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Effects of Legal Access to Cannabis on Scheduled II–V Drug Prescriptions

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A B S T R A C T

Background: Co-prescribing of scheduled drugs is endemic in the United Sates, increasing health risks to patients and the burden on healthcare systems.
Purpose: We conducted a pragmatic historical cohort study to measure the effect of enrollment in a state-authorized United States' Medical Cannabis Program (MCP) on scheduled II–V drug prescription patterns.
Procedures: Eighty-three chronic pain patients, who enrolled in the New Mexico MCP between April 1, 2010 and October 3, 2015, were compared with 42 nonenrolled patients over a 24-month period (starting 6 months before enrollment for the MCP patients) using the Prescription Monitoring Program. The outcome variables include baseline levels and pre- and postenrollment monthly trends in the number of drug prescriptions, distinct drug classes, dates prescription drugs were filled, and prescribing providers.
Findings: Twenty-eight MCP patients (34%) and 1 comparison group patient (2%) ceased the use of all scheduled prescription medications by the last 6 months of the observation period. Age- and sex-adjusted regressions show that, although no statistically significant differences existed in pre-enrollment levels and trends, the postenrollment trend among MCP patients is statistically significantly negative for all 4 measures (decreases in counts of −0.02 to −0.04, *P* values between <.001 and .017), whereas the postenrollment trend is 0 among the comparison group. Controlling for time-invariant patient characteristics suggested that MCP patients showed statistically significantly lower levels across all 4 measures by 10 months postenrollment.
Conclusions: Legal access to cannabis may reduce the use of multiple classes of dangerous prescription medications in certain patient populations.

The potential for addiction and health risks associated with using multiple scheduled drugs places additional direct monetary and health costs on patients and healthcare systems because of an increased number of side effects, risky drug interactions, dependency, and overdose.[1] For example, co-prescription of opioids and benzodiazepines in combination with drugs of abuse contribute to an estimated 144 American deaths every day.[2–6] Despite their existence in 29 states, it remains unknown how enrollment in state-authorized Medical Cannabis Programs (MCPs) affect scheduled II–V prescription drug use and the associated burden on health system resources.

Increased patient access to MCPs could impact prescription drug activity in a variety of ways. Potentially, MCPs might drive increased prescribing of medications as a result of side effects of cannabis use (eg, agitation or somnolence). Alternatively, access to cannabis could lead to a reduction in scheduled prescription drug use, if it treats patients' underlying condition(s) more effectively than scheduled drugs requiring a prescription. Studying the relationship using randomized control trials is not legally feasible because of cannabis' schedule I status. However, an observational study of Medicare Part D claims across states with and without MCPs showed that prescription medication use declined following medical cannabis legalization.[7] Similar results were found in a recent prospective open-label study conducted in Israel.[8] Medical cannabis laws have also been associated with reduced opioid-related deaths,[9,10] suggesting that some people that would otherwise be using opioids (either legally or illegally), are using medical cannabis instead.[11–13]

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We conducted a pragmatic historical cohort study to test whether enrollment in the New Mexico MCP causes a reduction in schedule II–IV prescription drug use as measured by the number and types of prescriptions filled. Additional outcomes included the frequency of schedule II–V prescription fills and the number of prescribing providers, which may more directly reflect the intensity of healthcare utilization, drug dependency, or diversion issues.

Methods

Study Design

Patients with a variety of chronic, debilitating health conditions are eligible for enrollment in the New Mexico MCP, enabling these patients to legally obtain and self-administer cannabis in various forms (eg, strain of whole dried flower, edible, or extract). Once enrolled in the MCP, patients are provided the option to use cannabis in place of, or in conjunction with conventional pharmaceutical medication treatments. At the pain rehabilitation clinic where the present study was conducted, the primary physician, a board-certified pain specialist, regularly offers patients that meet the inclusionary criteria the option to enroll in the MCP; which approximately one-third of eligible patients ultimately decide to pursue.

