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Opioid Prescriptions in Older Medicare Beneficiaries After the 2014 Federal Rescheduling of Hydrocodone Products

Yong-Fang Kuo, PhD^{*,†,‡,§}, Mukaila A. Raji, MD^{*,†,‡}, Victor Liaw[¶], Jacques Baillargeon, PhD^{‡,§}, and James S. Goodwin, MD^{*,†,‡,§}

^{*}Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas

[†]Sealy Center on Aging, University of Texas Medical Branch, Galveston, Texas

[‡]Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, Texas

[§]Institute for Translational Science, University of Texas Medical Branch, Galveston, Texas

[¶]College of Natural Sciences, University of Texas at Austin, Austin, Texas

Abstract

OBJECTIVES—To examine how an October 2014 Drug Enforcement Administration policy reclassified hydrocodone product from schedule III to II has affected older adults, who are among the largest consumers of prescription opioids in the United States.

DESIGN—Retrospective cohort study.

SETTING—United States.

Address correspondence to Yong-Fang Kuo, PhD, Department of Preventive Medicine and Community Health, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX. yokuo@utmb.edu.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Appendix S1. The steps for cohort construction.

Appendix S2. Rates of opioid prescription by type of opioid in 2013 and 2015.

Appendix S3. Characteristics of Medicare enrollees in 2013 and 2015.

Appendix S4. Adjusted prevalence ratios for any, prolonged, and high-dose opioid prescription, 2013 versus 2015.

Appendix S5. Absolute and relative changes in rates of any opioid prescriptions from 2013 to 2015, by participant characteristics.

Appendix S6. Absolute and relative changes in rates of high-dose opioid prescriptions from 2013 to 2015, by participant characteristics.

Appendix S7. Absolute and relative changes from 2013 to 2015 in prolonged opioid prescriptions, by state.

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PARTICIPANTS—A 20% sample of Medicare Part D beneficiaries aged 65 and older from 2013 through 2015 (> 2,500,000 beneficiaries each year)

MEASUREMENTS—From January 2013 to December 2015, we calculated the monthly prevalence of opioid prescriptions and the prevalence of individuals who received prescriptions for a 90-day supply or longer (prolonged), as well as hospitalizations related to opioid toxicity in 2013 and 2015.

RESULTS—From 2013 to 2015, the proportion of Medicare Part D enrollees who received a hydrocodone prescription in a year decreased from 21.9% to 18.3%. Monthly rates for hydrocodone prescriptions declined significantly in 2014. The risk of receiving prolonged opioid prescriptions decreased by approximately 7% in the multivariable analyses comparing 2015 to 2013 (prevalence ratio=0.93, 95% confidence interval (CI)=0.93–0.94). Medicare enrollees with an original entitlement because of disability or with Medicaid eligibility had smaller decreases in prolonged prescriptions and, unexpectedly, small increases in high-dose prescriptions. Opioid-related hospitalizations did not change significantly, but opioid-related hospitalizations without a documented opioid prescription increased (odds ratio=1.24, 95% CI=1.03–1.50).

CONCLUSION—The 2014 change in hydrocodone from schedule III to schedule II was associated with modest decreases in rates of opioid use in the elderly. The unexpected increase in opioid-related hospitalizations without documented opioid prescriptions may represent an increase in illegal use.

Keywords

Opioid; Medicare; Overdose; Regulation

The number of Americans addicted to and dying from prescription opioids has reached an epidemic level.^{1–3} This crisis has stimulated growing public awareness and regulations, including expansion of prescription drug monitoring programs, prescriber education in opioid use and safe prescribing, and new state and federal laws and policies.^{4–15} In October 2014, the U.S. Drug Enforcement Administration (DEA) reclassified all hydrocodone products from schedule III to schedule II,^{16,17} with a prescription limit of a 30-day supply and no refills allowed.

