RESEARCH ARTICLE

Association of opioid fills with centers for disease control and prevention opioid guidelines and payer coverage policies: physician, insurance and geographic factors

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Abstract

Background The Centers for Disease Control and Prevention (CDC) issued guidelines and certain healthcare payers have made pharmacy coverage changes (PCC) focusing on regulating prescription opioids. *Aim* We evaluated differences in the rate of first-time opioid fills at doses ≥ 50 morphine milligram equivalents (MME)/day and first-time opioid fills with benzodiazepine fill overlap following the CDC guidelines and following a PCC between provider types, geographic locations, and insurance types. *Method* We used OptumLabs® Data Warehouse claims data between 2014 and 2018. Subjects were opioid naïve non-cancer care patients, 18 years and older who had an identified chronic pain condition ICD diagnosis within 2 weeks prior to their first-time opioid fill. We used multiple treatment period segmented regression analysis with interaction terms to test the differences between primary care providers (PCPs) and specialist providers (SPs), urban and rural primary care service areas (PCSAs), and Medicare Advantage (MA) and commercially insured patients (CIPs) in their first-time opioid fill patterns. *Results* Prescribing first-time opioid fills at doses ≥ 50MME/day declined following the CDC guidelines and PCC, the decline was greater among SPs than PCPs and in rural PCSAs than urban PCSAs. Also, following the CDC guidelines, the decline was greater among MA patients however following the PCC the decline was greater among CIPs. There were no differences in rate of first-time opioid fill with benzodiazepine overlap between groups. *Conclusion* Responses to the CDC opioid guidelines and a PCC differed between PCPs and SPs, urban and rural PCSAs, and when prescribing to MA and CIPs. Understanding these differences is important to help inform future guidelines.

Keywords CDC opioid guidelines · Insurance type and geography · Opioids · Payer coverage change · Provider specialty

Impacts on practice

- Response to the CDC guidelines and payer coverage change with first-time opioid fills at doses ≥ 50MME per day differed based on provider specialty, patient insurance type and geography. Specialist providers also adopted the CDC guidelines and had a larger decline in rate of first-time opioid fills at doses ≥ 50MME per day than primary care providers following the guidelines.
- Also, following the payer coverage change, decline in rate of first-time opioid fills at doses ≥ 50MME per day was larger in rural PCSAs than urban PCSAs and among commercially insured patients than among the Medicare Advantage patients.
- Understanding these differences is crucial to better refine current guidelines and inform future guidelines and payer coverage change targets.

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- Health payers could be incentivized to create additional policies addressing first-time opioid prescribing at doses ≥ 50MME per day especially in commercially insured patients, because they have a higher level of first-time opioid prescriptions at doses ≥ 50MME per day than Medicare Advantage patients.
- Commercial health payers can provide more guidance and strategies on opioid initiation practices as CMS is doing for Medicare patients.

Introduction

Drug overdose is a leading cause of death among people under 50 years in the US [1], and during the current Covid-19 pandemic, overdose deaths have spiked even further [2]. In 2016, drug overdose resulted in 63,632 deaths, 66% of which involved prescription and illicit opioids (such as heroin and fentanyl) overdose [3]. Following the onset of the Covid-19 pandemic in the US in March 2020, there has been a further spike in drug overdose deaths and 92,476 drug overdose deaths were reported in 2020 [4], with over 60% of the deaths attributed to synthetic opioids [5]. Increase in prescription opioid distribution has been linked with a rise in opioid related deaths [6]. During 2016, greater than 40% of all US opioid overdose deaths involved a prescription opioid [7]. Prescription opioid related overdose deaths were also on the rise and increased by 10.6% between 2015 and 2016 [8]. Primary care (PC) providers and specialists all prescribe opioids, however PC providers account for about 50% of prescribed opioids dispensed [9, 10], and family medicine and internal medicine providers compared to other specialties, are associated with the greatest number of prescription opioid fatalities [11]. Hence, the Centers for disease control and prevention (CDC) in March 2016 released opioid prescription guidelines for chronic pain to PC providers [12] in a bid to reduce the risk associated with opioid prescribing. However, because clinicians often adopt evidence-based recommendations from outside of their own areas of practice [13–16], specialist providers also adopted the CDC guideline [17]. Hence, this study evaluates differences in response to two CDC guideline recommendations on first-time opioid fill patterns between PC and specialist providers. Also, since patient health plans are known to affect physician prescribing habits [18, 19], we also evaluate how changes in first-time opioid fills following the CDC guideline differ between commercially insured patients compared to Medicare Advantage (MA) patients. MA is a Medicare-approved plan from a private company that offers an alternative to traditional fee-for-service Medicare (a public health insurance program in the United States that primarily provides health insurance for persons aged 65 and older) [20] while commercial health insurance is a private health insurance plan typically for persons younger than 65 and is not administered by the government. 67% of Americans have commercial insurance, and 55% of private insurance is employer sponsored [21]. Lastly, the opioid overdose death rate is higher in rural areas than urban areas [22, 23]. However, evidence is scarce regarding whether uptake of the CDC guidelines aimed at reducing overdose deaths differs between rural and urban areas. Primary care service areas (PCSA) are the smallest geographic area that have been mapped out such that most of the of patients living in these areas use primary care services form within the area. Hence, we also evaluate how responses to the CDC guidelines differ between rural and urban PCSAs.

