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Association Between US State Medical Cannabis Laws and Opioid Prescribing in the Medicare Part D Population

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IMPORTANCE Opioid-related mortality increased by 15.6% from 2014 to 2015 and increased almost 320% between 2000 and 2015. Recent research finds that the use of all pain medications (opioid and nonopioid collectively) decreases in Medicare Part D and Medicaid populations when states approve medical cannabis laws (MCLs). The association between MCLs and opioid prescriptions is not well understood.

OBJECTIVE To examine the association between prescribing patterns for opioids in Medicare Part D and the implementation of state MCLs.

DESIGN, SETTING, AND PARTICIPANTS Longitudinal analysis of the daily doses of opioids filled in Medicare Part D for all opioids as a group and for categories of opioids by state and state-level MCLs from 2010 through 2015. Separate models were estimated first for whether the state had implemented any MCL and second for whether a state had implemented either a dispensary-based or a home cultivation only–based MCL.

MAIN OUTCOMES AND MEASURES The primary outcome measure was the total number of daily opioid doses prescribed (in millions) in each US state for all opioids. The secondary analysis examined the association between MCLs separately by opioid class.

RESULTS From 2010 to 2015 there were 23.08 million daily doses of any opioid dispensed per year in the average state under Medicare Part D. Multiple regression analysis results found that patients filled fewer daily doses of any opioid in states with an MCL. The associations between MCLs and any opioid prescribing were statistically significant when we took the type of MCL into account: states with active dispensaries saw 3.742 million fewer daily doses filled (95% CI, −6.289 to −1.194); states with home cultivation only MCLs saw 1.792 million fewer filled daily doses (95% CI, −3.532 to −0.052). Results varied by type of opioid, with statistically significant estimated negative associations observed for hydrocodone and morphine. Hydrocodone use decreased by 2.320 million daily doses (or 17.4%) filled with dispensary-based MCLs (95% CI, −3.782 to −0.859; $P = .002$) and decreased by 1.256 million daily doses (or 9.4%) filled with home-cultivation–only-based MCLs (95% CI, −2.319 to −0.193; $P = .02$). Morphine use decreased by 0.361 million daily doses (or 20.7%) filled with dispensary-based MCLs (95% CI, −0.718 to −0.005; $P = .047$).

CONCLUSIONS AND RELEVANCE Medical cannabis laws are associated with significant reductions in opioid prescribing in the Medicare Part D population. This finding was particularly strong in states that permit dispensaries, and for reductions in hydrocodone and morphine prescriptions.

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Opioid prescribing has dramatically increased over the past 15 years. During this time, physicians became more willing to use opioid medications to treat chronic and acute pain in the community[1,2] as the medical community increasingly recognized the historic undertreatment of pain and began to conceptualize pain as the "fifth vital sign."[3-5] Opioid prescribing increased from around 148 million prescriptions in 2005 to 206 million prescriptions by 2011.[6] Coincident with the increase in prescription opioids, the United States experienced an acceleration in opioid-related mortality. Annual opioid-related mortality (including heroin) increased from 14 910 deaths in 2005 to 33 091 in 2015.[7] However, even though overall prescriptions for opioid medications decreased from 206 million in 2012 to around 169 million in 2015,[6] opioid prescribing rates remains 3 times higher than in 1999. A significant component of the opioid mortality crisis is often attributed to prescription opioids.[8-11] Thus, there is reason to suspect that controlling the demand for opioid prescriptions could aid in the public health battle against unintentional opioid mortality.

One policy option that may have the unintended consequence of ameliorating the opioid crisis is the legalization of medical uses for cannabis. Since California approved the first medical cannabis law (MCL) in 1996, 29 states and the District of Columbia have approved some form of MCL.[9,12-15] All states with approved MCLs include a list of approved medical conditions that qualify a patient for access to cannabis.[16] Chronic pain is listed as an approved condition (either directly, or by implication) in every state MCL. In addition to explicit state legislative endorsement, there is increasing clinical evidence that cannabis can be used to manage pain.[17-23] In January 2017, the National Academies of Sciences, Engineering, and Medicine released a comprehensive review of the clinical peer-reviewed literature and determined that there is "conclusive evidence" that cannabis can be used safely and effectively to treat chronic pain.[24] Interestingly, recent evidence suggests that cannabis use is rising fastest in the population older than 50 years[25]—which is the group most likely to have the conditions for which the evidence for cannabis benefit is strongest.

