

Dose and Duration of Prescriptions for Opioids in Mississippi, 2012 and 2014



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Introduction: Long-term opioid therapy has been associated with adverse health outcomes including drug abuse, addiction, overdoses, myocardial infarction, fractures, sexual dysfunction, and motor vehicle accidents.¹ Some of these illnesses, such as drug abuse and addiction, are dose dependent.² To determine the frequency distribution of high-dose and long-term opioid prescriptions in Mississippi, we analyzed prescription monitoring program data (PMP). We quantified high-dose prescriptions using morphine milligram equivalents (MME), a measure that converts opioids of various strengths into a standard value. The duration of treatment was assessed by the days of supply recorded for each prescription. Our study examined Mississippi residents and opioids prescribed as pain relievers only.

Dose of Opioid Prescriptions, 2014: The Centers for Disease Control and Prevention (CDC) recommends that clinicians carefully consider all risks and benefits when prescribing a daily opioid dosage of ≥ 50 MME and avoid prescribing a daily dosage of ≥ 90 MME.³ The reason for this clinical guidance is the increased risk for overdose and other adverse effects caused by daily dosage of ≥ 50 MME. Based on these guidelines, we stratified opioid prescriptions into three groups:

1. Opioid prescriptions for < 50 MME
2. Opioid prescriptions for ≥ 50 but < 90 MME
3. Opioid prescriptions for ≥ 90 MME (high-dose)

The majority of prescriptions (78.4%) were for < 50 MME per day (Figure 1). Prescriptions with a daily dosage of > 50 MME totaled 725,225 (21.6%), of which 14.3% were for prescriptions of ≥ 50 but < 90 MME per day and 7.3% were for high dose prescriptions of ≥ 90 MME per day.

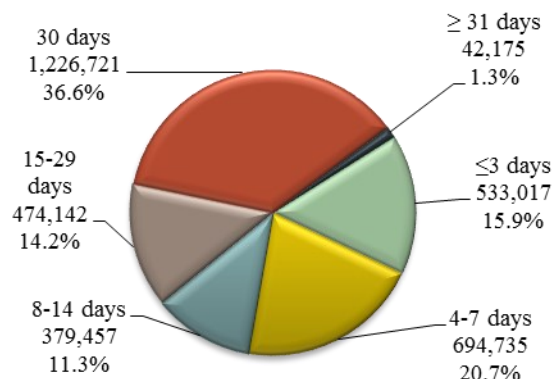
Length of Opioid Prescriptions, 2014: In addition to dosage, the CDC also highlights the importance of treatment duration. These guidelines recommend opioid treatment for acute pain not exceeding 3 days. The recommendations also suggest that chronic pain management requiring over 7 days of opioid treatment should be done only after thorough clinical evaluation and risk assessment. Based on these CDC guidelines, we defined prescriptions for durations of ≤ 7 days as a short-term opioid treatment.

Our findings revealed that only 36.6% of all prescriptions were short-term: 15.9% were for ≤ 3 days and 20.7% were for the range of 4-7 days. Nearly two-thirds (63.4%) of all prescriptions were for more than a week and over one third (36.6%) had a duration of 30 days (Figure 2).

Figure 1. Morphine Milligram Equivalents: Daily Dosage per Prescription, MS, 2014



Figure 2. Prescription Duration, MS, 2014



Changes from 2012 to 2014: To assess the changing dynamics of opioid consumption and prescribing practices, we compared prescription opioid numbers and rates between 2012 and 2014. Prescriptions were stratified by daily dosage of MME as well as prescription duration. Table 1 presents number of prescriptions, MME, and days of supply and Figure 3 displays the overall prescription rates and the rates of the different prescription subcategories.

PRESCRIPTION OPIOIDS	2012	2014	Change (%) 2012 and 2014
Prescriptions dispensed	3,375,323	3,356,455	-0.6%
Prescriptions analyzed for this report*	3,373,265	3,350,247	-0.7%
MME			
Total MME	2,221,339,404	2,336,236,612	5.2%
Average MME per Rx	658.5	698.2	6.0%
Average daily MME per Rx	41.2	41.1	-0.2%
Days of supply			
Total days of supply	54,646,214	56,807,230	4.0%
Prescriptions for < 30 days	2,211,680	2,081,351	-5.9%
Prescriptions for ≥ 30days	1,161,585	1,268,896	9.2%

*Some prescriptions were excluded from the analyses. The exclusion criteria are described in the "Data Analysis" section on page 4.

