State Medical Marijuana Laws and the Prevalence of Opioids Detected Among Fatally Injured Drivers

June H. Kim, MPhil, MHS, Julian Santaella-Tenorio, DVM, MSc, Christine Mauro, PhD, Julia Wrobel, MS, Magdalena Cerdà, DrPH, Katherine M. Keyes, PhD, Deborah Hasin, PhD, Silvia S. Martins, PhD, and Guohua Li, MD, DrPH

Objectives. To assess the association between medical marijuana laws (MMLs) and the odds of a positive opioid test, an indicator for prior use.

Methods. We analyzed 1999–2013 Fatality Analysis Reporting System (FARS) data from 18 states that tested for alcohol and other drugs in at least 80% of drivers who died within 1 hour of crashing (n = 68 394). Within-state and between-state comparisons assessed opioid positivity among drivers crashing in states with an operational MML (i.e., allowances for home cultivation or active dispensaries) versus drivers crashing in states before a future MML was operational.

Results. State-specific estimates indicated a reduction in opioid positivity for most states after implementation of an operational MML, although none of these estimates were significant. When we combined states, we observed no significant overall association (odds ratio [OR] = 0.79; 95% confidence interval [CI] = 0.61, 1.03). However, age-stratified analyses indicated a significant reduction in opioid positivity for drivers aged 21 to 40 years (OR = 0.50; 95% CI = 0.37, 0.67; interaction $P < .001$).

Conclusions. Operational MMLs are associated with reductions in opioid positivity among 21- to 40-year-old fatally injured drivers and may reduce opioid use and overdose. (*Am J Public Health.* 2016;106:2032–2037. doi:10.2105/AJPH.2016.303426)

See also Galea and Vaughan, p. 1901.

In 1996, California Proposition 215, a voter-initiated medical marijuana law (MML), received 55.6% of the popular vote and became law. Proposition 215 provided criminal protections for patients as well as defined caregivers, who in turn could cultivate the marijuana that physicians could now recommend.[1] Since then, 22 additional states and the District of Columbia have enacted their own MMLs, either by voter initiative or through state legislation. Of these laws, the MMLs in Connecticut, Maine, Massachusetts, Minnesota, New York, and the District of Columbia are the only ones that do not allow marijuana to be recommended or authorized for severe or chronic pain,[2] and they tend to be more medically oriented and restrictive.[3]

In the United States, nonmalignant chronic pain afflicts a growing proportion of adults.[4] The prescription of opioids for the treatment of this type of pain has also increased.[5,6] However, despite the legitimate benefits conferred by these drugs, the potential for harm has caused some concern,[7,8] perhaps because of large increases in opioid use disorders[9,10] and opioid overdoses[11,12] observed within the last 2 decades. Furthermore, recent policies aimed at reducing the supply of opioid prescriptions (e.g., prescription drug monitoring programs) may have also inadvertently led to recent increases in heroin overdoses.[13] Alternatives for the treatment of chronic pain are clearly needed.[14]

Marijuana may offer a substitute to opioids in many states with MMLs.[15,16] Unfortunately, data on treatment efficacy is limited, in large part because of current federal scheduling. Regardless, severe or chronic pain is among the most common indications cited by medical marijuana patients.[17] In theory, we would expect the adverse consequences of opioid use to decrease over time in states where medical marijuana use is legal, as individuals substitute marijuana for opioids. In a recent study of MMLs and opioid overdoses,[18] state MMLs were associated with reductions in the annual rate of state-level opioid overdoses. The relationship between MMLs and other indicators of opioid use or adverse consequences needs to be further examined, as this relationship potentially identifies actionable points of intervention on a growing opioid epidemic (e.g., expanding eligible medical conditions for marijuana to include chronic pain).

