

Appendix 1 (as supplied by the authors): Supplemental material

Supplemental Table S1. Search Strategy

Database	Search strategy
MEDLINE	<ol style="list-style-type: none"> 1. exp Opiate substitution therapy/ 2. Methadone/ 3. Methadone.mp. 4. MMT.mp. 5. Cannabis/ 6. Marijuana Abuse/ 7. Marijuana Smoking/ 8. Medical Marijuana/ 9. Cannabis.mp. or marijuana*.mp. 10. THC.mp. or hash*.mp. or ganja.mp. or hemp.mp. or bhang*.mp. 11. 1 or 2 or 3 or 4 12. 5 or 6 or 7 or 8 or 9 or 10 13. 11 an 12 14. Limit 13 to humans
EMBASE	<ol style="list-style-type: none"> 1. exp opiate substitution treatment/ 2. exp methadone treatment/ 3. exp methadone/ 4. Methadone.mp. 5. MMT.mp. 6. exp cannabis/ 7. exp "cannabis use"/ 8. exp cannabis addiction/ 9. exp cannabis smoking/ 10. exp medical cannabis/ 11. Cannabis.mp. or marijuana*.mp. 12. THC.mp. or hash*.mp. or ganja.mp. or hemp.mp. or bhang*.mp. 13. 1 or 2 or 3 or 4 or 5 14. 6 or 7 or 8 or 9 or 10 or 11 or 12 15. 13 and 14 16. Limit 15 to humans
PsycINFO	<ol style="list-style-type: none"> 1. exp methadone maintenance/ 2. methadone.mp. 3. MMT.mp. 4. exp cannabis/ 5. exp marijuana usage/ 6. cannabis.mp. or marijuana*.mp. 7. THC.mp. or hash*.mp. or ganja.mp. or hemp.mp. or bhang*.mp. 8. 1 or 2 or 3

Database	Search strategy
	9. 4 or 5 or 6 or 7 10. 8 and 9 11. Limit 10 to humans
CINAHL	1. (MH "Methadone") 2. "Methadone" 3. "MMT" 4. (MH "Cannabis") 5. (MH "Medical Marijuana") 6. "marijuana" or "cannabis" 7. "THC" or "hash*" or "ganja" or "hemp*" or "bhang*" 8. 1 or 2 or 3 9. 4 or 5 or 6 10. 7 and 8 (limiters – human)

Supplemental Table S2. Individual Study Characteristics by Outcomes

A. Illicit Opioid Use

Study	Country	Study Design	Sample Size (% Female)	Cannabis Use Definition	Outcome	Statistical Analysis	Results
Best, 1999 (1)	UK	Cross sectional	200 (30%)	Method: MAP Definition: Categorical; daily users, occasional users (used cannabis but not on all 30 days in previous months), and non-users Timing: Baseline	Method: MAP Definition: Continuous ; Mean number of days of heroin use in the past 30 days from MAP Timing: Baseline	ANOVA; post-hoc Scheffe test	F=11.07, p<.0001, such that non-users had more occasions of heroin use than occasional and daily users
Epstein, 2003 (2)	USA	Secondary RCT analysis (3 separate analyses), 12 months	408 (40.44%)	Method: Diagnostic Interview and urinalysis Definition: Dichotomized cannabis use and cannabis abuse/dependence diagnosis Timing: Baseline and 12 months	Method: Urinalysis Definition: Relapse to heroin among patients who achieved abstinence (3 consecutive weeks of opioid abstinence) Timing: Time to lapse	Cox proportional-hazard regression	Cannabis use: First two trials: HR = 1.54 (0.93–2.56); $\chi^2=2.78$, p=0.095 Third trial: HR = 0.90 (0.48-1.65); $\chi^2=0.13$, p=0.72 Cannabis abuse/dependence: First two trials: HR = 1.16 (0.63-2.13); $\chi^2=0.22$, p=0.64 Third trial: HR = 2.09 (0.76-5.76); $\chi^2=1.66$, p=0.19
Levine, 2015 (3)	USA	Retrospective cohort, 1 year	290 (40.34%)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: Baseline within the First month of drug testing	Method: Urinalysis Definition: Continuous ; Proportion of UDS results negative	Logistic Regression	Not significant, but statistics not reported.