Several single-center studies showed a decrease in opioid prescribing rates after the rescheduling.^{18–21} A national study using data from U.S. pharmacies also reported a decrease in prescribing rates for hydrocodone and prescription opioids overall from 2011 to 2015.²² In our previous study using national commercial health insurance data for individuals aged 18 to 64, we reported a 26% relative decrease in hydrocodone prescribing and an 11% relative decrease in total opioid prescribing from 2013 to 2015.²³

No previous studies have focused on the effect of the hydrocodone rescheduling on the older Medicare population. Medicare enrollees are at least 5 times as likely to be diagnosed with opioid abuse as commercial health insurance enrollees.²⁴ Older adults are particularly susceptible to toxicity and adverse effects from opioid use.^{25–30} Understanding the effect of regulating opioid accessibility for Medicare enrollees, particularly those with prolonged prescriptions, is critical to the development of effective public health interventions.

The current study examined the association between the hydrocodone rescheduling policy and changes in opioid prescribing rates and related outcomes from 2013 to 2015 for older Medicare Part D beneficiaries. We hypothesized that the 2014 rescheduling would be associated with declines in opioid prescriptions. We also hypothesized that hospitalizations from opioid overdoses would decrease. Our primary focus was to assess prescriptions for prolonged use—defined as at least 90 days supply in a year—but we also report on prescriptions for any opioid and for high-dose opioids.

METHODS

Source of Data

This was a retrospective cohort study using enrollment and claims data for a 20% national sample of Medicare beneficiaries enrolled between 2012 and 2015. This included Medicare beneficiary summary files, Medicare Provider Analysis and Review files, Outpatient Standard Analytic Files, Medicare Carrier files, and Prescription Drug Event files. The University of Texas Medical Branch Institutional Review Board approved the research.

Establishment of the Study Cohorts

We constructed different study cohorts for different outcomes. The steps for each cohort generation are included in Supplementary Appendix 1.

Opioid Prescription

We used National Drug Code, product name, therapeutic class description, and DEA class code from the 2015 Red-Book Select Extracts database to classify opioid treatment into the following categories: hydrocodone, nonhydrocodone schedule II opioids, nonhydrocodone schedule III opioids, and tramadol. Opioids given by injection were not included in the study.

We categorized opioid users as enrollees who had at least one opioid prescription in the study year. Prolonged opioid prescription was defined as having a 90-day supply or longer in a study year. To determine high-dose prescriptions, we calculated the daily morphine milligram equivalent dose (MME), which summarizes opioids with different ingredients and strengths to estimate the daily opioid level.³¹ The formula for MME is [(strength per unit) x (quantity prescribed) x (MME conversion factor)]/(daily supply).

We classified enrollees who had an opioid supply of 100 MME or more per day for longer than 30 days in 1 year as high-dose users. For example, a 100 MME is equivalent to approximately 100 mg of hydrocodone per day.

Outcomes of Opioid Use

Acute hospitalization related to potential overdose was identified using *International Classification of Diseases, Ninth Revision* (ICD-9) discharge diagnoses at any position listed in the claim, including opioid-related poisoning (965, E850.1, E950.0, E980.0) or opioid-specific adverse event (E935.0, E935.1, E935.2) plus an overdose diagnosis (276.4, 292.1, 292.8, 486, 496, 518.81, 518.82, E950-E959) from the same admission.²⁸

Beneficiary and Regional Characteristics

Medicare enrollment files provided information on beneficiary age, sex, race and ethnicity, and original entitlement. We used a Medicaid indicator in the enrollment file as a proxy for low income. Education and household income were obtained according to ZIP code from the 2011 to 2015 American Community Survey³² and categorized according to quartile. Elixhauser comorbidity measures³³ were generated from all claims in the 12 months before each study year and categorized according to number of morbidities (0, 1, 2, 3). We categorized type of residential area into metropolitan, nonmetropolitan urban, and rural using Rural-Urban Continuum Codes.³⁴

Statistical Analyses

The proportion of beneficiaries with opioid prescriptions in each category (any opioid, hydrocodone, nonhydrocodone schedule II, nonhydrocodone schedule III, tramadol) was calculated according to month from January 2013 to December 2015. For each beneficiary at each month of study, we used a 90-day look-back period to examine the most recent prescription date and the total days' supply of that prescription. Beneficiaries who had at least 1 day of opioid supply available in the month under study contributed to the numerator of the prevalence estimate for that month. We then analyzed the monthly trend of any opioid prescription using an interrupted time-series model. In this analysis, we examined the change in trend across three time periods: preimplementation (2013), implementation (2014), and postimplementation (2015).

