# Declines and Pronounced Regional Disparities in Prescription Opioids in the United States

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## Abstract

**Background:** The United States (U.S.) opioid epidemic, including the misuse of prescription drugs, is a significant public health crisis due to the risk of addiction and overdoses. Despite guidelines and several policies that have been implemented to combat these issues, drug overdoses continue to increase. This study aimed to assess the changes in opioid prescriptions between 2010 and 2019. We hypothesized that a decrease in opioid prescriptions would be observed but that there would be substantial state level variability.

**Methods:** Data was obtained from the U.S. Drug Enforcement Administration's Automation of Reports and Consolidated Orders System. Data from 2010 to 2019 was collected for 10 prescription opioids (codeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone and tapentadol) and was analyzed.

**Results:** The peak years for all 10 prescription opioids were identified individually between 2010 and 2013 except for codeine (2015). There was a -51.96% overall decrease in opioid distribution. The largest decrease was observed in Florida (-61.61%) and smallest in Texas (-18.64%). While the largest quantities of opioid distribution were observed in Tennessee (520.70 morphine milligram equivalent or MME per person) and Delaware (251.45) in 2011 and 2019, respectively, the smallest MMEs were observed in Nebraska (153.39) and Minnesota (90.49), respectively. The highest to lowest state ratio of opioid use, corrected for population, was 3.39-fold in 2011 to 2.78-fold in 2019. Moreover, the distribution between hydrocodone and codeine, and hydromorphone and codeine increased significantly from 2011 to 2019, $p < 0.05$.

**Conclusion:** Following the peak year for each opioid, a steady decline in opioid distribution was revealed. However, the extent of prescription use varied 3.39-fold in 2011 and 2.78-fold in 2019 by state. Moreover, there was an overall 42.99% decline in total opioid distribution across the U.S. from 2011 to 2019. If evidence-based medicine was being practiced, we would have expected that two states with similar rates of acute pain (e.g., North and South Dakota) should have similar use patterns for prescription opioids. However, we observed pronounced regional variability. The observed regional differences may partially be due to variability in state-level legislative changes that were implemented to combat the opioid epidemic or other factors. Additional research focused on the relationship between policy changes and prescription opioids is warranted.

## Introduction

The current rate of opioid prescriptions coupled with the risk of opioid addiction and unintentional overdose is a persistent public health concern. The aforementioned, intertwined with the observed increase in opioid overdose-related deaths, promoted the public health concern to a nationwide United States (U.S.) epidemic (1). The current rate of opioid prescriptions may be attributed to an increased prevalence of chronic pain, limited knowledge regarding long-term opioid use, and pharmaceutical companies capitalizing on false claims regarding the non-addictive nature of opioids (2). Since the emergence of heightened opioid utilization, the number of opioid-related deaths has steadily risen from 1999 to 2019 across the U.S. (3). In 2019 alone, a total of 70,630 drug overdose deaths occurred, corresponding to an age-adjusted rate of 21.6 per 100,000 population and a 4.3% increase from the 2018 rate (20.7) (1). However, despite the increasing mortality rate, the opioid prescription per capita expanded 7.3% between 2007 and 2012 with marked prescription rate increases in family medicine, general practice, and internal medicine (4). Given the stable prescription rates and increased pervasiveness of adverse outcomes, a sizable intervention was necessary to control this problem. With the plan to trigger nationwide transformation, the U.S. Department of Health and Human Services declared the opioid epidemic a public health emergency in 2017 (5).

