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Original article

Unemployment and opioid overdose death patterns in the United States from 2017 to 2019

Patrones de desempleo y muerte por sobredosis de opioides en Estados Unidos de 2017 a 2019

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Key contribution of the study

Objective	To determine an association between unemployment and opioid overdose death.
Study design	Retrospective spatial cluster
Information source	US Bureau of Labour Statistics, Center for Disease Control
Population/ sample	Unemployment and opioid-related deaths in Americans aged 18 years and older in the United States from 2017 to 2019
Statistical analysis	Moran's global I and local I values, Poisson regression, choropleth maps
Main findings	Opioid-related deaths appear to be associated with unemployment rates in the US during 2017 and 2019, but less so in 2018.

Abstract
Introduction: Unemployment has been linked to increased opioid-related harms such as opioid overdose deaths. Identifying hotspots and coldspots across the United States (US) can be crucial to understanding health resources and leveraging strategies, policies and programs to reduce the burden of opioid-related harms.
Objective: To determine an association between unemployment and opioid overdose death.
Methods: Using data from the US Bureau of Labour Statistics and the Center for Disease Control from 2017 to 2019, we describe how unemployment correlates with opioid overdose deaths in the US. Spatial clustering analyses were carried out to generate Moran's global I values and create hotspot maps leveraging Moran's local I to identify clusters and trends over time.
Results: There was an autocorrelation of opioid overdose death rates with surrounding states, particularly in the Midwest, Northeast and Southeast in 2017 and 2019. In contrast, only certain states in the Northeast showed greater clustering in 2018. A Poisson regression model showed a positive association between unemployment and opioid overdose deaths for the years 2017 and 2019. Overall, 2018 did not follow similar patterns seen in 2017 and 2019 in terms of the correlation between unemployment and opioid overdose rates.
Conclusions: Opioid-related deaths appear to be associated with unemployment rates in the US during 2017 and 2019, but less so in 2018
Keywords: opioid death, overdose, opioid-related harm, unemployment, social determinants of health

Resumen
Introducción: El desempleo se relaciona al incrementó de los efectos negativos de opioides, como muerte por sobredosis. Identificar puntos críticos en EE.UU. puede ser crucial para redireccionar recursos de salud y mejorar estrategias, políticas y programas para reducir la carga de daños relacionados con los opioides.

Objetivo: Determinar la asociación entre el desempleo y la muerte por sobredosis de opioides.
Métodos: Utilizando datos de la Oficina de Estadísticas Laborales de EE.UU. y los CDC entre 2017 a 2019, describimos la correlación del desempleo con las muertes por sobredosis de opioides. Se realizaron análisis de agrupamiento espacial para generar valores globales del índice I de Moran y crear mapas de puntos críticos para identificar agrupaciones y tendencias.
Resultados: Se observó una autocorrelación de las tasas de mortalidad por sobredosis de opioides con las de los estados circundantes, en particular en el Medio Oeste, el Noreste y el Sureste en 2017 y 2019. En contraste, solo ciertos estados del Noreste mostraron una mayor agrupación en 2018. Un modelo de regresión de Poisson mostró asociación positiva entre el desempleo y muertes por sobredosis de opioides en 2017 y 2019. En general, 2018 no siguió patrones similares a los observados en 2017 y 2019 en la correlación entre el desempleo y las tasas de muerte por sobredosis.
Conclusiones: Las muertes relacionadas con opioides parecen estar asociadas con las tasas de desempleo en EE. UU. durante 2017 y 2019, pero en menor medida en 2018.
Palabras clave: opioides, mortalidad, sobredosis, daños relacionados con opioides, desempleo, determinantes sociales de la salud

Introduction

It is estimated in the United States (US) that over 4 million people annually suffer from opioid use disorder (OUD), which is associated with a 10 times higher risk of death (1,2,3). The rate of opioid overdose deaths in the US has been increasing each year by over 25% and topping over 100,000 deaths annually since 2013, making this the most pressing non-infectious public health crisis of the last decade (4). In order to determine where resources are most needed, it is vital to evaluate public health trends and identify populations most at risk of opioid-related deaths (5,6).

