PRELIMINARY DRAFT

The Impact of Medical Marijuana Legalization On Prescription Medication Use and Costs in Medicare Part D

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In the past 20 years the drive to legalize medical marijuana has gained national attention with the public and policy makers. However, little is known about whether medical marijuana is being used clinically to any significant degree. Using data on all prescriptions filled by Medicare Part D enrollees in the U.S. from 2010 to 2013 we found that the use of prescription drugs for which marijuana could serve as a clinical alternative fell significantly once a medical marijuana law was put in place. Overall savings to the Medicare program when states implemented MMLs was estimated to be over $153.6 million per year by 2013. Medical marijuana availability has a significant effect on prescribing patterns and spending in Medicare Part D.

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1. Introduction

In the past 20 years the drive to legalize medical marijuana has gained national attention with the public and state policy makers. Research began to emerge in the late 1980's that marijuana has a positive effect on the lives of many people suffering from a variety of ailments. Nevertheless, marijuana is still federally classified as a Schedule I drug (the most restrictive category) in the Controlled Substances Act, which means that it is deemed to have "no currently acceptable medical use in treatment in the United States," a high potential for abuse, and "a lack of accepted safety for use… under supervision" (O'Keefe 2013). This classification imposes significant barriers to obtaining marijuana products for clinical use, or even for primary research projects regarding the pharmacological and behavioral impact of marijuana use. Despite such barriers, 23 states and the District of Columbia have adopted laws legalizing marijuana for medical purposes by of the beginning of 2016. Surprisingly, although there is a rapidly growing literature about spillover effects of medial marijuana laws (MMLs), almost nothing is known about how these state health policies affect clinical care and health care sector spending. In this paper we will investigate how implementing state-level MMLs changes prescribing patterns and program and patient expenditures for FDA-approved prescription drugs under Medicare Part D.

2. Background

There is significant variation between state policies surrounding medical marijuana, a situation that may reflect variations in each states' public opinion norms

about the use of marijuana (Cerdá, Wall et al. 2012). Every state that currently allows medical marijuana requires a licensed physician to recommend the drug, and requires that it be done only if the patient presents with a "legitimate illness."[1] Home cultivation of marijuana is sometimes permitted, although it is not an efficient way of obtaining the product a for many patients, because the process for growing a viable marijuana plant is very slow (O'Keefe 2013, Pacula, Boustead et al. 2014). In 2007 New Mexico became the first state to pass an MML that included state regulated dispensaries as a source of the drug. Every state since 2009 that has passed an MML has included some form of regulated dispensary program (O'Keefe 2013). Some states allow caregivers to distribute marijuana, although states differ in the definition of caregiver and to how many patients each caregiver is legally allowed to distribute (O'Keefe 2013, Pacula, Boustead et al. 2014). Lastly, the legal possession limit differs immensely from state to state. For example, Montana allows 1 ounce and 4 plants per person, while Oregon allows 24 ounces and 24 plants per person (Chu 2014).

Research surrounding the positive or negative effects of the medical use of marijuana has been extremely mixed. Historically, opponents of medical marijuana legalization have cited addiction, criminal activity, marijuana being a gateway drug, and lack of demonstrated medical value as reasons for keeping the drug illegal. However the causal link between the use of marijuana and the use of harder drugs, as well as the link between medical marijuana and criminal activity, has never been definitively proven. In fact, Anderson and coauthors reported in a 2013 study that estimated plausibly causal

[1] These illnesses include: chronic pain, nausea, cachexia, wasting syndrome resulting from HIV, glaucoma, acquired immune deficiency syndrome, and cancer among others Klofas, J. and K. Letteney (2012). The Social and Legal Effects of Medical Marijuana: State Legislation and Rules, Working Paper, Center for Public Safety Initiatives, Rochester Institute of Technology..

effects of MML implementation that traffic fatalities dropped 8-11% following the passage of state medical marijuana legislation (Anderson, Hansen et al. 2013). In contrast, Wall et al. reported that states that have passed an MML had significantly higher rates of marijuana use and abuse than their non-medical marijuana approving counterparts, though the estimated effects were largely associations (Wall, Poh et al. 2011). In a later study, Harper and colleagues (attempting to replicate Wall et al.) found that when causal methods were employed, the effect of MMLs on drug use largely disappeared (Harper, Strumpf et al. 2012). These findings are representative of an unsettled literature, where later studies that use causal methods tend find mixed evidence for significant effects.

One issue that has received surprisingly little attention is the question of whether medical marijuana is actually being used clinically to any significant degree. To the extent that marijuana is used by physicians to manage the conditions for which it has clinical evidence, then one would expect it to be primarily a substitute for existing prescription medications - for patients who did not respond to prior therapy, or who respond better to marijuana. Nonetheless, there are no published studies that investigate whether the introduction of medical marijuana changes the prescribing patterns for FDA-approved pharmaceuticals. In this article, we ask two straightforward questions. Does implementing an MML change prescribing patterns in Medicare Part D for traditional (FDA-approved) drugs that treat conditions marijuana may itself treat? If so, what is the effect on overall spending (programmatic and patient out of pocket) from such changes?

3. Data

3.1. Evidence for Clinical Uses and Effectiveness of Marijuana

The clinic evidence for the efficacy of marijuana in treating a variety of ailments is mixed. In order to synthesize the numerous studies that have been published in the past few decades we will use two primary sources: an influential summary of the clinical marijuana literature conducted under the auspices of the Institute of Medicine (Joy, Watson Jr et al. 1999); and a recent and very comprehensive meta-analysis of the clinical uses of marijuana (Whiting, Wolff et al. 2015). These two sources highlight nine broad categories of illness where sufficient studies have been conducted to justify some preliminary conclusions. They are listed in Table 2, which summarizes the discussion below.

Anxiety Disorders: Marijuana's treatment effect for managing anxiety has not been extensively studied. The meta analysis conducted by Whiting et al. (2015) found only one study which evaluated patients with Generalized Anxiety Disorder in a statistically rigorous manner. This study (judged to have a high risk of bias) found that marijuana was associated with an improvement in the levels of anxiety reported by patients. Four more studies were evaluated which examined the level of anxiety in patients with chronic pain. While these studies also found a beneficial effect, they were not limited to patients with anxiety disorders and so were not deemed conclusive. Nonetheless, some indication of effect was noted.

Depression and Mood Disorders: Depression has also not been studied extensively. In fact, the 2015 meta-analysis by Whiting et al. found no studies evaluating the effect of marijuana on depression that fulfilled their inclusion criteria. The authors did

find five studies on other ailments that included depression as an outcome measure, two with an unclear risk of bias and three with high risk of bias. Three of these studies found no treatment effect, and one parallel-group trial found a beneficial effect for one dosage level, and no difference between placebo and treatment for two other dosage levels.

Glaucoma: The 2015 meta-analysis found one very small crossover trial that found no difference between the placebo and cannabinoids on intraocular pressure in glaucoma patients. The 1999 IOM study by Joy et al. (1999) found that although glaucoma was one of the most commonly cited medical reason for marijuana, data do not support its clinical use in managing glaucoma. Although they did find a large treatment effect on intraocular pressure the dosage required was relatively high, and the decrease of intraocular pressure was incredibly short-lived. Consequently, marijuana was deemed impractical as a therapy and no further study was recommended.

Nausea: The treatment effect of cannabinoids on nausea and vomiting associated with chemotherapy for cancer treatment has been widely studied. The 2015 meta-analysis found 28 studies, 23 with a high risk of bias and 5 with an unclear risk. Every cited study found that marijuana reduced nausea symptoms when compared to a placebo, but this result was not statistically significant in all cases. Joy et al. (1999) also found scientific support for the treatment effect of marijuana for nausea and vomiting as a result of chemotherapy.

Pain Management: Pain is the most common malady for which people seek treatment according to Joy et al. (1999). The authors of the IOM review found scientific support for the treatment of pain in chemotherapy patients, spinal chord injury patients, neuropathic patients, stroke patients, chronic pain and insomnia patients, and AIDS

patients. The recent 2015 meta-analysis found 28 studies assessing the treatment effect of marijuana on chronic pain patients (two with a low risk of bias, 9 with unclear risk, and 17 at a high risk). The average number of chronic-pain patients in these studies who reported a reduction of pain of at least 30%, was greater with marijuana than with placebo. Both sources endorse existing evidence regarding the effectiveness of marijuana as a treatment of chronic pain.

Psychosis and Seizure Disorders: The effect of marijuana on psychosis and seizure disorders has not been studied extensively. The 2015 meta-analysis only reviewed two studies on psychosis, both with a high risk of bias. These two trials found no difference in the severity of psychotic symptoms between patients treated with marijuana and those treated with the placebo. Seizures studies were not included in the 2015 meta-analysis, and the 1999 Joy et al. review did not find enough evidence to support clinical studies in this area.

Sleep Disorders: Whiting et al. (2015) found two studies that evaluated the effect of cannabinoids on sleep disorders. One study had a high risk of bias, but found a greater benefit in marijuana over the placebo. The second study was a cross-over trial with a low risk of bias, which found that cannabinoids were associated with an improvement in insomnia and an increase in restfulness. Whiting et al. found another nineteen studies that did not focus on sleep disorders specifically but included sleep as an outcome variable. These studies provided models evidence to support the claim that marijuana may improve patient sleep time and quality.

Spasticity: Finally, spasticity was evaluated in the 1999 Joy et al. study. The IOM reviewers concluded that the evidence was too weak to make a reliable claim about

marijuana's treatment effectiveness. Whiting et al. (2015) found fourteen studies assessing spasticity due to multiple sclerosis (MS) or paraplegia. All of theses studies included a placebo control group, but none had an active comparator. Only studies involving patients with MS reported sufficient data to allow for meta-analytic estimation. Cannabinoids were associated with an improvement in spasticity compared to the placebo group, but this combined effect did not reach statistical significance.

3.2. Determining Drugs to Study

Marijuana, in addition to being one of the most widely used recreational drugs in the U.S., is also often credited in the popular press with being an effective treatment for an extremely broad range of conditions. However, as discussed above, the peer-reviewed clinical research is much more circumspect regarding what conditions may be effectively treated or managed using marijuana. As shown in Table 1, states have largely restricted authorized uses of marijuana to a much smaller set of conditions. We will study nine such categories that either have some evidence of clinical effectiveness (discussed above) or are very commonly cited in state medical marijuana enabling legislation (even if the clinical evidence is pessimistic, such as for spasticity). Our study conditions are: anxiety, depression, glaucoma, nausea, pain, psychosis, seizures, sleep disorders, and spasticity. We will examine the degree to which physicians changed their prescribing patterns for drugs used to treat these broad categories of diagnoses. Several steps are required to determine which drugs to study.

Before drugs can be marketed in the United States, manufacturers must receive approval from the Food and Drug Administration (FDA). Approval of a new drug is

based upon submission of detailed clinical trials evidence by the manufacturer; if the evidence established that the product is safe and effective, the drug is approved for marketing. Critically for this paper, when drugs are approved, they are always approved for specific diagnoses or indications. For example, when Forest Pharmaceuticals submitted an approval for their new drug Lexapro (escitlaopram) they requested approval for the product to be used in the treatment of "major depressive disorder" and were given approval – and a required to use a specific label – for that purpose. Physicians were then able to prescribe the drug for their patients with that diagnosis. When physicians prescribe a drug for one of the conditions that is mentioned on the approved FDA label it is called an "on-label use" of the product. In subsequent years, Forest Pharmaceuticals conducted additional clinical trials and submitted evidence that Lexapro is useful in treating other conditions, and were successful at expanding the label to include generalized anxiety disorder.