Overall Opioid Prescriptions: The number of opioid prescriptions and overall prescription rates decreased marginally from 2012 to 2014 (Table 1 and Figure 3).

MME and Days of Supply - Totals: Unlike the number of opioid prescriptions, the total MME increased by 5.2%. Similarly, the total number of days of supply expanded by 4.0% from 54,646,214 in 2012 to 56,807,230 in 2014, an increase of more than 2 million days of opioid supply (Figure 4 and Figure 5).

Morphine Milligram Equivalents - Averages:

- **Average MME per Rx:** The average MME per prescription grew by 5.9% from 658.5 MME per prescriptions in 2012 to 698.2 MME per prescription in 2014 (Table 1).
- **Average Daily MME per Rx:** Because the duration of prescription increased, the average daily prescription contained a marginally lower dosage of 41.1 MME in 2014 as compared to 41.2 MME in 2012. Similarly, the rates of high-dose prescriptions (≥ 90 MME) demonstrated only a slight upward movement from 8.0 in 2012 to 8.2 per 100 residents in 2014 despite the overall significant increase in the MME totals (Figure 3).

Prescription Duration: The increase in total days of supply was attributable to two opposing trends. First, the number of short-term prescriptions declined. Second, the number of 30-day prescriptions climbed by 10.1% (Table 2). This resulted in a growth in the rates of opioid prescriptions issued for ≥ 30 days: Such prescriptions increased from 38.9 in 2012 to 42.4 opioid prescriptions per 100 persons in 2014 (Figure 3).

Figure 3. Prescription Rates per 100 Residents by Type of Prescription, MS, 2012 and 2014

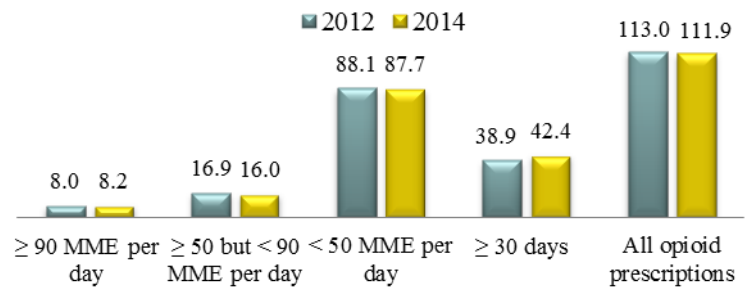


Figure 4. Total Morphine Milligram Equivalents, MS, 2012 and 2014



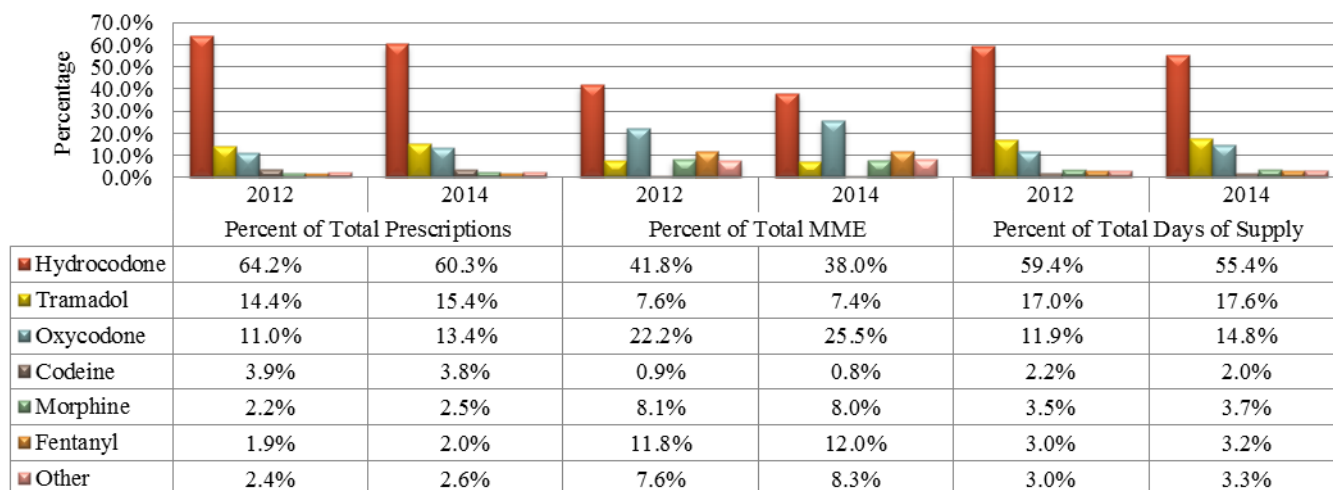
Figure 5. Total Days of Supply, MS, 2012 and 2014



