). The rate begins to increase for the following several years (2014: 6.9; 2015: 8.0; 2016: 11.8; 2017: 17.6). After a small downtick from 2017 to 2018 (16.4), two increases followed in 2019 (18.5) and 2020 (27.8).



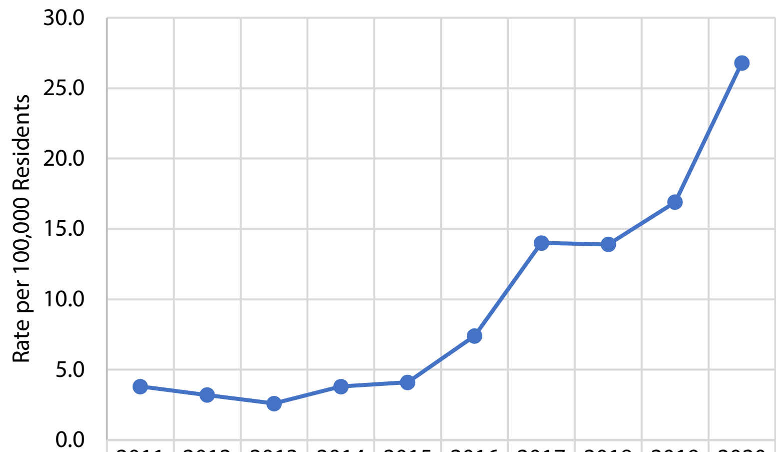
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	5.3	5.5	5.3	6.9	8.0	11.8	17.6	16.4	18.5	27.8

Year

(IDOH Stats Explorer, 2020)

Figure 2: Deaths from drug poisoning involving any opioid pain reliever in Indiana per 100,000 Residents, 2011-2020

Deaths from drug poisoning involving any opioid pain reliever per 100,000 residents is published by Indiana Department of Health Stats Explorer. The rate decreased from 2011 (3.8) to 2012 (3.2) to 2013 (2.6), followed by several increases in 2014 (3.8), 2015 (4.1), 2016 (7.4), and 2017 (14.0). The rate decreased slightly lower in 2018 (13.9), followed by two increases in 2019 (16.9) and 2020 (26.8).



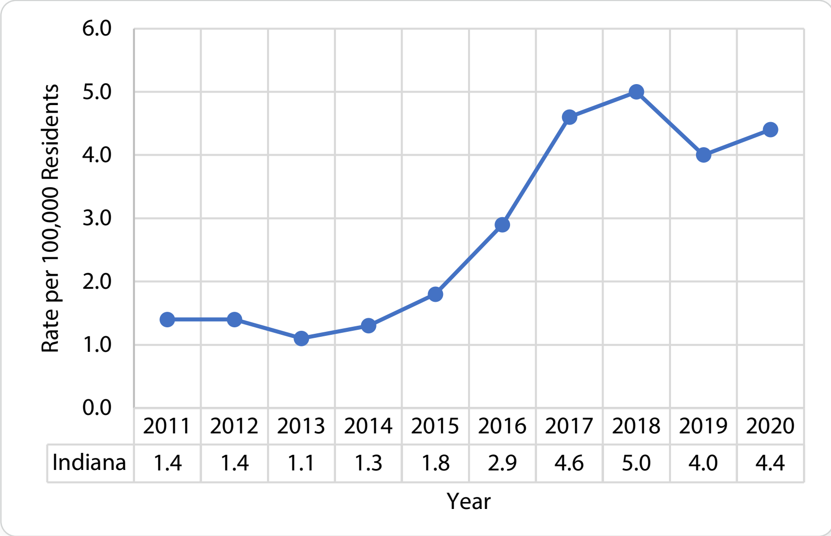
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	3.8	3.2	2.6	3.8	4.1	7.4	14.0	13.9	16.9	26.8

Year

(IDOH Stats Explorer, 2020)

Figure 3: **Deaths from drug poisoning involving benzodiazepines in Indiana per 100,000 Residents, 2011-2020**

Drug poisoning deaths per 100,000 residents in Indiana involving benzodiazepines is provided by Indiana Department of Health Stats Explorer. Rates in 2011 and 2012 were both 1.4, followed by a decrease in 2013 (1.1). For the next several years, increases in rates occurred (2014: 1.3; 2015: 1.8; 2016: 2.9; 2017: 4.6; 2018: 5.0). The rate decreases in 2019 (4.0), followed by another increase in 2020 (4.4).

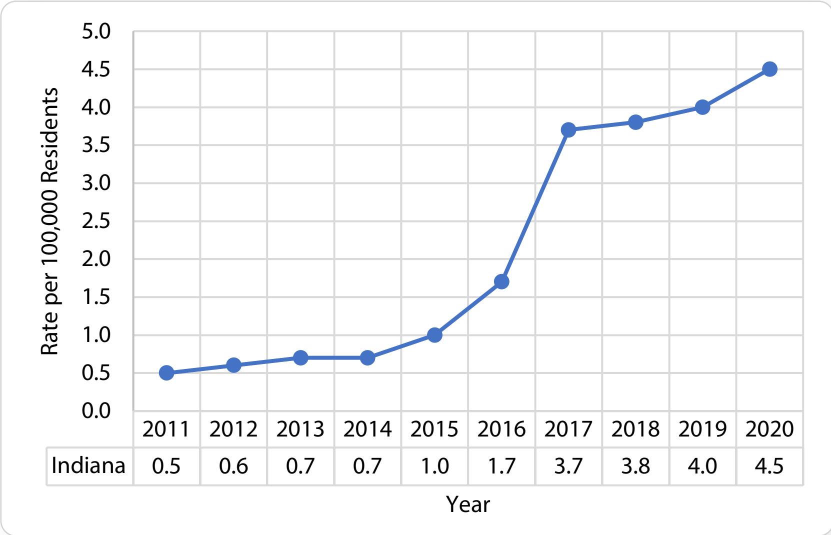


	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	1.4	1.4	1.1	1.3	1.8	2.9	4.6	5.0	4.0	4.4

(IDOH Stats Explorer, 2020)

Figure 4: **Deaths from drug poisoning involving cocaine in Indiana per 100,000 Residents, 2011-2020**

Indiana Stats Explorer publishes data on deaths in Indiana per 100,000 residents from drug poisonings involving cocaine. Rates slightly increased from 2011 (0.5) to 2012 (0.6) to 2013 (0.7), and leveled off in 2014 (0.7). Increases followed in 2015 (1.0), 2016 (1.7), 2017 (3.7), 2018 (3.8), 2019 (4.0), and 2020 (4.5).

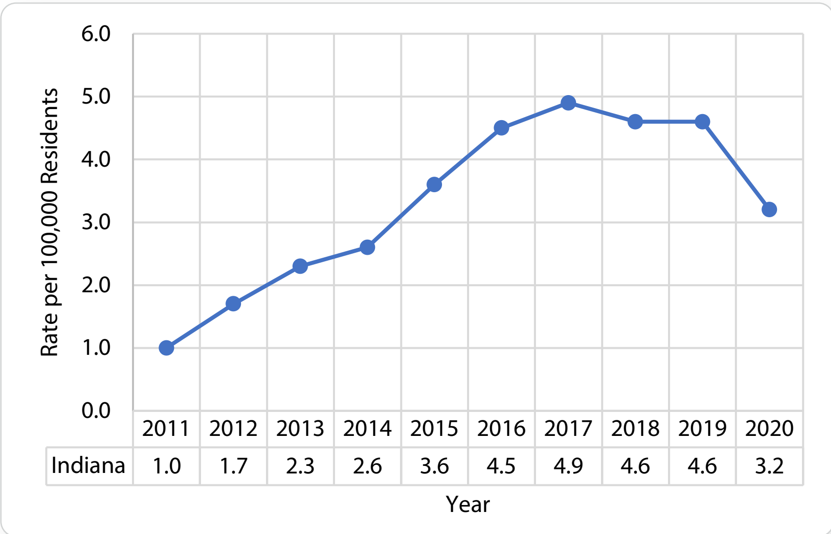


	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	0.5	0.6	0.7	0.7	1.0	1.7	3.7	3.8	4.0	4.5

(IDOH Stats Explorer, 2020)

Figure 5: **Deaths from drug poisoning involving heroin in Indiana per 100,000 Residents, 2011-2020**

Deaths per 100,000 residents from drug poisonings involving heroin in Indiana are published by Indiana Department of Health Stats Explorer. Rates, following 2011 (1.0), increased for several years (2012: 1.7; 2013: 2.3; 2014: 2.6; 2015: 3.6; 2016: 4.5; 2017: 4.9), followed by a decrease in 2018 (4.6). After leveling off in 2019 (4.6), the rate decreased in 2020 (3.2).

