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Decline in opioid prescribing after federal rescheduling of hydrocodone products

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Abstract

Purpose—To examine differences in opioid prescribing by patient characteristics and variation in hydrocodone combination product (HCP) prescribing attributed to states, before and after the 2014 Drug Enforcement Administration's reclassification of HCP from schedule III to the more restrictive schedule II.

Methods—We used 2013–2015 data for 9,202,958 patients aged 18 to 64 from a large nationally representative commercial health insurance program to assess the temporal trends in the monthly rate of opioid prescribing.

Results—HCP prescribing decreased by 26% from June 2013 to June 2015; the rate of prescriptions for any opioid decreased by 11%. Prescribing of non-hydrocodone schedule III opioids increased slightly while prescribing of non-hydrocodone schedule II opioids and tramadol was stable. Absolute decreases in HCP prescribing rates were larger in patients being treated for cancer (−2.26% vs −0.7% for non-cancer patients, P<0.0001) and in those with high comorbidities (−2.13% vs −0.55% for those with no comorbidity, P<0.0001). Differences in the absolute and relative changes in HCP prescribing rates among states were large; for example a relative decrease of 46.7% in Texas and a 12.7% increase in South Dakota. The variation in HCP prescribing attributable to the state of residence increased from 6.6% in 2013 to 8.7% in 2015.

Conclusions—The 2014 federal policy was associated with a decrease in rates of HCP and total opioid prescribing. The large decrease in the rates of HCP prescribing for patients with actively treated cancer may represent an unintended consequence.

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Conflicts of Interest: None.

Keywords

Opioids; Laws; Public Policy

INTRODUCTION

The rise in the prescribing of opioid analgesics for chronic non-cancer pain over the last decade has contributed to the epidemic of opioid-related addiction, overdose, and mortality in the US.[1–4] State laws and federal policies implemented to curb this epidemic have had varying effects.[5–14] The prescribing of schedule II opioids (classified as high abuse potential) is more tightly regulated by federal rules. Individual states have more input in regulating the prescribing of schedule III opioids (classified as moderate abuse potential). For example, states can make additional laws to make schedule III opioids prescribing almost as restrictive as schedule II.[5, 7, 9–14] Previous studies showed that inter-state variation was smaller for schedule II than for schedule III opioids, suggesting a larger impact of federal policies on the former.[7, 10]

In 2014, the Drug Enforcement Administration (DEA) reclassified all hydrocodone combination products (HCP), the most frequently prescribed opioids in the US, from schedule III to schedule II.[15–17] This limited all new HCP prescriptions to a maximum 30-day supply with no refills. A study based on data from US pharmacies showed a 22% decline in hydrocodone combination prescriptions and a 5% increase in non-hydrocodone opioid prescriptions within 12 months of the 2014 federal DEA policy.[18] Studies from single center health systems or poison centers reported similar changes.[19–24].The current study used data for patients aged 18 to 64 years from a large national commercial health insurance program to examine the impact of the 2014 federal policy on opioid prescribing by patient characteristics and across states.

Studying the effect of the 2014 federal policy in this population is important because persons aged 18 to 64 represent a high-risk population for opioid-related toxicity.[25, 26] This population demonstrated a significant and progressive increase—from 2003 to 2013—in the prevalence of prescription opioid use disorders, frequency of use, and overdose deaths.[26] In addition, the commercial insurance cohort under study represents a population with considerable access to prescription opioids. Any policy that restricts prescribing or affects refilling of specific prescription opioids, as in the 2014 federal policy, has potential to affect prescribing of opioid analgesics in this population.

We hypothesized that the 2014 federal policy would be associated with declines in HCP prescribing. We also hypothesized that there would be a larger decrease in HCP prescribing for non-cancer pain patients than for cancer patients.[2, 3, 15] Lastly, we hypothesized that there would be a decrease in the state-to-state variation in HCP prescribing with the increase in federal regulation.