One such indicator is the prevalence of opioid use. Although opioid use can be difficult to measure, tested opioid positivity in blood or urine is objective, and it provides a clear indicator of any prior opioid use, for medical or recreational purposes. Although we know of no representative general population data with tested opioid positivity among living participants, toxicological tests for substances among drivers fatally injured in car crashes represents a potential data source. Repeated annual panels of drivers killed in crashes in states with and without MMLs are available; in some states, data are uniformly collected for the majority of deceased drivers. Furthermore, states that do not

ABOUT THE AUTHORS

June H. Kim, Julian Santaella-Tenorio, Katherine M. Keyes, Deborah Hasin, Silvia S. Martins, and Guohua Li are with the Department of Epidemiology and Christine Mauro and Julia Wrobel are with the Department of Biostatistics, Columbia University, New York, NY. Magdalena Cerdà is with the Department of Emergency Medicine, University of California, Davis.

Correspondence should be sent to June H. Kim, MPhil, MHS, Department of Epidemiology, Columbia University, 722 W 168th St, Rm 228D, New York, NY 10032 (e-mail: jhk2171@columbia.edu). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

This article was accepted July 31, 2016.
doi: 10.2105/AJPH.2016.303426

have an MML but eventually pass one are more similar to states in which an MML has already been passed, reducing the possibility of bias in comparing MML and non-MML states.[19] Thus, our aim was to empirically assess whether, among drivers who died within 1 hour of a traffic collision, crashing in a state with an MML was associated with a reduced likelihood of opioid positivity compared with crashing in a state that would eventually pass an MML but had not yet done so.

TABLE 1—State Medical Marijuana Law (MML) Operational Status Among the 18 States That Performed Majority Testing on Its Drivers Who Died Within 1 Hour of Crashing: United States, 1999–2013

State	Effective Date[a]	Operational Date[b]	First Year Coded as Operational	MML Status (No.)[c]	% of Drivers Tested
California	Nov 96	Nov 96	1999	After (20 614)	92.3
Washington	Nov 98	Nov 98	1999	After (3 649)	91.1
Hawaii	Dec 00	Dec 00	2001	Before (38), After (388)	97.2
Colorado	Jun 01	Jun 01	2002	Before (687), After (2373)	85.9
Vermont	Jul 04	Jul 04	2005	Before (122), After (264)	93.0
Montana	Nov 04	Nov 04	2005	Before (489), After (932)	89.8
Rhode Island	Jan 06	Jan 06	2006	Before (267), After (225)	99.2
New Jersey	Oct 10	Dec 12	2013	Before (2 679), After (167)	93.0
Connecticut	Oct 12	Not operational	. . .	Before (1 616)	97.2
Massachusetts	Jan 13	Not operational	. . .	Before (2 267)	82.0
New Hampshire	Jul 13	Not operational	. . .	Before (889)	94.0
Illinois	Jan 14	Not operational	. . .	Before (5 803)	88.8
Maryland	Jun 14	Not operational	. . .	Before (2 504)	88.7
North Dakota	. . .	. . .	. . .	Never (710)	87.2
Ohio	. . .	. . .	. . .	Never (7 328)	85.2
Pennsylvania	. . .	. . .	. . .	Never (7 280)	80.5
Virginia	. . .	. . .	. . .	Never (4 775)	82.9
West Virginia	. . .	. . .	. . .	Never (2 328)	94.6

Note. "Majority testing" is defined as testing at least 80% of a state's drivers who died within 1 hour of crashing.
Source. Fatality Analysis Reporting System.
[a]MML effective dates are based on when (month and year) the law went into effect.
[b]Operational dates are based on when (month and year) allowances for home cultivation or the presence of active dispensaries came into effect.
[c]Numbers of drivers who died before and after the operational date of the MML. ("Never" indicates that the state never implemented any type of MML.)

METHODS

We obtained study data from the Fatality Analysis Reporting System (FARS), which provides a census of all crashes on public roads that result in a traffic fatality. This includes data from police records, state administrative files, and medical records on the persons, vehicles, and circumstances related to each crash.[20] To limit any false positive drug testing results, we restricted our sample to drivers who died within 1 hour of crashing from 1999 to 2013 (n = 215 384).

