

Supporting Information

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Toward a Deeper Understanding of Gut Microbiome in Depression: The Promise of Clinical Applicability

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Supplementary Tables

**Towards a deeper understanding of gut microbiome in depression:
the promise of clinical applicability**

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Table S1. Characteristics of studies investigating gut microbiota composition in patients with depression.

Study	People	Study design	groups	Age (Years) (mean±SD) Patients Control	Sex (M/F) Patients Control	BMI Patients Control	Comorbidity	Drug treatment in patients	Diagnostic criteria	Severity measure	Severity (mean±SD) Patients Control	Sample	Storage	Gut microbiome estimation	Sequencing region	Microbial biomarkers from comparisons	Microbial biomarkers selection
Aizawa E et al. 2016 ¹¹	Japanese	Case-control	MDD (N=43) Control (N=57)	39.4(10.0) 42.8(12.7)	25/18 22/35	23.2(3.6) 22.3(3.7)	In MDD: 14 IBS; In controls: 7 IBS	In MDD: 28 Imipramine	DSM-IV	HAMD-21	16.9(6.8) NA	Fecal samples	-4°C and -80°C	RT-qPCR for Bifidobacterium and Lactobacillus	NA	MDD and Controls	MannWhitney U test: p < 0.05
Bai S et al. 2021 ¹²	Chinese	Case-control	MDD (N=60) Control (N=60)	35.62(17.10) 35.13(15.79)	21/39 24/36	20.90(2.30) 21.19(4.29)	NA	NA	DSM-IV, HAMD-17 > 17	HAMD-17	25.36(0.01) 0.67(0.93)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	LEfSe: p < 0.05 and LDA > 2.0
Bai S et al. 2022 ¹³	Chinese	Case-control	MDD (N=56) Control (N=56)	35.11(16.79) 35.71(15.99)	18/38 20/36	20.94(2.37) 21.23(4.27)	NA	NA	DSM-IV-TR	HDRS	24.86(5.94) 0.71(0.95)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	LEfSe: p < 0.05 and LDA > 2.0
Cao JR et al. 2021 ¹⁴	Spanish	Case-control	Active MDD (N=46) Remission MDD (N=22) Control (N=45)	42.1 45.85 44.72	10/36 5/17 11/34	-	-	-	DSM-IV-TR, HDRS≥14	HDRS	21.17 10.54 0.08	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Active MDD and Controls	Kruskal-Wallis test followed by Bonferroni-adjusted analysis: p < 0.05
Chahwan B et al. 2019 ¹⁵	Australian	Case-control	Depression (N=71) (N=68 provided stool samples) Controls (N=20)	36.05(11.99) 35.95(11.74)	22/49 5/15	-	-	In depression: 38 Antidepressant, 46 Psychological treatment	DSM-IV MINI; ICD-10	BDI-II	28.43 (9.90) 2.80 (2.78)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Clinical/Subclinical Depression and Controls	Kruskal Wallis test with the False Discovery Rate (FDR) correction: adjusted p < 0.05 Spearman's Correlations (with FDR correction for multiple testing): adjusted p < 0.05
Chen DL et al. 2021 ¹⁶	Chinese	Case-control	UC (N=31) UC with depression (N=31) Control (N=31)	44.16(11.49) 41.94(13.42) 43.13(10.98)	17/14 16/15 16/15	22.8(1.9) 22.1(2.1) 22.4(2.6)	ulcerative colitis	NA	SDS≥53	SDS	-	Fecal samples	-80°C	16S rRNA gene sequencing-pyrosequencing	V3-V4	UC with depression and Controls	ANOVA: p < 0.05
