Supplementary Table 1. Search Strategy

PubMed: November 14, 2019

- 1. "cannabis use disorder"/4158
- 2. "pharmacotherapy"/3135179
- 3. 1 and 2/1028
- 4. Limit 3 to (Clinical Trial, Human population, and English Language)/100

MEDLINE: November 14, 2019

- 1. Exp cannabis dependence.mp. or exp Marijuana Abuse/6268
- 2. Exp pharmacotherapy.mp. or exp Drug Therapy/1346508
- 3. 1 and 2/298
- 4. Limit 3 to (English Language and Humans)/253

EMBASE: November 14, 2019

- 1. Exp cannabis addiction/9646
- 2. Exp pharmacotherapy.mp. or exp drug therapy/2796749
- 3. 1 and 2/1009
- 4. Limit 3 to (English Language and Humans)/929

PsycINFO: November 14, 2019

- 1. Exp Marijuana Usage or marijuana abuse.mp or cannabis dependence.mp or exp "Cannabis Use Disorder"/ or "cannabis use disorder"/6569
- 2. Exp pharmacotherapy.mp. or exp drug therapy/146907
- 3. 1 and 2/466
- 4. Limit 3 to (English Language and Humans)/432

Cochrane Central Register of Controlled Trials: November 14, 2019

- 1. Exp cannabis dependence.mp. or Marijuana Abuse/653
- 2. Exp pharmacotherapy.mp. or exp drug therapy/7331
- 3. 1 and 2/30

Supplementary Table 2. Secondary outcomes

Study	Abstinence	Adverse events	Withdrawal Severity	Cravings Severity	CUD Severity
Allsop 2014	Not reported	13/27 vs. 12/24	1.88 (1.64) vs. 2.22 (1.62)	1.87 (2.28) vs. 1.81 (2.26)	4.11 (5.29) vs. 4.04 (5.21)
Carpenter 2009	8/36 vs. 4/30	15/36 vs. 8/30	3.1 (1.9) vs. 1.9 (1.9)	Not reported	2.5 (1.4) vs. 2.3 (1.6)
Carpenter 2009b	4/40 vs. 4/30	18/40 vs. 8/30	4.0 (2.1) vs. 1.9 (1.9)	Not reported	2.7 (1.5) vs. 2.3 (1.6)
Cornelius 1999	Not reported	0/11 vs. 0/11	Not reported	Not reported	40.2 (8.5) vs. 47.5 (8.5)
Cornelius 2010	7/34 vs. 8/36	0/34 vs. 0/36	Not reported	Not reported	3.88 (2.51) vs. 3.61 (1.92
D'Souza 2019	Not reported	20/46 vs. 11/24	7.65 (1.32) vs. 9.04 (2.08)	Not reported	Not reported
Gray 2012	11/58 vs. 6/58	24/58 vs. 27/58	Not reported	Not reported	Not reported
Gray 2017	33/153 vs. 36/149	41/153 vs. 41/149	Not reported	Not reported	Not reported
Hill 2017	1/10 vs. 1/8	2/10 vs. 4/8	Not reported	51.7 (14) vs. 52.3 (10.4)	Not reported
Johnston 2014	6/16 vs. 6/22	12/16 vs. 14/22	1.24 (1.66) vs. 1.25 (1.97)	Not reported	3.07 (4.04) vs. 3.85 (3.91)
Levin 2004	6/13 vs. 5/12	3/13 vs. 1/12	19.22 (10.15) vs. 12.83 (10.22)	27.56 (36.71) vs. 16.83 (28.94)	Not reported
Levin 2011	14/79 vs. 12/77	53/79 vs. 45/77	4 (4.7) vs. 5 (5.4)	Not reported	Not reported
Levin 2013	6/51 vs. 19/52	51/51 vs. 29/52	Not reported	Not reported	Not reported
Levin 2016	17/61 vs. 19/61	47/61 vs. 46/61	4.8 (0.61) vs. 5.5 (0.77)	42.4 (16.9) vs. 40.1 (15.4)	Not reported
Lintzeris 2019	18/61 vs. 11/67	15/61 vs. 17/67	30.7 (28.9) vs. 43.6 (37.3)	27.2 (18.9) 31.2 (15.2)	Not reported
Mason 2012	Not reported	15/25 vs. 20/25	1.5 (1.0) vs. 0.4 (1.0)	0.2 (0.1) vs. 0.75 (0.3)	1.4 (1.6) vs. 1.6 (0.7)
McRae-Clark 2009	5/23 vs. 2/27	22/23 vs. 21/27	7.73 (8.99) vs. 7.00 (7.73)	19.95 (16.29) vs. 26.9 (15.75)	Not reported
McRae-Clark 2010	8/19 vs. 6/19	19/19 vs. 16/19	Not reported	25.51 (13.28) vs. 25.55 (15.97)	Not reported
McRae-Clark 2015	8/88 vs. 4/87	73/88 vs. 66/87	Not reported	46.4 (1.79) vs. 45.8 (1.48)	Not reported
McRae-Clark 2016	2/41 vs. 2/35	25/41 vs. 28/35	Not reported	49.9 (2.55) vs. 46.7 (0.11)	Not reported
Miranda 2017	Not reported	14/40 vs. 1/26	Not reported	Not reported	Not reported
Penetar 2012	Not reported	0/10 vs. 0/12	3.0 (0.51) vs. 4.1 (0.97)	1.2 (0.31) vs. 1.5 (0.26)	Not reported
Sherman 2017	0/8 vs. 0/8	1/8 vs. 2/8	Not reported	Not reported	Not reported
Trigo 2018	5/20 vs. 7/20	16/20 vs. 16/20	4.5 (0.6) vs. 4 (1)	7.0 (2.0) vs. 9.0 (2.0)	Not reported
Weinstein 2014	7/26 vs. 3/26	2/26 vs. 1/26	Not reported	Not reported	Not reported