We excluded drivers younger than 15 years (n = 507) or with missing data on age (included categories = 15–20, 21–40, and ≥ 41 years) or gender (n = 50). In addition, although the FARS provides data for all states, toxicological testing of fatally injured drivers is inconsistently performed across states.[21] States that do not perform drug and alcohol testing on the majority of their drivers may be selectively testing drivers that appear impaired.[22] Thus, we restricted our analysis to include only states that tested at least 80% of fatally injured drivers (n = 70 683) from 1999 to 2013 (18 states; Table 1), a threshold consistent with previous studies.[23–25] Although testing for New Mexico was above this threshold, because there were inexplicably low numbers of drivers testing positive for drugs, we deemed data from this state to be unreliable and excluded them.[22,26] Finally, we also excluded drivers with missing outcome data (n = 2289; 3.2%). In total, we included 68 394 deceased drivers from 18 states.

Measures

Drug and alcohol test results. Blood or urine specimens were tested for drugs through gas–liquid chromatography, mass spectrometry, and radioimmunoassay techniques.[27] For each driver, the FARS records up to 3 nonalcoholic drugs detected in the blood or urine. If multiple drugs are detected, the FARS records results in the following priority order: narcotics, depressants, stimulants, marijuana, and other.[20] In accordance with the FARS coding manual,[28] we based prior opioid use on the coding of any narcotic (codes 100–295). The FARS determines driver's blood alcohol content and drug content separately; we coded blood alcohol content as negative, positive, or missing.

State medical marijuana laws. Because state MMLs vary in how medical marijuana is provided and made available,[29] we coded only states that provided access to medical marijuana (through either one's own or collective cultivation or through public or private dispensaries) as having an operational medical marijuana law, and we based operational dates on when access was made available. For example, New Hampshire and Illinois have effective dates within or immediately after our study period (2013 and 2014, respectively); however, because they did not allow home cultivation and dispensaries were not operational until after our study period, we coded these states as negative throughout. For states that implemented an operational MML during our study period, we coded MML status as positive for all years following the operational date of availability and negative for the preceding periods. If the law became operational during the first half of the year (i.e., before July 1), we coded MML status as positive starting with that year. If the law became operational during the second half of the year, we coded MML status as positive starting with the subsequent year, as follows: Hawaii, 2001; Colorado, 2002; Vermont, 2005; Montana, 2005; Rhode Island, 2006; New Jersey, 2013. We coded California and Washington as positive for MML status for the entire study period. We considered the remaining states that had not yet passed an operational MML as negative throughout the study period (North Dakota, Ohio, Pennsylvania, Virginia, and West Virginia). Additionally, in the state-combined analysis, we controlled for whether the state had ever passed a medical marijuana law.[19] This included the states with an operational MML at any point during the study period as well as states with laws that were not yet operational (Connecticut, Massachusetts, New Hampshire, Illinois, and Maryland).

State prescription drug monitoring program laws. Prescription drug monitoring programs (PDMPs) may confound any association between state MMLs and individual opioid use if PDMPs are associated with the timing of state MMLs and an independent cause of opioid use. To account for this, we used 4 time-varying measures of PDMP characteristics obtained from LawAtlas: (1) "PDMP mandatory," which requires health professionals to report their prescribing; (2) "PDMP real-time," which requires that prescribing data be updated at least once weekly; (3) "PDMP proactive," which requires proactive identification of suspicious prescribing, dispensing, or purchasing; and (4) "PDMP oversight," which requires an oversight board. These indicators have been used previously to characterize variations across PDMP programs.[30] In this study, we compared the absence of all of these PDMP characteristics with the presence of 1 or of 2 or more of them.

State-Combined Analysis

First, to help characterize our study population, we ran cross-tabs between MML status and multiple driver and state-level characteristics. To assess the average impact of MML across states, we used a multilevel logistic regression with a random effect for state of crash and fixed effects for year of crash, presence of PDMP characteristics, and driver's age category, gender, and blood alcohol content. The 2 main independent variables were operational MML status and whether the state had ever passed an MML (model 1). This specification allowed us to compare drivers crashing in states after an operational MML was implemented with drivers crashing in states before one was implemented. This reduced bias related to comparing states with and without an MML, as states that will eventually adopt an operational MML are more comparable to states with a current law than to states that have never passed a law.[19] Furthermore, to test whether the effect of operational MML varied by age category, we included separate interaction terms between age category and the 2 main independent variables. We report the test of overall significance for the interaction between age category and operational MML status; if it is significant, we present age-stratified estimates.