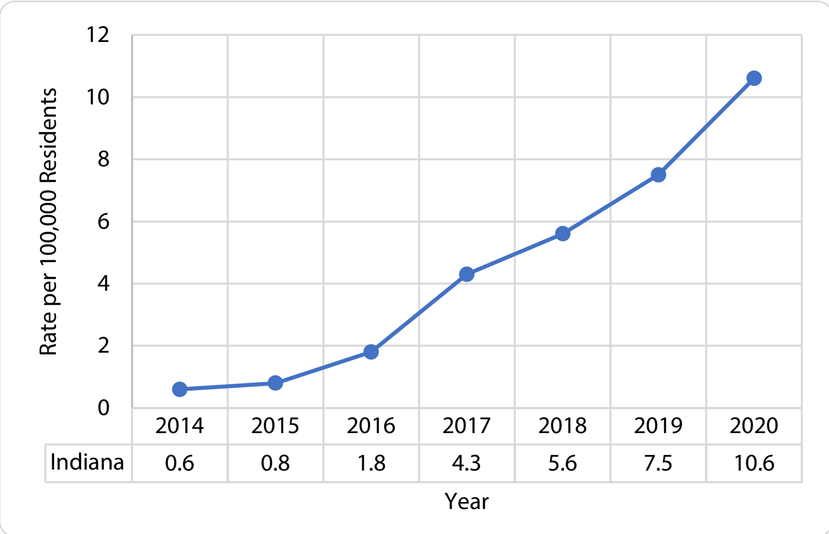


	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	1.0	1.7	2.3	2.6	3.6	4.5	4.9	4.6	4.6	3.2

(IDOH Stats Explorer, 2020)

Figure 6: **Deaths from drug poisoning involving psychostimulants other than cocaine in Indiana per 100,000 Residents, 2014-2020**

Drug poisoning deaths involving psychostimulants other than cocaine per 100,000 residents in Indiana is published by Indiana Department of Health Stats Explorer. From 2014 (0.6) to 2020 (10.6), rates increased every year (2015: 0.8; 2016: 1.8; 2017: 4.3; 2018: 5.6; 2019: 7.5).



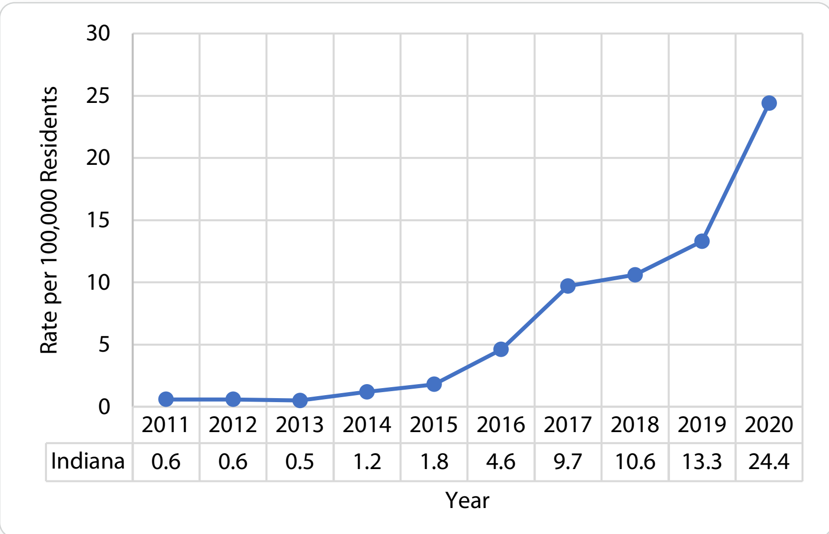
	2014	2015	2016	2017	2018	2019	2020
Indiana	0.6	0.8	1.8	4.3	5.6	7.5	10.6

(IDOH Stats Explorer, 2020)

Figure 7: **Deaths from drug poisoning involving synthetic opioids in Indiana per 100,000 Residents, 2011-2020**

Indiana Department of Health Stats Explorer publishes data on deaths per 100,000 in Indiana from drug poisonings involving synthetic opioids. Rates were relatively stable from 2011 (0.6) to 2012 (0.6) to 2013 (0.5), followed by increases for every year following (2014: 1.2; 2015: 1.8; 2016: 4.6; 2017: 9.7; 2018: 10.6; 2019: 13.3; 2020: 24.4).

Deaths from drug overdose involving any opioid in Indiana are published by the Indiana Drug Overdose Dashboard.

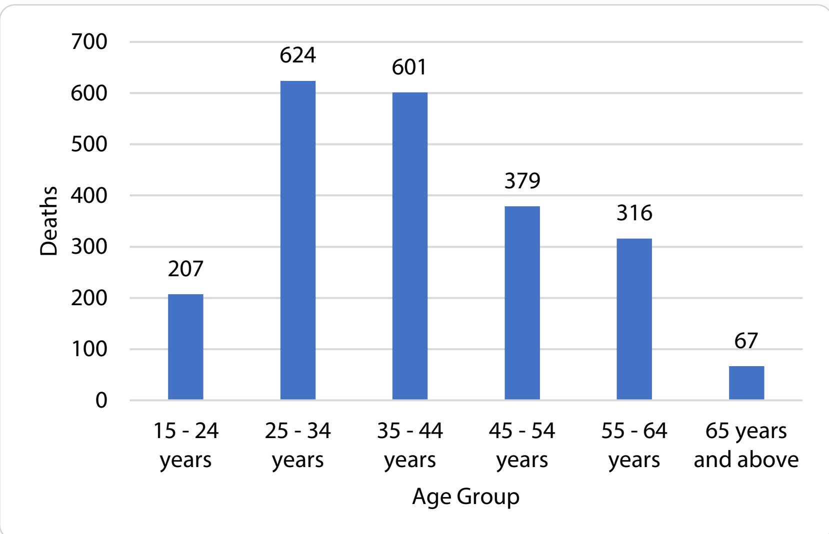


	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Indiana	0.6	0.6	0.5	1.2	1.8	4.6	9.7	10.6	13.3	24.4

(IDOH Stats Explorer, 2020)

Figure 8: **Deaths from drug overdose involving any opioid in Indiana by Age, 2021**

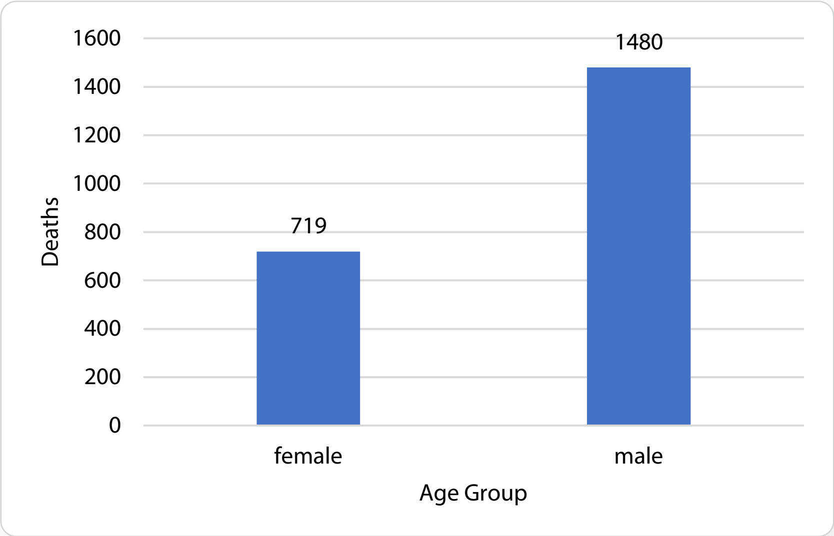
In 2021, the age group with the least deaths was those aged 65 and older, with 67 deaths. Those aged 15 to 24 years old accounted for 207 deaths, followed by 55 to 64 years old (316) and 45 to 54 years old (379). Those aged 35 to 44 had the second highest count with 601 deaths, beaten out only by those aged 25 to 34 years old (624).



