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US Adult Illicit Cannabis Use, Cannabis Use Disorder, and Medical Marijuana Laws 1991-1992 to 2012-2013

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IMPORTANCE Over the last 25 years, illicit cannabis use and cannabis use disorders have increased among US adults, and 28 states have passed medical marijuana laws (MML). Little is known about MML and adult illicit cannabis use or cannabis use disorders considered over time.

OBJECTIVE To present national data on state MML and degree of change in the prevalence of cannabis use and disorders.

DESIGN, PARTICIPANTS, AND SETTING Differences in the degree of change between those living in MML states and other states were examined using 3 cross-sectional US adult surveys: the National Longitudinal Alcohol Epidemiologic Survey (NLAES; 1991-1992), the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; 2001-2002), and the National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III; 2012-2013). Early-MML states passed MML between NLAES and NESARC ("earlier period"). Late-MML states passed MML between NESARC and NESARC-III ("later period").

MAIN OUTCOMES AND MEASURES Past-year illicit cannabis use and *DSM-IV* cannabis use disorder.

RESULTS Overall, from 1991-1992 to 2012-2013, illicit cannabis use increased significantly more in states that passed MML than in other states (1.4-percentage point more; SE, 0.5; P = .004), as did cannabis use disorders (0.7-percentage point more; SE, 0.3; P = .03). In the earlier period, illicit cannabis use and disorders decreased similarly in non-MML states and in California (where prevalence was much higher to start with). In contrast, in remaining early-MML states, the prevalence of use and disorders increased. Remaining early-MML and non-MML states differed significantly for use (by 2.5 percentage points; SE, 0.9; P = .004) and disorder (1.1 percentage points; SE, 0.5; P = .02). In the later period, illicit use increased by the following percentage points: never-MML states, 3.5 (SE, 0.5); California, 5.3 (SE, 1.0); Colorado, 7.0 (SE, 1.6); other early-MML states, 2.6 (SE, 0.9); and late-MML states, 5.1 (SE, 0.8). Compared with never-MML states, increases in use were significantly greater in late-MML states (1.6-percentage point more; SE, O.6; P = .01), California (1.8-percentage point more; SE, 0.9; P = .04), and Colorado (3.5-percentage point more; SE, 1.5; P = .03). Increases in cannabis use disorder, which was less prevalent, were smaller but followed similar patterns descriptively, with change greater than never-MML states in California (1.0-percentage point more; SE, 0.5; P = .06) and Colorado (1.6-percentage point more; SE, 0.8: P = .04).

CONCLUSIONS AND RELEVANCE Medical marijuana laws appear to have contributed to increased prevalence of illicit cannabis use and cannabis use disorders. State-specific policy changes may also have played a role. While medical marijuana may help some, cannabis-related health consequences associated with changes in state marijuana laws should receive consideration by health care professionals and the public.

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Supplemental content

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Corresponding Author: Deborah S. Hasin, PhD, Department of Psychiatry, Columbia University Medical Center, 1051 Riverside Dr, Unit 123, New York, NY 10032 (deborah.hasin@gmail.com). ver the last 20 years, laws and attitudes regarding cannabis have changed. As of November 2016, 28 states have passed medical marijuana laws (MML). Many adults now favor legalizing recreational use, and fewer view cannabis as risky. Despite this view, while some can use cannabis without harm, and potential consequences include impaired functioning, vehicle crashes, and addiction. Strip over time, the prevalence of adult illicit use and related consequences has increased. Over the simportant. State MML may be one such factor.

Little is known about MML and adult cannabis outcomes. Two national studies^{17,27} showed greater use and DSM-IV-diagnosed disorders in MML states but did not examine differences before and after MML. One national study²⁸ did so, finding increased post-MML cannabis use and cannabis disorders. However, this study only addressed 2004 to 2012, adults 20 years and older, and 10 states that changed MML status.²⁸ To our knowledge, no study of differences before and after MML has used adult national data predating all MML, differentiated between earlier and more recent periods, or separately examined particular states. Differences between states that passed MML early vs late are important because the national normative context differed for early-MML states, when few such laws existed, and late-MML states, enacted when more states had MML. Also, earlier data can show if trends in cannabis use and disorder in late-passing states began prior to their MML. Further, California and Colorado warrant separate, secondary examination. In 1996, when California passed the first MML, its cannabis rates were higher than other states,²⁹ and thus its MML may have had little additional effect. Colorado (MML passed in 2000) experienced unique policy changes in 2009-2010 (eAppendix 1 in the Supplement) followed by increases in medical user applications from 500 per month to greater than 10 000 per month and from no known dispensaries to greater than 900, 30-34 potentially exerting additional impact on cannabis outcomes during the later period.³⁵

We examined MML, illicit cannabis use, and cannabis use disorders in 3 cross-sectional adult surveys: the 1991-1992 National Longitudinal Alcohol Epidemiologic Survey (NLAES), 36,37 the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), 38-40 and the 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III). 41,42 Over this period, the national context for MML changed. In 1991-1992, no Americans lived in MML states; in 2001, 18.9% lived in MML states, 43 and in 2012, more than one-third (34.3%) lived in MML states. 44 We therefore addressed 3 questions. First, between 1991-1992 and 2012-2013 (the overall study period), were changes in the prevalence of illicit cannabis use and disorders greater in states that ever had MML vs never had MML? Second, between 1991-1992 and 2001-2002 (for convenience, termed the earlier period), did changes in prevalence differ between states that did and did not pass MML during this time, including and excluding California? Third, between 2001-2002 and 2012-2013 (for convenience, termed the later period), did changes in

Key Points

Question Are US state medical marijuana laws one of the underlying factors for increases in risk for adult cannabis use and cannabis use disorders seen since the early 1990s?

Findings In this analysis using US national survey data collected in 1991-1992, 2001-2002, and 2012-2013 from 118 497 participants, the risk for cannabis use and cannabis use disorders increased at a significantly greater rate in states that passed medical marijuana laws than in states that did not.

Meaning Possible adverse consequences of illicit cannabis use due to more permissive state cannabis laws should receive consideration by voters, legislators, and policy and health care professionals, with appropriate health care planning as such laws change.

prevalence differ between never-MML states, states passing MML during the earlier period, and states passing MML during the later period? In investigating the later period, we again kept California separate and also separated Colorado, given its 2009-2010 changes. 30-34

Methods

Study Design and Participants

The NLAES, 36,37 NESARC, 38-40 and NESARC-III41,42 surveyed adults 18 years and older in households and group quarters, using similar multistage sampling designs. 20,36,39-42,45 Sample weights were adjusted for selection probabilities and nonresponse. Field procedures were similar across surveys, except that the NLAES used paper-and-pencil interviews whereas the NESARC and NESARC-III used computer-assisted interviews. Because trained interviewers used similar procedures in all surveys, respondents were similarly exposed to interview questions, permitting examination of trends over time. 20,42,45-47 Quality assurance included training, supervision, and callbacks to verify respondent data. 36,39-42 The NLAES and NESARC protocols and consent procedures were approved by the institutional review boards at the US Bureau of the Census and the Office of Management and Budget; written consent was provided. The NESARC-III protocols and consent procedures were approved by institutional review boards at the National Institutes of Health and Westat; consent was verbal but recorded electronically, as approved by both institutional review boards. Overall response rates were 60% to 84%. 36,39-42 Eleven states in which primary sampling units were not randomly selected in NESARC-III were excluded from analyses (Table 1), yielding 41764 participants from the NLAES, 41184 from the NESARC, and 35549 from the NESARC-III, totaling 118 497 participants. Sample demographic characteristics are shown in eTable 1 in the Supplement.

Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS), a structured diagnostic interview, was used to assess substance use and *DSM-IV* substance use

disorders. All 3 surveys included the same questions about illicit use in the prior 12 months, including cannabis. Illicit use was defined to participants as use without a prescription or other than prescribed, eg, to get high (eAppendix 2 in the Supplement). In the NLAES, information about cannabis was assessed only if participants used 12 or more times. For consistency with the NLAES, we analyzed cannabis use and disorders among NESARC and NESARC-III participants who used cannabis 12 or more times. Any illicit cannabis use in the past 12 months was analyzed, providing a consistent timeframe for use and disorders.