- *CDC Guideline 5* "When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day" [12].
- *CDC Guideline 8* "Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible" [12].

Guideline 5 discouraging starting opioid prescriptions at doses ≥ 50 morphine milligram equivalents (MME) per day aims to mitigate opioid complications which increase at higher doses such as overdose and death [24, 25]. Guideline 8 discouraging starting opioid prescription overlapping with benzodiazepines is crucial since both benzodiazepines and opioids cause respiratory suppression, and when taken together, increases the likelihood of overdose deaths [24]. Studies have shown that the CDC guidelines were associated with reduction in opioid prescription at doses ≥ 50 MME per day and opioid fills with benzodiazepine overlap [26, 27], however it is unknown whether these reductions differed between prescribing provider types, patient insurance types and location in urban or rural primary care service areas (PCSAs).

Some US healthcare payers also implemented payer coverage changes to help reinforce the CDC guidelines. For example, a healthcare payer implemented the following coverage change: on the 1st of March 2018, members new to opioid therapy (no use in the last 120 days) were limited to a maximum dosage of 49 MME per day [28]. Higher doses (≥ 50 MME per day) will still covered for certain circumstances such as pain due to sickle cell crisis [28]. It is unknown whether the changes following this payer

coverage change differ between prescribing provider type, patient insurance type and location in urban or rural primary care service areas (PCSAs).

Aim

Firstly, the study evaluates if the changes in first-time opioid fills at doses ≥ 50MME per day associated with introduction of the CDC guidelines and payer pharmacy coverage change differed between PC providers and specialist providers (see Table 1 for provider specialty classification), Medicare Advantage (MA) and commercially insured patients, and between urban and rural PCSAs.

Secondly, the study evaluates if the changes in first-time opioid fills with benzodiazepine overlap associated with introduction of the CDC guidelines differed between PC providers and specialist providers, MA and commercially insured patients, and between urban and rural PCSAs. For the second aim we only evaluate differences following the CDC guidelines since there was no payer coverage change discouraging opioid fills with benzodiazepine overlap.

Ethics approval

This study was considered IRB exempt by the University of Minnesota Institutional Review Board (IRB ID:

Table 1 Patient and provider characteristics on first-time opioid fill

	N (%)/Mean (SD)
AGE	57.68 (16.52)
MEAN NUMBER OF COMORBIDITIES (ELIXHAUSER)	1.79 (1.96)
SEX	
Female	314,603 (57.1)
Male	236,366 (42.9)
INSURANCE TYPE	
Commercial	325,948 (59.2)
MA	225,021 (40.8)
PCSA	
Urban	457,934 (83.1)
Rural	93,035 (16.9)
CENSUS REGIONS	
South	259,786 (47.1)
Midwest	157,502 (28.6)
West	77,191 (14.0)
Northeast and others	56,490 (10.3)
ALL FIRST-TIME OPIOID FILLS ACROSS PROVIDER SPECIALTIES	
PRIMARY CARE PROVIDER TYPE	*160,447 (29.1)*
Family practice specialty	99,091 (17.9)
Internal medicine specialty	55,507 (10.1)
OB/GYN and Pediatrics specialty	5,849 (1.1)
SPECIALIST PROVIDER TYPE	*233,308 (42.4)*
Emergency medicine specialty	47,729 (8.7)
Internal medicine subspecialist	14,937 (2.7)
Cardiologist, pulmonologist, neurologist, critical care medicine, gastroenterologist, dermatologist, nephrologist, hematologist, geriatrician, rheumatologist, endocrinologist, immunologist, allergist, addiction medicine and infectious disease specialist	
Surgeon specialty	
Thoracic surgeon, colon and rectal surgeon, neurosurgeon, urologist, orthopedic surgeon, oncologist, plastic surgeon, vascular surgeon, general surgeon, hand surgeon and otolaryngologist surgeon	148,205 (26.9)
Other specialists	
Radiologist, rehabilitation medicine, nuclear medicine, neuropathologist, pathologist, ophthalmologist, podiatrist MD and psychiatrist	22,437 (4.1)
OTHER/UNKNOWN PROVIDER TYPE	
Other, unknown specialty	*157,214 (28.5)*

PCSA, Primary Care Service Areas; OB, Obstetrics; GYN, Gynecology

STUDY00012681) on 4/6/2021, because the data was existing and deidentified.

Method

Study population

First-time opioid fills for patients were identified between January 1, 2014 and December 31, 2018 from OptumLabs® Data Warehouse (OLDW) [29] claims database, a nationwide claims database of de-identified administrative medical and pharmacy claims for commercial and MA enrollees containing information on over 100 million enrollees [30]. The database contains longitudinal health information on enrollees and patients, representing a mix of ages, ethnicities, and geographical regions across the United States. Study subjects were required to have 6 months of continuous enrollment with medical and pharmacy coverage prior to their first-time opioid fill—baseline period. The study subjects were also required to be opioid naïve in the baseline period (have no prior opioid fill in the prior 6 months to their current first-time opioid fill). Fills of all first-time opioid doses including tramadol (but excluding buprenorphine and methadone, opioids frequently used to treat opioid addiction) were captured in the study period. Patients with any cancer diagnosis codes or hospice care codes (see appendix (ESM)) in the baseline period were excluded. Patients were required to be 18 years or older and have an identified chronic pain condition ICD (International Classification of Diseases) diagnosis identified via literature review [31–58] and board-certified physician recommendations (see appendix (ESM)) within 2 weeks prior to first-time opioid fill.

Outcome variables

The unit of observation was the first opioid fill per patient in the study period. We had two study outcomes: (1) first-time opioid fills with a starting daily dose ≥ 50 MME per day, calculated using the CDC formula "MME per day = strength per unit x (Number of units/days' supply) x MME conversion factor" [25, 59], and (2) first-time opioid fills with benzodiazepine [60] overlap, indicating when patients had a concurrent benzodiazepine fill days' supply overlapping with their first-time opioid fill day. Outcomes following the CDC guidelines and/or pharmacy coverage changes were evaluated to see if they differed between PC providers and specialist providers, commercially insured and MA patients, and rural and urban PCSAs.

Because the payer coverage change restrict first-time opioid coverage at doses ≥ 50 MME per day, patients may have either opted to pay out of pocket to get higher doses or providers may have reduced their first-time opioid fill doses

to just under 50 MME per day to get covered. Hence, we inspected the dosage distribution of first-time opioid fills before and after the payer policy change to verify whether after the payer coverage change, the first-time opioid fills ≥ 50 MME per day were reduced to just under 50 MME per day (40 to 49MME/day) just so they could be covered.

Exposure measures

The primary exposure variables were CDC guideline release and a payer coverage change. Other covariates included patient age in years at the time of first-time opioid fill, sex, patient insurance type (commercial or MA), residence in an urban or rural primary care service area (PCSA), and number of Elixhauser comorbidities [61] in the baseline period. Each of the Elixhauser comorbidities are flagged as an indicator variable in the baseline and the total number of Elixhauser comorbidities in the baseline are counted per patient and treated as a continuous variable in the models.