The relationship between economic conditions and opioid-related harms is ambiguous (7). Recent data has speculated that several socioeconomic factors may be associated with an increased risk of opioid overdose death, including gender, race/ethnicity and highest education achieved (8). However, little is known if employment or household income is associated with opioid overdose deaths (8,9,10). Unemployment has been linked to an increase in opioid prescribing, misuse, hospitalizations and incarcerations in the US in several studies, all of which are risk factors for opioid-related death (9,10,11,12). European studies have also commented on how patterns of opioid-related harms mirror a country's economic prosperity, but this has yet to be proven in the US and could possibly yield inconclusive results given the country's rapidly changing relationship with opioid prescribing and differences in healthcare infrastructure (13,14). Studies in Australia and Canada have found evidence that unemployment is strongly associated with opioid misuse but have yet to prove if this association translates to opioid overdose deaths (10,11,14).

Using US data from 2017 to 2019, we describe how unemployment correlates with opioid overdose deaths. Through spatial clustering analysis, we compared the association of opioid overdose death rates in each US state with neighbouring states to identify hotspots. The years 2017, 2018 and 2019 were chosen as they were before the COVID-19 pandemic, which presents a unique variable for both unemployment and opioid-related harms. Our objective was to determine if there was an association between unemployment and opioid overdose death to begin assessing how to efficiently address the opioid epidemic in the US.

Materials and methods

Data sources

US citizens of working age were included in the analyses, defined as age 15 to 64 years.15 The exposure was defined as the rate of unemployment among the labour force per state per year, which was obtained from the US Bureau of Labour Statistics (BLS). The US BLS is responsible for assessing the economic activity of the country, focusing on annual labour market activity and productivity (16,17,18,19). The outcome was defined as the rate of opioid overdose deaths per state per year, which was collected by the National Center for Health Statistics and shared by the Center for Disease Control (CDC). The dataset summarized the 12-month incidence of opioid-related deaths for each state from 2015 to 2021, detailing the number of opioid-related deaths, and specifically, the number of opioid overdose deaths (20).

Data cleaning

Using data from the US BLS, population-adjusted unemployment rates were collected for each state for the years 2017, 2018 and 2019. Using the dataset from the CDC, the number of opioid overdose deaths was extracted for each state for the same time period. No missing values were reported. In order to compare the exposure and outcome as a similar variable (i.e., in percents), the number of opioid overdose deaths for each state was manually population-adjusted to obtain opioid overdose death rates, standardized to the 2017 US population. All rates were calculated and reported as percents (%), as has been done in previous literature and documented by the BLS.

A shapefile was obtained from the US Census Bureau and uploaded into QGIS 3.22, a geographic information system software (21). It contained the 50 states, along with islands such as American Samoa, the Commonwealth of the Northern Mariana Islands, Guam, the US Virgin Islands and Puerto Rico. Data was not collected or used in these analyses for jurisdictions beyond the 50 states, thus these islands were manually removed from the shapefile. Following this, QGIS 3.22 was used to merge 2017 data from the master dataset onto the cleaned shapefile, attributing values for unemployment and opioid overdose death rates for each state onto the map. This was repeated for 2018 and 2019 data from the master dataset, ultimately obtaining three updated U.S. shapefiles corresponding to each year.

Data analysis

Spatial clustering analysis

Understanding how opioid overdose deaths are clustered can help provide information on spatial trends of opioid abuse (22). One of the most reputable methods to facilitate spatial understanding is through Moran's I statistic (22). Both Moran's global I statistic and Moran's local I statistic were used to evaluate opioid overdose death clustering. Moran's global I is an index of spatial autocorrelation indicating the extent to which a characteristic in a region is predictive of that same characteristic in neighbouring regions. In this study, Moran's global I was used to help determine if the rate of opioid overdose deaths in one state was predictive of that in surrounding states within the US. Moran's local I is a hotspot index used to identify hotspots or coldspots in terms of autocorrelation (i.e., if states are positively or negatively correlated with the states around them with respect to opioid overdose death rates).