State-Specific Sensitivity Analysis

As a sensitivity analysis, we explored state-specific effects of an MML on opioid positivity using a "difference-in-difference" approach. In this method, state fixed effects are used to capture within-state changes in the outcome among the exposed group, which is then contrasted with the change in outcome observed among an unexposed control group. Under the assumption that the pre-intervention trend is similar in the 2 groups, any differences between states with and without an MML (measured or not) that may also influence opioid positivity (e.g., societal norms) is "differenced" out and does not bias effect estimates.[31] Although statistical power is limited in such analyses, they are useful in showing state-specific effects, and can be used to compare results from other designs and modeling specifications. We conducted state-specific analyses on 4 states with at least 3 years of data before and after an MML became operational: Colorado (1999–2004), Montana (2002–2007), Vermont (2002–2007) and Rhode Island (2003–2008). For each comparison, besides the state of interest, we included as controls only those states in our sample that performed majority testing (i.e., ≥ 80% of drivers who died within 1 hour of crashing) and did not have an operational MML during each 6-year period. Each difference-in-difference analysis first used all eligible states and then repeated the analysis only in states that ever passed an MML, regardless of whether it was operational or not. Sample size limitations precluded the ability to obtain age-stratified estimates. Results are provided in Table A and Figure A (available as a supplement to the online version of this article at http://www.ajph.org). We conducted all analyses using Stata SE version 13 (StataCorp LP, College Station, TX). The technical appendix (available as a supplement to the online version of this article at http://www.ajph.org) provides information required to replicate our analyses.

RESULTS

Among our sample of 68 394 deceased drivers, approximately 41.8% were fatally injured in states that had an operational MML, 25.4% died in states before an operational law went into effect, and 32.8% died in states that had never passed an MML (Table 2). The mean age of all deceased drivers was approximately 41 years, and most (> 75%) were male. There was also a relatively stable level of alcohol involvement across MML status, although there was more missing alcohol data for deceased drivers in states before an MML was operational (6.4%) than in states with an operational MML (2.1%) or in states that had never had an MML (3.7%). In addition, although nearly all states had some form of PDMP, the presence of PDMP characteristics appeared to vary by operational MML status (Table 2). Figure 1 displays trends in opioid positivity across the study years by the MML status of the state in which the deceased drivers crashed.

State-Combined Analysis

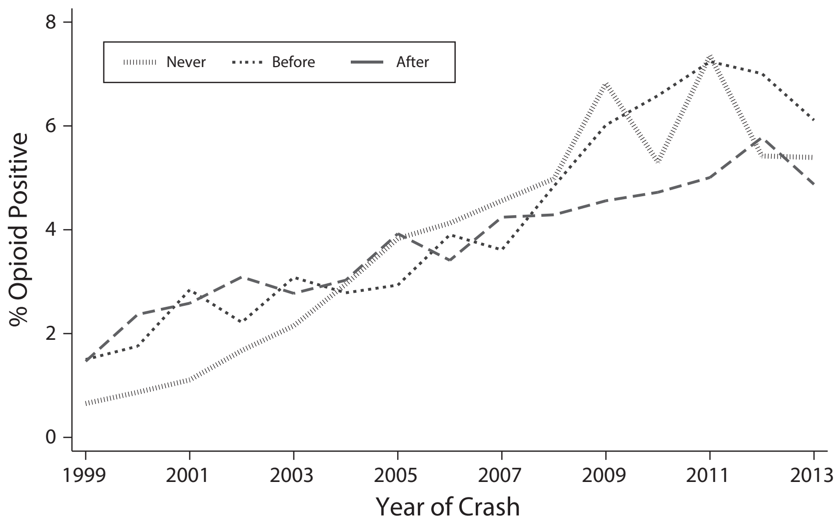
In the overall sample, after we adjusted for driver's age, gender, blood alcohol content, a state-level indicator of whether the state had ever passed a medical marijuana law, and PDMP characteristics, crashing in a state with an operational MML versus crashing in one where an MML was not yet operational was not associated with the odds of opioid

