THE MISSISSIPPI OPIOID EPIDEMIC PROJECT

2016 Update on Dose and Duration of Prescriptions for Opioids in Mississippi, Rates and Trends

MISSISSIPPI STATE DEPARTMENT OF HEALTH

Epidemiological Report
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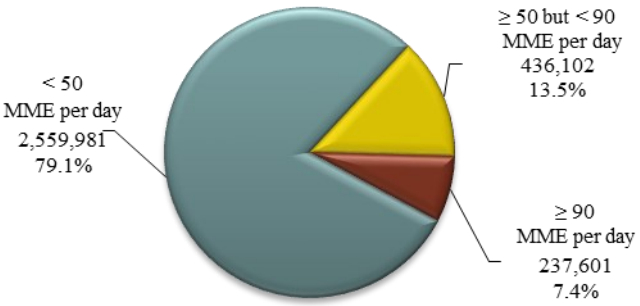
Introduction: Long-term opioid therapy has been associated with adverse health outcomes including drug abuse, addiction, overdoses, myocardial infarction, fractures, sexual dysfunction, and motor vehicle accidents.[1] Some of these illnesses, such as drug abuse and addiction, are dose dependent.[2] To 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, 2016: 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)

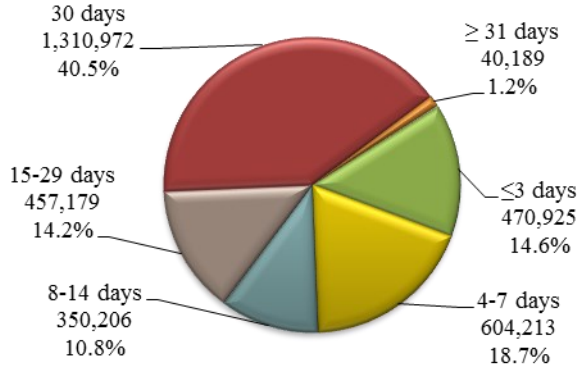
The majority of prescriptions (79.1%) were for < 50 MME per day (Figure 1). Prescriptions with a daily dosage of > 50 MME totaled 673,703 (20.9%), of which 13.5% were for prescriptions of ≥ 50 but < 90 MME per day and 7.4% were for high-dose prescriptions of ≥ 90 MME per day.

Figure 1. Morphine Milligram Equivalents: Daily Dosage per Prescription in MS, 2016



Length of Opioid Prescriptions, 2016: 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 33.3% of all prescriptions were short-term: 14.6% were for ≤ 3 days and 18.7% were for the range of 4 -7 days. Nearly two-thirds (66.7%) of all opioid prescriptions were for more than a week and all over one third (40.5%) had a duration of 30 days (Figure 2).

Figure 2. Prescription Duration in MS, 2016



Changes from 2012 to 2016: To assess the changing dynamics of opioid consumption and prescribing practices, we compared prescription opioid numbers and rates between 2012 and 2016. 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.

Table 1. Number of Prescriptions (Rx), Morphine Milligram Equivalents (MME), and Days of Supply, MS, 2012 and 2016

PRESCRIPTION OPIOIDS	2012	2016	Change (%) 2012 and 2016
Prescriptions dispensed	3,375,323	3,238,334	-4.1%
Prescriptions analyzed for this report*	3,373,334	3,233,684	-4.1%
MME			
Total MME	2,222,314,716	2,312,774,965	4.1%
Average MME per Rx	658.8	715.2	8.6%
Average daily MME per Rx	41.3	40.4	-2.2%
Days of supply			
Total days of supply	54,647,583	57,986,245	6.1%
Prescriptions for < 30 days	2,211,714	1,882,523	-14.9%
Prescriptions for ≥ 30days	1,161,620	1,351,161	16.3%

*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 opioid prescription rates decreased from 2012 to 2016 (Table 1 and Figure 3).