This increasing clinical evidence raises the question of whether cannabis access could sway patients away from opioid use. Recent work by 2 of us (A.C.B. and W.D.B.)[26] found substantial substitution away from pain medications (without differentiating the type of pain medication) prescribed by physicians in the Medicare Part D program between 2010 and 2013 for states with active MCLs. A 2017 follow-up study[27] by the same authors found similar results for the fee-for-service component of state Medicaid programs from 2007 to 2014. While these 2 studies were the first to demonstrate reductions in prescription use for large populations in the community, neither focused on how opioid medication use changed as MCLs went into effect. If nonnarcotic nonsteroidal anti-inflammatory drugs were the prescriptions that declined when MCLs went into effect, the potential for MCLs to induce reductions in opioid use would be questionable. In addition, those articles did not distinguish between the type of MCL; they did not identify whether the effect differed for states that permit access to medical cannabis via dispensaries compared with the effect in states that require home cultivation only. Clearly, the opportunity cost for accessing cannabis will be lower if patients can go to a dispensary rather than spend several months engaged in cultivation, and so the potential benefits for opioid diversion could be quite different across the type of MCL.[28] As the National Institute of Drug Abuse now states on its web site: "[S]ome preliminary studies have suggested that medical cannabis legalization might be associated with decreased prescription opioid use and overdose deaths, but researchers don't have enough evidence yet to confirm this finding."[29]

We examined associations between any MCL and between separate dispensary-based and home-cultivation-only-based MCLs and the number of daily doses of opioids filled in Medicare Part D at the state level from 2010 to 2015.

Key Points

Question What is the association between US state implementation of medical cannabis laws and opioid prescribing under Medicare Part D?

Findings This longitudinal analysis of Medicare Part D found that prescriptions filled for all opioids decreased by 2.11 million daily doses per year from an average of 23.08 million daily doses per year when a state instituted any medical cannabis law. Prescriptions for all opioids decreased by 3.742 million daily doses per year when medical cannabis dispensaries opened.

Meaning Medical cannabis policies may be one mechanism that can encourage lower prescription opioid use and serve as a harm abatement tool in the opioid crisis.

Methods

Data for this analysis was aggregated and made publicly available by the Centers for Medicare & Medicaid Services (CMS). Since no individual information is included in the public data, the research did not involve human subjects, and no approval was required from the University of Georgia IRB.

Medicare is a US federal insurance program established in 1965 to (initially) cover outpatient and inpatient medical services for people 65 years or older and people with disabilities or end-stage renal disease. Medicare Part D, enacted as a result of the Medicare Modernization Act of 2003, is the optional prescription drug benefit plan available to Medicare enrollees to which more than 70% of enrollees are subscribed. The CMS maintains records of all prescription drugs purchased through the Medicare Part D program in the Medicare Part D Prescription Drug Event (PDE) Standard Analytic Files. Public use versions of these data were made available under a Freedom of Information Act request by ProPublica for the calendar years 2010 to 2012 and were released directly by CMS for the calendar years 2013 to 2015. The raw PDE data are compiled to the physician-drug level each year and contain data on all prescription drugs filled under Medicare by all Part D enrollees whether they were in stand-alone Part D plans or had

prescription coverage under a Medicare Advantage Prescription Drug plan. We retained only those observations associated with physicians operating in a US state or Washington, DC (eg, prescriptions filled on overseas military bases or in a US territory were excluded). From 2010 to 2015, the time period we studied, there were 132.6 million physician-drug-year observations. Each record in the PDE data represents a specific drug prescribed by each physician in each year.

For this study, we used the total number of daily doses prescribed by each physician. Drugs were identified by the First Databank generic or brand name, as supplied in the PDE data. We retained all generic and brand opioids. Opioid brand and generic names were taken from all entries in the 2011 and 2016 US Food and Drug Administration Orange Book associated with the following pharmaceutical classes: Full Opioid Agonist (MoA), Opioid Agonist (EPC), Partial Opioid Agonist (EPC), and Partial Opioid Agonists (MoA). We further grouped each drug by the following generic product groupings: hydrocodone, oxycodone, fentanyl, morphine, methadone, and all other opioids. Buprenorphine products were excluded from the analyses because they are indicated for substance use disorder, not pain management. In addition, Medicare Part D does not cover methadone for substance use disorder; thus, methadone is prescribed only for pain management in Medicare Part D. The complete list of unique drug names used is presented in the eAppendix in the Supplement.

