

# Association of Opioid Utilization Management With Prescribing and Overdose

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From 2008 to 2017, almost 300,000 individuals in the United States died from an opioid-related overdose,<sup>1</sup> and harms from the opioid epidemic continue to accrue, including among Medicare beneficiaries.<sup>2-4</sup> Although heroin and illicit fentanyl account for a substantial proportion of opioid overdoses, more than 17,000 people in the United States died from prescription opioids in 2017,<sup>4</sup> and the continued oversupply of prescription opioids remains a key driver of the epidemic. Although most of the harms from the opioid epidemic, to date, have accrued among people younger than 65 years, opioid-related mortality is rising more rapidly among people 65 years and older than for any other age group.<sup>4</sup>

Given the role that opioid prescribing has played in driving substance use disorders, overdoses, and other adverse events, health care insurers are an important stakeholder in efforts to address the epidemic, including through the design of coverage and reimbursement policies.<sup>5-14</sup> Formulary design and utilization management strategies can be used to reduce prescribing of select opioids,<sup>5-10</sup> although some forms of quantity limits appear to be ineffective at reducing opioid prescribing.<sup>11</sup> However, few papers<sup>8-10</sup> have assessed the relationship between these policies and opioid misuse or overdoses, with some papers documenting reductions in misuse<sup>8,9</sup> or overdoses<sup>9</sup> associated with utilization management and other analyses examining how drug utilization review programs<sup>12</sup> and prescription drug management programs<sup>15</sup> may affect opioid prescribing patterns.

Despite the insights that these studies provide, little is known regarding how utilization management programs for opioids in the Medicare Part D program are associated with opioid supply, conditional on filling a prescription, nor is there robust evidence on the association between utilization management and subsequent overdoses. We conducted a retrospective cohort study of Medicare beneficiaries to examine these associations, focusing on individuals filling 1 or more opioid prescriptions over a 7-year period. We hypothesized that prior authorization requirements, which allow insurers to make more individualized assessments of the suitability of a prescription before authorizing it, would be associated with fewer overdoses.

## ABSTRACT

**OBJECTIVES:** Deaths from prescription opioids have reached epidemic levels in the United States, yet little is known about how insurers' coverage policies may affect rates of fatal and nonfatal overdose among individuals filling an opioid prescription.

**STUDY DESIGN:** Retrospective cohort study using 2010-2016 Medicare claims data for beneficiaries with 1 or more filled prescriptions for a Schedule II opioid.

**METHODS:** Outcomes were opioid volume dispensed in morphine milligram equivalents (MME), number of days supplied, and number of pills dispensed on each prescription and emergency department or inpatient stay associated with an opioid overdose during a prescription or within 7 days of the end of the prescription.

**RESULTS:** A total of 7.03 million prescriptions for Schedule II opioids were dispensed over 1.87 million Part D beneficiary-years. The 7.03 million opioid prescriptions were associated with 8.5 opioid overdoses per 10,000 prescriptions. Prior authorization was associated with larger opioid volumes per prescription (103.6 MME; 95% CI, 36.2-171.0). Step therapy was associated with a greater number of days supplied (0.62 days; 95% CI, 0.10-1.13) and more pills dispensed (6.12 pills; 95% CI, 2.17-10.1). Quantity limits were associated with smaller opioid volumes (24.3 MME; 95% CI, 12.3-36.3) and fewer pills dispensed (2.35 pills; 95% CI, 1.77-2.93). In adjusted models, beneficiaries filling an opioid requiring prior authorization experienced 3.3 fewer overdoses per 10,000 prescriptions (95% CI, 0.41-6.2).

**CONCLUSIONS:** Opioid utilization management among these beneficiaries was associated with mixed effects on opioid prescribing, and prior authorization was associated with a decreased likelihood of subsequent overdose. Further work exploring the impact of utilization management and insurer policies is needed.

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## TAKEAWAY POINTS

Utilization management policies may affect prescription opioid prescribing and overdoses, with differential effects for prior authorization, step therapy, and quantity limits among older adults.

- ▶ Prior authorization was associated with more opioid volume but fewer overdoses.
- ▶ Step therapy was associated with an increase in days and pills supplied but not overdoses.
- ▶ Quantity limits were associated with smaller opioid volumes and fewer pills.

## METHODS

## Data and Sample

We performed a retrospective cohort study using Medicare parts A, B, and D claims for a 5% representative sample of the US Medicare population from 2010 to 2016. We restricted our sample to individuals who were enrolled in a stand-alone Medicare Part D prescription drug plan, not enrolled in a Medicare Advantage plan, 65 years or older, and not eligible for low-income subsidies. These restrictions ensured that our sample included individuals who were in a Medicare Part D plan; had claims data from which we could identify overdose emergency department (ED) visits and hospitalizations; were not eligible due to disability or kidney disease, which would present additional confounders; and chose their own plan, because many low-income subsidy enrollees are autoenrolled in a plan. Following prior literature, we also excluded from our sample individuals who had a cancer diagnosis or used hospice care at any time.<sup>16,17</sup> We further restricted the sample to enrollees for whom we identified at least 1 prescription for a Schedule II opioid, which is deemed by the Drug Enforcement Administration to have a high potential for misuse, based on the National Drug Code on the prescription claim. This restriction excludes cough and cold preparations that contain opioids but does include hydrocodone-containing products, which were rescheduled from Schedule III to Schedule II at the end of 2014.<sup>18,19</sup> We used the classification in effect in September 2019.

