Published in final edited form as:

J Rural Health. 2020 March ; 36(2): 177–186. doi:10.1111/jrh.12368.

Rural-Urban Trends in Opioid Overdose Discharges in Missouri Emergency Departments, 2012–2016

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Abstract

Purpose: Opioid overdose death rates rose 36% from 2015 to 2016 in Missouri, indicating a worsening of the opioid overdose epidemic. To better understand urban and rural differences in nonfatal opioid overdoses treated in Missouri emergency departments, this paper analyzed hospital billing data from emergency departments due to opioid overdose from 2012 to 2016.

Methods: Emergency department records meeting the opioid overdose case definition were aggregated into 6 progressively rural groups using the National Center for Health Statistics (NCHS) urban-rural county classification from 2013. These data were analyzed to determine significant trends amongst and between the geographic groups.

Findings: Generally, the magnitude of opioid overdose morbidity decreased as levels of rurality increased, using annual percentage change as the metric of change. Over the study period, Missouri's most urban counties had significantly higher rates of opioid overdose and saw larger percentage increases in rates compared to more rural areas. Statewide, all rural-urban classifications experienced increases in heroin overdose morbidity; however, there was extreme variation in the trajectory of those increases. Heroin overdose rates were much higher in urban areas than rural areas. Conversely, rural and urban areas saw relatively similar patterns for non-heroin opioid overdoses, though overall magnitude of these increases was more modest across all geographic groups.

Conclusions: The results from this analysis can help inform prioritization of strategies and resources to implement activities addressing the opioid overdose epidemic. Using a rich hospital discharge database could allow for further analysis of subpopulations to enhance personalization and customization of care.

Keywords

emergency departments; Missouri; nonfatal overdose; opioids; rural-urban

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The opioid overdose epidemic has become an increasingly large public health crisis in the United States; however, this problem did not emerge overnight. This epidemic can be described as 3 overlapping waves, starting in the 1990s with an increase in deaths related to natural and semisynthetic opioids (including the most commonly prescribed opioid pain relievers such as oxycodone and hydrocodone). In the last 15 years, over 188,000 people died from overdoses involving opioids in the United States.[1] The second wave of the epidemic began in 2010 with increases in the number of heroin deaths. For 2016, the heroin-related death rate increased substantially (over 4-fold) since 2010 and over 15,000 Americans died from heroin.[2,3] Mortality involving heroin overdose now exceeds natural and semisynthetic opioids (eg, hydrocodone, oxycodone) and is lagging just behind synthetic opioids other than methadone as the leading cause of opioid-related death.[3] Beginning in 2013, the third wave includes the large and drastic increases in deaths related to synthetic opioids other than methadone, which is likely driven by illicitly manufactured fentanyl and fentanyl analogs. Fentanyl is a synthetic and short-acting opioid analgesic and is 50–100 times more potent than morphine. The death rate for synthetic opioids other than methadone has now surpassed all other opioids in the last 5 years, and in 2016 over 19,000 Americans died from synthetic opioids.[4] In 2016, more than two-thirds of drug overdose deaths nationwide involved an opioid. Opioid deaths in 2016, including both illicit and prescription opioids, increased by more than 5-fold compared to 1999.[4] The most recent estimates indicate that opioid-involved deaths increased 28% from 2015 to 2016.[3] During this time period there was a 100% increase in deaths due to synthetic opioids other than methadone (eg, illicitly manufactured fentanyl).[3]

Though data on opioid overdose deaths provides the mortality burden of this epidemic, emergency department (ED) data are another source that can be used to create a more informed narrative on the opioid crisis. ED data have the additional benefit of a reduced time lag in comparison to receiving finalized death certificates, which can better assist states in not only identifying opioid-involved overdose, but also in responding more effectively by quickly providing resources to communities in need. Most recent estimates from 16 states across the United States indicate a 30% increase in opioid overdose visits to EDs from July 2016 through September 2017.[5] Vivolo-Kantor et al[5] also found increases for most states in the United States, with some states showing larger increases than other states. In addition, disparities between levels of urbanization were examined. Though all urbanization levels saw large increases, large fringe metropolitan areas witnessed the largest increases (54%), indicating a potential worsening of the epidemic in certain types of geographic areas.[5] Tracking opioid overdose deaths by geographic areas and urbanization is critical to inform and target interventions.

To better track the trends of this epidemic in states across the United States, the Centers for Disease Control and Prevention (CDC) initiated the Enhanced State Opioid Overdose Surveillance (ESOOS) program in 2016, which now funds 32 states and the District of Columbia to report on nonfatal and fatal drug overdoses in a timelier manner through September 2019. Funded state health departments are required to provide quarterly reports on 2 of the 3 following indicators: suspected drug, opioid, or heroin overdoses treated in the EDs. Stratifications by sex, age group, and county are also reported. Additionally, biannual opioid-involved mortality data from medical examiners/coroners are reported, which includes toxicology reports and death scene investigations, allowing more data on the specific drugs involved in fatal overdose. The purpose of the ESOOS program is to capture these data so that response efforts can effectively target areas most in need of intervention.