Clinical medicine is not so straightforward as simply treating patients according to pre-approved FDA drug labels. Physicians are permitted to prescribe a drug to treat conditions for which it is not formally approved. When this happens the drug is said to be used "off-label." For example, beta-blockers, such as metaprolol and propranolol, have been used for decades to treat hypertension, cardiac dysrhythmias, and other diseases. Clinicians have noted that beta-blockers also control physical sensations associated with anxiety (such as rapid heartbeat, tightness in the chest, and trembling), and that when patients do not feel these sensations, their psychological experience of anxiety is significantly reduced. As a result, these drugs are widely prescribed for situational and other forms of anxiety. Lin et al. (2006) estimate that 52% of prescriptions

for beta-blockers were off-label from 1999-2002. (Lin, Phan et al. 2006) Recent studies have indicated that more than a third of all drugs prescribed in the U.S. are written for some off-label indication. (Bradford, Turner et al. 2015)

Consequently, it would not generally be sufficient to study the impact of MML on the use of drugs that are FDA-approved to treat the conditions listed above; defining the set of study drugs in that fashion could potentially exclude many drugs that are actually used to treat the conditions in clinical practice. To address this, we gathered data on prescription drug use from the Pharmacy Event Files of the Medical Expenditure Panel Survey (MEPS) maintained by the Agency for Healthcare Research and Quality (AHRQ). The MEPS is a large longitudinal survey of individuals and households, representative of the U.S. population. The survey has been conducted continuously since 1996. Approximately 35,000 individuals (representing around 12,000 households) are surveyed three times per year over a two year period as part of the Household Component (HCP) of the survey.

One component of the MEPS-HC is the Prescription Drugs event file. These files record all prescriptions filled by MEPS-HC respondents. Included in the file are details of each prescription event, including the First Data Bank brand (or generic) name and up to three recorded diagnostic reasons for the prescription as reported by the respondent. Diagnoses are coded into ICD-9 codes by MEPS staff. Using the MEPS, it is possible to identify all drugs that are prescribed for each diagnosis code – whether the drugs are being used off-label or on-label. We extracted all prescription events for the years 2007 through 2011 and retained all prescriptions records that had at least one ICD-9 codes

from the nine broad classification of conditions we studied for which marijuana is commonly cited as a treatment, which are listed in Table 2.

Once we identified the complete set of all prescriptions that MEPS-HC respondents reported were prescribed for these conditions, we eliminated all drugs that were recorded fewer than 100 times over the entire 2007-2011 time period. (There were many products that were listed only a handful of times over the five years for a given diagnosis, which we assumed was evidence that the use of the specific product for that condition was so non-standard as to not warrant inclusion.) Three of the potential marijuana-treatable conditions – anorexia, cachexia, and Tourette's – were reported so infrequently in the MEPS-HC Prescription Drug file that there were no drugs that reached the 100 mention threshold. Consequently, we did not include those conditions in the analysis.

The resulting data contained all prescription products used to treat the target diagnosis categories, both on- and off-label. We chose to be more parsimonious and restrict ourselves to the set of drugs that were more closely tied to the on-label options. In order to identify the more conservative set of drugs, we identified all the drugs from the set described above that were actually on-label using data on FDA-approved indications for each product in the Merck Manual, a commonly used pharmacological compendium. We then compiled a list of all drugs that were in the same drug class (using the Multim Tier-2 classification code) as these on-label options. These sets of "in the same drug class as an on-label option" prescription drugs – one set for each condition listed above – were the basis of our main analyses discussed below. For this "in-class" set of drugs we identified all prescription product in the MEPS that were in the same Multum Lexicon (second-

level) drug categories as the on-label drugs used to treat the disease groupings listed in Table 2.

Recall that drug classes are assigned according to whether any drug in that class is observed to be used to treat the general category of diagnosis on-label in the MEPS. Thus, for example, bupropion, is used on-label to treat anxiety (as Wellbutrin, or its generic alternatives). However, bupropion is also used on-label to treat smoking cessation (as Chantix, or its generic alternatives). As a result "smoking cessation agents" appear as one of the drug classes we use to select the Medicare Part D records we will include in the study. Rather than potentially leaving out some drugs that are widely used clinically to treat a target diagnosis, we chose to be inclusive in our list of candidate drug classes. So, while "smoking cessation agents" would not generally be associated with treatment for anxiety or depression, they do appear in our list of drug classes in which there is at least one on-label alternative (see Table 2). This will potentially leave in drugs for which turning on an MML will have no theoretical effect, which will drive the estimated treatment effect toward zero. In this sense, our estimated impact of implementing a MML will be conservative.

3.3. Extracting Medicare Part D Prescription Data

Beginning in January of 2006, Medicare enrollees had the option of purchasing a prescription drug benefit plan under the Medicare Part D program, which was initiated by the George W. Bush administration as part of the Medicare Modernization Act of 2003. After 2006, enrollees who want prescription drug coverage have three basic options: enroll in Medicare Parts A and B and purchase a separate prescription drug plan

(typically part of a retiree benefit program); enroll in a Medicare Advantage plan (Medicare Part C) which offers comprehensive inpatient, outpatient and prescription coverage; or purchase a Part D plan as a supplement to the traditional Medicare Parts A and B. Part D is available to all Medicare enrollees (both aged and disabled), including low-income enrollees dually eligible with Medicaid, at a monthly premium cost (base premium costs are $34.10 for 2016 (Cavanaugh 2015)). By 2015 the program enrolled over 39 million beneficiaries, accounting for nearly 72 percent of all Medicare enrollees.

The Centers for Medicare and Medicaid Studies (CMS) maintains records of all prescription drugs purchased through the Medicare Part D program in what is known as the Medicare Part D Prescription Drug Event (PDE) Standard Analytic File. Public use versions of this data were made available under a Freedom-of-Information Act request by ProPublica for the calendar years 2010 - 2012; CMS has made an essentially identical data set available for 2013. This PDE data is compiled by CMS to the physician-drug level each year. Drug names are assigned by linking the NDC code to a generic or brand name (where applicable) using the First DataBank drug names.[2] The data also includes basic data on the prescribing physicians, including NPI number, sex, specialty and location of home and business address.[3] The ProPublica and CMS public use files contain data on all prescription drugs filled under Medicare by all Part D enrollees (approximately 35.7 million enrollees in 2013), whether they were in stand-alone Part D plans (approximately 23 million enrollees in 2013) or had prescription coverage under a

[2] Note that since drugs are listed by NDC code, there will be different lines of data for different formulations - e.g., extended release vs. immediate release - and package sizes.
[3] For the years 2010-2012, when the data originates from the ProPublica FOIA request, only physician NPI numbers appeared in the actual public use PDE data. We merged information on physicians characteristics and practice location on to the analysis file by NPI number and the CMS National Plan and Provider Enumeration System.

Medicare Advantage Prescription Drug plan (approximately 13 million enrollees in 2013).[4] We retained only those observations associated with physicians operating in a U.S. State and Washington D.C. (e.g., prescriptions filled on overseas military bases or in a U.S. territory were excluded).

Each record in the PDE data represents a specific drug prescribed by each physician in each year. Thus, each prescribing physician will have as many records in the data as the number of unique drugs he or she prescribed in each year. Data elements include the number of unique prescriptions that were filled (initial prescription for the year and any refills), total days treatment supplied and total drug costs to the Medicare program. Drug costs include the amounts paid by the Part D drug plan, from any government subsidies, and amounts paid from any other third-party payors (including Medicaid). Importantly, costs also include any out-of-pocket payments made by the beneficiaries themselves.

3.4. Constructing the Analysis Data Sets

The Medicare Part D data (from both the ProPublica FOIA and CMS direct release) contain over 87 million physician-drug-year observations. We processed the data nine times, once for each of the broad diagnosis categories we had identified from the literature as being containing conditions for which marijuana is a potential therapy. During each pass through the data, we kept any records that were associated with a drug identified as being in the class for which some on-label option treatment option existed for the diagnosis group in question. These drug specific observations were then

[4] Due to privacy concerns, any drug that was prescribed 10 or fewer times by a physician in any year will was excluded from the PUF for that physician. Thus, in 2013 the PUF captures 86.8% of all Part-D filled drugs. Missing drugs are largely those that are very rarely prescribed.

aggregated to the physician level – such that each observation represented the total (in daily doses and cost) for each physician of all the drugs that were prescribed for each of our nine disease categories in each year. We saved the observations thus identified in separate analysis data sets - one for each diagnosis group. We merged data on county-level demographics from the Area Resources File. These variables included factors that were expected to influence the aggregate demand for drugs dispensed under Medicare Part D. We also constructed an indicator variable that equaled one whenever the prescriptions were filled in a state and year with an effective MML in place (i.e., where there was approval for state residents to use either home-grown marijuana or purchase in a dispensary and where a dispensary was actually open). This MML indicator is the key policy variable of interest. Finally, we constructed year and state indicator variables.

The resulting nine data sets, at the disease/physician/year level, were used for our main analyses. Means for all of the variables in each of the diagnosis-determined data sets are presented in Table 3. These primary data sets ranged in size from 588,808 observations to over 2,496,608 observations. Our models (discussed below) were run separately for each set of data.

In addition to the main analysis, we also repeated the data construction procedures outlined above twice, so that we could conduct sub-analyses by whether we could observe the drug being on-label or not. First, we repeated the data construction process keeping only observations that were determined to be themselves on-label treatment options for some ICD-9 code within the broad definition of the study conditions. We will refer to this data as the strictly on-label observations. Since, as mentioned above, off-label use is widespread and constituting as much as 35% to 40% of all prescriptions

written on average, we also created a version of our disease specific data where the observation were from the disunion of the prior two data sets: that is, the drug was from a class where there was at least one on-label option to treat an ICD-9 code within the disease class, but the particular drug was itself not on-label. We will refer to this data as the off-label data. Note, that this is not the set of drugs that were ever observed to have been used off-label to treat a relevant ICD-9 drug in the MEPS; that data would contain many more drugs, a large number of which would be approved for conditions that appear far-removed from the conditions under study. Rather than attempt to impose clinical judgment (which we do not possess) on those issues, we chose to restrict ourselves to drugs that while off-label nonetheless are in classes where some on-label option exists.

4. Conceptual Framework

From the perspective of the market for existing prescription drugs, the implementation of a medial marijuana law in a given state is essentially isomorphic to introducing a new prescription option: patients and physicians would then have a new treatment option which would compete with existing therapeutic alternatives. While it is true that the new option (medical marijuana) is not covered by any insurance plan, this is not unknown for new prescription drugs, and in any event would be the same as introducing a new FDA-approved drug with a very high price.

Conceptually then, our empirical model is based upon a model of uncertainty and learning in the prescription drug market, as explored by Coscelli and Shum and Crawford and Shum. (Coscelli and Shum 2004, Crawford and Shum 2005) The essential characteristics of the prescription drug market, in this framework, are that decisions are

made in an environment of uncertainty and that uncertainty is both general (viz. the average treatment effect) and individual (viz. the idiosyncratic patient response to any given drug). Patients are assumed to possess unobservable symptomatic and curative response parameters to each available drug conditioned on their clinical diagnosis. Physicians are unable to observe these parameters, and so must estimate (with error) which drug would be the most effective on both dimensions for the patient. Thus, initial prescribing following diagnosis is an exercise in experimentation. The quality of any given match will vary with the diagnosis (some patients have less uncertain response parameters for some conditions). Physicians, and patients, then learn about the match quality of each drug used over time. If the Bayesian updating is such that learned match quality falls below the expected match quality of a drug that has not been sampled, the patient will switch.