Contrast	Direct				
to Placebo	Comparisons	Random Effects Model	RR	95%-CI	P-Score
Nabilone	1.00		0.40	[0.10; 1.66]	0.89
Vilazodone	1.00		0.76	[0.57; 1.02]	0.83
Gabapentin	1.00		0.75	[0.52; 1.09]	0.83
Oxytocin	1.00		0.50	[0.06; 4.47]	0.76
N-acetylcysteine	2.00	+	0.94	[0.71; 1.23]	0.68
FAAH-inhibitor	1.00	+	0.95	[0.55; 1.64]	0.63
Nabiximols	3.00	+	0.99	[0.77; 1.26]	0.62
Dronabinol/Lofexidine	1.00	÷	1.02	[0.84; 1.25]	0.58
Dronabinol	1.00	+	1.15	[0.90; 1.46]	0.44
Buspirone	2.00	(2)	1.14	[1.00; 1.29]	0.44
Lithium	1.00	+	1.18	[0.77; 1.80]	0.44
Atomoxetine	1.00	<u>→</u>	1.18	[0.98; 1.43]	0.40
Escitalopram	1.00		2.00	[0.19; 20.72]	0.34
Nefazodone	1.00	+	1.56	[0.77; 3.17]	0.29
Bupropion SR	1.00	+	1.69	[0.85; 3.35]	0.24
Divalproex Sodium	1.00		2.77	[0.33; 23.14]	0.24
Venlafaxine XR	1.00	*	1.78	[1.40; 2.26]	0.18
Topiramate	1.00		9.10	[1.27; 65.11]	0.04
		0.1 0.5 1 2 10			

Favors drug Favors placebo Rate ratio for adverse events

Contrast to Placebo	Direct Comparisons	Random Effects Model	RR	95%-CI	P-Score
Nabiximols N-acetylcysteine Buspirone Bupropion SR Nefazodone Dronabinol Gabapentin Vilazodone	2.00 2.00 2.00 1.00 1.00 1.00 1.00	*	0.33 0.39 0.63 0.75 0.83 0.97 1.00	[0.04; 3.09] [0.07; 2.28] [0.15; 2.60] [0.05; 11.51] [0.05; 12.77] [0.06; 15.31] [0.07; 15.12] [0.16; 18.04]	0.80 0.78 0.69 0.63 0.60 0.57 0.57
Atomoxetine Divalproex Sodium Venlafaxine XR Dronabinol/Lofexidine Topiramate	1.00 1.00 1.00 1.00 1.00 0.01	0.1 1 10	- 3.00 2.77 - 5.10 5.00 - 9.10	[0.13; 69.20] [0.33; 23.14] [0.25; 103.61] [0.60; 41.55] [1.27; 65.11]	0.36 0.34 0.26 0.23 0.14