This study uses data analyzed as part of ESOOS to measure the disparities in nonfatal opioid overdoses (including heroin and non-heroin opioid overdoses) among urban and rural areas in the state of Missouri. By some metrics in Missouri, opioid-involved deaths have seen larger increases than national averages. Missouri has consistently been approximately 15% higher than the United States average for opioid overdose deaths over the last decade.[1] Over time, deaths involving opioids have increased drastically in Missouri and, in 2016, the state's 908 opioid overdose deaths were more than 8 times the total in 2001. From 2015 to 2016 alone, Missouri saw a 36% increase in all opioid-involved deaths, largely driven by a 26% increase in deaths involving heroin and a 152% increase in deaths involving synthetic opioids other than methadone.[3] In a recent report from CDC,[5] Missouri witnessed a 21% increase from July 2016 through September 2017 in nonfatal opioid overdose visits seen in EDs. However, the scale and scope of opioid-related morbidity may vary widely across Missouri's 115 counties, and grouping these counties by rurality allows for exploration of differences in spatial patterns for various opioid overdose subcategories. This study further examines these urban and rural differences using the most up-to-date hospital billing data from EDs for 2012–2016.

Methods

Study Population

Morbidity data utilized in this analysis are from the Patient Abstract System (PAS) maintained by the Missouri Department of Health and Senior Services (MDHSS). By state statute, all Missouri licensed hospitals are required to submit inpatient, emergency room, and select outpatient discharges to MDHSS, resulting in an annual file that includes well over 3 million records. Among other variables, these patient records contain basic demographic information such as age, race, sex, and county of residence, as well as information about the purpose of the visit (eg, diagnosis codes). The study population for this analysis included all ED visits in the PAS from January 1, 2012, through December 31, 2016, for Missouri state residents ages 11 years and older. Rates per 10,000 residents were generated using US Census Bureau estimates for the resident county population ages 11 and older and were not age-adjusted.

Opioid Overdose Case Definition

The definitions for opioid, heroin-specific and non-heroin opioid overdose were developed in collaboration with the CDC through the ESOOS cooperative agreement. Opioid overdose cases for Missouri residents were identified and further classified into 1 of the 2 mutually exclusive subtypes described below based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) discharge diagnosis codes assigned by hospital staff. The first 5 of 23 discharge diagnosis code fields were used to categorize opioid overdose discharges with either ICD-9-CM (covering 2012 through September 2015) or ICD-10-CM codes (covering October 2015 through the remainder of 2016). The first category, *all opioid overdoses*, included codes for poisoning by opium (T40.0X1A or T40.0X4A), other opioids (T40.2X1A or T40.2X4A), methadone (T40.3X1A or T40.3X4A), synthetic narcotics (T40.4X1A or T40.4X4A), unspecified narcotics (T40.601A or T40.604A), other narcotics (T40.691A or T40.694A), or heroin (T40.1X1A or T40.1X4A). The second category, *heroin overdoses*, included only codes T40.1X1A or T40.1X4A. The final category, *non-heroin opioid overdoses*, included all opioid codes except T40.1X1A or T40.1X4A. Visits that included an opioid code (eg, T40.691A) and a heroin code (T40.1X1A) were coded as *heroin overdose*. Hospitalization billing data from 2016 used in this analysis are considered provisional as the annual file is not finalized until all out-of-state records are received, generally in mid-summer. Our case definition includes codes for unintentional and undetermined drug poisoning intent using only the initial encounter to remove potential duplicate visits. A record containing both subtypes of opioid overdose was categorized as a heroin overdose.

Analytic Plan

ED records for the study period of 2012–2016, identified in the PAS as meeting the opioid overdose case definition, were aggregated into categories based on the patient's county of residence using the National Center for Health Statistics (NCHS) urban-rural county classification from 2013.[6] This methodology uses metropolitan and micropolitan statistical area designations, as well as overall Metropolitan Statistical Area (MSA) population size and principal city population estimates, to categorize Missouri counties into 6 progressively rural groups (see Figure 1). The most urban designation, Large Central Metro (LCM), included only 2 counties in Missouri, which contain the core cities of Kansas City and St. Louis. A total of 14 counties met the criteria for the Large Fringe Metro (LFM), and these counties surround the 2 LCM counties in the state. The Medium Metro (MM) classification included the third largest city in the state, Springfield, as well as several counties that surround it. In addition, 1 county in Missouri that is a part of the Northwest Arkansas metro falls in this classification. Progressively smaller, less dense urban areas are categorized as Small Metro (SM), which includes counties associated with or near Joplin, Columbia, Jefferson City, St Joseph, and Cape Girardeau. Finally, the Micropolitan (MCO) class includes counties that contain cities with a population between 10,000 and 50,000 persons. The majority of Missouri's counties (59) fell into the most rural classification of Noncore (NC). The LFM contains the highest percentage of Missouri's population with 38%. By comparison, the NC contains 14% and the smallest group by population is the MM with 8% (Table 1).

These data were then analyzed across time, space, and specific type of opioid overdose diagnosis. Ninety-five percent confidence intervals were used as the primary significance test to determine meaningful differences between data points for county groupings, specific years within the study period, or the study period as a whole. Frequencies in the numerator determined whether the Poisson (when numerator frequencies exceeded 500) or inverse gamma methodology was used to develop confidence intervals. All database management and some statistical testing were completed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Further testing through regression analysis was conducted using the National Cancer Institute's Joinpoint Regression Program version 4.5.0.1 to assess linear trends and calculate annual percentage change (APC).

Results

All Opioid Overdose

The rate of all opioid overdose-related ED discharges increased significantly, by more than 100% (3.08 to 6.33) from 2012 to 2016, with an APC of 22.0% (Table 2). This doubling of ED discharge rates reflects a steady rise from 2012 to 2014, followed by a surge of cases from 2015 to 2016.