Following this declaration and the resulting shift in mentality regarding the devastating effects associated with the over-prescription of opioids, a strategic nationwide plan to combat the epidemic remained unestablished. Instead, the task to develop strategies aimed at curbing the epidemic was left to the individual states, creating an opportunity for opioid legislative disparities nationwide. State legislators have independently created legislation guiding the prescribing of opioids for a multitude of conditions such as acute pain, chronic pain, cancer, terminal condition, palliative care, etc. For example, in Florida, House Bill 21 was enacted that would require certain registered practitioners to complete a specified board-approved continuing education course to obtain authorization to prescribe controlled substances, adopt rules establishing certain guidelines for prescribing controlled substances for acute pain, provide requirements for pharmacists for the dispensing of controlled substances to persons not known to them, and authorize a pharmacist to dispense controlled substances upon receipt of an electronic prescription if certain conditions are met (6). Further, prescribers are asked to develop a written plan for assessing each patient's risk of aberrant drug-related behavior, which may include drug testing, pill counting, and close monitoring from the physician (6). In 2019, Texas signed House Bill 2174 which states that a practitioner may not issue a prescription for an opioid in an amount that exceeds a 10-day supply or provide for a refill of an opioid for acute pain. The law does not limit how many times the 10-day supply may occur and does not apply to cancer, hospice, or chronic pain management (7). Nevada adopted the AB 474 and SB 59 in 2018 which has five major requirements; two units of CME per licensing cycle required for all licensed prescribers, Mandated Registry and Use of Prescription Monitoring Programs, New Prescriptions Requirements, New Prescribing Guidelines for Controlled Substances, and Overdose Reporting (8). North Carolina's 2017 house bill 243 extends standing orders for an opioid antagonist to community health groups, requires supervising physicians to personally consult with physician assistants and nurse practitioners who prescribe certain Schedule II and III controlled substances for long-term use, requires electronic prescribing of certain Schedule II and III controlled substances, and establishes maximum limits for initial prescription of certain Schedule II and III controlled substances (9). Each state has implemented what they believe to be the best approach at combating the epidemic; whether these laws are being enforced as well as their direct effects on opioid prescribing patterns is debatable. What is clear, however, is the lack of and need for either collaborative nationwide opioid legislation or a governing body tasked with the oversight and enforcement of the opioid legislation created by the states.

The observed variation in prescription opioid trends across the U.S. despite the implementation of new opioid legislation suggests that additional extraneous factors may be limiting the extent of its impact. Specifically, racial-ethnic disparities may partially explain the observed patterns, as emergency department physicians were less likely to prescribe opioids to non-Hispanic blacks for abdominal and back pain as compared with non-Hispanic whites due to the increased incidence of drug-seeking behaviors associated with this patient population (10). Moreover, the incidence of opioid-related overdose deaths documented in lower-income white regions in California may also support the involvement of socioeconomic status as an influential factor in prescription-opioid rates (11). Furthermore, women were more likely than men to receive opioid prescriptions relative to men (12). These factors, alongside other variables, may not only impact the efficacy of imposed legislation but may also influence the overall production of specific opioids that are more frequently prescribed or beneficial for patients with certain health conditions. Therefore, additional analyses focused on stratifying opioid prescription rates based on influential factors may be necessary to explain the observed trends.

The morphine milligram equivalent (MME) per capita in 2016 in the U.S. was 1,124 (13) which is appreciably higher than other developed countries or the U.S. Territories (14). However, even this belies the pronounced variability between states. There was a 5-fold difference between the lowest (North Dakota = 485) and highest (Rhode Island = 2,624) states (13). Examination of individual opioids revealed a 3-fold state level difference for fentanyl (15), 18-fold for meperidine (16), and 20-fold for buprenorphine (17).

Utilizing the above knowledge, this study aimed to confirm previously observed declining trends in opioid prescriptions by analyzing 10 opioids between 2010 and 2019. Additionally, through the identification of the state(s) with the highest and lowest decline in prescription rates, regional disparities in efforts to combat the opioid epidemic were examined. Through a direct comparison, opioid prescribing patterns for each of the 10 opioid drugs were evaluated. Lastly, to assess the relationship between the supply and demand of the analyzed opioids, the drugs' production quotas were compared to opioid prescription rates across the U.S. Through these means, this study expected to identify decreasing opioid prescription rates across the U.S. in the period of 2010 to 2019. The largest opioid prescription decline was hypothesized to be seen in regions that are most proactive in implementing and enforcing opioid prescribing reduction policies and identify risk factors that may predispose certain Americans to fall victim to the opioid epidemic.

