

Table 2: Systematic Review Summary Table

S/N	Study (Author, Year)	Population & Sample Size	Participants' Characteristics (Age, Gender, SES)	Study Location	Study Design & Setting	Type of Mental Health Disorder	Type of Intervention	Intervention Details	Key Findings & Impact	Barriers to Implementation	Recommendations	Quality Rating
Objective One												
1	Ganes h et al., 2022	n=28 healthy volunteers (Phase 1); Phase 2 subsample n=10; all with ≥1 prior cannabis exposure	Median age ≈25–26 years; 12 women (≈43%); race ~16 White/8 Black/4 other; smokers 18%; frequent cannabis users 25%; BMI ~26; SES not Reported	USA	Two-phase, double-blind, randomized, placebo-controlled, counterbalanced crossover human laboratory study	Acute psychotomimetic effects/psychosis-like symptoms in healthy volunteers	CBD pretreatment + THC challenge (vs placebo/alone)	IV THC 0.035 mg/kg (~2.5 mg/70 kg) over 20 min; IV CBD 2.5, 5, or 7.5 mg over 2 min immediately before THC (CBD:THC ratios ~1:1, 2:1, 3:1); outcomes: PANSS (positive/negative/general/total), CADSS, VAS “high/anxious”, EEG neural noise (Lempel-Ziv complexity)	CBD attenuated THC-induced psychotomimetic effects and neural noise; maximal attenuation at 1:1 CBD:THC (PANSS-positive and LZC significant); 2:1 significant in THC “responders” subgroup; no reduction in THC subjective “high”; 3:1 most attenuated anxiety	Small total N (esp. Phase 2 n=10); laboratory IV route (limited ecological validity); only partial counterbalancing; healthy volunteers (not clinical populations); short-term outcomes only	Replicate in larger samples (incl. clinical psychosis), test broader CBD:THC ranges and real-world routes; standardize biomarkers (e.g., LZC) in trials; consider harm-reduction guidance around ~1:1 CBD:THC; account for individual vulnerability/genetics	Moderate
2	Chestre et al., 2021	CHR cohort	Age: mostly 16–35 (mean ≈22–23); Gender: ~53% male in CHR; Ethnicity: majority White; SES: not reported	Multicentre: 11 sites across Europe, Australia, South America (HCs from London, Amsterdam, Den Haag,	Prospective cohort (longitudinal), baseline + 12m + 24m assessments; CHR defined by CAARMS; controls matched on age/gender	Clinical High Risk (CHR) for psychosis; outcomes: transition to psychotic disorder, persistence of CHR symptoms, functioning (GAF)	Exposure (no treatment): cannabis use metrics	Baseline cannabis status (never/ex/current); age at first use (≤15 vs >15); frequency (daily/weekly/<weekly); potency (>10% THC	No significant association between any baseline cannabis measure and transition to psychosis (HRs ns), persistence of symptoms,	Self-report cannabis measures; 36% missing follow-up cannabis data; no biological verification; possible cessation before baseline; heterogeneity within CHR;	Future studies should track within-subject cannabis changes over time; include biomarkers (urine/blood/hair); oversample adolescents for early use; analyze CHR subgroups ; reduce missingness; adjust for	Moderate