Primary care service areas (PCSAs) are standardized systems of known geographical units that measure access to primary care resources, utilization, supply and associated outcomes [62]. Patients were assigned to PCSAs using their zip codes according to the Dartmouth Atlas [63]. A single PCSA is made up of several census tracts. The population-weighted proportion of census tracts that were classified with a USDA rural–urban commuting area (RUCA) codes of 3 or lower [64] was calculated. If the weighted proportion was greater than or equal to 0.75, that PCSA was considered to be metropolitan or urban and if less than 0.75, the PCSA was considered to be non-metropolitan or rural.

Statistical analysis

We used a segmented regression discontinuity linear probability model with interaction terms to test the difference in immediate change in level and monthly change in rate over time in fill of first-time opioid at doses ≥ 50MME/day before and after the CDC guidelines and before and after the payer coverage change between groups (Fig. 1). Similarly, a segmented regression discontinuity linear probability model with interaction terms was used to test the difference in immediate change in level and monthly change in rate over time in fill of first-time opioid fill with benzodiazepine overlap before and after the CDC guidelines between groups. We chose a linear probability model over a logit model to produce readily interpretable estimates and show the difference between groups in how much the fill patterns change after release of the CDC guidelines and a payer coverage change [65–67]. The groups compared are as follows: PC providers and specialist providers, prescribing to commercially insured and MA patients; and patients receiving care in urban and rural PCSAs.
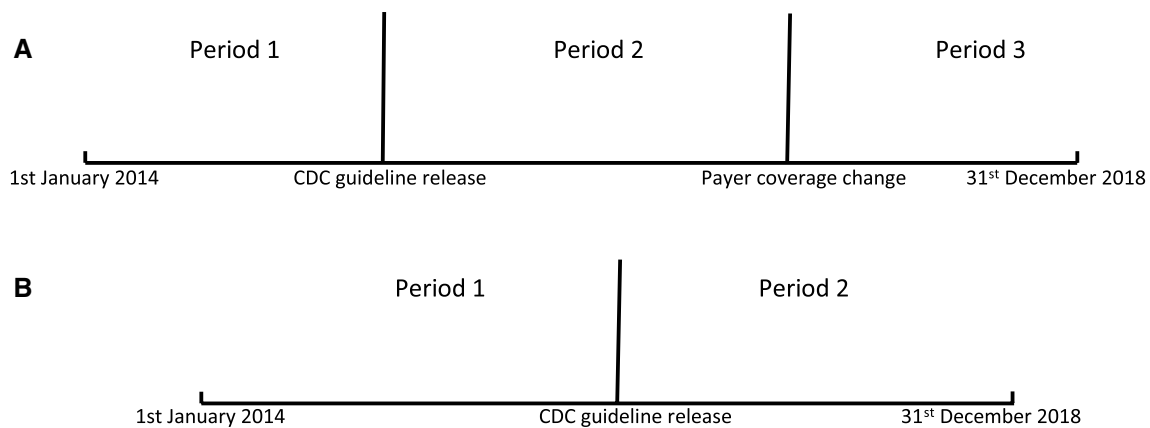
Fig. 1 Three Time Period Diagram for First-time Opioid Dose ≥ 50MME/day and Two Time Period Diagram for First-time Opioid Fill Overlap with Benzodiazepine. Key: CDC guideline release = March 15, 2016, pharmacy coverage change = March 1, 2018, figure A represents the timeline for first-time opioid dose ≥ 50MME/day and figure B represents the timeline for first-time opioid fill overlap with benzodiazepine. The interrupts were the exact months of the issuance of the CDC guideline and the payer coverage change

All models controlled for age, sex and number of Elixhauser comorbidities in the baseline. All analyses were performed using DbVisualizer version 10.0.15 [68] and Stata 14 [69].

Results

As shown in Table 1, the study sample comprised of 550,969 subjects of which 57.10% were female. Mean age was 57.68 (SD 16.52); 59.16% were commercially insured (others had insurance through the MA program); and 83.11% lived in urban PCSAs. The mean number of Elixhauser comorbidities per patient prior to first-time opioid prescription was 1.79 (SD 1.96). Of all first opioid prescription fills during the study period 14.13% had doses ≥ 50MME per day, and 6.39% overlapped with a benzodiazepine fill.

Figure 2 shows the dosage distribution of first-time opioid fills before and after the payer policy change and verifies that indeed after the payer coverage change, the first-time opioid fills ≥ 50 MME per day were reduced to just under 50MME per day (40 to 49MME/day) so they could be covered.