The unit of analysis for our study was the individual prescription, which allowed us to attribute overdoses to specific sets of utilization management characteristics. We also computed beneficiary-years as the unduplicated count of beneficiary identifiers by calendar year.

## Exposures and Outcomes

Our primary exposure of interest was whether a given prescription was covered by 1 of 3 types of utilization management: prior authorization, which requires approval from the insurer before a prescription may be dispensed; step therapy, which requires an individual to try another therapy before receiving a prescription subject to step therapy; or quantity limits, which stipulate a maximum number of units of a medicine (eg, pills, capsules, tablets) that can be dispensed within a specific time frame. Prescriptions could have multiple policies in effect at once, typically either a prior authorization or step therapy requirement with a quantity limit.

We examined 4 outcomes: (1) prescription opioid volume, as assessed by morphine milligram equivalents (MME), a method of

standardizing opioids across different molecules, formulations, and doses; (2) number of days supplied; (3) number of pills dispensed; and (4) whether there was an ED visit or inpatient stay attributable to an opioid overdose within a specified window after the dispensing date. We used published conversion factors from the CDC to calculate MME,<sup>20</sup> and we identified overdoses using *International Classification*

*of Diseases, Ninth Revision* and *Tenth Revision* codes for accidental poisonings, as well as from combinations of codes for adverse effects of an opioid and 1 or more indicators of a serious adverse effect (see **eAppendix Table 1** [eAppendix available at [ajmc.com](http://ajmc.com)]).<sup>17</sup> For each opioid prescription, we defined an interval starting on the day the prescription was filled and lasting for the number of days supplied by the prescription. We attributed an overdose to a prescription if the overdose occurred in that window or within 7 days after the end of the interval. In sensitivity analyses, we also used a 30-day window after the end of the interval. This method of attribution allowed for an overdose to be attributed to more than 1 opioid prescription.

## Control Variables

We used RxHCC codes, which are used by Medicare to risk adjust Medicare Part D plan payments to control for clinical conditions. Because some codes were rare, we aggregated codes with a prevalence below 1% into a single indicator. We controlled for demographic characteristics using a cubic polynomial in age and indicators for gender, race/ethnicity, and year. Finally, because we were interested in the associations with utilization management within a given drug, we also included indicators for the dispensed drug, which we defined based on its generic name and whether it was a short-acting or long-acting formulation.

## Analyses

We first examined descriptive statistics for beneficiaries and prescriptions in total and after stratifying by each type of utilization management of interest. Before exploring the association between utilization management and overdoses, we first established an association between utilization management and opioid prescribing patterns. To assess the association between utilization management and opioid prescribing, we estimated Poisson regression models with MME, days supplied, or quantity dispensed as the dependent variable. We estimated models with no controls, and adjusted models that included a cubic polynomial in age and indicators for gender, race, year, RxHCCs, and the drug that was dispensed. We allowed for more than 1 policy indicator to be one in our models. Next, we estimated a series of logistic regression models of the association between utilization management and opioid overdose. As with the Poisson models, we estimated both unadjusted and adjusted models.

For all models, we computed predicted means with and without each of our utilization management variables and the difference between the predicted mean levels. The difference between the

**TABLE 1.** Characteristics of Part D Medicare Beneficiaries Receiving Prescription Opioids and Their Prescriptions, 2010-2016 (N = 1,866,131 beneficiary-years; N = 7,032,250 prescriptions)<sup>a</sup>