				upon entry into MMT	for opioids was calculated within the first year Timing: 12 months in treatment		
Lions, 2014 (4)	France	Secondary RCT analysis, 45 weeks	158 (15.19%)	Method: Opiate Treatment Index Definition: Dichotomous; Daily users vs. non-daily users Timing: Baseline and 12 months	Method: Opiate Treatment Index Definition: Dichotomous; Opiate users vs. non-opiate users (used opiates at least once in the past month) Timing: 12 months	Multiple logistic regression	Pre-treatment daily cannabis: OR=1.46 (0.61-3.77), ns In-treatment daily cannabis: OR=2.81 (1.22-6.48), p<.05
Nava, 2007 (5)	Italy	Prospective cohort, 12 months	121 (14%)	Method: Self report, Urinalysis Definition: Dichotomous; long term users (more than 6 months) and currently smoking at least 7 times per week vs. non-users never exposed to marijuana smoking. Timing: Baseline	Method: Urinalysis Definition: Continuous ; Percentage positive opioid screens (missing specimens considered positive) Timing: Urine samples were collected once a week	Hierarchical linear modelling	Cannabis users: z=-3.42, p<.001, such that there was a reduced percentage of positive opioid urines. Non-cannabis users: z=-3.18, p<.001, such that there was a reduced percentage of positive opioid urines.
Nirenberg, 1996 (6)	USA	Prospective cohort, 6 months	70 (1.42%)	Method: Urinalysis Definition: Dichotomized cannabis use;	Method: Urinalysis; Definition: Continuous ;	ANOVA	Dichotomized cannabis use: F(1,68)=0.90, p=.35, ns Four groups:

				and Categorical 4 groups: Group 1 - cannabis abstainers (0 positive screens); Group 2 - intermittent cannabis users (0%-33.3% positive screens); Group 3 - moderate cannabis users (33.3% to 66.6% positive screens); Group 4 - consistent cannabis users (66.6%-100% positive screens) Timing: 45 weeks	Percentage positive opioid UDS Timing: 45 weeks		F(3,66)=1.13, p=.34, ns
Proctor, 2016* (7)	USA	Retrospecti ve cohort, 12 months	2410 (40.41 %)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: Intake, 3, 6, 9, and 12 months	Method: Urinalysis Definition: Dichotomo us; users vs. nonusers Timing: 3, 6, 9, 12 months	Logistic Regression	3 months: Intake cannabis: OR=1.17 (0.83- 1.63) 6 months: Intake cannabis: OR=0.59 (0.32- 1.10) 9 months: Intake cannabis: OR=0.63 (0.24- 1.66) 12 months: Intake cannabis: OR=0.23 (0.05- 1.16)
Saxon, 1996 (8)	USA	Prospective cohort, 18 months	353 (38.20 %)	Method: Self report Definition: Categorical; seven-point scale ranging from 0 "never" to 6 "four or more times per day".	Method: Urinalysis Definition: Dichotomo us; Considered opioid users if reported use of any	Cox regression model	r=0.06; B=0.05, ns

				Timing: 6 months prior to baseline	opioid drug other than their prescribed medication, or if they reported having administered their prescribed medication by snorting or injection in the previous 6 months. Percentage of opioid positive urine screens over 18 months Timing: 18 months		
Scavone, 2013 (9)	USA	Retrospective cohort, 9 months	91 (36.56 %)	Method: Self-report, Urinalysis Definition: Dichotomized cannabis use Timing: Baseline (self-report) and In-treatment (initial 9 months of MMT enrolment)	Method: Urinalysis Definition: Continuous Timing: 9 months	ANCOVA	r(82)=.018, p=.873, such that there was no significant relationship between frequency of cannabis use in treatment and opiate use.
Somers, 2012 (10)	Ireland	Retrospective cohort, 15 months	123	Method: Urinalysis Definition: Dichotomous cannabis use Timing: Baseline and in-Treatment; intake, 3, 9 and 15 months	Method: Urinalysis Definition: Dichotomous; Subjects with less than 20 % of samples positive for heroin	Logistic regression	Baseline: OR: 0.88 (.67-1.15) 3 month: OR: 0.79 (.58, 1.1) 9 month: OR: 0.78 (.55, 1.2) 15 months: OR: 1.45 (.82, 2.5) Total: AOR: 0.32 (.06, 1.66)

					Timing: 3,9,15 months		
Wasserman, 1998 (11)	USA	Prospective cohort, 6 months	74 (40.54 %)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: Baseline cannabis (first week) and cannabis as a time-dependent variable included in analyses	Method: Self-report or urinalysis; Definition: Dichotomous; Participants dichotomized as having used heroin during the period from week 2 through the 6-month follow-up assessment or not. Timing: 6 month follow-up	Cox proportional hazards regression	$\chi^2=8.39$, $p<0.004$, such that baseline cannabis use significantly increased the risk of a lapse to heroin. $\chi^2=7.62$, $p<0.006$, such that cannabis as a time-dependent variable significantly increased the risk of a lapse to heroin. 6-month follow-up: $\chi^2=7.90$, $p<0.005$, such that such that baseline cannabis use significantly increased the risk of a lapse to heroin
Zielinski, 2017 (12)	Canada	Cross-sectional	777 (46.7%)	Method: MAP Definition: Dichotomized cannabis use in the past 30 days Timing: Baseline cannabis	Method: Urinalysis Definition: Dichotomous; participants with any positive screens of illicit opioids Timing: 3 month testing period	Multivariable logistic regression analysis	OR: 1.16, 95%CI: 0.77, 1.75, $p=0.49$

Notes: "Dichotomized cannabis use" means users vs. non-users or at least one positive urine screen vs. none unless otherwise specified. MAP: Maudsley Addiction Profile; HR: hazard ratio; ANOVA: analysis of variance; RCT:

randomized controlled trial; ns: not significant; UDS: urine drug screen; MMT: methadone maintenance treatment; ANCOVA: analysis of covariance; OR: odds ratio. *Proctor et al. (2016) had too many results to present in this table, so we included only intake cannabis values in relation to opioid use at all time points. See study for more results.