TABLE 2—Characteristics of Drivers Who Died Within 1 Hour of Crashing by State Status of Medical Marijuana Law (MML), Pooled Across the Years 1999–2013: United States

	Operational Status[a] of State MML		
Characteristic	Crashed in States After MML Was Operational, No. (%)	Crashed in States Before MML Was Operational, No. (%)	Crashed in States That Had Never Passed an MML, No. (%)
Total	28 612	17 361	22 421
Age, y			
15–20	3 264 (11.4)	2 116 (12.2)	2 767 (12.3)
21–40	12 889 (45.1)	7 523 (43.3)	9 172 (40.9)
≥ 41	12 459 (43.5)	7 722 (44.5)	10 482 (46.8)
Gender			
Male	22 377 (78.2)	13 467 (77.6)	17 026 (75.9)
Female	6 235 (21.8)	3 894 (22.4)	5 395 (24.1)
Alcohol involvement			
Sober drivers	17 068 (59.7)	9 394 (54.1)	13 080 (58.3)
BAC > 0.01 g/dL	10 965 (38.3)	7 074 (40.8)	8 553 (38.2)
Missing data	579 (2.0)	893 (5.1)	788 (3.5)
PDMP indicators			
None	11 231 (39.3)	7 827 (45.1)	5 024 (22.4)
1	6 670 (23.3)	2 144 (12.4)	11 213 (50.0)
≥ 2	10 711 (37.4)	7 390 (42.6)	6 184 (27.6)

Note. BAC = blood alcohol content; PDMP = prescription drug monitoring program.
Source. Fatality Analysis Reporting System.
[a]An operational medical marijuana law is defined as an effective law with allowances for either home cultivation or access to dispensaries.

positivity (odds ratio [OR] = 0.79; 95% confidence interval [CI] = 0.61, 1.03; Table 3). Tests of interaction between an operational MML and age indicated that the association between MML and opioid positivity varied significantly by age ($\chi^2 = 48.7$; $P < .001$). After we adjusted for both individual and PDMP characteristics (Table 3), compared with drivers aged 21 to 40 years who crashed in states before an operational MML, drivers of the same age range who crashed in states with an operational MML had lower odds of opioid positivity (OR = 0.50; 95% CI = 0.37, 0.67). We observed no significant associations for other age groups.



Source. Fatality Analysis Reporting System.

FIGURE 1—Opioid Positivity Trends in States Before vs After Passing an Operational Medical Marijuana Law (MML) Compared With States That Have Never Had an MML: United States, 1999–2013

State-Specific Sensitivity Analysis

Figure A plots the prevalence of opioid positivity for each MML state compared with the observed average among control states with no operational MML. For each state comparison (Table A), we contrast the count and percentage of opioid positivity before and after an operational MML was implemented (and the before-vs-after difference) with those of 2 overlapping controls groups: (1) controls in states that had performed majority testing (all eligible controls) and (2) controls only in states that had passed an MML. The difference-in-difference estimate signifies the estimated change in opioid positivity associated with an operational MML. For example, after we adjusted for state and year of crash as well as driver's age, gender, and blood alcohol content, Montana experienced a 1.7% reduction (risk difference = –1.72; 95% CI = –5.5, 2.1) in opioid positivity after its MML became operational relative to the expected change in opioid positivity among states that had ever passed an MML (Table A). Although none of these state-specific estimates were significant, there were trends in all states toward a reduction in opioid positivity.

