Title

Spatial Analysis of Opioid Prescription and Overdose Rates in the United States

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Introduction

It is widely known that today's opioid crisis is considered an epidemic, but it can be difficult to determine which areas need more governmental support, and which areas have been successful in limiting the amount of overdose deaths. Luckily, spatial analysis can reveal patterns or potential causes of opioid-related deaths. Previous research states that the opioid crisis is composed of three waves: potentially inappropriate opioid prescribing (PIP), increase in heroin use and misuse, and entry of fentanyl into opioid markets. In general, PIP is associated with an increase in opioid overdoses, but the relationship between the two isn't quite clear. This analysis is aimed to determine the spatial relationship between overdose rates and opioid prescription rates in the United States and form a conclusion about how exactly they are related.

Background

It is widely known, and highly publicized, that the current opioid crisis is an epidemic. In the past, the only national emergencies were infectious diseases, such as the Ebola virus and the H1N1 influenza, or natural disasters, like Hurricane Katrina (Noe, Hodge, & Gostin, 2017). Today, opioid related mortality is a national emergency. There was a total of 21,088 fatal opioid overdoses in 2010; that number increased 156% to 33,091 in 2015, only a few years later (Noe et al., 2017). Opioids are the second leading cause of poisoning among emergency departments, right after alcohol intoxication (Nelson, Juurlink, & Perrone, 2015).

Recent research highlighted by Kiang, Basu, Chen, & Alexander (2019) has suggested that the current opioid epidemic is actually made up of three separate epidemics, each with its own distinct characteristics, which are referred to as 'waves'. From the 1990s to around 2010, opioid overdoses were usually associated with prescription painkillers, such as oxycodone; this is the first wave of the epidemic. The second wave is characterized by the distinct, significant increase in heroin-related deaths starting around 2010. Around 2013, the third, and current, wave emerged as a result of an increase of illicit, chemically-manufactured opioids. These synthetic opioids are incredibly potent; accidental skin absorption or inhalation can be fatal (Noe et al.,

2017). Other illicit drugs can be laced with a synthetic opioid, like fentanyl, which can also be lethal.

Some users abuse opioids in search of a euphoric effect, but many others misuse opioids to avoid experiencing withdrawal resulting from chronic opioid use. Opioids like oxycodone are often prescribed to individuals experiencing chronic pain; in the United States, one-third of people report experiencing chronic pain (Noe et al., 2017). Yes, prescription opioids are very effective for pain relief, but they are also extremely addictive. The majority of opioids misused by individuals originate from prescription medication (Nelson et al., 2015), whether it be an individual's own prescription being misused, or a prescription belonging to someone else. This abuse of prescription opioids, associated with the first wave of the epidemic, then leads to the second wave: increased heroin abuse. A whopping 80% of new heroin users have already abused prescription opioids (Noe et al., 2017). The third wave, associated with an increase in synthetic opioids, emerges when users start wanting something stronger, and more potent, than heroin.

The current opioid crisis is an *epidemic* across the entire country, but it can be difficult to determine which areas need more governmental support, and which areas have been successful in limiting the amount of overdose deaths. Spatial analyses of opioid-related overdoses can help inform policymakers at the local, state, and national level by identifying and determining trends and patterns of opioid-related deaths. As detailed by Stopka, Amaravadi, Kaplan, Hoh, Bernson, Chui… & Rose (2019), a new mandate within Massachusetts required several government agencies to report data trends among opioid overdose events; much more thorough analyses could then be performed utilizing this new comprehensive database of individual level data. It is important to study the geographic distribution of the opioid crisis as a tool to develop effective policy that will target opioid-related mortality and monitor opioid-related events more efficiently (Rolheiser, Cordes, & Subramanian, 2018). Analyzing spatial patterns of prescription opioid acquisition (i.e. determining how "saturated" or clustered an area is) can be very informative to understand overdoses, develop new policies, and prevent potential addiction since overdose deaths are directly related to improper opioid prescribing habits (Rolheiser et al., 2018). Analysis of trends in the geographic distribution of opioid abuse and overdoses on a more local level is essential to devise more relevant, geographically specific policies. Hot spot analysis of opioid-related mortality rates, as detailed by Kiang et al. (2019), can help determine for effective policies depending on the needs of a specific population. Other cluster analyses, as detailed by Brownstein, Green, Cassidy, & Butler (2010), could also be beneficial to identify areas of increased risk. The purpose of this paper is to use spatial analyses in order to determine the spatial relationship between overdose rates and opioid prescription rates.