METHODS

Study Design and Data Sources

We conducted a retrospective cohort study using de-identified administrative health data from Clinformatics Data Mart™ (CDM, Optum Insight, Eden Prairie, MN).[27] Data analyzed were from: the Member file, which includes information on demographic factors, region of residence, and insurance enrollment date; the Medical file, which includes all inpatient and outpatient encounter information, including diagnosis codes, procedure codes, and encounter dates; and the Pharmacy file, which includes medication name, date of fill, formulation, dose, quantity, and days of supply.

Study Population and Variables of Interest

During the study period (January 1, 2013 through December 31, 2015), 9,202,958 persons aged 18–64 years met the study's inclusion criterion of having at least 13 months of continuous coverage. This study was approved by the Institutional Review Board at the University of Texas Medical Branch at Galveston.

Measures

Opioid Prescribing—We used National Drug Code (NDC) therapeutic class description and DEA class code from the 2015 RedBook Select Extracts database, to classify opioid treatment into hydrocodone combination products (HCP), non-hydrocodone schedule II opioids, non-hydrocodone schedule III opioids, and tramadol.[28] Tramadol was in its own comparator category because prior studies showed a shift in prescribers' behavior with a substitution of the less-restricted tramadol for the newly up-scheduled HCP.[18–22, 24]

The unit of measurement is the prevalence of opioid prescription defined as any opioid prescribed to enrollees, with at least one opioid prescription in the study year. Our unit of measurement is the monthly rate of opioid prescribing. To estimate the monthly prevalence of opioid prescribing for each of the four categories, we generated denominators of all insured adults aged 18–64 years for each month of observation from January 2013 through December 2015. To be included in the denominator for a given month, the beneficiary was required to have had complete enrollment for the month and for the 12 preceding months. For each patient at each month of study, we used a 90-day look back period to examine the most recent prescription date and the total duration (days) of that prescription period. Patients who had at least one day of opioid prescription available in the month under study contributed to the numerator of the prevalence estimate for that month. Patients who received prescriptions for more than one opioid category during a given month contributed to the numerator of each opioid category for that month.

Patient Characteristics—Patient age was categorized at each month of observation. Race or ethnicity are not reported in the CDM. We examined all conditions included in the Elixhauser comorbidity index, with the exception of cancer, using a 12-month lookback period.[29] The Elixhauser comorbidity index comprises thirty conditions including drug and alcohol abuse, depression, and psychoses (eTable 2).[29] Patients were classified as having cancer if they had an International Classification of Diseases, ninth revision, clinical

modification (ICD-9-CM) diagnosis code for any solid cancer or leukemia/lymphoma with the exception of non-melanoma skin cancers (eTable 1).[30] Among patients with cancer, those who received radiation or chemotherapy treatment and those who were hospitalized with a primary diagnosis of cancer in the prior year were classified as 'actively treated.[30]

Statistical Analysis

The proportion of patients with opioid prescribing in each of the four categories was calculated by month, from January 2013 to December 2015, and stratified by patient characteristics. Categorical variables were analyzed using chi-square tests. Absolute differences in rates of HCP prescribing by patient characteristics were assessed by testing the interaction of each covariate with year of prescription using General Estimating Equation (GEE) models. Multilevel multivariable analyses — using a hierarchical generalized linear mixed model (HGLMM) with a binomial distribution and logit link with patients nested within states and adjustment for patient clinical and demographic characteristics — were conducted to estimate variation in HCP prescribing attributed to states at two time points: 2013 versus 2015.

The time trend in HCP prescribing was examined by piecewise regression including five joinpoints. The first four joinpoints were pre-specified and represented the key dates associated with HCP rescheduling. The fifth joinpoint was selected based on our inspection of the data when the decline in the rate of HCP prescribing reached a plateau. Trends in the prescribing of other prescription opioids over time were analyzed using jointpoint regression analysis with a maximum of five possible jointpoints. A sequential application of the permutation test using 4,500 possible randomly permuted datasets and Bayesian information criterion methods were used to determine the optimal number of jointpoints.[31] All tests of statistical significance were 2-sided. Analyses were performed by DA and YFK with SAS version 9.4 (SAS Inc., Cary, NC) and Jointpoint Regression Program, Version 4.4.0.0 (NCI).[31] Maps were constructed using ArcGIS 9.3.