We also calculated the proportion of beneficiaries receiving any opioid prescriptions, prolonged opioid prescriptions, and high-dose prescriptions in 2013 and 2015. These were further stratified according to participant and regional characteristics for each study year. Modified Poisson regression models—adjusted for the fixed effect of states, participant and regional characteristics, months of follow-up, and clustering effect within beneficiaries—were constructed to evaluate the prevalence ratio in these prescriptions measured and hospitalizations for opioid toxicity between 2013 and 2015. For beneficiaries with overdose hospitalizations, we calculated and compared the proportion of those who did not receive an opioid prescription preceding at least 1 day's supply in the 6 months before their first hospitalization using logistic regression. All tests of statistical significance were two sided. Analyses were performed using SAS Enterprise version 7.12 at the CMS Virtue Research Data Center (SAS Institute, Inc., Cary, NC). Maps were constructed using ArcGIS 9.3 (Esri, Redlands, CA).

RESULTS

Opioid Prescription in the Medicare Population from 2013 to 2015

In December 2013, the DEA announced their intention to move hydrocodone from schedule III to II. The final rule was published in August 2014 and implemented in October 2014. Figure 1 shows the monthly rate of hydrocodone, schedule II (excluding hydrocodone), schedule III (excluding hydrocodone), and tramadol prescriptions from January 2013 through December 2015. For hydrocodone prescription and prescriptions of any opioid, the rates appear stable in 2013 and the first half of 2014, followed by a decrease in rate in

September through November, followed by a stable rate in 2015. With the interrupted time series analysis applied to the preimplementation (2013), implementation (2014), and postimplementation (2015) periods, the slope of the monthly rate in 2013 and 2015 did not differ significantly from 0. In 2014, the slope was -0.079% per month (95% confidence interval (CI) $= -0.102$ to -0.055 , $p < .001$).

All subsequent analyses compared rates in 2013 and 2015. Supplementary Appendix 2 shows the change between 2013 and 2015 in rates of prescriptions for the different types of opioids. The hydrocodone prescribing rate decreased from 21.9% in 2013 to 18.3% in 2015. There were small but significant increases in nonhydrocodone schedule II and III prescribing (from 10.2% to 10.6% for schedule II, from 3.3% to 4.0% for schedule III, each $p < .001$). The tramadol prescribing rate was unchanged. Prescriptions for any opioid decreased from 37.0% in 2013 to 34.9% in 2015. The MME per person year for all Medicare beneficiaries (with and without opioid prescriptions) decreased from 102 mg in 2013 to 91 mg in 2015. Medicare enrollees in 2015 were slightly younger than those in 2013 and had higher socioeconomic status and fewer comorbidities (Supplementary Appendix 3). In multivariable analyses adjusting for these participant and regional characteristics, the risk of receiving any opioid prescription in 2015 was 4.3% (prevalence ratio (PR) $= 0.957$, 95% CI $= 0.955$ – 0.959) lower than in 2013 (Supplementary Appendix 4). The risk of receiving prolonged (PR $= 0.934$, 95% CI $= 0.931$ – 0.937) and high-dose (PR $= 0.931$, 95% CI $= 0.919$ – 0.944) prescriptions in 2015 was 7% lower than in 2013 (Supplementary Appendix 4).