## Methods

### Data collection

Opioid production data was obtained from the U.S. Drug Enforcement Administration's Production Quotas System, and opioid distribution data was obtained using the U.S. Drug Enforcement Administration's Automation of Reports and Consolidated Orders System (ARCOS) (U.S. Department of Justice, Drug Enforcement Administration (DEA), Division of Diversion Control, 2019). ARCOS is a publicly available reporting system mandated by the DEA that reports detailed and comprehensive drug information from manufacturing to distribution. Information on 10 opioid prescription drugs was collected: codeine, fentanyl base, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone and tapentadol. Population data was obtained from the U.S. Census. All procedures were reviewed and approved by Geisinger Commonwealth School of Medicine's and the University of New England's Institutional Review Board.

### Data analysis

The MME for each opioid drug was determined. These values were calculated using the appropriate multipliers: codeine 0.15, fentanyl base 75, hydrocodone 1, hydromorphone 4, meperidine 0.1, morphine 1, oxycodone 1.5, oxymorphone 3, and tapentadol 0.4 (13, 18). The multiplier for methadone was defined as both 8 and 12, based on whether it was utilized for narcotic programs (13, 18). Methadone utilized in narcotic programs was not included in the methadone prescription value. To isolate the peak opioid prescription year, the weight in grams of each opioid was obtained from ARCOS from 2010 to 2019. Weights for each opioid were converted to their MME values and were then summated for all 10 opioids across all 50 states. To assess changes in opioid prescriptions from 2011 to 2019, heat maps demonstrating the percent change across all 50 states per capita were produced using JMP. The per capita use of each opioid drug for each state was calculated using the respective population estimate according to the U.S. Census. Using these values, ratios for the 95th:5th and 70th:30th percentiles were calculated. Furthermore, Spearman correlations were calculated for all the opioid drugs. Lastly, to assess the relationship between the supply and demand of the analyzed opioids, the drugs production quotas were compared to opioid prescription rates across the U.S. All figures were constructed utilizing the GraphPad Prism version 8.

## Results

Examination of total opioid production quotas from 2010 to 2019 revealed a gradual increase beginning in 2011 that remained relatively stagnant until 2016 when a pronounced decline was observed. Many opioids, including methadone and oxycodone, exhibited a similar trend in their production. However, others such as codeine remained consistent throughout this timeframe (Figure 1A).

Analysis of opioid distribution during the same time period identified 2011 as the peak year for total opioid distribution in the U.S. (Figure 1B). The peak year for each opioid was 2010 for oxycodone and meperidine; 2011 for hydrocodone and oxymorphone; 2012 for morphine and tapentadol; 2013 for hydromorphone and fentanyl base; and 2015 for codeine. Since 2011, total opioid prescription for the ten pain medications analyzed has continued to steadily decline, despite the increase in total opioid production. A -45.4% decline from 2011 to 2019 and an -11.3% decline from 2018 to 2019 was observed.

Comparison of total opioid prescriptions per capita across the U.S. in 2011 (Figure 2A) and 2019 (Figure 2B) revealed an overall decrease of -51.96% in opioid distribution, but also considerable state level differences. Tennessee (520.70), Nevada (491.38), Delaware (476.15) and Florida (452.12) had significantly ($p < 0.05$) increased levels of total opioid distribution relative to the national average in 2011 (Figure 2C). Alabama (251.45) and Delaware (238.71) had significantly increased distribution relative to the mean in 2019 (Figure 2D). Moreover, analysis of changes in individual opioid prescription rates revealed the largest increase for codeine, which had a 143% increase in per capita distribution from 2011 to 2019. In contrast, oxycodone demonstrated the largest decrease of 50.09% in per capita distribution from 2011 to 2019. Furthermore, there was a 3.31-fold difference between the highest (Florida = -61.61%) and lowest (Texas = -18.64%) state opioid prescription decline. Figure 2E demonstrates the observed percent difference for total opioid prescription from 2011 to 2019.