Differences in response between primary care and specialist providers

Table 2 shows the difference between PC versus specialist providers associated changes in first-time opioid fill at doses ≥ 50MME per day and first-time opioid fill with benzodiazepine overlap following the CDC guideline release and payer coverage change.

Following the CDC guideline release, we found no difference in the immediate change in level of first-time opioid fill at doses ≥ 50MME per day between PC and specialist providers, however, specialist providers had a stronger decline in the rate of associated fills (change in trend) than PC providers by 16.55 in every 10,000 fills (CI 8.39 to 24.71, $P < 0.001$). After the payer coverage change in March 2018, specialist providers had a larger immediate decline in level of first-time opioid fills at doses ≥ 50MME per day by 846 per 10,000 (CI 722.65 to 969.95, $P < 0.001$) than PC providers. Following the payer coverage change, specialist providers also had a stronger decline in the rate of associated fills (change in trend) by 93.86 per 10,000 fills (CI 78.90 to 109.42, $P < 0.001$) than PC providers.

With regards to first-time opioid fill with benzodiazepine overlap, following the CDC guideline release, we found no difference in the immediate change in level or change in rate of fills (change in trend) between PC and specialist providers.

Differences in response between commercially insured and medicare advantage patients

Table 3 shows the difference in associated changes in first-time opioid fill at doses ≥ 50MME per day and first-time opioid fill with benzodiazepine overlap following the CDC guideline release and payer coverage change when prescribing to MA compared with commercially insured patients.

Following the CDC guideline release, we found no difference in the immediate decline in level and decline in rate of prescribing (change in trend) of first-time opioid fills at doses ≥ 50MME per day between MA patients compared to commercially insured patients. However,

Table 2 Differences in response to CDC guidelines and payer coverage changes in prescribing first-time opioid dose ≥ 50MME per day and first-time opioid with benzodiazepine overlap between primary care and specialist providers

	First-time opioid dose ≥ 50MME per 10,000 Fills (n = 393,755) [P][CI]	First-time opioid fill with benzodiazepine overlap per 10,000 Fills (n = 393,755) [P][CI]
Specialists pre-CDC guideline slope	10.25 [P < 0.001]	− 2.90 [P = 0.003]
	[6.75 to 13.74]	[− 4.84 to − 0.97]
Primary care minus specialists pre-CDC guideline slope	− 15.49 [P < 0.001]	0.99 [P = 0.515]
	[− 19.80 to − 11.19]	[− 1.99 to 3.97]
Specialists immediate change post-CDC guideline	− 94.53 [P = 0.040]	− 32.64 [P = 0.140]
	[− 184.81 to − 4.25]	[− 75.96 to 10.68]
Primary care minus specialist immediate change post-CDC guideline	62.21 [P = 0.271]	47.28 [P = 0.181]
	[− 48.58 to 172.99]	[− 22.06 to 116.61]
Specialist post-CDC guideline change in slope	− 11.97 [P < 0.001]	− 4.53 [P < 0.001]
	[− 18.63 to − 5.32]	[− 6.73 to − 2.33]
Primary care minus specialist post-CDC guideline change in slope	16.55 [P < 0.001]	− 0.96 [P = 0.590]
	[8.39 to 24.71]	[− 4.44 to 2.52]
Specialists immediate change post-payer coverage change	− 943.81 [P < 0.001]	
	[− 1046.18 to − 841.44]	
Primary care minus specialists immediate change post-payer coverage change	846.30 [P < 0.001]	
	[722.65 to 969.95]	
Specialist payer coverage change in slope	− 121.78 [P < 0.001]	
	[− 134.13 to − 109.42]	
Primary care minus specialist payer coverage change in slope	93.86 [P < 0.001]	
	[78.90 to 109.42]	
Constant	3442.722 [P < 0.001]	890.61
	[3366.76 to 3518.68]	[845.35 to 935.86]

P, P value; CI, 95% Confidence Interval; CDC, Center for Disease Control and Prevention. Models adjusted for patient age, gender, number of Elixhauser comorbidities, insurance type (commercial insurance versus MA) and location in urban or rural primary care service area