Characteristics	All	Prior authorization		Step therapy		Quantity limits	
		Yes	No	Yes	No	Yes	No
<b>Beneficiary characteristics</b>							
Age in years, mean (SD)	74.1 (6.97)	75.6 (7.93)	74.1 (6.97)	74.4 (7.79)	74.1 (6.97)	74.2 (6.97)	74.0 (6.99)
Annual fills, mean (SD)	2.10 (1.78)	2.81 (2.06)	2.10 (1.78)	3.08 (2.11)	2.10 (1.78)	2.12 (1.80)	2.09 (1.75)
Female sex, %	63.4	68.3	63.4	71.6	63.4	62.9	65.1
Race, %							
White	94.9	97.4	94.9	95.5	94.9	94.9	94.9
Black	3.37	1.59	3.37	2.96	3.37	3.36	3.35
Other	1.74	1.04	1.74	1.50	1.74	1.74	1.71
No. of beneficiaries	1,866,131	3654	1,864,162	2331	1,865,049	1,402,121	497,117
<b>Prescription characteristics</b>							
MME, mean (SD)	960.0 (1547.7)	2932.2 (3277.5)	955.1 (1537.7)	2403.8 (2431.1)	957.5 (1544.5)	965.8 (1508.1)	942.9 (1658.7)
Days supplied, mean (SD)	19.2 (13.3)	24.7 (11.7)	19.2 (13.3)	25.1 (10.4)	19.2 (13.3)	19.5 (13.1)	18.4 (13.9)
Quantity dispensed, mean (SD)	71.0 (59.5)	49.0 (48.6)	71.0 (59.5)	56.3 (48.3)	71.0 (59.5)	70.3 (56.5)	72.8 (67.5)
Prior authorization, %	0.25	100	0	0	0.25	0.33	0.031
Step therapy, %	0.17	0	0.17	100	0	0.20	0.087
Quantity limits, %	74.7	96.8	74.6	87.2	74.6	100	0
Overdose [per 1000 prescriptions]							
Within 7 days of end of prescription	0.85	1.08	0.85	1.56	0.85	0.89	0.76
Within 30 days of dispensing	0.89	1.14	0.89	1.72	0.89	0.92	0.81
No. of prescriptions	7,032,250	17,610	7,014,640	12,151	7,020,099	5,248,855	1,783,395

MME, morphine milligram equivalents.

<sup>a</sup>Data are from Medicare claims files for 2010-2016.

predicted mean levels provides a measure of the association between utilization management and the dependent variables.

Results were considered statistically significant if the 2-sided *P* value was less than .05 using a sandwich estimator of the variance accounting for within-beneficiary correlations.

### Sensitivity Analyses

We conducted 3 sensitivity analyses. First, because utilization management measures may be correlated, we estimated models with each measure separately. Second, because utilization management policies might affect the prescription length, we defined an absolute measure of overdose risk by attributing overdoses in the 30-day period following the date a prescription was filled to that prescription. Third, because overdoses may occur outside the hospital or ED, we performed analyses in which any death was considered an outcome of interest, although cause-of-death data were not available to us.

### Ethics

The study was approved by the University of North Carolina at Greensboro Institutional Review Board and the CMS Privacy Board.

## RESULTS

### Study Sample

Our sample included 1.87 million Medicare beneficiary-years (of an initial sample of 12.4 million beneficiary-years) in which 7.03 million prescriptions for Schedule II opioids were filled from 2010 to 2016 (Table 1). The beneficiaries had a mean (SD) age of 74.1 (6.97) years and the mean (SD) number of prescriptions filled by each beneficiary was approximately 2.1 (1.78). Almost two-thirds of all beneficiaries were female and almost 95% were White. The average prescription provided the equivalent of 960.0 (SD, 1547.7; median, 450) MME over 19.2 (SD, 13.3; median, 20) days in 71.0 (SD, 59.5; median, 60) pills. Among these prescriptions, 17,610 (0.25%) were subject to prior authorization, 12,151 (0.17%) were subject to a step therapy requirement, and 5.25 million (74.7%) were subject to a quantity limit. ED visits for opioid overdoses from the dispensing date to within 7 days of the end of the prescription were uncommon, occurring for 8.5 of every 10,000 opioid prescriptions.

Individuals who filled prescriptions subject to prior authorization or step therapy were slightly older (aged 75.6 and 74.4 years,

**TABLE 2.** Association of Prescription Opioid Utilization Management With Opioid Volume and Prescription, 2010-2016 (N = 1,866,131 beneficiary-years; N = 7,032,250 prescriptions)<sup>a</sup>

Utilization management	MME		Days supplied		Quantity dispensed	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Prior authorization						
No	955.1 (946.9-963.2)	959.3 (953.2-965.4)	19.2 (19.2-19.2)	19.2 (19.2-19.2)	71.0 (70.8-71.3)	71.0 (70.7-71.2)
Yes	2929.4 (2728.4-3130.4)	1062.9 (995.8-1130.0)	24.4 (23.6-25.2)	18.9 (18.2-19.5)	49.3 (46.2-52.5)	69.8 (67.0-72.7)
Difference (yes – no)	1974.4*** (1774.1-2174.7)	103.6** (36.2-171.0)	5.20*** (4.43-5.96)	-0.34 (-0.96 to 0.29)	-21.7*** (-24.8 to -18.5)	-1.12 (-3.95 to 1.70)
Step therapy						
No	957.5 (949.3-965.7)	959.8 (953.7-965.9)	19.2 (19.2-19.2)	19.2 (19.2-19.2)	71.0 (70.8-71.2)	71.0 (70.7-71.2)
Yes	2411.5 (2217.2-2605.8)	1012 (943.0-1081.0)	24.9 (24.3-25.6)	19.8 (19.3-20.3)	56.5 (53.1-59.8)	77.1 (73.1-81.0)
Difference (yes – no)	1454*** (1260.0-1648.0)	52.2 (-17.1 to 121.5)	5.74*** (5.12-6.35)	0.62* (0.10-1.13)	-14.5*** (-17.9 to -11.2)	6.12** (2.17-10.1)
Quantity limits						
No	948.4 (934.6-962.2)	978.4 (966.4-990.4)	18.4 (18.3-18.5)	19.3 (19.2-19.3)	72.8 (72.3-73.3)	72.7 (72.2-73.3)
Yes	963.9 (955.9-971.9)	954.1 (947.9-960.2)	19.5 (19.4-19.5)	19.2 (19.1-19.2)	70.3 (70.1-70.6)	70.4 (70.1-70.6)
Difference (yes – no)	15.5* (3.12-27.9)	-24.3*** (-36.3 to -12.3)	1.09*** (1.02-1.16)	-0.076 (-0.17 to 0.014)	-2.44*** (-2.90 to -1.97)	-2.35*** (-2.93 to -1.77)