Favors drug Favors placebo Rate ratio for losses due to adverse events

Contrast to Placebo	Direct Comparisons	Ra	ndom	Effect	ts Mod	el	SMD	95%-CI	P-Score
Dronabinol/Lofexidine	1100		-	+				2.37; 0.37]	0.84
FAAH-inhibitor	1.00		-					2.26; 0.56]	0.79
Nabiximols	3.00		-				-0.39 [-1	1.21; 0.43]	0.66
Dronabinol	1.00			-			-0.20 [-1	1.55; 1.16]	0.56
Lithium	1.00			*			-0.01 [-1	1.47; 1.46]	0.48
Bupropion SR	2.00		_	- 0			0.02 [-1	1.04; 1.09]	0.46
Nefazodone	1.00			-			0.08 [-1	1.25; 1.40]	0.44
Buspirone	1.00			-			0.09 [-1	1.34; 1.51]	0.44
Divalproex Sodium	1.00		_	_			0.61 [-0	0.94; 2.15]	0.26
Gabapentin	1.00			+	-	\neg	- 1.08 [-0).36; 2.53]	0.12
		-2	-1	0	1	2			

Favors drug Favors placebo Standardized mean difference for cannabis withdrawal

Contrast to Placebo	Direct Comparisons	Random Effects Model	SMD	95%-CI P-Score
Gabapentin	1.00 -		-2.42	[-3.53; -1.32] 0.99
Bupropion SR	1.00		-1.02	[-2.24; 0.20] 0.82
Nabiximols	3.00	-	-0.36	[-0.92; 0.20] 0.66
Nabilone	1.00	+	-0.05	[-1.28; 1.19] 0.48
Atomoxetine	1.00	-+-	-0.00	[-1.04; 1.03] 0.46
Buspirone	2.00		0.02	[-0.64; 0.67] 0.44
Dronabinol/Lofexidine	1.00		0.14	[-0.75; 1.03] 0.38
Divalproex Sodium	1.00		0.31	[-0.82; 1.45] 0.32
Vilazodone	1.00		1.69	[0.71; 2.66] 0.01
		-3 -2 -1 0 1 2 3		

Favors drug Favors placebo Standardized mean difference for cannabis cravings

Contrast	Direct	Bandom Effects Model	CMD	05% CL D Soors
to Placebo	Comparisons	Random Effects Model	SMD	95%-CI P-Score
Fluoxetine	2.00		-0.28	[-1.19; 0.64] 0.66
Lithium	1.00 -	*	-0.19	[-1.47; 1.09] 0.59
Gabapentin	1.00	-	-0.16	[-1.40; 1.08] 0.57
Nabiximols	1.00		0.01	[-1.22; 1.25] 0.47
Nefazodone	1.00		0.13	[-1.08; 1.34] 0.41
Bupropion SR	1.00		- 0.26	[-0.94; 1.47] 0.33
		-1 -0.5 0 0.5 1		