				Melbourne)				vs <10%); dependence (DSM-IV); CEQ-based; outcomes via CAARMS; functioning via GAF	or functional outcome after appropriate modeling; contrasts with some epidemiological case-control data	follow-up limited to 2 years; retrospective recall of early use	confounders (alcohol/other drugs, genetics)	
3	Ahmed et al., 2021	11 controlled studies (THC and CBD). Across CBD trials: 152 stable outpatients + 45 acutely psychotic inpatients; THC trials included ~ 25 stable outpatients (some overlap across reports). Sample sizes per study ranged n=3–88 .	Age mostly young–middle adult (several <30; others ~40s); 58–89% male across trials; ethnicity variably reported; SES not reported .	Multi-country across included trials (not one site)	Systematic review of prospective RCTs/controlled human lab studies (single-dose and 4–6-week trials), using GRADE to appraise bias/directness.	Schizophrenia spectrum disorders (schizophrenia, schizoaffective; early psychosis in some)	THC and/or CBD (monotherapy or augmentation)	THC: IV 2.5–5 mg; smoked 3.6% THC; oral 15 mg. CBD: 300–1,280 mg/day (single dose or 4–6 weeks); 800 mg CBD ≈ amisulpride on symptoms; augmentation at 600 mg (null) vs 1,000 mg (improved positive symptoms). fMRI/ ¹ H-MRS in some trials.	Overall: insufficient evidence that THC or CBD improve symptoms/cognition. One IV-THC RCT worsened psychosis and learning/recall; low-dose THC in CUD samples showed resting-state network normalization on without symptom change. CBD results mixed: 800 mg similar to amisulpride (fewer EPS/weight/prolactin), 1,000 mg adjunct reduced positive symptoms ; other trials null ; single-dose CBD showed partial	Heterogeneity in dose, route, duration; small samples; inconsistent inclusion/exclusion of CUD/ongoing cannabis use ; variable antipsychotic statuses; some industry funding ; short follow-up; limited biological verification; indirectness (imaging surrogates).	Run larger, well-powered RCTs with standardized dosing/route/duration; stratify by CUD and monitor substance use longitudinally with biomarkers ; examine CBD dose–response and head-to-head vs antipsychotics; include clinically meaningful outcomes (symptoms, cognition, functioning) alongside mechanistic imaging.	Moderate

									circuit normalization on and ↑ hippocampal glutamate.			
4	Choi et al., 2024	47,100 U.S. adults	Age: 18+; Gender: Mixed; SES: Mixed	USA	Cross-sectional survey	Mental illness (general), chronic illness, cannabis use disorder (CUD)	CBD use (alone or co-use with cannabis)	Self-reported CBD and cannabis use within past 12 months; outcomes—CBD-only, cannabis-only, and CBD+cannabis co-use; correlates analyzed using generalized linear models	20.6% reported CBD use; 63% of CBD users also used cannabis; CBD-only use higher among women, older, higher SES, those with chronic/mental illness, and high risk perception; co-users had highest risk for chronic illness, mental illness, and substance use problems	Cross-sectional design limits causality; self-report bias; no verification of product content/dose; possible underreporting	Longitudinal research on mental health outcomes of CBD vs. co-use; assess pharmacological purity and drug interactions; issue public health warnings on potential side effects and drug–drug interactions	High
Objective Two												
5	Sexton et al., 2016	1,429 self-identified medical cannabis users (out of 2,404 eligible respondents)	Age range 15–80 years (M = 36.3); Gender: 54.6% male, 45.4% female; Ethnicity: 86.5% Caucasian; Income: 47.4% < \$40,000; Education: 37% bachelor's or higher; Employment: 47.7% full-	Predominantly Washington State (USA); respondents from 18 countries	Anonymous online cross-sectional survey; self-selected sample recruited via dispensaries, social media, and university websites	Broad range: pain, anxiety, depression, headaches, nausea, muscle spasticity (mental health symptoms included depression and anxiety)	Medical cannabis	44-item online questionnaire assessing conditions treated, perceived efficacy, route, dosage, substitution for prescription drugs; PROMIS Global Health for physical	Most common conditions: pain (61.2%), anxiety (58.1%), depression (50.3%). Users reported an 86% average symptom improvement ; 59.8%	Self-selected convenience sample; overestimation of efficacy due to self-report and placebo effects; lack of randomization or control; underrepresentation of minorities and certain illnesses; online-only recruitment	Conduct controlled trials to verify efficacy and safety; expand inclusion of underrepresented clinical populations (e.g., cancer, epilepsy); explore harm-reduction and substitution effects for opioids; refine public health policy based on patient-reported outcomes	Moderate

