INTERACTIVE POLICY EFFECTS OF THE 2010 OXYCONTIN REFORMULATION

by

Joseph Bradford Baan

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ABSTRACT

In this paper I estimate the additional effects counties with active Prescription Drug Monitoring Programs and Medical Marijuana Laws felt after the 2010 OxyContin reformulation compared to counties without these laws. I also estimate the effect of each additional Substance Abuse Treatment facility as well after the reformulation. I find that counties with PDMPs and MMLs see the morphine equivalent of a 6.557 and 4.681 grams decrease in the Oxycodone shipped to pharmacies for every 1000 people. Each additional SAT is associated with a 0.11 Morphine Grams Equivalent decrease. For reference 6.557 represents about 3% of the county average of MGE in Oxycodone.

INTRODUCTION

After being released in 1995 OxyContin quickly rose to the top as a long lasting pain reliever. “Beginning in the late 1990s, pharmaceutical companies selling high-dose opioids seized upon a notion, based on flimsy scientific evidence, that regardless of the length of treatment, patients would not become addicted to opioids.” said David Kessler who was the FDA commissioner from 1990 to 1997 describing the shift towards long lasting pain relief. The effects are still with us today and OxyContin 40 mg is still the most popular Oxycodone product in the United States (DEA, 2020). Oxycodone (the active ingredient) can be prescribed generically as an immediate release drug, but OxyContin is the only extended release version available in the United States. An immediate release drug means that patients will receive the whole dosage quickly and the effect will also wear off quickly. For example, Percocet is another opioid with the Oxycodone active ingredient and is avaiable in dosages of 2.5mg to 10mg per pill. For OxyContin the dosages range from 10mg to 80mg, and a 160mg dosage was released in July 2000 but was discontinued by 2001. By including a timed release ingredient doctors could now prescribe OxyContin to be taken on a twelve hour schedule which is as effective as immediate release Oxycodone dosed every four to six hours.

In an attempt to combat prescription drug abuse of OxyContin, The U.S. Food and Drug Administration (FDA) approved a reformulation of Purdue Pharma’s OxyContin in 2010, which made the pills harder to crush and dissolve in water. Before the reformulation, abusers could bypass the timed release and receive the full dose immediately, by crushing or dissolving the pills. A report from the National Vital Statistics Survey (NVSS) and the Center for Disease Control (CDC) in 2018 showed that in 2011 Oxycodone (the active ingredient in OxyContin)

was the number one most mentioned drug in drug overdose reports where at least one drug was mentioned.

I identify the effect of the reformulation on opioid shipments to retail pharmacies, specifically look at how the reformulation had different effects for different areas based on Prescription Drug Monitoring Programs (PDMP), Medical Marijuana Laws (MML), and access to Substance Abuse Treatment facilities (SAT). These are other actions state and local governments have taken independently of the reformulation that could have interesting combination effects with the reformulation on prescription drug abuse. Alpert, Powell and Pacula (2018) use this reformulation to identify a possible substitution effect between OxyContin and Heroin. The reformulation was very effective at reducing OxyContin misuse, but that for every percentage point reduction in OxyContin misuse, they find that heroin-related deaths increase by 3.1 for every 100,000 people. My contribution to the literature is to examine the legal supply of OxyContin as well as other opioids. My main interest is the interactions between the implementation of the reformulation and PDMP laws, medical marijuana laws, access to substance abuse treatment facilities, and pre-2010 exposure to Oxycodone.

The data I use comes from the Drug Enforcement Administration (DEA) and is maintained under the Automation of Reports and Consolidated Orders System (ARCOS) program. The DEA describes ARCOS as an automated drug reporting system which monitors DEA controlled substances from their point of manufacture through commercial distribution to point of sale or distribution at the dispensing/retail level.

These data are address-level daily observations of all shipments of monitored drugs in the United States from 2008-2012. For my analysis, I aggregate to county and month. This is

because the treatment effect of the OxyContin reformulation was implemented at the national level in August of 2010. My outcome of interest is the Morphine Grams Equivalent (MGE) of opioids shipped to point of sale per capita.

I find that there is an interactive effect of PDMPs/MMLs/SATs and the reformulation. These policies are associated with a strong decrease in the Oxycodone per capita that was shipped to pharmacies after the reformulation. PDMPs were associated with about 6.557 MGE decrease in Oxycodone per capita post reformulation. For MMLs the affect was about 4.681 MGE per capita decrease, and each additional SAT in a county was associated with 0.11 MGE decrease. For the average county this is about a .704 MGE per capita decrease in the Oxycodone shipped associated with SATs.

LITERATURE REVIEW

Prescription drug abuse is a recurring theme in local and national news. This abuse has been the target of many policies, and it was a critical point of our 2020 election. In this literature review I start by taking a look at previous studies that have worked with the OxyContin reformulation. Then I look at Prescription Drug Monitoring Programs (PDMPs) which hope to track and prevent doctor shopping and over-prescribing. These are one of the main policies attempting to control the supply of opioids and as of 2020 50/50 states have adopted a PDMP (PDMP TTAC, 2020). Next is literature on access to substance abuse treatment facilities. Finally substitution effects of opioids and medical and recreational marijuana.

Oxycontin Reformulation

In 2010 the FDA approved a new reformulation of Purdue Pharma's OxyContin which would make the individual pills harder to crush or dissolve in water. This led to a decrease in OxyContin misuse as intended, however it also led to an increase in heroin deaths. Specifically in areas that had higher rates of OxyContin misuse pre reformulation. (Alpert, Powell, Pacula. 2018). Some estimate the spillover effect of the reformulation to be so great, that every single death avoided by OxyContin overdose was replaced by a heroin overdose death (Evans et al 2019). Furthermore, (Beheshti, 2019) finds that the reformulation was associated with 76% of new hepatitis C cases and 53% of new hepatitis B cases from 2011 till 2015 due to the increase needle usage after uses switched to heroin.

Prescription Drug Monitoring Programs

One form of government response to the opioid crisis are Prescription Drug Monitoring Programs. PDMP laws establish a system to track controlled substance prescriptions within and sometimes between states. These PDMPs are electronic databases that provide timely information about prescribing and patient prescription history to health care administrators (CDC, 2019).The goal of these programs is to combat doctor shopping as well as over prescribing by doctors. Doctor shopping is when patients attempt to get multiple prescriptions of controlled substances by visiting multiple providers in a short time, or where patients attempt to get a prescription under false pretenses. These programs would allow for doctors to see a patient's prescription history, which would ideally allow the doctors to make informed prescription decisions.