The 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. The raw Medicare Part D PDE files include the number of daily doses filled per physician and drug. "Daily dose" represents the number of days' treatment dispensed for each drug. For example, if the standard use of a drug and strength were for a patient to take 2 pills per day, and a prescription was dispensed in a bottle that contained 60 pills, then the prescription would represent 30 daily doses. The CMS determined "standard use" for each drug and provided the adjusted daily dose calculation in the raw data. Note that since the PDE data identifies drugs only by name rather that by the National Drug Code (which captures dosage strength), we cannot calculate morphine milligram equivalents. We also conducted secondary analyses in which the dependent variables were the sum of all prescriptions (in millions) written in each of the 6 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). Between 2010 and 2015, 9 states (Arizona, Connecticut, Delaware, Illinois, Massachusetts, and Minnesota) implemented some form of MCL; 14 states and the District of Columbia had some form of active MCL for the entire time period (Alaska, California, Colorado, District of Columbia, Hawaii, Maine, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, and Washington); 27 states had not implemented (though some had passed) an MCL by the end of 2015 (Alabama, Arkansas, Florida, Georgia, Idaho, Iowa, Indiana, Kansas, Kentucky, Louisiana, Maryland, Mississippi, Missouri, Nebraska, New Hampshire, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, West Virginia, Wisconsin, and Wyoming).[30,31]

There is considerable variation among state policies surrounding medical cannabis. Home cultivation of cannabis is sometimes permitted.[32,33] Currently, 15 states allow at least some patients to cultivate a predetermined amount of cannabis at home. Since 2009, every state that has passed an MCL has included some form of regulated dispensary program.[32] Currently, 24 states and the District of Columbia have MCLs that include a dispensary program, although dispensaries are not yet active in some states; we characterize a state as having a dispensary-based MCL only if some dispensary has been opened. The distinction between access points for medical cannabis (home cultivation or dispensaries) is an important yet infrequently studied aspect of cannabis policy.[34] Dates for the implementation of MCLs used in this study are listed in the online eAppendix in the Supplement. We did not try to assess the association between recreational cannabis laws and opioid prescribing because only 9 of 306 observations had recreational legalization turned on. However, we did include the variable in the model as a potential confounder.

Our analysis proceeded in 2 stages. The data were aggregated to the state level, with 1 observation per state per year. In the first stage we determined the association between any MCL and all opioid prescribing using adjusted linear regression models. We estimated 2 versions of these adjusted models: 1 with an indicator variable for any type of MCL and 1 with indicator variables for dispensary MCLs and home cultivation only MCLs (the 2 policy indicators were mutually exclusive). In the second stage we determined the association between MCLs and state aggregate prescribing for hydrocodone, oxycodone, fentanyl, morphine, methadone, and all other opioids separately. All regression models included a set of state-level covariates (listed in the footnotes of **Tables 1**, **2**, and **3**, and discussed in detail in the online eAppendix in the Supplement) and a linear time trend and state fixed effects. Standard errors were clustered at the state level using the Stata xtreg command with the "vce(cluster *clustvar*)" option (version 14; StataCorp). We tested our data for parallel trends in prescribing between "never-MCL" states and pre-MCL years for states that implement the policy during our study period; we cannot reject the null hypothesis of parallel trends, which supports the use of our models (see online eAppendix eTable 8 in the Supplement).

Results

The mean utilization of any opioid in Medicare Part D between 2010 and 2015 was 23.08 million daily doses per year (**Table 4**). Mean annual daily doses for the major subcategories of opioids (in millions) were 11.78 for hydrocodone, 0.834 for oxycodone, 1.381 for fentanyl, 1.703 for morphine, 0.673 for methadone, and 6.715 for our "other opioid" grouping.

In the adjusted (regression) model in which the dependent variable was the number of daily doses filled for any type of opioid (in millions) we found that MCLs of any sort were as-

Table 1. Daily Doses Prescribed for All Opioids[a]

Variable[b]	Coefficient (95% CI)[c]	Percentage Change	*P* Value
Modeling any type of MCL as 1 variable			
MCL in effect	−2.211 (−4.574 to 0.152)	−8.5	.06
Modeling MCL by type with separate variables			
Medical cannabis dispensary open	−3.742 (−6.289 to −1.194)	−14.4	.005
Medical cannabis home cultivation allowed	−1.792 (−3.532 to −0.052)	−6.9	.04

Abbreviation: MCL, medical cannabis law.

[a] There were 306 observations for each model. Ordinary least-squares regression coefficients from models in which the dependent variables are total opioid prescriptions. Percentage changes from the average "no MCL" state level of prescribing are in parentheses. Data are aggregated to all prescriptions in opioid category by state and year.

[b] The MCL coefficient from a model in which MCL is measured as being any type. Variables included in all models but not shown in this table: whether state has adopted legal recreational cannabis, whether the state has an operational electronic prescription drug monitoring program; Herfindahl index of physician market competition, percentage of the population below the poverty line, percentage of population enrolled in Medicare, percentage of Medicare in Medicare Advantage plans, total state population, a time trend, and state fixed effects.