(IDOH, Indiana Drug Overdose Dashboard, 2021)

Figure 9: Deaths from drug overdose involving any opioid in Indiana by Gender, 2021

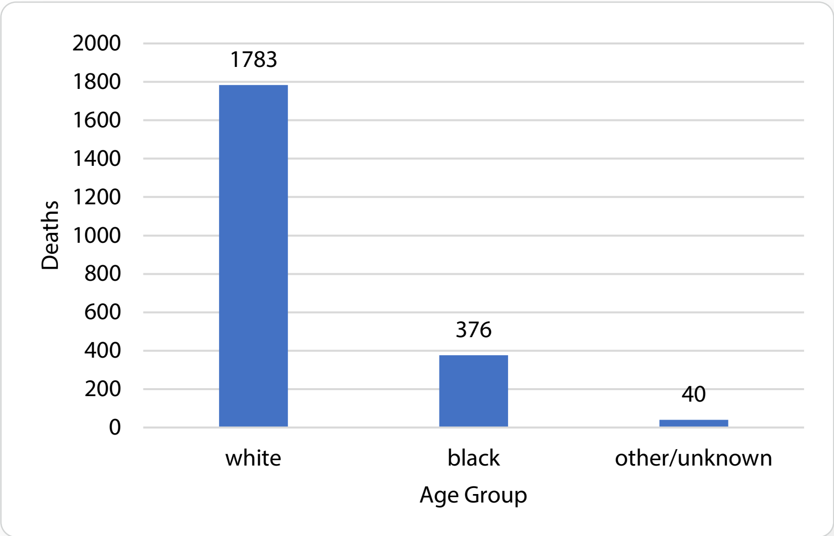
Males (1480) accounted for more deaths from drug overdoses involving any opioid than women (719).



(IDOH, Indiana Drug Overdose Dashboard, 2021)

Figure 10: Deaths from drug overdose involving any opioid in Indiana by Race, 2021

Whites (1783) accounted for more deaths from drug overdoses involving any opioid than blacks (376), along with another 40 deaths in the other/unknown category.



(IDOH, Indiana Drug Overdose Dashboard, 2021)

Regional analysis of factors affecting opioid overdose deaths

We perform a county wide assessment of factors affecting opioid overdose deaths in Indiana with the most recent data available at the time of analysis. To evaluate of Indiana's community-level vulnerability to opioid-related overdose we followed a count regression model based weighted ranking approach with mean standardized covariates and an opioid-involved overdose mortality outcome to calculate county-level vulnerability scores (Sawyer et al., 2021. Data was collected from the 92 counties in the state of Indiana for the purpose of this study. The outcome variable of interest is opioid related overdose mortality, that is deaths from drug poisoning involving any opioid. The outcome of interest is a count response and is quantitative in nature. The predictor variables used for this analysis were selected based on features used for previous vulnerability assessments and are all quantitative in nature. Most of the information comes from the online public health statistics data portal of the Indiana Department of Health and including overdose deaths caused by opioids, emergency room visits linked to opioids, and chronic HCV diagnoses (Indiana Department of Health, 2021).

Data on arrests connected to opioids were gathered from the Indiana Laboratory Information Management System, and information on the rate of opioid prescriptions was found from online CDC county level retail opioid prescription maps that displayed data from the IQVIA Xponent database. The Substance Abuse and Mental Health Services Administration's (SAMHSA) treatment locator and the Indiana Department of Health both provided address-level 2021 services data. This was used to evaluate county-level availability to harm reduction and treatment for opioid use disorder (OUD) (Administration for Mental Health and Substance Abuse Services, 2021). From the American Community Survey of the Census Bureau, we compiled demographic and social determinants of health indicators at the county level. We used county-level 5-year estimates from the years 2015 to 2019 for all ACS metrics. Utilizing a rural-urban classification system created especially for Indiana, the Purdue University Indiana County Classification System was used.

Data and Indicators:

Outcome Indicator - opioid related overdose mortality: Number of deaths from drug poisoning involving any opioid were used as the core outcome indicator in this analysis. Opioid-related overdose mortality refers to deaths that are caused by an overdose of opioids, including prescription painkillers, heroin, and synthetic opioids like fentanyl. Overdose deaths can occur when individuals take opioids in quantities or frequencies that are higher than prescribed, or when they use opioids in combination with other drugs or alcohol. Overdose deaths can also occur when individuals use opioids that have been contaminated with other substances, such as fentanyl or other synthetic opioids.

Core Indicator Variables: Six features are identified to have a strong association with the outcome of interest in previous vulnerability assessments and based on subject matter expertise (Sawyer et al., 2021; Michelle et al., 2017). The following features are used as core indicators in regional analysis.

Median Income: This is based on the income distribution of all households in a county, including those with no income. The median income is a statistical measure that represents the income level at which half of the households in each county earn more, and the other half earn less.

Opioid-Related Arrests: Number of arrests with laboratory-confirmed opioids per 100,000 population. Opioid-related arrests refer to arrests made by law enforcement officials for crimes related to the use, possession, sale, or distribution of opioids, such as heroin, fentanyl, and prescription painkillers. These arrests may involve individuals who are addicted to opioids and engage in criminal behavior to obtain or fund their drug use, or individuals who are involved in the illegal manufacture, distribution, or sale of opioids. Opioid-related arrests can also include arrests for driving under the influence of opioids or other drugs, as well as arrests related to drug trafficking, prescription fraud, or theft of prescription drugs.

Opioid-Related Emergency Department Visits: This is related to non-fatal emergency department visits involving any opioid overdose per 100,000 population. Opioid-related emergency department visits refer to visits to hospital emergency departments or urgent care centers that are related to the use or misuse of opioids, including prescription painkillers, heroin, and synthetic opioids like fentanyl. These visits may be due to a range of issues related to opioid use, including overdose, withdrawal symptoms, infections related to injection drug use, and other health complications caused by opioid abuse.

Chronic HCV Cases: These are confirmed and probable cases of chronic HCV per 100,000 population. Chronic HCV (Hepatitis C virus) refers to a long-term infection of the liver caused by the Hepatitis C virus. HCV is a blood-borne virus that can be transmitted through exposure to infected blood, such as through sharing needles or other injection equipment, receiving a blood transfusion prior to 1992, or through sexual contact with an infected person.

Opioid Dispensing Rate per 100 persons: The opioid dispensing rate refers to the number of opioid prescriptions that are filled by pharmacies or other healthcare providers within a certain population or geographic area over a given period. Specifically, it represents the number of opioid prescriptions dispensed per 100 persons in a specific population during a certain time frame, usually one year. This metric is often used by public health officials and policymakers to monitor the use of opioid medications and to identify potential areas where interventions may be needed to address high rates of opioid prescribing, misuse, or overdose.

Drug Submission: Drug submission refers to the process by which a pharmaceutical company applies to a regulatory agency seeking approval to market a new drug or to make changes to an existing drug, such as a new formulation or dosage form.

Other Covariates: Variables that measure county-level demographics and socioeconomic determinants were included in the study. These are the percentage of households that are female-led, Average household size, percent of residents with a disability, Black or African American population in the county: Percentage of the population that was non-Hispanic White, non-Hispanic Black or African American, and Hispanic or Latino. The unemployment rate, Population under 18 years, and The Gini index. Treatment service facilities: Calculated as the number of OUD services per 100,000 population. OUD services included syringe services programs (SSPs), sometimes known as needle exchange programs, and service locations offering MOUD, as well as OUD therapy and counseling services. A rural-urban covariate: This classification system splits counties into rural, rural/mixed, and urban categories by population density, size of the largest city or town, and a subjective indicator (county identity), Median income in the past 12 months, Total Population in each county, HIV Incidence Rate per 100,000, and Number of food insecure persons and children in the county.

The list of data sources and the year of data acquisition are provided in the Appendix A.

Regional Opioid Vulnerability Index

Number of opioid-related overdose mortality across the different counties in the state of Indiana are explored with respect to core indicators and other covariates to identify trends and patterns. One of the primary objectives of the study is to identify the Indiana localities that are at risk of fatal opioid overdose. Bivariate and multivariate negative binomial regression models for the opioid death counts are applied to estimate regression coefficients. Negative Binomial Regression models are fitted based on two approaches. Technically known as frequentist approach is uses available data only while Bayesian approach is based on both data and prior information on core indicators and other covariates. Bivariate analysis measures the level of association between each individual indicator and the outcome variable of interest (opioid-involved overdose mortality) while multivariate analysis measures association among core indicators and the outcome after adjusting for other covariate information. Graphs on trends and patterns and estimates regression coefficients from four modeling approaches [bivariate and multivariate negative binomial models under frequentist and Bayesian approaches] are presented under appendix D. All data preparation and analysis were performed using R programming software and the Stan probabilistic package which fits Negative Binomial Regression models, Bayesian models, and specify priors using R package rethinking version 1.59.