Days of Supply Categories	2012 Number	2014 Number	Difference 2012 and 2014	Change (%) 2012 and 2014
≤3 days	557,207	533,017	-24,190	-4.3%
4-7 days	739,014	694,735	-44,279	-6.0%
8-14 days	427,310	379,457	-47,853	-11.2%
15-29 days	488,149	474,142	-14,007	-2.9%
30 days	1,114,138	1,226,721	112,583	10.1%
≥ 31 days	47,447	42,175	-5,272	-11.1%

Major Opioids, 2014: The top three prescribed opioids in 2014, hydrocodone, tramadol, and oxycodone, accounted for 89.2% of all opioid prescriptions. Although nearly two-thirds (60.3%) of all opioid prescriptions were for hydrocodone, this drug accounted for only 38.0% of the total MME and for 55.4% of the total supply days during 2014 in Mississippi (Figure 6). Oxycodone, an opioid 1.5 times more potent than hydrocodone, accounted for 13.4% of all opioid prescriptions. Prescription oxycodone, however, was responsible for 25.5% of the total MME and for 14.8% of the total days of supply in 2014. Presented in figure 6 are also the percentages of total prescriptions, MME, and days of supply for all six major opioids dispensed in Mississippi during 2012 and 2014.

Figure 6. Major Opioids: Percentages of Total Prescriptions, Total MME, and Total Days of Supply, MS, 2012 and 2014



Oxycodone: While the number of prescriptions for hydrocodone declined by 6.7% (144,661 prescriptions), the number of prescriptions for oxycodone increased by 21.3% (78,928 prescriptions) from 2012 to 2014. In addition, our analysis uncovered that the increase in the overall MME and days of supply between 2012 and 2014 was due, mainly, to a surge in the number of oxycodone prescriptions (Table 3).

- The total MME increased by 114,897,208 in 2014 compared to 2012. Oxycodone prescriptions accounted for 90.2% (103,648,693) of this increase.
- Similarly, oxycodone prescriptions were responsible for 86.9% (1,878,284) of the increase in the total days of supply (2,161,016) during the study period (Table 2).

The reasons for such a spike in oxycodone prescriptions between 2012 and 2014 are unclear. It is important to note, however, that oxycodone is a potent and popular opioid for recreational use. During 2014, oxycodone was the third most frequent substance recorded in drug overdose deaths nationwide with 5,856 (12.4%) of all deaths, preceded only by the illicit drugs heroin and cocaine.⁴

Table 3. Number of Prescriptions, Morphine Milligram Equivalents (MME), and Days of Supply by Major Opioids, MS, 2012 and 2014

Drug	Total Number of Prescriptions			Total MME			Total Days of Supply		
	2012	2014	Difference 2012 and 2014	2012	2014	Difference 2012 and 2014	2012	2014	Difference 2012 and 2014
Hydrocodone	2,165,252	2,020,591	-144,661	928,040,325	888,010,811	-40,029,514	32,444,879	31,450,209	-994,670
Tramadol	485,907	517,318	31,411	169,197,192	173,152,018	3,954,826	9,273,852	10,026,173	752,321
Oxycodone	370,217	449,145	78,928	492,564,759	596,213,452	103,648,693	6,508,235	8,386,519	1,878,284
Codeine	132,452	125,979	-6,473	19,780,871	18,491,056	-1,289,815	1,178,939	1,112,857	-66,082
Morphine	75,176	82,824	7,648	180,937,100	187,303,199	6,366,099	1,912,494	2,079,596	167,102
Fentanyl	62,442	68,655	6,213	261,510,391	280,445,801	18,935,410	1,667,527	1,822,489	154,962
Other	81,819	85,735	3,916	169,308,766	192,620,275	23,311,509	1,660,288	1,929,387	269,099
All	3,373,265	3,350,247	-23,018	2,221,339,404	2,336,236,612	114,897,208	54,646,214	56,807,230	2,161,016