Opioid overdoses presenting to EDs are increasing statewide; however, the increases for the 2 most urban categories, LCM and LFM, are notable. These categories have 2016 rates that are 2–3 times higher than the MM, SMC, MCO, and NC groups (Table 2 and Figure 2). Additionally, the rate increases were much steeper than the gradual gains seen in the 4 other more rural areas. The APCs for the 2 most urban areas of LCM and LFM (25.0% and 26.2%, respectively) were significant. The greatest increases occurred between 2014 and 2016, where rates doubled from 4.99 (LCM) to 9.92 and 4.38 to 8.73 (LFM). Furthermore, these 2 groups also account for nearly 75% of all fatal opioid overdoses statewide during the study period.

Three of the middle density categories (MM, SM, and MCO) each experienced 2016 opioid overdose discharge rates that were more than 1.5 times higher than their rates in 2012, though the overall linear trend for the MM counties did not reach statistical significance.

The most rural areas in Missouri, NC counties, saw the smallest increases in overall rates of opioid overdose-related discharges. The discharge rate for these counties was highest in 2015, but this rate was half that of the rates in the most urban categories of LCM and LFM. Overall, the NC rate for 2016 was the second lowest of the 6 categories (only SM was lower). However, NC counties experience the third highest absolute number of overdoses (roughly 9% of the Missouri total) for the study period.

Heroin Overdose

Heroin overdose ED discharge counts increased more than 190% statewide during the study period—this subtype of opioid overdose has been the greatest driver of change in Missouri. Though frequencies are low in some NCHS groups, heroin overdose ED discharges and associated rates had increases from 2012 to 2016 for all urbanization levels, and all trends were statistically significant (using APC), except the MM area (Table 3 and Figure 3). Across the entire study period, residents of the most urban region of Missouri (LCM) had over a 650% increased risk (risk ratio 7.62) of being discharged from the ED for a heroin-related overdose than their most rural (NC) counterparts (LCM rate: 4.04, NC rate: 0.53). Missouri's 2 most urban groupings, LCM and LFM, account for almost 90% of the fatal heroin overdoses in the state during this study period.

While regions other than LCM and LFM have lower overall rates, these more rural areas experienced the largest percentage increases in the state over the study period, heralding the spread of heroin overdose outward from the most urban regions in more recent years. In 2012, 92% of all heroin-related overdose discharges occurred among residents living in the 2 most urban classifications (LCM and LFM); however, by 2016 that number had dropped to 87%, with the least dense population areas seeing increased burden (increases from 5% to 8% of the total burden in MCO and NC areas during the study period). While NC areas had relatively lower heroin overdose rates compared to other urbanization levels in 2016, they were more than 5 times higher than the 2012 rates.

The MM region, the smallest in terms of population of the 6 groupings, experienced both small overall counts and large increases of heroin overdose. Less than 3% of heroin cases in Missouri during this time period were attributed to residents in MM counties. While the total percent change between 2012 and 2016 for MM was over 500%, the overall linear trend did not reach significance. The greatest percentage increase during the study period for this area occurred in 2013–2014, where heroin-specific discharges jumped from 8 cases to 26.

Non-heroin Opioid Overdose

Results for non-heroin opioid overdoses reflect a different pattern. Statewide non-heroin opioid overdose discharges happen less frequently than heroin-related discharges, and rates have remained considerably more stable than the heroin trends over the same time period. Missourians experienced a 29% increase in non-heroin opioid overdose discharges during the study period, compared to the 190% increase for heroin-specific discharges. Though not statistically significant, the portion of time between 2014 and 2016 shows steep increases for the LCM region, with APC fluctuations from −14.1% (2012–2014) to +31.8% (2014–2016).

Statewide linear trends over time did not show significant APC changes, though the second most urban group of counties, LFM, saw a significant upward trend in non-heroin opioid overdose ED discharges with an APC of 17.6% (Table 4) during the study period. This cohort comprised 27% of statewide non-heroin opioid overdoses in 2012, which increased to nearly 40% by 2016.

The most rural grouping, NC, saw a significant decrease in non-heroin opioid overdose ED discharges. Rates fell from 2.16 to 1.75 over 5 years—a decrease of nearly 20%. This contrasts with a significant increase in heroin-specific ED discharges for the NC class during the same time, though it should be noted that the non-heroin opioid overdose rates continue to be higher than heroin-specific rates for NC counties. Early in the study period (2012) NC rates were commensurate with LCM rates; however, trends have since diverged, specifically in 2016 when the LCM rate was significantly higher than the rate for NC counties. Between 2013 and 2014, the NC rate was significantly higher than the LCM rate. However, by 2015, the rates for these 2 classes were nearly identical, and in 2016, the LCM rate was much higher than the NC rate (Figure 4).

Discussion

To better understand urban and rural differences in nonfatal opioid overdoses treated in Missouri EDs, this paper analyzed hospital billing data from ED discharges due to opioid overdose, including heroin, from 2012 to 2016. Our findings indicate that, overall, Missouri saw increases in nonfatal opioid (106%), heroin (185%), and non-heroin opioid (27%) overdose rates from 2012 to 2016. However, we identified disparities in rural and urban areas throughout the state whether or not the overdose involved heroin. Missouri's more urban counties (LCM and LFM) had significantly higher rates of overdose for the entire study period and moreover, those urban counties have seen larger percentage increases in rates compared to their more rural counterparts. The differences between rural and urban areas in Missouri warrant additional exploration.