Crucially in this model, risk aversion will serve as a source of switching costs, and reduce the incentive to switch. This is because risk aversion generates a risk premium which increases the opportunity cost of sampling a new drug simply because the curative and symptomatic treatment effects for the untested drug are uncertain while these treatment effects are known for the sampled drug. Thus, risk aversion introduces something like a status quo bias. This implies that when a new treatment option is introduced, patients may not immediately switch to it even if the average treatment profile is superior to existing options. This status quo bias will be larger where the uncertainty surrounding the average and idiosyncratic treatment effects from the new drug is higher. Therefore diffusion is likely to be gradual, and may accelerate after some

time has passed and physicians build up experience with the new drug, thereby decreasing uncertainty.

However, the model by Crawford and Shum does not take into account any demand expansion that might take place as a result of a new product being introduced. One key force in demand expansion is that when new products are available then information sets change. Information sets could be changed due to advertising or because a new product stimulates discussion of the disease in the media. (Bradford, Kleit et al. 2006) For example, Keith (Keith 1995) and Ruben (Rubin 1991) argue that one primary effect of direct to consumer advertising is that it informs patients of the potential that they have a disease, or informs patients who have been diagnosed of the possibility of effective therapy, and so new patient go to their physician to seek treatment. Thus, even if advertising has no effect on changing any individual patient's demand elasticity, it could nonetheless increase consumption by bringing new patients into treatment. While medical marijuana is not the object of direct to consumer advertising campaigns, it is very frequently the object of intense media coverage. Such media coverage can serve the same role as advertising, and may indeed be as effective at stimulating demand.

These two theoretical forces will work together to alter the use of existing prescription drug in ways that will either increase or decrease use. We assume that medical marijuana, like the large majority of new approved drugs, is a net substitute for existing FDA-approved products for any given diagnosis. However, in a world characterized by match quality heterogeneity, risk averse patients and changing information sets, just because marijuana is a substitute for existing products does not immediately imply that the demand for those products will fall when an MML is in

effect. When MMLs are being passed and implemented, the set of people who know, or believe, that they have a defined set of conditions should rise due to the public discourse. This is the effect highlighted by Keith and Ruben. (Rubin 1991, Keith 1995) New information will drive more people to seek medical attention – and these people should have lower severity of illness on average than the population seeking treatment before the MML policy debate (otherwise, they would have already sought care). So, patient populations – and the population of people at risk for using both marijuana and existing FDA-approved drugs – rise. Once patients consult with physicians, then the heterogeneity and status quo biases can act. For some patients and for some diagnoses, the evidence for the relative effectiveness of marijuana may be sufficiently high that physicians overcome the status quo bias and recommend trying marijuana (though they cannot technically prescribe it); in that circumstance, consumption of FDA-approved products should fall.

For other patents and for some diagnoses– most notably glaucoma – the expected treatment effect of marijuana is not large enough to overcome the persistence in drug choice for prescription drugs; in that case, patients will still need to be treated, so they receive an FDA-approved drug and the use of those products actually rise on aggregate (due to more patients being at risk of use). Glaucoma is one of the most widely approved conditions in the text of states' medical marijuana legislation; however the clinical evidence is very strong that while marijuana sharply reduces intra-ocular pressure, the effect lasts only about an hour (Joy, Watson Jr et al. 1999). So, new patients who seek glaucoma treatment after learning about the potential benefits from marijuana are very likely to receive a prescription for an FDA-approved product (the visual trajectory for

untreated glaucoma is very ominous); thus we expected prescribing for glaucoma drugs to remain unchanged or even rise in the face of an MML.

Thus, whether prescription drug use rises or falls for a given category of disease when medical marijuana becomes available is an empirical question. We could have some ex ante expectations, though. To determine which disease groupings we might expect the largest patient expansion effect from the media coverage of an MML, we conducted a search of all English language, North American newspapers for unique articles that included the terms "medical marijuana" and each of the nine disease groups we studied in this paper over the 2010 – 2013 time frame. The number of newspaper articles for each disease group are shown in Figure 1. Broadly, we see four groups. Psychosis and pain stand out as being the least and most discussed in the media (respectively). Depression, anxiety and sleep disorders were roughly grouped together with around 100 unique articles each. Seizures, glaucoma, nausea and spasticity were grouped together with approximately 200 articles each. So, as we move from left to right in the figure, we expect larger increases in people seeking care following the publicity surrounding and implementation of a MML.

However, as discussed above, the medical evidence for effectiveness of marijuana for each condition varies significantly. So, for a disease like glaucoma with a great deal of popular discussion about a marijuana treatment effect but also relatively clear clinical evidence that the effect is inadequate for therapy, combined with the fact that glaucoma has a very serious trajectory if left untreated, we expect to see an increase in FDA-approved drugs following implementation of an MML. On the other hand, with a condition like chronic pain with a great deal of popular attention and associated positive

clinical evidence we would expect to see a large reduction in prescription drug use as more new patients are diverted to try marijuana. This effect will be somewhat muted due to the Crawford and Shum type risk aversion influences, and may therefore grow larger over time as physicians and patients use marijuana and the uncertainty surrounding average and idiosyncratic treatment effects falls.

We test the general predictions of this framework using data on all Medicare Part-D prescriptions written in the contiguous U.S. states from 2010-2013.

5. Empirical Models

5.1 General Models

We implemented the conceptual model outline above using a simple difference-in-difference regression framework estimated separately for each of the diagnostic groupings: anxiety; depression; glaucoma; nausea; pain; psychosis; seizures; sleep disorders; and, spasticity. Models had the general form:

$$(1) \qquad y_{istd} = \beta_d + X_{st}\underline{\beta} + MML_{st}\delta + \nu_i + \tau_t\alpha_s + \varepsilon_{istd}$$

where: y_{istd} = prescriptions filled or daily doses filled by the i^{th} physician in the s^{th} county in the t^{th} year for the d^{th} diagnosis category; X_{st} are county characteristics; MML_{st} is an indicator variable for whether a medical marijuana law was in effect in state s during year t; ν_i is a vector of physician practice specialty indicator variables; τ_t is vector of year indicator variables; α_s is a vector of state variables; and ε_{istd} are error terms which were clustered at the physician level. Physician characteristics include sex and a set of

specialty indicator variables. State characteristics include the percent of the population that reports marijuana user and state indicator variables. Characteristics of the county included in the models were: an HHI for daily doses written by physicians at the disease / county level; percent of the county below the federal poverty line; median county income (in 10,000s); deaths in county (in 1000s); Medicare ED visits (in 10,000s); unemployment rate in county; percent of population enrolled in Medicare; county population (in 100,000s); percent of county population in urban area as of the 2010 census; percent county population that is Black; percent county population that is Hispanic; percent county population that is other race; and MDs per 10,000 population. Physician specialty indicator variables are: Internal Medicine; Hospice Care; Emergency Medicine; OB/GYN; Preventative Medicine; Psychiatry and Psychiatrics; Pain Medicine; Surgery; Optometry; Physical Medicine; and Oncology.

In addition, while the regression represents a difference-in-differences specification, there are actually three categories of states with respect to medical marijuana laws: those that never had an effective MML during the 2010-2013 time period (the "never" states); those that switched from no MML to having an effective MML in place during the 2010-2013 time frame (the "switcher" states); and those state that always had an MML in effect during those years (the "always" states). We therefore estimated the models in the regression two times: first, we estimated the difference-in-differences specification in (1) across all states; second, we estimated the difference-in-differences models only across "never" and "switcher" states. One could argue that the second approach represents the purest form of difference-in-differences estimator.

5.2. Estimating Changes in Costs

To put our ultimate findings in perspective, we conducted one additional exercise. As mentioned above, the Medicare Part D utilization data also contains information on total spending that resulted from the filled prescriptions; these dollar amounts include Medicare payments, government low-income subsidies, and patient out-of-pocket costs. We used this data to calculate costs per daily dose for each observation in our original drug-level data, and then estimated the total reduction in expenditure associated with an MML using prescription-level data on doses filled. We used a drug-level analysis for the cost saving estimate (rather than our main physician-level analysis) to calculate total program savings in order to avoid double-counting, since prescription products may be in multiple disease categories in our data. For example, some SSRIs would be used to treat anxiety, depression, psychoses, or sleep disorders and those drugs appear in each of those three condition specific analysis files. So, adding up estimated the dollar value changes from the main models calculated on the physician-condition level would over-estimate savings.

In order to arrive at a correct estimate of the net total savings to Medicare associated with states adopting medical marijuana laws, we first estimated the utilization models at the drug level and applied the coefficient on the MML indicator to each physician/drug/year observation to estimate changes to utilization; those utilization changes were multiplied by the calculated per unit Medicare and enrollee spending for the drug. We then pooled all of the resulting predicted cost changes into a single data set and eliminated any duplicates. In order to be conservative, when a physician/drug/year observation appeared more than once (for example, when it was in both the anxiety and

depression sets), we kept the observation that had the smallest estimated cost saving. With these unduplicated estimates of changes to total spending associated with Medicare Part-D in hand, we then calculated programmatic and enrollee savings induced by implementing MMLs for each year in our data.

6. Results

Before estimating the regression models on prescribing frequency and volume, we first ran a series of simple bivariate comparisons across observations occurring in states and times where there as an MML in effect compared to observations occurring in states and times without an effective MML in place. We conducted these bivariate tests for the whole sample, the on-label sample, and the off-label sample. It is worth recalling that we are using a true census of filled prescriptions under Medicare Part D, so, any observed differences are the true differences; in a real sense, standard errors and tests of significance are redundant. Nonetheless, we did conduct standard t-tests on differences in daily doses filled across MML and non-MML regimes for each of the clinical condition groups to assess the statistical strength of the difference in the number of prescriptions filled and the number of daily doses filled.[5] The t-tests for differences in prescriptions written are presented in Tables 4.a – 4.c. For the full sample (on- and off-label) we found that for each clinical condition group, except for glaucoma, the number of filled prescriptions fell by between 422 to 3645 prescriptions per physician per year. These reductions were all significant at very high levels of confidence, with t-statistics

[5] The t-tests we present were calculated on the data sets containing all drugs in Multum Lexicon classes where there was at least one confirmed on-label option to treat the relevant medical conditions. The t-test findings were essentially the same when run across the more restrictive set of only on-label options.

ranging from 32.96 up to 49.11. Generally speaking, the bivariate results were similar for the on-label only and off-label only samples. There were three notable exceptions to this. The first two involve pain and seizure disorder prescribing, where the raw differences were much more pronounced in the off-label sample than the on-label sample. This is consistent with the generally higher rates of off-label use to treat those conditions.

The third striking difference was for glaucoma. Glaucoma stood out as different from the other disease groupings in the full sample. Recall from our discussion above that there is reason to suspect ex ante that we might even see increases in FDA-approved prescriptions written after an MML goes into effect because of the patient population expansion effect, the very clear evidence that marijuana cannot be an effective therapy for glaucoma, and the clinical imperative to not leave glaucoma untreated. In Table 4.a. we saw that for glaucoma, prescription daily doses filled actually increased when an MML was in effect, though the difference was small in magnitude. The distinctiveness of glaucoma prescribing is further emphasized in Tables 4.b and 4.c. The on-label use of prescription drugs rose significantly in times when an MML was in effect, at around 1555 more daily doses per physician per year. However, off-label use of glaucoma treating drugs actually fell (like with other conditions) – though again, the magnitude of the effect was relatively small (around 96 daily doses per year).