Chen JJ et al. 2018 ¹⁷	Chinese	Case-control	MDD-female (N=24) control-female(N=24) MDD-male (N=20) control-male(N=20)	41.5(11.53) 43.95(12.11) 40.35(11.05) 42.80(15.13)	0/24 0/24 20/0 20/0	22.01(2.17) 22.63(2.43) 22.22(2.18) 22.50(2.25)	3 female patients had coexisting anxiety disorders. 2 male patients had coexisting anxiety disorders.	-	DSM-IV	HDRS-17	23.04(4.93) - 23.9(3.68) -	Fecal samples	-80°C	16S rRNA gene sequencing-Roche 454 sequencing	V3-V5	Female and male MDD and corresponding controls	LEfSe: p < 0.05 and LDA > 2.0
Chen JJ et al. 2020 ¹⁸	Chinese	Case-control	MDD-young(N=25) control-young(N=27) MDD-middle-aged (N=45) control-middle-aged(N=44)	24.0(3.74) 24.96(2.31) 44.96(7.76) 47.16(8.07)	7/18 8/19 14/31 10/34	22.13(2.24) 21.53(2.37) 22.64(2.64) 23.23(2.33)	NA	In young MDD: 7 medications In middle-aged MDD: 14 medications	DSM-IV	HDRS-17	22.64(3.18) 0.29(0.61) 23.0(4.61) 0.34(0.74)	Fecal samples	-80°C	16S rRNA gene sequencing-Roche 454 sequencing	V3-V5	Young and middle-aged MDD and corresponding controls	LEfSe: p < 0.05 and LDA > 2.0
Chen T et al. 2021 ¹⁹	Chinese	Case-control	UC with depression (N=16) UC (n=19)	41.31(12.2) 43.68(12.73)	7/9 10/9	22.49(2.64) 21.08(3.44)	Ulcerative colitis (UC)	NA	PHQ-9;10	PHQ-9	13.75(3.96) 2.26(1.35)	Fecal samples	-	qRT-PCR for Akkermansia muciniphila	NA	UC with depression and UC	One-way analysis of variance (ANOVA) with Tukey-Kramer test: p < 0.05

Chen Y et al. 2021 ^[50]	English	Cross-sectional associations	Depression (N=113693)	56.23	51162/62 531	--	--	--	PHQ-9	PHQ-9	2.71 (3.64)	Fecal samples	--	16S rRNA gene sequencing-Illumina HiSeq platform	V4	Cross-sectional associations with depression symptom measures	Linear regression model: p < 0.05
Chen YH et al. 2021 ^[51]	Chinese	Case-control	MDD-female (N=62) Control-female(N=46) MDD-female (N=20) Control-female(N=21)	39.58 (12.66) 36.93(8.58)	0/62 0/46	21.99(2.93) 22.24(2.92)	NA	In MDD: 26 Antidepressants for a short period of time --	DSM-5 HAM-D-17:18	HAMD-17	27.97(4.63) NA	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform Shotgun metagenomic sequencing-Illumina NovaSeq 6000	V3-V4 NA	MDD and Controls	LEIS: p < 0.05 and LDA > 2.4 Wilcoxon test followed by FDR correction: p < 0.05
Chen Z et al. 2018 ^[52]	Chinese	Case-control	MDD (N=10) Control (N=10)	43.9(13.8) 39.6 (9)	5/5 5/5	23.5(2.0) 22.6(1.5)	NA	In MDD: 2 SSRIs or SNRIs treatment	DSM-IV HAM-D-17:20	HAMD-17	25.6(4.7) NA	Fecal samples	-80 °C	Metaproteomics: phylogenetic analysis of bacterial peptides	NA	MDD and Controls	Mann-Whitney test: p < 0.05 and fold change >1.5
Cheng S et al. 2020 ^[53]	European	Cross-sectional associations	MDD (N=135458) Control (N=344901)	--	--	--	--	--	DSM-III, DSM-IV, ICD-9, or ICD-10	--	--	Fecal samples	--	Microbiota-related gene set enrichment analysis (GSEA)-Illumina MiSeq Illumina HiSeq2000 Illumina HiSeq	--	Cross-sectional associations between MDD and gut microbiota using published GWAS data	Unspecified
Chung YE et al. 2019 ^[54]	Chinese	Case-control	MDD (N=36) Control (N=37)	45.83 (14.08) 41.19 (12.73)	8/28 14/23	22.80 (4.21) 23.95(3.92)	NA	In MDD: 31 Antidepressant use	DSM-5	BDI	19.18 (12.47) 4.54 (4.85)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq/MiniSeq platforms	V3-V4/V4	MDD and Controls	Analysis of composition of microbiomes (ANCOM): p < 0.05