R Studio® v1.3.1073 was used to carry out spatial clustering analyses using the rgdal, spdep, sf, and tmap packages. To first assess the distribution of opioid overdose death rates, a histogram was constructed and indicated that a quantile classification would be most appropriate to create a choropleth map of opioid overdose death rates per year. Next, states were given weights depending on the number of states neighbouring them. To do this, zero-policy was used whereby a value of 0 was assigned to any state that did not have neighbours (i.e., Alaska). Moran's global I was evaluated by regressing the opioid overdose death rate in a state against the "lagged" weighted average opioid overdose death rate in surrounding states. This produced a scatter plot of autocorrelation with a line of best fit and a slope representing Moran's global I ranging from -1 to 1, where a value of 0 indicated the absence of autocorrelation. Another estimate of Moran's global I was generated, along with a p-value, using syntax for the Moran's global I test. Following this, Monte Carlo simulation was used to generate a density plot showing the distribution of values expected if opioid overdose deaths were distributed at random. The resulting line indicating the value for Moran's global I was assessed to determine the probability of obtaining this result by chance alone. Finally, Moran's local I estimates were bound to the US shapefile to create a spatial clustering map, with quantile breaks of autocorrelation of opioid overdose death rates. Areas of darker colour indicated a higher degree of positive correlation with surrounding states.

Poisson regression analysis

A two-way scatter plot comparing unemployment and opioid overdoses deaths was created with a line of best fit. As the plot showed an association between unemployment and opioid overdose deaths, further investigations were undertaken using STATA BE 17. A Poisson regression model was fit to assess the association between unemployment and opioid overdose deaths in the US in 2017, 2018 and 2019. We used this generalized linear model since count/rate-based data was used. Using this model, the incidence rate ratio (IRR) and 95% confidence intervals were reported. The IRR represented a ratio comparing the incidence rate of opioid overdose deaths in the exposed (i.e., being unemployed) to the incidence rate of opioid overdose deaths in the unexposed (i.e., being employed). Another two-way scatter plot of observed versus predicted values of opioid overdose deaths was created with a line of best fit. To assess the fit of the model, the plot was inspected to see if the points were scattered around the line of best fit.

Results

Spatial clustering

Histogram

The histogram displaying the frequency of opioid overdose death rates in 2017 indicated that most states had rates lower than 0.04%, showing a right-tailed skewed distribution. A similar trend was seen in 2018, where most states had rates lower than 0.05%, again showing a right-tailed skewed distribution. However, in 2019, opioid overdose death rates showed a range of rates with a majority between 0.01% to 0.04% (Appendix 1).

Choropleth map

The choropleth map for 2017 found that Alaska and the states bordered around the intersection of the Midwest, Northeast and Southeast areas had a high degree of opioid overdose death rates compared to the rest of the US (Figure 1a). The choropleth maps for 2018 and 2019 showed an even greater degree of opioid overdose death rates in the states bordered around the intersection of the Midwest, Northeast and Southeast areas (Figures 1b, 1c). This trend was also observed in states nearing the West and Southwest border. Alaska showed decreased opioid overdose death rates in 2018 and 2019 compared to 2017. Refer to Appendix 2 for US divisions.