			time, 14.1% disabled					and mental well-being	substituted cannabis for prescription drugs (mostly opioids); perceived mental and physical health scores similar to U.S. population; 41% sought high-CBD strains for anxiety/depression			
6	Sarris et al., 2020	13 human clinical studies/case series included (from 310 screened; search to July 2019)	Heterogeneous across included studies; mixes of out/inpatients, mostly adults; varying inclusion of cannabis use/CUD	Multinational literature (no single site)	Systematic review of clinical trials & case studies on whole-plant cannabis and plant-derived isolates for psychiatric disorders	Anxiety (incl. social anxiety), PTSD, insomnia, schizophrenia/psychosis, depression, bipolar disorder, ADHD	Medicinal cannabis & plant-derived cannabinoids (CBD, THC, nabiximols)	Routes: oral, inhaled, sublingual. Typical CBD doses 200–1200 mg/day; nabiximols ~2.7 mg THC + 2.5 mg CBD per spray; emphasis on avoiding high-THC in vulnerable groups	Evidence nascent : tentative support for CBD in social anxiety (acute) and as adjunct in schizophrenia ; case/weak observational signals for PTSD and insomnia ; no benefit for depression with high-THC; CBD not effective for mania; limited/nominal findings in ADHD	Small samples, heterogeneous designs/doses/routes, limited RCTs, blinding difficulties (THC psychoactivity), regulatory constraints, variable inclusion/exclusion of CUD, pharmacogenomic variability	Avoid high-THC, especially in youth and those with anxiety/psychosis; start low/titrate slow; screen for psychosis, CUD, CV/respiratory risks, pregnancy; monitor function/driving/occupational safety; prioritize high-quality RCTs on CBD (alone/with THC), dose-finding, pharmacogenomics, and long-term safety	Moderate
7	Bonaccorso et al., 2019	27 studies reviewed	Age: Mixed; Gender: Mixed; SES: Mixed	International (multinational literature)	Systematic review	Substance use disorders, psychosis, anxiety	CBD, nabiximols	Doses across studies: oral/sublingual CBD (ranging 300–1500 mg/day); duration: acute	Limited but emerging evidence for CBD's therapeutic potential in psychosis ,	Limited number of studies; variability in formulations	Conduct large-scale, well-controlled RCTs on CBD across psychiatric conditions; explore long-term safety ,	Moderate

								to 8-week trials; comparison groups: placebo, standard care, or antipsychotics	anxiety, and substance use disorders; minimal evidence for depression or sleep; CBD generally well-tolerated with few adverse effects; low abuse potential		dose-response, and specific subpopulation effects	
8	McKee et al., 2021	31 RCTs	Age: Adults; Gender: Mixed; SES: Mixed	Global (multi-country trials)	Systematic review & meta-analysis	Schizophrenia, anxiety, cannabis/opioid/tobacco use disorder, ADHD, PTSD, OCD, anorexia nervosa, Tourette's disorder	Cannabinoid-based products (CBPs) including THC, CBD, or mixed formulations	Oral, oromucosal, or inhaled CBPs; varying THC/CBD ratios; short-term interventions (acute to several weeks)	Limited evidence supporting acute symptom relief for select psychiatric disorders (notably schizophrenia and anxiety); no robust mid- or long-term benefits observed; no evidence supporting cannabis flower use for any psychiatric disorder	Heterogeneity in interventions, small sample sizes, variable cannabinoid content, lack of long-term follow-up, inconsistent outcome measures	Urgent need for large-scale, hypothesis-driven RCTs ; focus on standardized CBP formulations and long-term efficacy/safety ; discourage cannabis flower as treatment	Moderate
9	Black et al., 2019	k=83 studies; k=40 RCTs (n=3,067)	Age: Mixed; Gender: Mixed; SES: Mixed	Multinational	Systematic review & meta-analysis	Depression, Anxiety, PTSD, ADHD, Tic/Tourette, Psychosis	Pharmaceutical THC (±CBD), pharmaceutical CBD, medicinal cannabis	Routes mostly oral/oromucosal; short durations (median 3.5–7 wks); few CBD-only or whole-plant cannabis RCTs	No evidence of benefit for depressive disorders/symptoms, ADHD, Tic/Tourette, PTSD, or psychosis. Very-low-	VariabilitySmall, short trials; indirectness (MH not primary in many RCTs); heterogeneity; incomplete reporting; few CBD/whole-plant studies;	Do not recommend cannabinoids for MH disorders at present. Prioritize large, diagnosis-specific, hypothesis-driven RCTs with standardized products, longer	Low