RESULTS

Figure 1 illustrates the monthly rate (%) of HCP prescribing for all enrollees from January 2013 through December 2015. Also shown are the rates for non-hydrocodone schedule II opioids, non-hydrocodone schedule III opioids, and tramadol. There was an overall decline in HCP prescribing during the three-year period, from 2.84% in the first quarter of 2013 to 2.04% in the first quarter of 2015, a 28.17% reduction ($P<0.0001$). Prescribing of opioid (regardless of schedule classification) decreased from 4.73% in June 2013 to 4.19% in June 2015, an 11.42% reduction, ($P<0.0001$).

Table 1 summarizes the joinpoints where the slopes in rate of opioid prescribing changed during 2013–2015. HCP prescribing rates slightly decreased during 2013, with a significantly larger decrease in early 2014 (Arrows A and B in Figure 1), followed by stable prescribing from March to August 2014 (Arrows B and C in Figure 1). This stable period was followed by the largest decrease between August and October of 2014 (Arrows C and D in Figure 1). After October 2014, the rate of HCP prescribing continued to decrease but the slope of the decrease was less after March of 2015 (the fifth joinpoint).

Schedule II (non-hydrocodone) opioids had no identified joinpoints—the joinpoint analysis found no significant changes in the slope of schedule II opioid prescribing over the 2013–2015 period (Table 1). Non-hydrocodone schedule III opioid prescribing showed a significant increase in slope during August to November 2014. The joinpoint analysis found a significant deflection in tramadol prescribing around October of 2013. This is not obvious on inspection of Figure 1, which is basically flat over the three-year period.

We next examined the decrease in HCP prescribing as a function of specific patient characteristics (Table 2). For this, we compared HCP prescribing in June 2013 to June 2015. The unadjusted rates are given for each characteristic, along with the absolute and relative differences in use between the two time points. The absolute declines in HCP prescribing were greater in the older groups, (e.g., 0.87% drop in 56–64 year olds vs 0.52% in 18–35 year olds). Women had higher rates of receiving HCP prescriptions than men did initially, and a larger absolute decrease in receiving HCP after the 2014 policy. Patients with higher comorbidity scores had the highest initial rate of being prescribed HCP, and greatest absolute decreases.

Among patients with a cancer diagnosis, we examined rates of HCP prescribing by whether or not they were being actively treated for cancer. Both groups had higher initial HCP prescribing rates (e.g., 8.8% for actively treated cancer patients, and 5.2% for not actively treated cancer patients, vs 2.7% for those who did not have a cancer diagnosis). Active cancer patients had a much larger absolute reduction in HCP prescribing than did non-cancer patients (-2.26 vs -0.70), resulting in very similar relative reductions in prescribing (25.7% vs 26.0%).

Figure 2 shows the rates of HCP prescribing by state before (A) and after (B) the change of HCP from schedule III to II. The colors of the maps divide states by quintile of 2013 HCP prescribing rates. States varied considerably in 2013, with the lowest rate in New Jersey (0.91%) and the highest rate in Alabama (5.66%). By 2015, only 9 of the states were in the top two quintiles and 33 were in the bottom two quintiles. There were also large differences in the relative changes in use among states, from a 46.7% decrease in Texas to a 12.7% increase in South Dakota (eTable 2).

We further examined the variation among states in HCP prescribing before and after the change in regulations using a multilevel model to estimate Intra-class Correlation Coefficients (ICCs) indicating the proportion of variance in HCP prescribing attributed to the state of residence. Variation attributable to state was actually higher after the change in HCP scheduling than before (ICC of 6.6% in June 2013 vs 8.7% in June 2015).