A defining assumption of the literature is that PDMPs are (or are not) homogeneous across states. Early research published in non-economics journals, such as (Haegerich et al., 2014) and (Li et al., 2014) found little to no effect of PDMPs on health or crime outcomes. This has been shown to be an incorrect conclusion, as more recent research has shown that "must access" mandates significantly increase the effectiveness of PDMPs on reducing bad opioid outcomes. There is quite a bit of variance between PDMPs across states. Some states require prescribers and/or dispensers to check the database before serving patients. This is the variation that has proved to be extremely important. The variation between states on mandatory access prescription drug monitoring programs (MA-PDMPs) is quite extreme and has changed over time. As of August 2019, five states (including Montana) do not require either prescribers or

dispensers to look up patients before serving them, twenty-five states only mandate the prescribers check, and twenty require both. For reference, in 2012 only twelve states mandated usage by prescribers, and thirteen states mandated usage by dispensers (PDMP TTAC, 2019).

For papers regarding PDMPs I started with Birk & Waddell, 2017 and Dave, Deza & Horn, 2019. These papers were the first papers of high quality that I found which address the previous assumption that all PDMPs are homogeneous and attempt to account for MA-PDMPs. Dave, Deza & Horn use the Prescription Drug Abuse Policy System (PDAPS) to differentiate PDMPs that have a mandatory access clause. Birk & Waddell instead categorize the attributes of these programs using information "obtained from the Prescription Monitoring Program database curated by Corey Davis at The Network for Public Health Law and the PDMP Center of Excellence at The Heller School for Social Policy and Management at Brandeis University". From there I looked for articles they cited and that had cited them.

The consensus of recent econometric studies is that mandatory access requirements have a significant negative effect on bad opioid outcomes, however when they treat PDMPs as homogeneous these negative effects are diluted and statistically indifferent from zero. These results include drug-abuse treatment admissions (Birk & Waddell. 2017) (Dave, Grecu & Saffer. 2019), 5-10% decrease in violent and property crime (Dave, Deza & Horn. 2019), as well as total prescriptions and length of prescriptions supplied (Buchmueller & Carey. 2018) (Buchmueller, Meille, & Carey. 2019). Birk and Waddell additionally look at "tenure of opioid use" and "intensity of opioid use" to give a compelling explanation of the mechanism through which MA-PDMPs are effective stating "These decreases in drug treatment admissions are mostly due to weakly attached drug users meaning low abuse and short time abusing" (Birk & Waddell, 2017).

Unfortunately there is evidence that users are shifting to heroin as a substitute, though these effects are strongest in areas with heavy heroin use before implementation. This effect is exclusive to MA-PDMPs, as optional access laws have no displacement effect (Mallat. 2019)

One common theme among these papers is they use a third party source for data on PDMP implementation dates and classification of mandatory access. As each program is passed individually, any attempt to categorize the legalese of the laws is open for interpretation. Horwitz et al. 2018 attempt to study the robustness of the results when comparing multiple data sources. They even compile their own data crediting their combined decades of legal research and law degrees. They found that the implementation of PDMPs and the effects of mandatory access clauses were very volatile with regards to data sources chosen. They provide their list of when PDMPs were actually implemented, which ones have MA clauses, and the criteria they used to create these data.

Substance Abuse Treatment

Substance Abuse Treatment is another possible government reaction to rising overdose deaths. Previous literature ï¬• nd that additional SATs in a county are associated with a reduction in drug related deaths (Swensen, 2015), as well as reductions in violent and ï¬• nancially motivated crimes in the county (Bondurant, Lindo, & Swensen 2018). These programs work with drug users to not only safely treat addiction, but also recently have been working to educate users on safer drug use and clean needle access. Their documented eï¬€ects as well as intended eï¬€ects both could have interesting interactions with the OxyContin reformulation.

Marijuana

The literature is clear and through regarding the substitution between opioids and marijuana. Laws allowing access to medical and recreational marijuana leads to a decline in opioid mortality rates (Chan, Burkhardt, Flyr. 2019), Morphine Equivalent of opioids prescribed, and total days supply prescribed (McMichael, Van Horn, Viscusi. 2020). Additionally there is a per dispensary negative eï¬€ect on opioid overdose deaths (Powell, Pacula, Jacobson. 2018) (Smith. 2019).

DATA

In July 2019, The Washington Post released to the public a dataset they obtained through Freedom of Information Act from the Drug Enforcement Administration (DEA) that was maintained under the Automation of Reports and Consolidated Orders System (ARCOS) program. The DEA describes this program: "ARCOS is an automated, comprehensive drug reporting system which monitors the flow of DEA controlled substances from their point of manufacture through commercial distribution channels to point of sale or distribution at the dispensing/retail level - hospitals, retail pharmacies, practitioners, mid-level practitioners, and teaching institutions." These data are address-level daily observations of all shipments of opioids in the United States and in US territories. In the past, similar data has only been released at the state quarterly level. Because these data are pharmacy by month, I will be able to use these data in new ways to address my outcomes of interest. In figure 1 I show trends in shipments tracked by ARCOS for Oxycodone and all other opioids where Oxycodone account for about 20% of total shipments among 13 other tracked opioids in my sample. I also show in the appendix, trends in shipments broken down by the 6 most common opioids in my data, accounting for about 75% of observations.

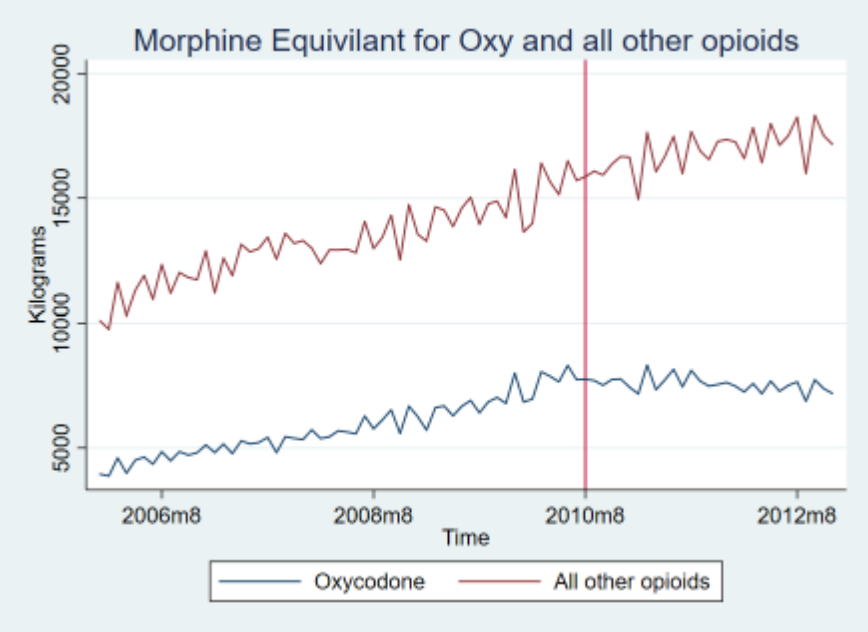

Figure 1: Total shipments in the U.S. Only Oxycodone is treated by the reformulation in 2010.

