Supplementary Online Content

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eAppendix

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix

Model confounding variables

For this study, we used the total number of daily doses prescribed by each physician. Our key dependent variable was the total number of daily doses (in millions) for any opioid medication prescribed in Medicare Part D in each state in each year. We also conducted secondary analyses where the dependent variables were the sum of all prescriptions (in millions) written in each of the six generic opioid groups in each state and year. The key independent variable was an indicator variable for states that had an MCL in place (an active law on the books and patients had active legal medical cannabis access). The data were aggregated to the state level, with one observation per state per year. We determined the association between any MCL and all opioid prescribing using adjusted linear regression models. We estimated two version of these adjusted models: one with an indicator variable for any type of MCL and one with indicator variables for dispensary MCLs and home cultivation only MCLs (the two policy indicators were mutually exclusive). We also determined the association between MCLs and state aggregate prescribing for hydrocodone, oxycodone, fentanyl, morphine, methadone, and all other opioids separately. All regression models included the following set of state-level covariates (and a linear time trend and state fixed effects):

For moderating factors directly associated with cannabis use:

- an indicator variable to capture whether state has adopted legal recreational marijuana. (Note: Two states, Colorado and Washington, had legalized recreational cannabis from the beginning of 2013 through 2015 and three states, Alaska, the District of Columbia, and Oregon, had legalized recreational cannabis in a significant part of 2015. Thus, only 9 of the 306 state/year observations had legalized cannabis turned on in our analysis. While we believe that there are too few legal recreational cannabis observations to support inferences associated with this variable, we nonetheless include it to allow for the potential that omitting it could introduce bias in our other estimated coefficients. Econometrically, including a variable, like legalized cannabis, which may have a "true" zero association does not introduce bias.)

For moderating factors directly associated with physician prescribing of opioids:

- an indicator variable to capture whether the state has an operational electronic prescription drug monitoring program.
- a Herfindahl index of physician market competitiveness; this variable is the sum of squared physician Medicare Part D prescribing market shares in each county (averaged over the state), and is a standard measure in economics of how competitive a market is (near zero reflects perfect competition and a one reflects pure monopoly).

For moderating factors that represent the underlying influence of the overall economic environment on the demand for opioids:

- the percent of the population below the poverty line;
- the percent of the population enrolled in Medicare;
- the percent of Medicare enrollees in Medicare Advantage (managed care plans that generally have stronger drug utilization management controls);
- and, total state population.

eTable 1: Opioid Brand and Generic Names Used in Analysis

Hydrocodone: ALOR, AZDONE, DAMASON, HYDROCODONE, HYSINGLA, IBUDONE, LORCET, LORTAB, MAXIDONE, NORCO, PANASAL, REPREXAIN, VICODIN, VICOPROFEN, ZOHYDRO, ZYDONE

Oxycodone: COMBUNOX, ENDODAN, OXECTA, OXYCOCET, OXYCODAN, OXYCONTIN, OXYFAST, OXYIR, OXYNORM, OYYCODONE, PERCOCET, PERCODAN, ROXICET, ROXICODONE, ROXIPRIN, TARGIN, TARGINACT, TARGINIQ, TROXYCA, TYLOX

Fentanyl: ABSTRAL, ACTIQ, DURAGESIC, DUROGESIC, FENTANYL, FENTORA, HALDID, INSTANYL, IONSYS, LAZANDA, MATRIFEN, ONSOLIS, SUBLIMAZE, SUBSYS

Morphine: ASTRAMORPH, AVINZA, DEPODUR, DURAMORPH, INFUMORPH, KADIAN, MORPHINE, MSIR, ORAMORPH, RESCUDOSE, ROXANOL

Methadone: AMIDONE, DISKETS, DOLOPHINE, HEPTADON, METHADONE, METHADOSE PHYSEPTONE, SYMORON, WESTADONE

Other opioid: BUTORPHANOL, CODEINE, COTANAL, DARVON, DEMEROL, DILAUDID, DROMORAN, EXALGO, HYDROMORPHONE, HYDROSTAT, LEVORPHANOL, MEPERIDINE, NALBUPHINE, NUBAIN, NUCYNTA, NUMORPHAN, OPANA, OXYMORPHONE, PENTAZOCINE, PROPOXYPHENE, STADOL, TALWIN, TAPENTADOL, TRAMADOL, ULTAM, ULTRACET

