

## Supplementary table of characteristics of included meta-analyses

### Balancing risks and benefits of cannabis use: umbrella review of meta-analyses of randomised controlled trials and observational studies

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Accepted: 27 June 2023.

Supplementary Table of characteristics of included meta-analyses.

Author, year	K	Population (age)	Type of cannabinoid #	Outcomes	Quality
<b>Meta-analyses of observational studies, or non-randomized studies</b>					
Asbridge, 2012[1]	9	General population (adolescents, adults)	THC	Car crash death/injuries	<b>M</b>
Bhagavan, 2020[2]	5	Insomnia (adults)	CBM	Sleep quality/quantity	<b>H</b>
Blest-Hopley, 2019[3]	12	General population (adolescents, adults)	Regular cannabis use	Brain executive and default mode network	<b>M</b>
Bogaty, 2018[4]	14	Psychosis (adolescents, adults)	Cannabis current use	Cognition	<b>M</b>
Borges, 2016[5]	16	General population (adolescents, adults)	Cannabis use	Suicide ideation, attempt, and suicide	<b>M</b>
Burns, 2012[6]	9	First episode psychosis (adolescents, adults)	Cannabis use	Duration of untreated psychosis	<b>L</b>
Chisini, 2019[7]	4	General population (adolescents, adults)	Cannabis use	Periodontitis	<b>L</b>
Conner, 2016[8]	31	Pregnant women (adult)	Marijuana use	LBW	<b>M</b>
De Carvalho, 2015[9]	6	General population (adolescents, adults)	Marijuana use	Head and neck cancer	<b>M</b>
Escelsior, 2021[10]	16	General population (adolescents, adults)	Cannabinoids	Self-injurious behaviour	<b>L</b>
Farooqui, 2019[11]	9	HCV+ NAFDL (adult)	Marijuana use	Liver fibrosis	<b>M</b>
Foglia, 2017[12]	15	Psychosis (adolescents, adults)	Cannabis use (current, past)	Antipsychotics adherence	<b>H</b>
Ghasemiesfe, 2019[13]	25	General population (adults)	Marijuana ever use, use>10y	Cancer (lung, head and neck, oral, testicular)	<b>H</b>
Ghasemiesfe, 2018[14]	22	General population (adolescents, adults)	Marijuana use	Sputum production and cough	<b>H</b>
Gibbs, 2015[15]	6	General population (adult)	Cannabis use	Mania symptoms	<b>M</b>
Goldenberg, 2017[16]	20	Mixed medical conditions~ (adult)	Cannabis, cannabinoids	Health related quality of life	<b>M</b>
Grant, 2002[17]	11	General population (adult)	Cannabis use	Cognition	<b>M</b>
Gunn, 2016[18]	6	Pregnant women (adult)	Cannabis use	Maternal anemia	<b>M</b>
Gurney, 2015[19]	3	General population (adults <50)	Cannabis use, current	Testicular cancer, non-seminoma	<b>M</b>
Hostiuc, 2018[20]	24	General population (adolescents, adults)	Cannabis use	Car events	<b>M</b>
Johnson, 2017[21]	13	General population (adolescents, young adults)	Cannabis use	Physical dating violence	<b>H</b>
Kamp, 2018[22]	5	General population (adults)	Cannabis use	Dopamine receptors, transporter and synthesis	<b>M</b>
Kiburi, 2021[23]	18	General population (adolescent)	Cannabis use	Psychosis	<b>H</b>
Kraan, 2016[24]	7	Ultra-high risk of psychosis (adolescents, adults)	Cannabis use	Psychosis (transition to)	<b>H</b>
Lev-Ran, 2014[25]	14	General population (adolescents, adults)	Cannabis use (normal, heavy)	Depression	<b>H</b>
Lorenzetti, 2019[26]	30	General population (adolescents, adults)	Regular cannabis use	Brain volume	<b>H</b>
Marchand, 2022[27]	16	Pregnant women (adults)	Marijuana use	LBW, SGA, preterm delivery, NICU, Apgar, head circumference	<b>L</b>
Moore, 2007[28]	35	General population (adolescents, adults)	Cannabis use	Depression, psychosis symptoms and suicidal ideation	<b>M</b>
Myles, 2012[29]	38	General population (adolescents, adults)	Cannabis use	Age at onset of schizophrenia and other psychoses	<b>M</b>
Noori, 2021*[30]	12	Chronic pain on opioids	Cannabis use	Opioid use	<b>L</b>
Power, 2021[31]	7	General population (adolescents, young adults)	Cannabis use, frequent/dependent	IQ, verbal IQ	<b>H</b>
Rabin, 2011[32]	8	Schizophrenia (adults)	Cannabis use	Cognition	<b>L</b>
Rocchetti, 2013[33]	14	General population (adolescents, adults)	Cannabis use	Hippocampal volume	<b>M</b>
Rodriguez-Almaraz,	5	Malignant CNS tumors (adults)	Cannabis use	Survival	<b>L</b>