DISCUSSION

The implementation of the 2014 federal policy restricting hydrocodone combination products (HCP) resulted in substantial decreases in the rates of opioid prescribing in the US. Between June 2013 and June 2015, the rate of HCP prescribing decreased by 26%; overall opioid prescribing (regardless of schedule) decreased by 11%—mostly driven by the decline in HCP prescribing. The decrease in refills, resulting from the up-scheduling of HCPs to

schedule II and concomitant elimination of refills, is one possible explanation for the decrease in HCP prescribing. The publication and implementation of the final federal policy rule coincided with a sharp drop in the rate of HCP prescribing from August to October 2014. Coinciding with this drop was a small but significant increase in the non-hydrocodone schedule III opioid prescribing, mostly codeine-combination products. The rate of prescribing of non-hydrocodone schedule II opioids and tramadol was stable over the three-year study period.

Unlike the previously reported increase in tramadol prescribing after the 2014 HCP up-scheduling,[14–20] we did not find this increase in our study population. Our national cohort included men and women aged < 65 with access to commercial insurance that covers prescription medications. Most prior studies were based on predominantly indigent, pediatric or veteran populations or from single health systems, hospitals, or poison centers.[16, 32, 33] It is possible that commercial health insurance medication carriers have specific programs to blunt the substituting of one opioid for another, as reported in prior studies.[18–24, 34] In particular, the health insurance carrier for the population who contributed data for our study implemented several programs (e.g. limiting number of refills of any opioid and requiring prior authorization) to reduce inappropriate opioid prescribing among its enrollees.[34] It is thus possible that the upticks in tramadol prescribing previously reported in other studies were mitigated in our sample by the impact of these programs.

Consistent with prior studies, increasing age, female gender, and high comorbidity scores were associated with higher rates of HCP prescribing.[7, 35–37] Patients with higher comorbidity scores had the highest initial rate of receiving prescribed opioids, and their absolute decreases were greatest. Actively treated cancer patients had substantially larger absolute reductions and similar relative reductions in the rate of HCP prescribing compared to non-cancer patients.[24, 38, 39] Several studies have raised concerns about the potential for unintended consequences of the federal policy on the adequacy of pain treatment in cancer patients undergoing chemotherapy and other cancer-specific interventions.[24, 39–42]

There were large inter-state variations in both the absolute and relative changes in the rates of HCP prescribing before and after the October 2014 federal policy, ranging from a 46.7% decrease in Texas to a 12.7% increase in South Dakota. The variation in HCP prescribing attributable to the state of residence may, in part, reflect quantitative and qualitative differences in laws and policies regulating prescription opioids at the state level, as well as the degree of enforcement of these laws.[5–10, 12, 13, 43] For example, the degrees of enforcement of Prescription Drug-Monitoring Programs in all US states vary from states to states with respect to the degree of inter-state data sharing, enrollment, access mandates, law enforcement access, and data collection interval.[13] Also, as of 2010, Florida had six categories of laws while Georgia has only one law regulating prescribing of opioid analgesics.[7] A careful examination of different state laws and opioid safe-use programs is key to understanding key components of effective state programs for possible adaptation and adoption by other states.

Contrary to our hypothesis, the variation in HCP prescribing attributable to states was actually higher after the 2014 federal policy than before. Others have noted similar

unexpected and paradoxical effects after implementation of opioid-related policies.[14] For example, an analysis of the impact of prescription monitoring programs aimed at reducing prescription opioid dispensing from retail pharmacies in Canada showed significant increases in prescription opioids dispensing over the study period (2005 to 2010) in most Canadian provinces and a widening of the inter-provincial variations in prescription opioids dispensing.[14] These unexpected results underscore the need for long-term monitoring and evaluation of the impact of opioid-related policy at provider, patient and health-system levels.

