Appendix

Table 1. Search Strategy and Eligibility Criteria

Component	Description
Databases Searched	PubMed, Google Scholar, Ovid MEDLINE
Search Terms	“fecal microbiota transplantation”, “FMT”, “comorbidity”, “gut-brain axis”, “mental health”, “depression”, “anxiety”, “irritable bowel syndrome”, “inflammatory bowel disease”, “gut dysbiosis”; with Boolean operators (AND, OR)
Publication Dates	2015–2025
Languages	English
Study Types	Primary research, clinical trials
Inclusion Criteria	Peer-reviewed studies examining FMT for GI and/or MH symptoms; studies involving phenotype transfer via FMT
Exclusion Criteria	Case studies, reviews, non-English publications
Total Included	24 studies

Table 2. Fecal Microbiota Transplantation to Cure Psychiatric Disorders – IBS Rodent Trials

Study	GI Condition(s)	GI Measure	Psychological Condition(s)	Psychological Measure	Donor	Recipient	Purpose of FMT	Conclusions
De Palma et al., 2017 [2]	IBS (via IBS fecal transplant)	Intestinal motility	Anxiety	Anxiety-like behaviour in mice	IBS-D patients (with and without GAD)	GF mice	Induce	IBS microbiota induced GI dysfunction and anxiety-like behaviour. Supports microbiota's causal role in IBS pathophysiology.
Kelly et al., 2016 [33]	Dysbiosis (via MDD fecal transplant)	Intestinal transit time, inflammation, microbiota composition	Depression	Anxiety / depression-like behaviours	MDD patients and healthy controls	GF mice	Induce	FMT from MDD patients induced dysbiosis, inflammation and anxiety/depression-like behaviours in mice.
Liu et al., 2020 [34]	Dysbiosis (via MDD fecal transplant)	Mitochondrial damage in intestinal epithelial cells	Depression	Anxiety / depression-like behaviours	MDD patients and healthy controls	GF mice	Induce	FMT from MDD patients induced anxiety/depression-like behaviours via the neuroendocrine-immune-mitochondrial pathway.
Li et al., 2019 [35]	Stress-induced IBS	Dysbiosis, gut inflammation	Anxiety, Depression	Anxiety / depression-like behaviours	CUMS-exposed mice	Antibiotic-treated mice	Induce	FMT induced GI dysbiosis and anxiety/depression-like behaviours. Supports the role of dysbiosis in IBS-like features and neuroinflammation.

Study	GI Condition(s)	GI Measure	Psychological Condition(s)	Psychological Measure	Donor	Recipient	Purpose of FMT	Conclusions
Cai et al., 2022 [28]	Stress-induced GI symptoms	Colonic motility, inflammation	Depression	Depressive behaviour, BDNF, glutamate, GABA levels	Healthy rats	CUMS-exposed rats	Treat	FMT reversed depressive behaviours, improved GI symptoms and restored balance of neurotransmitters and immune markers.
Rao et al., 2021 [36]	Stress-related GI issues	Dysbiosis, neuroinflammation, intestinal barrier integrity	Depression	Depression-like behaviours, neuro-inflammation	Healthy rats	CUMS-exposed rats	Treat	FMT decreased depressive behaviours, reduced inflammation and improved GI integrity. Supports FMT for GI and MH symptoms in IBS.

Notes: BDNF = brain-derived neurotrophic factor; CUMS = chronic unpredictable mild stress; FMT = fecal microbiota transplantation; GABA = gamma-aminobutyric acid; GAD = generalized anxiety disorder; GF = germ-free; GI = gastrointestinal; IBS = irritable bowel syndrome; IBS-D = diarrhea-predominant irritable bowel syndrome; MDD = major depressive disorder; MH = mental health.

Table 3. Fecal Microbiota Transplantation to Cure Psychiatric Disorders – IBS Human Trials

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
Kurokawa et al., 2021 [37]	OLT	IBS (IBS-SSS)	Depression (HAM-D, QIDS), anxiety (HAM-A)	Healthy donor (excl. Obesity, IBD, Atopic dermatitis, recent antibiotic use)	IBS, FDr, and FC patients (excl. Liver and/or renal dysfunction, malignant tumour history, pregnancy, severe psychiatric disorders, < 20 years of age)	6 out of 12 patients with clinical HAM-D and 3 out of 5 patients with clinical HAM-A scores reduced to normal levels following FMT. Depression and anxiety scores improved FMT improved GI, depression, and anxiety scores. Supports therapeutic potential of FMT.
El-Salhy et al., 2020 [39]	RCT	IBS (IBS-SSS, Birmingham IBS-S)	Fatigue (FAS), QoL (IBS-QoL)	'Superdonor' (screened medical history, lifestyle habits, exposure to infectious agents, sexual behaviour, substance use, blood test for GI, metabolic and inflammatory markers, and liver and thyroid function. Analyzed fecal	IBS patients (18-85, >175 in IBS-SSS. Excl. systemic disease, immune deficiency, pregnant, abdominal surgeries, severe psychiatric disorder, substance abuse, recent probiotic use, IBS medication use)	FMT significantly improved GI and MH symptoms for three months.