Conclusions: The overall opioid prescription rates in Mississippi remained almost the same in 2014 compared to 2012. By contrast, morphine milligram equivalents and days of supply rose during the same period. Such an increase occurred despite substantial evidence in support of numerous adverse effects associated with high-dose and long-term opioid consumption. The planned ongoing evaluation of more recent PMP data will monitor these trends as there has been a mounting public health response to the opioid epidemic and increasing national and state media coverage of this crisis.⁵

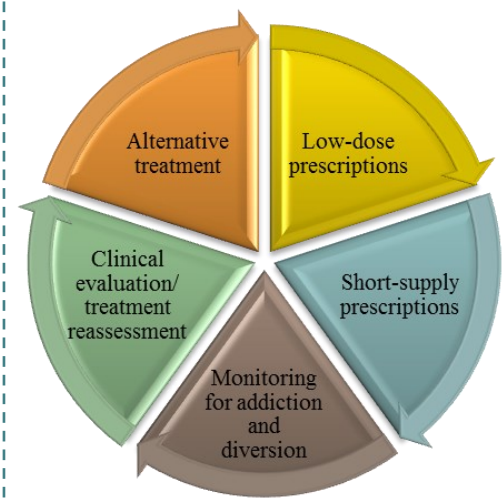
For example, research has demonstrated that a daily dosage of 50 to 99 MME increases opioid overdose risk by 3.7-fold and a daily dosage of 100 MME or more increases it by 8.9-fold.⁶ Our findings identified that one fifth of all opioid prescriptions dispensed in Mississippi during 2014 had a daily dosage greater than 50 MME per day. In other words, nearly three-quarters of a million prescriptions carried an elevated risk for opioid-related mortality.

Research also has shown that the length of the initial episode of opioid treatment is an important determinant of chronic opioid use. A recent CDC study estimates that 13.5% of all patients with an initial opioid treatment of ≥ 8 days continue to use opioids a year later.⁷ Finally, the effectiveness of long-term opioid therapy for chronic non-cancer-related pain has been questioned because of weak evidence.⁸ According to a 2018 study published in the *Journal of the American Medical Association*, opioid treatments for moderate to severe chronic non-malignant pain are not more effective than non-opioid treatment options.⁹ Despite associated medical harms and uncertain clinical effectiveness, the number of prescriptions for 30 days or longer increased in Mississippi between 2012 and 2014.

Public Health Implications: Our study demonstrates the importance of a comprehensive evaluation of prescribing trends. In addition to prescription numbers, such an approach measures the strength and length of opioid treatment, two important risk factors for opioid-related harms. While our study determined an escalation in dose and duration of opioid prescriptions between 2012 and 2014, further investigation is needed to establish the driving forces behind such prescribing practices. Empirical research, however, has shown that opioid consumption could increase due to phenomena such as the development of drug tolerance, physical dependence, psychological dependence (addiction), and drug diversion.¹⁰

The CDC has built a resourceful website on clinical guidelines for opioid prescribing, dosage calculations, non-opioid treatment options, assessing benefits and harms of opioid therapy, and pharmacists' educational tools. To access the short but informative CDC brochures, visit: <https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html>. To learn more about the Mississippi Prescription Monitoring Program data, visit: <http://www.mbp.ms.gov/Pages/Prescription-Monitoring.aspx>.

Figure 7. Prescription Opioid Misuse: The Clinical Prevention Path



Data Analysis: We applied the following CDC algorithm for calculating MME per day: Strength per unit x (quantity/days of supply) x MME conversion factor.¹² We excluded records with missing values for strength and days of supply as well as records with quantity $\geq 10,000$ and days of supply > 360 days.

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