Of note, the decrease in HCP prescribing started months before the final implementation of the law on October 2014. This decrease likely reflects the effects of media activities and myriad public hearings on prescribing behaviors of physicians before the official implementation date. Prior studies have described similar effects.[14, 43,44] For example, the reported decrease in prescription opioid use and misuse among the Canadian residents of Ontario reflected not just the policy interventions but also the effects of media reporting and public hearings on prescription use disorders surrounding the policy implementations.[14, 44] The media reporting not only affect MD prescribing behaviors but also patient expectations regarding pain control.[44]

Our study has limitations. First, information on severity of pain was not available. Second, the study population examined — aged 18 to 64 and members of commercial insurance plans — is not representative of the entire US population. Third, we were restricted to measuring opioids obtained by prescriptions. Other sources of opioids may be particularly prevalent among working-age populations.[4, 45] Fourth, prescription claims reflect what was dispensed, not whether it was consumed. Finally, information on race, ethnicity, and socioeconomic status was not available for the study population. Past studies showed an association of socio-demographic factors with rates of use, misuse, and toxicity of prescription and non-prescription opioids.[25, 45–47]

Our study also has important strengths, including a large sample size in all US states. The present study added to the existing body of literature in by improving our understanding of: a) the differential effects of the 2014 federal policy in subpopulations at high risk of pain under-treatment—the actively treated cancer patients and patients with multiple comorbidities or/and multiple sources of pain-causing conditions and; b) the extent to which these effects vary by state. The changes in HCP prescribing before and after the federal policy allows for natural experiments of examining how characteristics such as different state opioid-related laws interact with the 2014 federal policy. The large decrease in opioid prescribing for patients undergoing active cancer treatment is surprising; the CDC federal guidelines specifically addressed over-prescribing of opioid analgesics for “chronic pain outside of active cancer treatment, palliative care, and end-of-life care.”[2, 38, 42]

Conclusions

The 2014 federal policy was associated with a decrease in rates of hydrocodone prescribing. The large decrease in rates of hydrocodone prescriptions in patients with actively treated cancer was unexpected. This may represent an unintended consequence of the federal policy

