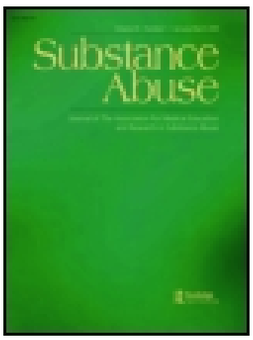

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ORIGINAL RESEARCH

County-level factors underlying opioid mortality in the United States

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ABSTRACT

Background: Mortality from overdoses involving opioids in the United States (U.S.) has reached epidemic proportions. More research is needed to examine the underlying factors contributing to opioid-related mortality regionally. This study's objective was to identify and examine the county-level factors most closely associated with opioid-related overdose deaths across all counties in the U.S. *Methods:* Using a national cross-sectional ecological study design, we analyzed the relationships between 17 county-level characteristics in four categories (i.e. socio-economic, availability of medical care, health-related concerns, and demographics) with opioid mortality. Data were extracted from the Robert Wood Johnson County Health Rankings aggregate database and Centers for Disease Control and Prevention (CDC)'s Wide-ranging Online Data for Epidemiological Research (WONDER) system. *Results:* There were 1058 counties (33.67% of 3142 nationally) with reported opioid-related fatalities. Median opioid-related mortality was 15.61 per 100,000 persons. Multivariate regression results indicate that counties with the highest opioid-related mortality had increased rates of tobacco use, HIV, Non-Hispanic Caucasians, and females and were rural areas, but lower rates of food insecurity and uninsured adults. The rates of tobacco use and HIV had the strongest association with mortality. Availability of either mental health or primary care providers were not significantly associated with mortality. Severe housing problems, high school graduation rate, obesity, violent crime, and median household income also did not contribute to county-level differences in overdose mortality. *Conclusions*: Future health policies should fund further investigations and ultimately address the most influential and significant underlying county-level factors associated with opioid-related mortality.

KEYWORDS

Opioid overdose; mortality; addiction; opioid use disorder

Introduction

Deaths from drug overdoses across the U.S. have reached epidemic proportions and overdoses have contributed to the deaths of more than 70,000 individuals annually, with greater than 67% of these involving opioids.[1,2] Buchanich et al (2016) found in their longitudinal study from 1979 through 2014 that drug poisoning mortality rates have risen 6% annually, across a variety of demographics.[3] The trend is continuing in all U.S. regions, and the Centers for Disease Control and Prevention (CDC) confirmed that opioid overdose emergency department visits increased nearly 30% from July 2016 through September 2017.[4] Overdose fatalities affect both economic and social welfare for individuals and communities.[5] To understand and develop strategies to address the opioid epidemic, we posit that it is essential to identify which county-level characteristics (or factors) are most closely associated with opioid-related mortality. Examining why certain regions have higher mortality could help shape future health policy, and guide government investments to curtail the epidemic, and improve health outcomes.

A recent geospatial analysis examined regions with the greatest disproportion between drug-related deaths and access to treatment.[6] The study identified high risk regions where additional resources to battle the epidemic are needed and suggested future research exploring underlying health factors related to overdose mortality. Another study using data through 2015 examined county-level differences in drug-related mortality and identified certain social factors strongly correlated with county mortality.[7] Other prior studies have focused on specific states;[8] urban versus rural regions;[9] young adults;[10] race;[11] or linear trends and disease progression over time.[12–14] Very few studies have attempted to more comprehensively identify county-level factors using recent data across the entire country.

Health outcomes are largely determined by the social and physical factors facing each individual in the community in which they live.[15] County-level factors influence the physical and social environment in which individuals live, which ultimately may impact their capacity for misuse of medications and illicit drugs. In this study we focus on four categories of factors, including socio-economic conditions, health-related concerns, availability of medical care, and