Author, year	K	Population (age)	Type of cannabinoid #	Outcomes	Quality
2020[34]					
Rogeberg, 2019[35]	12	Drivers (adult)	Cannabis, THC positive	Car crash and car crash culpability	L
Ruisch, 2018[36]	36	Pregnant women (adult)	Cannabis use	Offspring conduct problems	M
Ruiz-Veguilla, 2012[37]	5	Psychosis (adolescents, adults)	Cannabis use	Neurological soft signs	M
Sabe, 2020[38]	20	Schizophrenia (adults)	Cannabis use	Negative symptoms	H
Sánchez-Gutiérrez, 2020[39]	7	First-episode psychosis (adolescents, adults)	Cannabis use	Cognition	L
Schoeler, 2016[40]	24	Psychosis	Cannabis use (continued, past)	Psychosis, relapse	M
Schoeler, 2016[41]	88	Healthy subjects, psychosis (adult)	Cannabis use	Cognition	L
Schreiner, 2012[42]	33	General population (adolescents, adults)	Cannabis use (past)	Cognition	CL
Schumacher, 2018[43]	11	General population (adolescent, adult)	Cannabis	Condom use	M
Scott, 2018[44]	69	General population (adolescent, adult)	Cannabis (current, past)	Cognition	H
Smith, 2014[45]	11	General population (adolescents, adults)	Cannabis (heavy use)	Behavioural inhibition	M
Sultan, 2018[46]	13	General population (NR)	THC	Heart rate change	M
Szoke, 2014[47]	29	General population (adult)	Cannabis use	Schizotypy	M
Wijarnpreecha, 2018[48]	3	HCV (adult)	Cannabis use	Advanced liver fibrosis	H
Xue, 2021[49]	10	General population (adolescents, adults)	Cannabis use	Anxiety	L
Zhang, 2015[50]	6	General population (adult)	Cannabis use	Lung cancer	L
<b>Meta-analyses of randomised controlled trials</b>					
Allan, 2018[51]	22	Mixed conditions <sup>A</sup> (adults)	CBM	Pain, spasticity, nausea and vomiting, AEs	H
Allende-Salazar, 2017[52]	32	Mixed conditions (chronic non-cancer pain) <sup>B</sup> (adults)	CBM	Pain	L
Amato, 2017[53]	41	Mixed conditions <sup>C</sup> (adults)	CBM	Nausea, AEs	H
Andreae, 2015[54]	5	Mixed conditions (chronic neuropathic pain) <sup>D</sup> (adults)	Cannabis (inhaled)	Pain	H
Aviram, 2017[55]	23	Mixed conditions <sup>E</sup> (adults)	CBM	Pain, AEs	L
Bahji, 2020[56]	9	Dementia (older persons)	Cannabinoids	Psychiatric symptoms	L
Bahji, 2020[57]	14	Anxiety (adults)	Cannabinoids	Anxiety, acceptability	H
Bajtel, 2022[58]	16	Mixed conditions <sup>F</sup> (adults)	CBM	Drowsiness, fatigue, headache, nausea	M
Black, 2019[59]	86	Psychiatric disorders (adults)	THC/CBD	Psychiatric symptoms	H
Chesney, 2020[60]	12	Mixed conditions <sup>G</sup> (children, adults)	CBD	AEs	H
Couch, 2018[61]	53	Crohn's (adults)	THC/CBD	Disease activity index	M
Da Rovare, 2017[62]	16	Multiple sclerosis/paraplegia (spasticity, adults)	CBM	Dizziness, dry mouth, nausea, somnolence	M
De Carvalho, 2020[63]	4	Treatment-resistant epilepsy (children, adults)	Cannabis, CBD	Seizures, AEs, Pain	L
De Vita, 2018[64]	18	Healthy subjects experimental pain (adults)	Cannabinoids	Pain	H
Doeve, 2020[65]	4	Inflammatory bowel disease (adults)	Cannabis	Remission, biomarkers, symptoms, quality of life	CL
Elliot, 2018[66]	23	Epilepsy (children)	CBD	Seizures, response, quality of life, sleep, vomit, diarrhea	M
Fu, 2018[67]	23	Multiple sclerosis (adult)	Cannabinoids	Spasticity, AEs	CL

