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Original Research Article Opioid overdoses: A demographic analysis of the upward trend in the USA

Maansi S Kulkarni^{1,*}

¹Boonshoft School of Medicine, Wright State University, Dayton, Ohio, USA



ARTICLE INFO	A B S T R A C T		
Article history: Received 02-02-2021 Accepted 27-02-2021 Available online 28-04-2021	This paper provides a comprehensive overview of opioid-related deaths within the United States over the past two decades. Analyzing data provided by the CDC from 1999 to 2018, The conclusions concerning the relationship were drawn between opioid deaths and state of residence, gender, race, urbanization, and year. Within the categorizes, all factors were statistically different. Furthermore, Dataworld information from 2011 to 2014 demonstrated that although the number of prescriptions fell, deaths did not. In addition, all		
<i>Keywords:</i> Opioid poisoning Opioid caused deaths demographic	factors and interactions between deaths, year, state of residence, and prescription were significant with the exception of the year and prescription interaction. One therefore can conclude that within this time period, illegal acquisition and consumption of opioids could potentially explain a rise in opioid-related deaths.		
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1. Introduction

In 2018, the CDC reported 67,367 deaths due to drug overdose in the US. Opioids contributed to 46,802 of these deaths or 70% of all cases. Opioid abuse has been consistently on the rise in the US over the past twenty years.^{1,2} More specifically, deaths due to opioid poisoning quadrupled in number from 1999 to 2013. For these reasons, health experts have labeled this issue as the "opioid epidemic". This alarming trend warrants investigation and analysis of demographics that could potentially explain why specific groups of individuals are disproportionately affected by the epidemic.

Literature concerning opioid-related morbidities and mortalities reveals that several trends exist between deaths and key demographic factors such as age, race, urbanization, and number of opioid prescriptions given within an area. For example, although all states saw an increase in number of deaths from 2001 to 2014, non-Hispanic whites accounted for 80% of these deaths.³ Hedegaard et al. studied how death rates for males have been consistently higher than the females over the period of 1999 to 2016.⁴ The study also

found increased death rates for all the age groups over this period.

Monnat et al. studied county-based deaths between 2002-2004 and 2014-2016, and concluded that economically disadvantaged communities experienced higher death rates.⁵ They attributed this trend to an over-prescribing of opioids. However, this relationship between socioeconomic standing and opioid-related deaths is complicated by the fact that a larger proportion of professional workers are experiencing a "syndemic"-that is, an increase in opioid overdoses specific to synthetics. Furthermore, although it is believed that rural areas have been hit the hardest by this epidemic, neighborhood heterogeneity exists. For example, although some rural areas like Appalachia and the Mountain West have experienced a dramatic increase in deaths, other rural areas like the Great Plains are experiencing relatively low cases.^{6,7} Thus, sweeping generalizations concerning opioid-related overdoses and neighborhoods are unfounded.

Furthermore, whether the aforementioned trends are statistically significant remain unclear. Seth et al. found it challenging to disentangle deaths caused by prescribed and illicit consumption of opioids.⁸ Additionally, most of the literature that can be found concerning opioid deaths simply

* Corresponding author.

E-mail address: maansi.kulkarni2019@gmail.com (M. S. Kulkarni).

stops at the state of residence level without considering urbanization effects or only evaluates certain categories within demographics. For example, although Heyman et al. found a relationship to explain state variation, their investigation only focused on non-Hispanic whites.³

This paper specifically looks at race, gender, urbanization, population, and number of prescriptions given within states of residence in an attempt to uncover statistically significant factors that could help explain opioid overdoses. This comprehensive analysis spans two decades. Thus, using the most recent data available, one can begin to evaluate the success of state-sanctioned programs—like monitoring and limiting opioids prescribed for pain management— that were put in place in order to combat this epidemic.