B. Treatment Retention

Study	Country	Study Design	Sample size (% female)	Cannabis Measurement	Outcome	Statistical Analysis	Results
Epstein, 2003 (2)	USA	Secondary RCT analysis, 12 months	408 (40.44%)	Method: Diagnostic Interview and urinalysis Definition: Categorical; Non-users, occasional users and frequent users Timing: Time to dropout	Definition: Retention in clinical trials up till follow up Timing: Did they complete the follow ups to 12 months	Survival analysis for treatment retention for all 3 trials	In all 3 trials, p-values ranged from p=.69 to p=.72 Further statistics not reported.
Joe, 1998 (13)	USA	Prospective cohort, 360 days	981 (39%)	Method: Self-report Definition: Dichotomous; At least weekly marijuana use or not Timing: Baseline	Definition: Whether clients stayed at least 360 days in outpatient methadone treatment. Timing: 360 days into treatment	Hierarchical linear regression model	b=0.13, SE=0.16, t=0.79, OR=1.14, ns
Levine, 2015 (3)	USA	Retrospective cohort, 1 year	290 (40.34%)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: Baseline within the First month of drug testing upon entry into MMT	Definition: Dichotomized into two groups: less than a year and more than a year Timing: 12 months after treatment	Logistic regression	Men: cannabis-negative: OR=5.00 (1.61-14.29), p=.01, such that less cannabis use predicted >1 year retention Women cannabis-negative: OR=9.09 (2.33-33.33),

							p<.001, such that less cannabis use predicted >1 year retention
Nava, 2007 (5)	Italy	Prospective cohort, 12 months	121 (13.22%)	Method: Self report, Urinalysis Definition: Dichotomous; long term users (more than 6 months) and currently smoking at least 7 times per week vs. non-users never exposed to marijuana smoking. Timing: Baseline	Definition: Percentage dropout from treatment measured Timing: 2 weeks, 3 months, and 12 months	Kaplan-Meier survival analysis	No significant association (values not reported).
Peles, 2006 (14)	Israel	Prospective cohort, 11 years	492 (27.24%)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: 13 months or month before dropout	Definition: Continuous; The number of days in clinic from first admission until the patient quit treatment or until the end of follow-up (11 years) Timing: 132 months	Fishers exact test	Cannabis use on admission: p=0.3, ns
Peles, 2008 (15)	USA and Israel	Prospective cohort, 12 months	794 (30.98%)	Method: Weekly urinalysis; Definition: Dichotomized cannabis use Timing: Baseline and	Definition: Continuous; Duration in clinic from first admission until the patient	Kaplan-Meier survival analysis with log rank for cumulative retention.	Tel Aviv: Positive THC on admission: log rank=0.2, p=.8 Positive THC after 1 year:

				in-treatment For follow-up, recorded cannabis use month after completion or one month before if early dropout	stopped treatment or until the end of the follow- up Timing: Analyzed 6 months retention and 1 year retention in treatment		log rank=1.8, p=.2 Las Vegas: Positive THC on admission: log rank=4.2, p=.04 Positive THC after 1 year: log rank=0.8, p=.4 Included in multivariate analysis but not significant (values not provided)
Saxon, 1996 (8)	USA	Prospective cohort, 18 months	353 (38.20%)	Method: Self report Definition: Categorical; seven-point scale ranging from 0 "never" to 6 "four or more times per day". Timing: 6 months prior to baseline	Definition: subjects remaining in treatment continuously after enrolment and those not remaining Timing: 18 months after enrolment	Cox regression analysis	r=0.06; B=1.08 (0.97- 1.2), ns
Scavone, 2013 (9)	USA	Retrospectiv e cohort, 9 months	91 (39.56%)	Method: Self- report, Urinalysis Definition: Dichotomized cannabis use Timing: Baseline (self- report) and In-treatment (urinalysis from initial 9 months of MMT enrolment)	Definition: Mean number of patients dropped out Timing: 9 months into treatment	Pearson correlation, chi square	Unfavourabl e discharge status: r(80)=.069, p=.567, ns Premature discharge status: $\chi^2 = 3.009$, p=.222, ns