<b>Author, year</b>	<b>K</b>	<b>Population (age)</b>	<b>Type of cannabinoid #</b>	<b>Outcomes</b>	<b>Quality</b>
Gazendam, 2020[68]	6	Surgery (adult)	CBM	Pain	<b>L</b>
Hauser , 2019[69]	4	Cancer (adult)	Nabiximol, THC	Pain, maintenance of opioid dosage, daily breakthrough opioid dosage	<b>H</b>
Hindley, 2020[70]	15	General population (adult)	THC/CBD	Psychiatric symptoms	<b>H</b>
Kopelli, 2020[71]	3	Schizophrenia (adult)	CBD	Total symptoms, cognition	<b>L</b>
Lattanzi, 2020[72]	3	Dravet syndrome (children)	CBD	Seizure, acceptability, AEs	<b>CL</b>
Lattanzi, 2020[73]	4	Dravet syndrome, Lennox-Gastaut (children)	CBD	Seizure	<b>CL</b>
Lattanzi, 2018[74]	2	Lennox-gastaut syndrome (children)	CBD	Seizure, tolerability, AEs	<b>H</b>
Lattanzi, 2018[75]	4	Treatment-resistant Dravet syndrome, Lennox-Gastaut (children)	CBD	Seizure, acceptability, tolerability, AEs	<b>M</b>
Lobos Urbina, 2016[76]	29	Cancer (adults)	Cannabinoids	Pain, quality of life, AEs	<b>L</b>
McKee, 2021[77]	31	Opioid use disorder and Cannabis use disorder (adults)	CBM	Opioid use and Cannabis use	<b>L</b>
McCartney, 2021[78]	80	General population (adults)	THC	Driving impairment, cognitive impairment	<b>L</b>
Meza, 2017[79]	7	Multiple sclerosis (adults)	Cannabinoids	Spasticity, pain, AEs	<b>L</b>
Morales, 2017[80]	4	Cancer (chemotherapy, adults)	Cannabinoids	Nausea, vomit, AEs	<b>L</b>
Mucke, 2018[81]	16	Mixed conditions <sup>H</sup> (chronic neuropathic pain, adults)	CBM	Pain, psychological distress, sleep problems	<b>H</b>
Mucke, 2018[82]	8	Cancer, HIV (adults)	CBM	Weight gain	<b>H</b>
Noori, 2021[30]*	5	Cancer pain on opioids	CBM	Constipation, nausea, opioid use, pain, sleep, vomit	<b>L</b>
Rodríguez, 2018[83]	9	Cannabis use disorder (adults)	CBM	Abstinence, craving symptoms, AEs	<b>L</b>
Ruthirakuhan, 2019[84]	6	Alzheimer's disease (elderlies)	CBM	Agitation, cognition, neuropsychiatric symptoms, BMI, Aes, tolerability	<b>H</b>
Sainsbury, 2021[85]	17	Mixed conditions (chronic, neuropathic pain, adults) <sup>I</sup>	CBM, THC/CBD	Pain	<b>L</b>
Spanagel, 2021[86]	26	Mixed conditions (chronic, neuropathic pain, adults) <sup>L</sup>	CBM, THC/CBD	Appetite, sleep	<b>H</b>
Simon, 2022[87]	4	Cancer with cachexia (adults)	Cannabinoids	Appetite	<b>L</b>
Smith, 2015[88]	23	Cancer (chemotherapy, adults)	CBM	Nausea vomit, dysphoria, euphoria, sedation, dizziness, discontinuation due to Aes, participant preference	<b>H</b>
Stockings, 2018[89]	91	Mixed conditions <sup>M</sup> (chronic pain, non-cancer, adults)	CBM	Pain	<b>H</b>
Stockings, 2018[90]	36	Epilepsy (any age)	CBM	Seizure, quality of life, Aes, tolerability	<b>M</b>
Sultan, 2017[91]	25	General population (adults)	CBM	Heart rate, blood pressure, blood flow	<b>M</b>
Thanabalasingam, 2021[92]	3	Parkinson's disease (adults)	Cannabinoids	Motor symptoms	<b>L</b>
Torres-Moreno, 2018[93]	17	Multiple sclerosis (adults)	CBM	Pain, spasticity, bladder dysfunction	<b>H</b>
Treves, 2021[94]	8	Mixed conditions <sup>N</sup> (children)	CBM, THC/CBD	Appetite, gastrointestinal AE, SAE, seizures,	<b>H</b>
Velayudan, 2021[95]	46	Mixed conditions <sup>O</sup> (adults)	CBM	Aes, acceptability, tolerability	<b>L</b>