Coccan D et al. 2021 ^[55]	French	Case-control	MDD (N=56) Control (N=56)	41.9(11.6) 41.9(12.7)	18/38 17/39	24(5.3) --	In MDD: 3 Diabetes	Antidepressant-free for at least 1 year at baseline Longitudinal intervention in MDD: 25 Venlafaxine; 19 Citalopram; 12 Escitalopram	DSM-IV-TR MINI HDRS-17≥18	HDRS-17	--	Plasma sample	-80°C	16S rRNA gene sequencing-MiSeq technology (Vaiomer,Labège, France)	V3-V4	MDD and Controls (baseline)	LEIS: p < 0.05 and LDA > 2.0
Dong Z et al. 2021 ^[56]	Chinese	Case-control	MDD (N=23) GAD (N=21) Control (N=10)	30.04(5.90) 30.43(7.95) 30.22(6.50)	7/16 7/14 4/6	21.87(3.00) 21.19(2.89) 21.45(2.80)	NA	NA	DSM-5 HAM-D-24 ≥20	HAMD-24	29.26(7.51) 12.10(5.25) NA	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	ANOVA: p < 0.05
Fontana A et al. 2020 ^[57]	Italian	Case-control	MDD (N=34) Control (N=20)	55.58(43.3-61.6) 37.7(30.6-58.0)	10/24 13/7	23.96(21.0-28.8) 22.7 (21.2-23.8)	In MDD: 8 Cardiometabolic comorbidities; In controls: 4 Cardiometabolic comorbidities	In MDD: 12 SSRI; 15 SNRI/TCA/Serotonin modulator; 7 Mood stabilizers; 7 Antipsychotics; 11 Any concomitant drugs	DSM IV-TR	--	--	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD (treatment responsive, treatment-resistant and untreated at the moment of sampling) and controls	Two-sample t-test and Mann-Whitney U test: p < 0.05
Heym N et al. 2019 ^[58]	English	Cross-sectional associations	Depression(N=40)	36.38(11.43) male:36.77(13.24) female: 36.19(10.72)	13/27	--	--	7 patients: contraceptives; 3 patients:blood pressure and statins; 1 patient:thyroid; 1 patient:stomach acid; 1 patient:acne; 1 patient:asthma	BDI-II	BDI-II	--	Fecal samples	-20 °C	16S rRNA-targeted oligonucleotide probes for Bif164 (bifidobacteria) and Lab158 (lactobacilli)	--	Psychological risk and resilience factors for depression	Pearson's zero-order correlations
Hoggard M et al. 2018 ^[59]	New Zealanders	Cross-sectional associations	Chronic rhinosinusitis (N=14) Control (N=12)	59.5(29-74) 41.5(21-76)	8/6 2/10	--	In CRS: 14 chronic rhinosinusitis, 6 Asthma, 3 Diabetes, 3 GERD, 12 Allergy (medications), 7 Allergy	In CRS: 3 antibiotics, 3 systemic corticosteroids, 6 topical corticosteroids;	--	PHQ-9	6(0-12) 4.5(0-11)	Simonasal swab and	--	16S rRNA gene sequencing-Illumina MiSeq platform	Unspecified	Cross-sectional associations with depression symptom measures	Spearman correlation and linear regression analysis

							(other), 4 Polyposis; Control: 2 Asthma, 1 Diabetes, 6 Allergy (medications), 6 Allergy (other)	Control: 1 antibiotics, 1 systemic corticosteroids, 4 topical corticosteroids				mucus samples					
Huang Y et al. 2018 ^[20]	Chinese	Case-control	MDD (N=27) Control (N=27)	48.7(12.8) 42.3(14.1)	7/20 7/20	23.8(2.8) 23.4(2.9)	NA	NA	ICD-10	--	--	Fecal samples	-80-C	16S rRNA gene sequencing-Illumina Hiseq2500	V3-V4	First episode MDD and Controls	LEIS: p < 0.01 and LDA > 2.0
Huang Y et al. 2021 ^[21]	Chinese	Case-control	Stroke+ affective disorder (N=20) Stroke+cognitive impairment (N=29) Stroke (N=27) Control (N=19)	61.6(11.37) 62.76(9.01) 62.19(8.75) NA	11/9 20/9 14/13 NA	--	In PSTD: 9 Hypertension, 5 Diabetes In PSCI: 17 Hypertension, 9 Diabetes In ST: 12 Hypertension, 4 Diabetes	--		Depress on score	7.05(2.87) 1.52(1.27) 2.26(1.81) NA	Fecal samples	-80-C	16S rRNA gene sequencing-Illumina MSeq platform	V3-V4	Stroke+affective disorder and stroke control	LEIS: p < 0.05 and LDA > 2.0