Figure 2 shows the trend in Oxycodone only. This figure shows similar results as previous studies (Alpert et al. 2018) with a strong upward trend in Oxycodone previous to the reformulation followed by a stagnation or decrease after. In figure 3 I look closer at the trend of all opioids other than Oxycodone. This graphs shows a strong upward trend with no break in August 2010.

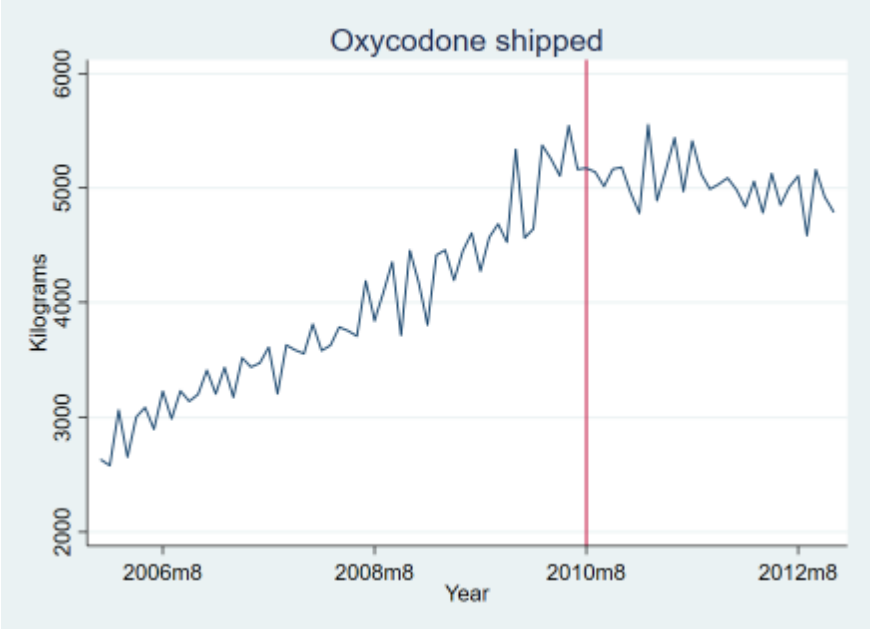

Figure 2: Total shipments in the U.S.

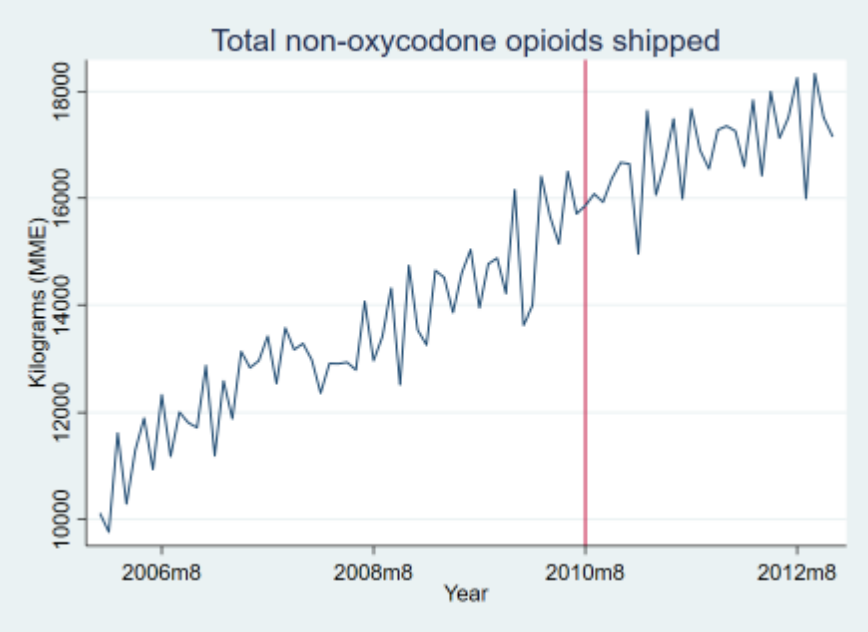

Figure 3: Total shipments across whole U.S. All drugs are converted using a MGE before aggregating

Again, these graphs show a similar trend of Oxycodone making a sharp turn after the reformulation in 2010. This trend has been documented in the past by other studies such as Alpert et al. 2018. I argue that, while their findings are significant, my data allow me to look past averages and find if there are additional trends in the drop off in shipments.

I converted all drug shipments from their original name and weight (eg Oxycodone 20 mg, Methadone 10 mg, etc.) into a morphine grams equivalent (MGE) using the morphine equivalent conversion factor provided by the ARCOS data. This conversion is a common tool used by physicians to understand how different doses of similar drugs will compound. For example, if a physician wanted to prescribe 50 mg of Vicodin and 30 mg of Percocet per day to a patient, they would be able to use a MGE conversion to find out that they would be prescribing about the equivalent of 100 mg of morphine per day. This gives my outcome of interest: MGE shipped to the point of final sale per month. I choose this as my outcome of interest because MGE is used by prescribers to compare strengths of different opioids. This allows me to interpret my results in a useful way, since active ingredients can be mixed to strengthen or weaken the effects of opioids. Simply reporting results in grams of Oxycodone could be misleading in a similar way as to reporting results in nominal dollars instead of real.

I drop all observations that are not marked as a final sale to a “chain pharmacy” or a “retail pharmacy” as defined by the DEA. I do this to limit my sample to the observations which the reformulation is most binding for. In a 2007 survey of drug diversion investigators, 39.4% of survey participants perceived doctor shopping to be the primary source of prescription drug diversion, and 35% marked prescription theft or forgery as the primary source. Additionally, chain and retail pharmacies such as CVS and Walgreens represent about 85% of the sample.

Next I aggregate to the pharmacy by month level. Finally I mark counties that had above the mean Oxycodone per capita shipped to them from 2006-2010. These counties I define as having high exposure to Oxycodone before the reformulation. Alpert et al. 2018 use a similar method in their study looking at the effects of the reformulation on OxyContin and heroin abuse. I also show this visually in figure 6 where I use a similar calculation at the state level, however I want to be clear that in my regressions I will be working at the county level.

In table 1 I show county by month averages of opioid shipments to chain and retail pharmacies measured in grams. This table is split up into the means over all counties, then means by counties that are below and above the average SATs per capita, then by counties that do and do not have MMLs active, then by counties that do and do not have PDMPs active. A main pattern that emerged is that Oxycodone per capita seems to shift slightly based on if counties have these policies in effect.

	All	SATs per 1k		Med. Marij.		PDMPs	
	County	Low	High	No	Yes	No	Yes
	mean	mean	mean	mean	mean	mean	mean
Grams Oxycodone	1,738	1,941	1,414	1,490	3,000	2,191	1,555
MGE Oxy 1k	18	18	19	18	21	20	17
MGE All 1k	67	66	70	65	77	66	68
MGE Non Oxy 1k	49	48	51	48	56	46	50
Total CTY SAT	6.4	5.3	8.2	5.4	12	5.6	6.8
Income per cap	33,856	33,781	33,974	33,395	36,201	34,319	33,669
Observations	204765	125723	79042	171153	33612	58769	145996

Table 1: County year averages. MGE Oxy, All, and Non-Oxy are morphine grams equivilant converted aggregates of Oxycodone, all opioids and all opioids except for Oxycodone. They are all measured as MGE per 1000 population in a county.