Author, year	K	Population (age)	Type of cannabinoid #	Outcomes	Quality
Wang, 2008[96]	31	Mixed conditions <sup>P</sup> (adults)	Cannabis	Aes	L
Wang, 2021[97]	32	Mixed conditions <sup>Q</sup> (chronic pain, adults)	CBM or cannabinoids	Pain	H
Watanabe, 2021[98]	47	Mixed conditions <sup>R</sup>	CBM	Hypotension, orthostatic hypotension	L
Whiting, 2015[99]	79	Mixed conditions <sup>S</sup> (NR)	CBM, THC/CBD	Aes	H
Wong, 2020[100]	43	Mixed conditions <sup>T</sup> (chronic pain, non-cancer, adults)	Cannabinoids	Pain	L
Zhang, 2021[101]	2	Schizophrenia (adults)	CBD	Psychotic symptoms	L

Legend. **ADHD**, attention-deficit/hyperactivity disorders; **AE**, adverse events; **BMI**, body mass index; **CBD**, cannabidiol; **CBM**, cannabis-based medications; **CNS**, central nervous system; **HCV**, hepatitis C virus; **HIV**, human immunodeficiency virus; **IQ**, intelligent quotient; **k**, number of studies included in the overall eligible systematic review with meta-analysis; **LBW**, low birth weight; **NAFLD**, non-alcoholic fatty liver disease; **NICU**, admission to neonatal intensive care unit; **NR**, not reported; **SGA**, small for gestational age; **SNP**, single nucleotide polymorphism; **THC**, tetrahydrocannabinol; \*, included both observational studies and randomized controlled trials; ~, fibromyalgia, HIV, IBD, neuropathic pain; #, specific SNPs are reported in Supplementary Table 8; **A**, neuropathic pain, cancer pain, chemotherapy; **B**, neuropathic pain, MS, diabetic neuropathy, HIV, fibromyalgia, muscular pain, rheumatoid arthritis, spasticity; **C**, multiple sclerosis, chronic pain, chemotherapy in cancer; **D**, (HIV, trauma, surgery, complex regional pain syndrome (CRPS) type I, spinal cord injury, peripheral neuropathy, or nerve injury; **E**, cancer pain, opioid resistant chronic cancer pain, advanced stage cancer pain, spinal cord injury, abdominal pain, chronic neuropathic pain, multiple sclerosis, brachial plexus root avulsion, chronic upper motor neuron syndrome, rheumatoid arthritis, HIV, allodynia, unilateral neuropathic pain, fibromyalgia, CRPS type I, knee osteoarthritis, central neuropathic pain, familial Mediterranean fever, diabetes; **F**, Alzheimer's Disease, Spinal cord injury, fibromyalgia, spasticity related pain, functional chest pain, Multiple Sclerosis, Dementia, gastrointestinal transit and postprandial satiation in healthy human subjects, IBD, capsaicin-induced pain and hyperalgesia, experimental heat pain; **G**, Fatty Liver Disease, diabetes mellitus type II, schizophrenia, healthy subjects, epilepsy; **H**, plexus root avulsion, HIV neuropathy, chronic central and PNP, central neuropathic pain in multiple sclerosis, chemotherapy-induced neuropathic pain, diabetic neuropathy, unilateral neuropathic pain, Chronic diabetic peripheral polyneuropathy in diabetes mellitus type 1 and 2, post-herpetic neuralgia, peripheral neuropathy, focal nerve lesion, radiculopathy or CRPS type 2 associated with allodynia, trauma, surgery, phantom limb pain; **I**, HIV, nerve injury, peripheral neuropathic pain, allodynia, diabetic neuropathy, radiculopathy, complex regional pain syndrome type 2, post-herpetic neuralgia, peripheral neuropathy, spinal cord injury, brachial plexus damage, multiple sclerosis, limb amputation; **L**, Dravet