In 2013, 10% of Medicare enrollees with aging as their original entitlement and approximately 27% of those with disability as their original entitlement received prescriptions for prolonged opioid use. Table 1 presents the rates and absolute and relative decreases in the percentage of enrollees receiving prolonged opioid prescriptions between 2013 and 2015, stratified according to participant and regional characteristics. The subpopulations that were white and aged 75 to 84, had disability as the reason for their original Medicare entitlement, were Medicaid eligible, and had more comorbidities experienced smaller relative decreases between 2013 and 2015. Beneficiaries living in rural areas had the smallest decreases in prolonged prescriptions received. Results of similar analyses for any opioid and high-dose opioid prescriptions are presented in Supplementary Appendices 5 and 6. Those with disability as the reason for their original Medicare entitlement and those who were Medicaid eligible unexpectedly had small increases in high-dose prescriptions.

Prolonged Opioid Prescription According to State in 2013 and 2015

Figure 2 shows the rates of prolonged opioid prescriptions according to state before (Figure 2A) and after (Figure 2B) the hydrocodone reschedule. The colors of the maps divide states according to quintile of the 2013 rates of prolonged opioid prescribing. In 2013, the lowest rate was in Hawaii (3.6%), and the highest rate was in Alabama (20.0%). By 2015, only 4 states remained in the top quintile, whereas 26 were in the bottom 2 quintiles. There were also differences between states in absolute changes from 2013 to 2015, from a 3.5% decrease in Alabama to a 0.2% decrease in North Dakota (Supplementary Appendix 7).

Individual Changes in Receipt of Opioid Prescriptions

We next examined changes in opioid prescriptions received in 2013 and 2015 at the individual level. Of enrollees who received an opioid prescription in 2013, 61.5% also received an opioid prescription in 2015. More than 75% of enrollees who received prolonged prescriptions in 2013 continued to receive prolonged prescriptions in 2015, whereas 10% received no opioid prescriptions in 2015. Only 5% of those who received high-dose prescriptions in 2013 received no prescriptions for opioids in 2015.

Association Between Hydrocodone Rescheduling and Hospitalizations Related to Opioid Overdose

The rate of opioid-related hospitalizations dropped from 56.4 per 100,000 in 2013 to 51.8 per 100,000 in 2015 (Table 2). After adjusting for participant and regional characteristics, length of observation, the fixed effect of states, and the clustering effect within beneficiaries, the relative risk of hospitalization in 2015 was insignificantly lower (PR=0.94, 95% CI=0.88–1.01) than in 2013. Beneficiaries on Medicare because of disability were approximately twice (PR=2.12, 95% CI=1.94–2.32) as likely as aging-entitled beneficiaries to have been hospitalized. In addition, beneficiaries with more morbidities had a much higher risk of hospitalization (e.g., PR=8.74, 95% CI=7.70–9.93 for beneficiaries with 3 morbidities vs those with no morbidity). Beneficiaries who were female, white, Medicaid eligible, or of lower socioeconomic status and those who were metropolitan residents were also at greater risk of hospitalization. Of Medicare beneficiaries hospitalized for opioid toxicity in 2013, 18.9% had received no opioid prescription in the 6 months before hospitalization. This percentage increased to 22.1% in 2015. In adjusted analyses, the adjusted odds of not having an opioid prescription for beneficiaries with opioid-related hospitalizations increased 24% from 2013 to 2015 (OR=1.24, 95% CI=1.03–1.50).

DISCUSSION

The 2014 rescheduling of hydrocodone was associated with decreases in rates of opioid prescription in Medicare beneficiaries aged 65 and older. The great majority of those who received prolonged or high-dose prescriptions in 2013 continued to receive prolonged or high-dose prescriptions in 2015, and only a small proportion discontinued opioid use entirely in 2015. The relative decreases between 2013 and 2015 that we observed were somewhat smaller than previously reported in other populations.^{18–23} Using pharmacy data, one study²² reported a 22% fewer dispensed hydrocodone combination product prescriptions in the 12 months after than the 12 months before rescheduling. We have previously reported a 26% relative decrease in hydrocodone prescriptions from a monthly rate of 2.7% in 2013 to 2.0% in 2015 in a commercially insured population aged 18 to 64.²³ This compares with a 18.7% relative decrease in monthly rate of hydrocodone prescription from 7.2% in 2013 to 5.8% in 2015 that we found in the older Medicare population. When comparing populations, assessing absolute and relative change is important. Younger populations have lower rates of opioid prescription use, so smaller absolute decreases can result in large relative changes.