While the simple bivariate comparisons demonstrate that – with the exception of glaucoma –fewer daily doses are filled after an MML for FDA-approved prescription drugs used to treat conditions in our selected disease groupings, this does not mean that the MML is the causal effect. To have more confidence in the association, we need to control for other factors that may be driving differences in prescribing across states that

do and do not have MMLs in effect. Thus, we conducted a series of multivariate regression analyses as specified in equation (1) above.

We sought to identify the causal impact of an effective MML in several ways. First, we included a rich set of county and state level controls, each capturing factors that would be expected to have independent effects on prescription drug aggregate demand. Second, we included year and state fixed effects to capture (in the least restrictive way) national secular trends in prescribing and any time-invariant differences between the states that might be driving prescribing in some way that might be correlated with MML implementation. With the inclusion of an effective MML indicator, time dummies and state dummies, the coefficient on the MML variable is the difference-in-differences estimate of the independent impact of the MML on prescribing.

However, our full analysis data sets for each condition group compares prescribing in three regimes: states that never had an MML from 2010 to 2013 ("never states"), states that adopted ("switched states") an MML sometime during 2010 to 2013; and states that had adopted an MML prior to 2010 ("always states"). While the MML indicator as specified above does represent a difference-in-differences estimate, we conducted a further sub-analysis by estimating (1) only for the "never states" and "switched states" to get a pure difference-in-difference, and thereby causal, effect.

We presented our MML coefficients for the measures of prescribing using the full state data in Table 5. The results for the difference-in-differences models were extremely consistent. For anxiety, depression, nausea, pain, psychosis, seizure disorders, and sleep disorders we found that implementing an effective MML led to a reduction in the number of daily doses written by a physician each year of between -265 (for depression) to -1826

(for pain). Each of these marginal effects were significant at the 1% level or better. As with our simple t-test, the estimated effect of an MML on glaucoma medications was insignificant. We also found that the impact of an MML on spasticity-related prescribing was also statistically insignificant when estimating the model on the full (on- and off-label) set of drugs.

The picture became somewhat more complex when we broke our sample into on-label only and off-label only prescriptions. As might be expected, the magnitudes of the estimated MML effects were somewhat different across on- and off-label drugs. The estimated MML effect for anxiety, depression, psychosis, and spasticity were a bit larger in on-label sample compared to the off-label sample (the MML effect was insignificant in the off-label sample in the case of spasticity). For example, physicians in states with an active MML wrote -816 fewer daily doses for on-label prescriptions for anxiety compared with only -272 fewer off-label anxiety related daily doses. The impact of an MML on prescribing for nausea, seizures, and sleep disorders was slightly larger in the off-label sample than the on-label one. The dominance of the effect of MMLs on the off-label sample was most pronounced in drugs to treat pain, where patients filled -2057 fewer off-label daily doses for pain when an MML was in effect, compared to only -175 fewer on-label daily doses.

However, as with the bivariate tests, the largest difference was seen for the glaucoma treating drugs. Recall that there was no statistically significant effect for an MML when all the drugs were combined (the first set of results in Table 6). However, when we examined only on-label treatments for glaucoma we found that the use of FDA approved on-label prescriptions actually rose substantially (by +1054 daily doses) once

an MML was put into effect, an effect which was statistically significant at better than the 1% level. However, off-label prescriptions in the classes of drugs used to treat glaucoma actually fell by -34 daily doses when an MML was implemented; the magnitude of this effect is quite small, despite it's statistical significance, and so it is probably better to view this as no change in off-label prescribing. Thus, as one would predict conceptually, glaucoma is different from all of the other conditions whose prescription treatments we examined: the potential treatment with marijuana is widely discussed in the media and widely approved by state legislatures; the clinical evidence of limited treatment efficacy is well established; and with respect to the drugs that the clinical community can have the most confidence in when MMLs are passed, utilization of on-label prescriptions goes up. This is consistent with a demand induced increase in diagnosis and treatment of this serious, and often asymptomatic, condition.

Table 6 presents the estimated MML effects restricting the analysis to only states that enacted an MML during the 2010-2013 time period and states that never had an MML during that time. The patterns found with this "pure" difference-in-difference model were identical to those found in the full sample (Table 5); only the magnitudes were changed, with the estimated MML effects being generally larger in the "changer vs. never" state samples.

For the sake of brevity the tables with the full model coefficients are presented only in the appendix. A number of other results are potentially interesting from our models. For example, we find that in all models, prescriptions are lower in states with a larger proportion of the population that reports using marijuana for any reason (independent of any MML). Perhaps surprisingly, physicians generally prescribe more

drugs in less competitive markets, as evidenced by higher values to the Herfinahl index (again, with the exception of glaucoma). Male physicians prescribe more daily does than female physicians. Counties with larger proportion African-American residents tend to have physicians who prescribe fewer daily doses, again with the exception of glaucoma (which is more prevalent among Blacks than whites). The effect of the percent Hispanic and for other race are mixed. Economic factors, such as poverty rates, unemployment rates and median household income are also generally important.

As an additional confirmation that our estimated MML effects are causally related to implementing an MML, and not due to some unobserved characteristic of states that influences both general prescribing and MML adoption, we conducted a series of falsification tests. For this, we selected prescriptions from four drug classes where there is no evidence of any beneficial (or harmful) effect from medical marijuana. These were: blood thinning agents; phosphorous stimulating agents; antivirals used to treat influenza; and antibiotics. We constructed analysis data sets for these drugs using the same process as with our main data (though, given that these were generally specific classes of drugs, we did not create separate on- and off-label data sets). We re-ran our main models on these drugs, using the specification in (1) above. We found no evidence of any effect of MML changes in these falsification models: estimated coefficients were between -51.6 and 15.5, with t-statistics that never approached significance at a reasonable level. Thus, we do not find evidence that there was some unobserved characteristic of prescribing in states with an MML that spuriously led to our main findings: when there was no theoretical reason to expect an effect from MMLs, we found none. This, we argue, strengthens the confidence we can have in the causal nature of our main findings. Details

of the specific drugs and full results from our falsification tests are presented in the Appendix.

7. Discussion

Since California passed the first law permitting (at the state level) residents to purchase and use marijuana for medical purposes, the issue of decriminalizing medical marijuana has been a frequent and often contentious topic of policy debate. As of the start of 2016, 23 states and Washington D.C. have approved medical marijuana, and there is a growing academic literature on the topic. Researchers have investigated negative externalities associated with medical marijuana, spillovers from medical marijuana to recreational use among adults and youth, and changes in traffic accidents following medical marijuana approval, among other similar topics. Remarkably, there is no literature that investigates the extent to which marijuana is actually used medically as a result of implementing MMLs at the state level. This is perhaps due to the fact that there are no data sources that combine detailed information on marijuana use with details on the use of traditional medical services. We provide the first, albeit somewhat indirect, evidence on the clinical impact of medical marijuana availability by examining the impact of medical marijuana laws (MMLs) on the use of all FDA-approved prescription drugs paid for by the Medicare Part D program.

We constructed nine data sets that contained annual prescription data aggregated to the physician / drug level; each analysis data set was defined by a broad disease category and contained only prescriptions that were in a drug class where there was at least one product that had FDA approval to treat the condition in question. We selected

conditions that were either widely mentioned in state MML approval legislation or were discussed in one of two meta analyses of the literature studying the clinical efficacy of marijuana. Our study conditions were: anxiety, depression, glaucoma, nausea, pain, psychoses, seizures, sleep disorders, and spasticity. Using difference-in-differences models, we compared prescribing patterns within states that did not have an MML to states (and years) for which an MML was in effect. Generally, we found that when an MML went into effect, prescribing for FDA-approved prescription drugs under Medicare Part D fell substantially. The only exception was for glaucoma-related drugs.

One remaining question is how to understand the importance of our estimated effects. Prescriptions fell for all conditions except glaucoma and spasticity, but how much of a change did this represent? To put our findings in perspective, we conducted one additional exercise. As discussed above, the Medicare Part D utilization data not only contains information on daily doses filled, it also measures the total spending that resulted from the filled prescriptions; these dollar amounts include Medicare payments, government low-income subsidies, and patient out-of-pocket costs. As a reminder, we used this data to calculate costs per daily dose for each observation in our original drug-level data, and then estimated the total reduction in expenditure associated with an MML using prescription-level data on doses filled.[6] Table 7 presents the ultimate calculations for net savings nationally by year. Our analysis suggested that prescription drug spending in the Medicare program fell by $103.9 million in 2010 and that cost saving had

[6] We used a drug-level analysis to calculate total program savings in order to avoid double-counting. Prescription products may be in multiple disease categories in our data. For example, some SSRIs would be used to treat anxiety, depression, psychoses, or sleep disorders. So, adding up the dollar values from the models in Table 4 would over-estimate savings. In order to arrive at a correct estimate of the net total savings to Medicare associated with states adopting medical marijuana laws, we pooled all of the predicted cost changes into a single data set and eliminated any duplicates. When a drug observation appeared more than once (for example, when it was in both the anxiety and depression sets), we kept the observation that had the smallest estimated cost saving.

risen to $153.6 million by 2013. This saving was accruing from only 18 states with implemented MML policies in 2013. Assuming the remaining states are of similar size, we would forecast that if all states had, *counterfactually*, adopted an MML by 2013, Medicare Part D programmatic spending would be $435.2 million lower than it would be with no state adoption.

Such reduced spending on Medicare does not represent a pure change in welfare, as some of the figure is surely a transfer of costs from the program to enrollees who would be purchasing marijuana out of pocket. But, in times of significant budget pressure, saving $435 million is not trivial: it would represent a bit less than 0.5% of total Part D spending for 2013. Thus, while lowering Medicare program costs is not a sufficient justification for approving marijuana for medical use – a decision which is complex and multidimensional – these programmatic savings should nonetheless be considered when marijuana policy changes are discussed.