Favors drug Favors placebo Standardized mean difference for CUD severity

Contrast	Direct	_						
to Placebo	Comparisons	Ran	dom Effects	3 Mode	ı	RR	95%-CI	P-Score
Venlafaxine XR	1.00					0.32	[0.11; 0.90]	0.93
Bupropion SR	1.00	_	*	_		0.75	[0.18; 3.16]	0.66
Dronabinol/Lofexidine	1.00					0.89	[0.39; 2.04]	0.62
Fluoxetine	1.00			_		0.93	[0.31; 2.75]	0.59
Vilazodone	1.00		*			0.85	[0.12; 6.33]	0.59
Nabilone	1.00 -		•		_	0.80	[0.05; 11.69]	0.59
Divalproex Sodium	1.00		-	_		1.11	[0.38; 3.26]	0.50
N-acetylcysteine	2.00		-			1.11	[0.60; 2.06]	0.50
Dronabinol	1.00		-	_		1.14	[0.45; 2.89]	0.49
Nabiximols	2.00		-	_		1.26	[0.62; 2.56]	0.43
Atomoxetine	1.00			_		1.33	[0.47; 3.79]	0.41
Lithium	1.00					1.38	[0.45; 4.19]	0.40
Nefazodone	1.00					1.67	[0.47; 5.86]	0.32
Escitalopram	1.00		\rightarrow		_	2.33	[0.59; 9.29]	0.21
Buspirone	2.00		- 	-	\neg	2.30	[0.82; 6.45]	0.18
		0.1	0.5 1 2	!	10			

Favors placebo Favors drug Rate ratio for abstinence

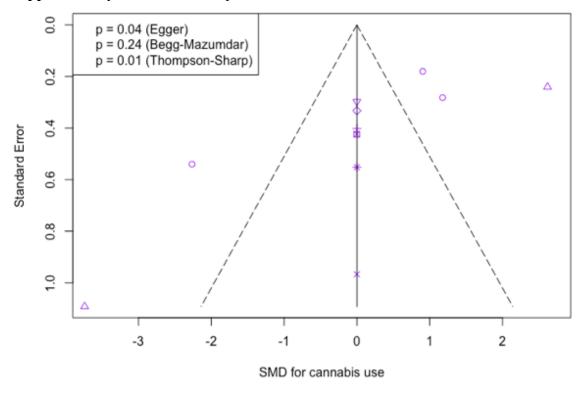
Supplementary Table 3. Cochrane risk of bias tool results for individual studies. Colours indicate the risk of bias per study domain: green = low risk of bias; yellow = unclear risk of

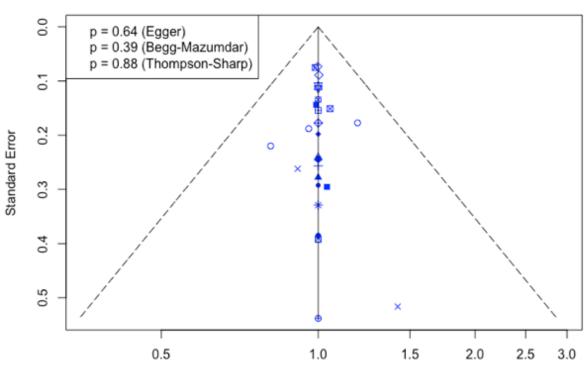
bias; and red = high risk of bias.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall Risk of Bias
Allsop 2014	•		•	•	•		•	
Carpenter 2009	?	•	•	•	•	•	•	•
Cornellus 1999	•	•	•	•	•	•	•	•
Cornellus 2010	•	•	•	•	•	•	•	•
D'Souza 2019	•	•	•	•	•	•	•	•
Gray 2012	•	•	•	•	•	•	•	•
Gray 2017	•	•	•	•	•	•	•	•
HIII 2017	•	•	•	•	•	•	•	
Johnston 2014	?	?	•	•	•	•	?	?
Levin 2004	?	?	•	•	•	•	•	?
Levin 2011	•	•	•	•	•	•	•	•
Levin 2013	•	•	•	•	•	•	•	•
Levin 2016	•	•	•	•	•	•	•	•
Lintzeris 2019	•	•	•	•	•	•	•	•
Mason 2012	•	•	•	•	?	•	•	•
McRae-Clark 2009	•	•	•	•	•	•	•	•
McRae-Clark 2010	•	•	•	•	•	•	•	•
McRae-Clark 2015	?	?	•	•	•	•	•	?
McRae-Clark 2016	•	?	?	?	•	•	•	?
Miranda 2017	•	•	•	•	•	•	•	•
Penetar 2012	?	?	•	•	•	?	•	?
Sherman 2017	?	?	•	•	•	•	•	
Trigo 2018	•	•	•	•	•	•	•	•
Weinstein 2014	?	?	•	•	•	•	•	?