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county demographics. Of these, the socio-economic factors, such as income, employment rates, and education, are more widely believed to contribute to disparities in overall health.[16,17] Health-related concerns, such as high rates of HIV or obesity, represent community concerns that are closely associated with quality of life and other outcomes.[7] Demographics are also important since certain demographic groups have a higher risk of overdose. For example, Boscarino and colleagues found that patients over 45 years and non-Hispanic white individuals are at higher risk of overdose than other groups.[18] Some studies have suggested that inner-city urban environments are more prone to drug deaths, while others suggest this is more prevalent in rural areas.[19] Dasgupta et al. (2018) theorized that the root causes of the current drug crisis were both "social and structural and are intertwined with genetic, behavioral, and individual factors,"[20] (p.185) and argue for a more comprehensive model to examine the contributory factors in drug-related deaths.[20]

Our aim is to identify which specific county factors have the largest association with opioid-related mortality across the U.S. Our conceptual framework operationalizes 17 measures related to the availability of medical care, socioeconomic factors, health-related concerns, and demographics.

Objective of the study

Although there is a general consensus about the importance of healthy social and physical environments, there is a need for more comprehensive research that empirically explores the association between county-level characteristics and opioid-related mortality rates. In this exploratory study, we aim to analyze the relationship between multiple county factors with opioid overdose deaths. We chose to use population-based data that represented factors that are commonly collected across all regions. We believe an ecological study using aggregate measures could help to provide more meaningful understanding of specific factors associated with opioid-related mortality at the county level. Better understanding could help shape comprehensive health policies and strategies to turn the tide on the opioid epidemic.

Methods

Study design

For the county level factors, we utilized the health data compiled by the Robert Wood Johnson (RWJ)/University of Wisconsin County Health Rankings initiative.[21] These data are collected for each county in the United States and represent a consolidated data repository extracted from multiple federal data sources, including the CDC, National Center for Health Statistics, U.S. Census, and Bureau of Labor Statistics, among others. This largely administrative dataset has been collected at the county level since 2010 and has been validated and used by numerous studies.[22–24] We obtained and analyzed data from the 2019 dataset for all 3142 counties across the U.S. Additional information regarding this database can be found on the County Health Rankings website (http://www.countyhealthrankings.org). For opioid-related mortality rates, we directly queried the CDC's Wide-ranging OnLine Data for Epidemiology (WONDER) database using the relevant opioid-related international classification of diseases (ICD) codes.[1] This study was approved through the Institutional Review Board of the University of Texas Health Science Center.

Measures

We chose as the dependent variable a population-adjusted measure of opioid-related mortality, calculated as the number of opioid poisoning deaths per 100,000 persons for each county, averaged over the most recent two-year period (2016–2017). This rate reflects all deaths from accidental, intentional, and undetermined opioid-related drug poisonings divided by the total population over the time period. This rate captures deaths involving opium, heroin, other opioids, methadone, synthetic narcotics and unspecified narcotics. We queried the WONDER system underlying cause of death data utilizing ICD-10 codes T40.0-T40.4, T40.6, X40-X44, and Y10-Y14. Additionally, some counties either had no deaths during this period or had missing values, which would be interpreted as zero since the CDC does not report detailed death data for counties with fewer than 10 deaths annually (per county). Therefore, there could be some counties excluded from our analyses which had some deaths, although missing data points are minimal, accounting for less than 4% of total overdose deaths. Since the distribution of the variable opioid-related mortality was non-normal, we used the natural log transformation for our analyses which was successful in reducing skewness and kurtosis within normal ranges.

Health behaviors and health-related concerns are theoretically associated with drug mortality.[25] Smoking is one example of an unhealthy behavior which has been linked with higher rates of drug usage, and specifically higher rates of illicit heroin use.[26] Obesity has been shown to be related to an increase in chronic pain prevalence and therefore higher use of prescriptions.[27] Intravenous drug use is a risk factor for HIV and could be linked to higher mortality.[28] In our analysis, we operationalized measures of health-related concerns: rates of tobacco use (smoking); obesity rates; and HIV prevalence.

Availability of medical care for substance use disorders improves the rate of successful long-term recovery.[6,29] As such, surrogate measures for medical care were included. Specifically, the rate of mental health providers (MHP) and primary care physicians (PCP) per capita within each county were captured. We also analyzed the uninsured rate for the county as an indicator of access to medical care.