on the adequacy of pain treatment in cancer patients. It will be important to assess whether the restriction of hydrocodone prescribing increase the rates of illicit opioid use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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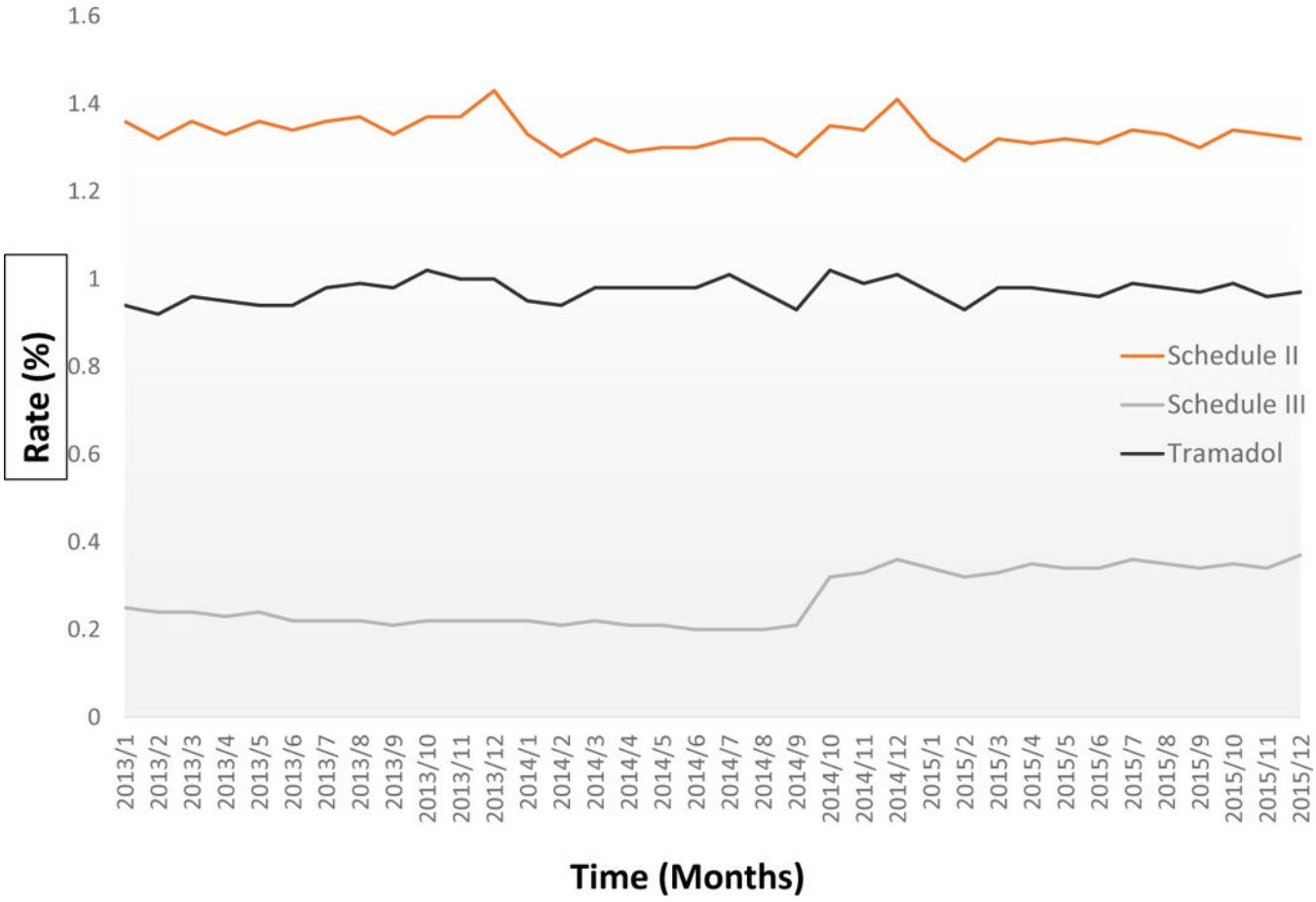
Appendix



Appendix Figure 1a*.

Change in opioid prescriptions from January 2013 to December 2015, stratified by opioid categories *The Figure 1a was enlarged version of figure 1 for easier visualization of the curves for schedule II, III, and tramadol. The Y-axis is from 0% to 1.6%.

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Key Points

- **Question**: Do opioid prescribing rates before and after the 2014 federal hydrocodone combination product (HCP) rescheduling policy vary by patient characteristics or state of residence?
- **Findings**: In the retrospective cohort study of 9,202,958 privately-insured patients, HCP prescribing decreased by 26% from 2013 to 2015; any opioid prescribing decreased by 11%; and variation by state of residence increased substantially. Patients with multi-morbidities and actively-treated cancer patients had largest decreases in HCP prescribing.
- **Meaning**: HCP prescribing decreased after the 2014 policy. The large decrease in HCP prescribing in actively-treated cancer patients was unexpected, and may represent an unintended consequence.