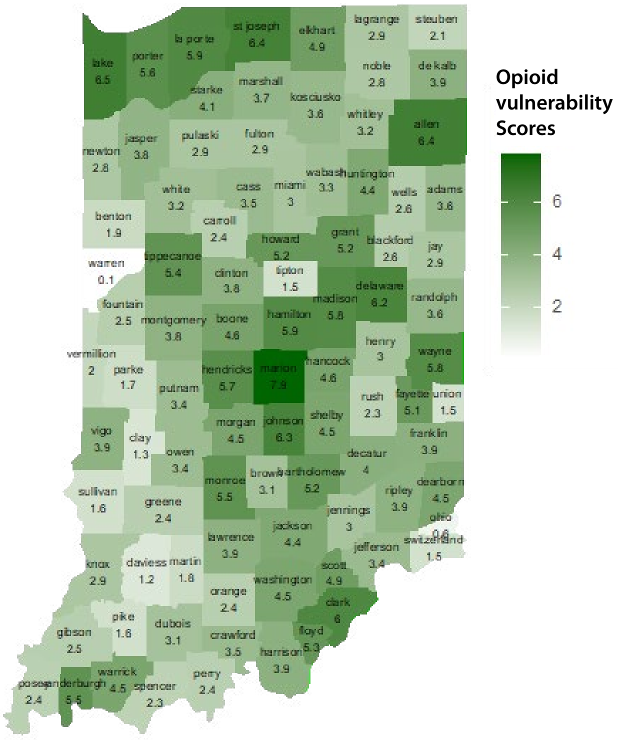
The vulnerability score for 2019 is calculated using significant indicators and the variables regression coefficient to compute each county's index score. We calculated quintile ranks for each of the core indicators and the remaining significant covariates. A quintile rank is a way of dividing a set of data into five equal groups, or quintiles, based on the values of the data. To calculate a quintile rank, the data set is first sorted in ascending order. Then, the total number of items in the data set is divided by five to determine the number of items in each quintile. The first quintile includes the lowest twenty percent of the data, the second quintile includes the next twenty percent, and so on up to the fifth quintile which includes the highest twenty percent of the data. Each item in the data set was assigned a quintile rank based on its position within the data set. Core indicators and the remaining significant covariates were ranked from highest to lowest, on a scale of 1 to 5 where higher scores (score = 5) indicated increased and lower scores (score = 1) indicated decreased vulnerability. Vulnerability scores were calculated using estimated regression coefficients of the significant indicators obtained from four models stated above. We weighted the quintile ranks by the variable's regression coefficient and calculated the vulnerability score by summing the weighted quintile ranks via the following equation.

$$VI_i = \beta_1 X_{i1} + \beta_2 X_{i2} + \ldots + \beta_p X_{ip}$$

where, VI_i represents vulnerability score for the i-th (i = 1,2,…92) county, β_j (j=1,2,…,p) is the j-th regression coefficient, and X_{ij} is the quintile rank for the j-th indicator variable.

Vulnerability scores resulted from frequentist multivariate analysis are presented in a geographical map below (See Map 1). Marion, Lake, Allen, St. Joseph, Johnson, Delaware, Clark, La Porte, and Hamilton are among the most vulnerable counties in order and recorded vulnerability scores are above 5.7. In addition, Union, Clay, Daviess, Ohio, Sullivan, Pike, Parke, Tipton, and Warren were among the least vulnerable counties with scores below 2. Results from frequentist bivariate analysis generate similar county wise ranking in terms of vulnerability scores and are presented in appendix D.

Map 1: Indiana county opioid vulnerability scores for 2019 (Multivariate negative binomial regression model)



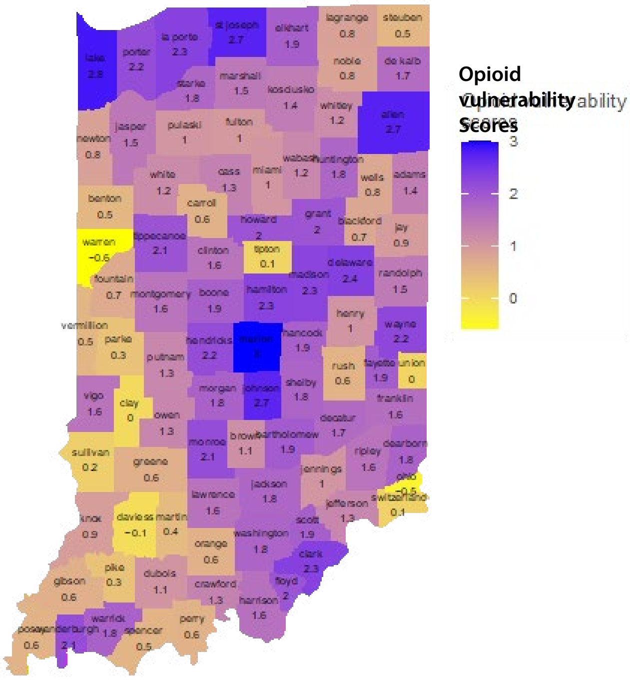
Data source: Vulnerability scores were calculated using count regression based method

Vulnerability scores for each county in the state of Indiana obtained using estimated regression coefficients from multivariate Bayesian approach are presented as geographical map as follows. Both frequentist Bayesian approaches generate similar county ranking in terms of opioid vulnerability indicating dominance of available data over prior information. Marion county is ranked highest, followed by Lake, St. Joseph and Allen County. Counties that appeared to be the least vulnerable in the frequentist approach are also the same as the counties recorded as the least vulnerable by Bayesian approach.

We calculated county wise crude death rates (CDR) from opioid related overdoses and presented as follows (See Map 2). CDR county map is representative of the vulnerability score map. It is to be noted that St. Joseph has the highest CDR followed by Fayette, Crawford, Marion, and Delaware county whereas Marion County reported the highest vulnerability score followed by Lake, St. Joseph, Allen, Johnson and Delaware county.

Map 3 shows the county opioid vulnerability scores using bayesian approach

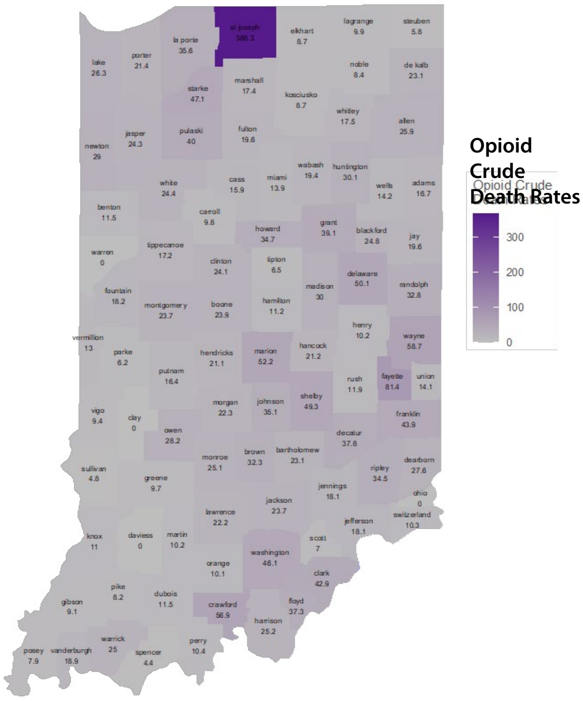
Map 3: Indiana county opioid vulnerability scores for 2019 (Multivariate negative binomial regression model Bayesian Approach)



Data source: Vulnerability scores were calculated using count regression based method

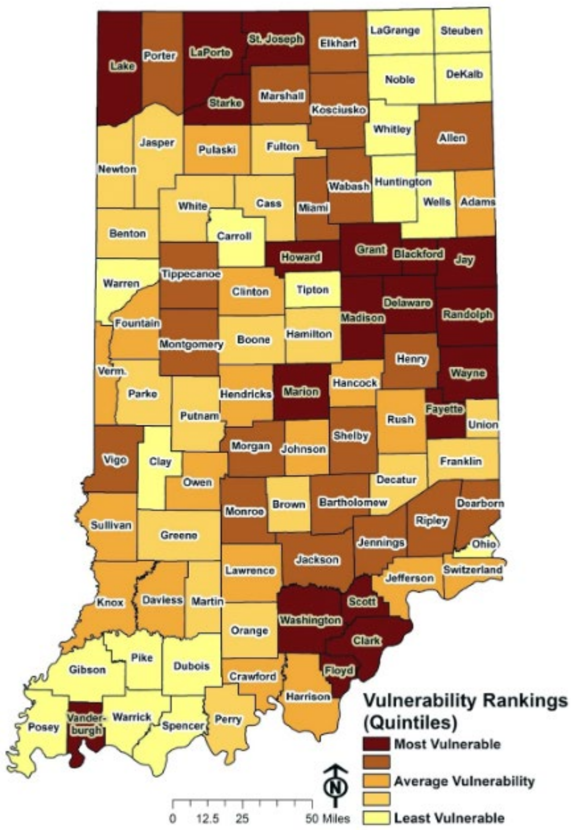
Map 4 shows the regional opioid vulnerability index derived by Sawyer et al. (2021) study for the 2017 data. We find similarities between Sawyer et al. and this study in terms of vulnerability indices across some counties for 2017 and 2019 data.