Although some single centers reported an increase in tramadol prescribing after the rescheduling,^{18–20} our findings of no change in tramadol prescribing are similar to our previous nationwide study in a younger, commercially insured population.²³

A number of other national efforts to reduce opioid abuse accompanied the hydrocodone rescheduling.^{6–15} The continued opioid epidemic despite these federal and state actions underscores the need for continuing community-wide education on the risks and limitations of opioids for chronic noncancer pain and prescriber education, starting in medical and nursing schools, on safe opioid prescribing and recognition of individuals at high risk of opioid use disorder.^{4,5,35–39} According to the 2016 Centers for Disease Control and Prevention guidelines for safe opioid prescribing for individuals without cancer, prescribers should keep opioid duration to less than 7-day use and consider discontinuation in long-term users.³⁵ It is important for prescribers to understand who these individuals are and why their opioid use persists.

One example from our study of a population at risk of prolonged use is disability-entitled beneficiaries, who experienced smaller decreases in prolonged or high-dose prescriptions received after the rescheduling of hydrocodone. These enrollees were aged 65 and older but had originally become eligible for Medicare before age 65 because of disability. Among Medicare enrollees aged 65 and older, the 10% who have disability as an original entitlement comprised 25% of prolonged opioid users and 40% of high-dose users in 2015. One explanation for the high rate of risky opioid use among disability-entitled enrollees is the clustering of known risk factors—mood disorders, cognitive disability, and back pain-related disorders—associated with opioid misuse.^{40,41}

A recent study reported that over half of all opioids prescribed in the United States were given to individuals with mental health disorders.⁴¹ High rates of chronic pain and heightened pain perception in this population, especially in the context of depression and addiction, suggest the need for a biopsychosocial interdisciplinary management approach to pain management, including case management and monitoring.^{29,36,42–44} Such an approach would need to address not only the pain syndrome, but also the myriad coexisting cognitive, emotional, physical, social, economic, and environmental drivers of high-risk opioid-related behaviors. This approach would also require substantial increases in funding from federal and commercial insurance to address current needs.

The 2014 hydrocodone rescheduling was associated with a small increase in high-dose opioids in the Medicaid-eligible Medicare population. This population tends to have low income and poor health status. It is possible that high-dose opioid prescriptions may serve economic and coping purposes.^{42–45} An economic purpose may relate to monetary gains from diversion and sale to others. Using prescription opioids may represent potentially pathological coping attempts to palliate despair and hopelessness associated with socioeconomic disadvantage, poor physical and mental health, and inability to work.

The introduction of the FDA regulations restricting extended-release and long-acting opioids and state-initiated programs of expanding access to opioid antidotes without prescription may lead to decreases in opioid-related hospitalizations,^{46,47} but our study did not find a

significant decrease in opioid-related hospitalizations from 2013 to 2015, although there was a nonsignificant 6% decrease in the adjusted PR. In a subgroup analysis, the proportion of those hospitalizations in which the beneficiary did not have a documented opioid prescription increased by 24% in the same period. It is important for prescribers to understand that their elderly Medicare beneficiaries might be obtaining opioids from sources that are not documented in their medical records. There is a need for additional research on why, where, and how these Medicare enrollees are obtaining opioids.^{36,48}