As part of a larger study approved by the University of New Mexico Institutional Review Board, we originally queried 147 patients who had enrolled in the MCP between April 1, 2010 and October 3, 2015. All patients in the study group had a diagnosis of "severe chronic pain," annually validated by 2 independent physicians, as required for MCP authorization. Throughout enrollment, patients received no direct medical supervision over their cannabis treatment, clinic visits were by patient request, and patients were not explicitly instructed to modify (eg, reduce) their prescription medication usage, in line with the clinic's mission to promote palliative care through patient education and self-management of available treatment options.

To assess scheduled II–V prescription drug patterns, Prescription Monitoring Program (PMP) records were retrieved over a 24-month period spanning from 6 months pre-enrollment through 18 months postenrollment. To create a comparison group, the PMP records were retrieved for a random sample of 53 chronic pain patients, who were given the option but chose not to participate in the MCP (between 2010 and 2015). To be eligible for the comparison group, patients had to have no legal ability to use cannabis, show no traces of cannabis use (via random drug screening throughout the observation period), and have been diagnosed with 1 of the 3 most common chronic pain diagnoses; *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* codes: M54.5 (chronic low back pain), M54.2 (cervicalgia, cervical spine pain), or M96.1 (postlaminectomy syndrome). PMP records dating from October 8, 2014 through October 8, 2016 were retrieved for the comparison group.

To identify changes in scheduled prescription patterns among people already using scheduled prescription medications, not patients newly seeking treatment, a second stage of sample filtering was conducted by excluding patients who did not fill any prescriptions in the first 6 months of the observation period (before enrollment in the MCP for the MCP patients). This resulted in a final sample of 83 MCP patients (63% male, $M_{age} = 51$ years, 65% chronic back pain, 26% other chronic musculoskeletal pain, 4% arthritis, 4% chronic headaches, 1% fibromyalgia) and 42 comparison group patients (69% male, $M_{age} = 58$ years, 100% chronic back pain).

Study Outcomes

To convert our patient-prescription level data into a patient-month level panel dataset, we aggregated by month the number of scheduled drug prescriptions (Rx), the number of distinct classes of scheduled drugs (Rx classes), the number of dates on which prescriptions for the drugs were filled (dates), and the number of distinct providers who prescribed the drugs (providers), resulting in 2962 patient-month level observations.

Statistical Analysis

We used 2-sided *t*-tests for continuous variables and χ^2 tests to compare dichotomous variables across the 2 patient groups. For our longitudinal analysis, we used a Poisson regression model to predict the number of events for each outcome by group, which we then depict graphically. For ease of interpretation, we used a least squares model to generate the results in tables. Incident rate ratios from a Poisson model are reported in the Table S1 of the Supplementary Appendix and follow the same pattern as the coefficients from the least squares model. We also perform a within-patient analysis of the effect of MCP enrollment, controlling for time-invariant patient characteristics through the use of individual dummy variables, which allow each patient to have a different intercept. Because group participation does not vary over time and pre-trends cannot be assumed to be parallel, we focus this analysis on the MCP patients. A placebo test using the same analysis within the comparison group is reported in the Supplementary Appendix. In the longitudinal analyses, standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary intrapatient correlation.

We perform 2 additional robustness checks to confirm that the same relationship between prescribing patterns and MCP enrollment existed for both prescriptions written by A.P.R. and those written by other doctors, as recorded in the PMP. Similar to the trend analysis for the overall sample, we regress the 2 outcomes (number of prescriptions written by A.P.R., number of prescriptions written by other providers) on a first period trend, a second period trend, age, sex, and individual fixed effects. We use the Zellner seemingly unrelated regression approach,[14] adjusting for the small sample size, with the outcomes of number of Rx written by A.P.R. and number of Rx written by other providers. (The seemingly unrelated regression approach takes into account correlation in the error terms across the 2 regressions. A Breusch-Pagan test of independence allowed us to reject independence of the error terms with a P value of less than .001.) During our sample period, 62 MCP patients filled 1488 prescriptions written by A.P.R., whereas 113 MCP patients filled 1142 prescriptions written by other providers. Fifty-one patients received prescriptions from both A.P.R. and other providers. Postestimation, we test whether the coefficients are the same across the 2 regressions.

Although this reduces the overall size of the sample, we also performed our main trend analysis excluding non-back pain patients. This makes our MCP and comparison groups more comparable in both size and diagnosis with a sample of 42 chronic back pain patients in our comparison group and 54 MCP patients with a chronic back pain diagnosis or 65% of the MCP patients in the sample.