2. Opioid poisoning and death

Opioids attach to and trigger opioid receptors on cells situated in many areas of the brain, spinal cord, and other organs, particularly those associated in feelings of pain and gratification due to increased dopamine release. They can alleviate pain and make a person feel tranquil and euphoric. However, they can have harmful effects of pinpoint pupils, drowsiness, confusion, and slowed breathing. The slowed breathing results in too little oxygen reaching the brain which can cause hypoxia. Hypoxia can result in coma, permanent brain damage, or even death. Heroin is about three times stronger than morphine while Fentanyl and its equivalents (acetylfentanyl, carfentanil, furanyl fentanyl, and butyrfentanyl), are about 100 times more powerful than morphine. They both reach brain faster than morphine and being highly potent have been linked with a spike in deaths from overdose poisoning.

3. Data acquisition and analysis

3.1. Database selection

The data collected by the CDC for the first analysis, limiting the dataset to opioid-related overdoses from 1999 to 2018.⁹ The death codes specified by the 10^{th} revision of the International Classification of Diseases or the ICD-10 for opioid overdose deaths were utilized. Within X40, which stands for unintentional deaths attributed to drug overdoses, category T40 includes all deaths in which opioids were identified as the major cause of death. T40 is further divided into deaths caused by opium (T40.0), heroin (T40.1), natural/semi-synthetic opioids (T40.2), methadone (T40.3), synthetic opioids that are not methadone (T40.4), and other unspecified narcotics (T40.6). These deaths were classified based on gender, race, population, state of residence, and urbanization for a total of 7,669 observations. The CDC uses the following race categorizes to organize opioid-related deaths: White, Black or African American, American Indian or Alaska Native, and Asian or Pacific Islander. Table 1

shows urbanization ranked on a 6-point scale as used by the CDC.

Table 1: CDC Urbanization Codes

2013 Urbanization Code	Definition
1	Large Central Metro
2	Large Fringe Metro
3	Medium Metro
4	Small Metro
5	Micropolitan (Nonmetro)
6	NonCore (Nonmetro)

Additionally, interest of the study was to investigate whether the number of opioids prescribed had any correlation with the amount of opioid-related deaths. Dataworld was used for the second analysis because although the CDC database provided information for the number of opioid prescriptions provided per year, it does not stratify this information based on state of residence, urbanization, race, and gender selections. In regards to number of prescriptions of opioids, Dataworld is superior as it at least provides this information by state and year.¹⁰ This dataset, however, only covers a timeframe from 1999 to 2014. Thus, the conclusions that one can make concerning the opioid overdoses in relation to over-prescription is limited as recent data is not readily available. For the same reason, one cannot make any conclusions concerning how number of prescriptions interact with factors of interest like gender, race, and urbanization. Lastly, of the 817 observations within the Dataworld dataset, 13 observations were labeled "suppressed" as particular states did not release information concerning the number of the deaths related to opioids for that year. These missing data points for the purpose of analysis were therefore excluded.

3.2. Hypothesis testing

Statistical analyses were performed with both data sets. A testing model with independent variables x_i that interact like

- $y = \beta_0 + \beta_{1, 1}x_1 + \beta_{2, 2}x_2 + \beta_{1, 2}x_1x_2 + \dots + \in \dots(1)$ The hypothesis used is
 - $H_0: \hat{\beta}_{1,1} = \beta_{2,2} = \beta_{1,2} = \dots = 0, and \dots (2)$
 - H_A : at least one of $\beta_{1, j} \neq 0$(3)

Rejection of H_0 implies that at least one of the independent variables contributes significantly to the model. F-test is utilized to test the above hypothesis with alpha = 0.05.

3.3. Data analysis

3.3.1. First analysis model

A visual display of the CDC-based dataset is provided in Figure 1 through 4 for the first analysis model. The scatterplots show variations between urbanization and deaths, race and deaths, year and deaths, and gender and deaths. Figure 1 demonstrates that large central metros have experienced more deaths than other areas. As one moves down the scale towards less urbanization, the deaths decreases.



Fig. 1: Urbanization and deaths scatterplot

Figure 2 confirms what Heyman et al. found: the majority of opioid-related deaths are experienced by whites. African Americans are the second most affected race, followed by Asian or Pacific Islander then American Indians or Alaska Natives.



Fig. 2: Race and deaths scatterplot

Figure 3 demonstrates an increase in the number of deaths from 1999 to 2018.



