Quality Research, Evidence of Effectiveness of Medical Cannabis

The research studies in the table below were each evaluated using the GRADE scale (Cochrane Methods Bias, n.d.; "What is GRADE?," 2012), a tool for assessing the quality of evidence, elucidating high, moderate, low, and very low evidence quality. All randomized experimental studies are initially rated as high quality; and observational studies began at low-quality rating. In this assessment, a study loses quality if it has serious risk of bias (from improper blinding of subjects and assessors, nonrandom sorting, patient dropout), confounding factors, imprecision, or inconsistency. Studies gain quality if the data show a large effect or dosage effect, or the study adequately controlled confounding factors.

The table below presents the moderate- to high-quality data asserting a positive effect of cannabis for qualifying conditions. The table preferentially displays therapeutic effects. Adverse effects and/or the absence of effect are not included in this table except for when they add perspective to currently debated therapeutic applications. For example, Hallak and colleagues (2010) detected no effect of CBD on schizophrenia symptomology. This is worth noting because CBD is often described as an antipsychotic (Russo & Guy, 2006), though the details and applicability of this effect continue to be researched.

The table groups the studies according to conditions with significant evidence and are preferentially grouped by qualifying condition. The conditions are listed in **bold** and subcategories are listed in *italics*. For example, Freeman et al., 2006, has data for *Incontinence* as a symptom of Multiple Sclerosis.

The studies are not generalizable. The conclusions of the studies can only be applied to the particular symptoms, conditions, and groups that were studied. The *Results* column notes the condition, symptoms, and sex of the subjects with statistically relevant results. Many of the studies can apply to more than one qualifying condition; when this occurs, those studies are grouped based on the primary qualifying condition of study (i.e., Cachexia instead of HIV).

Study	Drug (Dosage), Delivery	Grade	Results
Cachexia			
Abrams et al., 2003	Cannabis (3.95% THC three doses daily), smoked and dronabinol (3.93% three doses daily), oromucosal	Moderate to low	Smoked and oral cannabinoids not unsafe for HIV patients in short term. Increased weight by fat (smoked, $p = 0.021$; dronabinol, $p = 0.004$). Results applicable to male patients. $N = 62$
Andries, Frystyk, Flyvbjerg, & Støving, 2014	Dronabinol (2.5mg twice daily), orally	Moderate to high	Significant weight gain of 1.00kg during dronabinol vs 0.34kg during placebo ($p = 0.03$). Results applicable to anorexic female patients. $N = 25$
Haney, Rabkin, Gunderson, & Foltin, 2005	Dronabinol (10mg, 20mg, and 30mg), orally and cannabis (1.8%, 2.8%, and 3.9% THC), smoked	Moderate to low	Cannabis and dronabinol significantly increased caloric intake in the low BIA group (10mg and 1.8% THC $p < 0.005$, 30mg and 3.9% $p < 0.01$) but not in the normal BIA group. Results applicable to male patients. $N = 29$
Haney et al., 2007	Cannabis (2.0%, 3.9% THC four times daily), smoked and dronabinol (5mg, 10mg four times daily), orally	High to moderate	Cannabis (3.9% THC) improved ratings of sleep ($p < 0.005$) in HIV patients. Dronabinol ($p = 0.008$) and cannabis ($p = 0.01$) dose dependently increased caloric intake by increasing the number of eating occasions, resulting in improved weight via fat gain. Results applicable to male patients. $N = 10$
Timpone et al., 1997	Dronabinol (2.5mg twice daily), orally	Moderate to low	Megestrol acetate showed greater weight gain than dronabinol ($p = 0.0001$) and combining the two did not lead to additive weight gain in patients with HIV. $N = 39$