Statistical analyses were conducted using STATA/SE 13.1 (StataCorp LLC, College Station, TX).

Results

Across the 24-month observation period, the monthly average number of *Rx* ranged from 0 to 10 (mean ± SD = 1.12 ± 1.26); distinct *Rx Classes* ranged from 0 to 4 (0.86 ± 0.86) with the 2 most frequent classes consisting of opioids (0.66 ± 0.82) and benzodiazepines (0.27 ± 0.63) respectively; dates prescription medications were filled ranged from October 29, 2009 to June 9, 2015 with monthly counts ranging between 0 and 9 (0.91 ± 0.98); and number of distinct providers ranged from 0 to 4 (0.70 ± 0.65).

Table 1 compares the average number of Rx during the first 6 months (before enrollment for the MCP patients) with the last

Table 1
Descriptive Statistics Across Patient Groups

	Overall (N = 125)	MCP (N = 83)	Comparison (N = 42)	Difference (MCP-Comparison)	*P* Value
Mean monthly Rx (1st 6 mo)	1.24 ± 0.99	1.18 ± 0.96	1.36 ± 1.07	−0.18	.351
Mean monthly Rx (last 6 mo)	0.92 ± 0.97	0.70 ± 0.84	1.37 ± 1.05	−0.67	<.001
Rx in last 6 mo = 0	23% (29)	34% (28)	2% (1)	27	<.001
Rx in last 6mo < Rx in 1st 6 mo	62% (78)	71% (59)	43% (18)	41	.002
Change in Rx	−0.32 ± 0.97	−0.48 ± 0.90	0.00 ± 1.03	−0.48	.007
Change in Rx Classes	−0.2 ± 0.62	−0.31 ± 0.62	0.01 ± 0.56	−0.32	.006
Change in dates	−0.26 ± 0.72	−0.39 ± 0.69	−0.02 ± 0.71	−0.37	.007
Change in providers	−0.21 ± 0.44	−0.29 ± 0.44	−0.04 ± 0.41	−0.25	.003
Age	53.65 ± 12.35	51.39 ± 11.52	58.11 ± 12.86	−6.72	.004
Male	65% (81)	63% (52)	69% (29)	23	.479

All "changes" compare the monthly average in the first 6 months of observation with the monthly average in the last 6 months of observation. Only patients filling at least 1 prescription during the first 6 months of observation are included in the sample. *P* values are from 2-sided *t*-tests for continuous variables and χ^2 tests for categorical variables.

6 months of our 2-year sample period. During the first 6 months of observation, there was no statistically significant difference in schedule II–IV prescriptions across the 2 groups. However, by the last 6 months, 1.5 years later, our MCP group had decreased their *Rx* by approximately 0.5, whereas the comparison group showed no change in their number of prescriptions, resulting in a statistically significant difference between the 2 groups ($P = .007$). Twenty-eight MCP patients and 1 comparison group patient ceased filling prescriptions altogether by the last 6 months of observation. The other measures, the number of Rx classes, the number of prescription dates, and the number of distinct providers follow a similar pattern; the MCP patients decrease their value of all measures reported in the PMP, while the comparison group increases. Building on the simple tests in Table 1, we expand our analysis in Figure 1 and Table 2 to incorporate the longitudinal aspect of our data and to control for age and sex. Figure 1 shows the predicted number of events from the Poisson regression model by month with linear trend lines. We include a scatter plot of the monthly raw means by group for reference. In all cases, the MCP group starts off at a lower level than the comparison group. For all 4 outcomes, the MCP group appeared to be either maintaining or increasing these counts before enrollment. No consistent pattern exists in the comparison group and any trend appears to be small. Postenrollment, the 2 trends clearly diverge, with the MCP group reducing by all measures while the comparison group increases or maintains activity for all measures.