Schiff, 2007 (16)	Israel	Retrospective cohort, 13 months	2,683 (14.07%)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: Baseline and in-treatment; 13 months into treatment	Definition: Dichotomized patients as 100% retention vs. lower Timing: 13 months into treatment	Logistic regression	OR=1.43 (1.15, 1.78), p<.001, such that there was a significant relationship between cannabis use and increased retention.
Weizman, 2004 (17)	Israel	Prospective cohort, 12 months	283 (NR)	Method: Urinalysis Definition: Dichotomous; Cannabis abuse vs. not; First assessed the percentage of tests positive for a given month (first month and 12th month); second considered that is a patient tested positive for cannabis for any consecutive 3 months during the first year of MMT, was considered a potential cannabis abuser. SCID used to confirm or disconfirm cannabis abuse status.	Definition: Treatment tenure was calculated based upon the overall number of days patients remained in treatment; Timing: 12 months into treatment	Cox regression survival analysis	Non-CAs vs CAs, B=-0.17; SE=0.13; Wald=1.57, p=0.21; r=0.00; Exp(B)=0.84 Analysis with heroin, cocaine, and BZD abuse as covariates did not significantly change the results.

				Timing: Baseline and 12 months			
White, 2014 (18)	USA	Retrospective cohort, 15-17 months	604 (39.40%)	Method: Urinalysis Definition: Dichotomized cannabis use Timing: First 3 months	Definition: Dichotomized retention as left MMT or remained in MMT Timing: 15-17 months	Chi square Fishers Exact Test	Baseline cannabis use: OR: 3.3 (1.6-6.8), p<.01, such that cannabis use was significantly associated with increased attrition rates. Positive ONLY for cannabis at baseline: 5% OR: 0.5 (0.7-9.8), p=1.00, ns

Notes: "Dichotomized cannabis use" means users vs. non-users or at least one positive urine screen vs. none unless otherwise specified. RCT: randomized controlled trial; SE: standard error; OR: odds ratio; ns: not significant; MMT: methadone maintenance treatment; THC: tetrahydrocannabinol; NR: not reported; SCID: Structured Clinical Interview for DSM disorders; CA: cannabis abuser.

C. Polydrug Use

Study	Country	Study Design	Sample size (% female)	Cannabis Measurement	Outcome	Statistical Analysis	Results
Best, 1999 (1)	UK	Cross sectional	200 (30%)	Method: MAP Definition: Classified participants as daily users, occasional users, and non-users; categorical Timing: Baseline	Method: MAP Definition: Measured alcohol and crack cocaine use; continuous Timing: 30 days after MAP	ANOVA; post-hoc Scheffe test	Alcohol: F=5.24, p<.01 Scheffe test: significant difference such that non-users of cannabis consumed more alcohol than occasional and daily users Crack cocaine: F=4.67, p<.05 Scheffe test: significant difference such that non-users of cannabis consumed more alcohol than occasional and daily users
Bleich, 1999 (19)	Israel	Prospective cohort, 12 months	148 (29.82%)	Method: Urinalysis Definition: A positive urine test for cannabis. A drug abuser for any substance of abuse was defined as having a positive urine test for that substance during the 12th month of treatment. Timing: 12 months into treatment	Method: Urinalysis Definition: Benzodiazepines; A positive urine test for benzodiazepines non-abusers vs. abusers Timing: 12 months into treatment	Chi square	Benzodiazepine: $\chi^2 = 7.77$, p=0.005, such that benzodiazepine abusers were more likely to currently abuse cannabis than non-abusers of benzodiazepine

Epstein, 2003 (2)	USA	Secondary RCT analysis, 12 months	408 (40.44%)	Method: Diagnostic Interview and urinalysis Definition: Categorical; Non-users, occasional users and frequent users Timing: Baseline and 12 months	Method: Urinalysis Definition: Continuous; Cocaine use from urinalysis Timing: Entire study duration	Multiple linear regression	Cocaine abstinence: Parameter estimate +/- SEM: 11.49 +/- 5.68, t=2.02, p=0.0438
Nirenberg, 1996 (6)	USA	Prospective cohort, 45 weeks	70 (1.43%)	Method: Urinalysis Definition: Dichotomous and Categorical; 4 groups: Group 1 - cannabis abstiners (0 positive screens); Group 2 - intermittent cannabis users (0%-33.3% positive screens); Group 3 - moderate cannabis users (33.3% to 66.6% positive screens); Group 4 - consistent cannabis users (66.6%-100% positive screens) Timing: 45 weeks	Method: Urinalysis Definition: Continuous; Cocaine and benzodiazepine use Timing: 45 weeks	ANOVA	Cocaine: F(3,66)=1.17, p=.33 such that there was no significant difference between the 4 cannabis groups and their use of cocaine. Benzodiazepines: F(3,66)=2.10, p=.11, such that there was no significant difference between the 4 cannabis groups and their use of benzodiazepine.