Fig. 2 Opioid Dose Distribution Before and After the Payer Coverage Change Note: Pre-payer change period is after the CDC guideline release but before the payer coverage change (April 2016 – February 2018)
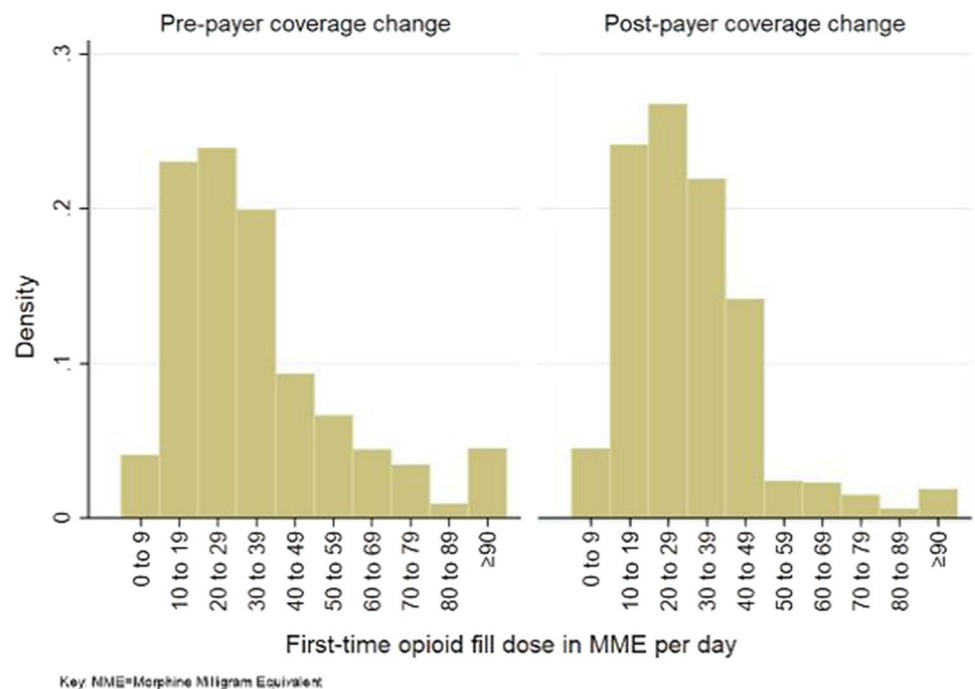
Key: MME=Morphine Milligram Equivalent

Table 3 Differences in response to the CDC guidelines and payer coverage changes in prescribing first-time opioid dose ≥ 50MME per day and first-time opioid with benzodiazepine overlap to MA versus commercially insured patients

	First-time opioid > 50MME All prescribers per 10,000 fills (n = 550,969) [P][CI]	First-time opioid fill with benzodiazepine overlap Per 10,000 fills (n = 550,969) [P][CI]
Commercially insured patients pre-CDC guideline slope	13.15 [$P < 0.001$] [10.51 to 15.78]	− 1.68 [$P = 0.032$] [− 3.22 to − 0.14]
MA insured patients minus commercially insured patients pre-CDC guideline slope	− 5.45 [$P = 0.008$] [− 9.44 to − 1.45]	− 0.13 [$P = 0.926$] [− 2.92 to 2.68]
Commercially insured patients immediate change post-CDC guideline	− 058.10 [$P = 0.118$] [− 130.87 to 14.67]	− 26.86 [$P = 0.146$] [− 63.08 to 9.35]
MA Insured patients minus commercially insured patients immediate change post-CDC guideline	− 54.51 [$P = 0.440$] [− 156.40 to 47.37]	− 11.69 [$P = 0.711$] [− 72.74 to 49.60]
Commercially insured patients post-CDC guideline change in slope	− 7.69 [$P = 0.007$] [− 13.16 to − 2.21]	− 5.59 [$P < 0.001$] [− 7.41 to − 3.77]
MA insured patients minus commercially insured patients post-CDC guideline Change in slope	− 4.26 [$P = 0.070$] [− 11.71 to 3.19]	− 1.08 [$P < 0.495$] [− 7.41 to 3.77]
Commercially insured patients immediate change post-payer coverage change	− 1148.64 [$P < 0.001$] [− 1239.12 to − 1058.15]	
MA minus commercially insured patients immediate change post-payer coverage change	1027.36 [$P < 0.001$] [913.88 to 1140.84]	
Commercially insured patients payer coverage change in slope	− 126.56 [$P < 0.001$] [− 137.08 to − 116.03]	
MA insured patients minus commercially insured patients payer coverage change in slope	111.323 [$P < 0.001$] [97.60 to 125.04]	
Constant	2561.01 [$P < 0.001$] [2500.30 to 2621.73]	926.321 [$P < 0.001$] [889.17 to 963.48]