Ishii W et al. 2019 ^[22]	Japanese	Case-control	Depression-OI (N=15) Nondepression-OI (N=41) Control (N=9)	13.6(1.6)* 12.3(3.8)	21/35* 3/6	18.8(2.9)* 18.0(2.2)	56 Orthostatic Intolerance; 33 Anxiety	NA	CDE:22	CDI	≥22	Fecal samples	-80-C	16S rRNA gene-Terminal-restriction fragment length polymorphism (T-RFLP)	--	Orthostatic Intolerance with depression and controls	Mann-Whitney test and Kruskal-Wallis test: p<0.017
Jackson MA et al. 2018 ^[23]	English	Cross-sectional associations	Depression(N=354) from all individuals(N=2737)	60(12)*	301/2436	26 (5)*	38 diseases(e.g., hypercholesterolaemia, respiratory allergies, anxiety, osteoarthritis, and hypertension)	51 prescription medications(e.g., statins, proton pump inhibitors, cholecalciferol, and calcium)	--	--	--	Fecal samples	-80 °C	16s rRNA gene sequencing-Illumina MSeq platform	V4	Cross-sectional associations with depression symptom measures	Beta coefficients of associations: p < 0.05
Jiang H et al. 2015 ^[24]	Chinese	Case-control	MDD-active (N=29) MDD-responded (N=17) Control (N=30)	25.3 (5.4) 27.1 (5.4) 26.8 (5.4)	18/11 9/8 15/15	20.3 (3.4) 21.8 (3.4) 19.6 (3.4)	--	In MDD: 38 SSRIs or SNRIs, 12 Atypical antipsychotic, 34 Benzodiazepines	DSM-IV HAMDS-24≥20	HAMDS -24	29.8 (7.6) 8.3 (4.6) NA	Fecal samples	-80-C	16S rRNA gene sequencing-Roche 454 sequencing	V1-V3	Active-MDD, Responding MDD and Controls	LEIS: p < 0.05 and LDA > 2.0
Jiang HY et al. 2020 ^[25]	Chinese	Case-control	CDE(N=24) Control (N=16)	37.2(7.2) 35.8(6.8)	13/11 9/7	23.6(7.1) 22.3(6.5)	--	In CDE: 11 Antidepressant; 16 Benzodiazepines; 9 Atypical antipsychotic; 7 Mood stabilizer	DSM-IV	HAMDS -24	25.3(6.8) 2.3(1.1)	Fecal samples	-80-C	16S rRNA gene sequencing-Illumina MSeq platform	V3-V4	Patients with current depressive episode (CDE) and controls	LEIS: p < 0.05 and LDA > 2.0
Kang Y et al. 2021 ^[26]	Chinese	Case-control	Post-stroke depression (N=67) Stroke (N=96)	55.9(18.61)	85/78	--	Stroke	NA	CCMD-3, HAMD-24: 8, SDS index ≥ 0.5	--	--	Fecal samples	--	Enterococcus faecalis, Escherichia coli and Bifidobacterium in feces were detected by ATB-expression semi-automatic microbial detection system	--	Post-stroke depression and stroke	Independent sample t-test: p < 0.05
Kelly JR et al. 2016 ^[27]	Irish	Case-control	MDD (N=34) Control (N=33)	45.8(11.5) 45.8(11.9)	21/13 19/14	26.2(4.5) 24.58(2.7)	7 patients: Dyslipidaemia, 3 patients: Hypertension, 5 patients: BPAD II, 4 patients: Anxiety disorder 4 patients: Dyslipidaemia, 3 patients: Hypertension	All patients:SSRIs	DSM-IV MINI	HAMD-17	19.5 (14) NA	Fecal samples	-80-C	16S rRNA gene sequencing Illumina Mseq platform	Unspecified	MDD and Controls	Mann-Whitney U test and Benjamini-Hochberg FDR-adjusted p-value ≤ 0.1

Kleiman SC et al. 2015 ²⁰	American	Cross-sectional associations	Anorexia Nervosa (N=16) Control (N=12)	28.0 (±11.7) 29.8 (11.6)	0/16 0/12	16.2 (1.5) 21.5 (1.9)	NA	NA	--	BDI	26.6 (13.4) NA	Fecal samples	~80-C	16S rRNA gene sequencing-454 Life Sciences Genome Sequencer FLX machine	V1-V3	Cross-sectional associations with depression symptom measures	Wilcoxon matched pairs rank test (-2 ≤ skewness ≤ 2) or the sign test (skewness ≤ -2 or ≥ 2); p < 0.05