MME and Days of Supply - Totals: Unlike the number of opioid prescriptions, the total MME increased by 4.1%. Similarly, the total number of days of supply expanded by 6.1% from 54,647,583 in 2012 to 57,986,245 in 2016, an increase of more than 3.3 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 8.6%, from 658.8 MME per prescriptions in 2012 to 715.2 MME per prescription in 2016 (Table 1).
- **Average Daily MME per Rx:** Because the duration of prescription increased, the average daily prescription contained a marginally lower dosage of 40.4 MME in 2016 as compared to 41.3 MME in 2012. Similarly, the rates of high-dose prescriptions (≥ 90 MME) demonstrated only a slight downward movement from 8.0 in 2012 to 7.9 per 100 residents in 2016 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 17.7% (Table 2). This resulted in a growth in the rates of opioid prescriptions issued for ≥ 30 days: Such prescriptions increased from 34.4% in 2012 to 41.8% opioid prescriptions per 100 persons in 2016 (Figure 3).

Figure 3. Prescription Rates per 100 Residents by Type of Prescription in MS, 2012-2016

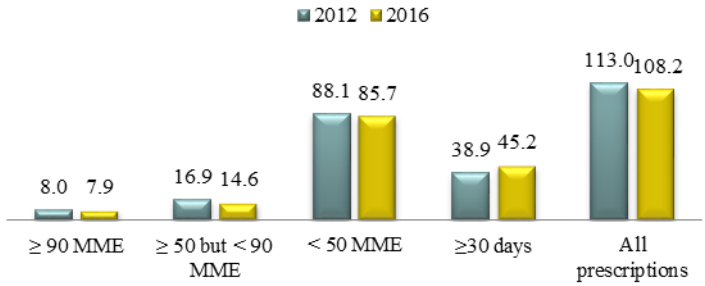


Figure 4. Opioid Prescriptions, Total Morphine Milligram Equivalents in MS, 2012-2016

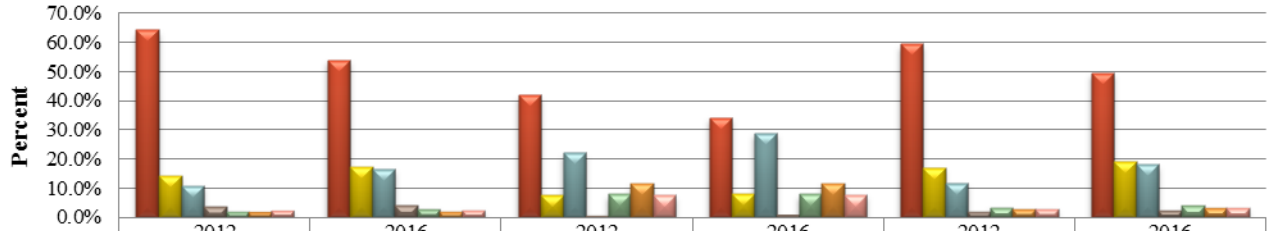
Figure 5. Opioid Prescriptions, Total Days of Supply in MS, 2012-2016

Table 2. Prescriptions by Days of Supply, MS, 2012 and 2016

Days of Supply Categories	2012 Number	2016 Number	Difference 2012 and 2014	Change (%) 2012 and 2014
≤3 days	557,224	470,925	-86,299	-15.5
4-7 days	739,021	604,213	-134,808	-18.2
8-14 days	427,310	350,206	-77,104	-18.0
15-29 days	488,159	457,179	-30,980	-6.3
30 days	1,114,173	1,310,972	196,799	17.7
≥ 31 days	47,447	40,189	-7,258	-15.3

Major Opioids, 2016: The top three prescribed opioids in 2016, hydrocodone, tramadol, and oxycodone, accounted for 87.9% of all opioid prescriptions. Although more than half (54.0%) of all opioid prescriptions were for hydrocodone, this drug accounted for only 34.3% of the total MME and for 49.5% of the total supply days during 2016 in Mississippi (Figure 6). Oxycodone, an opioid 1.5 times more potent than hydrocodone, accounted for 16.7% of all opioid prescriptions. Prescription oxycodone, however, was responsible for 28.9% of the total MME and for 18.1% of the total days of supply in 2016. 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 2016.