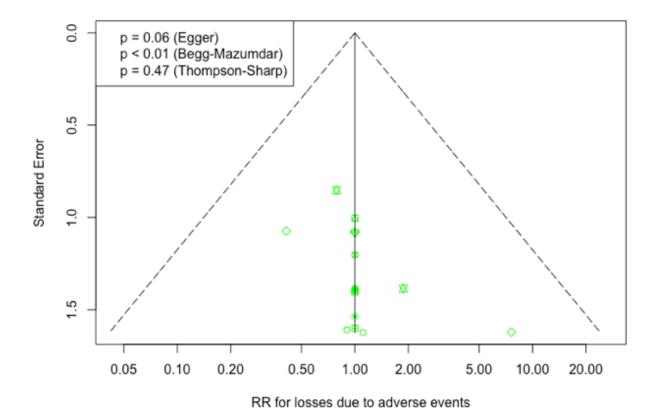
Study	Randomization	Allocation	Participant blinding	Assessment blinding	Attrition bias	Selective reporting	Other bias	The overall risk of bias
Allsop 2014	Low risk	High risk	Low risk	Low risk	Low risk	High risk	Low risk	High risk
Carpenter 2009	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Cornelius 1999	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk
Cornelius 2010	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
D'Souza 2019	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Gray 2012	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Gray 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Hill 2017	Low risk	High risk	High risk	High risk	High risk	Low risk	Low risk	High risk
Johnston 2014	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk
Levin 2004	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk
Levin 2011	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Levin 2013	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Levin 2016	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Lintzeris 2019	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Mason 2012	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
McRae-Clark 2009	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
McRae-Clark 2010	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
McRae-Clark 2015	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
McRae-Clark 2016	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Unclear risk
Miranda 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Penetar 2012	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear risk
Sherman 2017	Unclear risk	Unclear risk	High risk	High risk	Low risk	High risk	Low risk	High risk
Trigo 2018	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Weinstein 2014	Unclear risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk

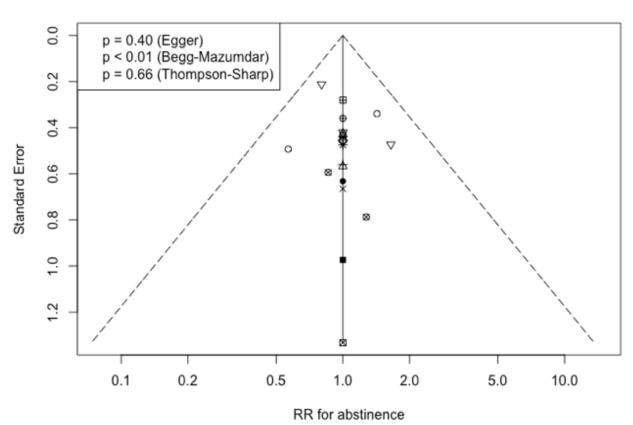
Supplementary Table 4. Funnel plots

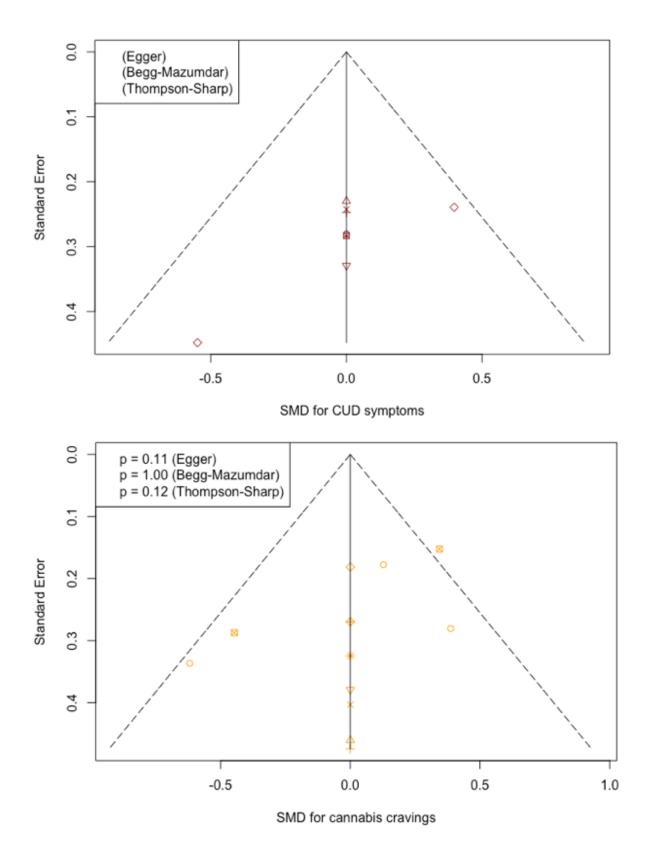


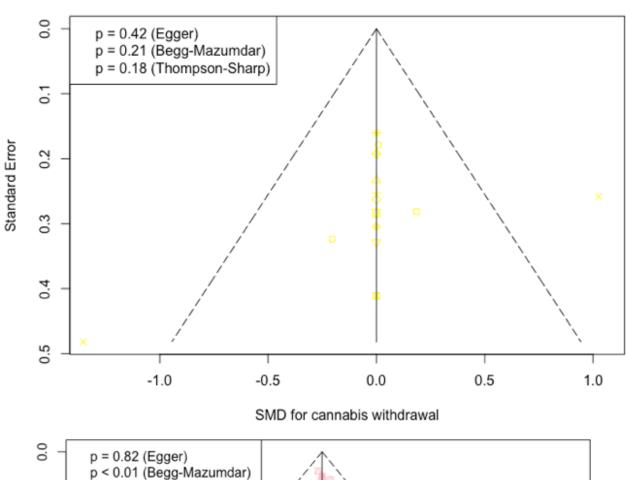


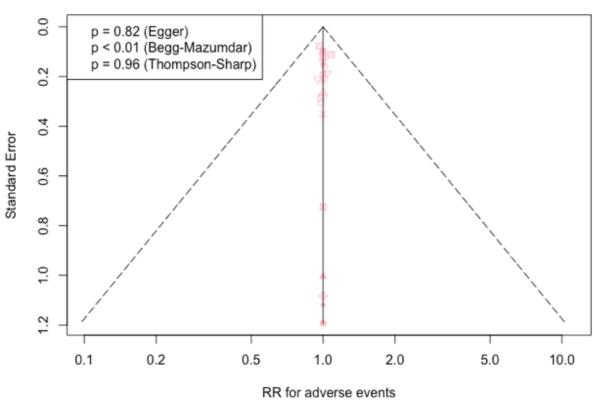
RR for retention in treatment











Supplementary Table 5. Sensitivity analysis after removing the high risk of bias studies.

Cannabis use (d) vs. placebo	Nabiximols -1.45 [-3.32; 0.41]
Califiable use (a) vs. placebo	Fluoxetine -2.30 [-4.75; 0.15]
	FAAH-inhibitor -3.60 [-6.86; -0.35]
	Lithium -0.43 [-3.65; 2.80]
	Gabapentin -0.88 [-4.09; 2.33]
	Topiramate -3.80 [-7.06; -0.54]
	Oxytocin 1.15 [-2.19; 4.48]
Retention in treatment (RR) vs. placebo	Nabiximols 1.15 [0.92; 1.42]
	Nefazodone 1.13 [0.69; 1.83]
	Bupropion SR 1.06 [0.67; 1.67]
	Fluoxetine 1.00 [0.89; 1.11]
	FAAH-inhibitor 0.99 [0.79; 1.24]
	N-acetylcysteine 1.06 [0.93; 1.21]
	Nabilone 0.80 [0.42; 1.52]
	Lithium 1.12 [0.79; 1.58]
	Divalproex Sodium 1.15 [0.40; 3.31]
	Dronabinol 1.27 [1.02; 1.57]
	Venlafaxine XR 0.96 [0.71; 1.30]
	Dronabinol/Lofexidine 0.88 [0.68; 1.15]
	Gabapentin 0.64 [0.30; 1.37]
	Buspirone 0.96 [0.74; 1.23]
	Atomoxetine 1.29 [0.60; 2.74]
	Vilazodone 0.70 [0.41; 1.21]
	Topiramate 0.62 [0.42; 0.91]
	Oxytocin 0.86 [0.53; 1.38]
	Escitalopram 0.62 [0.35; 1.11]
Treatment discontinuation (RR) vs. placebo	Nabiximols 0.88 [0.66; 1.19]
, , ,	Nefazodone 0.89 [0.57; 1.40]
	Bupropion SR 0.95 [0.65; 1.38]
	Fluoxetine 1.06 [0.23; 4.89]
	FAAH-inhibitor 1.04 [0.35; 3.12]
	N-acetylcysteine 0.87 [0.66; 1.15]
	Nabilone 1.60 [0.39; 6.62]
	Lithium 0.69 [0.20; 2.35]
	Divalproex Sodium 0.92 [0.51; 1.66]
	Dronabinol 0.58 [0.36; 0.96]
	Venlafaxine XR 1.07 [0.65; 1.76]
	Dronabinol/Lofexidine 1.26 [0.78; 2.05]
	Gabapentin 1.29 [0.84; 1.97]
	Buspirone 1.05 [0.80; 1.37]
	Atomoxetine 0.83 [0.48; 1.44]
	Vilazodone 1.28 [0.87; 1.89]
	v nazouone 1.20 [0.07, 1.07]