Table 2 includes information on the statistical significance of the results in Figure 1. Each panel represents a separate regression. By construction, the intercepts across all 4 measures for the comparison group are all statistically significantly different from 0. The difference between the intercepts for the comparison group and the MCP patients is not statistically significant for any of the outcome measures. The first period trends are insignificant for both groups, perhaps partly because of the limited time period analyzed. The overall trend in the second period is statistically insignificant. The last

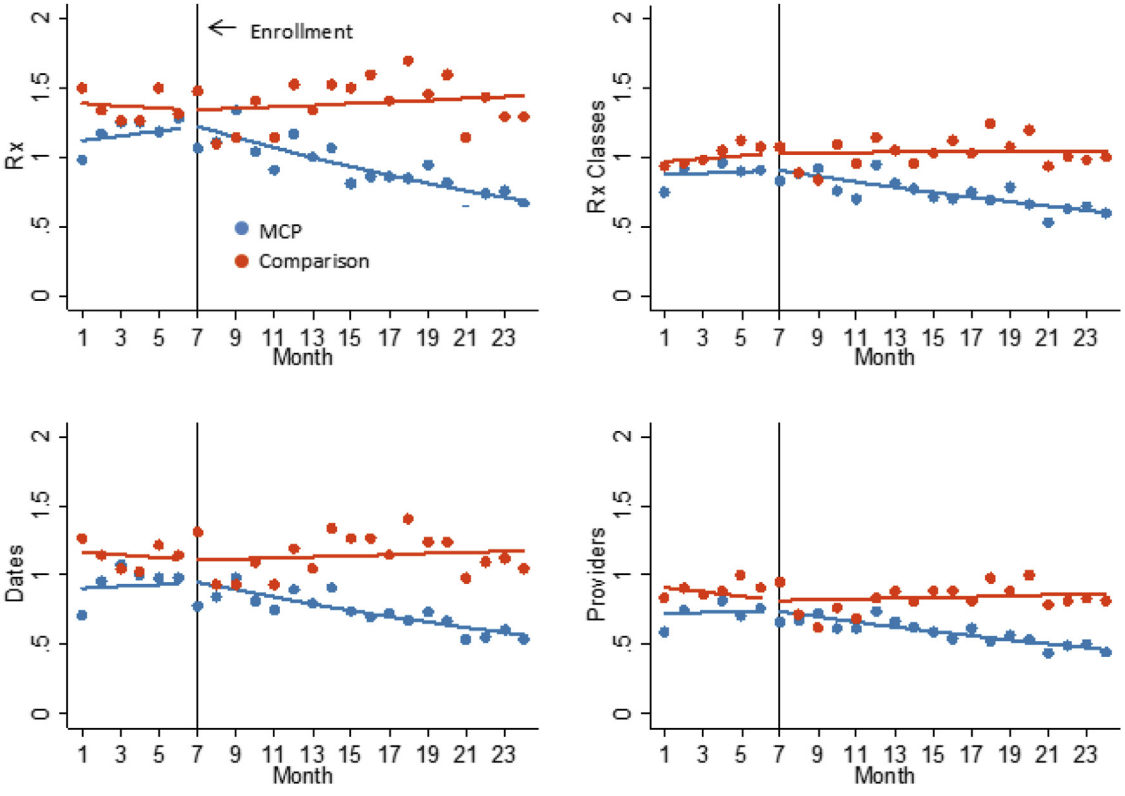

Fig. 1. Prescribing patterns of PMP data.