DISCUSSION

In this study, we assessed whether, among comparable samples, implementing an operational MML was associated with reductions in opioid positivity. We did this by comparing drivers crashing in states with an operational MML with drivers crashing in states before a future MML became operational. We performed this comparison in 2 disparate ways: by grouping drivers across states (i.e., the state-combined analysis) and by comparing before-versus-after trends

TABLE 3—Estimated Odds Ratios of Testing Positive for Opioids Among Drivers Who Died Within 1 Hour of Crashing: United States, 1999–2013

Variable	OR[a] (95% CI)
Before an operational law was implemented (Ref)	1
After implementation, by age	
Overall	0.79 (0.61, 1.03)
15–20 y	0.95 (0.55, 1.64)
21–40 y	0.50 (0.37, 0.67)
≥41 y	1.04 (0.79, 1.37)

Note. CI = confidence interval; OR = odds ratio. For test of overall interaction of age-stratified estimates, $\chi^2_2 = 48.7$ ($P < .001$).

Source. Fatality Analysis Reporting System.

[a]Multilevel model includes a random intercept for state of crash and adjusts for operational medical marijuana law (MML) status, driver's age category (and the interaction with MML for age-stratified estimates), whether the state had ever passed an MML (and its interaction with age for age-stratified estimates), the presence of 1, ≥2, or no prescription drug monitoring program characteristics, and year of crash, plus driver's characteristics (gender and blood alcohol content).

within the same state (i.e., the state-specific analysis). We found that among 21- to 40-year-old deceased drivers, crashing in states with an operational MML was associated with lower odds of testing positive for opioids than crashing in MML states before these laws were operational. Although we found a significant association only among drivers aged 21 to 40 years, the age specificity of this finding coheres with what we know about MMLs: a minimum age requirement restricts access to medical marijuana for most patients younger than 21 years, and most surveyed medical marijuana patients are younger than 45 years.[17,32] Although the uptake of medical marijuana has been historically concentrated among young adults, we would expect to see similar reductions in opioid use among older cohorts if medical marijuana is increasingly embraced by older generations.

Our findings among those aged 21 to 40 years are consistent with previous findings that MMLs are associated with a 25% reduction in the annual rate of opioid overdose[18] and that states permitting medical marijuana dispensaries experience a slight decrease in opioid treatment admissions and in opioid overdose mortality.[30] Few studies have previously attempted to explain this mechanism. One study assessed opioid use among a large representative sample,[33] but it found no impact of MMLs on self-reported use. However, the survey question that captured opioid use only assessed "nonmedical use" of pain medications, limiting the information on medication used legitimately for pain. It is possible that the weight of any benefit is mostly conferred on patients who have legitimate need for pain medications. For example, in 1 study conducted in Utah, the majority of opioid overdose decedents in 2008 and 2009 had previously been prescribed opioids for their own conditions.[34]

One other study found that MMLs were not associated with the quantity of opioids dispensed at the state level,[30] suggesting that any reductions in opioid overdoses may not be reflected in the overall sales of opioids. However, if MMLs are in fact reducing opioid overdoses, it follows that this mechanism would entail reductions in individual opioid use, which may not be characterized by an aggregate measure of opioids dispensed at the state level. By contrast, the findings in our study suggest that MMLs are associated with reductions in opioid positivity, an indicator for previous use, at least among drivers aged 21 to 40 years who died within 1 hour of crashing.

Limitations and Strengths

This study has several notable limitations. First, we cannot infer causation in the study; however, the results can be used to assess the plausibility of some alternative explanations. For example, the observed association could be explained by other factors (e.g., increased highway safety expenditures after MML implementation) or by differential selection into the study (e.g., opioid-exposed drivers are less willing to drive in MML states). Although these alternative explanations cannot be ruled out, the number of fatally injured drivers was remarkably consistent across years and states (online Table A), making such biases less likely. For example, in the 3 years prior to implementing its MML, Colorado had 687 drivers who died within 1 hour of crashing; in the following 3 years, it had 691 such deaths.

Second, because we included only a subset of states in our analysis, our results may not be generalizable to all of the United States. However, this was necessary to limit biases related to outcome-dependent selection (e.g., selective testing of inebriated drivers). Although our findings may apply only to deceased drivers in these states, we would expect to see similar findings across comparable samples living in states with and without an MML.