Moran's global I

Moran's global I was generated by calculating the slope of the regression line from the scatter plot. Values of 0.122, 0.139 and 0.348 were generated for the years 2017, 2018 and 2019, respectively. These Moran's global I values were compared to those obtained from running a Moran's global I test, which generated values of 0.267 (p-value= 0.0004) for 2017, 0.135 (p-value= 0.0170) for 2018 and 0.324 (p-value= 0.0002) for 2019. Overall, values generated from the regression model were similar to those obtained from the test. This overall increased trend in Moran's global I values from 2017 to 2019 signified increased spatial clustering of opioid overdose death rates. This indicated that opioid overdose death rates in neighbouring states were correlated with, and perhaps predictive of, surrounding states.

Density plot

All three density plots obtained from the Monte Carlo simulation indicated that the calculated Moran's global I were well to the right of the expected range. This provided evidence that the calculated Moran's

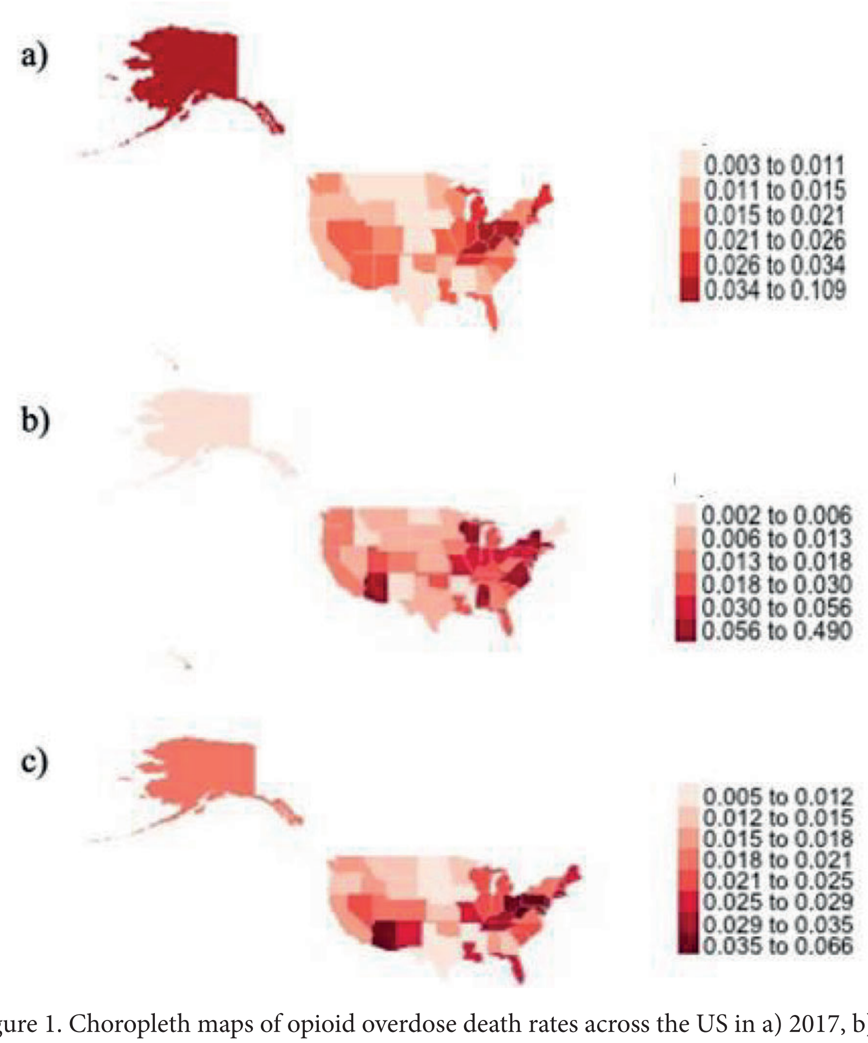

Figure 1. Choropleth maps of opioid overdose death rates across the US in a) 2017, b) 2018 and c) 2019. Rates represented as percentage (%)

global I was not due to chance alone but rather due to opioid overdose death rates being spatially autocorrelated (Appendix 3).

