Table 1—Characteristics and Outcomes of 12 Studies Included in the Integrative Review of Individual-Level Cannabis Substitutions

Authors Year	Frame	Sample Description	Size	Prevalent (%) substitution of cannabis for… Alcohol	Opioids	Illicit Drugs	Rx Drugs
Reiman, 2007	MCP, offline San Francisco, CA, 2006	Ages 18 to 78, *M* = 40 26% women, 59% NHW	130	50.0		46.9	73.8
Reiman, 2009	MCP, offline San Francisco, CA	Ages 18 to 81, *M* = 39 32% women, 66% NHW	350	40.0		26.0	65.8
Lucas et al., 2013	MCP, offline British Columbia	Ages 17 to 71, *M* = 44 33% women, 72% NHW	404	41.0		36.1	67.8
Boehnke et al., 2016	MCP, online Ann Arbor, MI, 2013-15	Ages 18 to 75 35% women	244		64.0		
Lucas et al., 2016	MCP, online & offline Canada, 2011-12	Ages 17-78, *M* = 40 32% women, 90% NHW	473	51.7		32.6	80.3
Corroon et al., 2017	MCP (60%) & RCU (40%) online USA,[a] 2013-16	18 to 65 or older 44% women, 86% NHW	2,774		35.8		13.6
Lucas & Walsh, 2017	MCP, online Canada, 2015	Ages 20 to 77, *M* = 40 27% women, 94% NHW	271	25.0	32.0	3.0	63.0
Piper et al.,	MCP, online	Ages 18 to 84, *M* = 48					

2017	ME, RI & VT, 2015-16	53% women, 95% NHW	1,513	42.0[b]	76.7 [b]	60.3 [b]
Reiman et al.,	MCP, online	Ages 20 to 60 or older				
2017	California	45% women, 64% NHW	2,897		61.0[c]	76.0
	HIV positive adults					
Mannes et al.,	MCP & RCU offline	Ages 18 to 55 or older, *M* = 47				
2018	Florida, 2014-17	31% women, 22% NHW	234	58.0[d]		
Boehnke et al.,	MCP, online	Ages 18 to 65 or older				
2019	USA[e]	59% women	1,321		53.0[f]	22.0[f]
	Pain patients prescribed opioids					
Ishida et al.,	RCU, online	Ages 18 to 65 or older				
2019	USA, 2017	47% women, 74% NHW	486		41.0[g]	

Summary statistics:				
Number of studies	7	7	5	9
Aggregated sample	3,375	9,506	1,628	10,133
Prevalence estimate (%)	43.1	53.2	28.3	48.7
95% confidence interval	41.4, 44.8	52.2, 54.2	26.1, 30.5	47.7, 49.7

Notes. MCP, medical cannabis patients; NHW, non-Hispanic white; RCU, recreational cannabis users; Rx, prescription.

[a] USA (83%), Europe (10%), Canada (4%) and other countries (3%).

[b] Respectively, reduced use "a lot:" 25.0%, 40.9% and 31.0%.

[c] 74% strongly agreed that cannabis allowed then to decrease their opiate dosage.

[d] MCP 58% less likely to drink hazardously. Hazardous alcohol use was defined as consuming 5 or more drinks on one occasion at least monthly or > 14 drinks per week for men, or 4 drinks on one occasion at least monthly or > 7 drinks per week for women over the past 12 months

[e] USA (97%) and Canada (3%).

[f] Substitutions resulted in the complete cessation of use: opiates (72%) and benzodiazepines (68%).

[g] Eight percent increased their opioid use.

