

Methadone Distribution Trends from 2017–2018 Across the United States

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Abstract

Background: The primary objective of this study is to explore methadone distribution patterns between the years of 2017 and 2018 across the United States (U.S.). This study builds upon previous literature that has analyzed prior years of U.S. distribution patterns, and further outlines state specific methadone trends.

Methods: The Drug Enforcement Administration's Automation of Reports and Consolidated Orders System was used to acquire methadone distribution amounts (grams) and number of narcotic treatment programs (NTPs). State population estimates were obtained from the 2010 Census published by the U.S. Census Bureau, Population Division. Methadone distribution weights and number of NTPs were compared from 2017 to 2018.

Results: From 2017 to 2018, there was a national decrease in methadone production quota (6.00%), total distribution (6.34%), and methadone distribution for both opioid use disorder (OUD) and pain (2.77% and 20.14%, respectively). Distribution for pain management per 100K population decreased in every state, while considerable variation was seen across states in regard to distribution for OUD per 100K population. Analysis of percent change in the number of NTPs also showed broad variation across states.

Conclusion: Total U.S. methadone distribution, distribution for OUD, and distribution for pain management all decreased between the years 2017 and 2018. State-specific analysis revealed an overall decrease in methadone distribution for the use of pain management across all 50 U.S. states and change in distribution for OUD showed a majority of states are decreasing in this regard. These trends lead us to question whether methadone's therapeutic role as an analgesic and as a treatment for OUD has decreased. Further analysis of federal and state legislation, as well as comparisons with other OUD pharmacotherapy distribution trends, may help to explain the observed results.

Introduction

Opioids interact with stereospecific and saturable binding sites within the nervous system and other tissues where their actions alter the release of various neurotransmitters including acetylcholine, norepinephrine, substance P, and dopamine (1–3). By mimicking endogenous enkephalins and endorphins, opioids modulate neurotransmission to produce global analgesic effects dependent upon opioid binding

specificity and receptor saturability (1). Methadone, a synthetic opioid, is considered a full agonist of the μ -opioid receptor and is known to have a long half-life relative to other opioids (4). After being identified as a potent pharmacotherapy option for those suffering from opioid use disorder (OUD), methadone has been demonstrated to decrease illicit opioid use, decrease HIV-associated risk behavior and reduce drug-related criminal behaviors (5, 6). In addition to its use as a treatment for opioid substance use disorders, methadone has been used clinically in the management of significant, chronic pain; no significant difference in pain relief between morphine and methadone in cancer patients has been noted (4, 7). Consequently, methadone is currently classified as a schedule II-controlled substance in the United States (U.S.) and is Food and Drug Administration (FDA)-approved for the following uses: (1) detoxification treatment of opioid addiction; (2) pain management in patients nonresponsive to non-narcotic analgesics (4, 6, 7).

Despite methadone's clinical uses, current research has shown there is a positive association between distribution rate and methadone overdose death rate (8). Both methadone distribution and methadone-associated deaths in the U.S. increased between the years 2002 and 2006, an average of 25% and 22% per year, respectively (9). Following the years of increasing distribution and associated deaths, a steady decline in methadone distribution occurred between 2007 and 2013 and a significant decrease in methadone volume distribution occurred between 2015 and 2016 (1, 10). Despite published methadone distribution trends being clearly outlined for this earlier time frame, data on more recent trends and state-specific trends is currently lacking. With significant uses in opioid recovery and pain management, as well as a link between methadone and overdose deaths, further research into the distribution of methadone in the U.S. could serve to benefit both the individual and public health sector. This study utilized the United States' Drug Enforcement Administration's Automated Reports and Consolidated Ordering Systems (ARCOS) comprehensive database to evaluate changes in the distribution of methadone in recent years. The years 2017 and 2018 are the most recent, complete datasets published. Investigation of methadone distribution trends using ARCOS will allow a greater understanding of the most up-to-date pattern of use in treatment of OUD and recent geographic fluctuations of methadone use within the United States.

Methods

Data sources

Distributed by the U.S. Drug Enforcement Administration (DEA), methadone yearly U.S. production quotas were obtained from final adjusted aggregate production quotas for Schedule I and II controlled substances for 2017 and 2018 via the Federal Registrar. State population estimates were obtained from the 2010 Census published by the U.S. Census Bureau, Population Division, to normalize data between states. Data related to methadone distribution amount (in grams) was extracted from the DEA's Automated Reports and Consolidated Ordering System (ARCOS) yearly drug summary data reports for 2017 and 2018. This federal program, mandated by the 1970 Controlled Substances Act, is a comprehensive drug reporting system that tracks the distribution of controlled substances, in grams, to pharmacies, hospitals, clinical providers, and Narcotic Treatment Programs (NTPs), and has been used in previous pharmacological trend studies (8, 10, 11). Methadone distributed to NTPs was classified as treatment of OUD. Methadone distribution to non-NTP locations, e.g. hospitals and pharmacies, was considered to be for pain management. Procedures were approved by the Institutional Review Board from the University of New England and Geisinger.

