NALOXONE PRESCRIBING AMONG HIGH-RISK INDIVIDUALS IN MISSISSIPPI MEDICAID

BACKGROUND

Opioid overdose is a serious problem in the United States with almost 450,000 people dying from overdoses involving opioids from 1999-2018[1]. In Mississippi, 65% of overdose deaths between 2017 and the first quarter of 2020 were opioid-related[2]. Prescription opioids are highly addictive and misuse can easily occur. It is estimated that the economic burden associated with prescription opioid misuse is approximately $78.5 billion annually in the United States[3]. The use of opioids in the treatment of chronic, non-cancer pain has increased substantially despite the risks associated with their use. In 2016, more than 11.5 million Americans reported misusing prescription opioids in the previous year[1].

Naloxone is an opioid antagonist shown to be safe and effective in preventing opioid overdose deaths by competitively binding mu opioid receptors and reversing signs of opioid intoxication[4]. Since the development of easy-to-use naloxone formulations, improving access to naloxone for patients at high-risk for an overdose has become a primary target for preventing opioid overdoses[5]. In 2016 the CDC Guidelines for Prescribing Opioids for Chronic Pain defined "high-risk" factors for opioid overdose such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 Morphine Equivalent Daily Dose [MEDD]), or concurrent benzodiazepine use[6]. Other factors have also been shown to increase an individual's risk for opioid overdose including chronic opioid use and having mental health issues such as depression[7].

One of the keys to preventing opioid overdose events is getting naloxone into the hands of individuals at high-risk for overdose. Many states, including Mississippi, have adopted standing orders making naloxone available by request directly from a pharmacist without requiring a prescription from a medical provider. In Mississippi, a naloxone standing order was initially implemented by the Mississippi State Department of Health (MSDH) on May 2018 and was renewed in May 2019[2,8]. According to one study, there has been a 9-11% decrease in the number of opioid-related deaths in states that have adopted a naloxone access law[9].

As recently as July 2020, the FDA released a drug safety communication recommending health care professionals discuss naloxone with all patients when prescribing opioid pain relievers or medications to treat opioid use disorder. At the September 2020 DUR Board Meeting, it was recommended that MS-DUR assess the utilization of naloxone among Medicaid beneficiaries at high-risk of experiencing an opioid overdose.

METHODS

A retrospective analysis was conducted using both point-of-sale and medical Mississippi Medicaid administrative claims data for Fee-for-Service (FFS) and the three Coordinated Care Organizations [CCOs: Magnolia (MAG), Molina Health (MOL), and UnitedHealthcare (UHC)] for the period from August 1, 2018, to August 31, 2020 (i.e., study period). Naloxone use was assessed for beneficiaries characterized as high-risk for experiencing an adverse event associated with opioid use. Beneficiaries with a cancer diagnosis were excluded from the analysis. High-risk events for opioid users identified in this analysis included: high MEDD, long-term opioid use, prior opioid overdose event, concomitant use of benzodiazepine, concomitant use of antipsychotic, and presence of other high-risk diagnoses. High MEDD was identified when beneficiaries had any day of opioid use with $\geq$ 90 MEDD. Long-term opioid use was defined as the continuous use of opioids with $\geq$ 50 MEDD for 90 days or more allowing for a 15 day gap during continuous use. Opioid overdose was identified if beneficiaries had any opioid overdose-related diagnosis or opioid-induced respiratory depression (OIRD) diagnosis. Concomitant use of benzodiazepines and concomitant use of antipsychotics were defined as any concomitant use of opioid and benzodiazepines or antipsychotics during the study period. Presence of other high-risk diagnoses included any diagnosis of alcohol dependence, opioid dependence, other substance abuse dependence, and depression. Claims for naloxone were identified using the national drug code (NDC). For each naloxone claim, the provider type was identified. High-risk events and naloxone use before an opioid overdose event were also identified. Naloxone use before opioid overdose was classified according to the months between a naloxone claim and opioid overdose (i.e., < 1 month, 1-3 months, and > 3 months). Moreover, for beneficiaries with claims for any high-risk event, their age, gender, and race were identified.