Fig. 3: Year and deaths scatterplot

Lastly, males experience more deaths compared to females, as displayed in Figure 4.



Fig. 4: Gender and deaths scatterplot

Using JMP software, a multiple linear regression was performed. The model's summary of fit demonstrated an R-squared value of 0.6029. The analysis of variance of the full model is shown in Table 2. The overall model is significant with a p-value of <0.0001. Table 3 shows that all individual sources, as well as the interaction between gender and race are significant as each has a p-value <0.001. The parameter estimates for the first model are tabulated in the Appendix. Figure 5 shows the normalized residuals vs. predicted deaths for the CDC data-based model. There are many outliers, as several of the points do not fall within a -3 to +3 range. There is no valid reason to question these data points and remove them from my analysis as the model is statistically significant without this manipulation.

Table 2: ANOVA tab

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	64	32161784	502528	180.38
Error	7604	21183963	2786	Prob>F
C. Total	7668	53345747		< 0.0001

Table 3: Effect tests						
Source	DF	Sum of Squares	F Ratio	Prob>F		
State	50	2618182	18.80	< 0.0001		
Urbanization	5	850052	61.03	< 0.0001		
Gender	1	63604	22.83	< 0.0001		
Race	3	1062602	127.14	< 0.0001		
Year	1	3987999	1431.50	< 0.0001		
Population	1	12408532	4454.05	< 0.0001		
Gender*Race	3	52452	6.28	0.0003		

3.3.2. Second analysis model

For the second model, multiple regression was performed using Dataworld data. The model included number of prescription opioids dispensed, state of residence, year, and the interactions between some of these independent. The decision to exclude certain interactions was based on the model's error when these interactions where computed. Table 4 shows the analysis of variance for the overall model which was significant with a p-value of <0.001. The model had a R-squared value of 0.9517 displaying good fit. Table 5 for this analysis demonstrated that all individual



Fig. 5: Normalized residuals plot

Sources and interactions for state of residence, year, and prescriptions dispensed are significant (p-value <0.05), with the exception of the interaction of year and prescriptions dispensed by retailers that year. Model parameter estimates are tabulated in the Appendix.

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	103	112685437	1094033	133.70
Error	699	5719541	8182	Prob>F
C.	802	118404977		< 0.0001
Total				

Table 5: Effect tests

Source	DF	Sum of Squares	F Ratio	Prob>F
State	50	93192839	227.79	< 0.0001
Year	1	1574386	192.41	< 0.0001
Prescription	1	49323	6.03	0.0143
Dispensed				
State*Prescription	50	8041030	19.65	< 0.0001
Dispensed				
Year*Prescription	1	26266	3.21	0.0736
Dispensed				

There was an increase in prescriptions dispensed by US retailers, reaching its zenith during 2011 (Figure 6). However, 2011 to 2014 demonstrates a downward trend in prescriptions dispensed.

Lastly, Figure 7 shows the normalized residuals vs. predicted deaths. Outliers are the points that fall outside the -3 to +3 range. There is no valid reason to question these data points and remove them from the analysis as the model is statistically significant without this manipulation.



Fig. 6: Prescription dispensed by US retailers vs. year



Fig. 7: Normalized residuals plot

4. Conclusions

Globally and particularly in the US, deaths due to opioids has become more prevalent of a health issue over the past two decades. In 2018, the number of opioid related deaths in the US was higher than the deaths due to motor vehicle crashes of 36,560. Factors of state of residence, urbanization, gender, race, year, population, and interaction between gender and race were found statistically different using multiple regression analysis. Additional analysis showed that factors of prescriptions dispensed, state, interaction of state and prescriptions dispensed were found to be significant. Moreover, the interaction between prescription dispensed and year was found to be not statistically significant. The fact that opioid related deaths are on rise while the prescriptions dispensed have been in decline suggests that the illegal acquisition and consumption of opioids is the next critical fight we have on hand.

5. Conflicts of interest

None.

6. Sources of funding

None.

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Author biography

Maansi S Kulkarni, Student

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