Data analysis

The following analyses were completed: (1) U.S. total methadone distribution to NTPs for management of OUD and distribution of the drug to other clinical locations for pain management (e.g., hospitals, pharmacies, practitioners) was calculated and converted to kg for each year (2017 and 2018); (2) percent change of methadone distribution from 2017 to 2018 for OUD and pain management for each state per 100K population quotient; (3) percent change in number of methadone NTPs from 2017 to 2018 for each state per 100K population quotient; (4) number of NTPs in 2018 for each state per 100K population quotient. Data analysis and figures were completed with GraphPad Prism, version 8.4.2 and Microsoft Excel.

Results

Both DEA production quota and total methadone distribution amount decreased between 2017 and 2018, 6.00% and 6.34%, respectively. However, production quotas were markedly higher than U.S. total distribution amount for both years. Additionally, distribution of methadone for OUD decreased by 2.77%, while use for pain decreased by 20.14% (Figure 1). Figure 2 demonstrates variability across individual states regarding percent change in methadone distribution amount for OUD. These changes range from a 173.63% increase, seen in North Dakota, to a 15.18% decrease seen in Maine. Overall, the majority of states saw decreases in methadone distribution for OUD between the years 2017 and 2018 (Figure 2). In contrast to distribution for OUD, distribution of methadone for pain management decreased in all 50 states, as well as the District of Columbia. These decreases ranged from a 41.58% decrease in Mississippi to a 5.9% decrease in the state of New York (Figure 3).

The majority of states saw an increase in the number of methadone NTPs per 100K population. Iowa showed the

largest percent increase of 74.84%, while Minnesota showed the largest percent decrease of -17.11% (Figure 4). Additionally, analysis of the number of NTPs per 100K in 2018 alone, showed Rhode Island had the largest number of NTPs per 100K, which contrasts many other states that had less than 1 NTP per 100K (44 states). Additionally, all states with more than one NTP per 100K are states found within the Northeast region (RI, VT, DE, MD, CT, MA). Wyoming was notably the only state without an NTP in 2018 (Figure 5). From a national standpoint, the number of methadone buyers for NTPs increased from 1,483 in 2017 to 1,572 in 2018, a 6.00% change.

Conclusion

From 2017 to 2018, the ARCOS database demonstrated an overall decrease in the total weight of methadone distributed in the United States. Every state demonstrated a decrease in percent change of methadone use for pain management, possibly suggesting a loss of demand for the drug's use as an analgesic. This is consistent with a recent ARCOS-based publication that shows decreases in the distribution of other opioids, including oxycodone, hydrocodone, and morphine, from 2013 to 2016 (10). Additionally, when comparing values on a national scale, an overall decrease in methadone distribution for OUD was documented. Although a minority of states (18) demonstrated a percent increase in methadone use for OUD, an overwhelming 31 states, plus the District of Columbia, demonstrated a percent decrease. This is excluding Wyoming, which had no methadone NTPs as of 2018. Interestingly, this national decrease in methadone use for OUD was accompanied by an increase of NTPs buyers in the United States. Many states in the Northeast that had the largest number of NTPs per 100K population (RI, PA, VT, MD, CT, MA) have shown decreases in the amount of distribution of methadone. Despite many states seeing decreases in methadone distribution during this time frame, there was a 173.63% increase in methadone distribution per 100K in North Dakota, however, there was no increase in the number of NTPs in this state. This may suggest an increasing demand

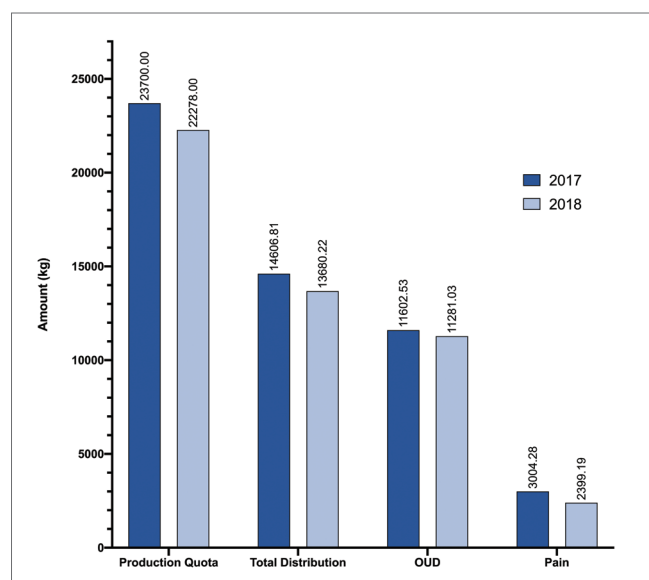


Figure 1: United States methadone distribution amounts and production quotas in kilograms for 2017 and 2018.