Peirce, 2009 (20)	USA	Secondary RCT analysis, 12 weeks	386 (44%)	Method: Urinalysis, breath sample Definition: Cannabis use defined as positive urine/breath sample given at study intake Timing: at intake Cannabis use disorder defined as the interview administered checklist of DSM-IV substance use disorder symptoms	Method: Urinalysis, breath sample Definition: Stimulant use measured as number of stimulant-negative urine results provided Timing: Throughout the 12 week study intervention	Mixed-model regression	Cannabis use at intake: B(SE) = -3.27 (1.33), p=0.014, such that participants showed more stimulant use (less negative urine tests). Cannabis use disorder: B(SE) = 3.89(1.49), p=0.010, such that participants showed less stimulant use (more negative urine tests).
Saxon, 1996 (8)	USA	Prospective cohort, 18 months	353 (38.20%)	Method: Self-reported seven-point scale ranging from 0 "never" to 6 "four or more times per day". Definition: Categorical; Timing: 6 months prior to baseline	Method: Urinalysis Definition: Continuous; percentage positive urine screens for any drug use then cocaine use, specifically Timing: 18 months in treatment	Cox regression model	Any drug use: Model 1: r=-0.05; B=0.06 Not included in second model. Cocaine use: Model 1: r=-0.08; B=-0.09 Model 2: B=-0.11, p<0.05, such that pre-treatment frequency of cannabis use predicted less cocaine use
Saxon, 1993 (21)	USA	Cross sectional	98 (0%)	Method: Urinalysis; Definition: Dichotomized cannabis use Timing: During the study period, specimens	Method: Urinalysis Definition: Continuous; screened for opiates, cocaine, and benzodiazepines. Timing: Weekly tests during entire treatment	Mann-Whitney U-test	THC+ vs. THC-: Percentage of urinalysis positive for other drugs of abuse was not significantly different between THC+ (median=6.5, mean

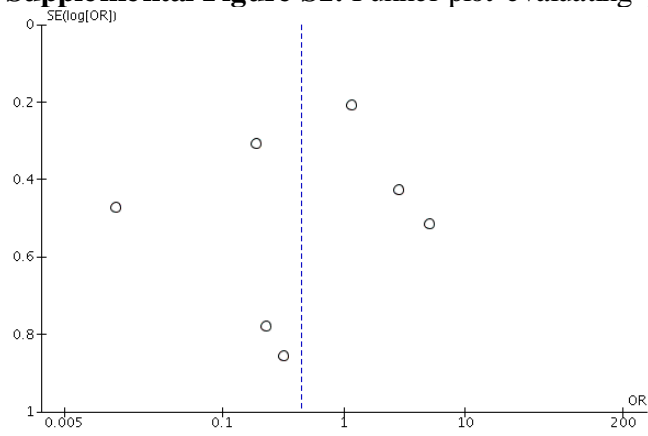
				were periodically tested for THC. The number of tests for THC per subject varied from 1 to 17 (median=4). THC testing was generally spread over the duration of the study so that subjects were tested periodically over a span of months.			rank=50.74) and THC-patients (median=6.3, mean rank=48.0; z=-0.48). Consistently THC+: Participants consistently THC+ had a smaller percentage of urinalysis positive for other drugs of abuse (median=3.25, mean rank=21.7) than those who were intermittently THC+ (median=8.2, mean rank=31.5; z=-2.27, p<0.05).
Scavone, 2013 (9)	USA	Retrospective cohort, 9 months	91 (39.56%)	Method: Self-report, Urinalysis Definition: Dichotomized cannabis use Timing: Baseline (self-report) and In-treatment (urinalysis from initial 9 months of MMT enrolment)	Method: Urinalysis Definition: Any illicit benzodiazepine use Timing: In-treatment (Initial 9 months of MMT enrolment)	Correlation	Benzodiazepine: r(91)=.374, p<.01, such that there was a positive correlation between rates of cannabis use and illicit benzodiazepine use during the initial nine months in treatment
Strain, 1991 (22)	USA	Cross sectional	66 (45%)	Method: Alcohol Research Center Intake Interview	Method: Alcohol Research Center Intake Interview Definition: Cocaine, sedative, and	Z-Test	Cocaine diagnosis: RR=0.69, ns Sedative diagnosis: RR=1.67, ns

				<p>Definition: Dichotomous; those with versus those without a history of a cannabis use diagnosis</p> <p>Timing: Interviews and assessments done in a series of two to three sessions</p>	<p>alcohol abuse/dependence diagnoses</p> <p>Timing: Interviews and assessments done in a series of two to three sessions</p>		<p>Alcohol diagnosis: RR=0.83, ns</p>
Weizman, 2004 (17)	Israel	Prospective cohort, 12 months	283 (NR)	<p>Method: Urinalysis</p> <p>Definition: Dichotomous; Cannabis abuse vs. not; First assessed the percentage of tests positive for a given month (first month and 12th month); second considered that is a patient tested positive for cannabis for any consecutive 3 months during the first year of MMT, was considered a potential cannabis abuser. SCID used to</p>	<p>Method: Urinalysis;</p> <p>Definition: Measured heroin, benzodiazepines, amphetamine, and cocaine abuse (they do not specify if they used SCID or something else to define abuse)</p> <p>Timing: 12 months</p>	ANOVA	<p>Benzodiazepines: F=18.48, p=0.000, such that CAs abused more benzodiazepines</p> <p>Amphetamines: F=9.29, p=0.003, such that CAs abused more amphetamines</p> <p>Cocaine: F=4.06, p=0.045, such that CAs abused more cocaine</p> <p>All abuse and dependency diagnoses: F=7.5, p=0.007, such that CAs had more other drug abuse and dependency diagnoses</p>