eTable 2: State Medical Cannabis Law Effective Dates (through 8/2016)				
State	Date MCL was Enacted	Date MCL was Effective	Date Home Cultivation was Permitted	Date Dispensary Opened in State
ALABAMA				
ALASKA	11/1998	3/1999	3/1999	
ARIZONA	11/2010	4/2011	4/2011	12/2012
ARKANSAS	11/2016			
CALIFORNIA	11/1996	11/1996	11/1996	11/1996 (a)
COLORADO	11/2000	6/2001	6/2001	7/2005
CONNECTICUT	6/2012	5/2012		10/2014
DELAWARE	5/2011	5/2011		6/2015
DC	5/2010	8/2010		7/2013
FLORIDA	11/2016			
GEORGIA				
HAWAII	6/2000	12/2000	12/2000	
IDAHO				
ILLINOIS	8/2013	1/2014		11/2015
INDIANA				
IOWA				
KANSAS				
KENTUCKY				
LOUISIANA				
MAINE	11/1999	1/2000	1/2000 (b)	4/2011
MARYLAND	4/2014	6/2014		
MASSACHUSETTS	11/2012	1/2013	1/2013	7/2015
MICHIGAN	11/2008	12/2008	12/2008	1/2009
MINNESOTA	6/2014	5/2014		7/2015
MISSISSIPPI				
MISSOURI				
MONTANA	11/2004	11/2004	11/2004	
NEBRASKA				
NEVADA	11/2000	10/2001	10/2001	8/2015
NEW HAMPSHIRE	7/2013	7/2013		6/2016
NEW JERSEY	1/2010	6/2010		12/2012
NEW MEXICO	3/2007	7/2007	7/2007	3/2009
NEW YORK	7/2014	7/2014		6/2016
NORTH CAROLINA				
NORTH DAKOTA	11/2016			
OHIO	6/2016			
OKLAHOMA				

OREGON	11/1998	12/1998	12/1998	7/2009
PENNSYLVANIA	4/2016	6/2016		12/2016
RHODE ISLAND	1/2006	1/2006	1/2006	4/2013
SOUTH CAROLINA				
SOUTH DAKOTA				
TENNESSEE				
TEXAS				
UTAH				
VERMONT	5/2004	7/2004	7/2004	6/2013
VIRGINIA				
WASHINGTON	11/1998	12/1998	11/1998	7/2014
WEST VIRGINIA				
WISCONSIN				
WYOMING				
(a) California has a complex history with dispensaries, which operated widely prior to the enactment of the MCL in 1996; dispensaries were first legally protected in 2003. (b) Caregivers can cultivate and sell, and were available as of December 1999.				
Note: Michigan prohibits dispensaries. Minnesota only permits liquid, oil, pill or vaporizer. Pennsylvania does not permit smoking or any dry leaf or plant form. New York does not permit smoking. Michigan initially had, but then repealed, a dispensary program.				
Sources are:				
ProCon.org (2017). "29 Legal Medical Cannabis States and DC - Laws, Fees, and Possession Limits." Retrieved June 5, 2017, from http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881.				
Powell, D., et al. (2015). Do Medical Cannabis Laws Reduce Addictions and Deaths Related to Pain Killers?, National Bureau of Economic Research. Appendix A.				
NORML (2015). "Medical Cannabis." Retrieved December 21, 2016, from http://norml.org/legal/medical-cannabis-2.				
Wen, H., et al. (2015). "The effect of medical cannabis laws on adolescent and adult use of cannabis, alcohol, and other substances." Journal of health economics 42: 64-80. Table 1.				
MPP (2016). State-by-State Medical Cannabis Laws: How to Remove the Threat of Arrest 2015. Washington, DC, Cannabis Policy Project.				
When sources conflict with one another, the earliest date is listed.				

eTable 3: Daily doses prescribed for all opioids, with state fixed effects and clustering