Participants with DSM-IV cannabis abuse or dependence in the past 12 months were coded positive for cannabis use disorder (abuse and dependence combined because their criteria reflect a single disorder⁴⁸). All AUDADIS versions included the same core questions covering cannabis disorder criteria. A minor difference between the NLAES and NESARC was that in the NLAES, criteria were assessed with 2 questions-1 on occurrence and 1 on recurrence-while in the NESARC and NESARC-III, single questions were used. 20,45 Also, the NLAES but not the NESARC included 4 items assessing the "social impairment" and "use despite health problems" dependence criteria. Comparisons between DSM-IV cannabis diagnoses in the NLAES with and without these 4 questions yielded nearly identical prevalence (1.12% vs 1.06%, respectively) and nearperfect concordance (k, 0.98), so these differences had little impact on results.

The NESARC and NESARC-III AUDADIS versions also had only minor differences. Four items were slightly reworded, 1 item was in the NESARC but not NESARC-III, and 1 item was in the NESARC-III but not NESARC. *DSM-IV* cannabis disorder diagnoses with and without these NESARC and NESARC-III items had near-identical prevalence and near-perfect concordance. ²⁰ Thus, these minor differences could not account for the substantial prevalence increases observed between surveys. Test-retest reliability and convergent validity of AUDADIS *DSM-IV* cannabis disorder diagnoses is documented extensively. ^{36,49-57}

State-Level MML Variables

A team of legal scholars, policy analysts, and economists reviewed state policies to determine the year of MML passage. ^{58,59} Three variables were then created (eTable 2 in the Supplement). One indicated participants in states passing MML between 1991 and 2012 (ever-MML states) vs others (never-MML states), 1 indicated participants in early-MML states vs non-early-MML states (ie, never-MML and late-MML states), and 1 indicated participants in early-MML states, late-MML states, and never-MML states. Early-MML states passed MML between 1991 and 2001 (in the earlier period). Late-MML states passed MML between 2002 and 2012 (in the later period). Never-MML states had no MML by 2012. Additional variables for secondary analyses represented California and Colorado separately.

Individual-Level and State-Level Control Covariates

Covariates included sex, age, education (less than high school vs others), race/ethnicity (Hispanic, non-Hispanic white, non-

Table 1. Difference in Predicted Prevalences of Past-Year Cannabis Use and *DSM-IV* Cannabis Use Disorder, 1991-1992 to 2012-2013: Never-MML States and Ever-MML States (Model 1)

	Model 1, Prevalence (S	Model 1, Prevalence (SE) ^a					
Outcome	Never-MML States ^b (24 States)	Ever-MML States ^c (15 States)					
Cannabis use							
1991-1992	4.54 (0.39)	5.55 (0.36)					
2012-2013	6.70 (0.39)	9.15 (0.54)					
Difference in prevalence	+2.17 (0.70) ^d	+3.60 (0.79) ^e					
DiD (ever-MML vs never-MML states)	[Reference]	+1.43 (0.48) ^f					
Cannabis use disorder							
1991-1992	1.35 (0.19)	1.48 (0.19)					
2012-2013	2.30 (0.22)	3.10 (0.34)					
Difference in prevalence	+0.96 (0.38) ^g	+1.62 (0.47) ^h					
DiD (ever-MML vs never-MML states)	[Reference]	+0.66 (0.30) ⁱ					

Abbreviations: DiD, difference-in-difference; MML, medical marijuana laws.

Hispanic black, and other; self-defined using US Census Bureau categories), marital status (unmarried vs others), urbanicity (metropolitan statistical areas vs others), and poverty (less than 100%, 100% to 200%, and greater than 200% of the federal poverty level⁶⁰). Following prior MML work, ^{27,59,61,62} US Census data were used to define 4 state-level covariates: percent male, percent white, percent younger than 30 years, and percent 25 years and older without a high school diploma.

Statistical Analyses

We examined whether the degree of change between surveys differed in participants by state MML status using difference-in-difference (DiD) tests. ^{63,64} By assuming that trends in non-MML states reflect what would have happened in MML states if they had not passed MML, DiD tests provide information about changes due to MML passage, with inferences strengthened if trends in MML and non-MML states did not differ

^a Prevalence based on participants in the 39 states included in all 3 surveys. States omitted: Alaska, Delaware, Hawaii, Idaho, Nebraska, New Hampshire, North Dakota, Rhode Island, South Dakota, West Virginia, and Wyoming. Prevalences back-transformed from marginal log-odds estimated from logistic regression interaction models (MML × survey) that included individual-level (sex, age, education, race/ethnicity, marital status, urbanicity, and poverty) and state-level (% male, % white, % <30 y, and % ≥25 y without a high school diploma) covariates. Predicted prevalences estimated by a model with a dichotomous MML variable (ever-MML states vs never-MML states).

^b Never-MML states (1996-2012): Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Minnesota, Mississippi, Missouri, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, and Wisconsin.

^c Ever-MML states (1996-2012): Arizona, California, Colorado, Connecticut, Maine, Maryland, Massachusetts, Michigan, Montana, Nevada, New Jersey, New Mexico, Vermont, Oregon, and Washington.

 $^{^{\}rm d}P$ = .003; change in never-MML states between 1991-1992 and 2012-2013.

 $^{^{\}rm e}$ P < .001; change in ever-MML states between 1991-1992 and 2012-2013.

 $^{^{\}rm f}$ P = .004, change in never-MML states between 1991-1992 and 2012-2013.

 $^{^{\}rm g}{\it P}$ = .01; change in never-MML states between 1991-1992 and 2012-2013.

 $^{^{}h}$ P = .001; change in ever-MML states between 1991-1992 and 2012-2013. i P = .03, change in never-MML states between 1991-1992 and 2012-2013.

before MML passage (ie, previous parallel paths⁶⁵). Difference-in-difference tests advantageously "difference out" fixed unmeasured factors and control for preexisting between-group differences⁶⁶ that might bias results. By standardizing groups across time to the overall weighted distribution of model covariates, use of predicted marginal prevalences in the DiD approach additionally eliminates varying measured covariates as explanations of results.

The 3 survey data sets were concatenated, adding a variable indicating survey. Models included survey (NLAES, NESARC, and NESARC-III), MML indicators, survey by MML interaction terms, and covariates. Sample weights in multivariable logistic regression models generated weighted predicted marginal prevalence estimates (back-transformed from marginal logodds) and SEs of cannabis outcomes in each survey within strata defined by MML variables. A first set of contrasts estimated between-survey change in predicted prevalences within MML strata. With a second set of contrasts, the DiD tests tested if these between-survey changes differed by MML strata. Difference-in-difference estimates differing significantly from 0 indicated differences in change between MML vs other states.

Separate models tested MML effects during the overall period (model 1), the earlier period (model 2), and the later period (model 3). In model 1 (1991-1992 vs 2012-2013), we evaluated MML effects by testing for differential changes between ever-MML states and never-MML states. In model 2 (1991-1992 vs 2001-2002), we evaluated early-MML effects by testing for differential changes in early-MML states vs remaining states (ie, late-MML and non-MML states), initially grouping California with other early-MML states (model 2A) and then examining California separately (model 2B). In model 3 (2001-2002 vs 2012-2013), we tested for differential changes between never-MML states (reference) and late-MML states, California, Colorado, and the other early-MML states.

We tested the parallel-path assumption⁶⁵ of DiD estimators for late-MML states and Colorado by comparing their trends with non-MML states during the earlier period. Sensitivity analyses testing robustness of findings included (1) adding originally excluded NESARC and NESARC-III participants who only used cannabis 1 to 11 times to models 1, 2, and 3; (2) adding participants from all states included in each survey to models 1, 2, and 3; (3) recoding cannabis disorder to include withdrawal as a seventh criterion⁴⁸; and (4) omitting participants aged 18 and 19 years for consistency with earlier research.²⁸ All analyses used SUDAAN version 11.0.1 (RTI International)⁶⁷ and included survey weights and stratification variables to account for the complex survey design. Results were inspected for meaningful change from models 1, 2, and 3 if DiD tests gained or lost significance. All P values were 2-tailed, and significance was set at P < .05.

