

TRANSIENT OPIOID USE AND SHORT-TERM ACUTE COPD EXACERBATIONS IN MS MEDICAID

BACKGROUND

Chronic obstructive pulmonary disease (COPD) impacts over 15 million Americans annually and is among the leading causes of death in the United States.¹ COPD patients are prone to repeated exacerbations resulting in acute worsening of respiratory symptoms leading to increased mortality, reduced quality of life and increased healthcare utilization costs.^{2,3,4,5,6} Many factors such as smoking, infection, poor medication adherence and other environmental factors are known to increase the risk of COPD exacerbations.^{7,8,9} The use of narcotic analgesics or opioids is also a factor associated with increased risk of COPD exacerbation.¹⁰ Previous research into the association between opioid use and COPD exacerbations has been limited to periods of historical use ranging from 30 to 180 days. There is little research examining the risk of COPD exacerbation and short-term opioid exposure duration. The objective of this study is to examine the association of transient opioid use and acute respiratory exacerbations among adults with COPD enrolled in the Mississippi Division of Medicaid (DOM).

METHODS

MS-DUR recently completed a special study to examine the impact of opioid use among beneficiaries with COPD. This study utilized a case-crossover design to examine the association between transient opioid use and acute COPD exacerbations with the DOM's claims data from 2013 to 2017. The use of a case-crossover design helps evaluate the impact of transient risk factors on abrupt outcomes with each subject serving as their own control. This means that each

¹ National Center for Chronic Disease Prevention and Health Promotion. Chronic Obstructive Pulmonary Disease. June 5, 2018. <https://www.cdc.gov/copd/maps/index.htm>. Accessed February 1, 2019.

² Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. *The Lancet*. 2007; 370(9589):786-796.

³ National Heart, Lung, and Blood Institute. Morbidity and Mortality: 2012 Chart Book on Cardiovascular, Lung, and Blood Diseases. 2012. Available: http://www.nhlbi.nih.gov/files/docs/research/2012_ChartBook_508.pdf, 2013.

⁴ Burt L, Corbridge S. COPD exacerbations. *The American Journal of Nursing*, 2013; 113(2): p. 34-43.

⁵ Shah T, Press VG, Huisingh-Scheetz M, White SR. COPD Readmissions: Addressing COPD in the Era of Value-based Health Care. *Chest*, 2016; 150(4): p. 916-926.

⁶ Seemungal TA, Donaldson GC, Paul EA, et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*. 1998; 157(5):1418-1422

⁷ Pavord ID, Jones PW, Burgel PR, Rabe KF. Exacerbations of COPD. *International Journal of Chronic Obstructive Pulmonary Disease*. 2016;11(Spec Iss):21.

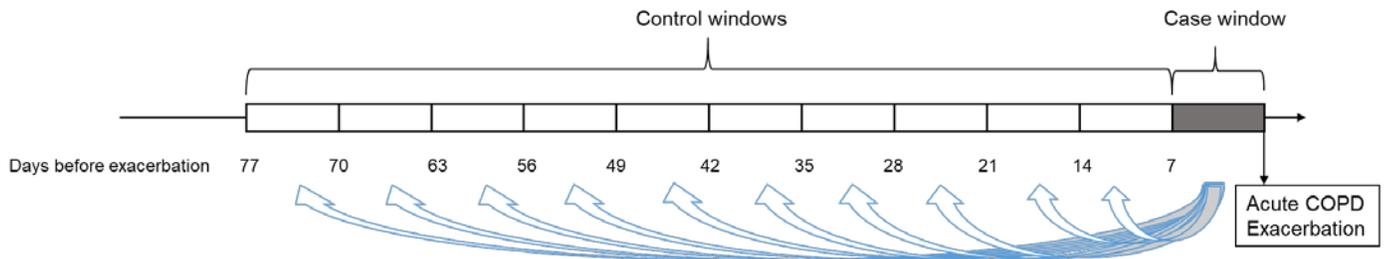
⁸ Seemungal TA, Hurst JR, Wedzicha JA. Exacerbation rate, health status and mortality in COPD—a review of potential interventions. *International Journal of Chronic Obstructive Pulmonary Disease*. 2009; 4: 203.

⁹ Halpin DM, Miravittles M, Metzendorf N, Celli B. Impact and prevention of severe exacerbations of COPD: a review of the evidence. *International Journal of Chronic Obstructive Pulmonary Disease*. 2017; 12:2891.

¹⁰ Samp JC, Joo MJ, Schumock GT, et al. Predicting Acute Exacerbations in Chronic Obstructive Pulmonary Disease. *Journal of Managed Care & Specialty Pharmacy*. 2018; 24(3): 265-279.

subject's short-term exposure just before an event of interest is compared with their exposure within the one or more control periods which are more remote from the case event.^{11,12} In this study opioid use within a 7-day case window immediately before each COPD exacerbation was compared to the same individual's opioid use in ten 7-day control windows. These successive 70 days before the case window are shown in Figure 1. A statistically significant result would represent transient exposure of opioid in 7 days increases the risk of acute COPD exacerbation.

Figure 1 Conceptual Framework of the Study Design



Both 2018 medical and pharmacy claims were used to determine the number of currently enrolled beneficiaries with COPD and any associated use of opioids during that year. This analysis provides data on the number of Medicaid beneficiaries diagnosed with COPD and potential opioid use impact on this disease in 2018.

¹¹ Maclure M, Mittleman AM. Should we use a case-crossover design? *Annual review of public health*. 2000;21(1):193-221.