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
				bacteria to ensure normobiotic)		
Huang et al., 2019 [40]	OLT	IBS-D subtype (IBS-SSS)	Depression, (HAM-D), anxiety (HAM-A), QoL (IBS-QOL)	Healthy donor (18-35 years old. Excl. pregnancy, substance or antibiotic use, history of disease related to gut flora, history of high-risk sexual behaviour)	Refractory IBS patients (unresponsive to treatments utilizing diet, antibiotics, probiotics, antidepressants or psychotherapies. Excl. pregnancy, severe disease)	FMT improved IBS GI symptoms and alleviated depression and anxiety scores at 1 month and 3 months after. Supports therapeutic use of FMT.
Mazzawi et al., 2018 [41]	OLT; FMT via colonoscopy	IBS (IBS-SSS, stool frequency)	Depression and anxiety (HAM-D), neuroticism (EPQ-N-12)	Healthy donors (excl. infectious agents and inflammation)	IBS patients	FMT reduced IBS severity and psychological distress at first (week 1) and second (week 3) visit following treatment, but not at visit

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
						3 (week 12). Supports short-term efficacy of FMT.
Mazzawi et al., 2022 [42]	RCT	IBS (IBS-SSS, stool frequency)	Depression and anxiety (HAM-D), neuroticism (EPQ-N-12)	First-grade relatives of recipient living in same household (>18 years old. Excl. history of disease, recent antibiotic or probiotic use, IBD, pregnant)	IBS patients (18-65 years old, >175 IBS-SSS. Excl. history of disease, recent antibiotic or probiotic use, IBD, pregnant)	No significant differences in depression or anxiety symptoms of 11 IBS patients in the 24 weeks following endoscopic FMT. The authors suggest small sample size contributed to Type II error.
Lahtinen et al., 2019 [43]	RCT	IBS (IBS-SSS)	Depression (BDI) and anxiety (BAI)	Healthy donor (Excl. long-term diagnoses or medication, history of high-risk sexual behaviour, substance use, exposure to infection)	IBS patients (18-73 years old. Excl. IBD, pregnant)	Transient GI response at 12-week follow-up, but did not differ from control. Association between the decrease of IBS symptoms and the improvement of BDI score. Single infusion FMT via colonoscopy cannot be recommended as a treatment for IBS.

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
Guo et al., 2021 [44]	RCT	IBS-D	Anxiety and depression (previous diagnosis)	Healthy Donor	IBS-D patients (Excl. abdominal surgery, virus, kidney disease, psychosis, pregnancy, active infection, abnormal thyroid function, recent use of prebiotics, probiotics, or antibiotics)	FMT improved IBS, depression, and anxiety symptoms throughout the 12 week trial. Supports FMT for GI and comorbid MH symptoms.
Tian et al., 2016 [45]	OLT	IBS (Rome III criteria, Wexner constipation scores)	QoL	Healthy Donor (Excl. illness, viruses, pregnant, use of probiotics, prebiotics or antibiotics)	Patients with STC (20-74 years old, unresponsive to alternative IBS treatments. Excl. psychiatric and GI disorders, pregnancy, use of probiotics, prebiotics, or antibiotics)	FMT improved GI symptoms and QoL throughout 12 week follow up.
Aroniadis et al., 2018 [46]	RCT	IBS-D (IBS-SSS)	QoL (IBS-QoL), Anxiety / depression (HADS)	Healthy donor	Patients with IBS-D	FMT did not induce significant symptom relief compared to placebo control group. Does not support FMT for anxiety, depression, and GI symptoms or QoL.

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
Holster et al., 2019 [47]	RCT	IBS (All subtypes; Rome III)	QoL (IBS-QoL), Anxiety / depression (HADS)	Healthy donor (Excl. long-term diagnoses or medication, history of high-risk sexual behaviour, substance use, exposure to infection, obesity, allergies)	Adult IBS patients (Excl. GI disease or surgery, dementia, severe depression, major psychiatric disorder, endometriosis, lactose intolerance, celiac disease, pregnancy, probiotic use, substance abuse)	FMT did not induce significant symptom relief compared to placebo control group. Does not support FMT for anxiety, depression, and GI symptoms or QoL.
Johnsen et al., 2020 [48]	RCT	IBS (non-constipated; Rome III, IBS-SSS)	Fatigue (FIS); QoL (IBS-QoL); Depression (self-assessment questionnaire)	Healthy donors	Adult IBS patients (18–75 years old)	FMT improved GI, QoL, and fatigue scores. Effects were maintained for 6 months, but had waning effect from 6 to 12 months. Supports transient effect of FMT.
Mizuno et al., 2017 [49]	OLT	IBS (Rome III, IBS-SSS)	Depression, (HAM-D), anxiety (HAM-A)	Healthy relatives (second degree; screened for	Adult IBS patients (Over 19 years old)	Improved GI, anxiety, and depression symptoms. Supports FMT as treatment for IBS and comorbid psychological symptoms.