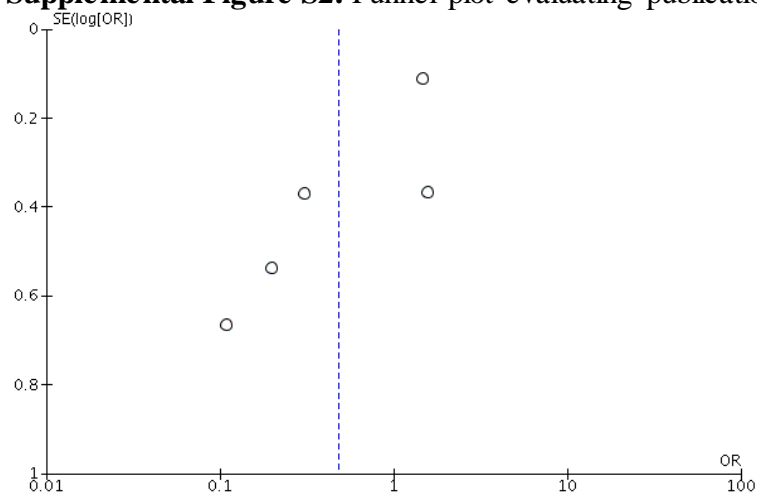
				confirm or disconfirm cannabis abuse status. Timing: Baseline and 12 months			
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Notes: "Dichotomized cannabis use" means users vs. non-users or at least one positive urine screen vs. none unless otherwise specified. MAP: Maudsley Addiction Profile; ANOVA: analysis of variance; RCT: randomized controlled trial; SEM: standard error of the mean; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; SE: standard error; THC: tetrahydrocannabinol; MMT: methadone maintenance treatment; RR: risk ratio; CA: cannabis abuser; SCID: Structured Clinical Interview for DSM disorders.

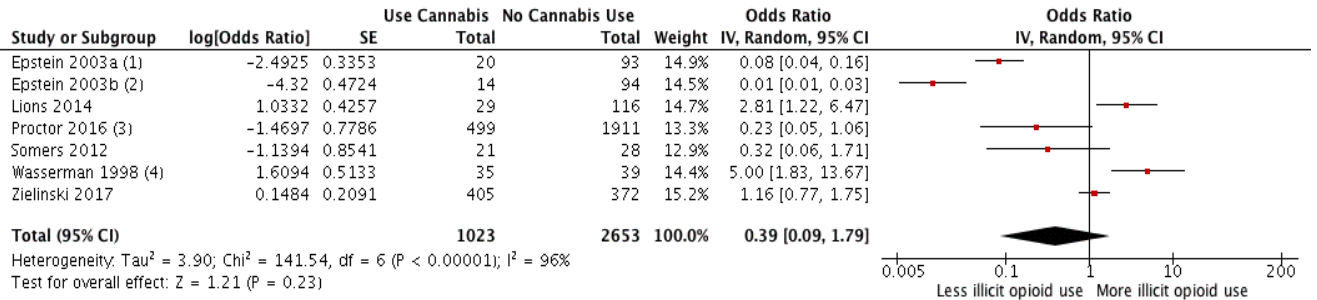
Supplemental Figure S1. Funnel plot evaluating publication bias for illicit opioid use



Supplemental Figure S2. Funnel plot evaluating publication bias for treatment retention.