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Study	Drug (Dosage), Delivery	Grade	Results
Cancer			
Johnson et al., 2010	THC:CBD (22mg–32mg/day THC, 20mg–30mg/day CBD), oromucosal	Moderate to low	THC:CBD caused 30% reduction in pain from baseline in patients unresponsive to opioids. THC:CBD patients used a median oral morphine dose lower than other treatments. THC:CBD had a significantly improved constipation score. (OR THC:CBD = 2.81, $p = 0.006$) $N = 177$
Chronic Pain			
Narang et al., 2008	Dronabinol (10mg and 20mg THC), orally	Moderate	Total pain relief at 8 hours (TOTPAR) improved (20mg $p = 0.01$, 10mg $p = 0.05$). Evoked pain (ESPID) decreased (20mg, 10mg $p < 0.05$). Significant reduction of pain over time (baseline vs week 2, $p = 0.01$; week 1 vs week 3, $p = 0.05$; week 2 vs week 4, $p = 0.05$). $N = 30$
Rheumatoid Arthritis			
Blake, Robson, Ho, Jubb, & McCabe, 2006	Sativex (max 6 doses daily), oromucosal	Moderate to low	Improvements in morning pain on movement ($p = 0.044$), morning pain at rest ($p = 0.018$), quality of sleep ($p = 0.027$), (DAS28 $p = 0.002$), and pain at present ($p = 0.016$). Results applicable to female patients. $N = 31$
Epilepsy			
Dravet syndrome			
Devinsky et al., 2017	CBD (20mg/kg/day), oromucosal	High to moderate	CBD decreased the median frequency of convulsive seizures per month (compared to placebo, $p = 0.01$). The Caregiver Global Impression of Change scale showed improvement in 62% of the CBD group (from baseline, $p = 0.02$). The frequency of total seizures of all convulsive types was reduced ($p = 0.03$). $N = 120$
Lennox-Gastaut syndrome			
Thiele et al., 2018	CBD (20mg/kg/day), orally	High	CBD decreased the median percentage of monthly drop by 43.9% (estimated median difference between placebo $p = 0{\cdot}013$). Monthly frequency of total seizures decreased by a median of 41·2% from baseline with CBD (difference from placebo $p = 0{\cdot}0005$). $N = 171$
Fibromyalgia			
Sleep			
Ware, Fitzcharles, Joseph, & Shir, 2010	Nabilone (0.5mg daily), orally	High	Improved sleep over amitriptyline 10mg (Insomnia Severity Index, adjusted difference = -3.25; CI, -5.26 to -1.24), marginally better on restfulness (difference = 0.48; CI, 0.01 to 0.95). Results applicable to female patients. $N = 29$
Pain			
Skrabek, Galimova, Ethans, & Perry, 2008	Nabilone (2mg daily), orally	Moderate to high	Significant decreases in the VAS ($p < 0.02$), Fibromyalgia Impact Questionnaire ($p < 0.02$), and anxiety ($p < 0.02$) at 4 weeks. $N = 40$*
HIV/AIDS			
Neuropathy			
Abrams et al., 2007	Cannabis (3.5% THC), smoked	Moderate	>30% reduction in pain from baseline ($p = 0.04$). 34% median reduction in chronic neuropathic pain (VAS $p = 0.03$). >30% reduction in pain was reported by 52% in the cannabis group (comparable to oral drugs used for chronic neuropathic pain). Results applicable to male patients. $N = 50$
Ellis et al., 2009	Cannabis (1%–8% THC), smoked	High	Decrease in pain intensity (Descriptor Differential Scale $p = 0.02$). 46% of cannabis patients achieved at least 30% pain relief. Results applicable to male patients. $N = 27$