Mortality data analyzed by Mack et al[7] found that opioid overdose death rates in rural counties across the United States increased from 2010 to 2015, but in 2016, rates seem to be more stable and the largest increases are now occurring in more urban areas. The dramatic increases in mortality seen nationally in urban areas are consistent with increases seen in the more urban areas in Missouri—especially for heroin overdoses. However, this trend in all opioid mortality is inconsistent with our findings that in the most rural areas of Missouri (NC counties), non-heroin opioid discharges were highest in 2013 and have decreased significantly since that time. Heroin-specific overdose discharge rates for this grouping have increased significantly, as well, though frequencies remain low compared to more urban groupings. On the other hand, the largest increases in opioid overdose death rates across the United States are now occurring in more urban areas.[3] Our data also support these findings, especially for heroin overdose where more urban areas witnessed large and significant percentage increases from 2012 to 2016.

While overdose mortality was not the focus of this study, Missouri resident opioid overdose deaths were examined using the same NCHS geographic categories and time period. Mortality data findings closely resembled emergency room discharge rates due to opioid overdose. LCM and LFM areas experienced the highest rates of opioid overdose deaths, having statistically significantly higher rates compared to the 4 more rural groupings during the entire study period. All geographic areas saw increases in heroin overdose death rates over the 5-year time period, while only LCM and LFM areas saw large percentage increases in non-heroin overdose deaths. In 2016, Missouri experienced an over 30% increase in opioid overdose deaths from the previous year and a 70% increase from 2012.

The reasons behind why we are seeing these increases are not entirely clear. More in-depth analysis of other types of data, including drug supply data or emergency medical services (EMS) data, could provide some additional context. Future analyses could also overlay county EMS data, ED discharges, and mortality data to explore these changes. In addition, law enforcement drug product reports from the Drug Enforcement Agency (DEA) could shed light on the types and amounts of opioids introduced and seized in the community.

Another important finding is that while increases in heroin overdose are driving increases in opioid overdoses across all urbanization levels, increases in non-heroin opioid overdose are also occurring in the more urban (LFM) locations. This may be due to the increase in availability and use of illicitly manufactured fentanyl (IMF) and fentanyl analogs in urban areas. In Missouri, evidence suggests that fentanyl analogs began infiltrating the opioid supply in LCM areas in 2015 and has since spread to LFM and MM areas.[8–10] With the high potency and rapid onset of reaction in the body, it is possible that the increase in overdose ED visits is driven by increases in the introduction of IMF in the drug supply. This is particularly true in situations where a drug user unknowingly uses IMF that has been mixed with the substances they purchase. Using our methodology, if a patient tests positive for both heroin and a non-heroin substance, like IMF, that record would be coded as a heroin overdose. However, we are not aware of the breadth nor the specificity of toxicology testing in all Missouri ED facilities.

Other states have shared reports of IMF distributed in counterfeit prescription pills or sold to individuals using substances with or without their knowledge that the product contains IMF[11,12]; thus, it is possible that this, too, is occurring in Missouri. More recently, anecdotal evidence from Missouri law enforcement officials indicates that sometimes IMF is being sought by individuals with substance use disorder.[9] In addition, IMF is now being found in other drug groups beyond opioids, including cocaine.[9] Unfortunately, because no specific ICD-10-CM code exists for IMF, and without additional information from hospital staff (eg, free text chief complaint or nurse triage notes), we cannot be certain how much IMF is playing a role in increasing overdose in urban Missouri areas.

Limitations

This study is not without several limitations. Foremost, this study focuses on nonfatal overdoses, which have nuanced implications that differ from those associated with fatal overdoses. It stands, however, that in Missouri the rate of fatal opioid overdoses during the study period was highest for the LCM category and comparatively significantly lower for the NC group, which mimics the findings of this nonfatal overdose analysis. Second, our case definition cannot take into consideration fluctuations in coding decisions and the coding changes precipitated by the transition from ICD-9-CM to ICD-10-CM, which occurred during the final 15 months of our study. It is possible that this transition may play a role in the increases or decreases witnessed. Third, no specific ICD-9-CM or ICD-10-CM code captures fentanyl overdoses, and it is likely that fentanyl overdoses are captured with both heroin overdose codes and codes for other or unknown narcotic. In our current classification scheme, cases with both a heroin and non-heroin opioid overdose code were classified as heroin; however, fentanyl overdoses have different presentation and treatment modalities than other non-heroin opioid overdoses.[8,13] Finally, several of the county groupings had low annual frequencies of opioid overdose-related ED discharges. During the 5-year study period, several of the NCHS classes, including MM, SM, and NC, have years in which there were less than 20 heroin-specific ED discharges. This makes rate comparisons unreliable and makes significant findings less likely.

Notwithstanding these limitations, this study has several strengths. The robust PAS dataset allows analysts to generate a fairly comprehensive understanding of an ED patient and the circumstances surrounding their visit and subsequent discharge. Geospatial analysis will allow public health professionals and others to address the specific needs of geographically granular areas in developing interventions related to the opioid overdose epidemic in Missouri.

Implications

By examining Missouri's opioid overdose epidemic by time, geography, and opioid subtype, findings from this study could better equip those responding to the crisis. These considerations heavily impact intervention strategies. For example, a greater understanding of how these factors are associated with a community could drive evidence-based programming and resource allocation. Furthermore, the results from this analysis can help inform prioritization of strategies and resources to implement activities to address the opioid overdose epidemic within the states. Using a rich hospital discharge database, like the Missouri PAS database described here, could allow for further analysis of subpopulations by age, sex, race, ethnicity, and other factors that could enhance the personalization and customization of care during this health crisis.