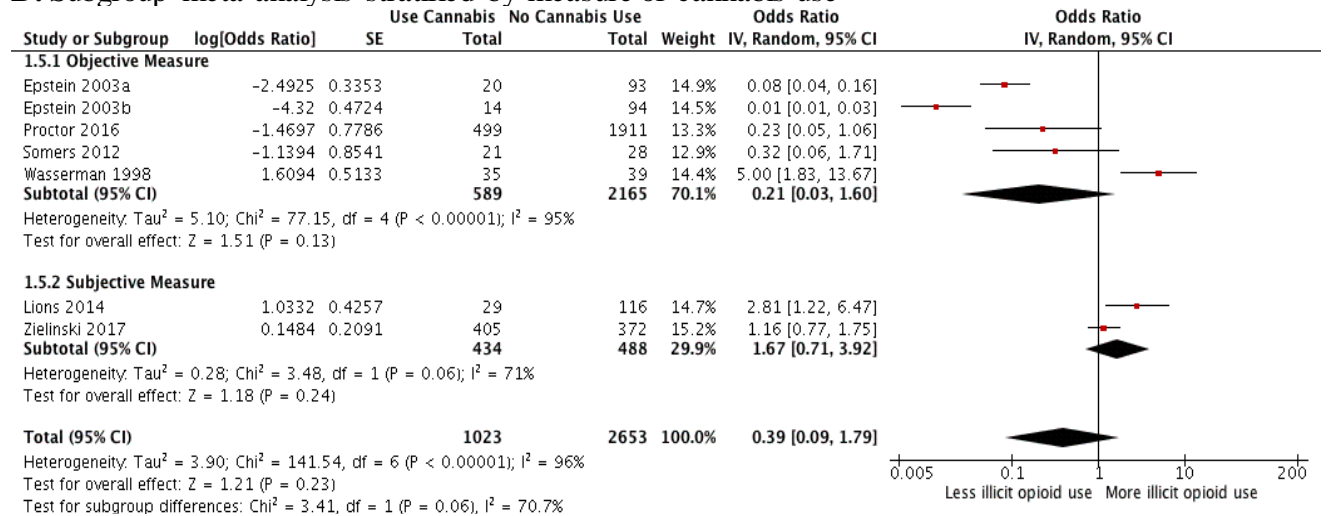
Supplemental Figure S3. Illicit opioid use during treatment by cannabis use meta-analysis
A. Meta-analysis forest plot for illicit opioid use



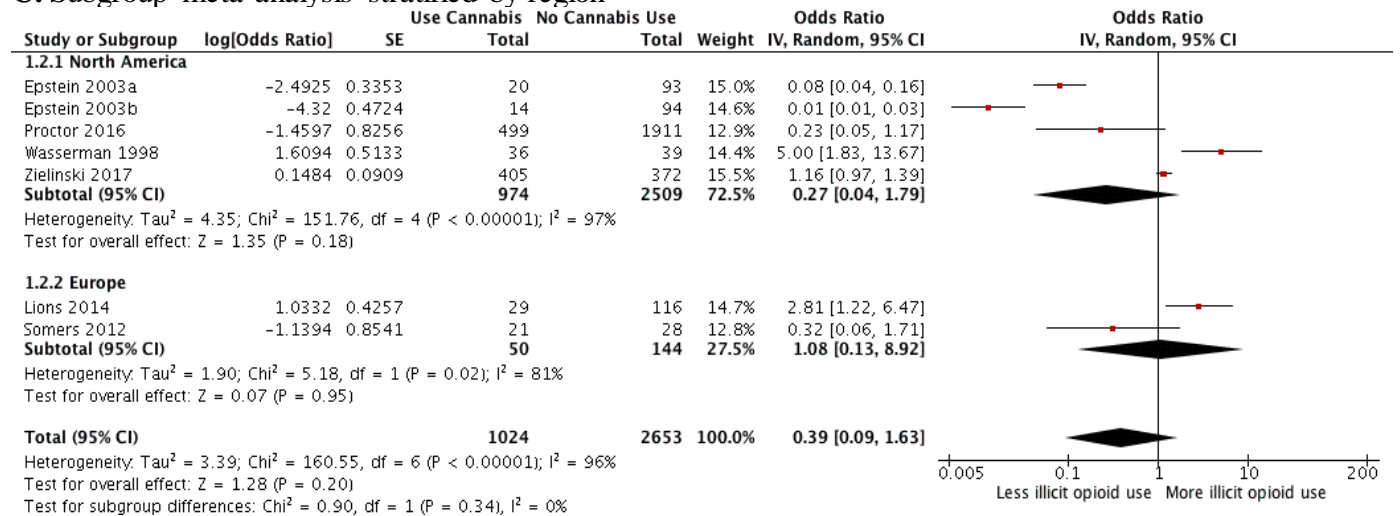
Footnotes

- (1) Combined results of two trials which were 8 weeks long
- (2) Results from one trial that was 12 weeks long
- (3) Prevalence reflects 12-month cannabis use, as baseline prevalence was not reported. Odds ratio reflects baseline cannabis use and 12-month opioid use.
- (4) Odds ratio as estimated in Epstein 2003