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
				pathogens and viruses)		
Halkjær et al., 2018 [50]	RCT	IBS (Rome III, IBS-SSS)	QoL (IBS-QoL)	Healthy donor (18-45 years old. Excl. medication use, virus, disease or infection, substance abuse, allergies, family history of high-risk conditions, history of high-risk sexual behaviours, recent tattoo, piercing, antibiotic use)	Adult IBS patients (IBS-SSS ≥175. Excl. other chronic GI disease, psychiatric disorder, substance abuse, pregnant)	FMT improved GI and QoL in both healthy donor FMT and placebo group. No significant difference between groups. Does not support FMT having treatment effects above placebo.

Notes: BAI = Beck anxiety inventory; Birmingham IBS-S = Birmingham IBS symptom score; BDI = Beck depression inventory; EPQ-N-12 = Eysenck personality questionnaire-neuroticism; FAS = fatigue assessment scale; FIS = fatigue impact scale; HADS = hospital anxiety and depression scale; HAM-A = Hamilton rating scale for anxiety; HAM-D = Hamilton rating scale for depression; IBD = inflammatory bowel disease; IBS-SSS = IBS severity scoring system; IBS-QoL = IBS quality of life questionnaire; OLT = open-label trial; QoL = quality of life; RCT = randomized controlled trial; Rome III = Rome III diagnostic criteria for functional gastrointestinal disorders; STC = slow transit constipation.

Table 4. Fecal Microbiota Transplantation to Cure Psychiatric Disorders – IBD Rodent Trials

Study	GI Condition(s)	GI Measure	Psychological Condition(s)	Psychological Measure	Donor	Recipient	Purpose of FMT	Conclusions
Yoo et al., 2022 [51]	IBD (UC/CD)	Colitis symptoms, hippocampal and colonic inflammation	Depression	Depressive-like behaviours in mice	IBD patients with depression (UC, CD), healthy donors, mice with stress-induced depression	GF mice, SPF mice	Induce and treat	FMT from IBD patients induces GI inflammation in GF mice. FMT from IBDD patients causes depression with GI inflammation in SPF mice. FMT from mice with stress-induced depression causes depression and GI inflammation and dysbiosis in SPF mice. FMT from healthy donors reverses these effects.
Jang et al., 2021 [52]	IBDD	Colitic symptoms, neuro-inflammation	Depression, (HAM-D), anxiety (HAM-A)	Anxious and depressive behaviours in germ-free mice	IBD patients with varying depression severity vs. healthy donors	GF mice	Induce and treat	FMT from IBD patients induced GI and MH symptoms in mice; donor depression severity influenced mouse behaviours; healthy donor FMT reduced symptoms.

Notes: IBDD = inflammatory bowel disease with depression; SPF = specific pathogen-free; UC = ulcerative colitis.

Table 5. Fecal Microbiota Transplantation to Cure Psychiatric Disorders – IBD Human Trials

Study	Study Design	GI Condition(s)	Psychological Condition(s)	Donor	Recipient	Conclusions
Ding et al., 2019 [53]	OLT	UC	QoL (EQ-5D)	Healthy donors (age 5-24. Excl. psychological disorder or behavioural abnormality, antibiotic use, tattoos or piercings, present or family history of disease/infection)	UC patients (documented diagnosis, moderate-severe active UC)	FMT was safe and effective for improving GI symptoms and QoL in UC patients, lasting at least one year following treatment.
Kilincarslan et al., 2020 [54]	OLT	UC, CD (Mayo score ≥6, Harvey-Bradshaw Index score ≥7)	General psychiatric symptoms (SCL-90-R), Depression (BDI), OCD (MOCI)	Donor (excl. neuropsychiatric or somatic illnesses, regular medication use)	IBD patients (excl. treatment of psychiatric or neurological disorder, substance abuse, acute psychotic state, and recent use of prebiotics, probiotics and antibiotics)	FMT reduced all psychological measures. Supports FMT for MH improvements in IBD treatment.
Wei et al., 2015 [55]	OLT	UC, CD	QoL (IBDQ)	Donor (excl. Recent antibiotic use, GI condition, disease/parasites.	IBD patients (18-70 years old. Excl. pregnant, infectious, prebiotic, probiotic or antibiotic use)	FMT improved QoL among IBD patients.

Notes: CD = Crohn's disease; EQ-5D = EuroQol-5 dimension; IBDQ = inflammatory bowel disease questionnaire; MOCI = Maudsley obsessive compulsive inventory; SCL-90-R = symptom checklist-90-revised.