	Topiramate 2.28 [1.06; 4.87]
	Oxytocin 2.00 [0.22; 17.89]
	Escitalopram 1.60 [0.90; 2.84]
Discontinuation due to adverse events (DD)	Nabiximols 0.33 [0.04; 3.09]
Discontinuation due to adverse events (RR)	Nefazodone 0.83 [0.04; 3.09]
vs. placebo	
	Bupropion SR 0.75 [0.05; 11.51]
	N-acetylcysteine 0.39 [0.07; 2.28]
	Divalproex Sodium 2.77 [0.33; 23.14]
	Dronabinol 0.97 [0.06; 15.31]
	Venlafaxine XR 5.10 [0.25; 103.61]
	Dronabinol/Lofexidine 5.00 [0.60; 41.55]
	Gabapentin 1.00 [0.07; 15.12]
	Buspirone 0.63 [0.15; 2.60]
	Atomoxetine 3.00 [0.13; 69.20]
	Vilazodone 1.71 [0.16; 18.04]
	Topiramate 9.10 [1.27; 65.11]
Cannabis withdrawal (<i>d</i>) vs. placebo	Nabiximols -0.39 [-1.21; 0.43]
	Nefazodone 0.08 [-1.25; 1.40]
	Bupropion SR 0.02 [-1.04; 1.09]
	FAAH-inhibitor -0.85 [-2.26; 0.56]
	Lithium -0.01 [-1.47; 1.46]
	Divalproex Sodium 0.61 [-0.94; 2.15]
	Dronabinol -0.20 [-1.55; 1.16]
	Dronabinol/Lofexidine -1.00 [-2.37; 0.37]
	Gabapentin 1.08 [-0.36; 2.53]
	Buspirone 0.09 [-1.34; 1.51]
Cannabis cravings (d) vs. placebo	Nabiximols -0.36 [-0.92; 0.20]
	Bupropion SR -1.02 [-2.24; 0.20]
	Nabilone -0.05 [-1.28; 1.19]
	Divalproex Sodium 0.31 [-0.82; 1.45]
	Dronabinol/Lofexidine 0.14 [-0.75; 1.03]
	Gabapentin -2.42 [-3.53; -1.32]
	Buspirone 0.02 [-0.64; 0.67]
	Atomoxetine -0.00 [-1.04; 1.03]
	Vilazodone 1.69 [0.71; 2.66]
Cannabis use disorder symptoms (<i>d</i>) vs.	Nabiximols 0.01 [-1.22; 1.25]
placebo	Nefazodone 0.13 [-1.08; 1.34]
	Bupropion SR 0.26 [-0.94; 1.47]
	Fluoxetine -0.28 [-1.19; 0.64]
	Lithium -0.19 [-1.47; 1.09]
	Gabapentin -0.16 [-1.40; 1.08]
Adverse events (RR) vs. placebo	Nabiximols 0.99 [0.77; 1.26]
(****) · 5. F ************************************	Nefazodone 1.56 [0.77; 3.17]
	Bupropion SR 1.69 [0.85; 3.35]
	FAAH-inhibitor 0.95 [0.55; 1.64]
	N-acetylcysteine 0.94 [0.71; 1.23]
	1. accepte youtine 0.74 [0.71, 1.23]