Moran's local I

The hotspot map indicated the extent to which states were autocorrelated. Positive Moran's local I values (i.e., states with darker shades of green) suggested that a state had similar patterns with respect to opioid overdose death rates in relation to its neighbours, contributing to a cluster. In contrast, negative Moran's local I values (i.e., states with yellow tones) indicated that a state had dissimilar patterns of opioid overdose death rates in relation to its neighbours, representing an outlier. In 2017, states in the North of the Midwest and West divisions and states at the intersection of the Midwest, Northeast and Southeast showed high similarity (Figure 2a). In 2018, states in the West and Southwest had relatively similar opioid overdose death rates to one another. In contrast, states in the Midwest, Northeast and Southeast predominantly had dissimilar opioid overdose death rates (Figure 2b). The map for 2019 showed similar trends to 2017, except for states in the West and Southwest that had negative Moran's local I values, indicating they were outliers (Figure 2c). This was compared to the choropleth map for 2019, which indicated that these states had different severities of opioid overdose death rates than their neighbouring states.

Poisson regression

Our Poisson regression model was used to generate IRRs to help determine the association between unemployment and opioid overdose deaths in the US. In 2017 and 2019, an IRR of 1.076 (95% CI: 1.069, 1.088) and 1.054 (95% CI: 1.045, 1.064), respectively, corresponded to a 7% and 5% increased risk of opioid overdose deaths for every 1% increase in unemployment. In 2018, an IRR of 0.780 (95% CI: 0.770, 0.791) indicated a protective effect of unemployment, where every 1% increase in unemployment was associated with a 22% decrease in opioid overdose deaths. The graphs of the predicted versus observed opioid overdose deaths showed a positive association with the points scattered around the line of best fit. The degree of scatter was greatest in 2018 and least in 2019, indicating that the model didn't fit the 2018 data as well as the other years (Appendix 4).

Discussion

Understanding the relationship between economic conditions and opioid-related adverse events is vital to tackling the opioid crisis (4). We examined this relationship using US data available for both variables