Socio-economic factors are especially important.[15,30] We included six variables with proposed relationships with drug mortality: graduation rate from high school, rate of unemployment, median household income, rate of violent crimes, rate of food insecurity in the community, and rate of severe housing problems. Severe housing problem

represents the percentage of adults living with either overcrowding, high housing cost, or lack of kitchen or plumbing facilities.

We included multiple demographic variables which could be related to geographic differences in drug deaths.[31–33] We examined geography (percentage rural areas), age (rate of senior citizens >65 years old), racial composition (percentage African American, percentage non-Hispanic Caucasian), and gender (percentage of females in the county).

Statistical analysis

We determined frequencies, proportions, median and interquartile ranges of all variables and evaluated the association of the factors under study with the mortality rate variable utilizing Pearson's correlation. We selected those with relevant correlations ($p < 0.10$) to be included in a multivariate regression model. In order to obtain optimal goodness of fit and meet the assumptions required to conduct linear regression, we normalized the distribution of the dependent variable (opioid-relatedd mortality rates) as well as of the covariates rate of HIV prevalence per 100,000 and rate of African American residents. We optimized the model using the stepwise backward selection and setting a significance threshold of p-value ≥ 0.10 for a covariate to be removed from the model. The covariates initially entered into the model were: rates of tobacco use/smoking, obese residents, and of food insecurity; HIV prevalence rate per 100,000, rates of uninsured adults, PCP, and high school graduation; rate of unemployed, median household income, rates of severe of housing problem and of rural areas; rates of seniors 65 years and older, African American, non-Hispanic Caucasian, and of females.

We report the model's coefficients, standardized betas, p-values, R-squared, and the mean variance inflation factor (VIF). The VIF measures the severity of inter-correlations and provides information about how much the variance of an estimated regression coefficient is increased due to collinearity. We determined the VIF of each covariate in the model and excluded covariates with values ≥ 5.[34] The goodness of fit of the multivariate model was evaluated with the Link test. To reduce type I error, we conducted separate regression models in three groups of counties selected at random in order to identify covariates that consistently resulted independently associated with opioid-related mortality. For regression analysis, a p-value <0.01 (two-tailed) was considered significant. All analysis was performed with Stata I/C version 15, StataCorp LLC, College Station, TX.

Results

Baseline characteristics

In 2017, across the 3142 counties in the U.S., there were 1058 (33.67%) with reported opioid-related deaths. The median drug mortality rate was 15.61 per 100,000 persons (IQR = 9.86–24.23).

On univariate analysis, opioid-related mortality was positively correlated with tobacco use, being a non-Hispanic Caucasian individual, living in a rural area, obesity, being 65 years or older and a higher rate of being unemployed. To a lesser degree, there were positive correlations between opioid-related mortality and other factors found in Table 1, such as an increased rate of food insecurity. There were

Table 1. Determinants of health of counties in study and correlation to the outcome in counties with reports of overdose deaths.