In Table 2 I show county by month demographic averages. I include this just to show that there are no spikes or gaps in my data and that the demographic variables I include are consistent and correct.

	2006 mean	2007 mean	2008 mean	2009 mean	2010 mean	2011 mean	2012 mean
Asian	.014	.014	.015	.015	.015	.016	.017
Black	.091	.092	.093	.093	.094	.094	.095
Native American	.018	.018	.019	.019	.019	.02	.02
White	.88	.88	.87	.87	.87	.87	.87
0-16	.2	.2	.2	.2	.2	.2	.19
16-30	.17	.17	.17	.17	.17	.17	.17
30-65	.45	.45	.45	.45	.46	.46	.45
65+	.099	.1	.11	.11	.12	.12	.13
Total pop	118,003	119,128	120,230	121,331	122,402	123,188	124,109
Observations	29393	29397	29407	29398	29385	29415	29416

Table 2: County year averages. Demographics are presented at rates of the total population.

Additionally I merge these data with data tracking the year Medical Marijuana Laws were passed from the National Conference of State Legislatures, data on when Prescription Drug Monitoring Programs were implemented provided by Dr Wendy Stock, county level demographics provided by SEER, and county Substance Abuse Treatment data provided by Dr Isaac Swensen. These data allow me to address my main effects of interest which are interactions between the implementation of the reformulation and PDMP laws, medical marijuana laws, access to substance abuse treatment facilities, and county demographics. In figures 4-6 I show visually which states have active PDMPs, MMLs, as well as which states I define as high exposure

pre reformulation. In figure 7 I show the average SATs per 10,000 population broken up into thirds. Finally in table 12 in the appendix I show the average number of active SATs in each state across my sample.

Figure 4: Highlighted states have an active Medical Marijuana Law during my sample

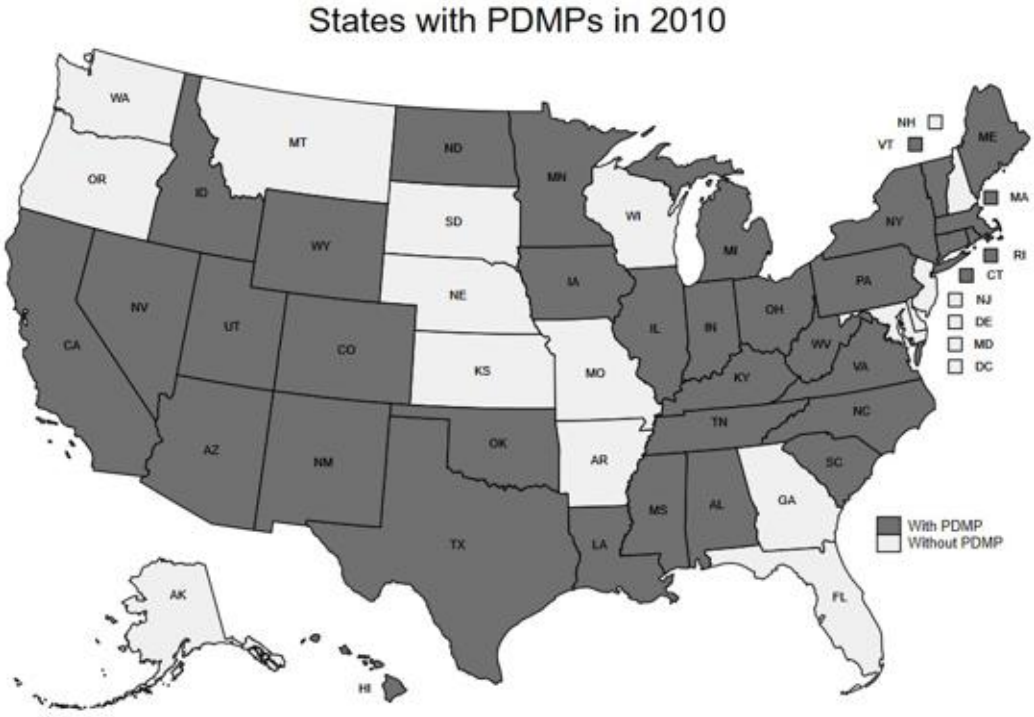

Figure 5: Highlighted states had an active Prescription Drug Monitoring Program as of 2010

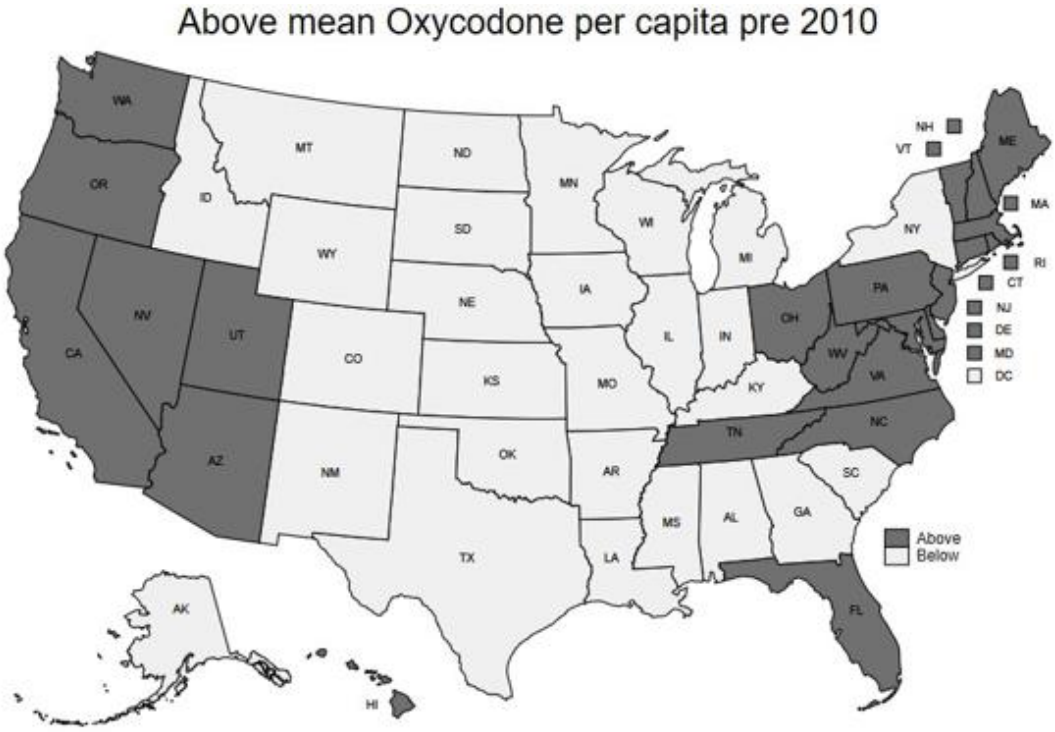

Figure 6: Highlighted states had above the mean Oxycodone per captia measured in grams shipped to chain and retail pharmacies from 2006-2010