P, P value; CI, 95% Confidence Interval; PCSA, Primary Care Service Area; CDC, Center for Disease Control and Prevention. Models adjusted for patient age, gender, number of Elixhauser comorbidities, insurance type (commercial insurance versus MA) and location in urban or rural primary care service area

following the payer coverage change there was a stronger immediate decline in level of prescribing first-time opioid fills at doses ≥ 50MME per day to commercially insured patients compared to MA patients by 1027.36 per 10,000 fills (CI 913.88 to 1140.84, $P < 0.001$). Following the payer coverage change, there was also a stronger decline in the rate of fill (change in trend) to commercially insured compared to MA patients by 111.32 per 10,000 fills (CI 97.60 to 125.04, $P < 0.001$).

With regards to first-time opioid fill with benzodiazepine overlap, following the CDC guideline release, we found no difference in the immediate change in level or change in rate of fills (change in trend) between commercially insured and MA patients.

Differences in response between urban and rural PCSAs

Table 4 shows the difference between urban PCSAs and rural PCSAs associated changes in first-time opioid fills at doses ≥ 50MME per day and first-time opioid fills with benzodiazepine overlap following the CDC guidelines and payer coverage change.

Following the CDC guideline release, we found no difference between the immediate change in level or change in rate (change in trend) of first-time opioid fills at doses ≥ 50MME per day between urban and rural PCSAs. However, following the payer coverage change, rural PCSAs had a larger immediate decline in level of first-time opioid fills at doses ≥ 50MME per day than urban PCSAs by 199.98 per 10,000 fills (CI 63.05 to 336.91, $P = 0.004$ but there was no difference between rural and urban PCSAs in the rate of decline (change in trend).

Table 4 Differences in response to the CDC guidelines and payer coverage changes prescribing first-time opioid dose ≥ 50MME per day and first-time opioid with benzodiazepine overlap between urban and rural PCSAs

	First-time Opioid Dose Fill > 50MME per 10,000 Fills (n = 550,969) [P][CI]	First-time Opioid Fill with Benzodiazepine Overlap per 10,000 Fills (n = 550,969) [P][CI]
Rural PCSA Pre-CDC guideline slope	11.65 [P < 0.001] [9.46 to 13.85]	− 2.20 [P = 0.002] [− 3.62 to − 0.79]
Urban PCSA minus rural PCSA Pre-CDC guideline slope	− 102.76 [P = 0.029] [− 12.08 to − 6.51]	3.87 [P = 0.025] [.48 to 7.26]
Rural PCSA immediate change post-CDC guideline	− 102.76 [P < 0.001] [− 160.17 to − 45.34]	− 22.82 [P = 0.165] [− 55.01 to 9.36]
Urban PCSA minus rural PCSA immediate change post-CDC guideline	54.67 [P = 0.438] [− 83.37 to 192.72]	− 49.68 [P = 0.191] [− 124.14 to 24.78]
Rural PCSA post-CDC guideline change in slope	− 10.93 [P < 0.001] [− 15.13 to − 6.723]	− 6.04 [P < 0.001] [− 7.65 to 4.44]
Urban PCSA minus rural PCSA post-CDC guideline change in slope	2.15 [P = 0.673] [− 7.81 to 12.10]	− 2.27 [P = 0.232] [− 6.00 to 1.46]
Rural PCSA immediate change Post-Payer coverage change	− 581.54 [P < 0.001] [− 644.66 to − 518.41]	
Urban PCSA minus Rural PCSA immediate change post-payer coverage change	199.98 [P = 0.004] [63.05 to 336.91]	
Rural PCSA payer coverage change in slope	− 80.35 [P < 0.001] [− 88.04 to − 72.65]	
Urban PCSA minus Rural PCSA payer coverage change in slope	16.02 [P = 0.060] [− 0.66 to 32.71]	
Constant	2544.05 [P < 0.001] [2490.48 to 2597.62]	1057.44 [P < 0.001] [1023.31 to 1091.57]

P, *P* value; CI, 95% Confidence Interval; PCSA, Primary Care Service Area; CDC, Center for Disease Control and Prevention. Models adjusted for patient age, gender, number of Elixhauser comorbidities, insurance type (commercial insurance versus MA) and location in urban or rural primary care service area

With regards to first-time opioid fills with benzodiazepine overlap, following the CDC guideline release, we found no difference in the immediate change in level or change in rate of fills (change in trend) between rural and urban PCSAs.