Spatial analyses of the opioid crisis involve the concept of autocorrelation, which describes exactly how a geographic variable is spatially related to itself. Spatial autocorrelation builds off Tobler's Law, which states that geographic variables near each other are more related than geographic variables far away (Chapman McGrew, Lembo, & Monroe, 2014). For the purposes of this analysis, geographic objects will either be neighbors, or they will not be neighbors (i.e. either they are 'near' or they are not), which depends on the method being used to classify an object's neighbors. For these analyses, Moran's Index will be calculated on both the

global level and the local level. In terms of spatial autocorrelation, a global measure derives a single value for the overall spatial pattern, while a local measure compares each object to its predetermined neighbors to determine the spatial pattern of each neighborhood. In general, Moran's Index uses both the geographic locations and the attribute value of each object. Values of Moran's Index range from -1, which would be a perfectly dispersed spatial pattern, to 1, which would be a perfectly clustered spatial pattern. A value of 0 would indicate complete spatial randomness. In order to determine whether the Moran's Index calculated indicates significant clustering or dispersion, the Index should be converted to a Z-score. The p-value associated with the Z-score will determine whether the Index is significant or not; the sign of the Z-score will determine whether the similar area attributes are clustered or dispersed. Global Moran's Index is a great indicator of spatial autocorrelation, but it could miss pockets of spatial autocorrelation. Global Moran's Index could indicate that there is no significant spatial pattern in the study area, but there could be hotspots, which are like little pockets of spatial autocorrelation, that were missed by the global measure. Local Moran's Index is termed Local Indicators of Spatial Autocorrelation, or LISA for short. LISA measures the similarity of one geographic object with a group of that object's predetermined neighbors. It is used to identify geographic objects whose neighbors have similar values, called local clusters, and geographic objects whose neighbors have very different values, called spatial outliers (Chapman McGrew et al., 2014).

It is very clear that the current opioid crisis is an epidemic. These significant increases in opioid abuse and overdoses cannot be ignored. The death toll for opioid-related overdoses has become catastrophic. In addition, needle-borne infections, such as human immunodeficiency virus (HIV) and hepatitis B or C, have become even more widespread as a result of needle use associated with opioids (Noe et al., 2017). Further spatial analyses are necessary to more effectively identify the relationship between opioid sales (i.e. prescriptions) and the increase in opioid-related mortality for the development of more effective and area-specific policy.

Methods

Descriptive statistics for both prescription and overdose data at the state and county levels will be calculated for analyses. In order to initially visualize the data, choropleth maps categorized by quantiles were produced for each variable. Counties with rates falling outside the interquartile range are identified as outliers (either high or low). Outliers at the state level were also identified for comparison. 1323 counties were identified as overdose rate outliers and 1475 counties were identified as prescription rate outliers. Outlier counties were placed into one of four categories: high-rate counties in high-rate states, low-rate counties in low-rate states, high-rate counties in low-rate states, and low-rate counties in high-rate states.