The study has limitations. First, Medicare Part D data do not contain information on whether beneficiaries took their prescribed opioids. Second, the indication for the opioid prescription is not available in Part D data. Third, information on severity of pain was not available. Although we doubt that overall pain prevalence changed substantially between 2013 and 2015 in the Medicare population, information about pain severity would allow investigators to better identify situations in which opioids are clearly not indicated. Fourth, we excluded beneficiaries with health maintenance organization enrollment and those without Part D coverage. Our results may not be generalizable to other Medicare populations. Also, the number of Medicare Part D enrollees has increased over time.⁴⁹ The 2013 and 2015 cohorts differed according to beneficiary characteristics (Supplementary Appendix 3). We controlled for these differences in our multivariable analyses. Fifth, states vary considerably in the stringency of regulations on opioid prescribing,⁵⁰ but we included states as a fixed effect in our multivariable analyses. Sixth, we did not include prescriber-level factors in this study. Providers play the ultimate role in opioid prescribing. This topic will require extensive additional analyses in further studies. Last, it is likely that our study underestimated total use of opioids because of the exclusion of opioid injections and lack of information on opioids obtained from sources other than prescriptions.

CONCLUSION

The 2014 hydrocodone rescheduling was associated with modest decreases in hydrocodone and overall opioid prescribing rates, but opioid-related hospitalizations did not decrease significantly. Also, high-risk groups such as disabled individuals did not experience decreases in opioid rates. As policy experts and clinicians move forward in their search for the proper balance between pain control and opioid overprescribing, refining public policy and clinical practice to target high-risk groups will be critical to reducing opioid overuse and adverse events.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Monthly opioid prescriptions according to type of opioid from January 2013 to December 2015. Points represent the rate of opioid supply for hydrocodone, schedule II drugs excluding hydrocodone, schedule III drugs excluding hydrocodone, tramadol, and any opioid supply during the month.

A:2013

B:2015

Figure 2.

Rates of prescriptions for prolonged opioid use before and after hydrocodone rescheduling in the 50 U.S. states in (A) 2013 and (B) 2015 based on quintiles of 2013 rates. [Color figure can be viewed at wileyonlinelibrary.com]

Absolute and Relative Changes in Rates of Prolonged Opioid Prescriptions from 2013 to 2015 According to Participant Characteristic

Table 1

Characteristic	n (%)		Change, %		P-Value ^d
	2013	2015	Absolute	Relative	
Overall	311,818 (11.9)	326,696 (10.7)	-1.2	-10.2	
Age					<.001
66–74	131,155 (11.7)	143,562 (10.4)	-1.3	-11.2	
75–84	111,157 (11.6)	114,295 (10.5)	-1.0 ^b	-9.0	
85	69,506 (13.0)	68,839 (11.7)	-1.2 ^b	-9.6	
Original Medicare entitlement					<.001
Age	234,646 (10.1)	244,601 (8.9)	-1.1 ^b	-11.3	
Disability	76,201 (26.7)	81,075 (25.6)	-1.0 ^b	-3.9	
End-stage renal disease	971 (19.1)	1,020 (16.8)	-2.3	-12.0	
Sex					.002
Male	82,727 (9.1)	93,287 (8.3)	-0.8	-8.8	
Female	229,091 (13.4)	233,409 (12.1)	-1.3	-9.9	
Race					<.001
White	257,712 (11.9)	277,158 (10.8)	-1.2 ^b	-9.7	
Black	29,435 (15.6)	27,961 (13.2)	-2.4	-15.5	
Hispanic	16,793 (11.0)	13,769 (9.8)	-1.2	-11.0	
Other	7,878 (6.7)	7,808 (5.9)	-0.8	-12.5	
Medicaid eligible					<.001