Table 2
Effect of MCP Enrollment on PMP Prescribing Patterns

Variables	Change in Rx (95% CI)	*P* Value
Comparison–intercept	1.46 (0.36–2.57)	.010
MCP–intercept	−0.29 (−0.80 to 0.23)	.276
Trend 1	−0.01 (−0.06 to 0.04)	.737
MCP*trend 1	0.02 (−0.04 to 0.08)	.503
Trend 2	0.01 (−0.01 to 0.02)	.502
MCP*trend 2	−0.04 (−0.06 to −0.02)	.001
	Change in Rx Classes (95% CI)	
Comparison–intercept	0.86 (0.31–1.41)	.002
MCP–intercept	−0.08 (−0.35 to 0.20)	.587
Trend 1	0.01 (−0.02 to 0.04)	.508
MCP*trend 1	−0.01 (−0.05 to 0.03)	.749
Trend 2	0.00 (−0.01 to 0.01)	.835
MCP*trend 2	−0.02 (−0.04 to −0.00)	.017
	Change in Dates (95% CI)	
Comparison–intercept	1.32 (0.50–2.14)	.002
MCP–intercept	−0.28 (−0.65 to 0.08)	.128
Trend 1	−0.01 (−0.05 to 0.03)	.663
MCP*trend 1	0.01 (−0.04 to 0.06)	.597
Trend 2	0.00 (−0.01 to 0.02)	.586
MCP*trend 2	−0.03 (−0.04 to −0.01)	.005
	Change in Providers (95% CI)	
Comparison–intercept	0.84 (0.36–1.31)	.001
MCP–intercept	−0.18 (−0.41 to 0.04)	.107
Trend 1	−0.02 (−0.03 to 0.00)	.114
MCP*trend 1	0.02 (−0.01 to 0.04)	.275
Trend 2	0.00 (−0.00 to 0.01)	.442
MCP*trend 2	−0.02 (−0.03 to −0.01)	<.001

CI, confidence interval.
We use generalized least squares and report the age- and sex-adjusted coefficients above. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.

line of each panel in Table 2 shows the differential trend in the second period among the MCP patients relative to the control group. In all cases, it is highly statistically significant and negative demonstrating that MCP enrollment is followed by reduction of all measures of PMP activity, in contrast to the lack of any change in PMP activity in the comparison group.

Finally, Table 3 compares levels of PMP activity in the first 3 months of our sample period with subsequent 3-month groups, controlling for time-invariant patient-level factors that could be confounding the effect of the MCP program in the regressions comparing trends across the 2 patient groups. Because MCP enrollment does not vary over time, these regressions include only MCP patients. For all 4 measures, counts in months 4 through 12 are not statistically significantly different from those in months 1 through 3. Suggesting that the effect of the MCP is not immediate but rather that MCP participation takes time to reduce PMP activity, statistically significant effects exist for months 16 through 24, and these effects are increasing in size with time. In other words, patients did not appear to make a dichotomous choice between types of treatments but rather MCP enrollment seems to have gradually crowded out the use of schedule II–IV prescription drugs as recorded in the PMP. The placebo test of the effect of the MCP is reported for the comparison group in Table S2 of the Supplementary Appendix and shows that, even after controlling for time-invariant patient characteristics, no statistically significant differences exist within the comparison group over the 2-year observation period.

Finally, the 2 follow-up analyses were performed to confirm the consistency of the results across doctors and when the sample is restricted to only those MCP patients with a diagnosis of chronic back pain, a group arguably more comparable to patients in the Comparison group, who all had diagnoses of chronic back pain. The comparison of the effect of MCP participation on prescriptions written by A.P.R. with those written by other providers is reported in Table 4. MCP patients do not experience a statistically significant change in the number of prescriptions filled by either provider before enrollment. Comparing across the regressions, the coefficients on the first 6-month trends are statistically significantly different from each other, although they are individually statistically insignificant. The coefficients on the second period trends are similar in magnitude, negative, and statistically significant. They are not statistically significantly different from each other, implying that the effect of enrollment reduces both prescriptions written by A.P.R. and prescriptions written by other providers at a similar rate.

Table 5 reports the results restricting the sample to just patients with chronic back pain. This reduces the imbalance in numbers and diagnoses between the MCP group and the comparison group. Despite the smaller sample size, the magnitude and statistical significance of the effect of the MCP program on all 4 outcomes is the same or greater than in Table 1.

Discussion

Our pragmatic preliminary study found that enrollment in the NM MCP was associated with significant reductions in scheduled II–V prescription drug activity and associated use of conventional

Table 3
Effect of MCP Enrollment on PMP Prescribing Patterns–Within Patient (MCP Only)