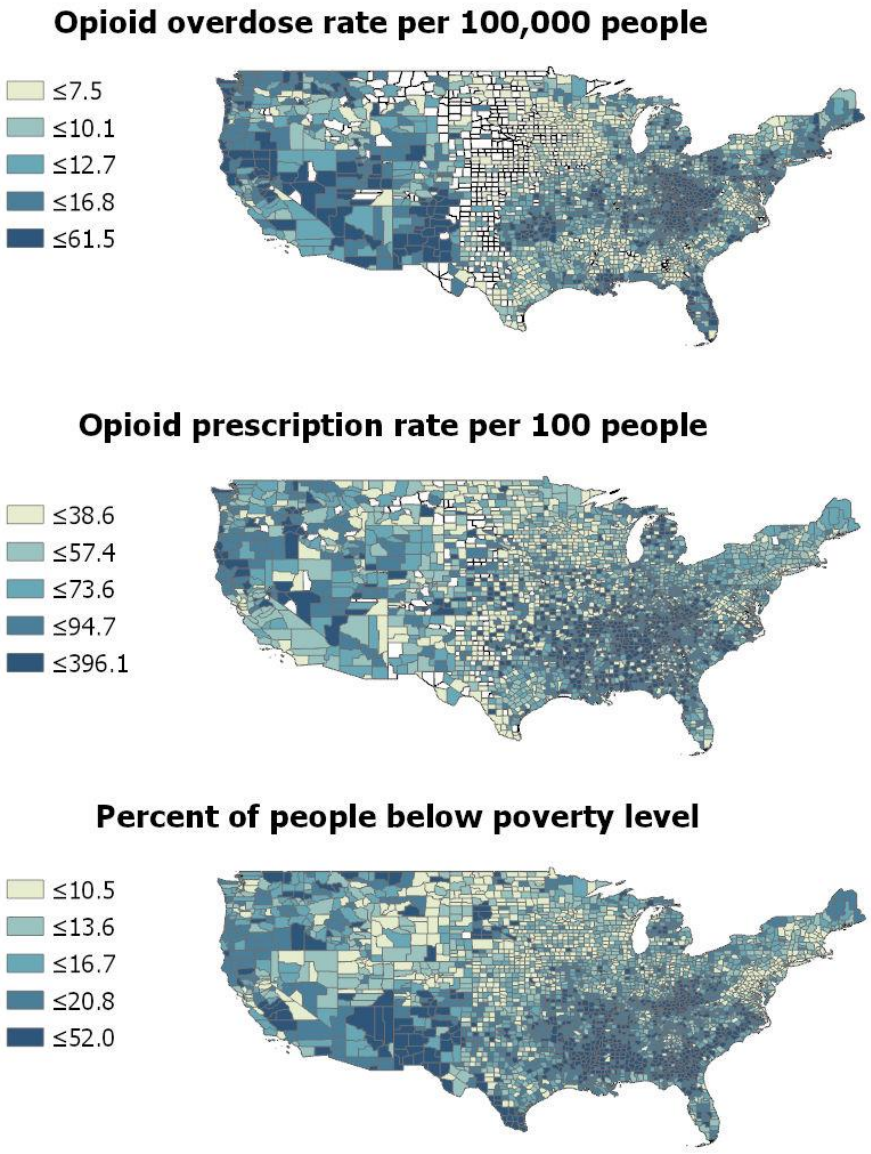

Figure 1: Choropleth maps categorized by quantiles for all variables used in analyses

Regression analyses detailed by Chen et. Al will be used to identify the relationship between both overdose and prescription rates. I will use the prescription rates as the independent variable and overdose rates as the dependent variable in order to determine whether the number of opioid prescriptions dispensed account for a significant portion of the variation in overdose rates. In addition, I will use a separate regression model to identify the relationship between overdose and poverty rates for more insight.

Global Moran's I will be used to determine the degree of clustering/dispersion in the data; a positive value would indicate that high-rate counties are close to other high-rate counties (i.e. more spatially clustered). It is possible that global Moran's I might have missed local clusters, i.e. hot spots, cold spots, or spatial outliers, so I will use Anselin Local Moran's I in

addition to global Moran's I. A high positive z-score would identify high-high and low-low clusters, while a low negative z-score would identify high-low and low-high outliers (Chen, Wang, Yu, Schoenfeld, Saltz, & Wang, 2017). For both Global Moran's I and Anselin Local Moran's I, an inverse distance conceptualization will be used with Euclidean distance and row standardization.

Data

Detailed mortality data on the CDC WONDER database website was filtered to only include all deaths caused by drug overdoses, grouped by county (n=3147) and by state (n=51). The dataset included the total number of deaths and total population counts for each county/state for all years available (1999-2017). Due to confidentiality constraints, any death counts totaling less than 10 are suppressed, so compiling the number of deaths and population counts for all years available minimized the number of counties with suppressed values. In the dataset used for analysis, 498 counties had suppressed values, but those counties made up less than 1% of the total population, so results will likely not be skewed. Excluding counties with suppressed data, overdose rates per 100,000 residents were calculated by dividing number of deaths by population, then multiplying by 100,000.

Prescription data was obtained from the CDC's U.S. Opioid Prescribing Rate Maps page, which included prescription rates at both county and state level from 2006 to 2017. The rate is computed as the number of retail opioid prescriptions dispensed per 100 residents per year. For the purposes of this analysis, datasets at both county and state level for 2006 and 2017 are used for comparison. For both years, state FIPS codes were added to the state level data and county names were split into two fields to separate the county name and state abbreviation.

On the same web page, the CDC included two summary tables: one showing national prescription data for each year 2006-2017, and one showing the number and percentage of counties with available prescription data for each year 2006-2017. The overall national opioid prescription rates in 2006 and 2017 were 72.4 and 58.7 prescriptions per 100 residents, respectively. In the 2006 dataset (n=3143), 87.6% of all counties had available prescription data; in the 2017 dataset (n=3142), 94.0% of counties had available prescription data.

Cartographic boundaries obtained from the U.S. Census Bureau's MAF/TIGER database were used to provide the locational data for both counties and states. For this analysis, the study area is limited to the 50 states and D.C.; territories such as Guam are not included in this study. Unnecessary features (i.e. territories) were removed from this data before joining with the tabular data to exclude analysis of any values outside the study area.