Variable	All Counties (n, %=3142, 100)	Counties with reported drug deaths (n, %=1058, 33.67)	Correlation with overdose rate/100,000 inhabitants	p-Value*
Health behaviors				
Rate of tobaccouse/smoking, median% (IQR)	17.32 (15.23 – 20.28)	17.27 (15.04 – 19.72)	0.375	≤0.0001
Rate of obese residents, median% (IQR)	31.80 (28.8 – 34.4)	30.70 (27.50 – 33.50)	0.256	≤0.0001
Rate of food insecurity, median% (IQR)	13.60 (11.4 – 16.3)	13.30 (11.40 – 15.60)	0.067	0.03
Prevalence of HIV per 100,000, median % (IQR)	122.35 (74.7 – 225.2)	131.70 (83.0 – 236.90)	−0.069	0.005
Clinical care				
Rate of uninsured adults, mean% (IQR)	13.57 (9.11 – 18.31)	11.04 (8.10 – 15.67)	−0.222	≤ 0.0001
MHP rate, median% (IQR)	0.09 (0.04 – 0.19)	0.15 (0.09 – 0.25)	−0.043	0.16
PCP rate, median% (IQR)	0.05 (0.03 – 0.07)	0.06 (0.04 – 0.08)	−0.094	0.002
Socioeconomic				
Graduation rate from high school, median% (IQR)	87.50 (82.35 – 92.26)	86.31 (81.35 – 91.63)	0.089	0.004
Rate of unemployment, median% (IQR)	4.97 (3.99 – 6.16)	4.87 (4.13 – 5.85)	0.129	≤ 0.0001
Median household income, median $ (IQR)	47,589 (41,072–55,308)	52,656.5 (46,093–61,882)	−0.199	≤0.0001
Rate of violent crime per 100,000, median% (IQR)	198.14 (112.74 – 325.44)	242.14 (147.39 – 394.79)	−0.054	0.08
Environmental				
Rate of severe housing problem, median% (IQR)	13.99 (11.45 – 16.68)	15.23 (13.11 – 17.98)	−0.195	≤ 0.0001
Rate of rural areas, median% (IQR)	59.47 (33.20 – 87.80)	30.43 (12.69 – 54.28)	0.257	≤0.0001
Demographics				
Age, rate of seniors 65 years and older, median% (IQR)	18.08 (15.49 – 20.82)	16.44 (13.97 – 18.71)	0.188	≤0.0001
Rate of African American, median% (IQR)	2.17 (.66 – 10.08)	4.62 (1.54 – 12.25)	−0.069	0.02
Rate of non-Hispanic Caucasian, median% (IRQ)	83.98 (64.90 – 92.71)	80.71 (64.35 – 90.14)	0.299	≤0.0001
Rate of females, median % (IQR)	50.33 (49.46 – 51.02)	50.72 (50.17 – 51.30)	0.072	0.02

*p-Value corresponds to Pearson's correlation.
$ denotes U.S. dollars; MHP denotes mental health providers; PCP: primary care providers.

Table 2. Multivariate linear regression model results ($n = 1031$) for counties with reported overdose deaths.

Factors in model	Coefficient	Standardized beta	VIF
Rate of tobacco use/smoking	0.072***	0.372	2.19
Rate of food insecurity	−0.035***	−0.182	1.92
Logarithm of prevalence of HIV/ 100,000 inhabitants	0.222***	0.265	2.45
Rate of uninsured adults	−0.029***	−0.221	1.64
Rate of unemployment	0.032	0.074	1.63
Rate of rural areas	0.003*	0.113	2.05
Rate of seniors 65 years and older	0.017	0.108	1.65
Rate of non-Hispanic Caucasian	0.008***	0.228	4.22
Rate of females	0.052**	0.094	1.21
R^2	0.32***		2.11

*$p = 0.002$; **$p = 0.004$; ***$p \leq 0.0001$.
Link test: hat = 0.946, p-value = 0.03; hat squared = 0.010, p-value = 0.90.
Model mean variance inflation factor = 2.11.
VIF: variance inflation factor.

negative correlations between a higher rate of being uninsured, higher median income, and increased rate of a severe housing problem with opioid-related mortality. Weaker negative associations were also found. (See Table 1)

Regression results

A multivariate linear regression model was used to examine the associations between these variables and opioid-related mortality. The covariates initially entered into the model were: rates of tobacco use/smoking, obese residents, and of food insecurity; HIV prevalence rate per 100,000, rates of uninsured adults, rates of PCP, and high school graduation rates; rate of unemployed, median household income, rates of severe of housing problem and of rural areas; rates of seniors 65 years and older, African American, non-Hispanic Caucasian, and the rates of female residents.

A total of 1031 (97.45%) counties were included in the multivariate model. The results suggest that a variety of factors are positively and independently associated with opioid-related deaths, including tobacco use, being infected with HIV, living in a rural county, being a Non-Hispanic Caucasian, and being female. We found a negative association between the rate of uninsured adults and the rate of food insecurity and the counties' opioid-related mortality rate. The R^2 of this model was 0.32 and the mean VIF was 2.11. We observed the rates of tobacco use and the logarithm of the rates of HIV were the covariates with the highest standardized betas, 0.372 and 0.265, respectively. We found these two covariates were consistently and positively associated with the outcome in the subgroup analysis, followed by the rate of food insecurity that retained its' negative standardized beta. Table 2 presents the regression results of the main model and Table 3 presents the subgroup analyses.