B. Subgroup meta-analysis stratified by measure of cannabis use

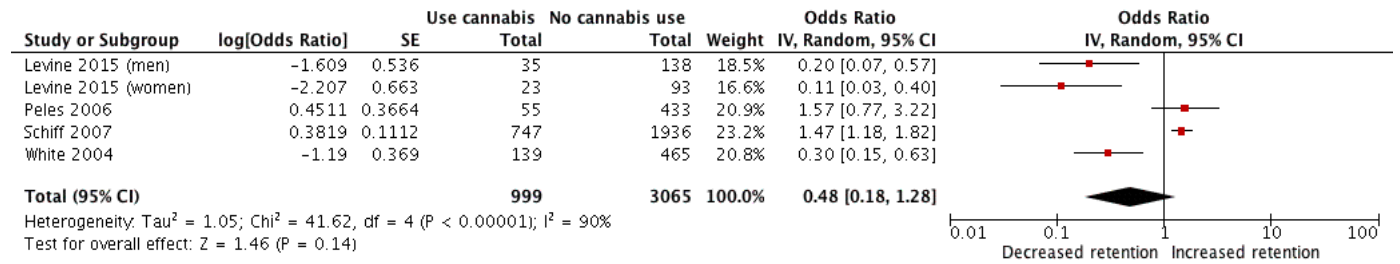


C. Subgroup meta-analysis stratified by region

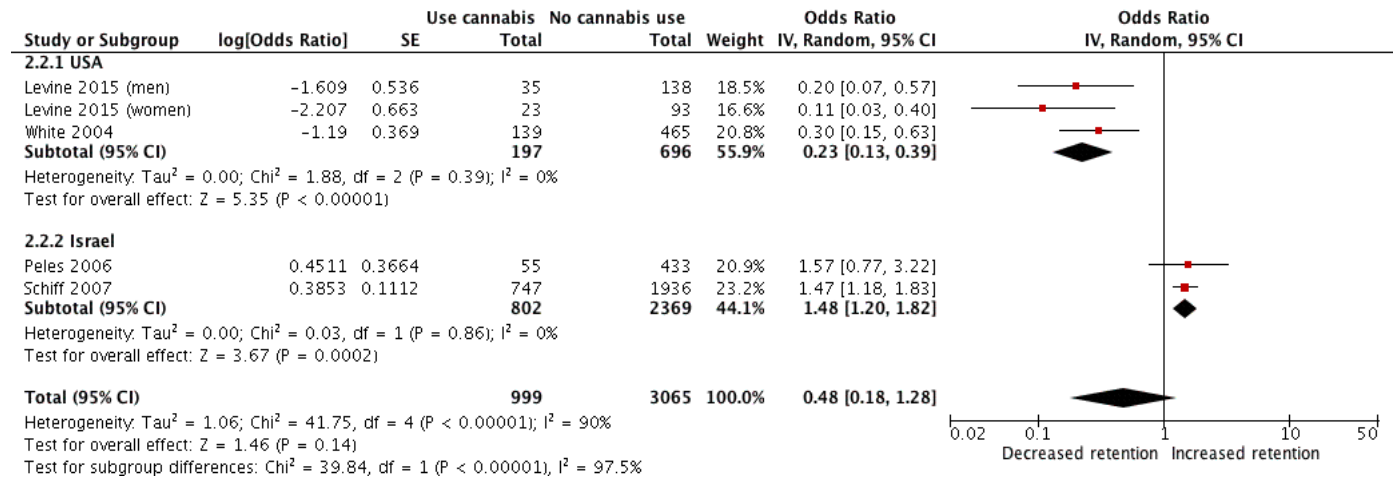


Supplemental Figure S4. Treatment retention meta-analysis

A. Meta-analysis forest plot for treatment retention



B. Subgroup meta-analysis stratified by country



Supplemental Statistical Methods:

Many of the odds ratios necessary for the meta-analyses were not reported in the publications we've referenced. Here we document how the statistics were calculated.

Formula for Standard Error:

$$SE(\log(OR)) = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

a = cannabis positive AND opioid positive

b = cannabis negative AND opioid negative

c = cannabis positive AND opioid negative

d = cannabis negative AND opioid positive

Calculation for Epstein 2003a:

- Opiate study + Cocaine study #1
- State that rate of relapse is 80% in non-users of cannabis
- N cannabis users = 126 (frequent + non-frequent users in cocaine study 1 and opiate study)
- N non-cannabis users = 89
- 113 absent from illicit opioids

OR = 0.189, SE = 0.307

2x2 Table

	+ opioids	- opioids	Total
+ cannabis	31	95	126
- cannabis	71	18	89
Total	102	113	215

Calculation for Epstein 2003b:

- Cocaine study #2
- Rate of relapse is 90% in non-users
- N cannabis users = 94
- N non-cannabis users = 99
- 94 absent from illicit opioids in total

OR = 0.013376, SE = 0.4724

OR = a*d/b*c

100/7476 = 0.013376

	+ opioids	- opioids	Total
+ Cannabis	10	84	94
- Cannabis	89	10	99
Total	99	94	193

Calculation for Wasserman 1998:

- **Information and relative risk calculation collected from Epstein et al., 2003**
- 35 people tested positive for cannabis
- Sample size is 74
- Opioid positives detected in 30 patients
- N non-cannabis users = 39
- 44 absent from illicit opioids
- Relative risk is (21/35)/(9/36) = 2.6

OR = 5.00, SE = 0.5133

References

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