	(1)	(2)
	All States	All States
	b/ci95	b/ci95
Medical cannabis law in effect	-2.211*	
	[-4.574,0.152]	
State had legalized recreational cannabis	-1.210**	-1.273***
	[-2.131,-0.290]	[-2.105,-0.442]
State prescription drug monitoring program in effect	-0.350	-0.222
	[-1.387,0.687]	[-1.246,0.801]
Medicare prescriber Herfindahl index	62.510	175.482
	[-157.369,282.389]	[-73.266,424.230]
Percent of population below Federal Poverty Level	1.593***	1.667***
	[0.756,2.430]	[0.833,2.501]
Percent of population enrolled in Medicare	35.248	26.511
	[-19.514,90.010]	[-25.736,78.758]
Percent Medicare in Medicare Advantage	50.074**	45.001**
	[10.743,89.406]	[8.706,81.295]
Total state population (in millions)	13.783***	13.503***
	[10.707,16.858]	[10.531,16.475]
Time trend	0.216	0.574*
	[-0.320,0.752]	[-0.021,1.168]
Medical cannabis dispensary open		-3.742***
		[-6.289,-1.194]
Medical cannabis home cultivation allowed		-1.792**
		[-3.532,-0.052]
Constant	-105.287***	-106.498***
	[-123.516,-87.059]	[-123.783,-89.214]
Number of Observations	306	306

OLS regression coefficients on a model where the dependent variable is total opioid prescriptions. Percentage changes from the average all state level of prescribing in parentheses. 95% confidence intervals in brackets. Data are aggregated to all prescriptions in opioid category by state and year. State fixed effects are included in all models, but not shown here. Standard errors are clustered by state.

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

eTable 4: Daily doses prescribed for opioids, by type with state fixed effects and clustering

	(1)	(2)	(3)
	Hydrocodone	Oxycodone	Fentanyl
	b/ci95	b/ci95	b/ci95
Medical cannabis law in effect	-1.404*	0.039	-0.133*
	[-2.895,0.087]	[-0.105,0.182]	[-0.272,0.006]
State had legalized recreational cannabis	0.164	-0.041	-0.129***
	[-0.385,0.713]	[-0.106,0.025]	[-0.212,-0.046]
State prescription drug monitoring program in effect	-0.475	0.008	0.008
	[-1.347,0.398]	[-0.067,0.082]	[-0.059,0.075]
Medicare prescriber Herfindahl index	-58.500	2.691	7.525
	[-180.464,63.464]	[-10.884,16.266]	[-8.013,23.062]
Percent of population below Federal Poverty Level	1.210***	0.047**	0.054**
	[0.431,1.989]	[0.004,0.090]	[0.013,0.096]
Percent of population enrolled in Medicare	49.321**	0.069	1.295
	[10.908,87.734]	[-2.578,2.716]	[-1.393,3.983]
Percent Medicare in Medicare Advantage	25.115*	-0.213	2.523**
	[-0.301,50.530]	[-1.831,1.406]	[0.627,4.418]
Total state population (in millions)	3.834**	0.058	0.679***
	[0.636,7.033]	[-0.103,0.220]	[0.190,1.168]
Time trend	-0.126	0.021	0.021
	[-0.475,0.222]	[-0.017,0.058]	[-0.018,0.059]
Constant	-40.172***	-0.368	-4.701***
	[-62.345,-17.999]	[-1.877,1.142]	[-7.977,-1.426]
Number of Observations	306	306	306

OLS regression coefficients on a model where the dependent variable is total opioid prescriptions. Percentage changes from the average all state level of prescribing in parentheses. 95% confidence intervals in brackets. Data are aggregated to all prescriptions in opioid category by state and year. State fixed effects are included in all models, but not shown here. Standard errors are clustered by state.

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

eTable 5: Daily doses prescribed for opioids, by type with state fixed effects and clustering

	(1)	(2)	(3)
	Morphine	Methadone	Other Opioid
	b/ci95	b/ci95	b/ci95
Medical cannabis law in effect	-0.246**	0.006	-0.472
	[-0.478,-0.015]	[-0.063,0.075]	[-1.241,0.296]
State had legalized recreational cannabis	-0.167**	-0.047	-0.989***
	[-0.331,-0.003]	[-0.114,0.019]	[-1.519,-0.460]
State prescription drug monitoring program in effect	-0.076	-0.007	0.192
	[-0.221,0.068]	[-0.042,0.028]	[-0.225,0.609]
Medicare prescriber Herfindahl index	39.159**	6.460*	65.175
	[6.636,71.682]	[-0.050,12.971]	[-36.876,167.226]
Percent of population below Federal Poverty Level	0.106***	0.041***	0.135
	[0.038,0.174]	[0.011,0.070]	[-0.198,0.468]
Percent of population enrolled in Medicare	-0.649	1.146	-15.934
	[-5.636,4.338]	[-0.255,2.546]	[-35.420,3.553]
Percent Medicare in Medicare Advantage	3.390**	-0.135	19.395***
	[0.202,6.578]	[-1.028,0.757]	[7.802,30.988]
Total state population (in millions)	1.403**	0.163**	7.645***
	[0.175,2.630]	[0.010,0.315]	[5.103,10.188]
Time trend	0.123**	0.009	0.168
	[0.031,0.216]	[-0.011,0.028]	[-0.125,0.462]
Constant	-10.750***	-1.264**	-48.032***
	[-18.207,-3.294]	[-2.446,-0.083]	[-63.322,-32.741]
Number of Observations	306	306	306