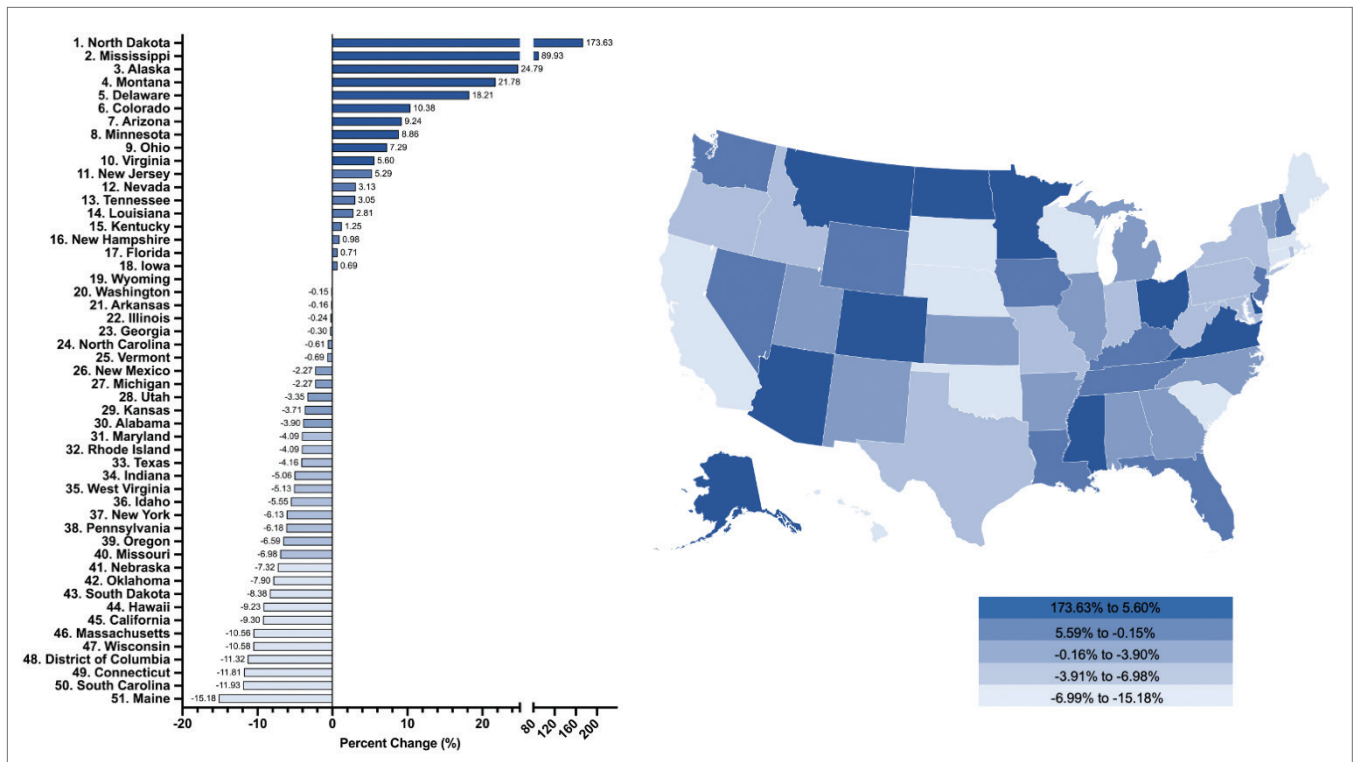


Figure 2: Percent change in methadone NTP distribution amount per 100K population from 2017 to 2018. States were ranked according to percent change and subsequently placed into groups of 10 for representation on the heat map.