Third, we used a broad measure of opioid use, which included any narcotic coded within the FARS. However, any resulting outcome misclassification is likely similar in states with and without medical marijuana laws (i.e., nondifferential), which would bias our results toward the null. This limitation is offset by the advantages of an objective measure of drug use, as most previous studies assessing the impact of medical marijuana laws have relied on self-reported measures.

There are also study strengths. First, few studies have assessed the association between state MMLs and opioid use at the individual level, and to our knowledge, this is the first to do so with an objective measure of opioid use. Second, although MMLs are heterogeneous across states, our classification of MML status was narrow and well defined. Although this degree of specificity did not allow us to explore other provisions of MMLs (e.g., criminal protection for patients), future studies should examine these as separate indicators with the potential to have disparate influences on substance use. Third, we accounted for the considerable state heterogeneity in both the measurement of our outcome (i.e., toxicological testing procedures) and trends in opioid use and opioid-related harms broadly. To correct for this in our state-combined analysis, we included a random intercept for state of crash and excluded states that did not perform majority testing. Furthermore, we also performed state-specific analyses that assessed within-state changes that eliminated most time-invariant sources of bias. Lastly, we observed consistent findings when making within-state and between-state comparisons, 2 models with varying assumptions.

Conclusions

Because of the uniqueness of our sample, it is worth noting again that our outcome is opioid positivity (i.e., prior opioid use), which is not necessarily indicative of driving impairment. This study was not designed to assess whether opioids increase crash risk. Instead, we assessed whether, among comparable samples, implementing an operational MML was associated with reductions in opioid positivity. Although previous studies have suggested that MMLs are associated with decreased opioid overdose mortality rates at the state level,[18,30] our study suggests 1 plausible mechanism underlying this association: in states with MMLs, fewer individuals are using opioids. If these laws are actually causing reductions in opioid use—an explanation consistent with our results—then the hypothesis that MMLs reduce opioid-related overdoses and treatment admissions is more plausible. However, as states with MMLs move toward legalizing marijuana more broadly for recreational purposes, future studies are needed to assess the impact these laws may have on opioid use. AJPH

CONTRIBUTORS

J. H. Kim developed the study concept and design, collected and analyzed the data, interpreted the results, and drafted the article. J. Santaella-Tenorio, C. Mauro, and J. Wrobel collected and analyzed the data and interpreted the results. M. Cerdà, K. M. Keyes, D. Hasin, S. S. Martins, and G. Li helped develop the study concept and design and helped draft the article.

ACKNOWLEDGMENTS

This study was supported by National Institute on Drug Abuse grants T32DA031099-01A1 (D. Hasin, principal investigator [PI]), R01DA037866-01 (S. S. Martins, PI), R01DA034244.

(D. Hasin, PI), R49CE002096 (G. Li, PI), and R21DA029670 (G. Li, PI).

HUMAN PARTICIPANT PROTECTION

Ethics approval was not needed for this work because it used publically available, anonymized data.

REFERENCES

1. Proposition 215, CA Health & Safety Code §11362.5 (1996).

2. Hill KP. Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: a clinical review. *JAMA*. 2015;313(24):2474–2483.

3. Williams AR, Olfson M, Kim JH, Martins SS, Kleber HD. Older, less regulated medical marijuana programs have much greater enrollment rates than newer "medicalized" programs. *Health Aff (Millwood)*. 2016;35(3):480–488.

4. Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: National Academies Press; 2011.

5. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs 2000. *Pain*. 2004;109(3):514–519.

6. Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. *Pharmacoepidemiol Drug Saf*. 2009;18(12):1166–1175.

7. Eriksen J, Sjogren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. *Pain*. 2006;125(1–2):172–179.

8. Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. *Exp Clin Psychopharmacol*. 2008;16(5):405–416.

9. Compton WM, Volkow ND. Major increases in opioid analgesic abuse in the United States: concerns and strategies. *Drug Alcohol Depend*. 2006;81(2):103–107.

10. Maxwell JC. The prescription drug epidemic in the United States: a perfect storm. *Drug Alcohol Rev*. 2011;30(3):264–270.

11. Okie S. A flood of opioids, a rising tide of deaths. *N Engl J Med*. 2010;363(21):1981–1985.

12. Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *MMWR Morb Mortal Wkly Rep*. 2011;60(43):1487–1492.

