

**Supplementary Table 1.** Per protocol generalized estimating equation (GEE) models of pain interference measured using the total PROMIS Pain Interference score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	21.95	21.12, 22.79	
Week 6	<b>-3.26</b>	-4.08, -2.44	<0.001
Week 12	<b>-2.98</b>	-3.95, -2	<0.001
Week 24	<b>-4.6</b>	-6.02, -3.17	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

PROMIS-Pain Interference scale range: 6-30

**Supplementary Table 2.** Per protocol generalized estimating equation (GEE) models of pain severity measured using the Numeric Pain Rating Scale.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	5.2	4.88, 5.53	
Week 6	<b>-0.6</b>	-0.94, -0.27	<0.001
Week 12	<b>-0.56</b>	-0.91, -0.2	<0.005
Week 24	<b>-1.19</b>	-1.7, -0.68	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

Numeric Pain Rating scale range: 0-10

**Supplementary Table 3.** Per protocol generalized estimating equation (GEE) models of anxiety severity measured using the total General Anxiety Disorder-7 score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	8.59	7.8, 9.37	
Week 6	<b>-1.7</b>	-2.37, -1.03	<0.001
Week 12	<b>-1.63</b>	-2.36, -0.9	<0.001
Week 24	<b>-2.24</b>	-3.5, -0.99	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

General Anxiety Disorder-7 scale range: 0-21

**Supplementary Table 4.** Per protocol generalized estimating equation (GEE) models of depression severity measured using the total Patient Health Questionnaire-9 score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	10.57	9.7, 11.43	
Week 6	<b>-2.4</b>	-3.06, -1.75	<0.001
Week 12	<b>-2.12</b>	-2.9, -1.34	<0.001
Week 24	<b>-2.79</b>	-4.29, -1.3	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

Patient Health Questionnaire-9 scale range: 0-27

**Supplementary Table 5.** Per protocol generalized estimating equation (GEE) models of quality of life measured using the total EQ-5D-3L score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	3.98	3.75, 4.21	
Week 6	<b>-0.46</b>	-0.66, -0.26	<0.001
Week 12	<b>-0.44</b>	-0.67, -0.22	<0.001
Week 24	<b>-0.56</b>	-0.96, -0.16	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

EQ-5D-3L scale range: 0-10

**Supplementary Table 6.** Stuart-Maxwell analysis of sleep hours categories.

<b>Comparison</b>	<b>n-paired</b>	<b>X<sup>2</sup> (df=3)</b>	<b>p-value</b>	<b>Effect Size</b>
Week 0 vs Week 6	163	27.2	<b>&lt;0.001</b>	0.24
Week 0 vs Week 12	144	24.8	<b>&lt;0.001</b>	0.24
Week 0 vs Week 24	125	16.1	<b>&lt;0.005</b>	0.21

Sleep hours analysis was based on categories of <5 hours, 5-6 hours, 6-7 hours, >7 hours.

**Supplementary Table 7.** Last Observation Carried Forward generalized estimating equation (GEE) models of pain interference measured using the total PROMIS Pain Interference score.

	<b><math>\beta</math></b>	<b>95% Confidence Interval</b>	<b>p-value</b>
<b>Time</b>			
Baseline	21.60	20.80, 22.50	
Week 6	<b>-1.86</b>	-2.43, -1.30	<0.001
Week 12	<b>-1.88</b>	-2.54, -1.22	<0.001
Week 24	<b>-2.50</b>	-3.11, -1.89	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

**Supplementary Table 8.** Last Observation Carried Forward generalized estimating equation (GEE) models of pain severity measured using the Numeric Pain Rating Scale.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	5.16	4.84, 5.47	
Week 6	<b>-0.34</b>	-0.57, -0.12	<0.001
Week 12	<b>-0.34</b>	-0.59, -0.10	<0.001
Week 24	<b>-0.55</b>	-0.78, -0.31	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

**Supplementary Table 9.** Last Observation Carried Forward generalized estimating equation (GEE) models of anxiety severity measured using the total General Anxiety Disorder-7 score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	8.27	7.52, 9.03	
Week 6	<b>-0.67</b>	-1.11, -0.23	<0.005
Week 12	<b>-0.76</b>	-1.24, -0.28	<0.005
Week 24	<b>-0.86</b>	-1.34, -0.38	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

**Supplementary Table 10.** Last Observation Carried Forward generalized estimating equation (GEE) models of depression severity measured using the total Patient Health Questionnaire-9 score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	10.20	9.36, 11.10	
Week 6	<b>-1.05</b>	-1.45, -0.65	<0.001
Week 12	<b>-1.09</b>	-1.57, -0.61	<0.001
Week 24	<b>-1.07</b>	-1.55, -0.59	<0.001

Bolded values are statistically significant at  $p < 0.05$ .

**Supplementary Table 11.** Last Observation Carried Forward generalized estimating equation (GEE) models of quality of life measured using the total EQ-5D-3L score.