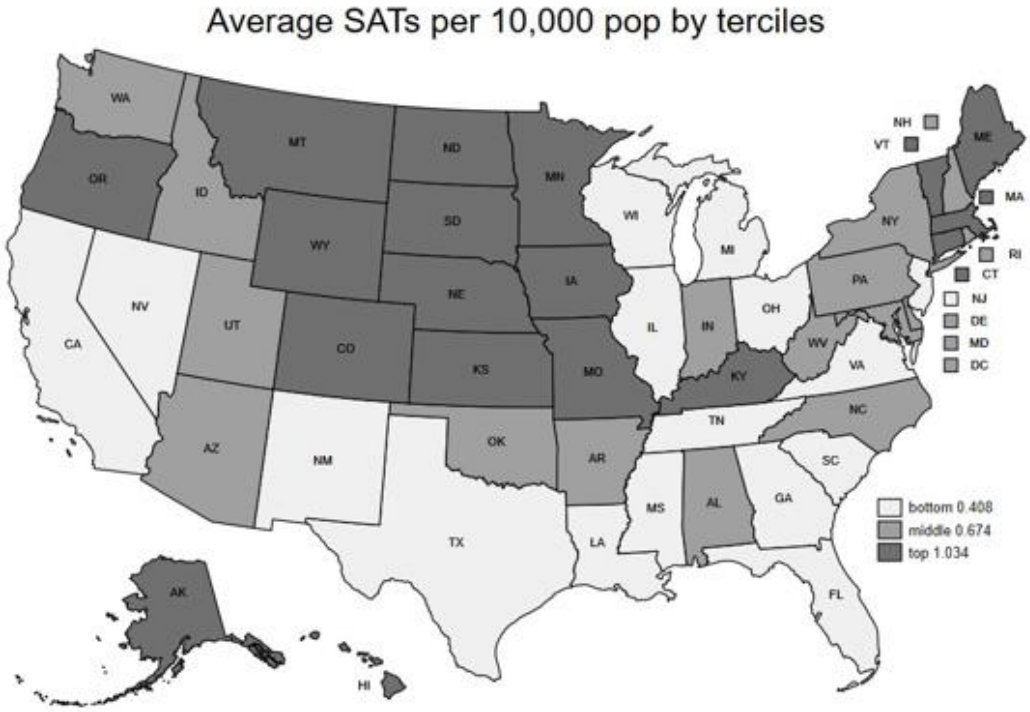

Figure 7: Average active Substance Abuse Treatment facilities per 10,000 population by percentile. The low is 0.215 in South Carolina, and the high is 1.574 in Maine.

METHODOLOGY

In my ideal experiment I could randomize treatment of the reformulation and of PDMPs/MMLs/SATs. However this is not realistic so I must rely on econometrics. A difference in difference model is a reasonable starting point to test this relationship. In this model I am comparing prescription opioid drug shipments to pharmacies within counties pre and post reformulation as well as across counties with and without PDMPs/MMLs/SATs. I show this in equation 1:

$$Y_{imy} = \beta_1 P_{my} \times Z_{imy} + \beta_2 P_{my} + \beta_3 Z_{imy} + \beta_4 X_{iy} + \theta_i + \gamma_m + \phi_y + \epsilon_{imy} \quad (1)$$

Where Y is total Oxycodone per capita shipped to pharmacy i in month m and year y, is my error term, and θ, γ, and φ are county, month, and year fixed effects. P is an indicator taking the value of 1 if the observation is after August 2010 when the reformulation occurred, and 0 otherwise. Finally, X is a vector of county demographics and income. I include month fixed effects to control for the cyclical nature of drug shipments, as well as any consistent monthly effects. Year fixed effects control for similar unobservable year-specific events that could affect drug shipments, such as the 2008 financial crisis for example. County fixed effects are also included to control for any possible time invariant effects that an individual county might possess.

Under this model I am now comparing observations from the same county between months in the same year and within the same month across years. Z represents one of the three separate state policies PDMPs/MMLs/SATs that I consider in this analysis, and so I would end up with three separate regressions. Z takes the value 1 for counties with active PDMPs or MMLs, and 0 otherwise. Alternatively, Z is the count of total SATs in a county because my measure of SATs is continuous. Under this difference in difference model I must assume that both counties with and without Z have similar trends in the pre reformulation period. In other words, I am assuming such states would trend similarly in the post-treatment period in the absence of changes in PDMPs/MMLs/SATs. However, 2010 was the middle of the opioid crisis and how some states were affected could be a factor in how they reacted. Using PDMPs as an example, in this model I would be assuming counties in states with PDMPs and counties in states without PDMPs would be trending similarly in the pre period, and would therefor would be trending similarly in the post period if there was no treatment. If states that enacted PDMP laws had different trends than states without, this specification would attribute the difference in the trends to the PDMPs. For example, state that experienced a rapid spike in opioid consumption before 2010 may have been more likely to enact PDMPs as a reaction. If this is true, then the estimates I find would be biased towards a positive effect as this model would attribute these pre trends to the PDMPs. To account for this possibility I add a third difference by comparing OxyContin to

all other opioids. I am now assuming that, without the reformulation or PDMPs, counties would have similar trends for OxyContin and all other opioids however I no longer have to assume counties in states with and without PDMPs have a similar trend in opioid use. Thus I propose my equation of interest:

$$Y_{imy} = \beta_1 P_{my} \times Z_{imy} \times O_i + \beta_2 P_{my} \times Z_{imy} + \beta_3 P_{my} \times O_i + \beta_4 Z_{imy} \times O_i + \beta_5 Z_{imy} + \beta_6 O_i + \beta_7 P_{my} + \beta_8 X_{iy} + \theta_i + \gamma_m + \phi_y + \epsilon_{imy} \quad (2)$$

Where Y is measured in units of Morphine Grams Equivalent (MGE) per capita shipped to county i in month m and year j. MGE is a universal method of converting and comparing all opioids used by physicians. This allows me to track all opioids not just Oxycodone in one model. P is an indicator taking the value of 1 if the observation is after August 2010 when the reformulation occurred and 0 otherwise. O is an indicator taking the value of 1 if the observation is measuring Oxycodone and 0 if it is measuring all other opioids. Z again represents the three separate state policies I consider, and so I end up with three separate regressions. For PDMPs and MMLs, Z takes the value of 1 if the policy is active and 0 otherwise. For SATs however, this becomes the interaction with the count of active SATs in a county. Finally, I will be clustering standard errors at the state level. This is because for

PDMPs/MMLs/SATs the variation in policy decisions will be done at the state level and, I must account for the fact that the error in these observations will not be independent and identically distributed. Clustering at the state level allows me to correct for this assumption I must make when using an ordinary least squares regression such as my main estimating equation.