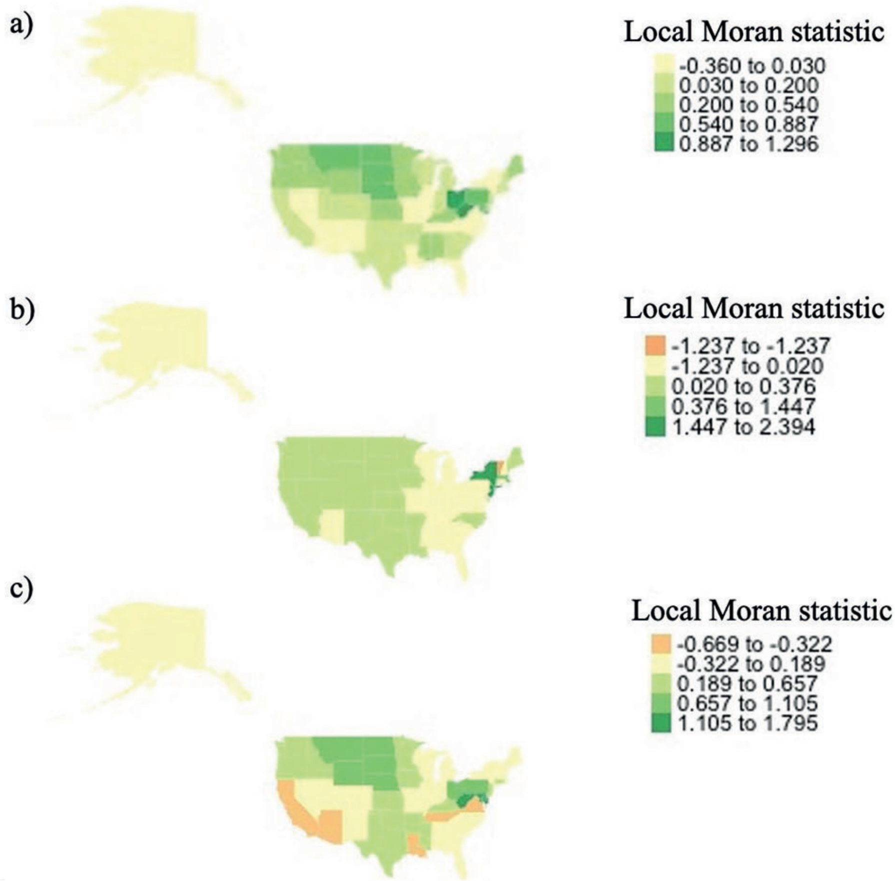

Figure 2. Horspot maps of opiod overdose death rates across the US in a) 2017, b) 2018 and c) 2019

from 2017 to 2019. These years were chosen as opioid data was not explicitly available prior to 2017 (i.e., death rates were combined with other substances, including alcohol) and we did not include data after 2019 as to not confound our results with the COVID-19 pandemic that preliminary data suggests negatively impacted the opioid crisis (4,7).

Our data suggested that opioid overdose death rates were spatially clustered across the US. Most noticeably, states at the intersection of the Midwest, Northeast and Southeast were highly positively correlated with each other in 2017 and 2019. During these years, trends with respect to the location and degree of clustering of opioid overdose deaths were similar and demonstrated by patterns found in the hotspot maps and the larger calculated Moran's global I values. This is not surprising given these areas have similar economic flux and taxation patterns, along with similar mental health policies and initiatives (23,24). In contrast, there was an overall lack of clustering in 2018, as indicated by the smaller Moran's global I value for 2018. One possibility for this may be the various initiatives brought on by the 2017 Tax Cuts and Jobs Act, which aimed to increase employment across the US but was inconsistently taken up by various jurisdictions in 2018 (23,24). By 2019, it was predicted that most neighbouring states had similar uptake of the Act (23,24). Further, while each state implements its own mental health initiatives, it has been noted that states in the Midwest have implemented more opioid harm reduction programs than other states, beginning in the early 2010s (23.24). This may account for some of the decreased mortality rates seen in this area. By contrast, the Southeastern states were slow to implement programs such as supervised injection sites and naloxone programs, which may further account for the higher mortality rates reported in these states (23,24). Our analyses suggested that spatial clustering was unlikely due to chance alone.

We reported that a 1% increase in unemployment was associated with a 7% and 5% increase in opioid overdose deaths in 2017 and 2019, respectively. These values are higher than those reported by the National Bureau of Economic Research, which concluded that as unemployment increased by 1%, opioid overdose deaths increased by 3.6% between 2003 to 2014 (25). This is not surprising given that other countries such as Australia and Canada have reported a significant spike in opioid overdose deaths starting in 2016 (25). This was unlike 2018, where unemployment appeared to confer a protective effect on opioid overdose deaths. Some reasons for this include the dramatic uptake of opioid abuse-deterrent formulations (ADF) by prescribers seen mid-2017 and 2018, but not subsequent years, and the increase in drug take-back programs which were heavily funded by the Drug Enforcement Administration (DEA) in 2018 compared to other years (27). The higher unemployment rates in 2017 and 2019 may also be attributable to Hurricanes Harvey, Irma and Dorian, major hurricanes documented to significantly affect nonfarm employment, namely hospitality and transportation (28,29,30).

Ultimately, it should be noted that 2018 did not follow similar patterns seen in 2017 and 2019. This could be due to the inability to consider factors such as increased initiatives to manage the opioid crisis and changes in opioid prescribing policies, which were largely taken up in 2018 compared to other years (23,24,26). Given these scattered and inconsistent results, it is difficult to precisely summarize the relationship between unemployment and opioid overdose deaths across the three years.