Results

Descriptive Predicted Prevalences of Illicit Cannabis Use and Disorder

Between 1991-1992 and 2001-2002, illicit use decreased and disorder changed little. Between 2001-2002 and 2012-2013, use

and disorder increased. eTable 3 in the Supplement presents predicted prevalences of use and disorder in the 39 states analyzed, by survey and MML status.

Change in Illicit Cannabis Use and Cannabis Use Disorder by State MML Status: 1991-1992 to 2012-2013 (Model 1)

Between 1991-1992 and 2012-2013, the predicted prevalence of illicit use increased by 3.6 and 2.2 percentage points in ever-MML and never-MML states, respectively (Table 1) (**Figure 1**A), a significantly greater increase in ever-MML than never-MML states (P = .004). The predicted prevalence of cannabis disorder also increased (1.6 and 1.0 percentage points) in ever-MML and never-MML states (**Figure 2**A), also a significantly greater change in the ever-MML states (P = .03).

Change During the Earlier Period: 1991-1992 to 2001-2002 (Models 2A and 2B)

From 1991-1992 to 2001-2002, when grouping California with other early-MML states in model 2A, the predicted prevalence of illicit use did not change significantly in early-MML states and decreased by 1.7 percentage points in non-early-MML states, which was not a significant difference. For cannabis disorders, change in all early-MML and non-early-MML states also did not differ significantly (model 2A) (Table 2).

Separating California from the other early states produced very different results in model 2B (Table 2) (Figure 1B and Figure 2B). Note that in 1991-1992, predicted prevalences of use and disorder were higher in California than other early-MML states (use: 7.59% vs 4.49%; P = .001; disorder: 2.08% vs 1.15%; P = .02). Nevertheless, for use, decreases in California and non-early-MML states (-2.0 vs -1.7 percentage points) did not differ significantly, nor did the slight decreases in cannabis disorder.

In contrast, in the other 5 early-MML states, prevalences of use and disorder increased. The change in remaining early-MML states differed from non-MML states for use (by 2.5 percentage points; P = .004) and disorder (1.1 percentage points; P = .02).

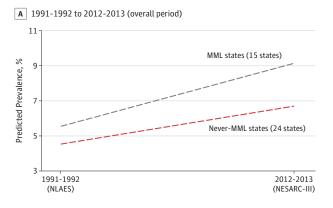
Change During the Later Period: 2001-2002 to 2012-2013 (Model 3)

From 2001-2002 to 2012-2013, predicted prevalences of illicit cannabis use and cannabis disorder increased by the following percentage points: never-MML states, 3.5 and 1.0, respectively; California, 5.3 and 2.0; Colorado, 7.0 and 2.7; other early-MML states, 2.6 and 0.1; and late-MML states, 5.1 and 1.7. Compared with change in never-MML states, increases in use were significantly greater in late-MML states (P = .01), California (P = .04), and Colorado (P = .03) (Table 3) (Figure 1C). Comparing increases in prevalence of cannabis disorder with never-MML states (the reference group), change in late-MML states was not significant (P = .12) but was greater at a trend level in California (P = .06) and significantly greater in Colorado (P = .04) (Table 3) (Figure 2C).

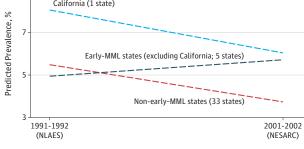
Parallel Paths Sensitivity Analyses

The pre-MML parallel-path assumption was supported by a lack of difference during the earlier period in changes between

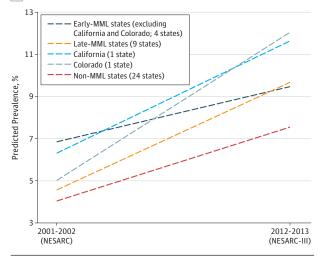
Figure 1. Medical Marijuana Laws (MML) and Marijuana Use in the Past 12 Months





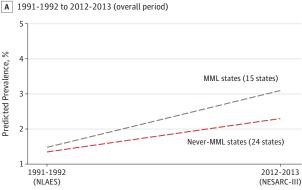


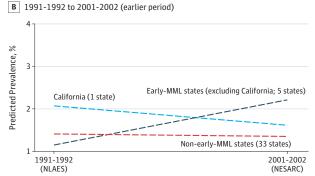
C 2001-2002 to 2012-2013 (later period)

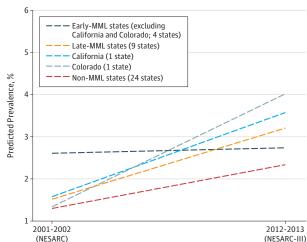


Prevalences predicted by logistic regression model 1 (A), model 2B (B), and model 3 (C). Models controlled for sex, age (18-29, 30-39, 40-49, and ≥50 years), education (<high school vs others), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, and other), marital status (unmarried vs others), urbanicity (metropolitan statistical areas vs others), and poverty (<100%, 100%-200%, and >200% of the federal poverty level). Early-MML states (1996-2001) include California, Colorado, Maine, Nevada, Oregon, and Washington. Late-MML states (2002-2012) include Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, and Vermont. Trend lines are included for visual comparison; they do not imply that the trend was linearly changing over time. NESARC indicates the National Epidemiologic Survey on Alcohol and Related Conditions; NESARC-III, the National Epidemiologic Survey on Alcohol and Related Conditions-III; NLAES, the National Longitudinal Alcohol Epidemiologic Survey.

Figure 2. Medical Marijuana Laws (MML) and *DSM-IV* Cannabis Use Disorder in the Past 12 Months







c 2001-2002 to 2012-2013 (later period)

Prevalences predicted by logistic regression model 1 (A), model 2B (B), and model 3 (C). Models controlled for sex, age (18-29, 30-39, 40-49, and ≥50 years), education (<high school vs others), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, and other), marital status (unmarried vs others), urbanicity (metropolitan statistical areas vs others), and poverty (<100%, 100%-200%, and >200% of the federal poverty level). Early-MML states (1996-2001) include California, Colorado, Maine, Nevada, Oregon, and Washington. Late-MML states (2002-2012) include Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, and Vermont. Trend lines are included for visual comparison; they do not imply that the trend was linearly changing over time. NESARC indicates the National Epidemiologic Survey on Alcohol and Related Conditions-III; NLAES, the National Longitudinal Alcohol Epidemiologic Survey.

Table 2. Differences in Predicted Prevalences of Past-Year Cannabis Use and DSM-IV Cannabis Use Disorder, 1991-1992 to 2001-2002: Non-Early-MML States and Early-MML States (Models 2A and 2B)

	Prevalence ^a (SE)				
	Model 2A ^b		Model 2B ^c		
Outcome	Non-Early-MML States All Early-MML States (33 States) ^d (6 States) ^e		All Early-MML States but California (5 States) California		
Cannabis use					
1991-1992	4.97 (0.44)	6.34 (0.48)	4.49 (0.53)	7.59 (0.71)	
2001-2002	3.29 (0.14)	5.24 (0.47)	5.26 (0.71)	5.58 (0.60)	
Change in prevalence	-1.69 (0.42) ^f	-1.10 (0.59)	+0.77 (0.87)	-2.01 (0.74) ^g	
DiD (early-MML states vs non-early-MML states)	[Reference]	+0.58 (0.62) ^h	+2.51 (0.85) ⁱ	-0.27 (0.80) ^j	
Cannabis use disorder					
1991-1992	1.43 (0.22)	1.73 (0.23)	1.15 (0.25)	2.08 (0.33)	
2001-2002	1.36 (0.08)	1.86 (0.28)	2.22 (0.42)	1.62 (0.28)	
Change in prevalence	-0.07 (0.21)	+0.14 (0.33)	+1.07 (0.49) ^k	-0.46 (0.37)	
DiD (early-MML states vs non-early-MML states)	[Reference]	+0.21 (0.35) ^l	+1.13 (0.47) ^m	-0.40 (0.40) ⁿ	

Abbreviations: DiD, difference-in-difference; MML, medical marijuana laws.

Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Vermont, Virginia, and Wisconsin.

non-MML states and late-MML states (eTable 4 in the Supplement) as well as non-MML states and Colorado (eTable 4 and eFigures 1 and 2 in the Supplement). Sensitivity analyses (eTable 5 in the Supplement) did not change results meaningfully, indicating robust main findings.

Discussion

In 3 cross-sectional national surveys spanning 20 years, we investigated whether increases in US adult illicit cannabis use and cannabis use disorders followed implementation of MML. Over the entire period, predicted prevalences of illicit use and disorders increased to a greater degree in states that passed MML than in other states. Holding population size and demographic distributions constant from 1991 to 2012, an additional 1.1 million adult illicit cannabis users and an additional 500 000 adults with a *DSM-IV*-diagnosed cannabis disorder may be attributable to medical marijuana law passage. Given the potential consequences of use and persistent disability associated with cannabis use disorders, ^{3,68} this represents a serious public health problem.

During the earlier period (1991-1992 to 2001-2002), prevalences in the 5 early-MML states (excluding California) increased in contrast to decreases in non-MML states and Cali-

fornia. In 1991-1992, the sharply higher rates of cannabis use and disorder in California than in other states (use, 69% higher; disorder, 80% higher) suggest that California, a bellwether state, differed from other states from the start, consistent with 1995 findings of higher cannabis use in California communities than elsewhere. ²⁹ Therefore, an already permissive environment in California may have overridden further MML effects. However, in other early-MML states, MML contributed to increased illicit use and disorder, contrary to a nationally decreasing trend.

During the later period (2001-2002 to 2012-2013), illicit use increased significantly more in late-MML states than in never-MML states. (The lack of significant differences in early-MML states could be due to absence of strong lagged effects, waning MML effects over time, or local factors.) Our inference that MML contributed to increased illicit use in late-MML states is strengthened by the lack of such differences in late-MML states during the earlier period (eTable 4 in the Supplement). Further, greater increases in cannabis use and disorder in Colorado than in never-MML states suggests that well-documented 2009-2010 policy changes and dispensary proliferation (eAppendix 1 in the Supplement) contributed to increases in use and disorder, particularly because similar increases did not occur there during the earlier period (eTable 4 and eFigures 1 and 2 in the Supplement). Substantial increases also occurred in California during

a Prevalence based on participants in the 39 states included in all 3 surveys. States omitted: Alaska, Delaware, Hawaii, Idaho, Nebraska, New Hampshire, North Dakota, Rhode Island, South Dakota, West Virginia, and Wyoming. Prevalences back-transformed from marginal log-odds estimated from logistic regression interaction models (MML × survey) that included individual-level (sex, age, education, race/ethnicity, marital status, urbanicity, and poverty) and state-level (% male, % white, % <30 y, and % ≥25 y without a high school diploma) covariates. Predicted prevalences estimated by a model with a dichotomous MML variable (non-early-MML states ys early-MML states).

^b Predicted prevalences estimated by a model with a dichotomous MML variable (early-MML states vs non-early-MML states).

^c Predicted prevalences estimated by an identical model to model 2A, except California was specified as a separate group.

^d Non-early–MML states: Alabama, Arizona, Arkansas, Connecticut, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland,

^e Early-MML states (1996-2001): California, Colorado, Maine, Nevada, Oregon, and Washington.

^f P < .001; change in non-early-MML states between 1991 and 2001.

g P = .009; change in California between 1991 and 2001.

 $^{^{}h}P = .35.$

 $^{^{}i}$ P = .004.

^j P = .74.

^k P = .03; change in all early-MML states but California between 1991 and 2001.

P = .55.

 $^{^{}m}P = .02.$

 $^{^{}n}P = .33.$

Table 3. Differences in Predicted Prevalences of Past-Year Cannabis Use and *DSM-IV* Cannabis Use Disorder, 2001-2002 to 2012-2013: Never-MML States, Early-MML States, and Late-MML States (Model 3)^a

	Model 3, Prevalence ^b (SE)							
Outcome	Never-MML States (24 States) ^c	All Early-MML States but California and Colorado (4 States) ^d	All Late-MML States (9 States) ^e	California (1 State)	Colorado (1 State)			
Cannabis use								
2001-2002	3.12 (0.15)	5.93 (0.81)	3.64 (0.31)	5.39 (0.59)	4.10 (0.62)			
2012-2013	6.62 (0.41)	8.55 (0.69)	8.74 (0.74)	10.72 (0.98)	11.13 (1.64)			
Change in prevalence	+3.50 (0.47) ^f	+2.62 (0.93) ^g	+5.11 (0.75) ^h	+5.33 (0.95) ⁱ	+7.03 (1.62) ^j			
DiD (ever-MML vs never-MML states)	[Reference]	-0.87 (0.89) ^k	+1.61 (0.63) ^l	+1.83 (0.89) ^m	+3.53 (1.54) ⁿ			
Cannabis use disorder								
2001-2002	1.29 (0.09)	2.61 (0.48)	1.51 (0.20)	1.57 (0.28)	1.34 (0.47)			
2012-2013	2.33 (0.24)	2.74 (0.49)	3.21 (0.47)	3.58 (0.55)	4.02 (0.81)			
Change in prevalence	+1.04 (0.28)°	+0.13 (0.61)	+1.70 (0.49) ^p	+2.00 (0.54) ^q	+2.68 (0.84) ^r			
DiD (ever-MML vs never-MML states)	[Reference]	-0.91 (0.61) ^s	+0.65 (0.42) ^t	+0.96 (0.49) ^u	+1.64 (0.77) ^v			

Abbreviations: DiD, difference-in-difference; MML, medical marijuana laws.

the later period, consistent with qualitative observations of marijuana dispensary proliferation, ⁶⁹ although centralized California dispensary documentation is lacking. Additional research is needed on late MML and cannabis use disorder and how major policy changes and their implementation ^{58,70} relate to public health consequences in MML states.

Increases in cannabis use associated with MML may have resulted from increasing availability, potency,⁷¹ perceived safety/acceptability,⁶¹ generally permissive attitudes (because other substance use and disorders also increased^{42,72,73}), greater use for coping with depression and anxiety (A.L.S., M.M.W., K.M.K., M.C., D.S.H.; unpublished data; 2017), or diminished economic opportunities.²¹ Future studies should investigate such mechanisms.

The previous study of pre-post MML changes in adults²⁸ also found post-MML increases in cannabis use and disorder, supporting our results. However, while this study had an important advantage in that consecutive years of survey data were analyzed, only 8 years were included, changes in only 10 MML states were examined, early-MML vs late-MML

effects were not addressed, and the survey did not differentiate between medical and illicit users, so medical use may have been included in its estimates. Finally, the diagnostic measure used in that study may have low sensitivity and validity. Thus, our examination of MML effects on adult illicit (ie, nonmedical) cannabis use contributes important new information.

To our knowledge, studies using DiD methods have not shown post-MML increases in adolescent cannabis use. ^{28,59,76-78} The reasons MML differentially affect adolescents and adults merit investigation.

Since 2012, 8 states have legalized recreational cannabis use. Research is needed on the effects of these laws, which may differ from MML.⁶¹

Limitations and Strengths

Study limitations are noted. Measures were self-reported. Diminished underreporting as cannabis gained acceptability could have influenced observed increases between the NESARC and NESARC-III, as could other methodological

^a States included were the 39 with data in all 3 surveys. States omitted: Alaska, Delaware, Hawaii, Idaho, Nebraska, New Hampshire, North Dakota, Rhode Island, South Dakota, West Virginia, and Wyoming. The predicted prevalences from the later period were estimated by a model with a trichotomous MML variable (early-MML states vs late-MML states vs never-MML states).

^b Predicted prevalences estimated by a model with a 5-level MML variable (early-MML states vs late-MML states vs California vs Colorado vs never-MML states). Prevalences back-transformed from marginal log-odds estimated from logistic regression interaction models (MML × survey) that included individual-level (sex, age, education, race/ethnicity, marital status, urbanicity, and poverty) and state-level (% male, % white, % <30 y, and % ≥25 y without a high school diploma) covariates.

^c Never-MML states (1996-2012): Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Minnesota, Mississippi, Missouri, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, and Wisconsin.