[c] MCL coefficients from a model in which dispensary-based or home cultivation only MCLs are measured separately.

Table 2. Daily Doses Prescribed for Opioids Using "Any Medical Cannabis Law" (MCL) Policy Variable, by Opioid Type[a]

Opioid Type, With MCL in Effect	Coefficient (95% CI)	Percentage Change	*P* Value
Hydrocodone	−1.404 (−2.895 to 0.087)	−10.5	.06
Oxycodone	0.039 (−0.105 to 0.182)	4.4	.59
Fentanyl	−0.133 (−0.272 to 0.006)	−8.5	.06
Morphine	−0.246 (−0.478 to −0.015)	−14.1	.04
Methadone	0.006 (−0.063 to 0.075)	0.8	.87
Other opioid	−0.472 (−1.241 to 0.296)	−6.0	.22

[a] There were 306 observations for each type of drug. Ordinary least-squares regression coefficients from models in which the dependent variables are total opioid prescriptions. Percentage changes from the average "no MCL" state level of prescribing are in parentheses. Data are aggregated to all prescriptions in opioid category by state and year. Variables included in all models but not shown here: whether state has adopted legal recreational cannabis, whether the state has an operational electronic prescription drug monitoring program, Herfindahl index of physician market competition, percentage of the population below the poverty line; percentage of population enrolled in Medicare, percentage of Medicare in Medicare Advantage plans, total state population; a time trend, and state fixed effects.

Table 3. Daily Doses Prescribed for Opioids Distinguishing MCL Policy Types, by Opioid Type[a]

Opioid	Coefficient (95% CI)	Percentage Change	*P* Value
Medical Cannabis Dispensary Open			
Hydrocodone	−2.320 (−3.782 to −0.859)	−17.4	.002
Oxycodone	0.081 (−0.043 to 0.205)	9.1	.19
Fentanyl	−0.152 (−0.332 to 0.028)	−9.7	.10
Morphine	−0.361 (−0.718 to −0.005)	−20.7	.047
Methadone	0.009 (−0.062 to 0.080)	1.3	.80
Other opioid	−0.998 (−2.190 to 0.194)	−12.8	.10
Medical Cannabis Home Cultivation Allowed			
Hydrocodone	−1.256 (−2.319 to −0.193)	−9.4	.02
Oxycodone	0.083 (−0.025 to 0.192)	9.3	.13
Fentanyl	−0.047 (−0.168 to 0.075)	−3.0	.44
Morphine	−0.149 (−0.364 to 0.065)	−8.5	.17
Methadone	0.035 (−0.017 to 0.087)	5.1	.18
Other opioid	−0.458 (−1.174 to 0.258)	−5.8	.20

[a] There were 306 observations for each type of drug. Ordinary least-squares regression coefficients from models in which the dependent variables are total opioid prescriptions. Percentage changes from the average "no MCL" state level of prescribing are in parentheses. Data are aggregated to all prescriptions in opioid category by state and year. Variables included in all models but not shown here: whether state has adopted legal recreational cannabis, whether the state has an operational electronic prescription drug monitoring program; Herfindahl index of physician market competition, percentage of the population below the poverty line, percentage of population enrolled in Medicare, percentage of Medicare in Medicare Advantage plans, total state population, a time trend, and state fixed effects.

sociated with a 2.211 million daily dose decrease in filled prescriptions (or 8.5% of the non-MCL state prescribing) (Table 1) compared with states that did not have an active MCL. While not statistically significant, the "any MCL" association is in the same direction as the results when MCLs are identified by type. When compared with having no MCL, we found that permit-

ting access via a dispensary was statistically significantly associated with a decrease in prescribing of 3.742 million daily doses (or 14.4%) annually (95% CI, −6.289 to −1.194; P = .005) and that access via home cultivation only was associated with a decrease of 1.792 million annual daily doses (or 6.9%) (95% CI, −3.532 to −0.052; P = .04).

The secondary analyses examined the association between MCLs separately by class of opioid. We found significant associations in both models in which we estimated the association of any MCL (Table 2) and in models in which we distinguished between dispensary and home-cultivation-only delivery modes (Table 3). Focusing in the results differentiating the type of MCL, we found that hydrocodone use decreased by 2.320 million daily doses (or 17.4%) filled with dispensary-based MCLs (95% CI, −3.782 to −0.859; P = .002) and decreased by 1.256 million daily doses (or 9.4%) filled with home-cultivation-only-based MCLs (95% CI, −2.319 to −0.193; P = .02). Morphine use decreased by 0.361 million daily doses (or 20.7%) filled with dispensary-based MCLs (95% CI, −0.718 to −0.005; P = .047). Associations between dispensary-based MCLs and fentanyl and "other opioid" use were not statistically significant at conventional levels but were in the same direction as with hydrocodone and morphine.