Discussion

Prior research has shown that county-level variations in socioeconomic factors are associated with higher drug-related mortality rates.[7,22] This study builds on these findings by expanding beyond these measures and examining other county-level factors with more recent and specifically opioid-related mortality data. We note several interesting findings as a result of our analyses, which are of an exploratory nature.

First, we found smoking and HIV infection rates are among the most significant modifiable health behaviors positively associated with opioid-related mortality. Tracking HIV incidence could aid in screening for OUD because according to the CDC, in 2017, 6% of new HIV diagnoses were in people who injected drugs.[35] The rate was even higher in preceding years.

We found that availability of primary and mental health medical care, as measured in this study, were not positively correlated with opioid-related mortality. This may be because mental health and primary care providers are not able to provide the medical care most needed by those at risk for an opioid overdose. Other studies have shown that access to providers for the treatment of specialized substance use disorder has been shown to have a relationship with mortality.[6] A recent study that divided U.S. counties into high and low risk for opioid-related mortality as defined by opioid-related mortality rates and access to providers who prescribe medication for OUD found that high-risk counties had fewer mental health and primary care providers.[36] An interesting future study could be to dichotomize opioid-related overdose mortality into high and low-risk counties and then to compare rates of primary, mental health, and MOUD providers at the county level.

While extensive research has argued that generally a range of factors are associated with health outcomes, here we empirically analyze cross-sectional data on specific socioeconomic, behavioral, availability of care, and environmental factors to understand their relative association on opioid-related mortality. Understanding which precise factors appear to be associated, and which ones do not, could help improve federal, state, and local health policy for additional studies and initiatives.

Despite the fact that the U.S. spends more for healthcare than other countries globally, the health outcomes of vulnerable populations has failed to improve. It is possible that more focused attention on preventative medicine and on strategies to reduce factors that are associated with morbidity and mortality is warranted.[37] A study in Finland found that unemployment had the highest hazards ratio for drug mortality.[38] An analysis of deaths in Florida found that time from most recent medical checkup, income, education level, age, and availability of MHP were the dominant factors.[39] Monnat analyzed data from across the country and found that average mortality rates were significantly higher in counties where there was more economic and family distress, as well as those areas more dependent on the mining industry.[7] Consistent with this, our study finds that unemployment is positively associated with opioid-related mortality rates.

Interestingly, while unemployment rates were positively and independently associated with higher opioid-related mortality, being uninsured, which would've been expected to have strong collinearity with unemployment, remained in the regression model and was actually negatively correlated

Table 3. Multivariable models of subgroups of counties with opioid-related rates.

Factors in model	Coefficient	Standardized beta	*p*-Value*	VIF
Subgroup 1 ($N = 190$)				
Rate of tobacco use/smoking	0.092	0.493	≤0.0001	2.40
Rate of food insecurity	−0.069	−0.360	≤0.0001	2.58
Logarithm of prevalence of HIV/100,000 inhabitants	0.0009	0.264	=0.001	1.92
Rate of uninsured adults	−0.024	−0.182	0.03	1.98
Rate of unemployment	0.062	0.133	0.09	1.77
Rate of rural areas	0.005	0.180	0.02	1.81
Rate of seniors 65 years and older	0.023	0.147	0.08	2.03
Rate of non-Hispanic Caucasian	0.004	0.103	0.32	3.15
Rate of females	0.042	0.070	0.31	1.40
R^2 adjusted	0.36			
Model VIF (mean)				2.12
Subgroup 2 ($N = 188$)				
Rate of tobacco use/smoking	0.095	0.480	≤0.0001	2.64
Rate of food insecurity	−0.071	−0.387	≤0.0001	2.20
Logarithm of prevalence of HIV/100,000 inhabitants	0.001	0.377	≤0.0001	2.21
Rate of uninsured adults	−0.021	−0.148	0.08	2.0
Rate of unemployment	0.027	0.079	0.30	1.64
Rate of rural areas	0.001	0.049	0.55	1.93
Rate of seniors 65 years and older	0.005	0.040	0.60	1.71
Rate of non-Hispanic Caucasian	0.011	0.326	0.02	5.88
Rate of females	0.044	0.089	0.18	1.26
R^2 adjusted	0.35			
Model VIF (mean)				2.38
Subgroup 3 ($N = 183$)				
Rate of tobacco use/smoking	0.072	0.372	≤0.0001	2.25
Rate of food insecurity	−0.020	−0.093	0.25	1.76
Logarithm of prevalence of HIV/100,000 inhabitants	0.0007	0.268	0.001	1.70
Rate of uninsured adults	−0.014	−0.107	0.16	1.54
Rate of unemployment	0.072	0.157	0.05	1.69
Rate of rural areas	−0.002	−0.080	0.40	2.47
Rate of seniors 65 years and older	0.016	0.083	0.27	1.59
Rate of non-Hispanic Caucasian	0.014	0.392	0.001	3.43
Rate of females	0.063	0.099	0.15	1.26
R^2 adjusted	0.34			
Model VIF (mean)				1.97