This analysis may have implications for public health, law enforcement, and service providers in Missouri and may be of interest to other Midwestern states that have similarly high rates of fatal and nonfatal opioid overdose. In addition to increasing rates of opioid overdose ED discharges statewide, rural and urban communities in Missouri face somewhat different challenges in addressing the epidemic. The sheer burden of the overdose crisis to these urban counties in Missouri cannot be understated. The most urban areas of LCM and LFM continue to respond to significantly high rates of heroin-specific discharges and deaths while contending with rising non-heroin opioid overdose discharge rates. The increase in non-heroin opioid overdose may be the result of the introduction of fentanyl to the opioid supply, either mixed into heroin or pressed into counterfeit prescription pills. The NC areas, which are Missouri's most rural, continue to see higher rates of non-heroin opioid overdose discharges than heroin-specific discharges, but a steady increase in heroin-related discharges with a decrease in non-heroin opioid overdose discharges indicates a shift may be occurring.

Funding:

This research was funded by the Centers for Disease Control and Prevention, #NU17CE924884 (Hunter, A., PI). The findings and conclusions in this paper of those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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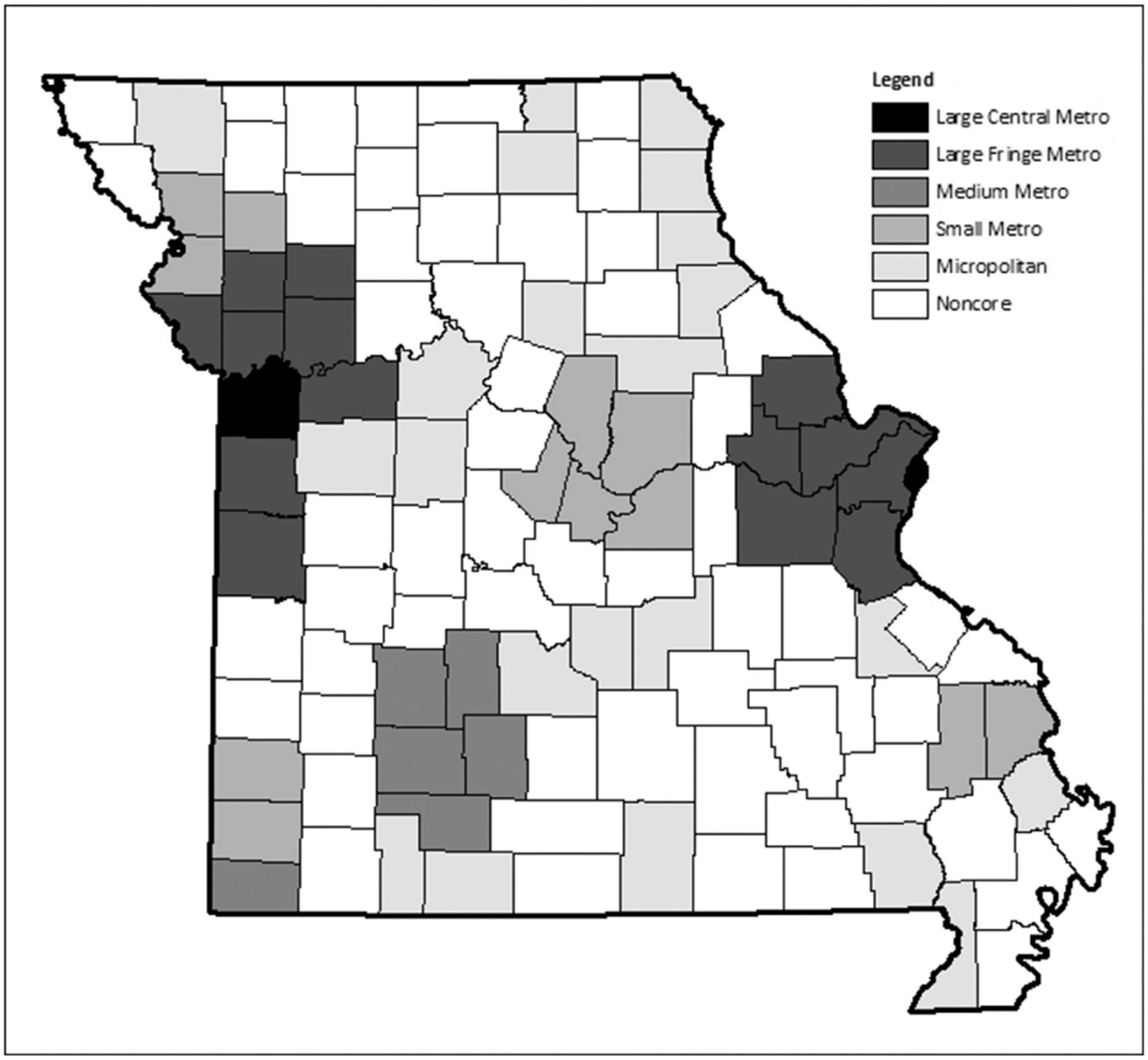

Figure 1.
NCHS Map—Missouri County Classifications.