	T	
	Nabilone 0.40 [0.10; 1.66]	
	Lithium 1.18 [0.77; 1.80]	
	Divalproex Sodium 2.77 [0.33; 23.14]	
	Dronabinol 1.15 [0.90; 1.46]	
	Venlafaxine XR 1.78 [1.40; 2.26]	
	Dronabinol/Lofexidine 1.02 [0.84; 1.25]	
	Gabapentin 0.75 [0.52; 1.09]	
	Buspirone 1.14 [1.00; 1.29]	
	Atomoxetine 1.18 [0.98; 1.43]	
	Vilazodone 0.76 [0.57; 1.02]	
	Topiramate 9.10 [1.27; 65.11]	
	Oxytocin 0.50 [0.06; 4.47]	
	Escitalopram 2.00 [0.19; 20.72]	
Abstinence (RR) vs. placebo	Nabiximols 1.26 [0.62; 2.56]	
. , ,	Nefazodone 1.67 [0.47; 5.86]	
	Bupropion SR 0.75 [0.18; 3.16]	
	Fluoxetine 0.93 [0.31; 2.75]	
	N-acetylcysteine 1.11 [0.60; 2.06]	
	Nabilone 0.80 [0.05; 11.69]	
	Lithium 1.37 [0.45; 4.19]	
	Divalproex Sodium 1.11 [0.38; 3.26]	
	Dronabinol 1.14 [0.45; 2.89]	
	Venlafaxine XR 0.32 [0.11; 0.90]	
	Dronabinol/Lofexidine 0.89 [0.39; 2.04]	
	Buspirone 2.30 [0.82; 6.45]	
	Atomoxetine 1.33 [0.47; 3.79]	
	Vilazodone 0.85 [0.12; 6.33]	
	Escitalopram 2.33 [0.59; 9.29]	

Supplementary Table 6. Medications included in this analysis and their current medical use

Agent	Mechanism of action	Clinical use
Nabiximols	A mixture of tetrahydrocannabinol (THC) and cannabidiol (CBD)	Spasticity in multiple sclerosis
Nefazodone	Serotonin antagonist and reuptake inhibitor (SARI)	Antidepressant
Bupropion sustained-release	Noradrenergic and dopaminergic reuptake inhibitor (NDRI)	Antidepressant, smoking cessation, attention-deficit hyperactivity disorder (ADHD)
Fluoxetine	Selective serotonin reuptake inhibitor (SSRI)	Antidepressant, anxiolytic
N-acetylcysteine	Glutathione precursor, role in glutamatergic neurotransmission	Acetaminophen overdose, treatment of several psychiatric disorders
Nabilone	Synthetic cannabinoid	Antiemetic, analgesic, nightmares in post-traumatic stress disorder
Lithium	Unclear, but appears to modulate secondary messenger systems	Mood stabilizer in bipolar disorder, augmentation agent in depression
Divalproex	An antagonist of the voltage-gated sodium channel that enhances gamma-aminobutyric acid (GABA) neurotransmission	Anticonvulsant, mood- stabilizing agent, anti- migraine agent
Dronabinol	Synthetic cannabinoid	Antiemetic, analgesic, appetite stimulant
Venlafaxine extended-release	Serotonin-norepinephrine reuptake inhibitor (SNRI)	Antidepressant, anxiolytic, analgesic for neuropathic pain
Lofexidine	α _{2A} adrenergic receptor agonist	Opioid withdrawal, hypertension
Buspirone	Non-benzodiazepine anxiolytic	Anxiety disorders
Atomoxetine	Noradrenergic reuptake inhibitor (NRI)	ADHD
Vilazodone	Serotonin reuptake inhibitor and 5-HT _{1A} receptor partial agonist	Antidepressant
Escitalopram	Selective serotonin reuptake inhibitor (SSRI)	Antidepressant, anxiolytic