Study	Drug (Dosage), Delivery	Grade	Results
Multiple Sclerosis			
Aragona et al., 2009	Sativex (average 15 doses daily), oromucosal	Moderate to low	Did not induce psychopathology and did not impair cognition. At dosages higher than those used, interpersonal sensitivity, aggressiveness, and paranoiac features might arise. *N* = 17
Collin, Davies, Mutiboko, & Ratcliffe, 2007	Sativex (max 48 doses daily), oromucosal	Moderate	Spasticity improved (NRS $p = 0.048$) and 40% of patients achieved >30% benefit ($p = 0.014$). *N* = 184
Collin et al., 2010	Sativex (max 24 doses daily), oromucosal	Moderate to low	In the per-protocol analysis, 36% achieved at least a 30% improvement in NRS spasticity scores ($p = 0.04$). N = 177
Corey-Bloom et al., 2012	Cannabis (4%THC), smoked	High	Significant decrease in modified Ashworth ($p = 0.001$), subjective pain score ($p = 0.008$), and highness ($p = 0.001$). *N* = 30
Vaney et al., 2004	Cannabis extract (2.5mgTHC, 0.9mg CBD. Max 30mgTHC daily), orally	Moderate	Lowered spasm frequency and improved mobility results not statistically significant. *N* = 57
Wade, Makela, Robson, House, & Bateman, 2004	Sativex (2.5mg–120mg daily), oromucosal	Moderate to low	Spasticity reduced (VAS $p = 0.001$). Improvement in quality of sleep ($p = 0.047$), and Guy's Neurological Disability scale scores ($p = 0.048$). *N* = 160
Wade, Collin, Stott, & Duncombe, 2010	Sativex (N/A), oromucosal	Moderate to low (pooled data)	~1/3 of patients gain at least a 30% improvement from baseline. A greater proportion of treated patients responded to the treatment (OR = 1.62, $p = 0.0073$), treated patients reported greater improvement (OR = 1.67, $p = 0.030$). *N* = 666
Zajicek et al., 2003	Cannabis extract (2mg–5mg THC, 1mg–25mg CBD per capsule), orally	High	Improvements in spasticity (Ashworth $p = 0.01$), pain ($p = 0.002$), sleep ($p = 0.025$), and spasms ($p = 0.038$). *N* = 657
Zajicek et al., 2012	Cannabis extract (5mg–25mg THC daily), orally	High to moderate	Relief from stiffness after 12 weeks (OR 2.26, $p = 0.004$). Rating scales had significant difference in muscle stiffness, body pain, muscle spasms, sleep quality at week 4 and increasing significance on week 8 for stiffness and body pain, and an increase in significance for spasms in week 12, but a decrease in significance in sleep and body pain (became nonsignificant) in week 12 (all significance values at least $p < 0.025$). *N* = 277
Multiple Sclerosis			
Neuropathies			
Langford et al., 2013	Sativex (max 12 doses daily), oromucosal	Moderate	At the end of the treatment, a significant difference in pain score (NRS $p = 0.028$) and sleep quality (NRS $p = 0.015$). *N* = 339
Turcotte et al., 2015	Nabilone (1mg twice daily), orally	Moderate to low	Significant differences in pain intensity (VAS $p = 0.01$). Patient perceived benefit higher with nabilone and gabapentin ($p < 0.05$). Results applicable to female patients. *N* = 15
Incontinence			
Freeman et al., 2006	Cannabis extract (2.5mgTHC with 1.25mg CBD or 2.5mg THC. Max 25mg daily), orally	High	Both treatments improved incontinence (cannabis extract, $p = 0.005$;THC, $p = 0.039$). Pad weight reduced in both treatments ($p = 0.001$). *N* = 630
Kavia, De Ridder, Constantinescu, Stott, & Fowler, 2010	Sativex (max 8 doses in 3 hr and 48 doses in 24 hr), oromucosal	Moderate to low	Patients failed to respond to anticholinergics before study. Significant differences in number of episodes of nocturia ($p = 0.010$), bladder capacity (Ordinary Bladder Capacity $p = 0.001$), number of voids/day ($p = 0.001$) total number of voids ($p = 0.007$), impression of change (Patient's Global Impression of Change $p = 0.005$), number of daytime voids ($p = 0.044$). Size of effect was greater for more severely affected subjects. Results applicable to female patients. *N* = 135

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Study	Drug (Dosage), Delivery	Grade	Results
Chronic Pain			
Rog, Nurmikko, Friede, & Young, 2005	Cannabis extract (2.5mg THC with 2.5mg CBD. Max 48 doses daily), oromucosal	High to moderate	Improvements in pain (NRS-11, $p = 0.005$; Neuropathic Pain Scale, $p = 0.044$) and sleep disturbances ($p = 0.003$). Treatment effect comparable to tramadol and pregabalin in treatment of peripheral neuropathic pain. Results applicable to female patients. $N = 66$
Svendsen, Jensen, and Bach, 2004	Dronabinol (max dose 10mg daily), orally	Moderate	Median spontaneous pain intensity lowered ($p = 0.02$) and pain relief score rose ($p = 0.035$). Number Needed to Treat = 3.5 (poor outcome) for 50% pain relief. $N = 24$
Nausea/Vomiting			
Meiri et al., 2007	Dronabinol (2.5mg–20mg daily), orally	Moderate to low	Nausea absence was significantly greater in active treatment groups ($p < 0.05$). Nausea intensity and vomiting/retching lowest with dronabinol. Dronabinol and ondansetron are similarly effective for chemotherapy-induced nausea and vomiting. Combination therapy with dronabinol and ondansetron was not more effective than either agent alone. $N = 61$
Söderpalm, Schuster, & de Wit, 2001	Cannabis (8.4mg and 16.9mg THC), smoked	High to moderate	Acute feelings of nausea were reduced (8.4mg $p < 0.05$, 16.9mg $p < 0.01$) and emesis was also decreased ($p < 0.05$). The higher dose of marijuana significantly reduced nausea at 20 min. However, its effects are very modest relative to ondansetron ($p < 0.05$). $N = 13$
Neuropathies			
Frank, Serpell, Hughes, Matthews, & Kapur, 2008	Nabilone (max 2mg daily), orally	Moderate to low	Dihydrocodeine is a better analgesic than nabilone (VAS $p = 0.01$). A small number of patients responded well to nabilone. $N = 96$ (33 of the 96 dropped out)
Karst et al., 2003	CT3 (a potent analog of THC-11-oic acid) (max 40mg and 80mg daily), orally	Moderate	Reduced pain 3 hours after intake (VAS $p = 0.02$). $N = 21$
Nurmikko et al., 2007	Sativex (max 48 doses daily), oromucosal	High to moderate	Significant decrease in pain (NRS $p = 0.004$). $N = 125$
Wallace et al., 2007	Cannabis (4%, 8% THC), smoked	High	4% THC produced delayed analgesia (Visual Analogue Scale of Pain Intensity $p = 0.027$), 8% THC cannabis produced an increase in pain (Visual Analogue Scale of Pain Intensity $p = 0.009$) after 45 minutes. $N = 19$
Ware, Wang et al., 2010	Cannabis (2.5%, 6%, and 9.4% THC, three times daily), smoked	High	Participants receiving 9.4% reported a lower average daily pain intensity (NRS $p = 0.023$), improved ability to fall asleep (easier, $p = 0.001$; faster, $p < 0.001$; more drowsy, $p = 0.003$), and improved quality of sleep (less wakefulness, $p = 0.01$). Anxiety and depression were improved with 9.4% (EQ-5D questionnaire $p < 0.05$). $N = 23$
Wilsey et al., 2008	Cannabis (7% THC or 3.5% THC), smoked	High	Decrease in pain (VAS $p = 0.02$). Equal anti-nociception at every time point with no difference between the doses over time ($p = 0.95$). Significant differences in measures of unpleasantness ($p < 0.01$) and global impression of change ($p < 0.01$). $N = 38$
Wilsey et al., 2013	Cannabis (3.53% or 1.29% THC), vaporized	Moderate to high	1.29% as effective as 3.53% THC in pain relief. Increasing cumulative analgesia over time (180 min $p < 0.0001$, 240 min $p = 0.0004$, 300 min $p = 0.0018$); analgesia remained stable afterward. Decreased levels of sharpness, burning, aching pain (both doses $p < 0.001$). 1.29% THC more effective for burning pain ($p < 0.0001$); significantly reduced aching more than the 3.53% THC and placebo ($p < 0.0001$). $N = 39$