RESULTS

Table 1a describes the demographic characteristics of beneficiaries prescribed opioids. During the study period there were 113,739 beneficiaries having opioid claims. Of those beneficiaries prescribed opioids, 30.7% (34,912) were classified as high-risk of experiencing an adverse opioid event. For those high-risk beneficiaries:

- 58.2% were between the ages of 18-45 years;
- 75.8% were female;
- Little difference in distribution between African Americans (46.4%) and Caucasians (45.3%).

Table 1a: Demographics of Beneficiaries Prescribed Opioids with High-Risk Event(s) for Opioid Overdose August 2018 - August 2020					
	Plan*				
	FFS	United	Magnolia	Molina	Total
Opioid users	20,380	37,858	42,894	12,607	**113,739**
Any high-risk event	7,627	11,573	13,272	2,440	**34,912**
Age					
< 18	413	851	962	121	**2,347**
18 - 45	4,219	6,533	7,545	2,009	**20,306**
46 - 65	2,854	4,115	4,680	310	**11,959**
65+	141	74	85	0	**300**
Gender					
Female	5,473	8,726	10,170	2,091	**26,460**
Male	2,153	2,847	3,102	349	**8,451**
Race					
Caucasian	3,716	5,332	5,637	1,146	**15,831**
African American	3,279	5,233	6,555	1,147	**16,214**
Other	632	1,008	1,080	147	**2,867**
Note: * Plan on the indext date of the earliest event					

Table 1b details the high-risk event types for beneficiaries classified as high-risk for having an adverse opioid event. A Beneficiary could be classified as having multiple high-risk events. A large majority of beneficiaries (88.7%) were found to have a high-risk diagnosis such as alcohol dependence, opioid dependence, other substance abuse dependence, or depression.

Table 1b: High-Risk Event Type among Beneficiaries Prescribed Opioids August 2018 - August 2020					
	Plan*				
	FFS	United	Magnolia	Molina	Total
Opioid users	20,380	37,858	42,894	12,607	**113,739**
Any high-risk event	7,627	11,573	13,272	2,440	**34,912**
High MEDD	290	604	811	173	**1,878**
Long-term opioid use	74	166	159	11	**410**
Opioid overdose	138	183	201	30	**552**
Concomitant use of benzodiazepine	915	1,959	2,158	239	**5,271**
Concomitant use of antipsychotic	920	1,765	2,066	242	**4,993**
High-risk diagnosis	6,867	10,188	11,668	2,231	**30,954**
Notes: A beneficiary may be represented under more than 1 high-risk event type. High MEDD: ≥ 90 MEDD; Long-term opioid use: ≥ 50 MEDD for 90 days or more (gap allowance: 15 days) ; High-risk diagnosis: alcohol dependence, opioid dependence, other substance use dependence, or depression * Plan on the indext date of the event;					

Naloxone use among high-risk beneficiaries was examined in Table 2. Only a small proportion (<2.0%) of beneficiaries characterized as high-risk had claims for naloxone during the study period.

When examining those naloxone claims, approximately one-fifth occurred prior to the qualifying high-risk event.

Table 2: Number of High-Risk Beneficiaries that Received Naloxone August 2018 - August 2020

Plan	High-risk event type	# of benes	# of benes with naloxone claims	# of benes with naloxone claims prior to high risk event
FFS	High MEDD	290	14	3
	Long-term opioid use	74	5	2
	Opioid overdose	138	4	2
	Concomitant use of benzodiazepine	915	19	3
	Concomitant use of antipsychotic	920	18	10
	High-risk diagnosis	6,867	70	8
United	High MEDD	604	31	7
	Long-term opioid use	166	19	6
	Opioid overdose	183	11	5
	Concomitant use of benzodiazepine	1,959	11	9
	Concomitant use of antipsychotic	1,765	30	7
	High-risk diagnosis	10,188	163	28
Magnolia	High MEDD	811	40	5
	Long-term opioid use	159	20	7
	Opioid overdose	201	3	1
	Concomitant use of benzodiazepine	2,158	3	12
	Concomitant use of antipsychotic	2,066	42	5
	High-risk diagnosis	11,668	182	24
Molina	High MEDD	173	1	0
	Long-term opioid use	11	1	0
	Opioid overdose	30	0	0
	Concomitant use of benzodiazepine	239	3	2
	Concomitant use of antipsychotic	242	2	2
	High-risk diagnosis	2,231	11	2