Strengths of the study include the use of robust and complete datasets, with no missing data. The data was obtained from comprehensive data sources, which collect surveillance population data. Our time period did not encompass the COVID-19 pandemic as more information is required on how this has affected unemployment and opioid overdose deaths in the US for meaningful analyses to be conducted. Some limitations exist for this study. We only studied three years as we chose to exclude data prior to 2017 due to possible misclassification of opioid overdose deaths, which were grouped together as opioid-related harms by the data source. For example, prior to 2014, deaths due to opioid overdoses were grouped in a general category with other substance use deaths. Our analyses may be strengthened and show a more accurate time-trend if more years were included. Furthermore, we did not adjust for potential confounders such as age, gender and race/ethnicity, nor did we stratify by variables such as the implicated opioid or laws surrounding opioid misuse. We also did not have data on psychiatric comorbidities, which would have allowed us to further comment on policies that impact other disorders such as depression that often present with OUD and can impact mortality (3). Finally, we analyzed unemployment rates from BLS based on tax reporting. Although considering informal employment could have strengthened our analyses, this may have biased our results due to their less specific and robust reporting in BLS.

Thus far, strategies aimed at restricting opioid supply and influencing prescriber practices have been largely explored to reduce the opioid crisis in the US. Our study suggests that strategies aimed at decreasing unemployment rates in certain jurisdictions should also be explored if we are to successfully tackle this multi-faceted public health issue.

Conclusion

The relationship between unemployment and opioid overdose deaths is not well characterized in the US. This is the first time spatial clustering was used to study opioid overdose deaths across the US as a whole. Using spatial clustering analyses and Poisson regression, we found that opioid overdose death rates appear spatially clustered.

Future research aimed at understanding other markers of economic prosperity, such as competitive and changing job markets and the cost of goods, as well as the take-up of various opioid harm reduction strategies is needed to substantiate these findings further. Furthermore, research incorporating complex variables (such as the COVID-19 pandemic and concurrent psychiatric conditions) and their impact on the relationship between unemployment and opioid overdose deaths is needed. By understanding this complex relationship, we hope that government officials and health workers can leverage strategies, policies and programs that consider socioeconomic factors to reduce the burden of opioid-related harms across the US.