Variables	Change in Rx (95% CI)	*P* Value
Months		
4–6	0.10 (−0.06 to 0.26)	.196
7–9	0.04 (−0.18 to 0.25)	.742
10–12	−0.10 (− 0.29 to 0.10)	.331
13–15	−0.18 (−0.34 to −0.01)	.034
16–18	−0.28 (−0.46 to −0.10)	.003
19–21	−0.33 (−0.54 to −0.12)	.002
22–24	−0.39 (−0.63 to −0.15)	.002
	Change in Rx Classes (95% CI)	
Months		
4–6	0.04 (−0.06 to 0.14)	.475
7–9	−0.00 (−0.14 to 0.13)	.954
10–12	−0.08 (−0.23 to −0.07)	.286
13–15	−0.11 (−0.25 to 0.01)	.077
16–18	−0.17 (−0.32 to −0.02)	.025
19–21	−0.21 (−0.37 to −0.06)	.007
22–24	−0.25 (−0.44 to −0.06)	.009
	Change in Dates (95% CI)	
Months		
4– 6	0.07 (−0.05 to 0.19)	.227
7–9	−0.05 (−0.21 to 0.11)	.558
10–12	−0.10 (−0.25 to 0.05)	.208
13–15	−0.10 (−0.23 to 0.03)	.130
16–18	−0.21 (−0.36 to −0.06)	.005
19–21	−0.26 (−0.42 to −0.10)	.002
22–24	−0.34 (−0.53 to −0.15)	.001
	Change in Providers (95% CI)	
Months		
4–6	0.03 (−0.06 to 0.12)	.523
7–9	−0.04 (−0.15 to 0.06)	.420
10–12	−0.08 (−0.19 to 0.04)	.199
13–15	−0.10 (−0.20 to −0.01)	.040
16–18	−0.17 (−0.28 to −0.07)	.001
19–21	−0.22 (−0.33 to −0.11)	<.001
22–24	−0.26 (−0.39 to −0.12)	<.001

CI, confidence interval.
The table above reports coefficients from 4 least squares regressions, one for each outcome variable. Only MCP patients are included in the sample analyzed. Individual dummy variables control for time-invariant patient characteristics. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.

Table 4
Effect of MCP Enrollment on PMP Prescribing Patterns Across Providers

Variables	A.P.R.		Other Providers		βA.P.R. = βOther
	Change in Rx (95% CI)	*P* Value	Change in Rx (95% CI)	*P* Value	*P* Value
Trend 1	0.02 (−0.00 to 0.03)	.051	−0.01 (−0.03 to 0.01)	.220	.039
Trend 2	−0.01 (−0.01 to −0.00)	.003	−0.01 (−0.02 to −0.01)	<.001	.333

CI, confidence interval.
The results of 2 separate regressions are reported with the outcomes of number of Rx filled that were written by A.P.R. and number of Rx written by other providers. The last column reports the *P* values from tests for whether a linear combination of the coefficients across the regressions is statistically significantly different from 0. We use generalized least squares and report the age-, sex-, and individual fixed effects-adjusted coefficients above. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.

pharmacies and prescribing providers. Co-prescribing of scheduled drugs is prevalent in modern medical practice but discouraged because of the risks of multiple side effects and interactions in the patient population. Interventions that can reduce polyprescription drug usage are worthwhile, both from a cost and patient health perspective. With the results showing a reduction across classes of drugs and the number of prescribing providers, it may be that cannabis is effective at treating multiple conditions currently treated by separate medications. Studies suggest that cannabis alone may be able to address comorbid health conditions typically concurrently treated by multiple scheduled prescription drugs [eg, chronic pain (opioids), PTSD (benzodiazepines), and muscle spasms (muscle relaxants)].[15–18] However, the addition of medical cannabis should be taken into account. Although 34% of the MCP patients cease to exhibit any evidence of scheduled drug consumption and an additional 36% reduce the number of prescriptions filled for scheduled drugs by the last 6 months of our sample period, it may be that they are simply replacing scheduled prescription drugs with scheduled cannabis.

The relative safety and efficacy of cannabis in comparison to that of the other scheduled medications taken by the patients in our sample is beyond the scope of this paper. However, the vast majority of documented side effects of cannabis use reported by patients appear to be relatively non-serious,[15,19] and cannabis is not associated with an increased risk of mortality in people with or without comorbid opioid, alcohol, or cocaine use disorders.[20–22] In contrast, overdoses associated with opioids, the most common class of prescription medication filled by the patients in our sample, are the leading cause of preventable mortality nationwide.[23,24] Benzodiazepines, the second most commonly filled prescription in our sample, are used by nearly 16% of the US population[25] and are also associated with an increased risk of death by suicide and accidental poisoning.[26–28] Long-term use is associated with increased risk for cognitive impairment, dementia, Alzheimer disease, and malignancy.[29–31]