OLS regression coefficients on a model where the dependent variable is total opioid prescriptions. Percentage changes from the average all state level of prescribing in parentheses. 95% confidence intervals in brackets. Data are aggregated to all prescriptions in opioid category by state and year. State fixed effects are included in all models, but not shown here. Standard errors are clustered by state.

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

eTable 6: Daily doses prescribed for opioids, by type with state fixed effects and clustering

	(1)	(2)	(3)
	Hydrocodone	Oxycodone	Fentanyl
	b/ci95	b/ci95	b/ci95
Medical cannabis dispensary open	-2.320***	0.081	-0.152*
	[-3.782,-0.859]	[-0.043,0.205]	[-0.332,0.028]
Medical cannabis home cultivation allowed	-1.256**	0.083	-0.047
	[-2.319,-0.193]	[-0.025,0.192]	[-0.168,0.075]
State had legalized recreational cannabis	0.099	-0.030	-0.124***
	[-0.458,0.656]	[-0.098,0.038]	[-0.205,-0.044]
State prescription drug monitoring program in effect	-0.389	0.004	0.014
	[-1.250,0.472]	[-0.071,0.079]	[-0.053,0.082]
Medicare prescriber Herfindahl index	9.781	0.290	11.169
	[-120.805,140.367]	[-12.061,12.642]	[-7.336,29.674]
Percent of population below Federal Poverty Level	1.258***	0.044**	0.055**
	[0.479,2.037]	[0.005,0.084]	[0.013,0.096]
Percent of population enrolled in Medicare	44.221**	0.148	0.851
	[6.992,81.450]	[-2.326,2.623]	[-1.920,3.622]
Percent Medicare in Medicare Advantage	22.293*	-0.243	2.154**
	[-1.356,45.941]	[-1.708,1.221]	[0.359,3.950]
Total state population (in millions)	3.660**	0.068	0.676***
	[0.636,6.685]	[-0.086,0.222]	[0.191,1.162]
Time trend	0.086	0.015	0.035
	[-0.283,0.454]	[-0.020,0.051]	[-0.013,0.083]
Constant	-40.982***	-0.309	-4.704***
	[-62.381,-19.582]	[-1.755,1.137]	[-8.045,-1.362]
Number of Observations	306	306	306

OLS regression coefficients on a model where the dependent variable is total opioid prescriptions. Percentage changes from the average all state level of prescribing in parentheses. 95% confidence intervals in brackets. Data are aggregated to all prescriptions in opioid category by state and year. State fixed effects are included in all models, but not shown here. Standard errors are clustered by state.

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

eTable 7: Daily doses prescribed for opioids, by type with state fixed effects and clustering