MME, morphine milligram equivalents.

\*P < .05; \*\*P < .01; \*\*\*P < .001.

<sup>a</sup>Cells show predicted means from Poisson regressions and 95% CIs based on a covariance matrix that is clustered on the beneficiary. Adjusted models control for a cubic polynomial in age, gender, race/ethnicity, year, RxHCCs with a prevalence greater than 1%, and the drug dispensed. Data are from Medicare claims files for 2010-2016.

**TABLE 3.** Association Between Prescription Opioid Utilization Management and Subsequent Fatal or Nonfatal Overdose, 2010-2016 (N = 1,866,131 beneficiary-years; N = 7,032,250 prescriptions)<sup>a</sup>

Utilization management	Overdoses per 1000 prescriptions	
	Unadjusted	Adjusted
Prior authorization		
No	0.85 (0.82-0.89)	0.86 (0.82-0.89)
Yes	1.05 (0.47-1.62)	0.52 (0.23-0.81)
Difference (yes – no)	0.19 (-0.39 to 0.77)	-0.33* (-0.62 to -0.041)
Step therapy		
No	0.85 (0.82-0.89)	0.85 (0.82-0.89)
Yes	1.54 (0.66-2.42)	0.72 (0.30-1.15)
Difference (yes – no)	0.68 (-0.20 to 1.56)	-0.13 (-0.56 to 0.29)
Quantity limits		
No	0.76 (0.70-0.82)	0.85 (0.78-0.93)
Yes	0.89 (0.85-0.92)	0.85 (0.82-0.89)
Difference (yes – no)	0.13*** (0.059-0.19)	0.0017 (-0.086 to 0.090)

\*P < .05; \*\*P < .01; \*\*\*P < .001.

<sup>a</sup>Cells show predicted means from logistic regressions and 95% CIs based on covariance matrix that is clustered on the beneficiary. Adjusted models control for a cubic polynomial in age, gender, race/ethnicity, year, RxHCCs with a prevalence greater than 1%, and the drug dispensed. Data are from Medicare claims files for 2010-2016.

respectively) and the average prescription was for a substantially greater MME (2932.2 and 2403.8, respectively). Differences in age and MME prescribed based on the presence of quantity limits were minimal.

### Association of Utilization Management With Opioid Volume and Days Supplied

**Table 2** characterizes the association between prescriptions subject to utilization management and those that were not. In unadjusted analyses, prescriptions with prior authorization provided an additional 1974.4 (95% CI, 1774.1-2174.7) MME and lasted 5.20 (95% CI, 4.43-5.96) days longer, despite covering 21.7 (95% CI, 18.5-24.8) fewer pills. However, after adjusting for demographic, clinical, and product factors, prior authorization was associated with 103.6 (95% CI, 36.2-171.0) greater MME per prescription, with no differences in the days supplied or quantity dispensed among opioids dispensed with prior authorization and their counterparts. Products dispensed with step therapy were dispensed with greater MME, days supplied, and quantity, although after adjustment, step therapy was associated with only a slight increase in days supplied (0.62 days; 95% CI, 0.10-1.13). Quantity limits were associated with 24.3 fewer MME (adjusted model: 95% CI, 12.3-36.3) as well

as a reduction of 2.35 pills (adjusted model: 95% CI, 1.77-2.93) in quantities dispensed.

### Association Between Utilization Management and Opioid Overdose

**Table 3** demonstrates the association between utilization management and subsequent opioid overdoses. Neither prior authorization nor step therapy was associated with overdoses in unadjusted analyses, but after adjustment, prescriptions subject to prior authorization were associated with 0.33 fewer overdoses per 1000 prescriptions (95% CI, 0.041-0.62). Quantity limits were associated with increased overdoses in unadjusted models (0.13 per 1000 prescriptions; 95% CI, 0.059-0.19) but not associated with overdoses after adjustment.

### Sensitivity Analyses

There were no substantive differences in our results when we estimated models with each utilization management measure entered separately (**eAppendix Table 2**), nor did we find substantive differences in our adjusted point estimates using alternative definitions of an opioid overdose (**eAppendix Table 3**) or sample inclusion criteria. The 1 exception to the latter was that quantity limits are associated with fewer overdoses or deaths in our unadjusted and adjusted models and, in unadjusted models, both prior authorization and step therapy are significantly associated with increased overdoses or deaths.