syndrome, Lennox-Gastaut syndrome, Tuberosclerosis complex, Schizophrenia, Opioid dependent, Chronic pancreatitis, Cannabis dependent, multiple sclerosis, Alzheimers disease, Parkinson disease or mixed/vascular dementia, miscellaneous cancer in chemotherapy, chronic headache, cocaine use disorder, brachial plexus lesion and neuropathy, phantom limb, Fibromyalgia; **M**, HIV, multiple sclerosis, brachial plexus avulsion, rheumatoid arthritis, Parkinson disease, fibromyalgia, chronic pancreatitis, spinal cord injury, chemotherapy, nociceptive pain, medication overuse headache pain, amyotrophic lateral sclerosis, diabetes, upper motor neuron syndrome, irritable bowel syndrome; **N**, autism spectrum disorder, cancer, cerebral palsy, Dravet syndrome, intellectual disability; **O**, healthy older, dementia, cancer patients with chemosensory alterations, obstructive sleep apnoea, Huntington disease, chronic pancreatitis, Alzheimer disease, cancer-related anorexia, cancer-related pain, chemotherapy induced nausea and vomiting, Parkinson disease, multiple sclerosis, intraocular pressure, diabetic peripheral neuropathic pain, fibromyalgia amyotrophic lateral sclerosis, cervical dystonia, rheumatoid arthritis, type 2 diabetes, chronic obstructive pulmonary disease, healthy controls, motor neurone disease; **P**, Multiple sclerosis, rheumatoid arthritis, neuropathic pain, brachial plexus avulsion, glaucoma, post-operative pain, chemotherapy, cancer, HIV, idiopathic Parkinson's disease; **Q**, Cancer-related chronic pain, Diabetic neuropathy, Peripheral neuropathic pain, Chronic neuropathic pain, Central neuropathic pain in multiple sclerosis, Spinal cord injury-related neuropathic pain, HIV-Associated Neuropathic Pain, Multiple sclerosis, Chronic upper motor neuron syndrome, Fibromyalgia, Endometriosis-related chronic pelvic pain, Vestibulodynia, Chronic abdominal pain, Chronic prostatitis/chronic pelvic pain syndrome, Rheumatoid arthritis, Osteoarthritis, Chronic refractory pain related to musculoskeletal system, Mixed chronic non-cancer pain, Medication overuse headache; **R**, Cannabis dependence, Cancer-related pain, Chronic noncancer pain, Fibromyalgia, Neuropathic pain, Chemotherapy-induced nausea and vomiting, Capsaicin-induced pain and hyperalgesia, dementia, Cervical dystonia, Anorexia associated with weight loss in patients with AIDS, Asthma, Pain management in healthy subjects, Ocular hypertension or early primary openangle glaucoma, multiple sclerosis, Neurogenic symptoms, Levodopa-induced dyskinesia, Primary anorexia nervosa, Analgesic effect in healthy patients, Postoperative pain, IBS, GERD; **S**, Chemotherapy with nausea and vomiting, chronic pain, HIV with loss of appetite, spasticity due to MS or paraplegia, depression, anxiety disorders, sleep disorders, glaucoma, or Tourette syndrome; **T**, multiple sclerosis, neuropathic pain, upper motor neuron syndrome, fibromyalgia, spinal cord injury, headache, diabetic neuropathy, osteoarthritis pain of the knee, chronic pancreatitis, functional chest pain, HIV, post-surgical and post-traumatic pain, brachial plexus avulsion, rheumatoid arthritis, chemotherapy. \*, has both observational studies and randomized controlled trials

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