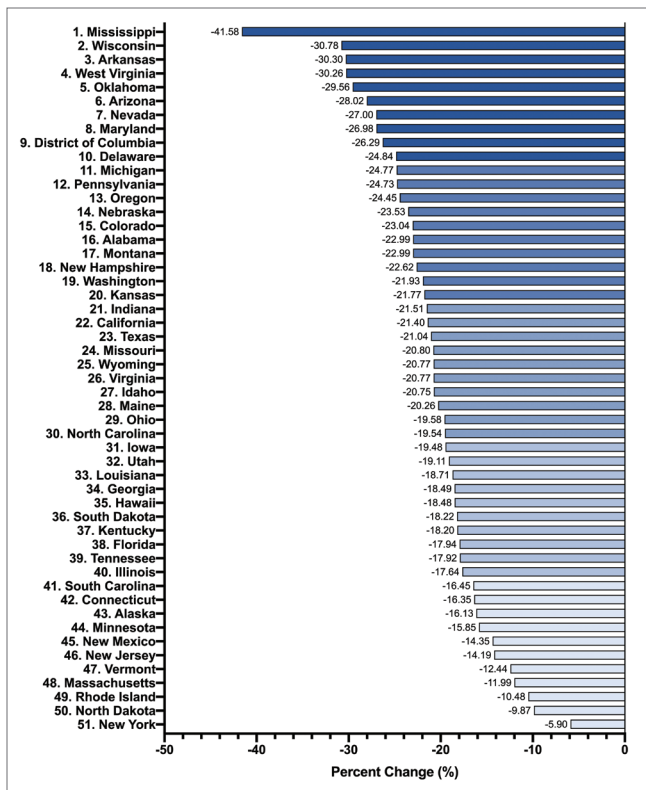


Figure 3: Percent change in methadone pain distribution amount per 100K population from 2017 to 2018.

within the state of North Dakota and therefore, a possible need for additional NTPs. Further exploration of state specific legislation and policy may help to explain these findings.

Moreover, total production quota for methadone decreased from 2017 through 2018. Despite this decrease, methadone production quotas remained noticeably higher than the total U.S. distribution for both 2017 and 2018. It may be possible that methadone produced in the U.S. is being exported to other countries; however, this would not explain the decrease in distribution of methadone within the U.S. These observed trends raise the question, is methadone becoming a less popular choice for treatment of opioid use disorder? When compared to an alternative OUD medication, buprenorphine (partial μ -agonist), methadone (full μ -agonist) demonstrates increased risk of death during treatment induction but is more successful at patient retention (12). Although difficult to weigh the risks and benefits between these two treatments, it must be noted that methadone use by weight from 2017 to 2018 dropped by 6.34%, while buprenorphine distribution by weight increased by 13.26% according to ARCOS data. Whether these differences are due to perceived benefits of buprenorphine, possible price differences or restricted access due to varying state legislature is unknown and of interest to explore in further research. Additionally, in 2016, the Comprehensive Addiction and Recovery Act was put into effect, which expanded the ability to prescribe buprenorphine to qualified nurse practitioners and physician assistants and also increased the maximum number of patients that these providers can treat with buprenorphine, or other schedule III, IV, or V narcotic for the treatment of OUD, from 100 to 275 patients (13). This federal legislation change may help to explain the opposing