The ratios between the 95th:5th percentiles were calculated for each of the Schedule II opioids for 2011 and 2019 (Figure 3). Analysis of the differences in the 95th:5th percentile ratio between 2011 and 2019 revealed an increase for codeine, hydrocodone, meperidine, and methadone, but a decrease for the remaining opioids. Interestingly, methadone was the only opioid to demonstrate a 95th percentile value increase from 2011 to 2019. The remaining opioids demonstrated decreases in their percentile ranks.

Table 1 demonstrates the Spearman's correlation for the various opioids. Interestingly, oxycodone had the most significant correlations with the other opioids in both 2011 and 2019. The strength of the correlation between oxycodone and morphine (0.50 and 0.51, respectively) and oxycodone and oxymorphone (0.50 and 0.61, respectively) increased from 2011 to 2019. However, between oxycodone and methadone (0.66 and 0.39, respectively) the strength of the correlation decreased. These trends were also observed for the Spearman's correlation

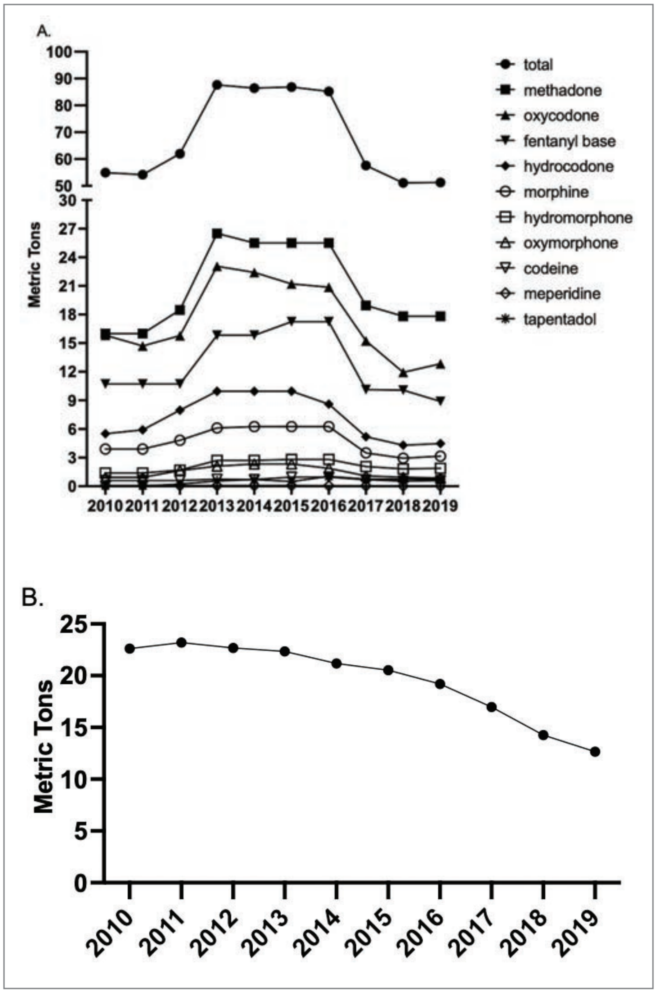


**Figure 1.** (A) Total opioid production and (B) distribution in morphine milligram equivalents across the United States from 2010 to 2019 as reported to the Drug Enforcement Administration's Automated Reports and Consolidated Orders System. Opioids analyzed were codeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, and tapentadol.

between the other opioids analyzed. Moreover, there was a moderate correlation revealed between hydrocodone and meperidine in 2011 (0.62) and 2019 (0.58). Furthermore, Fisher r to Z transformations were calculated to determine whether there were any changes in the strength of the correlations between opioids in 2011 and 2019. These analyses revealed a significant increase in the strength of the correlation between codeine and hydrocodone ($p < 0.05$), codeine and hydromorphone ($p < 0.01$), hydrocodone and methadone ($p < 0.05$), and methadone and oxycodone ($p < 0.05$). Additionally, a significant difference was identified between the correlation for methadone between 2011 and 2019 ($p < 0.05$).