Figure 1: Media Coverage of Medical Marijuana by Condition

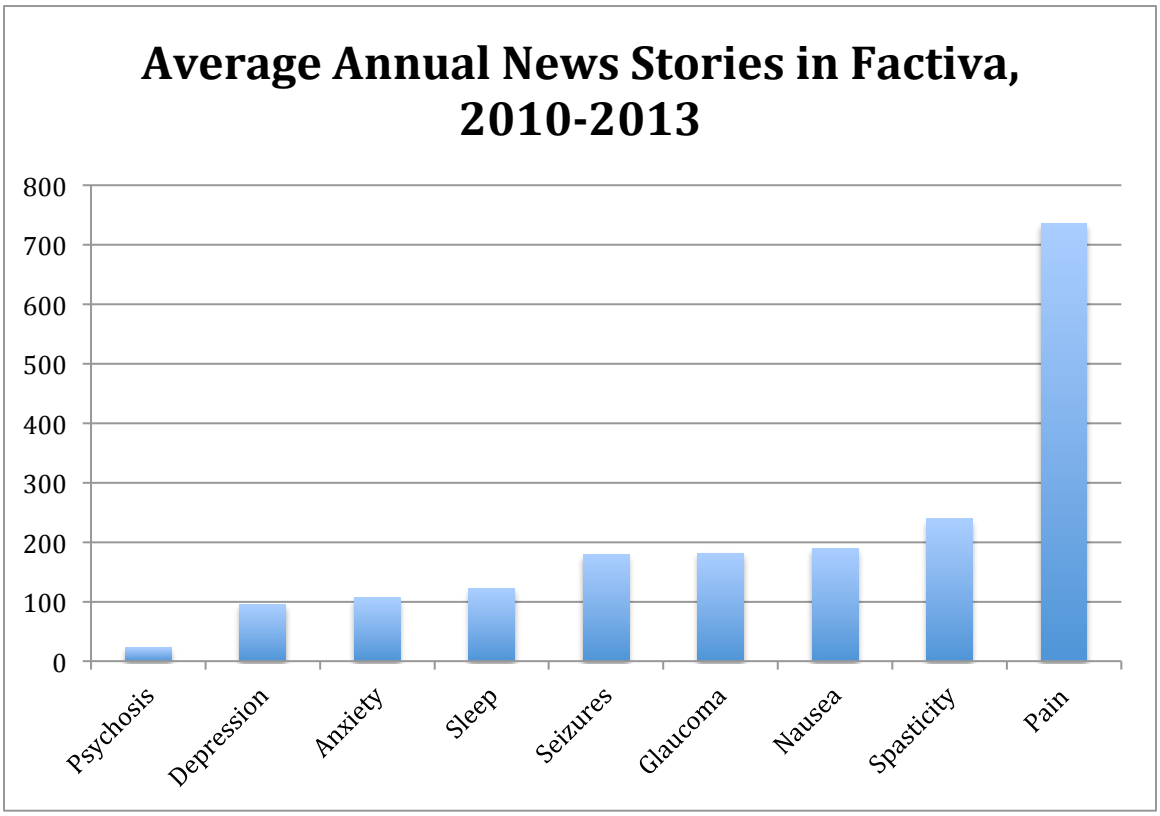

Table 1: Conditions Which Are Approved Reasons to Access Medical Marijuana

Condition	AK	AZ	CA	CO	CT	DE	DC	HI	IL (a)	ME	MD	MA	MI	MN	MT	NV	NH (a)	NJ	NM	NY	OR	RI	VT	WA	Number of States for Which Condition is Mentioned
Multiple sclerosis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	24
Cancer	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	23
HIV/AIDS	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	23
Cachexia	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X		X	X	X	X	22
Pain	X	X	X	X		X		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	21
Muscle spasms	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X	X		X	X	X	X	21
Epilepsy	X	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X		X	21
Glaucoma	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X		X	X		X	20
Seizures	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X			X	X	X	X	20
Nausea	X	X	X	X		X		X	X	X	X		X		X	X	X	X	X		X	X	X	X	19
Crohn's		X			X			X	X	X	X	X	X	X	X	X	X	X	X	X		X		X	17
ALS		X				X	X		X	X		X	X	X			X	X	X	X					12
Hepatitis		X				X			X	X	X	X	X				X		X			X		X	11
PTSD		X	X		X	X			X	X			X			X			X						9
Spasticity	X	X			X										X		X	X	X	X				X	9
Alzheimer's		X				X			X	X	X		X				X				X	X			9
Inflammatory Bowel									X	X							X	X		X				X	6
Parkinson's					X				X			X					X			X					5
Anorexia			X								X								X					X	4

Note: Conditions listed by at least 4 states.

Table 2: Medical conditions studied and associated drug classes for which there is at least one approved on-label option.

Condition	Clinical Evidence of Effect		Drug Classes with at Least One On-Label Option
	Joy et al. (1999)	Whiting, et al. (2015)	
Anxiety	Present	Very low	anticonvulsants; anxiolytics, sedatives and hypnotics; antidepressants; and smoking cessation agents
Depression	-	Very low	anticonvulsants; antidepressants; antipsychotics; and smoking cessation agents
Glaucoma	Insufficient	-	opthalmic preparations
Nausea	Present	Low	antiemetic/antivertigo agents; antidiarrheals; and proton pump inhibitors
Pain	Present	Moderate	antimalarial agents; analgesics; anticonvulsants; antiemetic/antivertigo agents; muscle relaxants; adrenal cortical steroids; respiratory inhalant products; antirheumatics; antidepressants; and functional bowel disorder agents
Psychosis	-	Low	anticonvulsants; anxiolytics, sedatives and hypnotics; antidepressants; and antipsychotics
Seizure Disorders	Insufficient	-	antiarrhythmic agents; and anticonvulsants
Sleep Disorders	-	Low or very low	anticonvulsants; anxiolytics, sedatives and hypnotics; and CNS stimulants
Spasticity	Insufficient	Low to moderate	immunostimulants; and muscle relaxants

Table 3: Variable Means and Standard Deviations on all drugs by approved class, Observations at the condition and physician level

	Anxiety Sample	Depression Sample	Glaucoma Sample	Nausea Sample	Pain Sample
Number of filled daily doses	10905.3	9212.8	2568.6	9785.2	30786.1
State MML is effective	0.285	0.284	0.266	0.275	0.281
FIPS HHI for daily doses	0.0173	0.0177	0.0197	0.0185	0.0159
Percent of state using marijuana	7.424	7.420	7.357	7.411	7.445
Prescriber sex	0.663	0.667	0.690	0.640	0.654
Percent of county below FPL	0.160	0.161	0.161	0.161	0.160
County median household income	52492.4	52384.7	51918.5	52422.8	52917.4
Number of deaths in county	7689.2	7649.3	7471.8	7654.6	7930.2
Number of emergency department visits in Medicare	54731.0	54444.3	52764.6	54373.2	56565.4
Unemployment rate in county	0.0845	0.0844	0.0846	0.0846	0.0843
Percent of population enrolled in Medicare	0.152	0.153	0.156	0.153	0.151
County total population	1092889.3	1086293.3	1054913.2	1083201.8	1123948.4
Percent of county population in urban area, 2010	0.839	0.837	0.823	0.833	0.849
Percent county population that is Black	0.131	0.131	0.130	0.131	0.135
Percent county population that is Hispanic	0.146	0.145	0.143	0.146	0.148
Percent county population that is other race	0.0839	0.0835	0.0801	0.0829	0.0851
Physicians per capita	0.000830	0.000828	0.000813	0.000827	0.000843
Observations	1884498	1850419	1191940	1443291	2496608

State and physician specialty indicator variables not shown.

Table 3: Variable Means and Standard Deviations on all drugs by approved class, Observations at the condition and physician level (continued)

	Psychosis Sample	Seizures Sample	Sleep Disorder Sample	Spasticity Sample
Number of filled daily doses	11102.6	9009.7	7382.6	1956.6
State MML is effective	0.284	0.284	0.285	0.263
FIPS HHI for daily doses	0.0172	0.0169	0.0175	0.0245
Percent of state using marijuana	7.424	7.431	7.419	7.297
Prescriber sex	0.667	0.671	0.669	0.661
Percent of county below FPL	0.160	0.161	0.161	0.163
County median household income	52534.2	52549.3	52413.7	50612.8
Number of deaths in county	7722.4	7811.4	7679.3	6662.4
Number of emergency department visits in Medicare	54946.2	55542.9	54614.7	47471.5
Unemployment rate in county	0.0845	0.0846	0.0846	0.0858
Percent of population enrolled in Medicare	0.152	0.152	0.152	0.158
County total population	1097070.9	1108137.5	1091548.7	936896.2
Percent of county population in urban area, 2010	0.840	0.842	0.838	0.796
Percent county population that is Black	0.131	0.133	0.131	0.127
Percent county population that is Hispanic	0.146	0.147	0.146	0.137
Percent county population that is other race	0.0840	0.0841	0.0836	0.0755
Physicians per capita	0.000831	0.000832	0.000827	0.000783
Observations	1962456	1992258	1816551	588808

State and physician specialty indicator variables not shown.

Table 4a: T-tests on number of daily doses filled on all drugs by approved class, Observations at the physician level by condition and effective MML in place

	No MML in Effect	With MML in Effect	Difference	T-Test Statistic
Anxiety	11,220.29	10,113.77	1,106.51	32.96
Depression	9,576.73	8,296.25	1,280.47	41.60
Glaucoma	2,551.40	2,616.04	-64.64	-4.06
Nausea	10,067.92	9,040.22	1,027.70	35.28
Pain	31,810.07	28,165.54	3,644.53	41.11
Psychosis	11,421.46	10,298.60	1,122.86	32.00
Seizure disorders	9,398.60	8,028.74	1,369.85	49.11
Sleep disorders	7,557.97	6,942.94	615.03	27.21
Spasticity	2,067.82	1,645.43	422.38	41.99

Table 4b: T-tests on number of daily doses filled on drugs approved on label for broad condition categories, Observations at the physician level by condition and effective MML in place

	No MML in Effect	With MML in Effect	Difference	T-Test Statistic
Anxiety	7,066.30	5,936.95	1,129.35	47.86
Depression	9,885.66	8,274.36	1,611.30	48.52
Glaucoma	5,791.83	7,347.22	-1,555.39	-20.89
Nausea	4,814.12	4,356.17	457.95	33.77
Pain	5,186.10	4,405.15	780.96	43.82
Psychosis	5,362.08	4,574.98	787.10	38.63
Seizure disorders	2,560.62	2,226.99	333.64	30.57
Sleep disorders	2,205.21	1,895.98	309.23	44.84
Spasticity	1,048.47	1,002.77	45.70	7.30

Table 4c: T-tests on number of daily doses filled on drugs not approved for broad condition categories, Observations at the physician level by condition and effective MML in place

	No MML in Effect	With MML in Effect	Difference	T-Test Statistic
Anxiety	7,906.82	7,299.31	607.51	26.32
Depression	4,680.37	4,146.17	534.21	35.26
Glaucoma	1,726.12	1,630.25	95.87	13.28
Nausea	7,604.01	6,739.72	864.29	38.87
Pain	32,392.43	29,407.86	2,984.58	32.97
Psychosis	9,243.14	8,412.99	830.16	30.43
Seizure disorders	8,330.70	7,128.52	1,202.18	49.31
Sleep disorders	6,797.49	6,285.31	512.18	25.02
Spasticity	1,831.48	1,409.97	421.51	43.85

Table 5: Daily doses prescribed for diagnoses in Medicare Part D, all states, 2010-2013

	Anxiety	Depression	Glaucoma	Nausea	Pain
	All Drugs (approved on-label and in class with at least one on-label option)				
State MML is effective	-562.1***	-264.6***	35.2	-541.3***	-1825.7***
	(-8.64)	(-4.08)	(0.94)	(-11.85)	(-14.23)
	Drugs with FDA approval (on-label) for some ICD-9 code in condition area				
State MML is effective	-815.5***	-902.6***	1053.6***	-85.7***	-174.9***
	(-13.69)	(-12.34)	(4.61)	(-3.46)	(-6.36)
	Drugs without FDA approval (off-label) for any ICD-9 code in condition area				
State MML is effective	-271.5***	-140.0***	-33.9**	-501.5***	-2056.7***
	(-7.05)	(-4.83)	(-2.42)	(-13.67)	(-14.95)

	Psychosis	Seizures	Sleep	Spasticity
	All Drugs (approved on-label and in class with at least one on-label option)			
State MML is effective	-518.9***	-486.1***	-361.7***	-31.9*
	(-7.40)	(-10.53)	(-8.13)	(-1.75)
	Drugs with FDA approval (on-label) for some ICD-9 code in condition area			
State MML is effective	-548.0***	-128.8***	-139.2***	-68.4***
	(-10.85)	(-5.87)	(-10.28)	(-4.93)
	Drugs without FDA approval (off-label) for any ICD-9 code in condition area			
State MML is effective	-364.8***	-420.7***	-324.9***	-5.71
	(-7.45)	(-11.13)	(-7.81)	(-0.33)

Data are aggregated to all prescriptions in disease category by physician. Other variables included but not shown are: county HHI for daily doses; percent of state using marijuana; prescriber sex; percent of county below FPL; county median household income; number of deaths in county; number of emergency department visits in Medicare; unemployment rate in county; percent of population enrolled in Medicare; county total population; percent of county population in urban area, 2010; percent county population that is Black; percent county population that is Hispanic; percent county population that is other race; physicians per capita; and state and year indicators. Standard errors are clustered at the physician level.