In drug-specific adjusted analyses (**eAppendix Figure**), prior authorization was associated with fewer opioid overdoses for long-acting fentanyl, long-acting methadone, and both short- and long-acting morphine; there was no association between prior authorization and overdoses attributable to oxycodone formulations, including long-acting oxycodone (eg, Oxycontin). Step therapy was associated with significantly fewer overdoses for tapentadol and morphine. Although there were statistically significant associations between utilization management and MME dispensed, days supplied, and quantity dispensed, the drugs for which there were such associations were not the same drugs as those that were associated with fewer overdoses.

## DISCUSSION

Because the oversupply of prescription opioids has played an important role in driving the opioid epidemic,<sup>21</sup> it is important to understand how coverage policies may affect opioid prescribing and fatal and nonfatal overdose. We used Medicare claims to examine these relationships among a large sample of Medicare beneficiaries who filled a prescription for a Schedule II opioid, focusing on 3 common forms of utilization management: prior authorization, step therapy, and quantity limits. Although nearly three-fourths of prescriptions were dispensed with quantity limits, both prior authorization and step therapy were uncommon, being applied to fewer than 1% of opioid prescriptions. However, those prescriptions were for significantly greater quantities of MME, even though the

difference in quantity of pills dispensed was small, indicating that these policies were more likely to be applied to high-dose opioid formulations. The utilization management strategies that we observed were associated with mixed effects on opioid prescribing, whereas prior authorization was associated with a decreased likelihood of subsequent overdose.

Although our study was not designed for causal inference, it nevertheless adds to a growing literature examining the role of prescription opioid coverage and reimbursement policies in the opioid epidemic. The previous literature on the relationship between utilization management policies and opioid overdoses has mostly assessed state Medicaid programs, suggesting that prior authorization policies reduce high-risk prescribing and, in some cases, reduce the incidence of overdose-related ED visits or hospitalizations.<sup>8-10</sup> Our investigation complements these papers by assessing these associations in a nationwide data set among Medicare plans with a wide variety of utilization management policies, tools, and cost-sharing provisions applied to a diverse set of opioid products.

Our main finding is that prior authorization policies are associated with a reduction in opioid overdoses, holding product and other factors constant. This finding is particularly surprising because these prescriptions provided greater MME, which one might hypothesize would be associated with greater, not lesser, harms.<sup>17</sup> On the other hand, once we normalize by the number of days supplied, the incremental MME per day for prescriptions subject to prior authorization is a more modest 6 MME/day, based on the ratio of total MMEs to days supplied. We speculate that prior authorization may have prompted greater scrutiny of patients' regimens by payers, pharmacists, and/or clinicians, leading to clinical changes (eg, discontinuation of concomitant benzodiazepines) that ultimately reduced patients' risks. We are also unable to rule out a substitution effect in which utilization management on one drug leads to increased prescribing of another, less tightly managed drug. Understanding this pathway is an important avenue of future research.

Our finding of no association between quantity limits and overdose is also interesting, but it must be interpreted with care because the quantity limits in effect in this time period were several-fold greater than the caps that Medicare has applied since 2019, when Medicare Part D plans limited prescriptions for opioid-naïve patients to a 7-day supply and alerted prescribers when a patient sought to fill a prescription that would result in a daily MME greater than 90.<sup>22</sup> Among the 3 utilization management strategies, only quantity limits were associated with a reduction in MME and quantities dispensed.

### Limitations

Our report has several limitations. First, our sample was limited to beneficiaries in a stand-alone Medicare Part D plan from 2010 to 2016, so our results may not generalize to other populations or time periods. We note, in particular, that our sample is less racially diverse than the population of Part D enrollees overall. Second, we relied on claims data to identify opioid-related overdoses, which

may misclassify some visits,<sup>23</sup> and our method of attributing overdoses to specific prescriptions is also imprecise. Third, we do not have any information on prescriptions that may have been written but ultimately went unfilled due to utilization management programs. Finally, we do not observe causes of death, so we cannot estimate an association with opioid-related mortality, but only with all-cause mortality.

## CONCLUSIONS

Although efforts are being undertaken by many stakeholders to address the opioid epidemic, many harms continue to accrue, with persistent and widespread nonmedical use and overdose of prescription opioids. Payers have an important role to play in affecting these trends. Despite this, remarkably little is known regarding how commonly utilization management programs have been applied to opioids and the impact that these programs have had. In this analysis of a broad and diverse group of Medicare beneficiaries, opioid utilization management was associated with mixed effects on opioid prescribing, with only quantity limits being associated with an overall reduction in MME. Strikingly, prior authorization was associated with a decreased likelihood of subsequent overdose in our adjusted models, despite being associated with greater MME prescribed. Further work is needed to elucidate the mechanisms accounting for this association, including potential mechanisms acting through who fills an opioid prescription, as well as to extend this work to other populations, especially those most vulnerable to opioid-related harms. ■

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**Authorship Information:** Concept and design (MSA, JWB, GCA); acquisition of data (MSA, VL, AP); analysis and interpretation of data (MSA, VL, AP, JWB, GCA); drafting of the manuscript (MSA); critical revision of the manuscript for

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**eAppendix to “Association of Opioid Utilization Management with Prescribing and Overdose”**

**eAppendix Table 1.** ICD-9 and ICD-10 Codes for Opioid Overdoses

**eAppendix Table 2.** Association between prescription opioid utilization management, opioid overdose, volume, and prescription duration (n=1866131 beneficiaries).