	(1)	(2)	(3)
	Morphine	Methadone	Other Opioid
	b/ci95	b/ci95	b/ci95
Medical cannabis dispensary open	-0.361**	0.009	-0.998*
	[-0.718,-0.005]	[-0.062,0.080]	[-2.190,0.194]
Medical cannabis home cultivation allowed	-0.149	0.035	-0.458
	[-0.364,0.065]	[-0.017,0.087]	[-1.174,0.258]
State had legalized recreational cannabis	-0.167*	-0.041	-1.009***
	[-0.357,0.023]	[-0.102,0.020]	[-1.498,-0.520]
State prescription drug monitoring program in effect	-0.063	-0.008	0.220
	[-0.205,0.078]	[-0.041,0.025]	[-0.196,0.636]
Medicare prescriber Herfindahl index	49.369**	6.403*	98.469
	[10.014,88.724]	[-0.621,13.427]	[-31.230,228.168]
Percent of population below Federal Poverty Level	0.111***	0.040***	0.159
	[0.039,0.183]	[0.011,0.069]	[-0.194,0.513]
Percent of population enrolled in Medicare	-1.570	1.094	-18.233*
	[-6.451,3.311]	[-0.362,2.549]	[-37.764,1.298]
Percent Medicare in Medicare Advantage	2.766*	-0.207	18.238***
	[-0.219,5.751]	[-1.043,0.630]	[7.184,29.291]
Total state population (in millions)	1.382**	0.164**	7.552***
	[0.175,2.589]	[0.014,0.315]	[4.928,10.176]
Time trend	0.158***	0.010	0.270
	[0.050,0.266]	[-0.013,0.032]	[-0.107,0.646]
Constant	-10.830***	-1.244**	-48.430***
	[-18.201,-3.458]	[-2.418,-0.069]	[-64.320,-32.539]
Number of Observations	306	306	306

OLS regression coefficients on a model where the dependent variable is total opioid prescriptions. Percentage changes from the average all state level of prescribing in parentheses. 95% confidence intervals in brackets. Data are aggregated to all prescriptions in opioid category by state and year. State fixed effects are included in all models, but not shown here. Standard errors are clustered by state.

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

eTable 8: Parallel Trends Test on Number of Daily Doses Filled

	Coefficient on Parallel Trend	Standard Error	T-Test Statistic	
Opioids	2.15	5.12	0.42	
Hydrocodone	1.21	2.87	0.42	
Oxycodone	0.03	0.18	0.16	
Fentanyl	0.21	0.28	0.75	
Morphine	-0.15	0.35	-0.42	
Methadone	0.03	0.15	0.21	
Other opioid	0.82	1.60	0.51	

Note: The coefficient is from an interaction with the time trend (year) variable and an indicator variable for whether the state will adopt an MML in a regression on state-level average daily doses filled for each clinical condition listed, as:

$$\overline{Doses}_{st} = \beta_0 + \beta_1 \cdot Time_t + \beta_2 \cdot 1(State\ will\ adopt\ MML) + \beta_3 Time_t \cdot 1(State\ will\ adopt\ MML) + \varepsilon_{st}$$

This model is run during the time periods when MML=0 for those states that ultimately adopt and for all time periods for states that never adopt. Observations after the year 2014 are dropped since all "ever adopting" states have adopted an MML by that year. The unit of observation is state level average daily doses per year. The test of parallel trends is a test of the null hypothesis that the coefficient on time***1**(State will adopt an MML) = 0. This hypothesis is not rejected for any of the conditions.

eTable 9: Placebo tests for effective MML parameter - opioids

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.12	0.017
Dispensary open	-0.11	0.068
Home cultivation only	-0.17	-0.0042
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 10: Placebo tests for effective MML parameter - hydrocodone

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.058	0.052
Dispensary open	-0.046	0.091
Home cultivation only	-0.096	0.041
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 11: Placebo tests for effective MML parameter - oxycodone

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.0051	0.0015
Dispensary open	-0.0053	0.0030
Home cultivation only	-0.0079	0.0024
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 12: Placebo tests for effective MML parameter - fentanyl

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.0075	0.00062
Dispensary open	-0.0079	0.0012
Home cultivation only	-0.0089	0.0025
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 13: Placebo tests for effective MML parameter - morphine

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.0078	0.0091
Dispensary open	-0.0084	0.014
Home cultivation only	-0.013	0.0096
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 14: Placebo tests for effective MML parameter - methadone

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.0028	0.00057
Dispensary open	-0.0033	0.00072
Home cultivation only	-0.0035	0.0012
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.

eTable 15: Placebo tests for effective MML parameter – other opioid

	(1)	(2)
	Lower Bound Placebo Estimate	Upper Bound Placebo Estimate
	mean	mean
Any MML in effect	-0.027	0.039
Dispensary open	-0.030	0.048
Home cultivation only	-0.036	0.049
Observations	101	101

Placebo estimates were based on 100 iterations with random assignment of effective MMLs, dispensary and home cultivation MMLs to non-MML states and pre-MML periods to all MML states. Lower and upper bounds of the placebo estimates were calculated using 95 percent confidence intervals on the estimated parameters using each repetition of the simulated placebo trials.