Map 2: Indiana county opioid Crude Death Rate (Crude Death Rate of different Counties in the State of Indiana 2019 dataset)



Data source: Crude Death Rate were calculated using Crude Death Rate Method

Map 4: Indiana opioid vulnerability ranking in 2017



Source: Sawyer et al., 2021"

Key Points:

- During COVID 19 there was an overall increase in overdoses deaths with an even larger increase found in Black and Native communities
- From 2019-202 there was a 53.1% increase in overdose deaths in the United States
- Fentanyl is 30-50x more potent than heroin
- In 2020 2,321 people in Indiana died from an opioid-related overdose
- Blacks and Hispanics have higher rates of opioid-related overdose deaths than Caucasians
- The 25-34 years old demographic accounted for the highest rate of overdoses in Indiana in 2021
- Males have a higher rate of overdose deaths than females
- Marion county has the highest opioid vulnerability score among counties in Indiana
- Multivariate count regression models are recommended for calculating county wise opioid vulnerability indices as these models provide better fit to the data on opioid related mortality with core indicators and other covariate information
- Drug poisoning involving synthetic opioids in Indiana have been increasing since 2014

Discussion

Deaths due to drug overdose has increased consistently within the last few years. This study reviewed the overdose death rate of several opioids and/or prescription drugs in the Indiana population. The rate was considered per 100,000 Indiana residents. Over the past ten years, Indiana saw an upward trend in drug related deaths across all drugs excluding heroin. When looking at the effects of any opioid from 2011-2020 there was a consistent increase over the nine-year time-span, with a slight drop between 2017-2018. Since 2018, there has been a consistent increase in drug related mortality. In most recent years, the rate increased by 9.3 in 2020 from 2019. Overdose mortality rates induced by pain relievers fluctuated amongst Indiana residents for four years before seeing a drastic increase between 2016-2017. Overdose deaths from to pain relievers continued to fluctuate between 2017-2018 until seeing another substantial increase between 2019-2020. Pain relievers related overdose deaths contributed to 9.9 more deaths in 2020 than in 2019. Drug related deaths due to overdosing on benzodiazepines also increased heavily between 2013-2017. Although, there was a quick decline between 2018 - 2019, overdose due to use of benzodiazepines increased again between 2019 - 2020. Drug poisoning associated with cocaine attributed overdose deaths saw a large increase from 2016-2017 and has continued to increase consistently through 2020. Drug poisoning was observed as the leading variable for opioid related deaths in Indiana. Many of these overdoses derived from both intentional and unintentional fentanyl use. Fentanyl, with a potency anywhere from 30-50 times higher than heroin, has been critical in the overdose death rates of Indiana residents. Heroin, overdoses showed the only decrease in rates in recent years. The death rate of drug poisoning associated with psychostimulants has increased consistently from 2011-2020. The death rate of drug overdoses related to synthetic opioids did not see a major increase until 2016. Since, the death rate has increase consistently, nearly doubling from 2019 to 2020.

The COVID-19 pandemic is an additional variable that has contributed to the increase in opioid related deaths. The nationwide mandated lockdown caused a surge in recreational drug use. Subsequently, the rate of opioid use and drug related overdoses increased during the pandemic. However, admittances into the emergency room due to overdose saw no increase. The gap between overdoses and overdose related emergency room admittances exhibit a clear indicator of the increase in overdose deaths during the pandemic. In 2021, young adults ranging from ages 25-34 were the biggest group to fall victim to opioid overdose mortality. The second largest group being adults ages 35-44. Overdose deaths in males largely outweigh the overdose rate amongst females contributing to twice as many deaths. Of these groups, African-Americans and Hispanics have a lower overdose death rate than Whites.

Indiana saw over 2,321 deaths due to opioid related overdose statewide in 2020. When examining vulnerability index scores based on multivariate count regression model under two inferential approaches provide, Marion county has the highest score of all the counties in Indiana under both approaches. Other counties like, Lake, St. Joseph, and Allen counties have a higher vulnerability index as well. These counties corresponding directly to cities with a bigger population, similar to what is observed in Indianapolis.

We present overall opioid-involved overdose vulnerability in order by quintile for all 92 Indiana counties. Quintile five represents the most vulnerable counties, while quintile one represents the least vulnerable counties. Summary measures, range and average for vulnerability scores and opioid involved overdose death counts are also displayed.

Table 1: **Summary data by quintiles**

Quintile 5	Quintile 4	Quintile 3	Quintile 2	Quintile 1
VI Scores Range: 5.23 - 7.86	VI Scores Range: 3.95 - 5.2	VI Scores Range: 3.20 - 3.94	VI Scores Range: 2.43 - 3.19	VI Scores Range: 0.06 - 2.42
Average VI Score: 5.96	Average VI Score: 4.55	Average VI Score: 3.61	Average VI Score: 2.82	Average VI Score: 1.73
Opioid Death Count Range: 29 - 510	Opioid Death Count Range: 10 - 26	Opioid Death Count Range: 6 - 10	Opioid Death Count Range: 3 - 6	Opioid Death Count Range: 0 - 2
Average Opioid Death Count: 76	Average Opioid Death Count: 15	Average Opioid Death Count: 8	Average Opioid Death Count: 4	Average Opioid Death Count: 1
Marion Lake Allen St. Joseph Johnson Delaware Clark LaPorte Hamilton Madison Wayne Hendricks Porter Monroe Vanderburgh Tippecanoe Floyd Howard	Grant Bartholomew Fayette Scott Elkhart Boone Hancock Morgan Warrick Dearborn Washington Shelby Huntington Jackson Starke Decatur DeKalb Franklin	Harrison Lawrence Ripley Vigo Montgomery Clinton Jasper Marshall Randolph Kosciusko Adams Cass Crawford Jefferson Owen Putnam Wabash White	Whitley Brown Dubois Henry Jennings Miami Pulaski Fulton Jay Knox LaGrange Newton Noble Wells Blackford Fountain Gibson Greene	Carroll Orange Perry Posey Rush Spencer Steuben Vermillion Benton Martin Parke Pike Sullivan Switzerland Tipton Union Clay Daviess Ohio Warren

There are multiple contributing factors that lead to use and misusage of opioids in the United States. These factors frequently affect Indiana residents, mainly young adults age 25-34. The COVID-19 pandemic was also a huge contributor to mental stressors that propelled the usage of opioids and subsequently, overdose rates. Indiana experienced extremely high prevalence rates of opioid use and overdose deaths within the past nine years.

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Technical/Supplemental Appendix

A. Data Source for Core Indicators and Covariates

Table A: Core Indicators and Sources

Variable	Label	Year	Data Source
ns-deaths	Opioid-involved overdose deaths	2020	IDOH stat explorer
Median income	Medium income (USD)	2019	ACS-2019
Arrests	Opioid-related arrest	2018	"indiana laboratory information management system https://hub.mph.in"
nf-ev-stats	Opioid-related emergency department visits	2021	IDOH stat explorer
hep-c-chronic-stat	Chronic HCV cases	2021	IDOH stat explorer
Opioid-dispensing-rate-per-100	Opioid prescriptions dispensation	2019	IDOH stat explorer
Drug submission	Drug submission	2019	IDOH stat explorer

Table A: Other indicators and sources

Variable	Label	Year	Data source
People-with internet	Percentage of the population with internet access	2019	ACS, 2019 5-year estimates
Gini-index	Gini index (a measure of inequility)	2019	ACS, 2019 5-year estimates
Population	Total population in each county	2019	ACS, 2019 5-year estimates
Median-income-12 months	Median income in the past 12 months	2019	ACS, 2019 5-year estimates
Owner occupied home	Owner occupied homes in county	2019	ACS, 2019 5-year estimates
Bik-AA-population	Black and african american population in county	2019	ACS, 2019 5-year estimates
Unemployed-persons	Percentage of unemployed population in county	2019	ACS, 2019 5-year estimates
Female led homes	Percentage of female led households	2019	ACS, 2019 5-year estimates
Average household size	Average household size in the county	2019	ACS, 2019 5-year estimates
No-diploma-25	Percentage of the population aboe 25 years of age without a school diploma	2019	ACS, 2019 5-year estimates
Disable	Percentage of the population with disbility both male and females	2019	ACS, 2019 5-year estimates
under-18	Percentage of under 18 population in county	2019	ACS, 2019 5-year estimates
Trt-service-faciliites	County-level opioid use disorder treatment service facilities	2021	Substance abuse & mental health services administration,2021
HIV-aids-stats	HIV incidence rate per 100,00	2020	IDOH stat explorer
Food-insecure-person	number of food insecure persons in the county	2020	Map the meal gap
Rural-urban-class	Classification of couties as rural/urban/mixed	2022	Classified manually according to existing literature