Kurokawa S et al. 2018 ²¹	Japanese	Case-control	IBS with depression (N=12) IBS without depression (N=5) Donors (N=17)	43.41(10.75) 51.41(18.11)	8/9 7/10	--	IBS	NA	HAMD≥8	HAMD-	--	Fecal samples	~80-C	16S rRNA gene sequencing-Illumina MiSeq platform	V1-V2	IBS with depression and donors	Paired-t-test: p < 0.05
Lai WT et al. 2021 ²⁰¹	Chinese	Case-control	MDD (N=26) Control (N=29)	43.73 (11.46) 39.41(10.96)	8/18 13/16	21.17 (2.17) 21.10(2.23)	NA	In MDD: 12 SSRIs, 7 SNRIs, 6 Other antidepressants	DSM-5	HAMD-17 NA	19.81 (2.95) NA	Fecal samples	~80-C	Shotgun metagenomic-Illumina HiSeq2500 sequencer	NA	MDD and Controls	LEfSE: adjusted p < 0.05 and LDA > 3.0
Liu P et al. 2017 ²¹¹	Chinese	Case-control	MDD (N=10) Control (N=10) MDD (N=60) Control (N=60)	36.2(10.1) 38.1(2.9) 20-85	6/4 6/4 --	23.8(1.9) 24.2(2.0) --	--	Longitudinal intervention (all patients received Escitalopram)	DSM-IV-TR HAM-D-17;23	HAM-D-17	>23 --	Fecal samples	~70-C	16S rRNA gene sequencing-Illumina MiSeq platform qRT-PCR for Streptococcus, Clostridium XI, Prevotella and Klebsiella	V3-V4 --	MDD and Controls	Double-sided Student's t-test and Wilcoxon's Sign Rank Test: p < 0.01
Liang Y et al. 2020 ²¹²	Chinese	Case-control	PSCCID (N=41) non-PSCCID (N=25)	69.63(9.35) 68.92(8.46)	17/24 14/11	25.14(3.62) 26.62(3.58)	In PSCCID: 24 Hypertension, 12 Diabetes mellitus; 15 Hyperlipidemia In non-PSCCID: 16 Hypertension, 6 Diabetes mellitus; 10 Hyperlipidemia	Unknown	HAMD≥8	HAMD	13.63(3.50) 5.56(2.58)	Fecal samples	~80-C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	PSCCID and non-PSCCID	LEfSE: p < 0.05 and LDA > 2.0
Liukiewicz P et al. 2021 ²¹³	Polish	Cross-sectional associations	MDD(N=16)	44.0 (34.3-56.3)	8/8	25.0 (22.4-26.7)	NA	Longitudinal intervention (all patients received Escitalopram)	ICD-10	HAMDS-24	23.0 (21.0-28.5)	Fecal samples	--	16S rRNA gene sequencing-Illumina NextSeq 500 platform	V4	Cross-sectional associations between with symptom severity (baseline)	Spearman's rank correlation
Liu P et al. 2021 ²¹⁴	Chinese	Case-control	MDD (N=66) Control (N=43)	24.20(9.60) 23.67(3.19)	27/39 20/23	21.46(4.61) 21.81(2.15)	NA	NA	DSM-IV, HAM-D-17;21	HAMD-17	20.07(4.20) 2.31(2.04)	Fecal samples	~80-C	16S rRNA gene sequencing-Illumina NovaSeq PE250 platform	V3-V4	MDD and Controls	LEfSE: p < 0.05 and LDA > 2.0
Liu RT et al. 2020 ²¹⁵	American	Case-control	MDD (N=43) Control (N=47)	21.9 (2.1) 22.1 (1.8)	5/38 13/34	--	NA	In MDD: 28 prescribed psychotropic medications In Control: 1 prescribed psychotropic medications	PROMIS Depression Score > 21, DSM-5	PROMIS Depressi on Score	25.0 (6.9) 9.3 (1.4)	Fecal samples	~80-C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	MDD and Controls	LEfSE: p < 0.05 and LDA > 2.0
Liu T et al. 2020 ²¹⁶	Chinese	Cross-sectional associations	IBS-D (N=84) Control (N=46)	41.76 (11.57) 38.30 (13.13)	46/24 25/21	23.36 (3.49) 23.63 (3.76)	IBS-D	--	HAMD/SDS	HAMD	13.23 (5.15)/49.89 (9.59) NA/NA	Fecal samples	~80-C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Cross-sectional associations with depression symptom measures	Spearman's correlation coefficient