In Table 3 MS-DUR examined the types of providers prescribing naloxone to beneficiaries classified as high-risk. As part of this analysis MS-DUR attempted to determine the proportion of naloxone claims generated at a pharmacy level through the MSDH's naloxone standing order. Using the national provider identifier (NPI) for physicians associated with the standing order during this time period, MS-DUR was able to distinguish claims executed through the naloxone standing order. Approximately 29% (183) of naloxone claims were processed through the MSDH's naloxone standing order.

Table 3: Number of Naloxone Claims by Prescribing Provider Type					
Provider Type	Plan				Total
	FFS	United	Magnolia	Molina	
Primary Care Physician	10	30	61	8	109
Department of Health*	21	74	73	15	183
Other Physician	17	44	44	3	108
Nurse Practitioner	15	34	32	3	84
Physician Assistant	1	3	4	0	8
Other Provider	3	1	2	0	6
Unkown	16	48	65	3	132
* Department of Health provider type: Providers associated with the MSDH Naloxone Standing Order					

The primary goal in naloxone prescribing is the prevention of opioid overdose events. For those beneficiaries that experienced an opioid overdose event, MS-DUR examined naloxone claims prior to that overdose event. (Table 4a) Of the 552 beneficiaries with an opioid overdose event during the study period:

- **56% (311) had a high-risk event prior to their opioid overdose.**
- **1.4% (8) had a naloxone claim prior to the overdose event.**

Table 4a: Naloxone Claims Prior to Opioid Overdose Events August 2018 - August 2020						
Plan	Opioid overdose events	Any prior high risk events	Prior naloxone claims	Prior naloxone claims timeline		
				< 1 month	1-3 months	> 3 months
FFS	138	74	2	2	0	0
United	183	104	5	2	0	3
Magnolia	201	114	1	0	0	1
Molina	30	19	0	0	0	0
Total	**552**	**311**	**8**	**4**	**0**	**4**

For those 311 individuals with a prior high-risk event that had a subsequent opioid overdose, MS-DUR examined the type of prior high-risk event present. (Table4b) **It was noted that a large proportion (87.8%) of individuals experiencing an opioid overdose had a prior high-risk diagnosis present.**

Table 4b: Type of Prior High-Risk Events Associated with Opioid Overdose Events August 2018 - August 2020							
Plan	Opioid overdose events	Any prior high risk events	Type of prior high-risk event				
			Prior high MEDD	Prior long-term opioid use	Prior concomitant use of benzodiazepine	Prior Concomitant use of antipsychotic	Prior high-risk diagnosis
FFS	138	74	11	5	17	14	63
United	183	104	20	6	30	13	94
Magnolia	201	114	24	7	22	15	99
Molina	30	19	2	1	4	4	17
Total	**552**	**311**	**57**	**19**	**73**	**46**	**273**

CONCLUSIONS

The opioid epidemic has greatly impacted the United States and placed many people at risk of opioid overdose events. Naloxone is an effective treatment for reversing the signs of opioid intoxication. Getting naloxone into the hands of individuals at high-risk of opioid overdose is key to preventing these events. Among Medicaid beneficiaries identified as high-risk of experiencing an opioid overdose, less than 2% had a naloxone claim. For those beneficiaries who experienced an overdose event, although 56% were classified as high-risk prior to their overdose event, only 1.4% had a naloxone claim prior to that overdose event.

RECOMMENDATION

1. DOM should distribute educational reminders to prescribers and pharmacists regarding the FDA's recent recommendation for naloxone, the covered status of naloxone products on the PDL, and the MSDH's Naloxone Standing Order.

References:

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