^d Early-MML states (except California and Colorado) (1996-2001): Maine, Nevada, Oregon, and Washington.

^e Late-MML states (2002-2012): Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, and Vermont.

f P < .001; change in never-MML states between 2001 and 2012.

g P < .001; change in all early-MML states (except California) between 2001 and 2012.

^h P < .001; change in all late-MML states between 2001 and 2012.

ⁱ P < .001; change in California only between 2001 and 2012.

^j P < .001; change in Colorado only between 2001 and 2012.

 $^{^{}k}P = .33.$

 $^{^{}I}$ P = .01.

 $^{^{}m}P = .04.$

 $^{^{}n}P = .03$

 $^{^{\}circ}\mathit{P}$ < .001; change in never-MML states between 2001 and 2012.

 $^{^{\}mathrm{p}}P$ = .001; change in all late-MML states between 2001 and 2012.

 $^{^{\}rm q}P$ < .001; change in California only between 2001 and 2012.

 $^{^{\}rm r}$ P = .002; change in Colorado only between 2001 and 2012.

s P = .14.

^t P = .12.

 $^{^{\}rm u}P = .06.$

 $^{^{\}vee}P = .04.$

issues.^{79,80} However, numerous other cannabis-related consequences also increased over this period, 10,17,19,22,24,25 supporting the validity of NESARC to NESARC-III comparisons. 75 In any case, there is no reason to expect that such methodological issues would have influenced potential differences between medical marijuana states and other locations. Also, the early and later periods were defined by dates of the surveys. Exploring other definitions of early and later in suitable data could contribute useful information, eg, before and after major policy changes. The treatment of California and Colorado is termed as secondary. While these results contribute important information, further research is needed on these states relative to the national context if suitable data can be found. Ideally, all 3 surveys would have included all 50 states. However, approximately equal proportions of ever-MML and never-MML states were excluded, and analyses suggested that omitted states would not have changed the results. Additionally, we used data sets from only 3 periods, precluding formal testing of the prior parallel-path assumption for the early-MML states. However, 2 smaller surveys conducted in 1984 and 1990⁸¹ suggest descriptively that early-MML states other than California did not begin their sharp increase prior to MML passage (eTable 6 and eFigure 3 in the Supplement; written personal communication, William Kerr, PhD, February 2017). Study strengths include that results contribute knowledge from more than 100 000 participants in 39 states across 2 decades. Topics for future research include whether other outcomes (eg, cannabis use frequency and other substance use) were affected by MML and whether individual or state characteristics modify MML effects.

Conclusions

This study suggests that MML contributed to increasing US adult illicit cannabis use and cannabis disorders. Policy and clinical professionals should recognize that cannabis disorders can be severe, 3.82 treatment needs are increasing, and treatment can be effective. Bare Medical marijuana laws may benefit some with medical problems. However, changing state laws (medical or recreational) may also have adverse public health consequences. A prudent interpretation of our results is that professionals and the public should be educated on risks of cannabis use and benefits of treatment, and prevention/intervention services for cannabis disorders should be provided.

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Acquisition, analysis, or interpretation of data: All authors.

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Supplementary Online Content

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- **eAppendix 1.** Justification for testing change in Colorado as a single state relative to never-MML states in the analysis of the later period (2001-2002 to 2012-2013)
- **eAppendix 2.** Interviewer statement preceding AUDADIS questions about drug use in NLAES, NESARC and NESARC-III
- **eTable 1.** Demographic characteristics of NLAES, NESARC, and NESARC-III samples, with participants in the 11 states not common to the 3 surveys excluded
- **eTable 2.** Years that medical marijuana laws (MML) were enacted for the 50 US states up to 2012 and how participants in these states were coded in Models 1-3
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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Justification for testing change in Colorado as a single state relative to never-MML states in the analysis of the later period (2001-2002 to 2012-2013)

Federal Context. Cannabis was established as a Schedule 1 substance by the Federal Drug Enforcement Agency (DEA) in 1970, and has remained so since then. Schedule 1 substances are defined as having no currently accepted medical use and a high potential for abuse. However, despite the definition of the federal stance towards marijuana as defined by the DEA, California passed the first medical marijuana law in 1996, and between then and 2009, fifteen additional states passed medical marijuana laws.

The 2009 Ogden Memo. Given these changes, in October 2009, U.S. Attorney General Eric Holder announced new formal guidelines for federal prosecutors in states that had enacted laws authorizing the use of marijuana for medical purposes. The guidelines were contained in a memorandum from Deputy Attorney General David W. Ogden in the U.S. Department of Justice known as the "Ogden Memo". The Ogden Memo reflected the shifting stance of the federal government over the last decade towards medical marijuana, despite the continuing Schedule 1 status of cannabis at the federal level.

The memo instructed federal prosecutors not to focus federal resources on prosecuting individuals who were clearly and unambiguously in compliance with state laws providing for the medical use of marijuana. Prior to the Ogden Memo, fears and uncertainty about federal law enforcement had limited state actions to disseminate medical marijuana. By directing federal prosecutors not to use federal resources to prosecute those complying with state medical marijuana laws, the Ogden Memo provided states with somewhat greater flexibility to adopt and implement medical marijuana laws.

The state context: caregivers and dispensaries. Many state medical marijuana laws have provisions for what are termed "caregivers". These are adults who agree to assist with patients' medical use of marijuana. Caregivers are permitted to possess but not use marijuana ¹. Many states also have regulations governing medical marijuana dispensaries, i.e., retail outlets where medical marijuana can be sold. Whether or not a state has specific provisions for dispensaries is considered by some experts^{2,3} to be an important consideration in analyzing the unintended consequences of state medical marijuana laws for outcomes such as illicit cannabis use.

Colorado's legal stance towards caregivers and dispensaries. Colorado passed its medical marijuana law in 2000. This law had a provision for caregivers, which the Colorado Department of Public Health and Environment (CDPHE) limited to five patients per caregiver. In 2007, a Denver District Judge ruled that the five-patient limit for caregivers violated state requirements, and overturned the rule. While in theory, that opened the door for caregivers to claim an unlimited number of patients and begin operating medical marijuana commercial operations (i.e., dispensaries), few did because of fear of federal prosecution. Attempts to reinstate the limit were unsuccessful.

Changes in Colorado in and after 2009. In July 2009 (preceding the Ogden Memo by three months), the Colorado Board of Health definitively rejected this limit on the size of patient loads for licensed medical marijuana caregivers (www.rmhidta.org). This effectively allowed caregivers to act as licensed dispensaries, or business entities, with unlimited patients⁴.

The Ogden Memo and the rejection by the Colorado Board of Health on limited patient loads for caregivers permitted rapid changes in Colorado (www.rmhidta.org), information that is well documented due to Colorado's centralized record-keeping. Between January and December of 2009, the number of applications to use medical marijuana increased from about 500 per month to over 10,000 per month. Through the end of 2008, Colorado had no known dispensaries. By spring, 2009, Colorado had over 250 dispensaries, and by mid-2010, over 900 dispensaries. In

addition, in 2010, the Colorado legislature passed HB-1284, which confirmed the legalized status of registered medical marijuana centers (dispensaries).

Subsequent to these legal changes to the distribution system for medical marijuana, data suggest that attitudes, availability, and use increased⁵, as did cannabis-involved fatal motor vehicle crashes⁶.

Other early-MML states and the Ogden Memo. A literature search of Pubmed, Scopus, Google Scholar and Google using the words "marijuana" or "cannabis" and the state name did not indicate other early-passing states (California, Oregon, Maine, Nevada) with accurate, comprehensive documentation of analogous post-Ogden policy changes with accompanying increases in medical marijuana applications and dispensaries. The lack of such changes was recently descriptively reviewed in a publication that should be online shortly. The Public Health Division of the Oregon Health Authority reported that medical marijuana card applications increased steadily since 1999, with a possible increase in the yearly rate in 2008, but without data on accompanying changes in the prevalence of cannabis-related consequences, while Oregon did not permit legal medical marijuana dispensaries until 2015.