This study had several limitations, especially with regard to sample selection and that we only observed MCP enrollment and scheduled prescription drug activity. The small convenience sample increased internal validity but likely decreased generalizability to other patient populations who might respond differentially to enrollment in the MCP. Individual-level cannabis use before and throughout the duration of the study in both the MCP and non-MCP groups was not collected. In addition, individual opioid use was not directly tested. It may be that some patients in the MCP group never used cannabis or switched to illegal sources of opioid medications. Another limitation is the PMP data do not track all prescription drug activity, prescriptions filled at Veterans Affairs and Indian Health Services clinics, out-of-state prescriptions, and methadone dispensed from methadone clinics. The PMP also did not allow us to control for time-varying individual level characteristics other than age, and important socioeconomic and health characteristics could have interacted with MCP enrollment and scheduled prescription drug usage patterns in dynamic ways.

Although he did not expressly instruct patients to reduce their prescription drug use, the referring physician might have subconsciously encouraged a greater reduction in prescription use among MCP patients than among the comparison group. However, the likelihood that this alternative factor drove our results is reduced by our analyses showing that the effect of MCP enrollment was similar in both size and statistical significance for scheduled medications prescribed by the referring physician (A.P.R) and for medications prescribed by other providers (unrelated to the research team).

Lastly, although some studies suggest a better risk profile, particularly than that of the opioids and benzodiazepines recorded in the PMP data, cannabis likely is psychologically addictive and may be associated with excessive health risks for some populations (eg, pregnant women and adolescents.).

In conclusion, a shift from prescriptions for other scheduled drugs to cannabis may result in less frequent interactions with our conventional healthcare system, and potentially improved patient health.

Table 5
Effect of MCP Enrollment on PMP Prescribing Patterns for Back Pain Patients

Variables	Change in Rx (95% CI)	*P* Value
Comparison−intercept	1.88 (0.63−3.12)	.003
MCP−intercept	−0.21 (−0.76 to 0.34)	.447
Trend 1	−0.01 (−0.06 to 0.04)	.738
MCP*trend 1	0.04 (−0.03 to 0.11)	.213
Trend 2	0.01 (−0.01 to 0.02)	.503
MCP*trend 2	−0.05 (−0.08 to −0.02)	<.001
	Change in Rx Classes (95% CI)	
Comparison−intercept	1.09 (0.51−1.68)	<.000
MCP−intercept	0.00 (−0.30 to 0.31)	.982
Trend 1	0.01 (−0.02 to 0.04)	.509
MCP*trend 1	0.01 (−0.04 to 0.05)	.774
Trend 2	0.00 (−0.01 to 0.01)	.835
MCP*trend 2	−0.03 (−0.05 to −0.01)	.005
	Change in Dates (95% CI)	
Comparison−intercept	1.62 (0.71−2.53)	.001
MCP−intercept	−0.26 (−0.65 to 0.13)	.187
Trend 1	−0.01 (−0.05 to 0.03)	.664
MCP*trend 1	0.03 (−0.02 to 0.09)	.209
Trend 2	0.00 (−0.01 to 0.02)	.586
MCP*trend 2	−0.04 (−0.06 to −0.01)	.002
	Change in Providers (95% CI)	
Comparison−intercept	1.02 (0.51 to 1.53)	.000
MCP−intercept	−0.16 (−0.40 to 0.08)	.182
Trend 1	−0.02 (−0.03 to 0.00)	.116
MCP*trend 1	0.03 (−0.00 to 0.06)	.054
Trend 2	0.00 (−0.00 to 0.01)	.443
MCP*trend 2	−0.02 (−0.04 to −0.01)	<.001

CI, confidence interval.
Only backpain patients are included in these regressions, which reduces the sample size by 23.2%, leaving 2304 patient-month level observations. We use generalized least squares and report the age- and sex-adjusted coefficients above. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.