									quality signal that THC(±CBD) yields small anxiety reduction in patients with other medical conditions (SMD −0.25; k=7; n=252). In psychosis, one study found worsening of negative symptoms with THC(±CBD) (SMD 0.36; n=24). Adverse events increased with THC(±CBD) (AEs OR 1.99; withdrawals due to AEs OR 2.78). Very few RCTs of CBD; pooled psychosis outcomes largely null; one study showed improved global functioning. No RCT support for medicinal cannabis flower.	blinding challenges in study designs; short duration of studies	follow-up, and robust safety monitoring. Avoid THC in psychosis; caution generally due to AEs.	
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10	Allan et al., 2018	31 systematic reviews included (46 review foci; median 7 RCTs per review; ~725 participants per meta-analysis)	Age: Mixed; Gender: Mixed; SES: Mixed	International (systematic review of global RCTs)	Systematic review of systematic reviews	Pain (neuropathic, cancer), nausea/vomiting (chemotherapy-related), spasticity (MS), and general adverse psychiatric/cognitive effects	Medical cannabinoids (THC, nabilone, dronabinol, nabiximols, inhaled or buccal cannabinoids)	Oral, buccal spray, and inhaled formulations; comparison with placebo or standard antiemetics; trials up to 15 weeks	Pain: Small improvement (RR = 1.37, NNT = 11) mostly for neuropathic pain. Nausea/vomiting: Strong effect (RR = 3.60, NNT = 3). Spasticity: Modest improvement (RR = 1.45, NNT = 7). Adverse events: Very common—NNH = 5–22 for dizziness, sedation, confusion, dissociation; psychosis rare but more frequent in naïve users. GRADE: <i>low–very low</i> certainty for most outcomes.	Short RCT durations; small sample sizes; heterogeneity; high bias risk; overrepresentation of experienced cannabis users; inconsistent dosing; limited psychiatric endpoints	Limit use to refractory cases (e.g., resistant nausea/spasticity); avoid in psychiatric vulnerability; use only standardized formulations (not smoked cannabis); monitor for cognitive/psychiatric side effects; improve RCT quality	Moderate
Objective Three												
11	Sorkhau et al., 2021	124 studies reviewed	Age: Mixed; Gender: Mixed; SES: Mixed	Global (multi-country primary studies)	Systematic review of cross-sectional & longitudinal human studies	Cognition (memory, attention, IQ), motivation, impulsivity, mood, anxiety, psychosis, psychosocial/educational/occupational functioning	Cannabis use exposure (not therapeutic use)	Exposure variables included frequency, potency (THC/CBD content), age of onset, and cumulative lifetime cannabis use	Frequent or early cannabis use, especially high-THC exposure, was associated with adverse behavioral outcomes , including cognitive	Heterogeneity in methodologies and exposure measurement; confounding variables (e.g., alcohol/tobacco use, socioeconomic factors); limited causal inference due to observational	Need for preventive strategies emphasizing delayed initiation and lower THC potency; education on potential cognitive and psychiatric risks; call for longitudinal research clarifying dose–response effects and	Moderate