While many qualitative sources of information (e.g., news reports and observations by those living in California) have suggested that California experienced equivalent rapid growth and proliferation of medical marijuana dispensaries since the Ogden Memo⁹, California's lack of centralized recordkeeping of permits and dispensaries has limited research there to cross-sectional studies of dispensaries within cities or counties^{10,11}. This has limited knowledge about policy changes and their immediate consequences for marijuana use and distribution in California as a whole, but suggests that changes in California be viewed in light of the qualitative information.

Therefore, given the documentation of the policy changes and their impact in Colorado, analyzing Colorado as a separate state during the later period is warranted.

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eAppendix 2. Interviewer statement preceding AUDADIS questions about drug use in NLAES, NESARC and NESARC-III

Now I'd like to ask you about your experiences with medicines and other kinds of drugs that you may have used ON YOUR OWN - that is, either WITHOUT a doctor's prescription (PAUSE); in GREATER amounts, MORE OFTEN, or LONGER than prescribed (PAUSE); or for a reason other than a doctor said you should use them. People use these medicines and drugs ON THEIR OWN to feel more alert, to relax or quiet their nerves, to feel better, to enjoy themselves, to get high or just to see how they work.

eTable 1. Demographic characteristics of NLAES, NESARC, and NESARC-III samples, with participants in the 11 states not common to the 3 surveys excluded

		NLAES	NESARC	NESARC-III	
		1991-1992	2001-2002	2012-2013	
		N=41,764	N=41,184	N=35,549	
		<u>.</u>	revalence (SE)		p-value ^a
Characteristic			` ,		•
Male		48.03 (0.31)	47.88 (0.32)	48.11 (0.29)	0.87
Age					
	18-29	25.02 (0.41)	21.78 (0.38)	21.62 (0.35)	< 0.001
	30-39	22.95 (0.26)	20.08 (0.25)	16.70 (0.28)	
	40-49	18.52 (0.25)	20.90 (0.27)	18.11 (0.30)	
	50+	33.50 (0.37)	37.24 (0.46)	43.58 (0.46)	
Race/Ethnicity					
	White	76.53 (0.46)	70.70 (1.64)	66.19 (0.82)	<0.001
	Black	11.23 (0.37)	11.33 (0.65)	12.02 (0.67)	
	Hispanic	7.75 (0.26)	11.77 (1.29)	14.91 (0.68)	
	Other	4.48 (0.17)	6.20 (0.48)	6.88 (0.25)	
Less Than HS b		19.39 (0.31)	15.66 (0.51)	13.10 (0.43)	<0.001
Poverty		· · · ·			
·	<100% FPL ^c	15.56 (0.35)	13.70 (0.40)	19.36 (0.46)	
	100-200% FPL	23.34 (0.29)	19.83 (0.40)	21.56 (0.37)	< 0.001
	>200% FPL	61.10 (0.41)	66.47 (0.68)	59.08 (0.71)	
Married		59.74 (0.39)	58.17 (0.52)	57.81 (0.52)	0.008
Urban		72.46 (0.66)	81.40 (1.60)	78.66 (1.56)	<0.001

SE = Standard Error

^a p-value corresponds to chi-squared test of differences in distribution of demographic characteristics across surveys.

^b HS = High school

^c FPL = Federal Poverty Level

eTable 2. Years that medical marijuana laws (MML) were enacted for the 50 US states up to 2012 and how participants in these states were coded in Models 1-3

State and Year passed MML up to 2012	Code for Model 1 ^a 1991-1992 to 2012-2013	Code for Model 2a ^b 1991-1992 to 2001-2002	Code for Model 2b ^b 1991-1992 to 2001-2002	Code for Model 3 ^c 2001-2002 to 2012-2013
California 1996	Ever-MML	Early-MML	Separate	Separate
(Alaska) ^d 1998				
Oregon 1998	Ever-MML	Early-MML	Early-MML	Early-MML
Washington 1998	Ever-MML	Early-MML	Early-MML	Early-MML
Maine 1999	Ever-MML	Early-MML	Early-MML	Early-MML
Colorado 2000	Ever-MML	Early-MML	Early-MML	Early-MML
(Hawaii) ^d 2000				
Nevada 2000	Ever-MML	Early-MML	Early-MML	Early-MML
Maryland 2003	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Montana 2004	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Vermont 2004	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
(Rhode Island) d 2006				
New Mexico 2007	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Michigan 2008	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Arizona 2010	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
New Jersey 2010	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
(Delaware) d 2011				
Connecticut 2012	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Massachusetts 2012	Ever-MML	Non-Early-MML	Non-Early-MML	Late-MML
Alabama	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Arkansas	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Florida	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Georgia	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(Idaho) ^d				
Illinois	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Indiana	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Iowa	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Kansas	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Kentucky	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Louisiana	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Minnesota	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Mississippi	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Missouri	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(Nebraska) ^d				
(New Hampshire) d	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
New York	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
North Carolina	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(North Dakota) d	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Ohio Never	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Oklahoma	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Pennsylvania	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML

South Carolina	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(South Dakota) d				
Tennessee	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Texas	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Utah	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Virginia	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(West Virginia) ^a				
Wisconsin	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(Wyoming) d				
Missouri	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(Nebraska) d				-
(New Hampshire) d				
New York	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
North Carolina	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(North Dakota) d				
Ohio Never	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Oklahoma	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Pennsylvania	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
South Carolina	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(South Dakota) d				•
Tennessee	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Texas	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Utah	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
Virginia	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(West Virginia) d				
Wisconsin	Never-MML	Non-Early-MML	Non-Early-MML	Never-MML
(Wyoming) ^d				

^a Ever MML state passed a law between 1996 and 2012; Non-MML states did not pass a law by 2012

^b Early-MML states passed a law between 1996 and 2001; Non-early-MML states did not pass a law between 1996 and 2001, and thus include states that passed a law between 2002 and 2012

 $^{^{\}rm c}$ Late-MML states passed a law between 2002 and 2012

^d Participants in these states were not included in all three surveys (NLAES, NESARC, NESARC-III) and therefore were excluded in primary analyses

eTable 3. Predicted US prevalence of past-year illicit cannabis use and past-year *DSM-IV* cannabis use disorder: overall and by medical marijuana law (MML) status^a

	1991-1992 ^b (NLAES) n=41,764	2001-2002 ^c (NESARC) n=41,184	2012-2013 ^d (NESARC-III) n=35,549	NLAES vs. NESARC	NESARC vs. NESARC-III
		% (SE)		% difference (SE)	% difference (SE)
Cannabis use ^e					
Overall	4.89 (0.35)	3.58 (0.14)	7.55 (0.39)	- 1.31 (0.34)	+ 3.97 (0.44)
				p<0.001	p<0.001
Never-MML states (no MML, 1996-2012) ^f	4.54 (0.39)	3.16 (0.16)	6.70 (0.39)		
Ever-MML states (MML passed 1996-2012) ^g	5.55 (0.36)	4.38 (0.27)	9.15 (0.54)		
Early-MML states (MML passed 1996-2001) h	6.05 (0.41)	5.24 (0.48)	9.77 (0.70)		
Late-MML states (MML passed 2002-2012) i	5.08 (0.54)	3.69 (0.31)	8.97 (0.70)		
<u>,</u>					
Cannabis use disorder ^J					
Overall	1.39 (0.17)	1.43 (0.08)	2.57 (0.23)	+ 0.04 (0.18)	+ 1.14 (0.26)
				p=0.82	p<0.001
Never-MML states (no MML, 1996-2012) ^f	1.35 (0.19)	1.31 (0.09)	2.30 (0.22)		
Ever-MML states (MML passed 1996-2012) ^g	1.48 (0.19)	1.67 (0.16)	3.10 (0.34)		
Early-MML states (MML passed 1996-2001) h	1.64 (0.22)	1.87 (0.29)	3.20 (0.42)		
Late-MML states (MML passed 2002-2012) i	1.31 (0.31)	1.52 (0.20)	3.20 (0.47)		