**eAppendix Table 3.** Association between prescription opioid utilization management and opioid overdose using alternative attribution methods and sample inclusion criteria (n=1866131 beneficiaries).

**eAppendix Figure.** Adjusted Drug-specific associations between prescription opioid utilization management, opioid volume, prescription length, quantity dispensed, and opioid overdose (n=1866131 beneficiaries).

**eAppendix Table 1. ICD-9 and ICD-10 Codes for Opioid Overdoses.**

Case Definition 1	
<b><u>ICD-9</u></b>	
9650	Poisoning by opiates
E8501	Accidental poisoning by methadone
E9500	Suicide and self-inflicted poisoning by analgesics, antipyretics, and antirheumatics
E9800	Poisoning by analgesics, antipyretics, and antirheumatics, undetermined whether accidentally or purposely inflicted
<b><u>ICD-10, def1</u></b>	<b><u>Description</u></b>
T400	Poisoning by opium
T402	Poisoning by other opioids
T403	Poisoning by, adverse effect of and underdosing of methadone
T404	Poisoning by, adverse effect of and underdosing of other synthetic narcotics
<b><u>Case definition 2 (1 code from each section on the same date); ICD-9 only</u></b>	
<b><u>Group 1 (Opioid specific adverse events)</u></b>	
E9350	Heroin causing adverse effects in therapeutic use
E9351	Methadone causing adverse effects in therapeutic use
E9352	Pother opiates and related narcotics causing adverse effects in therapeutic use
<b><u>Group 2 (Overdose diagnostic codes)</u></b>	
276.4	Mixed acid-base balance disorder
292.1	Drug induced psychotic disorder
292.8	Other specified drug-induced mental disorder
486	Pneumonia, organism unspecified
496	Chronic airway obstruction, not elsewhere classified
518.81	Acute respiratory failure
518.82	Pother pulmonary insufficiency, not elsewhere classified
780.0x	General symptoms
780.97	Altered mental status
786.03	Apnea
786.05	Shortness of breath
786.09	Other respiratory abnormalities
786.52	Painful respiration
799.0x	Asphyxia and hypoxemia
E950-E959	Suicide and self-inflicted injury

Notes: Adapted from Dunn et al.<sup>17</sup>.

**eAppendix Table 2.** Association between prescription opioid utilization management, opioid overdose, volume, and prescription duration (n=1866131 beneficiary-years ).

	Milligrams Morphine Equivalent		Days supplied		Quantity dispensed		Overdose within 7 days	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Prior Authorization	1977.1*** [1776.7,2177.5]	99.9** [33.0,166.7]	5.49*** [4.72,6.27]	-0.36 [-0.98,0.26]	-22.0*** [-25.1,-18.9]	-1.46 [-4.26,1.35]	0.23 [-0.37,0.82]	-0.33* [-0.62,-0.039]
Step Therapy	1446.3*** [1252.6,1640.0]	47.5 [-21.7,116.6]	5.90*** [5.26,6.53]	0.63* [0.11,1.15]	-14.7*** [-18.1,-11.4]	5.92** [1.99,9.86]	0.71 [-0.18,1.61]	-0.12 [-0.55,0.31]
Quantity limits	22.9*** [10.5,35.3]	-23.6*** [-35.5,-11.6]	1.11*** [1.04,1.18]	-0.076 [-0.17,0.014]	-2.52*** [-2.98,-2.05]	-2.35*** [-2.93,-1.77]	0.13*** [0.060,0.19]	0.00021 [-0.088,0.088]

Predicted means from Poisson (MME, days, and quantity) logistic (overdose) regressions. Adjusted models control for a cubic