Discussion

The CDC guidelines currently focus on PC physicians because they account for about half of all prescribed opioids dispensed [9, 10]. However, it is known that healthcare providers adopt knowledge from other specialties to improving clinical practice and patient safety [13–16]. Hence, specialist providers may have adopted the CDC guidelines in addition to the payer coverage change.

We found that compared with PC physicians, specialist providers appeared to have a larger reduction in first-time opioid fills at doses ≥ 50MME per day following the CDC guidelines. Likewise, specialist providers appeared to have a larger reduction in first-time opioid fills at doses ≥ 50MME per days following payer coverage change

than PC providers. This may stem from the fact that specialist providers had a higher rate of first-time opioid fills at doses ≥ 50MME per day prior to the CDC guideline release and payer coverage change, therefore these providers had more room for dose reduction than PC physicians.

Post-CDC guideline release, immediate decline in level or subsequent decline in rate of first-time opioid fills at doses ≥ 50MME per day did not differ between MA and commercially insured patients. However, following the payer coverage change, commercially insured patients had a larger decline in level and rate (change in trend) of first-time opioid fills at doses ≥ 50MME per day than MA patients. This may be due to the more comprehensive nature of the MA plans in lowering cost sharing and increasing access to medications, in contrast, commercially insured patients who are more bound by the payer coverage change. Further encouragement from Center for Medicare and Medicaid services (CMS) through release of additional technical guidance on strategies for reducing first-time opioid fill doses such as that in 2018 [70], may be beneficial in MA plans.

Following both the CDC guidelines and pharmacy coverage change, there was no difference in immediate decline and change in rate (change in trend) of first-time opioids fill at doses ≥ 50MME per day between rural than urban PCSAs. However, following payer coverage change, there was a larger immediate decline in level of first-time opioids fill at doses ≥ 50MME per day in rural than urban PCSAs. This may also be because rural PCSAs had a higher rate of first-time opioid fills at doses ≥ 50MME per day prior to the pharmacy coverage changes, therefore they had more room for dose reduction than urban PCSAs. However, following the payer coverage change, the change in rate of decline (change in trend) of first-time opioid fills at dose ≥ 50MME per day did not differ between rural and urban PCSAs.

Limitations

Our results show an association rather than a causal effect of guidelines and payer/pharmacy coverage changes on provider prescribing behavior, and causality cannot be inferred from observational study designs. In the claims data, we observe only opioid fills, not all written prescriptions by providers, and the data may be missing fills for patients who pay out of pocket. Finally, our analysis evaluates at the national level and may not have accounted for some state level policies on opioid prescribing during the study period (For example, Nevada and Arizona limit opioid prescribing doses to 90 MMEs per day, Maine limits to 100 MME per day, and Rhode Island limit to 50 MME per day) [71]. Similarly, healthcare organizations may have specific policies we are not able to observe.

Conclusion

The study leveraged a large US claims database with a large sample size to show that response to the CDC guidelines and payer coverage change with first time opioid fills at doses ≥ 50MME per day differed between provider specialty. Understanding these differences is crucial to better refine current guidelines and inform future guidelines and payer coverage change targets. Likewise, factors that influence response to guidelines such as patient insurance types and location in urban or rural PCSAs should also be considered when developing future guidelines. Health payers could also be incentivized to create more policies addressing first-time opioid prescribing behavior, especially in commercially insured patients, because they have a higher level of being prescribed first-time opioids at doses ≥ 50MME per day. Commercial payers could provide more guidance and strategies on opioid initiation practices as CMS is doing for Medicare patients. Clinical pharmacists can also help

counsel patients on recommended guidelines and opioid risks during opioid dispensing.

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