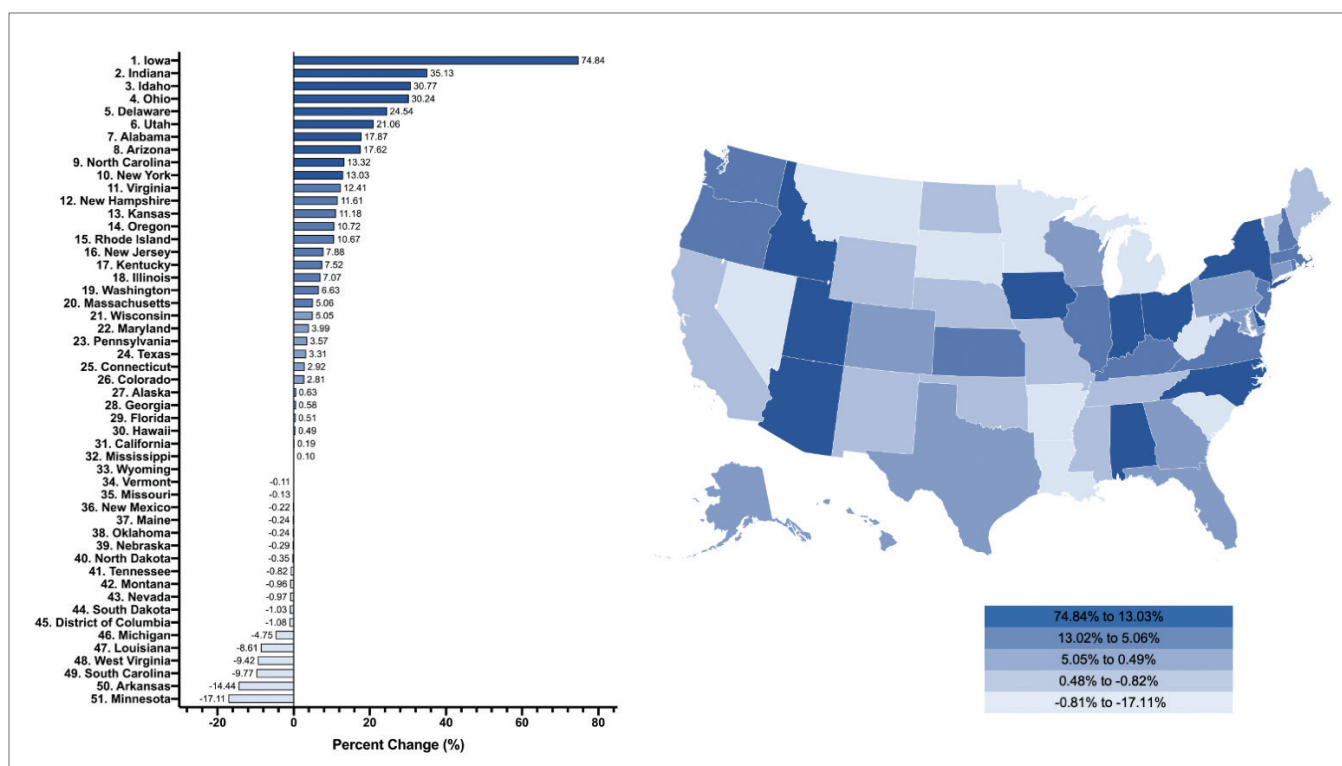


Figure 4: Percent change in number of NTPs per 100K population from 2017 to 2018. States were ranked according to percent change and subsequently placed into groups of 10 for representation on the heat map.

distribution trends of methadone and buprenorphine and warrants further exploration.

In an effort to further analyze methadone trends across the U.S., incorporation of the 2019 methadone data set from ARCOS will be merged with this data set upon its publication. A more in depth look into federal and specific state legislation, as well as any recent changes to these laws, may help to explain the different trends uncovered. Furthermore, comparison of ARCOS methadone distribution trends to Medicaid enrollee information in matching years is also desired to assess any correlations. In the future, analysis of opioid use per state could be compared to these results to explore a possible correlation with the distribution patterns of methadone within each state. Zip codes provided by the ARCOS database can also be utilized for a county analysis within each state. Particularly, a state-specific approach of analysis for Pennsylvania is of relevant interest as Geisinger Commonwealth School of Medicine's place of residence.

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Disclosures

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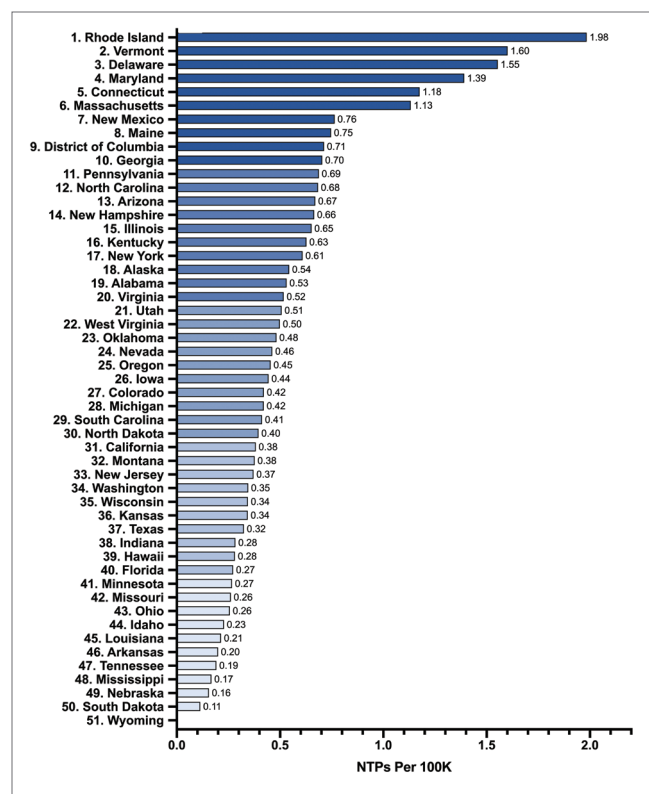


Figure 5: Number of methadone NTPs per 100K population in 2018.

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