- ^a States included were the 39 with data in all three surveys. States omitted: Alaska, Delaware, Hawaii, Idaho, Nebraska, New Hampshire, North Dakota, Rhode Island, South Dakota, West Virginia and Wyoming.
- ^b National Longitudinal Alcohol Epidemiology Study (NLAES); Differences in predicted prevalence:
 - Cannabis <u>use</u>: Ever- vs. Never-MML states, p=0.003; Early- vs. Never-MML states, p=0.002; Late- vs. Never-MML states, p=0.08; Late- vs. Early-MML states, p=0.17.
 - Cannabis <u>use disorder</u>: Ever- vs. Never-MML states, p=0.45; Early- vs. Never-MML states, p=0.19; Late- vs. Never-MML states, p=0.39; Late- vs. Early- MML states, p=0.39.
- ^c National Epidemiologic Survey On Alcohol & Related Conditions (NESARC); Differences in predicted prevalence:
 - Cannabis <u>use</u>: Ever- vs. Never-MML states, p<0.001; Early- vs. Never-MML states, p<0.001; Late- vs. Never-MML states, p=0.12; Late vs. Early-MML states, p=0.01.
 - Cannabis <u>use disorder</u>: Ever- vs. Never-MML states, p=0.06; Early- vs. Never-MML states, p=0.07; Late- vs. Never-MML states, p=0.32; Late- vs. Early-MML states, p=0.33.
- ^d National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III); Differences in predicted prevalence:
 - Cannabis <u>use</u>: Ever- vs. Never-MML states, p<0.001; Early- vs. Never-MML states, p<0.001; Late- vs. Never-MML states, p<0.001; Late- vs. Early-MML states, p=0.29.
 - Cannabis <u>use disorder</u>: Ever- vs. Never-MML states, p=0.006; Early- vs. Never-MML states, p=0.02; Late- vs. Never-MML states, p=0.03; Late- vs. Early-MML states, p=0.99.
- ^e Prevalences back-transformed from marginal log-odds estimated from logistic regression interaction models (MML x survey) that included individual and state covariates. Overall prevalences estimated from a model with a 3-level MML variable (never vs. early vs. late). "Never-" and "Ever-MML" prevalences estimated from a model with a dichotomous MML variable (never vs. ever). "Early-MML" prevalences in 1991-1992 estimated from a model with a dichotomous MML variable (early- vs. non-early). "Late-MML" prevalences at times and "Early-MML" prevalences in 2001-2002 and 2012-2013 estimated from a model with a 3-level MML variable (never vs. early vs. late).
- ^f Never-MML states (1996-2012): AL, AR, FL, GA, IL, IN, IA, KS, KY, LA, MN, MS, MO, NY, NC, OH, OK, PA, SC, TN, TX, UT, VA, WI
- ⁹ Ever-MML states (1996-2012): AZ, CA, CO, CT, ME, NV, OR, MD, MA, MI, MT, NJ, NM, VT, WA
- ^h Early-MML states (1996-2001): CA, CO, ME, NV, OR, WA
- ⁱ Late-MML states (2002-2012): AZ, CT, MD, MA, MI, MT, NJ, NM, VT
- ¹ Prevalences estimated in models analogous to those for cannabis use.

eTable 4. Testing the parallel paths assumption for Colorado and the late-MML states: differences in predicted prevalences of past-year cannabis use and *DSM-IV* cannabis use disorder during the earlier period, 1991-1992 to 2001-2002^a

	Never-MML	All Early-MML states but California and	All Late-MML		
	states [24 states] ^b	Colorado [4 states] ^c	states [9 states] ^d	California [1 state]	Colorado [1 state]
Outcome	No MML before 2012	Passed MML 1991-2001	Passed MML 2002-2012	Passed MML 1996	Passed MML 2000
Cannabis use	before 2012		revalence ^e (SE)	1990	2000
1991-2001	4.39 (0.42)	4.58 (0.63)	5.00 (0.54)	7.15 (0.71)	4.03 (0.84)
2001-2002	3.12 (0.15)	5.93 (0.81)	3.64 (0.31)	5.39 (0.59)	4.10 (0.62)
				1	
Change in prevalence	- 1.26 (0.40) ^f	+ 1.35 (1.02)	-1.36 (0.63) ^g	- 1.75 (0.72) h	+ 0.07 (1.02)
				T-	
Difference in difference (DiD) (vs. Never-MML states)	(reference)	+ 2.61 (0.99)	- 0.10 (0.53)	-0.49 (0.75)	+ 1.33 (1.03)
DiD p-value		0.01	0.85	0.52	0.20
Cannabis use disorder		Р	revalence ^e (SE)		
1991-2001	1.27 (0.20)	1.07 (0.31)	1.28 (0.31)	1.95 (0.31)	1.24 (0.39)
2001-2002	1.29 (0.09)	2.61 (0.48)	1.51 (0.20)	1.57 (0.28)	1.34 (0.47)
Change in	+ 0.03	+ 1.54 (0.56) ⁱ	+ 0.23 (0.37)	- 0.38 (0.36)	+ 0.10 (0.61)
prevalence	(0.19)	, ,	, ,	, ,	,
Difference in		. 1 51 (0 55)	. 0.24 (0.22)	-0.41 (0.37)	. 0.07 (0.60)
difference (DiD)	(reference)	+ 1.51 (0.55)	+ 0.21 (0.32)	-0.41 (0.37)	+ 0.07 (0.60)
(vs. Never-MML states)	(1616161106)				
DiD p-value		0.007	0.52	0.28	0.91

SE = Standard Error; participants in states not common to all 3 surveys are excluded

^a States included were the 39 with data in all three surveys. States omitted: Alaska, Delaware, Hawaii, Idaho, Nebraska, New Hampshire, North Dakota, Rhode Island, South Dakota, West Virginia and Wyoming. The predicted prevalences from the earlier period were estimated by a model with a 5-level MML variable (Early-MML states (ex. Colorado and California) vs. Late-MML states vs. California vs. Colorado vs. Never-MML states)

^b Never-MML states (1996-2012): Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Minnesota, Mississippi, Missouri, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin

^c Early-MML states (except California and Colorado) (1996-2001): Maine, Nevada, Oregon, Washington

d Late-MML states (2002-2012): Arizona, Connecticut, Maryland, Massachusetts, Michigan, Montana, New Jersey, New Mexico, Vermont

e Prevalences back-transformed from marginal log-odds estimated from logistic regression interaction models (MML X survey) that included individual (sex; age; education; race/ethnicity; marital status; urbanicity; poverty) and state covariates (% male; white; <30 years old; ≥25 years without a high school diploma).

f p=0.002, change in Never-MML states between 1991 and 2001

g p=0.03, change in all Late-MML states between 1991 and 2001

^h p=0.02, change in California only between 1991 and 2001

i p=0.008, change in all Early-MML states but California and Colorado between 1991 and 2001

eTable 5. Difference-in-difference (DiD) results of sensitivity analyses for models 1-3

Model	Model 1	Model 2a	el 2a Model 2b			Model 3		
Time period	1991-2012		1991-2001		2001-2012			
Exposure	Ever MML	All Early-	All Early-	CA	Early-	Late-	CA	CO
Group	States	MML	MML States	[1 state]	MML	MML	[1 state]	[1 state]
	[15 states]	States	but California		States	States		
		[6 states]	[5 states]		[4 states]	[9 states]		
Reference	Non-MML	Non	-Early MML stat	es		Non-MMI	L states	
Group	states		[33 states]			[24 sta	ates]	
	[24 states]							
			Difference in dif		iD) ^a			
Inclusion of t	hose who use	d cannabis	only 1-11 times	, lifetime				
Cannabis	1.91 (0.51) ^b	0.73	2.52 (0.88) ^c	0.08	-0.46	1.91	2.45	3.89
use		(0.62)		(0.80)	(0.92)	(0.65) ^d	(0.98)e	(1.69) ^f
CUD 1	0.72 (0.31) ^g	0.26	1.18 (0.48) ^h	-0.35	-0.94	0.70	0.96	1.82
		(0.35)		(0.40)	(0.62)	(0.43)	(0.49)	(0.78) ¹
Inclusion of i	ndividuals in a	all 50 states						
Cannabis	1.47 (0.48) ^j	0.44	2.53 (0.84) ^k	-0.49	-0.80	1.58	1.85	3.79
use		(0.61)		(0.80)	(0.87)	(0.63) ¹	(0.88)m	(1.60) ⁿ
CUD 1	0.68 (0.30)°	0.22	1.18 (0.46) ^p	-0.43	-0.86	0.65	0.93	1.69
		(0.34)		(0.41)	(0.58)	(0.41)	(0.48)	(0.77) ^q
Cannabis use	e disorder, inc	luding withou	drawal as a diag	Inostic crit	terion			
CUD 1	0.69 (0.30) ^r	0.29	1.24 (0.51 ^s	-0.35	-1.07	0.62	0.92	1.75
		(0.37)		(0.41)	(0.62)	(0.42)	(0.48)	$(0.79)^{t}$
Excluding inc	dividuals age	18-19						
Cannabis	1.24 (0.47) ^u	0.43	2.17 (0.80) ^v	-0.30	-0.59	1.27	1.70 ^x	3.72
use		(0.61)	` ,		(0.82)	(0.63) ^w	(0.84)	(1.26) ^y
CUD 1	0.60 (0.29) ^z	0.04	0.78 (0.45)	-0.44	-0.60	0.56	0.99	1.78
		(0.33)		(0.40)	(0.53)	(0.37)	(0.50)	$(0.63)^{aa}$

Note: We present exact p-values only for estimates with significance p<0.05.