## Discussion

There are several key findings to this report. This study identified 2011 as the peak year of opioid prescriptions in the U.S., and a consistent decline in prescription rates since that point. These findings are consistent with the literature assessing opioid prescription trends at earlier time periods

| 2011 | A | B | C | D | E | F | G | H | I | Mean | Standard Error |
|---|---|---|---|---|---|---|---|---|---|---|---|
| codeine (A) | 1.00 | | | | | | | | | 0.15 | 0.05 |
| fentanyl base (B) | 0.31 | 1.00 | | | | | | | | 0.23 | 0.04 |
| hydrocodone (C) | 0.17* | 0.16 | 1.00 | | | | | | | 0.13 | 0.09 |
| hydromorphone (D) | 0.16* | 0.28 | -0.30 | 1.00 | | | | | | 0.13 | 0.09 |
| meperidine (E) | -0.10 | 0.10 | 0.62 | -0.22 | 1.00 | | | | | 0.10 | 0.09 |
| methadone (F) | 0.08 | 0.06 | -0.15* | 0.40 | -0.20 | 1.00 | | | | 0.16 | 0.10 |
| morphine (G) | 0.33 | 0.39 | 0.24 | 0.29 | 0.18 | 0.35 | 1.00 | | | 0.26 | 0.07 |
| oxycodone (H) | 0.19 | 0.26 | -0.12 | 0.44 | 0.02 | 0.66* | 0.50 | 1.00 | | 0.29 | 0.09 |
| oxymorphone (I) | 0.25 | 0.36 | 0.32 | 0.18 | 0.16 | 0.35 | 0.28 | 0.50 | 1.00 | 0.32 | 0.04 |
| tapentadol (J) | 0.01 | 0.14 | 0.24 | -0.04 | 0.38 | -0.08 | -0.21 | 0.13 | 0.51 | 0.12 | 0.08 |

| 2019 | A | B | C | D | E | F | G | H | I | Mean | Standard Error |
|---|---|---|---|---|---|---|---|---|---|---|---|
| codeine (A) | 1.00 | | | | | | | | | 0.08 | 0.08 |
| fentanyl base (B) | 0.07 | 1.00 | | | | | | | | 0.15 | 0.06 |
| hydrocodone (C) | 0.54* | 0.33 | 1.00 | | | | | | | 0.12 | 0.12 |
| hydromorphone (D) | -0.31* | 0.14 | -0.33 | 1.00 | | | | | | 0.06 | 0.08 |
| meperidine (E) | 0.17 | 0.29 | 0.58 | -0.07 | 1.00 | | | | | 0.17 | 0.09 |
| methadone (F) | -0.10 | -0.26 | -0.45* | 0.31 | -0.39 | 1.00 | | | | -0.02** | 0.10 |
| morphine (G) | 0.13 | 0.31 | 0.26 | 0.30 | 0.26 | 0.13 | 1.00 | | | 0.25 | 0.05 |
| oxycodone (H) | 0.10 | 0.05 | 0.02 | 0.25 | 0.21 | 0.39* | 0.51 | 1.00 | | 0.29 | 0.07 |
| oxymorphone (I) | 0.12 | 0.24 | 0.14 | 0.16 | 0.10 | 0.23 | 0.29 | 0.61 | 1.00 | 0.27 | 0.06 |
| tapentadol (J) | -0.03 | 0.21 | 0.03 | 0.05 | 0.34 | -0.02 | 0.02 | 0.43 | 0.49 | 0.17 | 0.07 |

**Table 1.** Spearman's correlations for opioid distribution per state corrected for population in 2011 and 2019. Boxes in blue and orange represent significant associations between the opioids of < 0.05 and < 0.01, respectively. * p < .05 for Fisher r to Z scores when comparing 2011 and 2019. ** t-test p < .05 versus 2011.