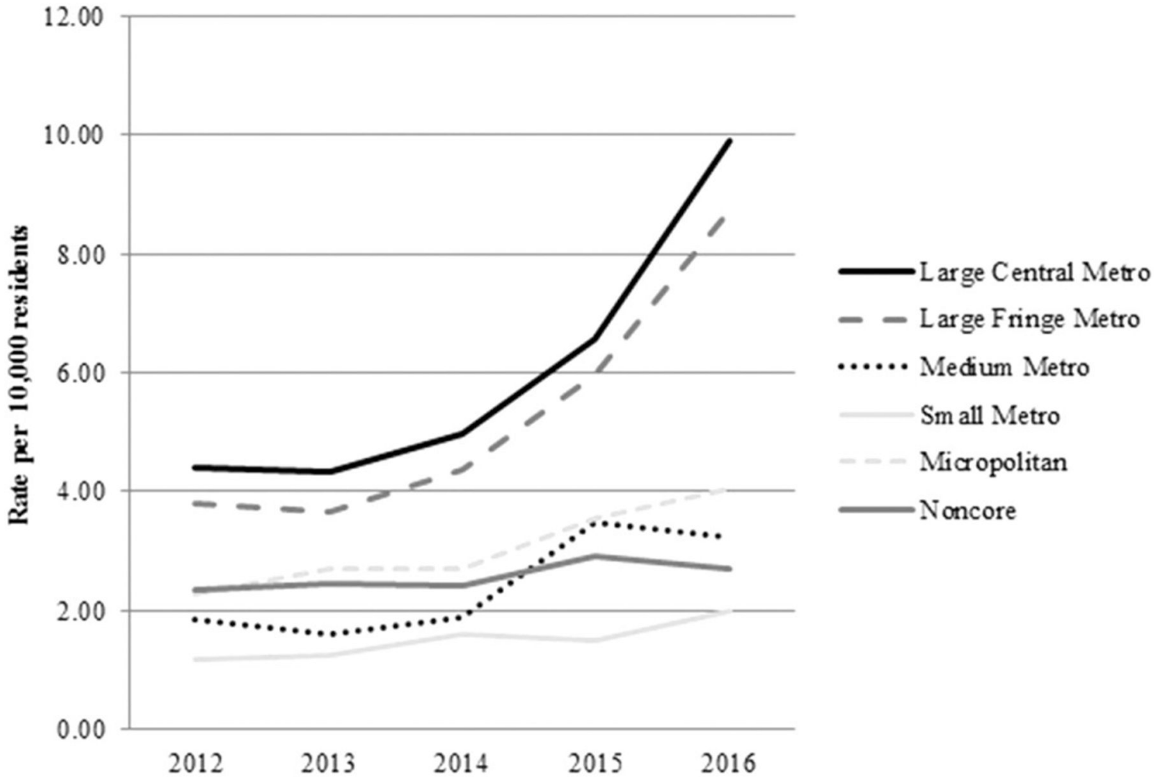

Figure 2.

Trends in Opioid Overdose ED Discharges From 2012 to 2016, Missouri by Urbanization.

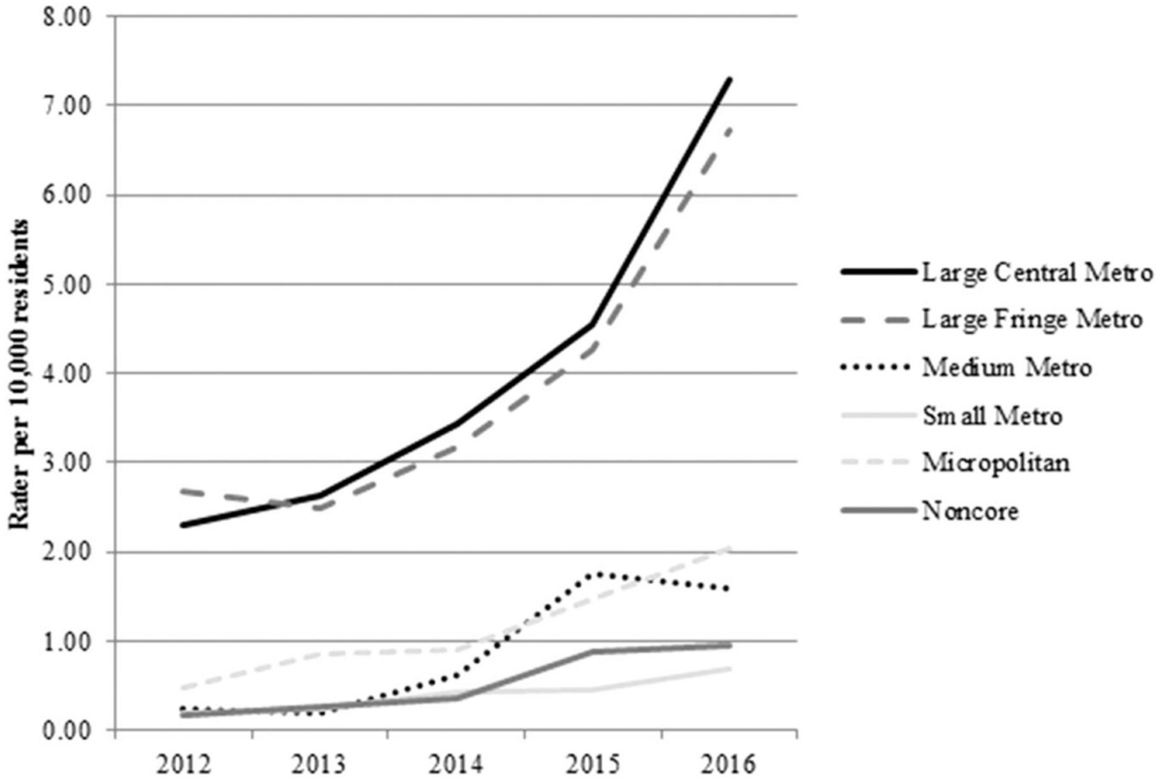

Figure 3.
Trends in Heroin-Specific Overdose ED Discharges From 2012 to 2016, Missouri by Urban-Rural County Classifications.