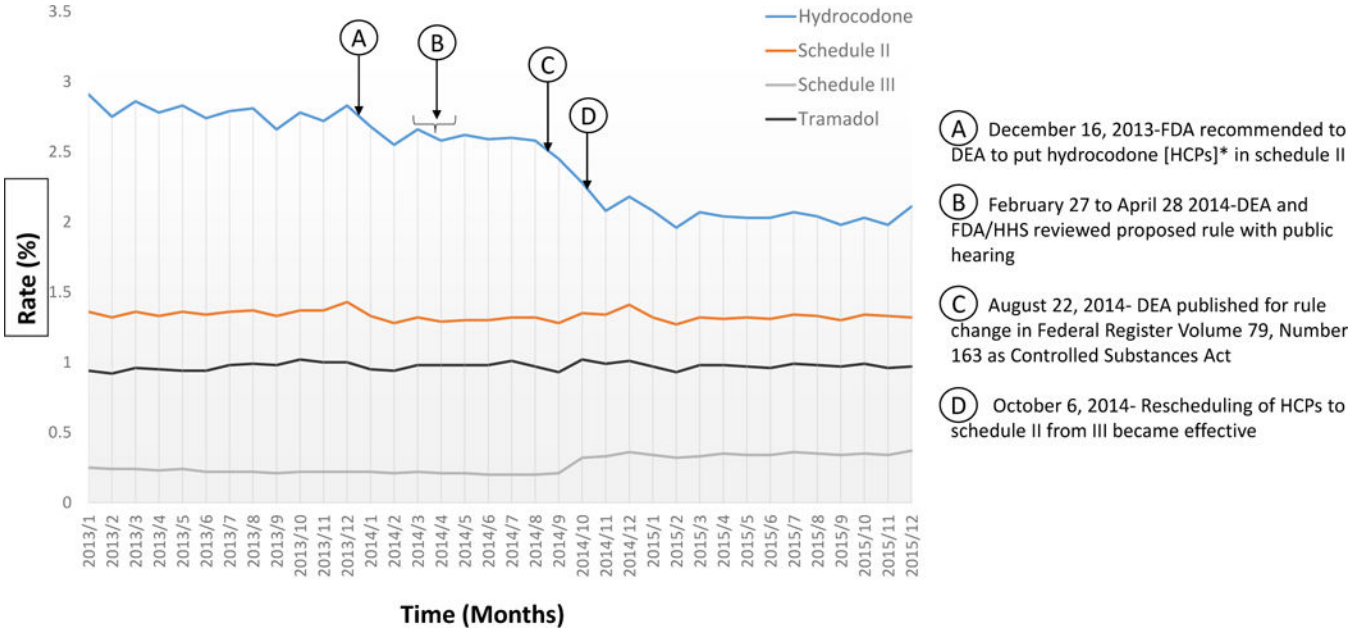

Figure 1.

Change in opioid prescriptions from January 2013 to December 2015, stratified by drug categories. [See enlarged version in appendix for better visualization].

*HCPs – Hydrocodone combination products

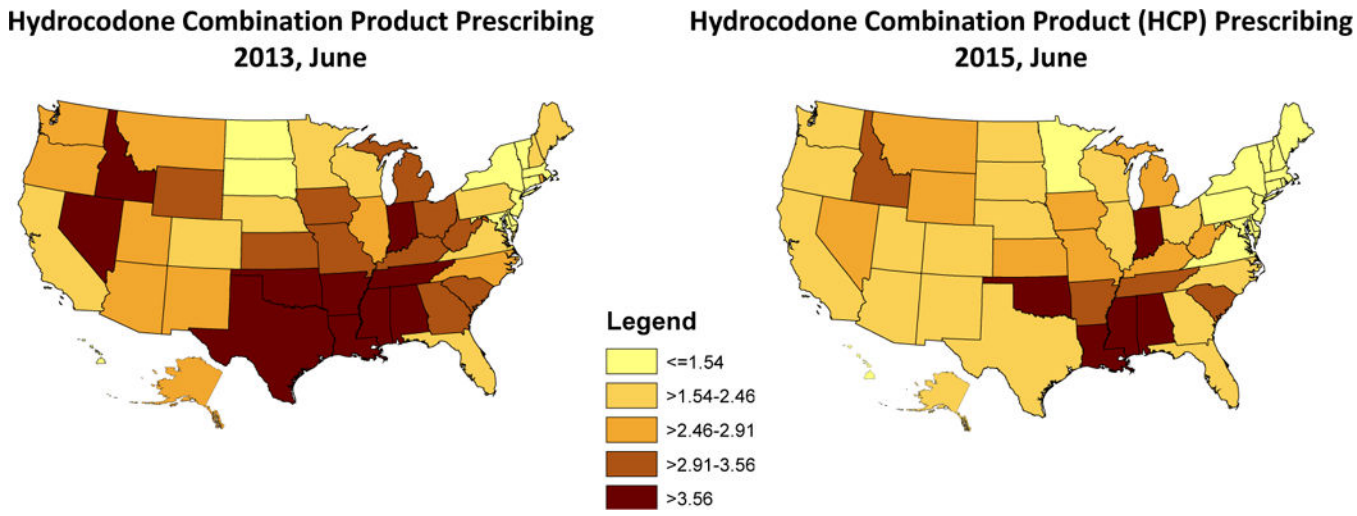

Figure 2.