(13, 19, 20, 21). It did not escape notice that the prescribing peak in 2011 was 5 years before the CDC issued its opioid prescribing guidelines (March 2016) and 6 years before rising overdoses resulted in the classification of the situation as a "national emergency" (July, 2017). There is a myriad of reasons that may explain the decline in opioid prescriptions, including individual legislative amendments implemented across the U.S. (22), PDMPs (23), increased awareness of the addictive nature of opioids (24), increased rates of opioid-related overdose mortalities (2), and heightened appreciation of the differences in biochemical characteristics of these opioids (22).

Comparison of the variation of opioid prescriptions across the U.S. between 2011 and 2019 based on each respective state's population revealed a substantial increase in codeine prescriptions. This increase may be attributable to the substitution of codeine and tramadol for pain management as compared with the typical protocol of hydrocodone (2). In fact, hydrocodone prescriptions following Emergency Department visits decreased by approximately 12% between 2012 and 2017 (2). Moreover, a pronounced decrease in oxycodone prescriptions was also identified in this analysis, which may have also contributed to the elevated rates of codeine prescriptions for pain management. The CDC reported a decline in oxycodone prescriptions between 2011 and 2017, statistics that are consistent with our findings (2). While the increase in codeine prescriptions may explain the opioid prescription trends observed in our study, additional research is necessary to substantiate our reasoning. Furthermore, the 95th percentile of methadone was the only opioid to demonstrate an elevated rate in 2019 as compared with the estimated rate in 2011. The observed increase in methadone prescriptions may be a result of the drug's efficacy in treating pain and cost-effectiveness (25). To further elucidate the observed trend, efforts should be directed at stratifying opioid prescription distribution and use between 2011 and 2019.

Drug overdose deaths have not homogeneously impacted the U.S. Although death determination is an extremely complicated process and data should be interpreted cautiously because of methodological differences between states (26), the eastern U.S. has had higher rates of overdoses (27). Similarly, opioid prescriptions were not homogeneous. Several positive associations between opioid prescriptions were identified using Spearman correlations, suggesting that prescribing a specific opioid may increase the likelihood of adding another