In addition, the 2013-2017 American Community Survey 5-Year Estimates database from the U.S. Census Bureau was used for county level poverty data, in which there is an estimate for the percent of people living below the poverty level. This data is used for extra demographic data in the analyses. This data did not require any preprocessing, except removing unnecessary columns.

Results

As mentioned earlier, outlier county rates were identified and placed into four categories. For overdose rates, 9.43% of counties were identified as high-rate counties in high-rate states, 12.9% were identified as low-rate counties in low-rate states, 2.07% were identified as high-rate counties in low-rate states, and 0.955% were identified as low-rate counties in high-rate states. For prescription rates, 13.76% of counties were identified as high-rate counties in high-rate states, 5.86% were identified as low-rate counties in low-rate states, 1.05% were identified as high-rate counties in low-rate states, and 3.82% were identified as low-rate counties in high-rate states.

Regression analysis indicated that prescription rates likely account for a significant portion of the variation in overdose rates. The x-coefficient calculated was 0.008760 and the intercept was calculated to be 11.9421. The F-statistic (6.345) and the t-value (2.519) were fairly large, and their associated p-values were small (0.0118). Regression analysis was also performed using poverty rates as the independent variable, but did not indicate a significant relationship between overdose and poverty rates. The x-coefficient calculated was -0.01257 and the intercept calculated was 12.77551. The F-statistic (0.4419) and the t-value (-0.665) were not large enough, and the p-value (0.506) was much too large to be statistically significant.

Global Moran's I was calculated for overdose, prescription, and poverty rates to determine the degree of clustering/dispersion in the data. In order to reject the null hypothesis (H_0: data is randomly dispersed), the z-score calculated and its associated p-value must be statistically significant. A positive z-value would indicate that similar area attributes tend to cluster in the study area, while a negative z-value would indicate that area attribute values are more dispersed than would occur by random chance. County level overdose rates revealed a Moran's I of 0.253488, z-score of 93.979899, and an associated p-value less than 0.01. County level prescription rates revealed a Moran's I of 0.217871, a z-score of 65.765820, and an associated p-value less than 0.01. County level poverty rates revealed a Moran's I of 0.289650, a z-score of 120.830153, and an associated p-value less than 0.01. Anselin Local Moran's I was calculated after global Moran's I to check for local clustering or dispersion patterns. Refer to Figure 2 for visualization.

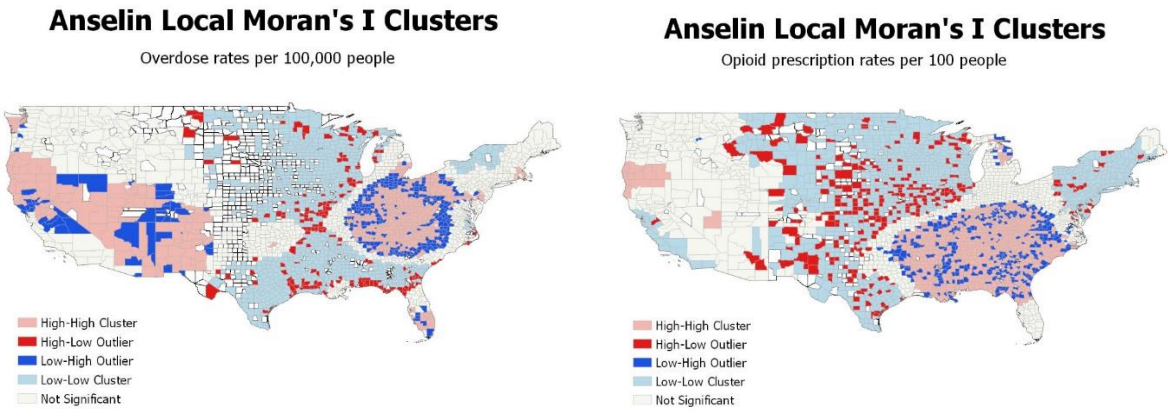

Figure 2: Anselin Local Moran's I maps for both overdose and prescription rates

Discussion

Regression analyses confirmed the direct linear relationship between overdose and prescription rates, which was expected; it is known that inappropriate prescribing of opioids causes an increase in opioid related deaths. It was expected that regression analyses would also indicate a direct linear relationship between overdose and poverty rates, but the regression model was unreliable.

Global Moran's I revealed that the data is more spatially clustered than would occur by random chance. All three coefficients and z-scores indicated statistically significant clustering, along with the associated p-values all being less than 0.01. Anselin Local Moran's I also revealed similar clustering patterns between the datasets, which was expected, considering the regression results.

In conclusion, it is highly likely that opioid overdose and opioid prescription rates are directly related, as shown in the analyses. Contrary to original expectations, poverty rates were not determined to be directly related to overdose rates.

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