Table 2—Characteristics and Outcomes of 11 Studies Included in the State-Level Meta-Analysis of Opioid Outcomes

Key comparison Reference	Population Places & cohort years Analytic samples	Research design Sampling frame Covariate adjustments	Outcome Descriptive statistics Risk Ratio (95% CI)
Medical marijuana legal or not			
Bachhuber et al., 2014	General population USA, 1999-2010 Census of deaths	Time series National Vial Statistics System 4 covariates	**Opioid overdose age-adjusted mortality** RR = 0.75 (0.63, 0.91)[a]
Powell et al., 2018	Medicare D & Medicaid enrollees USA, 1999-2013 Census of deaths	Difference-in-differences National Vial Statistics System 10 covariates	RR = 0.77 (0.61, 1.01)[*]
Shover et al. 2019	Systematic extension of Bachhuber et al. (2014) to 2017	Time series National Vital Statistics System 8 covariates	RR = 1.23 (1.02, 1.48)
Kim et al., 2016	Fatally injured drivers Aged 15 or older USA, 18 states, 1999-2013 68,394	Multi-level Difference-in-differences Fatality Analysis Reporting System 6 covariates	**Driver died within 1 hour of crash** **Opioid positive blood test** 4.5% vs 6.0% OR = 0.79 (0.61, 1.03)[*] *Drivers aged 21 to 40* OR = 0.50 (0.37, 0.67)

Shi, 2017	Hospitalized population USA, 27 states, 1997-2014 Census of hospitalized people	Time series State Inpatient Databases 6 covariates	**Opioid dependence or abuse related hospitalizations** OR = 0.77 (0.59, 0.93)[b] **Opioid pain reliever overdoses after discharge** OR = 0.87 (0.75, 0.98) OR_{pooled} = 0.84 (0.75, 0.95)
Bradford et al., 2018	Medicare Part D enrollees USA, 2010-2015 Census of prescriptions	Historical cohort CMS Prescription Drug Event Standard Analytic Files 12 covariates	**Opioid prescriptions** RR = 0.91 (0.82, 1.01)[*c]
Wen et al., 2018	Medicaid enrollees USA, 2011-2016 Census of prescriptions	Difference-in-differences CMS State Drug Utilization Data 13 covariates	RR = 0.94 (0.88, 1.00)[d]
Shah et al., 2019	Privately insured aged 18 or older USA, 2006-2014 4,840,562	Multi-level historical cohort LifeLink Claims Database Area Health Resource File 18 covariates	**Prescription opioid use during past year** OR = 0.95 (0.94, 0.96) **Chronic prescription opioid use** RR = 0.93 (0.91, 0.95) **High-risk prescription opioid use** OR = 0.96 (0.94, 0.98) OR_{pooled} = 0.95 (0.94. 0.96)[e]
Özlük, 2019	Young adults aged 18 to 39 USA, 1996-2014 186,144	Panel study Medical Expenditure Panel Study 16 covariates	**Per capita prescription opioid spending** OR = 0.46 (0.26, 0.83)

Recreational marijuana legal or not

	General population	Time series	**Opioid-related deaths**
Livingston et al., 2017	Colorado , vs Nevada & Utah, 2000-2015 Census of deaths	CDC WONDER 3 covariates	6.5% decrease in opioid deaths in RML states OR = 0.51 (0.26, 0.97)
	Medicaid enrollees	Difference-in-differences	
Shi et al., 2019	USA, 14 states & DC, 2010-2017 Census of deaths	Medicaid State Drug Use Data 6 covariates	**Opioid prescriptions** RR = 0.68 (0.51, 0.85)[f]

Notes. CDC, Center for Disease Control and Prevention; CI, confidence interval; CMS, Center for Medicare and Medicaid Services; OR, odds ratio; MML, medical marijuana legalization; PDMP, prescription drug monitoring program, RML, recreational marijuana legal; RR, rate ratio; WONDER, Wide-Ranging Online Data for Epidemiological Research.

[*] $p < .10$.

[a] Heart disease mortality and septicemia deaths were null.

[b] Medical marijuana dispensaries had no independent effect.

[c] Medical marijuana dispensaries had an independent effect: RR = 0.86 (0.77, 0.96).

[d] Systematically replicated among states where recreation use is legal: RR = 0.94 (0.88, 0.99).

[e] No effect observed for prescription use of antihyperlipidemics or antihypertensives: OR_{pooled} = 1.00 (0.99, 1.01).

[f] Systematically replicated with two related outcomes: total opioid dosage and spending.