¹ CUD = DSM-IV Cannabis Use Disorder

^a Changes in predicted marginal prevalence of marijuana outcome within MML-exposed group of states over time period are compared to changes within reference group of states.

 $^{^{}b}$ p<0.001 c p= 0.006 d p=0.004 e p=0.02 f p=0.02 g p=0.02 h p=0.02 i p=0.02 j p=0.003 k p=0.004 l p=0.01 m p=0.04

 $^{^{}n}p=0.02$ $^{o}p=0.03$ $^{p}p=0.01$ $^{q}p=0.03$ $^{r}p=0.03$ $^{s}p=0.02$ $^{t}p=0.03$ $^{u}p=0.01$ $^{v}p=0.009$ $^{w}p=0.05$ $^{x}p=0.05$ $^{y}p=0.004$

^z p=0.04 ^{aa} p=0.006

eTable 6. Difference in prevalences of past-year cannabis use, 1984 to 1990: data from Alcohol Research Group National Surveys 7 and 8 of adults 18 years and older^a, grouped as California, other early-MML^b states, and nonearly-MML states

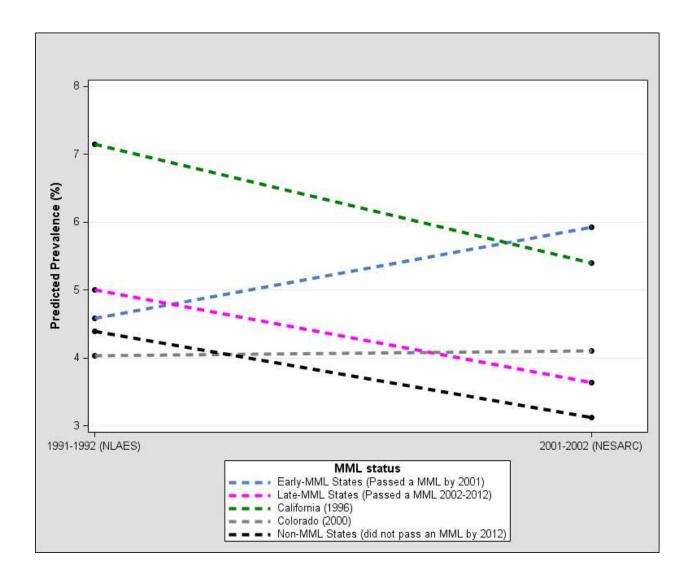
Outcome	Non-Early MML states	California	Other Early MML states b
	No MML	Passed MML	Passed MML
	before 2012	1996	1998-2000
Past-year cannabis use		Prevalence ^c	
1984 (National Alcohol Survey 7 d)	9.44	12.72	12.29
1990 (National Alcohol Survey 8 e)	8.84	10.04	11.77
Difference in prevalence	-0.60	-2.68	-0.52
Difference in Difference (DiD)		-2.08	+0.08
(vs. Non-Early MML states)	(reference)		3.00

^a Polcin DL, Korcha R, Greenfield TK, Bond J, Kerr W. Twenty-one-year trends and correlates of pressure to change drinking. Alcohol Clin Exp Res. 2012 Apr;36(4):705-15, funded by P50AA005595
^b Other Early-MML states: Maine, Nevada, Oregon, Colorado, Washington

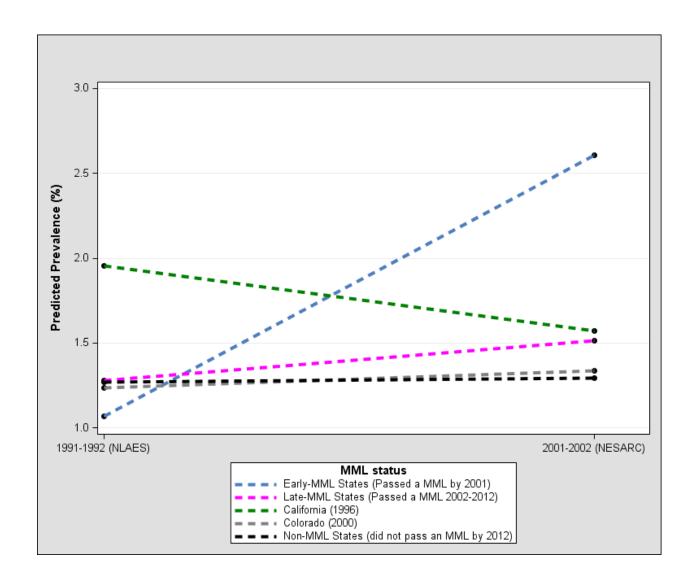
^c Weighted prevalences

^d N = 5,221, response rate: 77% ^e N <u>= 2,058, response rate: 70%</u>

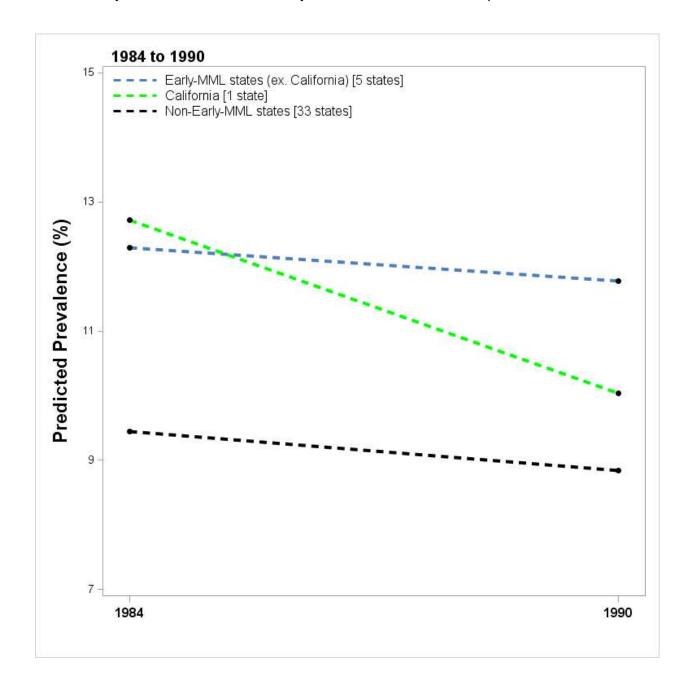
eFigure 1. Medical marijuana laws (MML) and cannabis use, past 12 months, during the earlier period (1991-1992 to 2001-2002): test of "parallel paths" assumption for late states and Colorado



eFigure 2. Medical marijuana laws (MML) and *DSM-IV* cannabis use disorder, past 12 months, during the earlier period (1991-1992 to 2001-2002): test of "parallel paths" assumption for late states and Colorado



eFigure 3. Past-year cannabis use, 1984 and 1990, from the National Alcohol Surveys of adults 18 years and older conducted by the Alcohol Research Group.



Early-MML states other than California include Colorado, Maine, Nevada, Oregon, and Washington (laws passed 1998-2000). Trend lines included for visual comparison; they do not imply that the trend was linearly changing over time