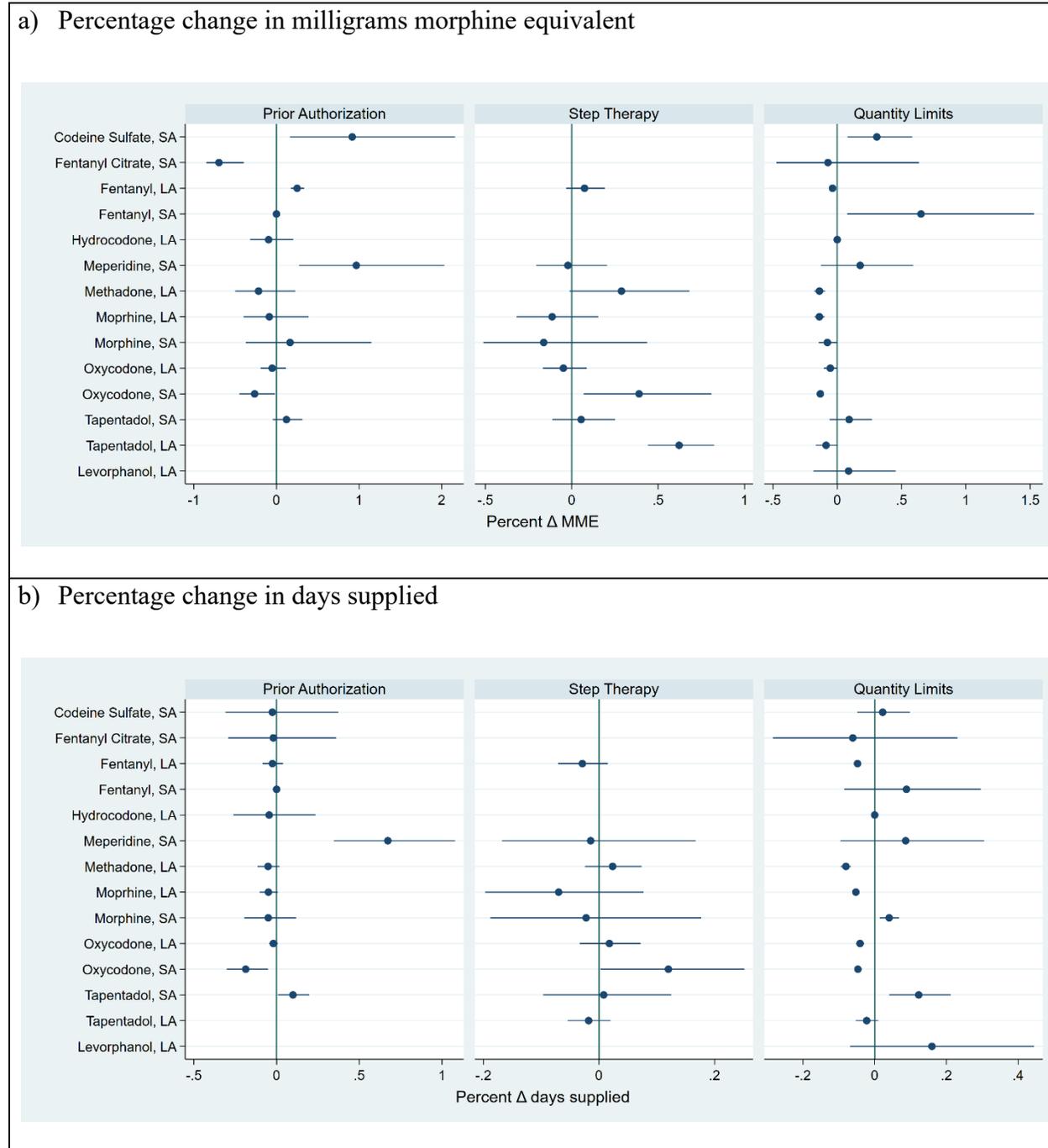
polynomial in age, gender, race/ethnicity, year, RXHCCs with a prevalence greater than 1%, and the drug dispensed. 95% confidence intervals based on covariance matrix that is clustered on the beneficiary. \*p<.05, \*\*p<.01, \*\*\*p<.001.

**eAppendix Table 3.** Association between prescription opioid utilization management and opioid overdose using alternative attribution methods and sample inclusion criteria (n=1866131 beneficiary-years ).