B. Distributions of the outcome variable (opioid-related overdose mortality) and core indicator variables

Figure B.1: Distribution of opioid related mortality

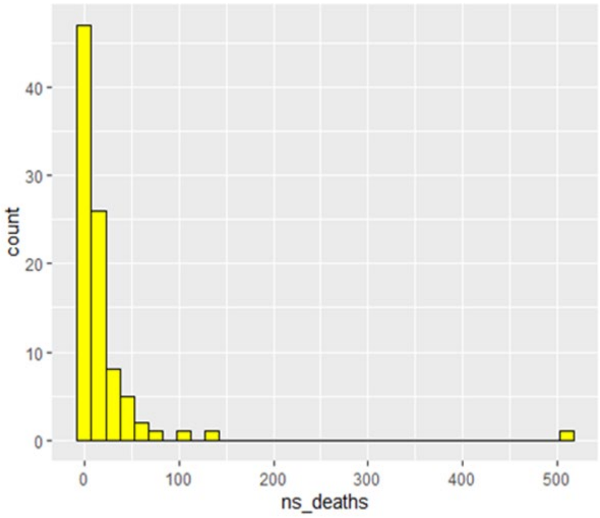
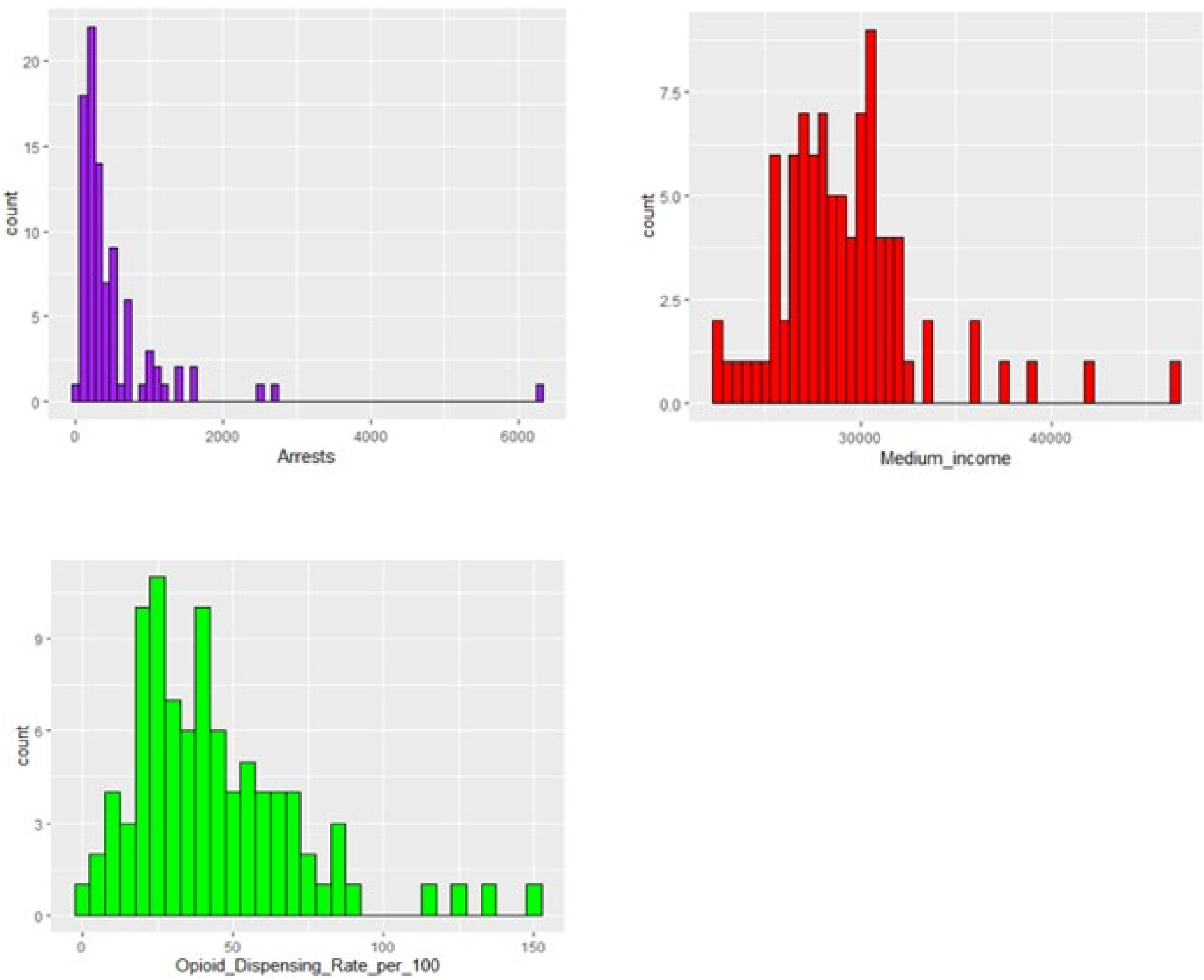
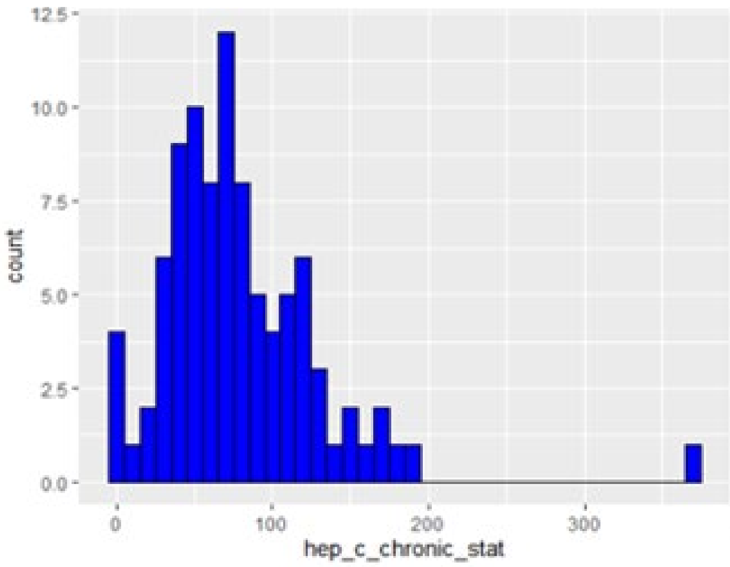