									impairment, increased impulsivity, emotional instability, anxiety, and risk for psychosis. Strongest evidence linked cannabis to psychosis and psychosocial dysfunction even in healthy populations. psychosis and cognitive impairments	designs; inconsistent THC/CBD dosage reporting.	distinguishing THC from CBD impacts.	
12	Berny et al., 2025	17 RCTs	Age: Mixed; Gender: Mixed; SES: Mixed	International (predominantly U.S., U.K., and Australia)	Systematic review & meta-analysis	Cannabis use disorder	Brief drug interventions	Brief counseling, motivational interviewing, or psychoeducation sessions; some with booster sessions; delivered in primary care, emergency departments, and general hospitals	No significant short-term or long-term reductions in cannabis use (OR = 1.20, 95% CI [0.90–1.62]; g = 0.01, 95% CI [–0.07–0.09]) or severity (g = 0.13, 95% CI [–0.07–0.33]). Sensitivity analysis indicated small significant reductions in long-term use when delivered in emergency departments.	Limited intervention intensity; heterogeneity in delivery settings and populations; inadequate long-term follow-up; variability in fidelity and clinician training; potential reporting bias.	BDIs may yield modest benefits in acute/emergency settings but lack efficacy for general cannabis reduction. Future trials should test extended or tailored intervention models and focus on higher-risk or treatment-seeking populations.	High

13	Sorkh u et al., 2024	78 studies (N ≈ 3,262 screened) including observati onal, longitudi nal, and one RCT	Adults and adolescents across diverse socioeconomic and cultural backgrounds; mixed-gender samples; clinical and general populations	Internatio nal (studies from North America, Europe, and other regions)	Systematic review of cross-sectional, longitudinal, and clinical studies	Major Depressive Disorder (MDD), Bipolar Disorder (BD), and related mood symptoms (mania, suicidality)	Cannabis use and cannabinoid exposure (THC/CBD; medical and non-medical)	Evaluated cannabis and cannabinoid (THC, CBD) use in relation to onset, course, and prognosis of mood disorders; included one RCT using adjunctive cannabidiol (150–300 mg/day)	Cannabis use associated with elevated depressive and manic symptoms, increased risk of developing MDD and BD, and poorer prognosis (e.g., greater symptom severity, suicidality, rapid cycling, hospitalizatio ns, and reduced treatment adherence). One RCT showed CBD safe but not clinically superior to placebo for BD. Abstinence studies suggested partial reversibility of cognitive/mo od deficits.	High heterogeneity across studies (measurement tools, cannabis potency, and confounders); few randomized trials; limited objective verification of cannabis use; absence of gender-specific analyses; reliance on self-report; difficulty isolating THC vs CBD effects.	potency, and confounders); few randomized trials; limited objective verification of cannabis use; absence of gender- specific analyses; reliance on self- report; difficulty isolating THC vs CBD effects. Routine screening of cannabis use in patients with mood disorders; public education on cannabis-related psychiatric risks; longitudinal and neurobiological studies to clarify causality; clinical trials on standardized cannabinoids; develop gender- sensitive interventions and safer symptom- management alternatives.	High
14	Moore et al., 2007	35 longitudi nal, populatio n-based studies (from 4,804 records)	Age: Mixed; Gender: Mixed; SES: Mixed	Internatio nal (multi- country cohorts)	Systematic review of of longitudinal studies; independent duplicate screening, extraction, quality assessment	Psychotic outcomes (incl. clinical psychotic disorders); affective outcomes (depression, anxiety, suicidal ideation)	Exposure (cannabis use) vs. non- use; observational (no clinical intervention)	Any/lifetime and frequency of cannabis use; dose- response examined (e.g., most- frequent users)	Psychosis: Any use ↑ risk (pooled adjusted OR = 1.41, 95% CI 1.20– 1.65); dose- response — most- frequent	Confounding factors; variability in study designs; reliance on observational data	Conduct randomized controlled trials; control for confounders; standardize measurement tools	High

									users OR = 2.09 (1.54–2.84). Effects persisted after addressing intoxication and confounding. Affective outcomes: results less consistent and less rigorously adjusted. Public-health impact: sufficient evidence to warn youth that cannabis can increase later psychosis risk.			
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