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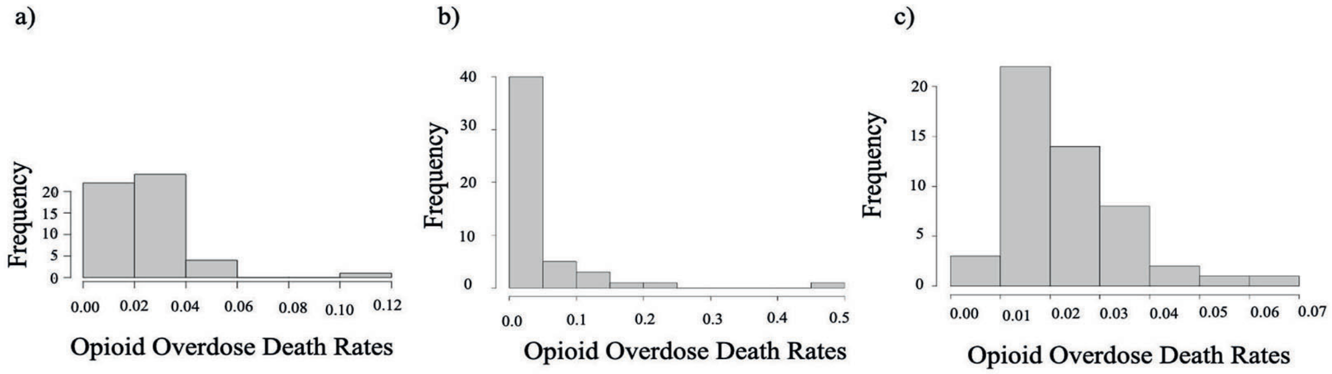
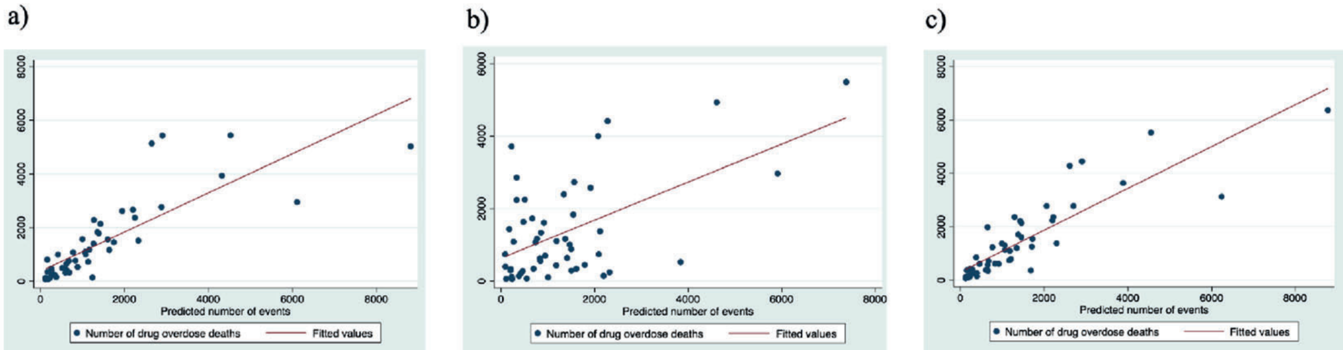
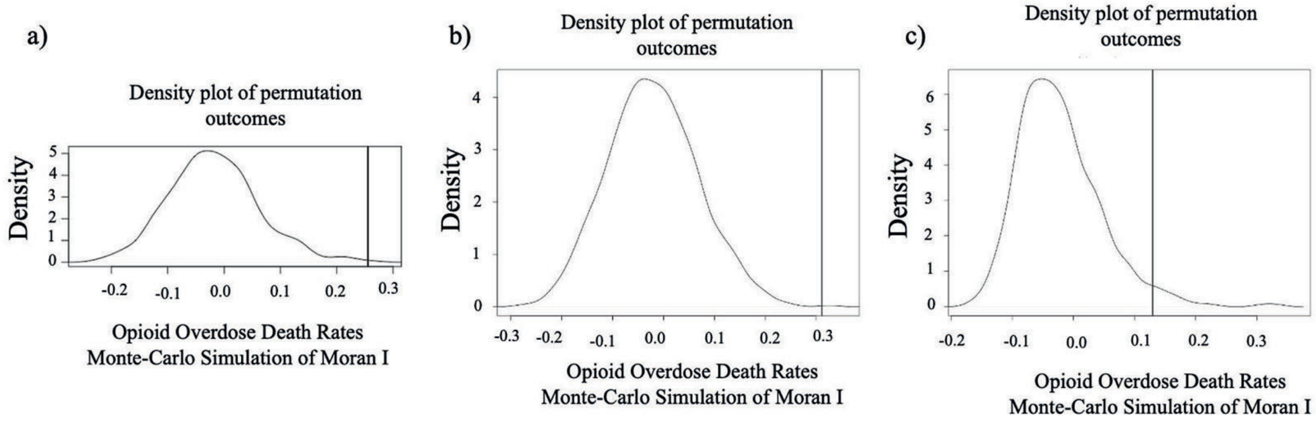


Appendix 1. Histogram of opioid overdose death rates in a) 2017, b) 2018 and c) 2019. Opioid overdose death rates represented as percents (%) and frequency as number of values corresponding to a rate.

Appendix 2. Divisions of the United States (obtained with permission from https://www.ducksters.com/geography/us_states/us_geographical_regions.php)



Appendix 3. Density plot of the Monte Carlo permutations to assess Moran's global I in a) 2017, b) 2018 and c) 2019



Appendix 4. Observed versus fitted values for Poisson regression models of the association between unemployment and opioid overdose deaths in a) 2017, b) 2018 and c) 2019