Study	Drug (Dosage), Delivery	Grade	Results
Neuropathies *(continued)*			
Diabetes			
Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015	Cannabis (1%, 4%, or 7% THC), vaporized	Moderate	There was a modest reduction in spontaneous pain (% reduction in pain: placebo, 61.2%; 1% THC, 66.7%; 4% THC, 70.3%; 7% THC, 65.5%, $p < 0.001$ for all). $N = 16$
Posttraumatic Stress Disorder			
Jetly, Heber, Fraser, & Boisvert, 2015	Nabilone (0.5mg–3mg at bedtime), orally	Moderate	Reduction in nightmares (CAPS Recurring and Distressing Dream scores $p = 0.03$), improved global impression of change (Clinical Global Impression of Change $p = 0.05$) and general well-being (General Well-Being Questionnaire $p = 0.04$). Results applicable to male patients. $N = 10$
Schizophrenia			
Hallak et al., 2010	CBD (300mg or 600mg), orally	Moderate	Single dose showed no effects on symptomology. $N = 28$
Spinal Cord Injury			
Pooyania, Ethans, Szturm, Casey, & Perry, 2010	Nabilone (max 1mg daily), orally	Moderate to low	Decrease in the spasticity (Ashworth "most involved muscle group" $p = 0.003$) and total Ashworth ($p = 0.001$). $N = 11$
Tourette Syndrome			
Müller-Vahl et al., 2002	THC (5mg, 7.5mg, 10mg), orally	Moderate to low	Significant improvement of self-reported tics (Tourette's Syndrome Symptom List $p = 0.015$) and obsessive compulsive behavior ($p = 0.041$). Objective scores showed improvement in simple motor tics ($p = 0.026$), complex motor tic ($p = 0.015$), all motor tics (simple and complex motor tics) ($p = 0.026$), and complex vocal tics ($p = 0.041$). Results applicable to male patients. $N = 12$

Notes

1. Brand-name and generic-name drug dosages:
   - Sativex (2.7mgTHC, 2.5mg CBD)
   - Dronabinol (2.5, 5, or 10mgTHC)
   - Nabilone (1mgTHC)
2. If dosage schedule is not mentioned (i.e., daily, twice daily, at bedtime, max in 24 hr), then the study only assessed a single dose.
3. An effect is considered statistically significant if the p value is greater than or equal to 0.05. Other significant effects are noted by confidence intervals, effects, and ratios (Page, 2014).
4. If more than 75% of patients in a study are one sex, then results are applicable to that sex. An * denotes that sex proportion of patients is not given.

Abbreviations

BIA = bioelectrical impedance analysis; CBD = cannabinol; CI = Confidence Interval; DAS = Disease Activity Score; NRS = Numerical Rating Scale; OR = Odds Ratio; VAS = Visual Analogue Scale; THC = tetrahydrocannabinol.