Looking now at my main coefficient of interest, β_1. The first difference is pre reformulation minus post. This is the building block for my model and this difference allows me to estimate the change across the reformulation. The second difference is the interaction with Z, where Z takes the values of 1 or 0 to mark if the observation is in a county with an active PDMP, or MML, or is alternatively the count of total active SATs in a county. This difference allows me to estimate the change in opioids shipped depending on if the county has an active PDMP/MML at the time. It also allows me to estimate the effect from each additional SAT in a given county. The third difference is all other opioids minus Oxycodone. This difference allows me to estimate the interaction between the reformulation and Z and their combined effect on Oxycodone compared to all other opioids. Using this model I am now estimating the interactive effect of the reformulation and Z on the MGE of all opioids per capita shipped to pharmacies, while subtracting out the change from pre to post for counties without Z, and the change from pre to post for all other opioids in counties with Z. Thus my coefficient of interest is now measuring the effect of

the reformulation interacted with Z on the MGE of Oxycodone per capita relative to all other opioids.

Additionally I report a dynamic model where I break the post period of my sample up into seven four-month periods. I do this to check for any unexpected lags or spikes, as well as to compare the short and semi-long run effects of the reformulation.

RESULTS

Difference in Difference Approach

In tables 3 and 4 I report results from a difference in difference set of models. Here I limit the outcome to only Oxycodone in Table 3 and then I limit the outcome to all other opioids in Table 4. Both of these variables are measured in MGE per 1000 population. In table 3 I find that all of the interactive effects of PDMPs/MMLs/SATs are not statistically different than zero. In Table 4 I find that the additional affect to counties in states with PDMPs is an increase of 4.897 MGE per capita of all other opioids not Oxycodone. The rest of my results are not statistically different than zero. However, in these tables the signs are consistent with what one might predict from the literature. As previously discussed in the methodology section, I am assuming that states with and without PDMPs would be trending similarly in the pre reformulation period, and continue with similar trends in the post period in the absence of the reformulation. These results could be due to the fact that the pre-treatment trends assumption is violated, which would cause my results to be biased. Again using the example of PDMPs, if counties with rapidly increasing opioid misuse are more likely to pass PDMPs, then any of the interactive effects of the reformulation and PDMPs would be biased towards a positive result. I interpret this to mean that using a triple difference model where I can directly compare Oxycodone to all other opioids is the most valuable model specification. Specifically, the triple difference model allows

me to use all other opioids as counterfactual, which accounts for different trends in states that pass

PDMPs. In the simple double difference model this is not the case.

	(1)	(2)	(3)
	Oxy per 1k	Oxy per 1k	Oxy per 1k
PDMP Law	-0.673		
	(0.711)		
Post x PDMP	-0.515		
	(0.821)		
Med. Marij. Law		0.0342	
		(1.308)	
Post x MML		-0.187	
		(0.731)	
Total CTY SAT			-0.0121
			(0.0286)
Post x SAT			0.00383
			(0.00770)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

Table 3: Each column represents a different regression where the outcome is MGE of Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Data tracking the year Medical Marijuana Laws were passed were collected from the National Conference of State Legislatures. Data on when Prescription Drug Monitoring Programs were implemented were provided by Dr. Wendy Stock. Data on county counts of active Substance Abuse Treatment facilities were provided by Dr Isaac Swensen. County demographics data were collected from the National Cancer Institute's SEER program. County income estimates were provided by Dr Isaac Swensen. Standard errors are clustered at the state level and are in parentheses for all regressions. PDMP is an indicator for if the county was in a state with and active Prescription Drug Monitoring Program. MML is an indicator for if the county was in a state with and active Medical Marijuana Law. SAT is a count of active Substance Abuse Treatment Facilities in the county.

	(1)	(2)	(3)
	Non Oxy 1k	Non Oxy 1k	Non Oxy 1k
PDMP Law	-7.303***		
	(1.655)		
Post x PDMP	4.897***		
	(1.559)		
Med. Marij. Law		1.475	
		(1.353)	
Post x MML		-1.613	
		(1.540)	
Post x SAT			0.00394
			(0.0145)
Total CTY SAT			-0.0224
			(0.0452)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

Table 4: Each column represents a different regression where the outcome is MGE of all opioids not Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. Standard errors are clustered at the state level and are in parentheses for all regressions. PDMP is an indicator for if the county was in a state with and active Prescription Drug Monitoring Program. MML is an indicator for if the county was in a state with and active Medical Marijuana Law. SAT is a count of active Substance Abuse Treatment Facilities in the county.

Main Results

Table 5 is my main results table where I estimate the additional impact PDMPs MMLs and SATs had on Oxycodone shipments in conjunction with the reformulation, in columns 1, 2, and 3 respectively. The outcome of interest for Table 5 is MGE per 1000 population. My coefficients of interest are the triple differences in rows 2, 4

and 6. Recall from the methodology that the triple difference model is preferable to the previous double difference because it allows me to account for the trends in all opioids. This method works by measuring the total amount of opioids shipped to pharmacies before and after the reformulation, then subtracting out the change from pre to post for states without Z, and the change from pre to post for non-Oxycodone opioids. Using this triple difference I am now estimating the change in MGE shipped to pharmacies from pre to post reformulation, in counties with active PDMPs/MMLs/SATs (Z), for Oxycodone. In column 1 I find that the reformulation is associated with an additional 6.557 decrease in the MGE per 1000 people of Oxycodone shipped to pharmacies in states with active PDMPs compared to all other opioids which see an increase of 5.341 MGE per 1000 population. This result is significant at the 99% confidence level. Column 2 shows a 4.681 MGE decrease in Oxycodone for states with active MMLs, this result is significant at the 90% confidence level. Finally, in column 3, each additional SAT in a county is associated with a 0.11 MGE per capita decrease after the reformulation, significant at the 99% confidence level.

	(1)	(2)	(3)
	MGE per 1k	MGE per 1k	MGE per 1k
Post x PDMP	5.341***		
	(1.574)		
Post x PDMP x Oxy	-6.557***		
	(1.352)		
Post x MML		1.393	
		(1.627)	
Post x MML x Oxy		-4.131*	
		(2.560)	
Post x SAT			0.0597**
			(0.0284)
Post x SAT x Oxy			-0.110***
			(0.0379)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Table 5: Each column represents a different regression where the outcome is the MGE of all opioids shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Data tracking the year Medical Marijuana Laws were passed were collected from the National Conference of State Legislatures. Data on when Prescription Drug Monitoring Programs were implemented were collected from PDMP TTAC. Data on county counts of active Substance Abuse Treatment facilities were provided by Dr Isaac Swensen. County demographics data were collected from the National Cancer Institute's SEER program. County income estimates were provided by Dr Isaac Swensen. Standard errors are clustered at the state level and are in parentheses for all regressions. PDMP is an indicator for if the county was in a state with and active Prescription Drug Monitoring Program. MML is an indicator for if the county was in a state with and active Medical Marijuana Law. SAT is a count of active Substance Abuse Treatment Facilities in the county. This is using a triple difference model where the Oxy indicator is interacted with all other treatment indicators to measure the additional effect the reformulation had on Oxycodone specifically.