	$\beta$	95% Confidence Interval	p-value
<b>Time</b>			
Baseline	3.91	3.69, 4.14	
Week 6	<b>-2.1</b>	-0.33, -0.08	<0.005
Week 12	<b>-2.4</b>	-0.38, -0.10	<0.001
Week 24	<b>-2.3</b>	-0.37, -0.09	<0.005

Bolded values are statistically significant at  $p < 0.05$ .

**Supplementary Table 123.** Post-hoc power analysis between Baseline and Week 24.

<b>Variable</b>	<b>Effect Size</b>	<b>Power</b>
<b>Pain Interference</b>	-0.727	1.000
<b>Numeric Pain Rating Scale</b>	-0.441	0.999
<b>General Anxiety Disorder-7</b>	-0.290	0.898
<b>Patient Health Questionnaire-9</b>	-0.365	0.981
<b>EQ-5D-3L</b>	-0.198	0.598
<b>Sleep Hours</b>	-0.039	0.072

$\alpha = 0.05$

**Supplementary Table 13.** Number of reported symptom side effects per time point.

	<b>Week 6</b>	<b>Week 12</b>	<b>Week 24</b>
<b>Symptom</b>			
None	50	50	56
Heart Racing	8	8	4
Fainting	2	0	1
Feeling High	19	16	12
Dizziness	14	11	9
Daytime Sleepiness	24	21	22
Headache	13	17	8
Dry Mouth	24	29	26
Nausea	6	8	7
Paranoid	5	5	2
Other	11	14	15

Multiple survey selections allowed per patient.

**Supplementary Table 14.** Number of reported side effects per time point.

	<b>Week 6 (N=184)</b>	<b>Week 12 (N=165)</b>	<b>Week 24 (N=139)</b>
Total Side Effects Reported	126	129	106
No Side Effects	50	50	56
<b>Side Effect N (% of total reported)</b>			
Dry Mouth	24 (19%)	29 (22.5%)	26 (24.5%)
Daytime Sleepiness	24 (19%)	21 (16.3%)	22 (20.8%)
Feeling High	19 (15.1%)	16 (12.4%)	12 (11.3%)
Dizziness	14 (11.1%)	11 (8.5%)	9 (8.5%)
Headache	13 (10.3%)	17 (13.2%)	8 (7.5%)
Heart Racing	8 (6.3%)	8 (6.2%)	4 (3.8%)
Nausea	6 (4.8%)	8 (6.2%)	7 (6.6%)
Paranoid	5 (4%)	5 (3.9%)	2 (1.9%)
Fainting	2 (1.6%)	0 (0%)	1 (0.9%)
Other*	11 (8.7%)	14 (10.9%)	15 (14.2%)

Different side effect selections allowed per patient. One selection represents 1 or greater instance of the respective side effect.

\*Indicates participants reporting any symptoms they have experienced not listed on questionnaires.

**Supplementary Table 15.** Internal consistency (Cronbach's Alpha) of multi-item validated questionnaires.

<b>Scale</b>	<b>Cronbach's <math>\alpha</math></b>
PROMIS Pain Interference	0.97
General Anxiety Disorder-7	0.91
Patient Health Questionnaire-9	0.90

**Supplementary Table 16.** Baseline characteristics of dropouts and non-dropouts in the MCRWE study.

	<b>Dropouts (N=137)</b>	<b>Non-Dropouts (N=139)</b>	<b>p-value</b>
<b>Age, mean (SD)</b>	47.2 (15.9)	49.6 (16.3)	>0.05
<b>Female Gender</b>	82 (63.1%)	91 (66.4%)	>0.05
<b>Previous MC Use</b>	60 (47.6%)	66 (50.4%)	>0.05
<b>Previous Recreational Cannabis Use</b>	77 (61.1%)	64 (49.2%)	>0.05
<b>Smoking Status (Tobacco):</b>			
Current	25 (19.4%)	17 (12.8%)	>0.05
Previous	52 (40.3%)	46 (34.6%)	>0.05
Never	52 (40.3%)	70 (52.6%)	>0.05
<b>*Pain Medication Use</b>			
NSAID	41 (31.5%)	40 (29.2%)	>0.05
Acetaminophen	52 (40%)	52 (38%)	>0.05
Opioid	43 (33.1%)	44 (32.1%)	>0.05
Gabapentinoid	31 (23.8%)	40 (29.2%)	>0.05
<b>*MC Indications:</b>			
Pain	105 (83.3%)	113 (86.9%)	
Sleep	56 (44.4%)	71 (54.6%)	>0.05
Anxiety/Depression	49 (38.9%)	45 (34.6%)	>0.05
<b>**Reported Symptom Improvement from Previous Cannabis Use:</b>			

Pain	46 (35.4%)	51 (37.5%)	>0.05
Sleep	35 (26.9%)	46 (33.8%)	>0.05
Anxiety	36 (27.7%)	36 (26.5%)	>0.05
Depression	22 (16.9%)	21(15.4%)	>0.05

All values displayed are n (%) unless stated otherwise.

\*Multiple selections allowed.

\*\*Regardless of primary MC indication.

SD: standard deviation, GERD: gastroesophageal reflux, MC: medical cannabis, NSAID: non-steroidal anti-inflammatory, PTSD: post-traumatic stress disorder

No significant difference in any variable ( $p>0.05$ ).