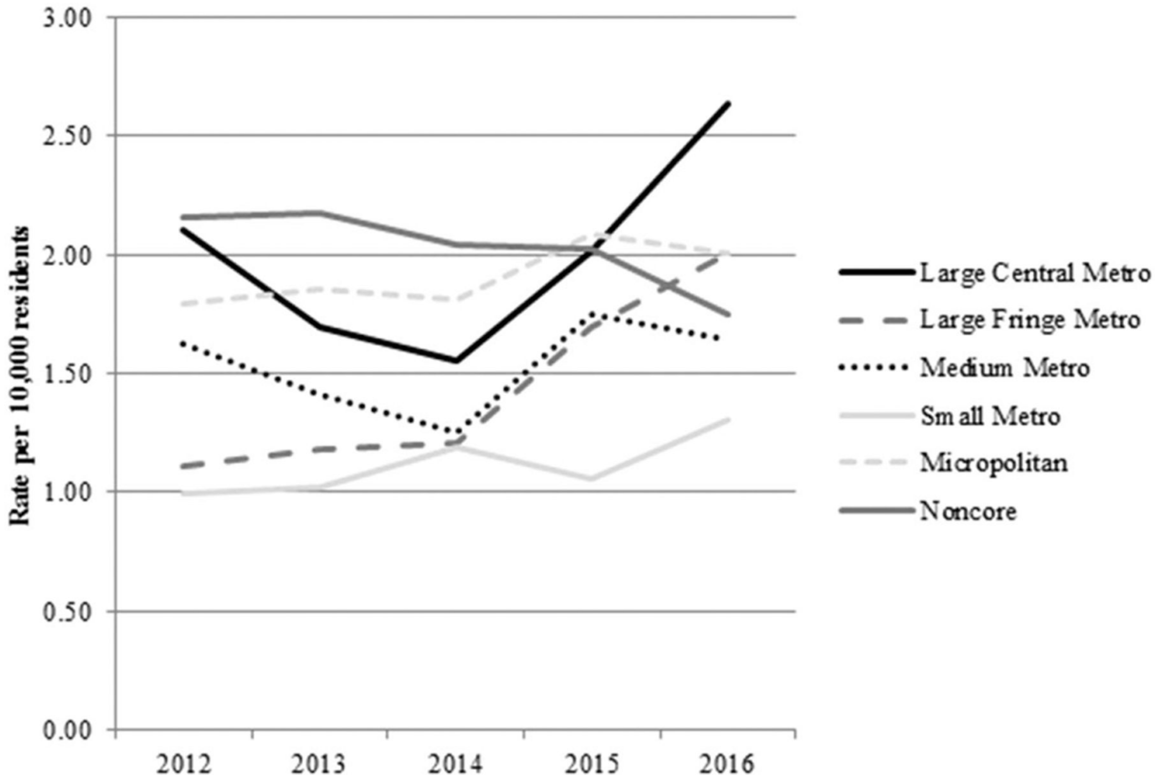

Figure 4.

Trends in Non-heroin Overdose ED Discharges From 2012 to 2016, Missouri by Urbanization.

Table 1

Population and Nonfatal Overdose Proportion (2012–2016) by NCHS Classification

NCHS Urban-Rural County Classification	Number of Counties	2015 Population	Percent of State Population	Percent of Opioid Overdoses	Percent of Heroin-Specific Overdoses	Percent of Non-heroin Overdoses
Large Central Metro	2	1,003,308	16.5%	24.0%	26.7%	19.9%
Large Fringe Metro	14	2,338,627	38.4%	49.3%	59.8%	33.6%
Medium Metro	6	479,099	7.9%	4.7%	2.8%	7.4%
Small Metro	12	713,167	11.7%	4.3%	1.9%	7.9%
Micropolitan	22	717,886	11.8%	8.5%	5.3%	13.4%
Noncore	59	831,585	13.7%	8.7%	3.0%	17.3%
Missouri total	115	6,083,672	100%	100%	100%	100%

Table 2

Rates of All Missouri Resident Opioid Overdose Emergency Department Discharges

NCHS Urban-Rural County Classification	Year 2012	2013	2014	2015	2016	2012–2016	Annual Percentage Change (APC)
Large Central Metro	4.39 (3.96–4.86)	4.33 (3.91–4.80)	4.99 (4.53–5.49)	6.56 (6.01–7.10)	9.92 (9.26–10.59)	6.05 (5.81–6.28)	25.0[a] (7.8–45.0)
Large Fringe Metro	3.80 (3.53–4.07)	3.66 (3.39–3.93)	4.38 (4.09–4.67)	5.96 (5.62–6.29)	8.73 (8.33–9.14)	5.32 (5.18–5.46)	26.2[a] (9.3–45.6)
Medium Metro	1.87 (1.47–2.34)	1.61 (1.24–2.05)	1.88 (1.49–2.35)	3.50 (2.95–4.11)	3.23 (2.71–3.83)	2.43 (2.21–2.64)	21.2 (−3.2 to 51.7)
Small Metro	1.17 (0.92–1.48)	1.25 (0.98–1.56)	1.62 (1.32–1.97)	1.51 (1.22–1.85)	1.99 (1.65–2.37)	1.51 (1.38–1.66)	13.5[a] (3.8–24.2)
Micropolitan	2.27 (1.91–2.68)	2.70 (2.30–3.15)	2.70 (2.30–3.15)	3.55 (3.09–4.06)	4.05 (3.59–4.59)	3.06 (2.86–3.25)	15.7[a] (8.5–23.3)
Noncore	2.34 (2.00–2.71)	2.45 (2.07–2.79)	2.41 (2.07–2.79)	2.90 (2.52–3.32)	2.71 (2.35–3.12)	2.56 (2.40–2.72)	4.8 (−1.5 to 11.6)
Missouri total	3.08 (2.92–3.23)	3.06 (2.91–3.21)	3.51 (3.35–3.67)	4.66 (4.47–4.84)	6.33 (6.12–6.55)	4.13 (4.06–4.21)	22.0[a] (8.8–36.8)