Dynamic Model

In Table 6 I report results from a dynamic model where the post period is split up into seven periods starting with August - December 2010. Beyond that there is nothing different than the regressions from Table 5, these are still triple difference models. I do this to look at how the reformulation interacted with these local policies over time. In all three columns I show a sharp decrease directly after the reformulation, followed by a small stutter back towards pre-reformulation levels, before steadily declining to new lows by the end of 2012.

Specifically looking at PDMPs, there is an initial decrease of 6.750 MGE of Oxycodone per 1000 population shipped to pharmacies in August - December 2010 for counties with active PDMPs. This steadily gets larger until there is a decrease of 8.577 MGE of Oxycodone by September - December 2012. For all periods there is a statistically significant negative effect of PDMPs on Oxycodone shipments at the 99% confidence level. In column 2 with MMLs, there is a initial decrease of 3.848 MGE per 1000 population however this effect is insignificant at any confidence level. This effect does grow to a decrease of 6.291 MGE per 1000 population for counties with active MMLs in September - December 2012 and this result is significant at the 95% confidence level. Finally looking at SATs in column 3, starting in August - December 2010 there is an initial decrease of 0.0801 MGE per 1000 population for each additional SAT in a county. This effect grows to 0.149 MGE for each additional SAT by September - December 2012. For SATs the effect on Oxycodone post reformulation is statistically significant

for at least the 95% confidence level for all periods. All of these results are similar to my main findings and suggest that were there more data available, my finding would grow over time suggesting that PDMPs MMLs and SATs all have a strong negative interaction with the 2010 reformulation on Oxycodone shipments to chain and retail pharmacies.

	PDMP	MML	SAT
	(1)	(2)	(3)
	MGE per 1k	MGE per 1k	MGE per 1k
Aug-Dec 10	-6.750***	-3.848	-0.0801**
	(1.250)	(2.442)	(0.0331)
Jan-Apr '11	-4.840***	-3.632	-0.0859**
	(1.524)	(2.630)	(0.0333)
May-Aug '11	-5.518***	-4.300	-0.0957***
	(1.512)	(2.734)	(0.0334)
Sep-Dec '11	-6.192***	-4.960*	-0.114***
	(1.379)	(2.713)	(0.0378)
Jan-Arp '12	-6.406***	-4.454*	-0.113***
	(1.404)	(2.560)	(0.0415)
May-Aug '12	-7.543***	-5.374**	-0.129***
	(1.463)	(2.531)	(0.0466)
Sep-Dec '12	-8.577***	-6.291**	-0.149***
	(1.583)	(2.501)	(0.0538)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Table 6: Each column represents a different regression where the outcome is the grams of Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Data tracking the year Medical Marijuana Laws were passed were collected from the National Conference of State Legislatures. Data on when Prescription Drug Monitoring Programs were implemented were collected from PDMP TTAC. Data on county counts of active Substance Abuse Treatment facilities were provided by Dr Isaac Swensen. County demographics data were collected from the National Cancer Institute's SEER program. County income estimates were provided by Dr Isaac Swensen. Standard errors are clustered at the state level and are in parentheses for all regressions. PDMP is an indicator for if the county was in a state with and active Prescription Drug Monitoring Program. MML is an indicator for if the county was in a state with and active Medical Marijuana Law. SAT is a count of active Substance Abuse Treatment Facilities in the county. This is using a triple difference dynamic model where the Post indicator is broken up into seven four month periods.

Alternative Models

Tables 7, 8, and 9 in the appendix I suggest as starting points for future work. These are triple difference models now looking at the interactive effects of the reformulation, PDMP/MMLs/SATs, and high exposure counties as well as below mean income per capita counties. These are two categories that have shown increased reactions to drug policy in previous literature and I believe there could be interesting substitution effects here, such as high income counties having a higher substitution rate towards other opioids. However, considering my previous discussions on the models I choose to use, I believe another interaction is required making these fully saturated quad difference models which is beyond the scope of this paper. I believe a model looking at the interaction between the reformulation, PDMPs, high exposure, and Oxycodone would find interesting results. Regardless, looking at Table 7 I find that counties with an active PDMP and that had high exposure to Oxycodone pre-treatment had a 7.310 MGE per 1000 population increase in the amount of non-Oxycodone shipped to pharmacies. I find a similar result for MMLs. This could indicate a substitution effect away from Oxycodone toward other opioids after the reformulation. However, I also find a similar effect, though much smaller, for Oxycodone using these models which leads me back to wanting to use a fully saturated quad difference model.

CONCLUSION

The results from Table 5 suggest that there is a strong complementary effect of PDMPs with the reformulation, with PDMPs being associated with a 6.557 decrease in the Oxycodone per 1000 population compared to all other opioids. This is about 3% of the county average of 215 MGE per 1000 population shipped every month. One possible explanation for the way PDMPs interact with the reformulation is by combating doctor shopping. As was explained previously, the reformulation made OxyContin abuse resistant, however one could still get high by simply taking multiple pills at once. It is possible that PDMPs prevented abusers from doctor shopping in an attempt to still abuse OxyContin. By the end of my sample PDMPs were associated with about a 8.577 MGE decrease in Oxycodone compared to all other opioids suggesting that there impact grew as time went on.

MMLs showed about a 4.681 MGE per 1000 population decrease which grew to a 6.291 MGE decrease by the end of my sample. While these results are noisier at the beginning of my sample, by the end there is a statistically significant decrease in Oxycodone associated with MMLs. These results are a bit smaller than the effects associated with PDMPs, as the change from MMLs is only about 2.9% of the sample mean Oxycodone per capita by the end of my sample. One possible explanation for this is a substitution effect between prescription opioids and medical marijuana, something that has been

documented before in previous literature (Maclean et al 2020) (Chan, Burkhardt, Flyr. 2019).

For SATs the average county has about 6.4 SATs. With a coefficient of -0.110 this means that the average county saw about a .704 MGE per 1000 population decrease in Oxycodone associated with those SATs. This is a bit of a smaller in magnitude effect than from PDMPs and MMLs however it is still very significant. I suggest that SATs may have interacted with the reformulation by allowing abusers an easy way out. Instead of switching to heroin or another prescription opioid, abusers may have seen the reformulation as their chance to admit into a SAT and treat their addiction.