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

Table 6: Daily doses prescribed for diagnoses in Medicare Part D, only states that changed or never had MML during 2010-2013

	Anxiety	Depression	Glaucoma	Nausea	Pain
	All Drugs (approved on-label and in class with at least one on-label option)				
State MML is effective	-801.8***	-431.5***	18.1	-569.9***	-2095.1***
	(-12.02)	(-6.52)	(0.48)	(-12.07)	(-15.89)
	Drugs with FDA approval (on-label) for some ICD-9 code in condition area				
State MML is effective	-1112.0***	-1186.0***	1036.5***	-115.5***	-218.3***
	(-18.17)	(-15.78)	(4.54)	(-4.53)	(-7.63)
	Drugs without FDA approval (off-label) for any ICD-9 code in condition area				
State MML is effective	-368.3***	-215.4***	-50.4***	-528.4***	-2285.0***
	(-9.30)	(-7.21)	(-3.54)	(-13.91)	(-16.18)

	Psychosis	Seizures	Sleep	Spasticity
	All Drugs (approved on-label and in class with at least one on-label option)			
State MML is effective	-754.7***	-577.7***	-542.4***	-40.0**
	(-10.52)	(-12.09)	(-11.89)	(-2.09)
	Drugs with FDA approval (on-label) for some ICD-9 code in condition area			
State MML is effective	-743.8***	-187.8***	-192.0***	-88.5***
	(-14.35)	(-8.28)	(-13.60)	(-6.25)
	Drugs without FDA approval (off-label) for any ICD-9 code in condition area			
State MML is effective	-523.0***	-486.4***	-488.3***	-9.55
	(-10.41)	(-12.40)	(-11.47)	(-0.52)

Data are aggregated to all prescriptions in disease category by physician. Other variables included but not shown are: county HHI for daily doses; percent of state using marijuana; prescriber sex; percent of county below FPL; county median household income; number of deaths in county; number of emergency department visits in Medicare; unemployment rate in county; percent of population enrolled in Medicare; county total population; percent of county population in urban area, 2010; percent county population that is Black; percent county population that is Hispanic; percent county population that is other race; physicians per capita; and state and year indicators. Standard errors are clustered at the physician level.

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

Table 7: Estimated annual dollar change in Medicare spending from MML, unduplicated across all conditions, by year for the average state and total for the program

	Change for Average State	Change for Total Program
2010	-7,989,304.18	-103,860,954.39
2011	-7,418,913.27	-111,283,699.06
2012	-7,944,388.20	-119,165,822.94
2013	-8,530,636.54	-153,551,457.67
For all years	-31,883,242.19	-487,861,934.07

Data is using all drugs in the classes of confirmed on-label indications. Estimates from model on all states except AK and HI with clustering at the physician level. Last row calculates the change in total 2010-2013 net Medicare expenditures for non-duplicated changes in use; cost savings were assigned to the diagnosis with the smallest estimated daily dose change.

References

Anderson, D. M., B. Hansen and D. I. Rees (2013). "Medical marijuana laws, traffic fatalities, and alcohol consumption." Journal of Law and Economics **56**(2): 333-369.

Bradford, W. D., A. Kleit, P. Neitert, T. Mcilwain and S. Ornstein (2006). "The effect of direct to consumer television advertising on physician prescribing behavior for the treatment of osteoarthritis." Health Affairs **25**(5): 1371-1377.

Bradford, W. D., J. L. Turner and J. W. Williams (2015). "Off-Label Use of Pharmaceuticals: A Detection Controlled Estimation Approach." Available at SSRN 2230976.

Cavanaugh, S. (2015). Annual Release of Part D National Average Bid Amount and other Part C &

D Bid Information C. f. M. a. M. Studies. Baltimore, MD, Centers for Medicare and Medicaid Studies.

Cerdá, M., M. Wall, K. M. Keyes, S. Galea and D. Hasin (2012). "Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence." Drug and alcohol dependence **120**(1): 22-27.

Chu, Y.-W. L. (2014). "The effects of medical marijuana laws on illegal marijuana use."

Coscelli, A. and M. Shum (2004). "An empirical model of learning and patient spillovers in new drug entry." Journal of Econometrics **122**(2): 213-246.

Crawford, G. S. and M. Shum (2005). "Uncertainty and learning in pharmaceutical demand." Econometrica **73**(4): 1137-1173.

Harper, S., E. C. Strumpf and J. S. Kaufman (2012). "Do medical marijuana laws increase marijuana use? Replication study and extension." Annals of Epidemiology **22**(3): 207-212.

Joy, J. E., S. J. Watson Jr and J. A. Benson Jr (1999). Marijuana and Medicine:: Assessing the Science Base, National Academies Press.

Keith, A. (1995). "Regulating information about aspirin and the prevention of heart attack." American Economic Review **85**: 96-99.

Klofas, J. and K. Letteney (2012). The Social and Legal Effects of Medical Marijuana: State Legislation and Rules, Working Paper, Center for Public Safety Initiatives, Rochester Institute of Technology.

Lin, H.-W., K. Phan and S.-J. Lin (2006). "Trends in off-label β-blocker use: A secondary data analysis." Clinical therapeutics **28**(10): 1736-1746.

O'Keefe, K. (2013). "State medical marijuana implementation and federal policy." J. Health Care L. & Pol'y **16**: 39.

Pacula, R. L., A. E. Boustead and P. Hunt (2014). "Words Can Be Deceiving: A Review of Variation Among Legally Effective Medical Marijuana Laws in the United States." Journal of drug policy analysis **7**(1): 1-19.

Rubin, P. (1991). "Economics of prescription drug advertising." Journal of Research in Pharmaceutical Economics **3**: 29-39.

Wall, M. M., E. Poh, M. Cerdá, K. M. Keyes, S. Galea and D. S. Hasin (2011). "Adolescent marijuana use from 2002 to 2008: higher in states with medical marijuana laws, cause still unclear." Annals of epidemiology **21**(9): 714-716.

Whiting, P. F., R. F. Wolff, S. Deshpande, M. Di Nisio, S. Duffy, A. V. Hernandez, J. C. Keurentjes, S. Lang, K. Misso and S. Ryder (2015). "Cannabinoids for Medical Use: A Systematic Review and Meta-analysis." JAMA **313**(24): 2456-2473.

APPENDIX

Full Results

Daily doses prescribed for diagnoses and confirmed drug class

	Anxiety	Depression	Glaucoma	Nausea	Pain
State MML is effective	-562.1***	-264.6***	35.2	-541.3***	-1825.7***
	(-8.64)	(-4.08)	(0.94)	(-11.85)	(-14.23)
FIPS HHI for daily doses	6832.6***	5487.8***	-1267.1***	8360.9***	41472.2***
	(6.47)	(6.03)	(-6.46)	(9.07)	(12.36)
Percent of state using marijuana	-67.0***	-49.8***	-16.5***	-61.2***	-256.2***
	(-4.99)	(-3.87)	(-2.91)	(-5.52)	(-8.29)
Prescriber sex	2208.1***	1788.8***	1475.8***	3672.4***	8527.5***
	(42.66)	(37.85)	(57.06)	(83.68)	(63.00)
Percent of county below FPL	-4435.7***	-2460.7**	797.3	-4607.2***	-12787.9***
	(-3.60)	(-2.21)	(1.50)	(-4.32)	(-3.76)
County median household income	-0.037***	-0.045***	-0.0017	-0.027***	-0.051***
	(-7.48)	(-9.86)	(-0.76)	(-6.34)	(-3.89)
Number of deaths in county	0.47***	0.28***	0.11***	0.32***	0.94***
	(13.42)	(9.04)	(6.33)	(10.99)	(10.38)
Number of emergency department visits in Medicare	-0.032***	-0.021***	-0.0087***	-0.026***	-0.074***
	(-15.79)	(-10.92)	(-7.97)	(-14.92)	(-13.75)
Unemployment rate in county	20671.5***	18860.0***	-848.3	14590.3***	71042.1***
	(9.96)	(10.28)	(-0.88)	(7.89)	(11.92)
Percent of population enrolled in Medicare	19149.2***	13256.3***	3474.5***	18807.8***	70736.6***
	(15.83)	(12.63)	(7.41)	(18.38)	(20.83)
County total population	-0.0018***	-0.0011***	-0.00032***	-0.0010***	-0.0033***
	(-10.72)	(-7.20)	(-3.73)	(-7.23)	(-7.43)
Percent of county population in urban area, 2010	-6308.5***	-4400.7***	228.9**	-6202.7***	-22754.5***
	(-22.16)	(-17.73)	(2.46)	(-25.51)	(-27.66)
Percent county population that is Black	-9997.9***	-9543.9***	757.9***	-5048.9***	-21715.5***
	(-22.11)	(-23.41)	(4.25)	(-13.03)	(-17.43)
Percent county population that is Hispanic	605.7	-2327.1***	1801.0***	3321.5***	5409.9***
	(1.26)	(-5.95)	(7.54)	(8.23)	(4.59)
Percent county population that is other race	-5789.1***	-7362.6***	868.7***	-2806.0***	-11549.4***
	(-10.49)	(-15.12)	(2.82)	(-5.83)	(-7.69)
Physicians per capita	-3758230.2***	-3170213.3***	243182.4***	-3032678.6***	-12071535.4***
	(-36.28)	(-33.58)	(4.95)	(-36.04)	(-46.70)
Internal Medicine	8563.7***	7065.6***	-831.6***	6695.4***	36200.2***
	(109.20)	(101.17)	(-28.92)	(113.98)	(158.83)
Hospice Care	-6615.8***	-4462.2**	-394.1	-6135.4***	-32846.3***