*Level of significance set at *p*-value ≤0.01.
VIF: denotes variance inflation factor.

with opioid-related mortality. It is possible our model lacks other explanatory variables that could interact with the rates of uninsured and partially explain these findings. Future studies should examine both direct and interaction effects of county characteristics. Monnat (2018) did find that economic conditions alone only partially explain differences in mortality.[7]

In our study, we found that being a rural county was positively associated with opioid overdose deaths, which has been shown in other studies.[9] These high-risk counties should be a focus for additional resources.

We found that multiple county characteristics were not significantly related. Among counties with opioid-related overdose deaths, high school graduation rates, and rates of violent crime were not significantly correlated with death rates. Food insecurity, obesity, and rates of available primary care providers also were not associated with mortality in the regression model.

Based on a better understanding of specific county-level characteristics, we believe that federal and local health departments can develop more active and targeted, community-based strategies to study and address these factors at the population level.[40]

There are limitations to this study. First, this is a cross-sectional ecological study which is inherently limited by the use of aggregate population data. We, therefore, do not suggest that our findings apply to every county, and we are also are not able to examine cause and effect relationships. However, our study uses large-scale data to identify relationships between complex county level factors and opioid mortality. We believe however that our findings are significant, and could be used to aide policy and county leadership public health measures specific to their own knowledge of their county. In addition, we relied on opioid-related mortality data during a the most recent years and newer data, when released by the CDC, could impact future findings and limit generalizability. Further, CDC death certificate data is somewhat limited based on classifications of death and issues surrounding proper coding. Regardless, it is the most complete national data source we can use. Longer, longitudinal data with additional measured variables might yield different patterns or findings. We included availability of primary care and mental health providers as factors, but did not look specifically at MOUD providers, which may have shown a correlation with lower opioid-related mortality as other studies have shown. Finally, there can be extensive variation even within counties, so future studies could examine mortality at a more granular geographical level. In addition, there are a number of counties where drug-related deaths were not analyzed since counties with <10

deaths are not released by the CDC in order to prevent identification of deceased individuals who died from an overdose. If mortality rates were known for these counties with few overdose deaths, the inclusion of their data might affect the findings.

Conclusion

Opioid-related mortality has reached epidemic proportions, and it is important to identify county-level factors most closely associated with deaths, in order to target health policy and community interventions. We found that counties with the highest opioid-related mortality had higher rates of unemployment, tobacco use, HIV, and were rural. There were also some surprising findings that warrant further investigation, such as the fact that counties which had higher uninsured were negatively correlated with opioid mortality. Interventions should focus resources in high-risk counties, while also doing more in depth studies of each correlated factor.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

Author contributions

Research conception and design (JL, TCL), collection of data (JL and TCL), analysis (MLC and JL), interpretation of the results (JL, KC, and MLC), writing (JL, KC), revision (KC, JL, TCL, MLC).

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