Liu Y et al. 2016 ²¹⁷	Chinese	Case-control	IBS-D (N=40) Comorbid IBS-D and MDD (N=25) MDD (N=15) Control (N=20)	38.5(13.6) 39.0(13.9) 44.8(14.9) 43.9(11.2)	28/12 14/11 4/11 7/13	22.6(3.1) 22.0(3.8) 22.0(3.2) 24.6(2.2)	IBS-D	NA	DSM-IV MINI	SDS	Data displayed in histogram	Fecal samples	~80-C	16S rRNA gene sequencing-Roche 454 sequencing	V1-V3	Depression and Controls	Wilcoxon rank-sum test with q value was used for correction: q < 0.05

Malden A et al. 2020 ^[61]	American	Cross-sectional associations	Depression(N=111)	35.7 (13.8)	51/60	–	–	–	SCID-4/II	PHQ-9	–	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform Metagenomic shotgun sequencing-Illumina sequencers	V4	Cross-sectional associations with symptom severity	LEfSe: p < 0.05 and LDA > 2.0
Mason BL et al. 2020 ^[78]	American	Case-control	Comorbid MDD and anxiety (N=38) Anxiety (N=8) MDD (N=14) Control (N=10)	39.2(10.6) 40.0(13.7) 41.9(12.0) 33.0(8.4)	7/31 0/8 3/11 4/6	30.4(5.8) 33.3(9.2) 31.0(5.8) 25.6(3.5)	Anxiety	In patients: 59 any medication; 30 Antidepressants; 15 Anti-anxiety medications	DSM-IV Axis I Disorders (SCID)	QIDS-SR	15.2(3.7) 10.9(3.9) 15.6(3.2) 1.3(0.9)	Fecal samples	-80°C	16s rRNA gene sequencing-Roche 454 Titanium platform 16S rRNA gene qPCR for Eubacteria, Enterobacteriaceae, Eubacterium rectale/Clostridium group (Clostridial cluster XIVa), Lactobacillus/Enterococcus, Bacteroides, Clostridium leptum group (Clostridial cluster IV)	V4 –	MDD and Controls	Kruskal-Wallis one-way ANOVA: p < 0.05 Within these clusters, p-values were adjusted to control the false discovery rate using the Benjamini and Hochberg method
Medina-Rodríguez EM et al. 2020 ^[62]	American	Case-control	MDD (N=10) Control (N=10)	47.2(12.8) 39.6(13.4)	2/8 2/8	33.9(6.7) 28.7(7.1)	In MDD: majority of patients had masked or fully expressed generalized anxiety disorder or other anxiety disorders; 2 Mania or hypomania	–	QIDS≥13	QIDS	15.0(1.8) 1.7(1.5)	Fecal samples	-80°C	qPCR	–	MDD and Controls	Mann Whitney U test: p < 0.05
Minichino A et al. 2021 ^[63]	British	Cross-sectional associations	Depression-anhedonia/ambivalence (N=786)	65.2 (7.6)	52/734	–	218 Obesity	22 Antidepressants	–	–	–	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	Cross-sectional associations with depression symptom (anhedonia/ambivalence)	Pearson's correlation analyses
Naserifardouei A et al. 2014 ^[62]	Norwegian	Case-control	Depression(N=37) Control (N=18)	49.2(13.9) 46.1(13.9)	17/20 7/11	25.9(4.2) 24.7(3.3)	NA	Depression medication, Blood pressure medication	ICD-10	MADRS	26.3(7.6) 7.2(4.8)	Fecal samples	-70°C	16S rRNA gene sequencing-Illumina MiSeq platform	Unspecified	Depression and Controls	PLS-DA
Pérez-Santiago J et al. 2021 ^[63]	American	Case-control	MDD (N=66) Control (N=61)	54(48-62) 54(48-62)	–	–	In MDD: 56 HIV In Controls: 36 HIV	–	DSM-IV	–	–	Fecal samples	–	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	Mann-Whitney or t test: p < 0.05
Qin Q et al. 2021 ^[64]	Chinese	Case-control	Depression (N=60) Control (N=60)	19.30(0.05) 19.85(0.11)	30/30 30/30	–	Test anxiety	NA	–	HAMD-17	10.95(3.95) 1.92(1.49)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina HiSeq 2000 platform	V4	Depression with test anxiety and Controls	One-way ANOVA followed by Tukey's multiple comparison test: p < 0.05