Altogether it seems that PDMPs are the best compliment to the 2010 OxyContin reformulation at significantly reducing the Oxycodone consumed in a county. These programs seem to be most effective and states have started to follow suit as all fifty states now are operating or participating in a PDMP as of 2020 (PDMP TTAC, 2020). I would propose that PDMPs, MMLs and SATs form an excellent triangle of prevention, substitution, and treatment for opioid abuse. By possibly preventing substitution towards other opioids with a PDMP, allowing access to a safer alternative for pain relief with a MML, and increasing access to addiction treatment with SATs a county could be prepared to, in the future, take complete advantage of an unexpected shock such as the 2010 OxyContin reformulation.

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APPENDIX A

EXTRA TABLES AND FIGURES

	(1) Non Oxy 1k	(2) Non Oxy 1k	(3) Non Oxy 1k
PDMP Law	-7.350***		
	(1.553)		
Post x PDMP	1.974		
	(1.224)		
Post x High exposure x PDMP	7.310***		
	(1.355)		
Med. Marij. Law		1.300	
		(1.284)	
Post x MML		-3.645**	
		(1.555)	
Post x High exposure x MML		3.696***	
		(1.148)	
Total CTY SAT			-0.0505
			(0.0448)
Post x SAT			-0.0289**
			(0.0115)
Post x High exposure x SAT			0.0837***
			(0.0279)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Table 7: Each column represents a different regression where the outcome is MGE of all opioids not Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Standard errors are clustered at the state level and are in parentheses for all regressions. This table is specifically looking at interactions between previous regressions and if the county had a high exposure to Oxycodone before the reformulation in 2010.

	(1) Oxy per 1k	(2) Oxy per 1k	(3) Oxy per 1k
PDMP Law	-0.462		
	(0.946)		
Post x PDMP	-1.742**		
	(0.727)		
Post x High exposure x PDMP	3.062***		
	(0.787)		
Med. Marij. Law		-2.000***	
		(0.443)	
Post x MML		-0.885	
		(0.592)	
Post x High exposure x MML		1.161**	
		(0.577)	
Total CTY SAT			-0.0437**
			(0.0178)
Post x SAT			-0.0373**
			(0.0153)
Post x High exposure x SAT			0.0781***
			(0.0206)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Table 8: Each column represents a different regression where the outcome is grams of Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Standard errors are clustered at the state level and are in parentheses for all regressions. This table is specifically looking at interactions between previous regressions and if the county had a high exposure to Oxycodone before the reformulation in 2010.

	(1) Oxy per 1k	(2) Oxy per 1k	(3) Oxy per 1k
PDMP Law	-0.0624		
	(0.762)		
Post x PDMP	-0.897		
	(0.703)		
Post x Below avg inc pc x PDMP	0.611		
	(0.464)		
Med. Marij. Law		1.761	
		(1.218)	
Post x MML		-0.785	
		(0.633)	
Post x Below avg inc pc x MML		1.111	
		(0.789)	
Total CTY SAT			-0.0213
			(0.0231)
Post x SAT			0.00632
			(0.00914)
Post x Below avg inc pc x SAT			0.123**
			(0.0511)
County effect	yes	yes	yes
Month effects	yes	yes	yes
Year effects	yes	yes	yes
CTY Demographics	yes	yes	yes
CTY Income per capita	yes	yes	yes

Standard errors in parentheses

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Table 9: Each column represents a different regression where the outcome is grams of Oxycodone shipped to chain and retail pharmacies per 1000 population. Outcome data were collected from the DEA's ARCOS dataset. The sample is from all 50 states from 2006-2012 measured at the county by month level. Standard errors are clustered at the state level and are in parentheses for all regressions. This table is specifically looking at interactions between previous regressions and if the county was below the mean income per capita.

State	SAT mean		State	SAT mean
AK	89		MS	173
AL	418		MT	191
AR	383		NC	1144
AZ	656		ND	53
CA	3523		NE	280
CO	591		NH	155
CT	525		NJ	693
DC	87		NM	215
DE	134		NV	111
FL	1366		NY	2486
GA	412		OH	1081
HI	153		OK	344
IA	424		OR	554
ID	173		PA	1768
IL	1043		RI	185
IN	752		SC	174
KS	319		SD	147
KY	625		TN	637
LA	346		TX	1073
MA	1262		UT	307
MD	719		VA	295
ME	527		VT	178
MI	1000		WA	765
MN	923		WI	708
MO	831		WV	229
			WY	111

Table 10: State averages of active SATs from 2006-2012.

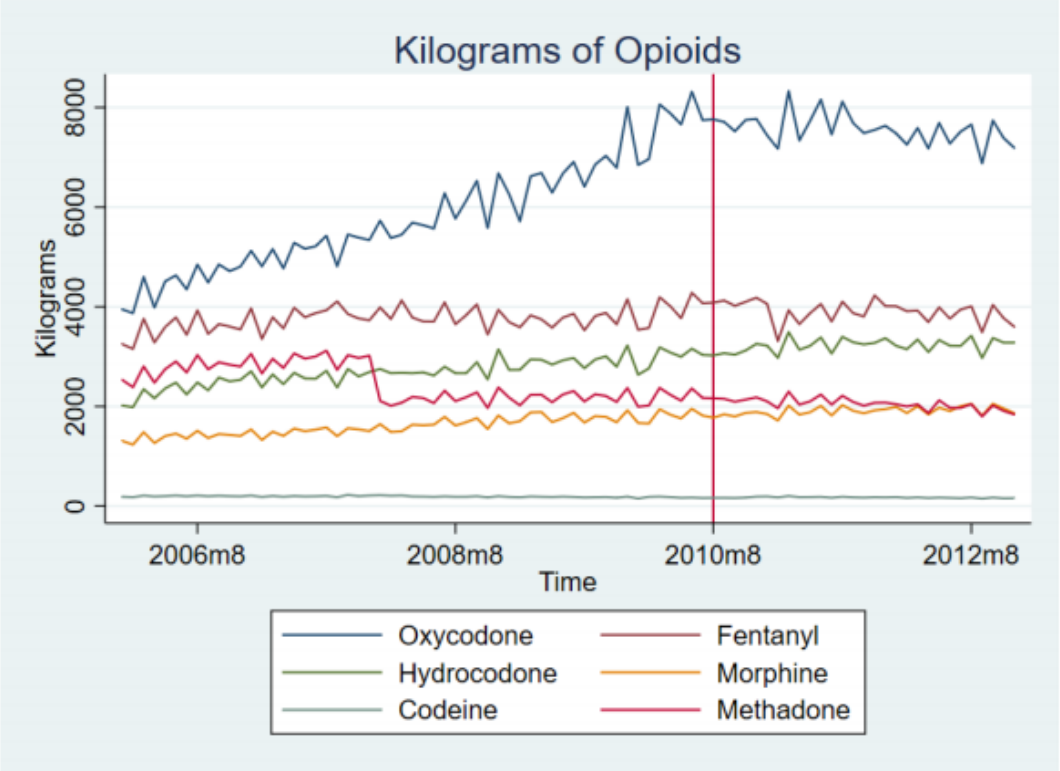

Figure 8: Total shipments in the U.S. Only Oxycodone is treated by the reformulation in 2010.