¹² Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *American journal of epidemiology*. 1991; 133(2): 144-153.

RESULTS

A total of 1,354 Medicaid beneficiaries and 1,972 COPD exacerbation events met the study inclusion criteria.

- 62.3% of the COPD exacerbations had an opioid prescription claim during the seven-day period preceding the occurrence.
- Transient opioid exposure was found to be associated with an 80.8% increase in the odds of an acute respiratory exacerbation (Table 1).
- When opioid exposure was measured as a continuous variable, each 25mg increase in MEDD was found to be associated with an 11.2% increase in the odds of an acute respiratory exacerbation.
- Other medications, such as benzodiazepines and β -blockers were also significantly associated with an increased risk of a COPD exacerbation.

TABLE 1: Conditional Logistic Regression of Opioid and Other Medication Use and Respiratory Exacerbation of COPD (FFS and CCOs, 2013-2017)				
	Use within 7-days of respiratory exacerbation			
	Odds Ratio	95% Confidence Interval	P-value	
Use of Opioid	1.81	1.60	2.05	< 0.001*
Use of Benzodiazepines ^a	2.22	1.72	2.86	< 0.001*
Use of β -blockers ^a	2.18	1.56	3.05	< 0.001*

^a Use was defined as presence of a prescription claim resulting in possession of the medication during the case or the control windows preceding each exacerbation event.

As of December, 2018, there were a total of 14,596 beneficiaries enrolled in Mississippi Medicaid who had diagnoses of COPD (Table 2).

- Beneficiaries with COPD were almost twice as likely to be female.
- Beneficiaries with COPD were more likely to be ≥ 45 years of age.
- Although COPD was more prevalent in the FFS program, there were also a large number of COPD patients in the Coordinated Care Organizations (CCOs).

TABLE 2: CHARACTERISTICS OF BENEFICIARIES WITH COPD DIAGNOSES ENROLLED IN DECEMBER 2018									
<i>(Excludes Nursing Home Residents and Dual-Eligibles)</i>									
		Pharmacy Program							
		FFS		UHC		MAG		MOL	
TOTAL		5,951		3,752		4,717		176	
Race	Caucasian	3,127	52.5%	1,820	48.5%	2,255	47.8%	90	51.1%
	African American	2,288	38.4%	1,285	34.2%	1,695	35.9%	64	36.4%
	Other	536	9.0%	647	17.2%	767	16.3%	22	12.5%
Gender	Female	3,876	65.1%	2,343	62.4%	2,983	63.2%	108	61.4%
	Male	2,075	34.9%	1,409	37.6%	1,734	36.8%	68	38.6%
Age	Less than 18	90	1.5%	183	4.9%	232	4.9%	13	7.4%
	18 - 44	317	5.3%	615	16.4%	675	14.3%	54	30.7%
	45 - 64	2,807	47.2%	2,943	78.4%	3,791	80.4%	109	61.9%
	65+	2,737	46.0%	11	0.3%	19	0.4%	0	0.0%

Table 3 provides information on opioid use among beneficiaries with COPD who were enrolled in Medicaid as of December 2018 for that calendar year.

- Overall, 58% of beneficiaries with COPD had one or more opioid prescriptions during 2018. The percentage of beneficiaries with COPD having opioid prescriptions was much higher in the CCOs than in FFS.
- Of this 58%, about three-fourths of beneficiaries with opioid prescriptions had a maximum morphine equivalent daily dose (MEDD) < 50.
- Although few patients received high opioid doses, analyses in the study conducted by MS-DUR indicated that any dose of opioid significantly increases the likelihood of an exacerbation event.

TABLE 3: OPIOID PRESCRIPTION USE AMONG BENEFICIARIES WITH COPD DIAGNOSES ENROLLED IN DECEMBER 2018									
<i>(Excludes Nursing Home Residents and Dual-Eligibles)</i>									
		Pharmacy Program							
		FFS		UHC		MAG		MOL	
TOTAL		5,951		3,752		4,717		176	
Number of Opioid Prescription Fills	0	4,742	79.7%	1,480	39.4%	2,071	43.9%	100	56.8%
	1	331	5.6%	470	12.5%	615	13.0%	29	16.5%
	2	171	2.9%	273	7.3%	381	8.1%	14	8.0%
	3	135	2.3%	183	4.9%	197	4.2%	9	5.1%
	4+	572	9.6%	1,346	35.9%	1,453	30.8%	24	13.6%
Maximum MEDD	< 50 MEDD	965	79.8%	1,672	73.6%	1,993	75.3%	56	73.7%
	50 - 89 MEDD	156	12.9%	419	18.4%	467	17.6%	15	19.7%
	90 - 119 MEDD	33	2.7%	83	3.7%	95	3.6%	2	2.6%
	120 + MEDD	55	4.5%	98	4.3%	91	3.4%	3	3.9%

CONCLUSIONS AND RECOMMENDATIONS

Opioid use is fairly common among beneficiaries with a diagnosis of COPD. Even at lower doses, opioid use increases the likelihood of an exacerbation event. The DOM is implementing an opioid edit to require a manual prior authorization (PA) when the cumulative MEDD exceeds 90. As noted in the yellow highlighted area in table 3, this edit requiring a subsequent manual PA will have minimal impact on the quantity of manual PAs required for opioid prescriptions written for beneficiaries with COPD. The results of these analyses highlight a need to educate providers on the increased risk of exacerbation events in COPD patients associated with short-term opioid use.

Recommendations:

1. MS-DUR should implement a provider education initiative to address the risk associated with short-term opioid use among beneficiaries with COPD.