	(-3.36)	(-2.22)	(-1.19)	(-4.60)	(-7.57)
Emergency Medicine	-8973.8***	-7205.5***	-3020.7***	-8757.2***	-25009.7***
	(-178.12)	(-166.71)	(-118.31)	(-127.58)	(-178.75)
OBGYN	-7199.4***	-5692.0***	-2598.9***	-6052.9***	-21296.1***
	(-97.07)	(-84.32)	(-78.89)	(-67.31)	(-114.02)
Preventive Medicine	-4202.0***	-2935.1***	-2396.1***	-4489.0***	-14295.5***
	(-7.51)	(-5.16)	(-23.48)	(-9.47)	(-11.05)
Psychiatry and Psychiatrics	11361.2***	15125.2***	-2415.6***	-6687.0***	787.7***
	(85.43)	(101.65)	(-74.53)	(-148.81)	(4.52)
Pain Medicine	9526.5***	10138.7***	-2710.0***	-7827.8***	30791.2***
	(15.87)	(18.25)	(-48.82)	(-48.22)	(18.13)
Surgery	-9207.0***	-7456.6***	-2907.6***	-8446.6***	-25493.4***
	(-162.50)	(-155.33)	(-80.57)	(-99.56)	(-157.57)
Optometry	-8701.5***	-8674.4***	438.2***	-8668.8***	-33874.6***
	(-34.95)	(-89.33)	(7.06)	(-30.81)	(-127.07)
Physical Medicine	-142.7	950.9***	-2615.4***	-6265.7***	-1140.5**
	(-0.74)	(5.39)	(-66.27)	(-53.14)	(-2.10)
Oncology	-12191.0***	-9853.8***	-1284.0***	-11697.9***	-42709.1***
	(-145.48)	(-138.38)	(-69.07)	(-170.72)	(-167.78)
Constant	9079.2***	9989.9***	495.9	7320.8***	43998.4
	(14.06)	(16.72)	(1.32)	(11.97)	(0.02)
Number of Observations	1870054	1836759	1186845	1432463	2472210

Data are aggregated to all prescriptions in disease category by physician. State and year indicator variables not shown. Standard errors clustered at the physician level

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

Daily doses prescribed for diagnoses and confirmed drug class

	Psychosis	Seizures	Sleep	Spasticity
State MML is effective	-518.9***	-486.1***	-361.7***	-31.9*
	(-7.40)	(-10.53)	(-8.13)	(-1.75)
FIPS HHI for daily doses	7782.2***	8050.0***	4515.6***	-236.2
	(7.13)	(8.44)	(6.30)	(-1.23)
Percent of state using marijuana	-66.3***	-70.6***	-49.3***	-11.4***
	(-4.64)	(-6.41)	(-5.44)	(-2.61)
Prescriber sex	2141.3***	2643.0***	1691.2***	495.6***
	(39.59)	(63.86)	(49.44)	(35.17)
Percent of county below FPL	-4712.7***	3132.4***	-539.9	2744.1***
	(-3.69)	(2.87)	(-0.63)	(7.51)
County median household income	-0.039***	-0.018***	-0.014***	-0.0067***
	(-7.66)	(-4.43)	(-4.12)	(-4.63)
Number of deaths in county	0.47***	0.25***	0.35***	0.011
	(12.83)	(9.09)	(15.27)	(1.15)
Number of emergency department visits in Medicare	-0.032***	-0.020***	-0.023***	0.00022
	(-14.84)	(-12.78)	(-17.58)	(0.41)
Unemployment rate in county	21931.6***	20650.1***	16007.8***	5970.7***
	(10.29)	(11.14)	(11.31)	(10.92)
Percent of population enrolled in Medicare	18859.6***	18059.0***	13635.7***	40.1
	(15.26)	(17.05)	(16.66)	(0.11)
County total population	-0.0018***	-0.00083***	-0.0013***	-0.000067
	(-10.16)	(-6.24)	(-12.02)	(-1.39)
Percent of county population in urban area, 2010	-6513.0***	-4853.5***	-4126.7***	192.7***
	(-22.13)	(-20.03)	(-21.60)	(3.09)
Percent county population that is Black	-9834.1***	-7777.7***	-5576.5***	-2317.1***
	(-20.96)	(-19.80)	(-18.20)	(-17.65)
Percent county population that is Hispanic	591.0	354.9	1221.6***	-1662.3***
	(1.20)	(0.98)	(3.68)	(-16.69)
Percent county population that is other race	-5866.3***	-4741.0***	-3105.1***	-1146.4***
	(-10.27)	(-10.55)	(-8.21)	(-7.52)
Physicians per capita	-3928540.5***	-2885795.9***	-2310094.0***	-239946.0***
	(-36.63)	(-35.37)	(-33.30)	(-7.67)
Internal Medicine	8865.8***	8555.6***	6334.0***	256.3***
	(110.12)	(130.63)	(117.95)	(15.31)
Hospice Care	-6173.2***	-6528.8***	-5123.1***	-62.4

	(-2.72)	(-4.52)	(-3.88)	(-0.17)
Emergency Medicine	-8885.0***	-7225.5***	-6044.7***	-1812.2***
	(-172.61)	(-173.87)	(-176.09)	(-66.25)
OBGYN	-7073.5***	-5924.0***	-4541.1***	-1019.0***
	(-93.07)	(-80.81)	(-79.58)	(-10.68)
Preventive Medicine	-3913.9***	-2854.3***	-2540.2***	149.6
	(-6.49)	(-5.05)	(-6.45)	(0.43)
Psychiatry and Psychiatrics	14650.7***	3401.3***	5828.9***	785.3***
	(91.34)	(43.06)	(74.04)	(17.68)
Pain Medicine	9620.0***	32097.0***	10867.8***	5465.7***
	(16.04)	(27.97)	(19.94)	(22.51)
Surgery	-9128.5***	-7520.8***	-6146.9***	-1058.4***
	(-158.70)	(-158.43)	(-159.63)	(-12.85)
Optometry	-10835.6***	-8379.4***	-5711.8***	-1336.0***
	(-96.17)	(-57.77)	(-31.80)	(-10.38)
Physical Medicine	-39.8	7673.4***	1533.7***	2061.2***
	(-0.20)	(20.94)	(8.73)	(19.12)
Oncology	-12251.7***	-10553.7***	-8493.4***	-1462.5***
	(-144.70)	(-149.26)	(-144.41)	(-21.28)
Constant	12990.9***	10020.3	5574.0***	702.6***
	(19.06)	(.)	(13.47)	(4.10)
Number of Observations	1947438	1977564	1803560	586307

Data are aggregated to all prescriptions in disease category by physician. State and year indicator variables not shown. Standard errors clustered at the physician level

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

Daily doses prescribed for diagnoses and confirmed drug class, strict D-in-D

	Anxiety	Depression	Glaucoma	Nausea	Pain
State MML is effective	-801.8***	-431.5***	18.1	-569.9***	-2095.1***
	(-12.02)	(-6.52)	(0.48)	(-12.07)	(-15.89)
FIPS HHI for daily doses	7005.8***	5701.8***	-1304.8***	8601.0***	43397.3***
	(5.99)	(5.65)	(-6.22)	(8.50)	(11.74)
Percent of state using marijuana	-7.58	4.82	-1.21	-37.9***	-130.5***
	(-0.44)	(0.29)	(-0.17)	(-2.72)	(-3.35)
Prescriber sex	2552.3***	2032.3***	1513.2***	3955.1***	9519.6***
	(42.03)	(36.17)	(55.41)	(77.58)	(60.80)
Percent of county below FPL	-3883.1***	-2594.4**	767.7	-4002.0***	-11022.1***
	(-2.79)	(-2.06)	(1.36)	(-3.38)	(-2.89)
County median household income	-0.045***	-0.051***	-0.0034	-0.030***	-0.060***
	(-8.23)	(-10.05)	(-1.39)	(-6.58)	(-4.16)
Number of deaths in county	0.52***	0.31***	0.10***	0.31***	0.94***
	(12.66)	(8.37)	(5.09)	(9.14)	(8.89)
Number of emergency department visits in Medicare	-0.049***	-0.030***	-0.0097***	-0.036***	-0.11***
	(-18.18)	(-12.30)	(-6.80)	(-15.92)	(-16.27)
Unemployment rate in county	26045.4***	22568.0***	1234.6	20006.9***	89469.5***
	(9.55)	(9.23)	(1.20)	(8.76)	(11.75)
Percent of population enrolled in Medicare	19152.7***	13220.6***	3184.2***	18810.9***	71939.4***
	(13.89)	(10.99)	(6.25)	(16.30)	(18.73)
County total population	-0.00085***	-0.00054***	-0.00017*	-0.00015	-0.00022
	(-4.11)	(-2.86)	(-1.74)	(-0.81)	(-0.39)
Percent of county population in urban area, 2010	-7261.7***	-5110.1***	126.7	-6890.4***	-25270.5***
	(-23.00)	(-18.60)	(1.27)	(-25.85)	(-27.90)
Percent county population that is Black	-11194.6***	-10263.0***	604.5***	-5583.1***	-23967.2***
	(-22.60)	(-22.89)	(3.27)	(-13.23)	(-17.51)
Percent county population that is Hispanic	300.6	-2650.7***	2026.2***	3376.3***	4578.1***
	(0.54)	(-5.84)	(7.62)	(7.31)	(3.35)
Percent county population that is other race	-13028.6***	-12309.1***	-935.7**	-10478.6***	-30072.3***
	(-15.90)	(-16.42)	(-2.51)	(-15.51)	(-13.87)
Physicians per capita	-3447767.3***	-2964114.9***	243014.3***	-2855837.2***	-11347930.3***
	(-29.60)	(-27.88)	(4.59)	(-30.87)	(-39.84)
Internal Medicine	8345.9***	7081.8***	-681.5***	6709.9***	36140.6***
	(91.99)	(85.87)	(-21.70)	(98.35)	(138.10)
Hospice Care	-6416.5***	-4333.9*	-341.1	-6297.3***	-33118.9***

	(-2.73)	(-1.78)	(-0.84)	(-3.99)	(-6.55)
Emergency Medicine	-9264.3***	-7537.8***	-2926.9***	-9104.6***	-25655.5***
	(-149.96)	(-141.52)	(-107.32)	(-115.16)	(-153.23)
OBGYN	-7521.9***	-6055.1***	-2530.5***	-6245.2***	-21980.1***
	(-87.43)	(-77.97)	(-70.79)	(-60.46)	(-100.85)
Preventive Medicine	-4570.2***	-3362.6***	-2311.5***	-4697.0***	-15414.8***
	(-6.35)	(-4.56)	(-18.39)	(-7.74)	(-9.57)
Psychiatry and Psychiatrics	12293.1***	15887.7***	-2326.0***	-6735.2***	1848.3***
	(78.26)	(91.24)	(-65.05)	(-126.84)	(9.12)
Pain Medicine	10711.1***	11212.1***	-2612.5***	-7957.8***	34580.5***
	(15.17)	(17.17)	(-42.86)	(-43.61)	(17.41)
Surgery	-9603.2***	-7872.4***	-2873.4***	-8798.9***	-26399.2***
	(-139.01)	(-134.33)	(-76.23)	(-91.83)	(-136.55)
Optometry	-9139.7***	-9091.9***	625.3***	-9156.6***	-35581.1***
	(-28.97)	(-81.04)	(9.07)	(-26.60)	(-114.37)
Physical Medicine	407.9*	1382.9***	-2501.5***	-6161.4***	493.9
	(1.69)	(6.30)	(-60.57)	(-43.07)	(0.73)
Oncology	-12109.4***	-9985.3***	-1328.5***	-11766.8***	-42823.7***
	(-126.47)	(-120.80)	(-62.69)	(-150.04)	(-148.29)
Constant	9170.7***	10598.7***	-22.5	8670.9***	42930.1
	(13.14)	(16.24)	(-0.06)	(14.58)	(.)
Number of Observations	1442723	1416836	939682	1125397	1931171

Data are aggregated to all prescriptions in disease category by physician. State and year indicator variables not shown. Standard errors clustered at the physician level