Ramirez-Carrillo E et al. 2020 ^[65]	Mexican	Cross-sectional associations	Depression (N=34 for adults, N=29 for children)	30.48(7.79) for adults 7.6(1.8) for children	16/18 for adults 13/16 for children	–	–	–	–	–	–	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	Cross-sectional associations with depression symptom	Phyloseq, vegan and ggplot2 packages in R
Rhee SJ et al. 2020 ^[66]	Koreans	Case-control	BD (N=42) MDD (N=30) Control (N=36)	34.2(10.8) 46.2(9.7) 43.0(5.6)	15/27 5/25 9/27	24.3(4.0) 24.4(4.3) 23.9(3.9)	NA	In BD: 6 Antidepressant; 32 Anticonvulsant or Lithium; 33 Antipsychotics In MDD: 26 Antidepressant; 1 Anticonvulsant or Lithium; 13 Antipsychotics	DSM-IV, DSM-5, MINI	HAMD-17	6.21(4.80) 6.07(5.43) –	Serum samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq System	V3-V4	MDD and Controls	ANCOM

Rhee SJ et al. 2021 ⁹¹	Koreans	Cross-sectional associations	Depression (N=69)	39.6(12.0)	18/51	24.2(4.1)	29 MDD patients, 40 BD patients	31 Antidepressant; 33 Anticonvulsant or lithium; 45 Antipsychotics	DSM-IV, DSM-5, MINI	HAMD-17	6.13(5.08)	Serum	-80°C	16S rRNA gene sequencing-Illumina MSeq platform	V3-V4	Cross-sectional associations with depression symptom measures	Multivariate association with linear models (MaAsLin2)
Rong H et al. 2019 ⁹²	Chinese	Case-control	BD (N=30) MDD (N=31) Control (N=30)	38.40 (8.33) 41.58(10.40) 39.47(10.22)	15/15 9/22 14/16	21.92 (2.22) 21.46(2.3) 21.97(3.18)	NA	In MDD: 13 SSRI; 8 SNRI; 6 Other antidepressants In BPD: 11 SSRI; 3 SNRI; 1 Other antidepressants; 7 Atypical antipsychotics	DSM-5	HAMD-17	20.37 (3.41) 20.23(3.11) --	Fecal samples	-80°C	Shotgun metagenomic-Illumina HiSeq2500 sequencer	--	MDD and Controls	Wilcoxon rank-sum test with FDR multiple testing correction; p < 0.05
Shen Y et al. 2021 ⁹³	Chinese	Case-control	MDD (N=30) Control (N=30)	44.83(11.00) 43.97(10.57)	13/17 15/15	23.99(2.05) 23.83(2.08)	NA	NA	MINI HAMD-17 ≥24	HAMD-17	--	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina HiSeq 2500 platform	V3-V4	MDD and Controls	Metastats (T test); p < 0.05
Simpson CA et al. 2020 ⁹⁴	Australian	Case-control	high-depression(N=33) low-depression(N=33)	16.84(1.11) 17.02(0.89)	7/26 13/20	--	Anxiety	NA	CESD	CESD	20.14(9.78) 10.59(5.75)	Saliva sample	-30°C	16S rRNA gene sequencing-Ion Torrent Personal Genome Machine	V4	High-depression and low-depression	Multivariate association with linear model analysis (MaAsLin2); p-value < 0.05 and FDR q-value < 0.25
Stevens BR et al. 2021 ⁹⁵	American	Case-control	Hypertension (N=18) MDD (N=7) MDD with Hypertension (N=8) Control (N=21)	59.9(17.6) 63.8(6.2) 67.0(10.7) 53.0(14.8)	8/10 3/4 3/5 8/13	37.5(13.4) 27.3(5.9) 34.2(10.5) 30.7(7.0)	In HTN: 8 Diabetes; 7 Chronic kidney disease; 2 Peripheral artery disease; 1 Stroke/Transient ischemia attack; 3 Atrial fibrillation; 1 Heart failure In MDD: 2 Diabetes; 2 Stroke/Transient ischemia attack In DEP plus HTN: 2 Diabetes; 3 Chronic kidney disease In Controls: 9 Diabetes; 2 Chronic kidney disease; 2 Heart failure	Unknown	DSM-5	--	--	Fecal samples	-80°C	whole metagenome shotgun sequencing (WMGS)-Illumina HiSeq4000	NA	Depression only and reference subjects	Pearson correlation heatmaps were generated based on relative Rho magnitudes