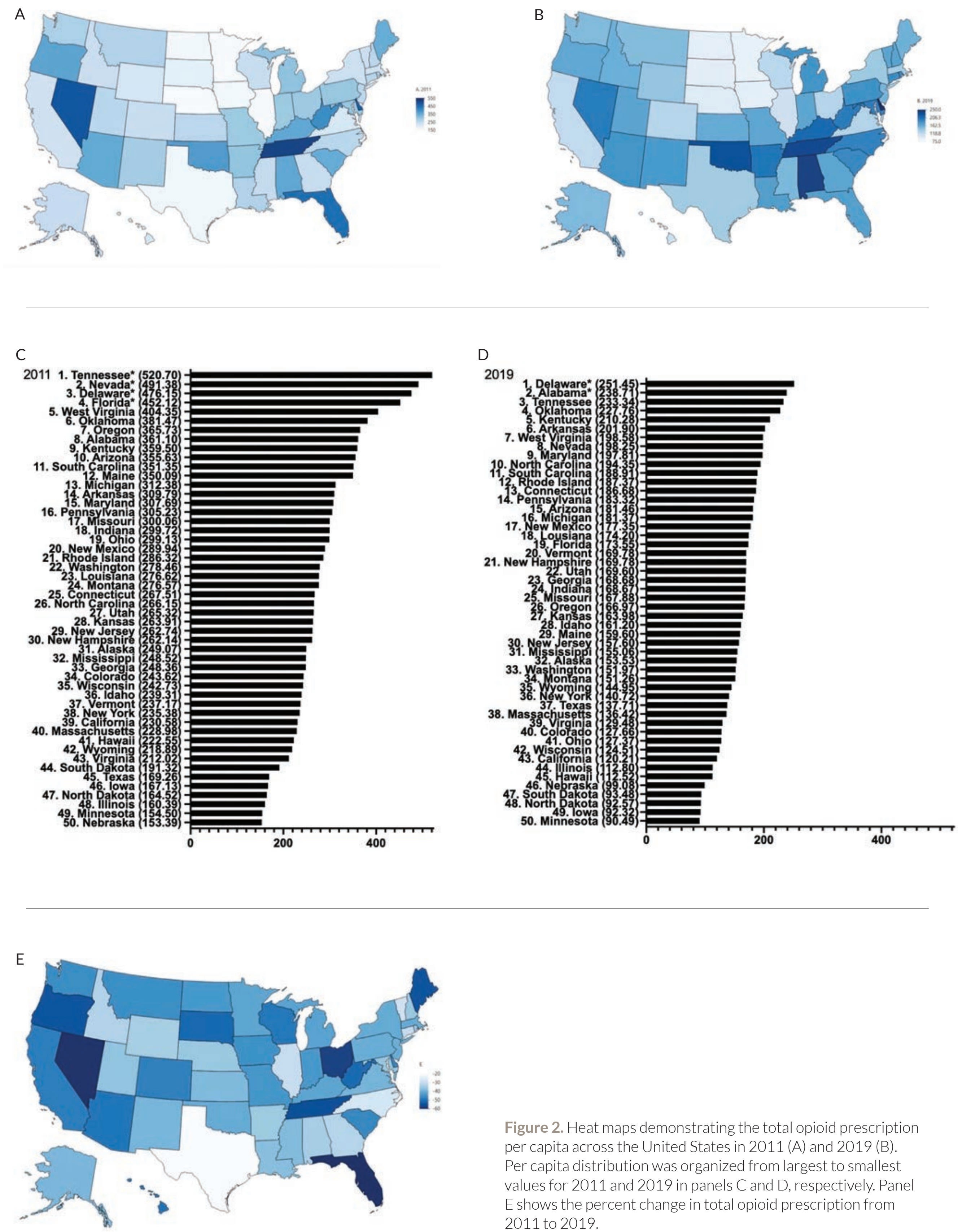


**Figure 2.** Heat maps demonstrating the total opioid prescription per capita across the United States in 2011 (A) and 2019 (B). Per capita distribution was organized from largest to smallest values for 2011 and 2019 in panels C and D, respectively. Panel E shows the percent change in total opioid prescription from 2011 to 2019.

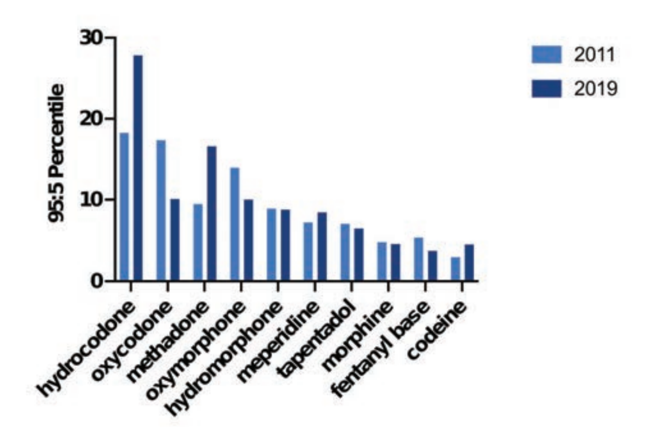


**Figure 3.** 95:5 percentile ratio for each of the prescription opioids analyzed.

opioid to the patient's pain management regimen. Interestingly, oxycodone was implicated in various of these associations in both 2011 and 2019. However, a specific reason for this finding remains unknown. This may be due to medical specialties having certain preferences for one opioid over another; for example, otolaryngologists commonly prescribe hydrocodone and oxycodone, while family medicine physicians tend to prescribe buprenorphine (28, 29, 30).