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

Daily doses prescribed for diagnoses and confirmed drug class, strict D-in-D

	Psychosis	Seizures	Sleep	Spasticity
State MML is effective	-754.7***	-577.7***	-542.4***	-40.0**
	(-10.52)	(-12.09)	(-11.89)	(-2.09)
FIPS HHI for daily doses	8042.9***	8179.1***	4548.1***	-310.4
	(6.65)	(7.77)	(5.73)	(-1.47)
Percent of state using marijuana	-5.44	-25.9*	-10.7	-5.25
	(-0.30)	(-1.79)	(-0.91)	(-0.86)
Prescriber sex	2475.7***	2918.2***	1928.0***	527.5***
	(38.95)	(59.88)	(48.46)	(31.17)
Percent of county below FPL	-4314.2***	4093.1***	324.5	2808.9***
	(-3.00)	(3.31)	(0.34)	(6.79)
County median household income	-0.047***	-0.020***	-0.017***	-0.0072***
	(-8.32)	(-4.25)	(-4.75)	(-4.40)
Number of deaths in county	0.52***	0.25***	0.40***	0.012
	(12.07)	(7.87)	(14.89)	(1.06)
Number of emergency department visits in Medicare	-0.049***	-0.031***	-0.037***	-0.0024***
	(-17.19)	(-14.80)	(-20.65)	(-3.33)
Unemployment rate in county	27514.5***	22639.5***	17755.9***	4491.3***
	(9.82)	(9.46)	(9.63)	(6.21)
Percent of population enrolled in Medicare	18824.2***	18557.3***	14142.5***	659.2
	(13.37)	(15.32)	(15.19)	(1.59)
County total population	-0.00084***	-0.000085	-0.00068***	0.000091
	(-3.89)	(-0.50)	(-4.95)	(1.43)
Percent of county population in urban area, 2010	-7478.3***	-5613.1***	-4855.7***	86.3
	(-22.93)	(-20.98)	(-22.91)	(1.26)
Percent county population that is Black	-11012.7***	-8287.5***	-6318.7***	-2369.2***
	(-21.45)	(-19.15)	(-18.87)	(-16.68)
Percent county population that is Hispanic	320.7	208.7	994.1***	-1912.3***
	(0.57)	(0.49)	(2.61)	(-16.40)
Percent county population that is other race	-13180.3***	-9069.8***	-7571.2***	-696.3***
	(-15.43)	(-13.54)	(-13.62)	(-3.02)
Physicians per capita	-3625338.0***	-2722549.6***	-2098397.7***	-219642.3***
	(-30.15)	(-29.90)	(-26.91)	(-6.25)
Internal Medicine	8674.5***	8493.6***	6105.0***	258.3***
	(92.91)	(111.74)	(99.19)	(13.00)
Hospice Care	-5893.1**	-6714.2***	-5023.5***	2.74

	(-2.16)	(-3.96)	(-3.22)	(0.01)
Emergency Medicine	-9178.2***	-7448.7***	-6175.0***	-1893.4***
	(-145.16)	(-148.20)	(-146.98)	(-64.66)
OBGYN	-7395.0***	-6344.9***	-4773.6***	-1168.2***
	(-84.04)	(-74.55)	(-72.90)	(-12.05)
Preventive Medicine	-4282.3***	-3187.7***	-2708.0***	55.5
	(-5.56)	(-4.35)	(-5.34)	(0.12)
Psychiatry and Psychiatrics	15661.8***	3752.7***	6459.8***	831.3***
	(83.08)	(40.89)	(69.97)	(16.13)
Pain Medicine	10811.7***	34893.9***	12074.0***	5978.2***
	(15.32)	(26.06)	(18.82)	(21.12)
Surgery	-9525.9***	-7846.0***	-6359.6***	-1136.3***
	(-135.65)	(-137.61)	(-136.23)	(-12.19)
Optometry	-11356.8***	-8884.6***	-5971.0***	-1387.8***
	(-86.68)	(-53.01)	(-26.31)	(-9.84)
Physical Medicine	514.1**	8665.6***	2074.0***	2284.1***
	(2.13)	(19.06)	(9.47)	(17.23)
Oncology	-12187.0***	-10590.8***	-8348.2***	-1575.6***
	(-125.94)	(-131.60)	(-125.57)	(-18.86)
Constant	15221.2***	5534.9***	5129.2***	1112.5***
	(21.00)	(8.83)	(11.22)	(5.75)
Number of Observations	1504909	1535191	1389848	461279

Data are aggregated to all prescriptions in disease category by physician. State and year indicator variables not shown. Standard errors clustered at the physician level

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

FALSIFICATION TESTS: The following models are estimated for drugs where there is no significant clinical literature or media discussion suggesting a link between marijuana use and the underlying conditions that these drugs address. Drugs were chosen in the following categories.

Blood thinning agents rank among the most commonly reimbursed drugs in Medicare Part D. We selected the following drugs from a list of blood thinners maintained by Micromedex (both brand and generic names may be included, in order to assure all prescriptions were identified in the Medicare Part D data): PRADAXA, DABIGATRAN, ARGATROBAN, BIVALIRUDIN, ANGIOMAX, REFLUDAN, LEPIRUDIN, DESIRUDIN, HEPARIN.

Phosphorus stimulating agents are prescribed to patients undergoing dialysis in order to maintain proper phosphorus levels in the blood. These drugs are also very commonly reimbursed in Medicare Part-D. We selected the following drugs from a list of phosphorus stimulants maintained by Micromedex (both brand and generic names may be included, in order to assure all prescriptions were identified in the Medicare Part D data): RENVELA, SEVELAMER, RENAGEL.

Certain anti-viral medications are prescribed to patients to shorten the duration of, and lessen the severity of, influenza infections. These drugs are also very commonly reimbursed in Medicare Part-D. We selected the following drugs from a list of anti-virals prescribed for flu maintained by Micromedex (both brand and generic names may be included, in order to assure all prescriptions were identified in the Medicare Part D data): OSELTAMIVIR, TAMIFLU, ZANAMIVIR, RELENZA, PERAMIVIR, RAPIVAB, SYMMETREL, AMANTADINE, FLUMADINE, RIMATANDINE.

Anti-biotic medications are prescribed to patients to treat bacterial infections. These drugs are also very commonly reimbursed in Medicare Part-D. We selected the following drugs from a list of antibiotics maintained by Micromedex (both brand and generic names may be included, in order to assure all prescriptions were identified in the Medicare Part D data): AMOXICILLAN, AMPICILLIN, AUGMENTIN, AVELOX, AZASITE, AZITHROMYCIN, BESIFLOXACIN, BESIVANCE, BIAXIN, BICILLIN, CILOXAN, CIPRO, CIPROFLOXACIN, CLARITHROMYCIN, DICLOXACILLIN, DIFICID, ERYTHROCIN, ERYTHROMYCIN, FACTIVE, FIDAXOMICIN, GATIFLOXACIN, ILOTYCIN, IQUIX, LEVAQUIN, LEVOFLOXACIN, MOXATAG, MOXEZA, MOXIFLOXACIN, NAFCILLIN, OCUFLOX, OFLOXACIN, PENICILLIN, PFIZERPEN, PIPERACILLIN, PROQUIN, QUIXIN, TAZOBACTAM, UNASYN, VIGAMOX, ZITHROMAX, ZOSYN.

Exhibit A3: Regression results for falsification tests, using conditions not shown to be affected by marijuana. Predicting physician annual daily doses of prescriptions, by drug group

	Blood Thinners	Phosphorus Stimulants	Anti-Flu Medications	Antibiotics
State MML is in effect	15.5	-51.6	11.1	-8.11
	(0.60)	(-1.07)	(0.51)	(-1.60)
FIPS HHI for daily doses	-647.5***	-5096.7***	84.5	60.5
	(-5.04)	(-10.33)	(1.00)	(1.53)
State percent (+12 years) consuming marijuana in past month	-18.2***	23.6*	2.69	0.19
	(-3.20)	(1.95)	(0.56)	(0.19)
Prescriber sex	291.2***	156.4***	-10.7	252.8***
	(23.49)	(4.07)	(-0.46)	(76.04)
Percent of county below FPL	110.1	1650.5	-462.4	567.6***
	(0.41)	(1.62)	(-1.47)	(7.25)
County median household income	-0.0011	-0.00082	-0.0043***	0.00035
	(-1.03)	(-0.21)	(-2.92)	(1.10)
Number of deaths in county	-0.026***	-0.019	0.036	0.0086***
	(-3.38)	(-0.94)	(1.40)	(3.92)
Number of emergency department visits in Medicare	0.00079*	-0.0017	-0.0011	-0.0011***
	(1.82)	(-1.33)	(-0.78)	(-8.02)
Unemployment rate in county	-630.0	2203.1	291.4	660.9***
	(-1.28)	(1.08)	(0.73)	(4.75)
Percent of population enrolled in Medicare	328.6	1390.7*	-741.7***	625.8***
	(1.34)	(1.95)	(-2.93)	(9.89)
County total population	0.00012***	0.00010	-0.00018	-0.00000078
	(3.18)	(1.05)	(-1.61)	(-0.07)
Percent of county population in urban area, 2010	437.6***	116.1	241.9***	15.2
	(8.89)	(0.76)	(5.52)	(1.16)
Percent county population that is Black	-410.1***	879.3***	50.3	-186.3***
	(-4.44)	(2.87)	(0.47)	(-7.33)
Percent county population that is Hispanic	-564.5***	1416.1***	-155.6	210.0***
	(-6.74)	(4.20)	(-1.62)	(7.02)

Percent county population that is other race	-909.6***	-178.0	250.0	23.4
	(-5.88)	(-0.35)	(1.24)	(0.47)
Physicians per capita	44670.9**	4048.6	135164.3***	-198.8
	(1.97)	(0.06)	(4.75)	(-0.03)
Internal Medicine	512.6***	782.6***	-111.4***	-14.4***
	(42.28)	(18.92)	(-9.93)	(-3.52)
Hospice Care	-727.1***	-1045.5***	-91.9	-28.9
	(-6.99)	(-5.02)	(-1.19)	(-0.32)
Emergency Medicine	-84.5	-762.9***	-246.2***	-414.8***
	(-0.85)	(-6.07)	(-6.20)	(-119.52)
OBGYN	-254.6***	-619.1***	-177.5***	-381.3***
	(-3.61)	(-3.45)	(-3.00)	(-53.87)
Preventive Medicine	-328.6***	-340.8	-188.3***	-264.6***
	(-3.95)	(-1.46)	(-3.32)	(-11.48)
Psychiatry and Psychiatrics	-276.9***	-787.8***	615.6***	-375.9***
	(-5.68)	(-4.29)	(25.31)	(-21.62)
Pain Medicine	-450.4**	-604.5**	254.2	-456.2***
	(-2.47)	(-2.14)	(0.83)	(-21.07)
Surgery	-275.5**	-852.8***	-38.0	-425.3***
	(-2.55)	(-7.17)	(-0.49)	(-61.24)
Optometry	-448.0***	-942.7***	-254.0***	88.9***
	(-3.00)	(-3.66)	(-7.31)	(3.56)
Physical Medicine	-400.6***	-967.9***	162.8***	-339.8***
	(-7.47)	(-7.70)	(3.27)	(-15.69)
Oncology	-758.2***	-1298.6***	271.7	-304.8***
	(-23.96)	(-6.69)	(1.53)	(-49.75)
Constant	-626.1***	-511.2	435.4***	-73.5*
	(-4.42)	(-1.22)	(3.13)	(-1.76)
Number of Observations	95990	48893	52152	970088

Source: Regression coefficients from authors' estimation models. Data are aggregated to all prescriptions in disease category by physician. State and year indicator variables are included, but the coefficients are not shown. Standard errors are clustered at the physician level.

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