[a] APC is significantly different from 0 at the alpha= 0.05 level 95% confidence intervals.

All rates are crude rates per 10,000 residents age 11 and older.

Table 3

Rates of Missouri Resident Heroin-Specific Overdose Emergency Department Discharges

NCHS Urban-Rural County Classification	Year 2012	2013	2014	2015	2016	2012–2016	Annual Percentage Change (APC)
Large Central Metro	2.29 (1.98–2.63)	2.64 (2.30–3.00)	3.44 (3.06–3.85)	4.54 (4.10–5.01)	7.28 (6.71–7.85)	4.04 (3.85–4.23)	35.8[a] (21.5–51.7)
Large Fringe Metro	2.69 (2.46–2.92)	2.48 (2.26–2.71)	3.17 (2.92–3.41)	4.26 (3.97–4.94)	6.72 (6.37–7.08)	3.87 (3.75–4.00)	29.6[a] (9.5–53.4)
Medium Metro	0.25 (0.12–0.45)	0.19 (0.08–0.38)	0.63 (0.41–0.92)	1.75 (1.37–2.20)	1.59 (1.23–2.02)	0.89 (0.77–1.03)	68.8 (−2.7 to 192.8)
Small Metro	0.18 (0.09–0.33)	0.23 (0.13–0.39)	0.43 (0.28–0.62)	0.46 (0.30–0.66)	0.68 (0.49–0.92)	0.40 (0.33–0.47)	37.9[a] (20.1–58.3)
Micropolitan	0.48 (0.32–0.69)	0.85 (0.63–1.11)	0.90 (0.67–1.17)	1.46 (1.17–1.80)	2.04 (1.70–2.44)	1.14 (1.03–1.27)	40.6[a] (25.5–57.4)
Noncore	0.18 (0.09–0.30)	0.27 (0.17–0.42)	0.37 (0.24–0.54)	0.88 (0.67–1.12)	0.96 (0.75–1.21)	0.53 (0.46–0.61)	55.9[a] (20.8–101.1)
Missouri total	1.53 (1.43–1.64)	1.57 (1.46–1.67)	2.05 (1.92–2.17)	2.88 (2.74–3.03)	4.37 (4.19–4.55)	2.48 (2.42–2.55)	33.6[a] (17.6–51.8)

[a]APC is significantly different from 0 at the alpha= 0.05 level 95% confidence intervals

All rates are crude rates per 10,000 residents age 11 and older.

Table 4

Rates of Missouri Resident Non-heroin Opioid Overdose Emergency Department Discharges

	Year						
NCHS Urban-Rural County Classification	**2012**	**2013**	**2014**	**2015**	**2016**	**2012–2016**	**Annual Percentage Change (APC)**
Large Central Metro	2.10 (1.81–2.43)	1.70 (1.43–2.00)	1.56 (1.30–1.84)	2.02 (1.73–2.34)	2.64 (2.31–3.01)	2.00 (1.87–2.14)	7.1 (−11.6 to 29.7)
Large Fringe Metro	1.11 (0.97–1.27)	1.18 (1.04–1.34)	1.21 (1.06–1.37)	1.70 (1.52–1.89)	2.01 (1.82–2.22)	1.45 (1.37–1.52)	17.6[a] (6.9–29.3)
Medium Metro	1.62 (1.25–2.06)	1.41 (1.07–1.83)	1.26 (0.94–1.65)	1.75 (1.37–2.20)	1.64 (1.28–2.08)	1.54 (1.37–1.72)	2.4 (−10.8 to 17.7)
Small Metro	0.99 (0.76–1.28)	1.02 (0.78–1.31)	1.19 (0.94–1.50)	1.06 (0.82–1.35)	1.31 (1.04–1.63)	1.12 (1.00–1.24)	6.3 (−2.0 to 15.4)
Micropolitan	1.79 (1.47–2.16)	1.86 (1.53–2.23)	1.81 (1.48–2.18)	2.09 (1.74–2.49)	2.01 (1.67–2.40)	1.91 (1.75–2.07)	3.6 (−1.2 to 8.6)
Noncore	2.16 (1.84–2.52)	2.18 (1.85–2.54)	2.04 (1.73–2.40)	2.02 (1.71–2.38)	1.75 (1.46–2.08)	2.03 (1.89–2.18)	(4.6)[a] (−8.9 to 0.1)
Missouri total	1.54 (1.44–1.65)	1.49 (1.39–1.60)	1.47 (1.36–1.57)	1.77 (1.66–1.89)	1.97 (1.85–2.09)	1.65 (1.60–1.70)	7.1 (−1.1 to 16.0)

[a]APC is significantly different from 0 at the alpha= 0.05 level 95% confidence intervals.

All rates are crude rates per 10,000 residents age 11 and older.