It is necessary to continue the battle against the opioid epidemic to eliminate opioid misuse, overdose, and deaths. While recent efforts may have significantly contributed to the observed decline in prescription opioids, additional strategies may be necessary to permanently remedy the issue. It has been speculated that this goal can be achieved by increasing patient awareness and education, implementing institutionalized prescription guidelines, and establishing patient-bedside standardized protocols focused on pain management (31). Furthermore, having individual states create their own legislative policies to combat the epidemic has led to varying outcomes and is perhaps not the path we should continue on any longer. This divisive solution could be remedied by creating a national PDMP system, updated in real time, which accounts for electronic prescriptions of all Schedule II and III opioids, patient diagnoses, overdose risk number calculated based on this history, and guidelines for alternative pain management to be explored with the patient (13). Furthermore, a nationwide mandate for the use of the CDC's Drug Overdose Surveillance and Epidemiology (DOSE) System alongside an increase in state funding for Enhanced State Opioid Overdose Surveillance (ESOOS) could prove effective (32, 33). Until that time comes, current potential solutions include individual states implementing limits to the high morphine equivalent daily dose prescription rate (22) and considering prescribing marijuana as an alternative for pain management (34). However, there is still room for improvement, and perhaps the U.S. could adopt and modify international guidelines like the UK to aid in curbing the epidemic further (35).

While we were able to successfully identify and isolate trends in opioid prescriptions between 2011 and 2019, this comprehensive database and our analysis has some caveats. We reported a decline in opioid prescriptions beginning in 2011 based on the distribution of the aforementioned opioids. However, other commonly prescribed opioids such as buprenorphine were not included in our analysis, and therefore may have influenced the peak year of opioid prescriptions. In addition, ARCOS data does not account for Schedule IV or V opioids (e.g., codeine and acetaminophen combination products) that could influence the total number of opioid prescriptions across the U.S. (13). Thus, future studies should analyze trends in opioid prescriptions by including information on these additional opioids collected from additional drug databases like PDMPs and electronic medical records. Moreover, racial, gender and socioeconomic disparities were not statistically accounted for in this study. However, the literature has demonstrated increased opioid use in female and Caucasian individuals (11, 36). Furthermore, current rates of opioid prescriptions are substantially increased in low-income white communities compared to low-income black communities, and black patients are less likely to be prescribed opioids than white patients (11, 37). Moreover, black patients who are prescribed opioids for chronic pain are tested more frequently for concomitant use of illicit drugs than white patients, which may reduce the risk of unintentional overdose for black patients due to drug interactions (38). These findings support the suggested propensity of low-income and racial disparities in opioid prescription rates. This may indicate a need to stratify the data based on these demographics to identify more specific trends in opioid prescriptions. Furthermore, given the extended period of comparison of opioid prescriptions, it is difficult to isolate even an association between implemented legislative amendments and the observed reduction in opioid prescriptions. To elucidate this relationship, future studies should be directed at examining trends in opioid prescriptions at specific periods based on legislative changes enacted since 2011 to determine their overall impact on the declining distribution. An economist might rightly argue that this descriptive study cannot differentiate between reduced demand for opioids by prescribers as well as patients versus reductions in supply imposed by the DEA's production quotas (Figure 1A) and subsequent shortages, particularly of parental formulations of fentanyl, hydromorphone, and morphine (39).

## Conclusion

Overall, we have demonstrated a pronounced decline in opioid prescription across the U.S. from 2011 to 2019, as well as sizeable and stable regional disparities in opioid distribution. We speculated that this decline may at least be due in part to legislative amendments implemented by various states and novel insurance policies, as well as the DEA opioid production quotas, to mitigate the opioid epidemic. While individual states have enacted legislative amendments they deemed necessary to combat the epidemic, further analysis regarding specific modifications and regulations may be necessary to illuminate the etiology behind the observed variation in the decline of opioid prescriptions across the U.S. Through these analyses, we may be able to identify additional strategies aimed at controlling the opioid epidemic and further increasing the rate of decline of prescription opioids.

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## Disclosures

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