13. Unick GJ, Rosenblum D, Mars S, Ciccarone D. Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid-related overdoses, 1993–2009. *PLoS One*. 2013;8(2):e54496.

14. Pizzo PA, Clark NM. Alleviating suffering 101—pain relief in the United States. *N Engl J Med*. 2012;366(3):197–199.

15. Reiman A. Cannabis as a substitute for alcohol and other drugs. *Harm Reduct J*. 2009;6:35.

16. Lucas P, Walsh Z, Crosby K, et al. Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: the impact of contextual factors. *Drug Alcohol Rev*. 2016;35(3):326–333.

17. Reinarman C, Nunberg H, Lanthier F, Heddleston T. Who are medical marijuana patients? Population characteristics from nine California assessment clinics. *J Psychoactive Drugs*. 2011;43(2):128–135.

18. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the united states, 1999–2010. *JAMA Intern Med*. 2014;174(10):1668–1673.

19. Wall MM, Mauro C, Hasin DS, et al. Prevalence of marijuana use does not differentially increase among youth after states pass medical marijuana laws: commentary on and reanalysis of US National Survey on Drug Use in Households data 2002–2011. *Int J Drug Policy*. 2016;29:9–13.

20. *FARS Analytic Reference Guide, 1975 to 2009*. Washington, DC: National Highway Traffic Safety Administration; 2010.

21. *State Laws and Practices for BAC Testing and Reporting Drivers Involved in Fatal Crashes*. Washington, DC: National Highway Traffic Safety Administration; 2004.

22. *Drug Involvement of Fatally Injured Drivers*. Washington, DC: National Highway Traffic Safety Administration; 2010.

23. Hingson R, Winter M, Heeren T. Alcohol and drug use in fatally injured drivers in states that test over 80% for both alcohol and drugs. Paper presented at: 19th International Conference on Alcohol, Drugs and Traffic Safety; August 22–26, 2010; Oslo, Norway.

24. Brady JE, Li G. Prevalence of alcohol and other drugs in fatally injured drivers. *Addiction*. 2013;108(1):104–114.

25. Romano E, Torres-Saavedra P, Voas R, Lacey J. Drugs and alcohol: their relative crash risk. *J Stud Alcohol Drugs*. 2014;75:56–64.

26. Keyes K, Brady J, Li G. Effects of minimum legal drinking age on alcohol and marijuana use: evidence from toxicological testing data for fatally injured drivers aged 16 to 25 years. *Inj Epidemiol*. 2015;2(1):1.

27. Li L, Zhang X, Levine B, Li G, Zielke HR, Fowler DR. Trends and pattern of drug abuse deaths in Maryland teenagers. *J Forensic Sci*. 2011;56(4):1029–1033.

28. *FARS Coding and Validation Manual*. Washington, DC: US Dept of Transportation, National Highway Traffic Safety Administration; 2008.

29. Pacula RL, Powell D, Heaton P, Sevigny EL. Assessing the effects of medical marijuana laws on marijuana use: the devil is in the details. *J Policy Anal Manage*. 2015;34(1):7–31.

30. Powell D, Pacula RL, Jacobson M. *Do Medical Marijuana Laws Reduce Addiction and Deaths Related to Pain Killers?* Cambridge, MA: National Bureau of Economic Research; 2015.

31. Hunt PE, Miles J. The impact of legalizing and regulating weed: issues with study design and emerging findings in the USA. *Curr Top Behav Neurosci*. 2015; Epub ahead of print.

32. Reiman A. Medical cannabis patients: patient profiles and health care utilization patterns. *Complement Health Pract Rev*. 2007;12(1):31–50.

33. Wen H, Hockenberry JM, Cummings JR. The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. *J Health Econ*. 2015;42:64–80.

34. Johnson EM, Lanier WA, Merrill RM, et al. Unintentional prescription opioid-related overdose deaths: description of decedents by next of kin or best contact, Utah, 2008–2009. *J Gen Intern Med*. 2013;28(4):522–529.