Figure B.2: Distributions of Core Indicators

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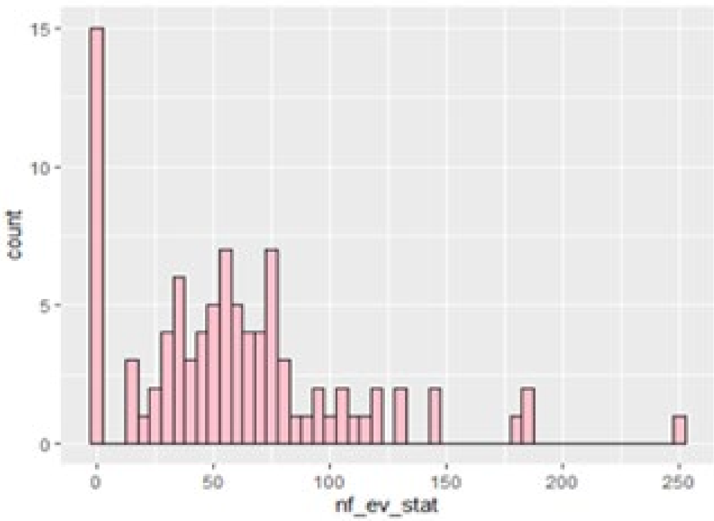
10.0
7.5
5.0
2.5
0.0
count
0
100
200
300
hep_c_chronic_stat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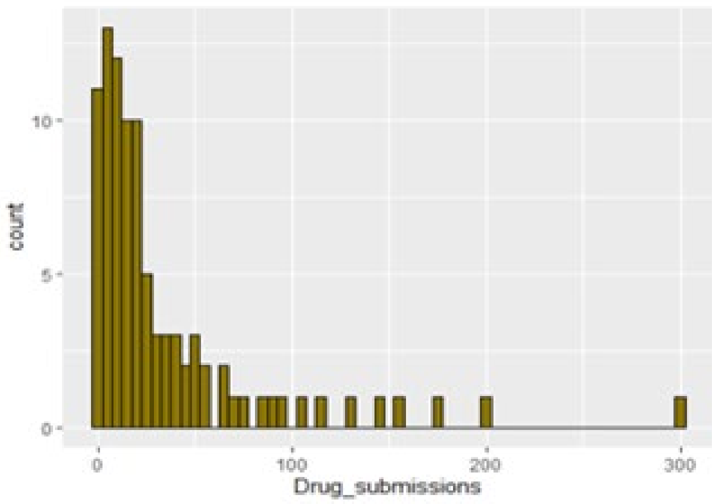
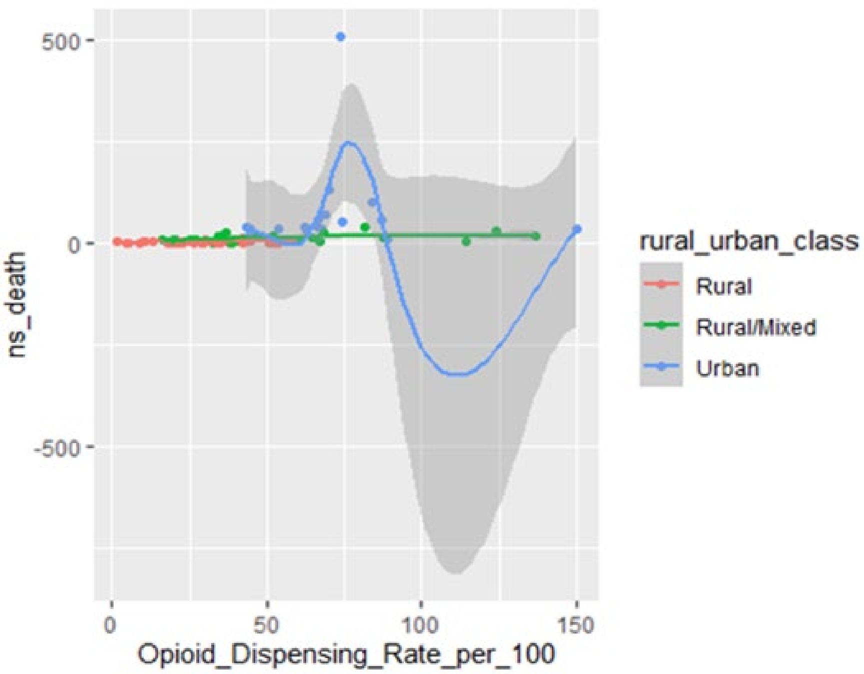
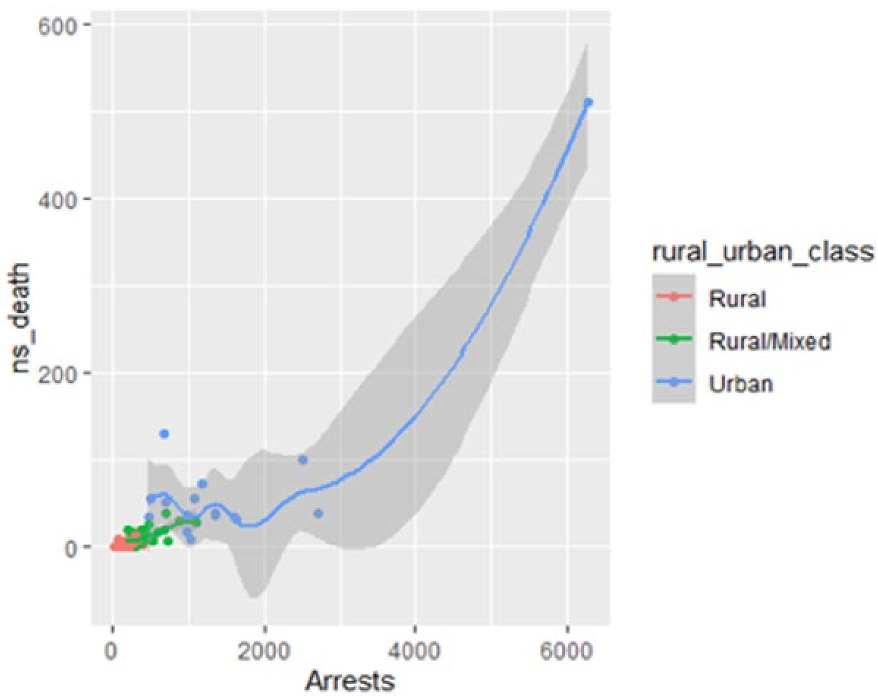
10
5
0
count
0
50
100
150
200
250
nf_ev_stat


10
5
0
count
0
100
200
300
Drug_submissions

C. Visualization of the relationship between opioid-related overdose mortality and core indicator variables by rural urban classification

Figure C.1:
Distribution of opioid related mortality





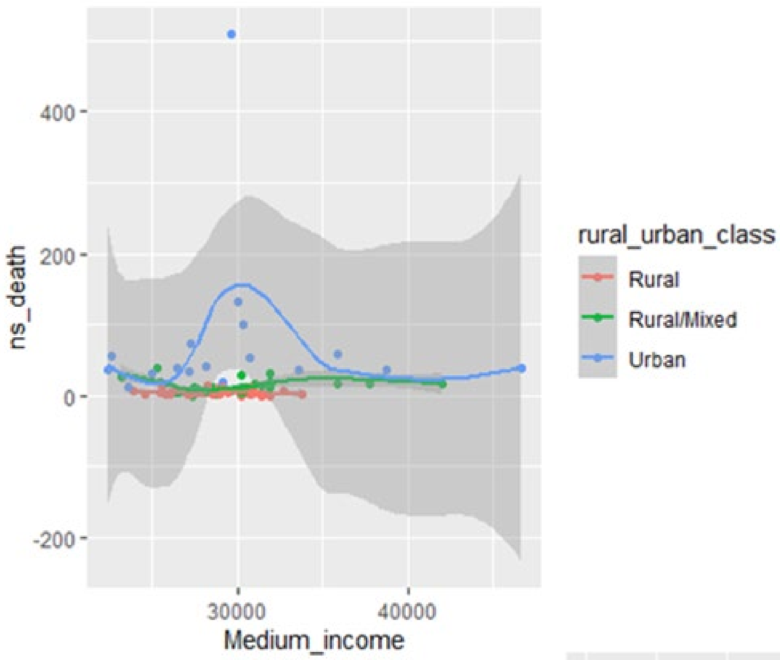
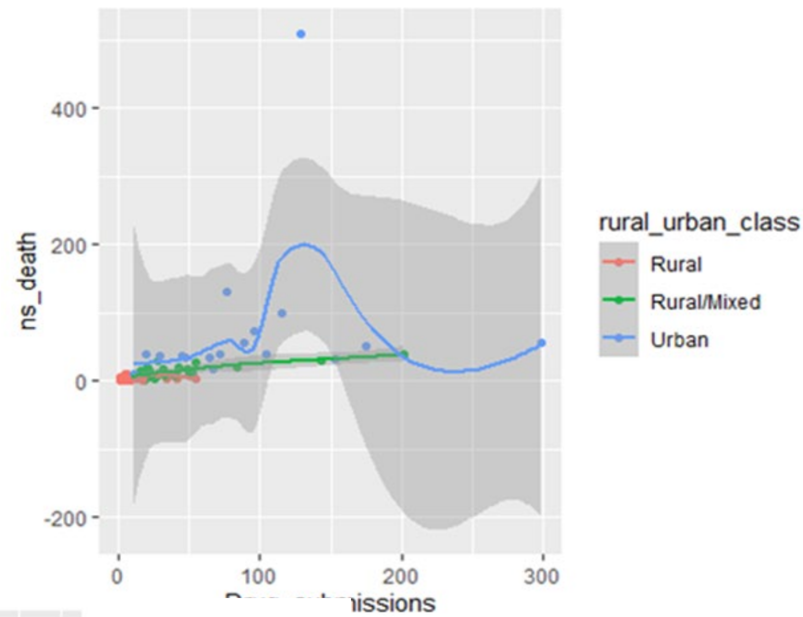
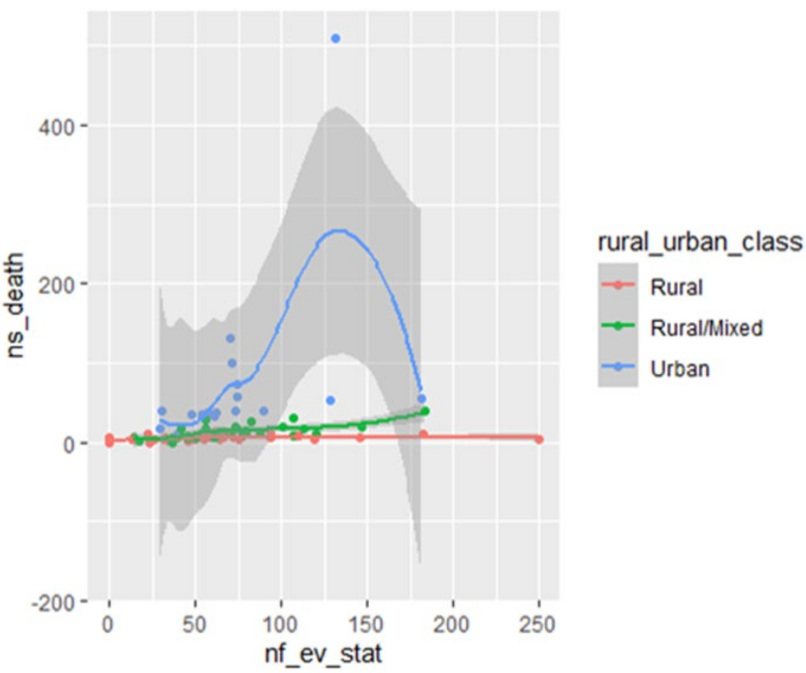