Table 4. Dependent, Cannabis Policy, and Other Independent Variables[a]

Variable	Mean (SD)
Filled daily doses, in millions, No.	
Any opioid	23.08 (24.34)
Hydrocodone	11.78 (13.60)
Oxycodone	0.83 (0.74)
Fentanyl	1.38 (1.24)
Morphine	1.70 (1.78)
Methadone	0.67 (0.72)
Other opioid	6.71 (7.33)
Medical cannabis law in effect	0.36 (0.48)
Medical cannabis dispensary open	0.19 (0.39)
Medical cannabis home cultivation allowed	0.20 (0.40)
State had legalized recreational cannabis	0.029 (0.17)
State prescription drug monitoring program in effect	0.79 (0.40)
Medicare prescriber Herfindahl Index	0.028 (0.02)
Percentage of population below federal poverty level	15.24 (3.09)
Percentage of population enrolled in Medicare	0.12 (0.02)
Percentage of Medicare enrollees in Medicare Advantage	0.26 (0.13)
Total state population (in millions)	6.18 (6.95)
Time trend	3.50 (1.71)

[a] There were 306 state and year observations. State indicator variables not shown. Means for categorical variables represent the average of the 0 (no) and 1 (yes) values across each state and year observation. The Herfindahl Index is a commonly used economic measure of market competitiveness; we have scaled the index to range from zero (perfectly competitive) to 100 (perfect monopoly). The time trend ranges from 1 to 6 (2010 to 2015, respectively).

Discussion

In analyzing data on all opioid prescriptions filled in the Medicare Part D program from 2010 through 2015, nationwide, we found in our multivariate regressions that use of outpatient opioid prescriptions decreased after states implemented MCLs. When we controlled for the type of MCL, we found a 14.4% reduction in use of any opioid associated with medical cannabis dispensaries and a 6.9% reduction in any opioid prescribing with home-cultivation-only MCLs. Secondary analyses by type of opioid found statistically significant negative associations with dispensary-based MCLs and daily doses filled of hydrocodone and morphine.

There is some evidence in the literature that MCLs are associated with reductions in opioid-related mortality. A recent state-level analysis found statistically significant and meaningful reductions in opioid mortality when any form of MCL was passed.[35] There are mechanisms that would explain this association. Most opioid overdoses are associated with legitimate opioid prescriptions.[10] Furthermore, a growing consensus suggests that cannabis can be used to effectively manage pain in some patients.[17,19-23,36,37] If initial licit prescriptions for opioids can be reduced, then there is a plausible theoretical pathway to anticipate that opioid misuse and abuse could also fall.

Limitations

This study has several limitations. We cannot determine whether the association between MCL and decreased opioid prescribing represents substitution for any individual patient because we cannot observe both prescription use and medical cannabis use in the same patient; otherwise, our results would be vulnerable to the ecological fallacy.[38] In addition, using our state-level aggregation, we cannot examine substate heterogeneity in the association. Perhaps the association between opioid use and cannabis access differs for rural compared with urban areas, areas with larger compared with smaller minority populations, or in areas that are medically underserved compared with areas with adequate clinician resources. Third, hydrocodone was upgraded to a Schedule II controlled substance in 2014, although since our data only go through 2015 we cannot determine if any of the change in use we observe was due to rescheduling. We do not have separate measures of the price of each drug paid by Medicare patients, which should affect utilization (although it is unlikely to be correlated with state MCLs, given Medicare reimbursement rules). Fourth, because we examine the association between MCLs and opioid prescribing in Medicare Part D, we cannot directly address the effect that cannabis laws may have on opioid use among other populations. Fifth, we only observe prescribing by drug name, and so we cannot convert daily doses into an intensity measure like morphine milligram equivalents.

Conclusions

In this study, we investigated whether medical cannabis access was associated with prescription opioid prescribing in Medicare Part D. We found that overall opioid prescribing in

Part D was lower when states permit access to medical cannabis. When examining data by individual drug classes, we found that prescriptions for hydrocodone and morphine had statistically significant negative associations with medical cannabis access via dispensaries; while not statistically significant, there were also negative associations between dispensary MCLs and fentanyl and "other opioid" use. Combined with previously published studies suggesting cannabis laws are associated with lower opioid mortality, these findings further strengthen arguments in favor of considering medical applications of cannabis as one tool in the policy arsenal that can be used to diminish the harm of prescription opioids.

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