Characteristic	n (%)		Change, %		P-Value ^a
	2013	2015	Absolute	Relative	
Yes	118,688 (19.5)	99,853 (19.1)	-0.5 ^b	-2.4	
No	193,130 (9.6)	226,843 (9.0)	-0.6	-6.7	
ZIP code education quartile					<.001
1 (low)	91,114 (15.1)	97,292 (13.8)	-1.3	-8.6	
2	85,337 (13.5)	88,606 (12.0)	-1.5	-11.2	
3	75,458 (11.2)	77,727 (10.0)	-1.3 ^b	-11.3	
4 (high)	59,909 (8.4)	63,071 (7.6)	-0.8	-10.0	
ZIP code income quartile					<.001
1 (low)	94,211 (16.2)	99,980 (14.6)	-1.5 ^b	-9.4	
2	84,840 (13.3)	89,185 (12.0)	-1.4 ^b	-10.4	
3	75,031 (11.1)	77,948 (9.9)	-1.2	-11.1	
4 (high)	57,736 (7.9)	59,583 (7.1)	-0.9 ^b	-10.8	
Location					<.001
Metropolitan	223,422 (11.1)	235,771 (10.0)	-1.2 ^b	-10.7	
Urban	77,632 (14.4)	79,881 (13.2)	-1.2	-8.4	
Rural	10,764 (14.1)	11,044 (13.3)	-0.8	-5.4	
Number of morbidities					<.001
0	56,515 (6.0)	58,347 (5.3)	-0.7	-12.4	
1	74,569 (10.6)	77,715 (9.5)	-1.1	-10.2	
2	59,363 (14.4)	62,895 (13.0)	-1.4	-9.6	

Characteristic	n (%)		Change, %		P-Value ^a
	2013	2015	Absolute	Relative	
3	121,371 (21.4)	127,739 (19.5)	-1.9	-8.8	

^aFrom modified Poisson regression model to examine interaction between each characteristic and year of observation. The model tested whether the relative changes in each category (e.g., age group) were different from each other. There were 2.62 million person-years in 2013 and 3.06 million in 2015. The n's given are the number of enrollees with each characteristics who received a prescription for prolonged opioid use.

^bInconsistencies in absolute changes are due to rounding.

Table 2

Risk of Probable Opioid Toxicity Hospitalization According to Beneficiary Characteristic and Year of Observation

Characteristic	Probable Opioid Toxicity Hospitalization		
	n	Per 100,000	Adjusted Prevalence Ratio ^a (95% Confidence Interval)
Year			
2013	1,499	56.35	1.00
2015	1,608	51.79	0.94 (0.88–1.01)
Age			
66–74	1,357	53.62	1.00
75–84	1,082	52.18	0.92 (0.85–1.00)
85	668	57.56	0.91 (0.83–1.01)
Original Medicare entitlement			
Age	2,228	43.36	1.00
Disability	859	139.74	2.12 (1.94–2.32)
End-stage renal disease	20	173.76	1.94 (1.24–3.03)
Sex			
Male	886	42.85	1.00
Female	2,221	60.07	1.32 (1.22–1.43)
Race			
White	2,685	55.99	1.00
Black	211	51.15	0.57 (0.49–0.66)
Hispanic	124	41.04	0.52 (0.42–0.63)
Other	87	34.22	0.57 (0.46–0.72)
Dually eligible			
Yes	1,056	90.62	1.45 (1.33–1.58)
No	2,051	44.59	1.00
Zip code income quartile			
1 (low)	767	59.49	1.13 (1.00–1.27)
2	784	55.87	1.10 (0.98–1.23)
3	825	55.62	1.12 (1.01–1.24)
4 (high)	731	46.00	1.00
Location			
Metropolitan	2,443	54.98	1.00
Urban	595	51.32	0.83 (0.75–0.92)
Rural	69	42.64	0.71 (0.55–0.91)
Morbidities			
0	309	15.02	1.00
1	483	31.51	2.04 (1.76–2.35)

Characteristic	Probable Opioid Toxicity Hospitalization		
	n	Per 100,000	Adjusted Prevalence Ratio ^a (95% Confidence Interval)
2	477	52.28	3.27 (2.83–3.79)
3	1,838	145.65	8.74 (7.70–9.93)

^aFrom modified Poisson regression model including year of observation, participant characteristics listed in table, months of observation, fixed effect of states, and clustering effect within participants.