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Supplemental Appendix

Table S1
Poisson Regression Results

Variables	Incident Rate Ratios (95% CI)	*P* Value
Rx		
Comparison–intercept	1.48 (0.60–3.67)	.396
MCP	0.79 (0.53–1.17)	.237
Trend 1	0.99 (0.96–1.03)	.738
MCP*trend 1	1.02 (0.97–1.07)	.396
Trend 2	1.00 (0.99–1.02)	.500
MCP*trend 2	0.96 (0.94–0.98)	<.001
Rx Classes		
Comparison–intercept	0.86 (0.46–1.58)	.620
MCP	0.92 (0.68–1.23)	.557
Trend 1	1.01 (0.98–1.04)	.505
MCP*trend 1	0.97 (0.95–1.04)	.854
Trend 2	1.00 (0.99–1.01)	.835
MCP*trend 2	0.97 (0.96–0.99)	.007
Dates		
Comparison–intercept	1.37 (0.61–3.11)	.446
MCP	0.75 (0.53–1.06)	.102
Trend 1	0.99 (0.96–1.03)	.665
MCP*trend 1	1.02 (0.97–1.07)	.521
Trend 2	1.00 (0.99–1.02)	.589
MCP*trend 2	0.97 (0.95–0.99)	.001
Providers		
Comparison–intercept	0.81 (0.43–1.54)	.526
MCP	0.80 (0.61–1.04)	.098
Trend 1	0.98 (0.96–1.00)	.104
MCP*trend 1	1.02 (0.98–1.06)	.259
Trend 2	1.00 (0.99–1.01)	.439
MCP*trend 2	0.97 (0.95–0.99)	<.001

We use a Poisson regression model rather than a negative binomial model because of a lack of evidence of overdispersion in the latter 3 outcome variables. Negative binomial results look similar for the total number of prescriptions, so we report the incident rate ratios for the Poisson model for the sake of consistency across outcomes. Age- and sex-adjusted incident ratios are reported above. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.

Table S2
Within-Patient Regression for the Comparison Group

Comparison	Change in Rx (95% CI)	*P* Value
Months		
4–6	−0.01 (−0.21 to 0.19)	.936
7–9	−0.13 (−0.43 to 0.18)	.402
10–12	−0.01 (−0.30 to 0.28)	.957
13–15	0.09 (−0.24 to 0.41)	.589
16–18	0.20 (−0.15 to 0.54)	.252
19–21	0.03 (−0.32 to 0.38)	.857
22–24	−0.03 (−0.42 to 0.36)	.871
Variables	Change in Rx Classes (95% CI)	*P* Value
Months		
4–6	0.13 (−0.03 to 0.28)	.104
7–9	−0.02 (−0.23 to 0.18)	.818
10–12	0.11 (−0.07 to 0.30)	.235
13–15	0.06 (−0.12 to 0.24)	.538
16–18	0.17 (−0.04 to 0.40)	.116
19–21	0.11 (−0.09 to 0.31)	.263
22–24	0.04 (−0.19 to 0.27)	.724
Variables	Change in Dates (95% CI)	*P* Value
Months		
4–6	−0.02 (−0.20 to 0.14)	.775
7–9	−0.10 (−0.34 to 0.15)	.434
10–12	−0.08 (−0.32 to 0.16)	.503
13–15	0.06 (−0.20 to 0.33)	.633
16–18	0.12 (−0.15 to 0.39)	.382
19–21	−0.00 (−0.27 to 0.27)	1.000
22–24	−0.06 (−0.35 to 0.22)	.655
Variables	Change in Providers (95% CI)	*P* Value
Months		
4–6	0.06 (−0.05 to 0.18)	.264
7–9	−0.10 (−0.24 to 0.03)	.133
10–12	−0.10 (−0.23 to 0.02)	.104
13–15	−0.01 (−0.15 to 0.13)	.908
16–18	0.02 (−0.13 to 0.18)	.768
19–21	0.02 (−0.14 to 0.19)	.760
22–24	−0.05 (−0.21 to 0.12)	.568

CI, confidence interval.
The table above reports coefficients from 4 least squares regressions, one for each outcome variable. Only comparison group patients are included in the sample analyzed. Individual dummy variables control for time-invariant patient characteristics. Standard errors are clustered at the patient level to control for heteroskedasticity and arbitrary correlation among patients.