Figure 6. Major Opioids: Percent of Total Presriptions, Total MME, and Total Days of Supply in MS, 2012 and 2016



	2012	2016	2012	2016	2012	2016
	Percent of Total Prescriptions		Percent of Total MME		Percent of Total Days of Supply	
Hydrocodone	64.2%	54.0%	41.8%	34.3%	59.4%	49.5%
Tramadol	14.4%	17.2%	7.6%	8.2%	17.0%	19.3%
Oxycodone	11.0%	16.7%	22.2%	28.9%	11.9%	18.1%
Codeine	3.9%	4.4%	0.9%	1.1%	2.2%	2.5%
Morphine	2.2%	2.9%	8.1%	8.0%	3.5%	4.0%
Fentanyl	1.9%	2.2%	11.8%	11.7%	3.0%	3.3%
Other	2.4%	2.6%	7.6%	7.8%	3.0%	3.3%

Major Opioids, 2012-2016: The overall decline in the number of prescriptions was attributable to a decrease in the number of hydrocodone prescriptions. All other major opioids exhibited an uptrend. While the number of prescriptions for hydrocodone declined by 19.4% (419,507 prescriptions), the number of oxycodone prescriptions increased by 46.2% (70,341 prescriptions). In addition, our analysis uncovered that the increase in the overall MME and days of supply between 2012 and 2016 was due, mainly, to a surge in the number of oxycodone prescriptions. As shown in Table 3, oxycodone prescriptions had the highest absolute increase of 176,581,792 MME among all prescription opioids. Similarly, oxycodone prescriptions had the highest absolute increase in the total days of supply, increasing by nearly 4 million days in 2016 compared to 2012. In other words, the percent increase in the totals of MME and days of supply for oxycodone prescriptions was 35.8% and 61.4%, respectively. The reasons for such a spike in oxycodone prescriptions 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] Tramadol, one of the opioids with low potency, had the second highest increase in days of supply nearing a surplus of two million days in 2012 compared to 2016.

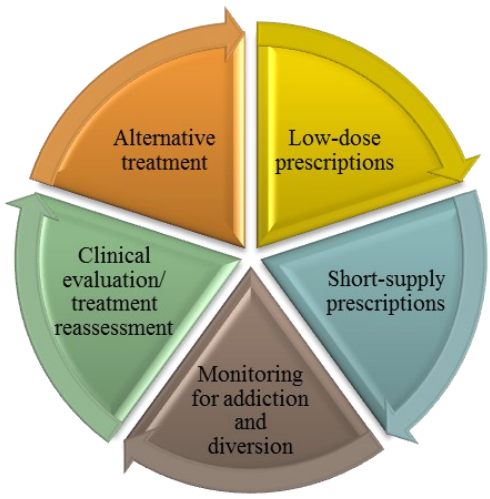
Table 3. Number of Prescriptions, Morphine Milligram Equivalents (MME), and Days of Supply by Major Opioids, MS, 2012- 2016

Drug	Total Number of Prescriptions			Total MME			Total Days of Supply		
	2012	2016	Difference 2012 and 2016	2012	2016	Difference 2012 and 2016	2012	2016	Difference 2012 and 2016
Hydrocodone	2,165,252	1,745,745	-419,507	928,040,325	792,424,747	-135,615,578	32,444,879	28,712,413	-3,732,466
Tramadol	485,907	556,248	70,341	169,197,192	188,366,632	19,169,440	9,273,852	11,201,669	1,927,817
Oxycodone	370,217	541,298	171,081	492,564,759	669,146,551	176,581,792	6,508,235	10,502,481	3,994,246
Codeine	132,452	143,110	10,658	19,780,871	24,035,645	4,254,774	1,178,939	1,454,711	275,772
Morphine	75,176	93,316	18,140	180,937,100	186,001,377	5,064,277	1,912,494	2,312,285	399,791
Fentanyl	62,511	71,410	8,899	262,485,703	271,482,192	8,996,489	1,668,896	1,894,022	225,126
Other	81,819	82,557	738	169,308,766	181,317,821	12,009,055	1,660,288	1,908,664	248,376
All	3,373,334	3,233,684	-139,650	2,222,314,716	2,312,774,965	90,460,249	54,647,583	57,986,245	3,338,662

Conclusions: The overall opioid prescription rates in Mississippi declined in 2016 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 increased in Mississippi between 2012 and 2016.

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 2016, 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.[11] We excluded records with missing values for strength and days of supply as well as records with quantity ≥ 10,000 and days of supply > 365 days.

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