Hydrocodone combination product (HCP) prescriptions before and after federal reschedule in US states.

Table 1

Joint points in trend of the monthly percentage of opioid prescribing between January 2013 and December 2015.

Opioids	Joint Point		Fitted Line	
	Time	95% CI	Time Period	Slope^ (p-value)
Hydrocodone-HCP *	12/2013		~12/2013	−0.0095 (0.0491)
	03/2014		12/2013~03/2014	−0.0462 (0.0100)
	08/2014		03/2014~08/2014	0.0012 (0.9203)
	10/2014		08/2014~10/2014	−0.1903 (<0.0001)
	03/2015		10/2014~03/2015	−0.0413 (0.0006)
			~03/2015	0.0034 (0.5615)
Schedule II **	No Joint Point	No Joint Point	No Joint Point	No Joint Point
Schedule III **	08/2014	07/2014, 09/2014	~08/2014	−0.0101(0.0000)
	11/2014	10/2014, 12/2014	08/2014~11/2014	0.1776(0.0015)
			11/2014~	0.0028(0.2259)
Tramadol **	10/2013	06/2013, 01/2014	~10/2013	0.0067(0.0200)
			10/2013~	−0.0007(0.2378)

* Based on the concurrency dates associated with hydrocodone combination product (HCP) schedule change, joinpoints for HCP were pre-specified in the piecewise regression model.

** Joinpoint analyses were conducted to locate the optimal joint points.

^ Slope is expressed as percentage change in opioid prescribing rate, for example −0.0095 means 0.95% decrease in monthly opioid prescribing rate.

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Table 2

Patient characteristics and hydrocodone combination product (HCP) prescribing before (June 2013) and after (June 2015) policy implementation in October 2014.

Characteristics	Hydrocodone Prescribing 2013		Hydrocodone Prescribing 2015		Absolute difference	% Reduction	p-value**
	N	Rate (%)	N	Rate (%)			
Overall	4846500	2.74	4182504	2.03	−0.71	25.91	
Age Group							<0.0001
18–35	1630799	1.69	1450431	1.17	−0.52	30.77	
36–45	1096662	2.53	936011	1.88	−0.65	25.69	
46–55	1208413	3.41	1015371	2.55	−0.86	25.22	
56–64	910626	3.99	780691	3.12	−0.87	21.80	
Sex *							<0.0001
Male	2397800	2.48	2125942	1.83	−0.65	26.18	
Female	2447931	3.00	2056057	2.23	−0.77	25.67	
Cancer							<0.0001
Yes (with Trt.)	21278	8.80	17253	6.54	−2.26	25.68	
Yes (no Trt.)	45323	5.21	38131	3.89	−1.32	25.34	
No Cancer	4779899	2.69	4127120	1.99	−0.70	26.02	
Number of Comorbidity ***							<0.0001
0	3794704	1.93	3293678	1.38	−0.55	28.50	
1	671760	4.64	563387	3.59	−1.05	22.63	
2	250196	6.40	211618	5.00	−1.40	21.88	
3 or more	129840	9.46	113821	7.33	−2.13	22.52	

Note: All the characteristics were significant at 0.01 level.

Trt. =Treatment

*Does not add up to total N because of missing values.

**p-value was determined by multinomial model for long vs. long-term prescribing characteristic, and by GEE for all other characteristics.

***All conditions in the Elixhauser comorbidity index, with the exception of cancer, were included. The index comprised 30 conditions including drug and alcohol abuse, depression, and psychoses.[29]