Figure C.3: Relationship between opioid-related overdose mortality and core indicator variables (opioid related arrests, opioid dispensing rate, medium income, drug submission, number of emergency visits) by rural urban classification





D. Estimates of Regression Coefficients by frequentist multivariate negative binomial model

Table D1: Regression coeeficient estimates: Bayesian multivarate approach

Variable	Estimates	10% CI	90% CI	Standard error	Rhat	mcse	Prior
Median income	0.6	-0.8	2.1	*1.250000*	*1.0*	*0.0*	*N(0,2.5)*
Chronic hepatitis	-0.1	-0.2	0.1	0.014000	1.0	0.0	N(0,2.5)
C cases							
Drug submission	-0.1	-0.2	0.1	0.128000	1.0	0.0	N(0,2.5)
Arrests	-0.1	-0.4	0.0	0.119000	1.0	0.0	N(0,2.5)
Opioid dispensing rate per 100	-0.1	-0.3	0.0	0.111000	1.0	0.0	N(0,2.5)
Opioid-related emergency visit	0.4	0.3	0.6	0.126000	1.0	0.0	N(0,2.5)
Gini index	0.2	0.1	0.4	0.110000	1.0	0.0	N(0,2.5)
median income 12 months	-0.6	-2.2	0.8	0.126000	1.0	0.0	N(0,2.5)
Average household size	0.0	-0.1	0.1	0.096200	1.0	0.0	N(0,2.5)
Treatment services facilities	0.2	0.1	0.5	0.142000	1.0	0.0	N(0,2.5)
Rural/mixed	0.2	-0.1	0.5	0.025000	1.0	0.0	N(0,2.5)
Urban	0.5	0.4	1.3	0.356000	1.0	0.0	N(0,2.5)

Estimates of Regression Coefficients by Bayesian multivariate negative binomial model

Variable	Estimates	10% CI	90% CI	Standard error	Rhat	mcse	Prior
Median income	0.6	-0.8	2.1	*1.250000*	*1.0*	*0.0*	*N(0,2.5)*
Chronic hepatitis	-0.1	-0.2	0.1	0.014000	1.0	0.0	N(0,2.5)
C cases							
Drug submission	-0.1	-0.2	0.1	0.128000	1.0	0.0	N(0,2.5)
Arrests	-0.1	-0.4	0.0	0.119000	1.0	0.0	N(0,2.5)
Opioid dispensing rate per 100	-0.1	-0.3	0.0	0.111000	1.0	0.0	N(0,2.5)
Opioid-related emergency visit	0.4	0.3	0.6	0.126000	1.0	0.0	N(0,2.5)
Gini index	0.2	0.1	0.4	0.110000	1.0	0.0	N(0,2.5)
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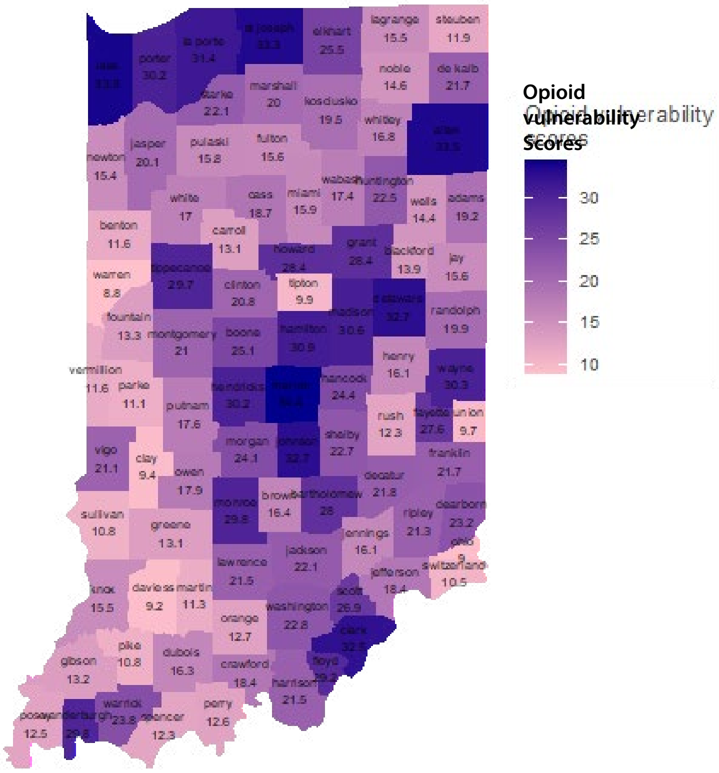
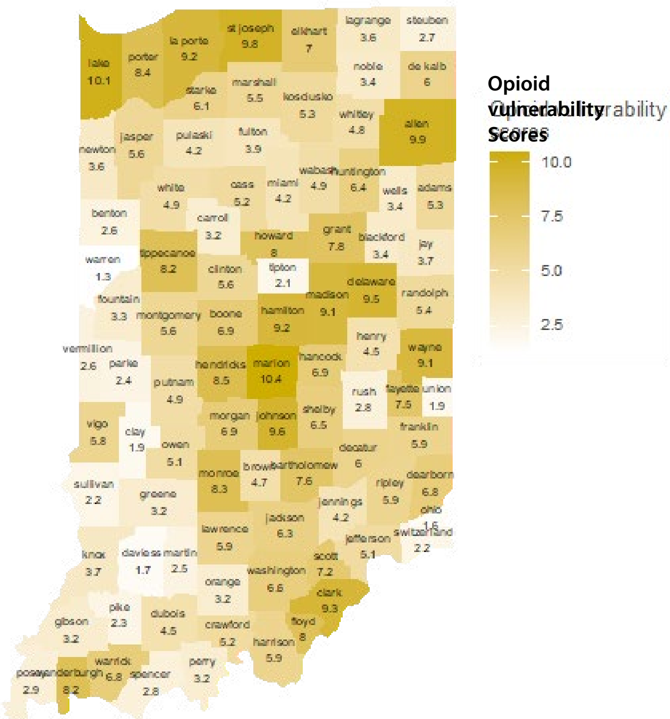
Average household size	0.0	-0.1	0.1	0.096200	1.0	0.0	N(0,2.5)
Treatment services facilities	0.2	0.1	0.5	0.142000	1.0	0.0	N(0,2.5)
Rural/mixed	0.2	-0.1	0.5	0.025000	1.0	0.0	N(0,2.5)
Urban	0.5	0.4	1.3	0.356000	1.0	0.0	N(0,2.5)

Map D.1: **Indiana county opioid vulnerability scores (Bivariate negative binomial regression model)**



Data source: Vulnerability scores were calculated using count regression based method

Map D.2: **County map for opioid vulnerability (with Bayesian bivariate negative binomial regression model)**



Data source: Vulnerability scores were calculated using count regression based method

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The views expressed here do not necessarily reflect the views of the DMHA

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