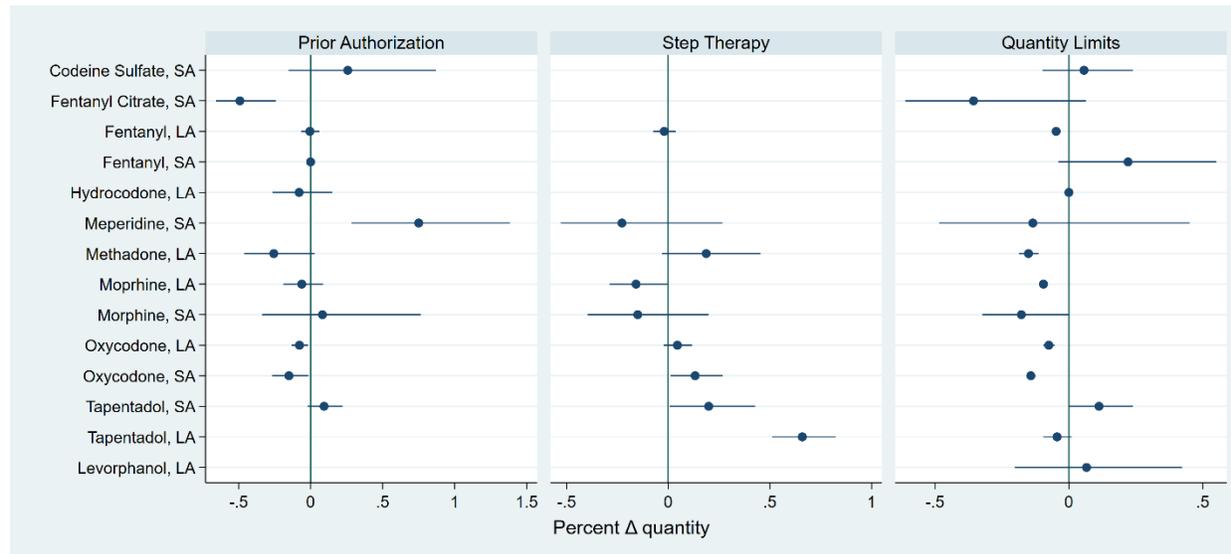
	Baseline		Within 30 days of dispensing date		Include deaths		Include people with cancer diagnosis or hospice use	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Prior Authorization	0.19	-0.33*	0.22	-0.27	1.95**	-0.42	0.36	-0.31*
	[-0.39,0.77]	[-0.62,-0.041]	[-0.37,0.81]	[-0.61,0.061]	[0.64,3.26]	[-1.12,0.28]	[-0.19,0.92]	[-0.59,-0.033]
Step Therapy	0.68	-0.13	0.81	-0.025	1.55*	-0.54	0.51	-0.21
	[-0.20,1.56]	[-0.56,0.30]	[-0.13,1.75]	[-0.50,0.45]	[0.13,2.97]	[-1.33,0.26]	[-0.22,1.23]	[-0.57,0.15]
Quantity limits	0.13***	0.0016	0.11**	0.016	-0.64***	-0.42***	0.092**	0.033
	[0.059,0.19]	[-0.087,0.090]	[0.039,0.18]	[-0.077,0.11]	[-0.76,-0.52]	[-0.57,-0.27]	[0.034,0.15]	[-0.041,0.11]
Mean	0.85	0.85	0.89	0.89	2.77	2.77	0.89	0.89

Predicted means from Poisson (MME, days, and quantity) logistic (overdose) regressions. Adjusted models control for a cubic polynomial in age, gender, race/ethnicity, year, RXHCCs with a prevalence greater than 1%, and the drug dispensed. 95% confidence intervals based on covariance matrix that is clustered on the beneficiary. \*p<.05, \*\*p<.01, \*\*\*p<.001.

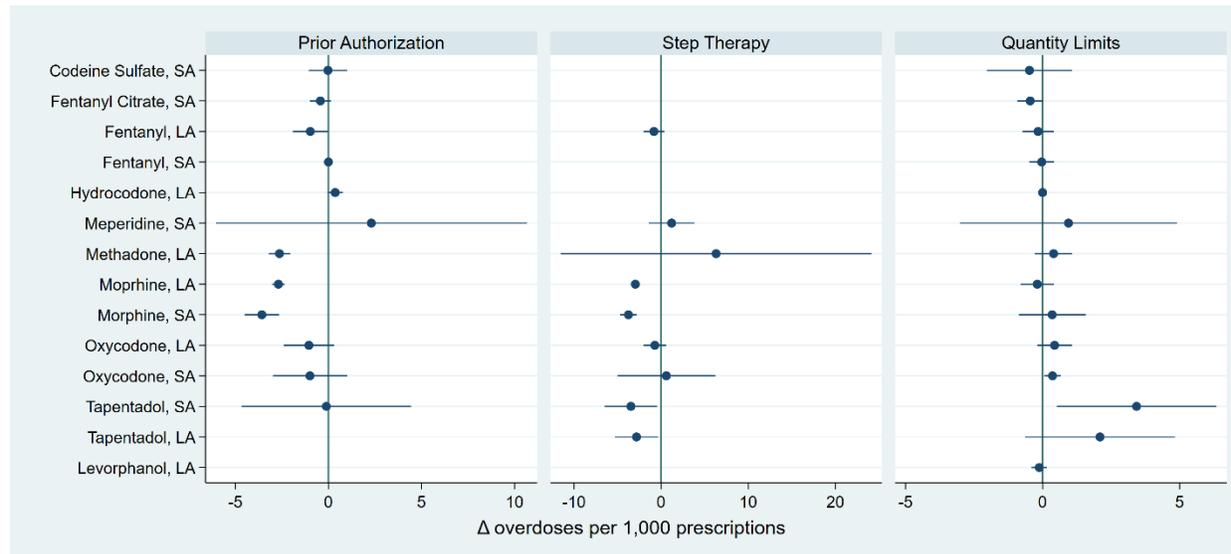
**eAppendix Figure.** Adjusted drug-specific associations between prescription opioid utilization management, opioid volume, prescription length, quantity dispensed, and opioid overdose (n=1866131 beneficiary-years).



c) Percentage change in quantity dispensed



d) Overdoses within 7 days of end of prescription



Models control for a cubic polynomial in age, gender, race/ethnicity, year, RXHCCs with a prevalence greater than 1%, and the drug dispensed. 95% confidence intervals based on covariance matrix that is clustered on the beneficiary.