Stevens BR et al. 2020 ⁷²	American	Case-control	MDD (N=20) Control (N=20)	mean: 34	10/10 6/14	--	NA	In MDD: 15 Antidepressant	DSM-IV	--	--	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MSeq platform	V3-V4	MDD and Controls	ALDE2 effect sizes for taxons assigned from ASVA. Displayed cutoffs are effect size >0.5 (NODEP) or <=0.5 (DEPR)
Strandwitz P et al. 2019 ⁹⁷	American	Cross-sectional associations	MDD (N=23)	19.65	8/15	--	NA	NA	DSM-IV-TR	--	--	Fecal samples	-80°C	16S rRNA gene sequencing-American Gut dataset	V4	Cross-sectional associations with depression symptom measures	Pearson
Szczesniak O et al. 2016 ⁹⁴	Norwegian	Case-control	Depression(N=34) Control (N=17)	49.2(13.9) ^f 46.1(13.9) ^f	17/20 ^f 7/11 ^f	25.9(4.2) ^f 24.7(3.3) ^f	NA	Depression medication; Blood pressure medication	ICD-10	MADRS	26.3(7.6) 7.2(4.8)	Fecal samples	-70°C	16S rRNA gene sequencing-Illumina MSeq platform	Unspecified	As described in Nasirifraei et al. (2014) Depression and Controls	PLS-DA
Taylor AM et al. 2020 ⁹⁸	American	Cross-sectional associations	Depression (N=133)	33.4(5.7)	60/73	30.9(6.7)	NA	NA	DASS-42	DASS-42-Depression Scale	3.4(4.6)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MSeq2000 platform	V4	Cross-sectional associations with depression symptom measures	Linear mixed modeling
Taylor BC et al. 2020 ⁹⁸	American	Case-control	MDD (N=34) Control (N=14)	53.8(9.1) [*]	41/7 [*]	--	HIV and HCV infections	--	DSM-IV, BDI-II ≥14	BDI-II	10.9(10.7)	Fecal samples	--	16S rRNA gene sequencing-Illumina MSeq platform	V4	MDD and Controls (Connected)	Kruskal-Wallis test: p < 0.05

Valles-Colomer M et al. 2019 ⁹⁷	Belgian Netherlands	Case-control	FGFP cohort: Depression (N=121) Control (N=933) Validation LLD cohort: Depression(N=115) Controls (N=948)	50.9 44.9	479/575 448/615	24.9 25.3	Unspecified	In FGFP cohort: 52 Antidepressant treatment In LLD cohort: 29 Antidepressant treatment	Unspecified	--	--	Fecal samples	-80°C	16S rRNA gene sequencing Illumina HiSeq 2500 System/Illumina MiSeq platform Shotgun metagenomics-Illumina HiSeq2500	V4	Two independent studies (Flemish Gut Flora Project [FGFP] and Dutch Lifelines DEEP [LLD]); Depression and Controls	Generalized linear models (GLMs): FDR <0.1
Wingfield B et al. 2021 ⁹⁸	English	Case-control	MDD (N=40) Control (N=43)	21.8(5.1) 20.4(3.9)	11/29 13/30	--	NA	NA	DSM-IV	--	--	Saliva samples	Room temperature	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	Wald test and Benjamini-Hochberg (FDR) correction: FDR < 0.05
Xu C et al. 2020 ⁹⁹	Chinese	Case-control	IBS-D (N=22) Comorbid IBS-D and MDD (N=13) MDD (N=15) Control (N=15)	40.7(3.1) 43.1(3.6) 42.3(3.0) 44.8(2.9)	12/30 6/7 6/9 5/10	22.9(0.7) 22.7(1.1) 21.3(0.7) 24.1(0.7)	IBS-D	NA	DSM-IV MINI	SDS	39.5(2.1) 64.5(3.6) 58.2(2.3) 28.7(1.4)	Fecal samples	-80°C	Metagenomic Sequencing-Illumina HiSeq™ platform	NA	MDD and Controls	One-way ANOVA: p < 0.05
Yang J et al. 2020 ¹⁰⁰	Chinese	Case-control	MDD (N=118) Control (N=118)	27.19(4.71) 26.86(5.24)	51/67 51/67	22.50(3.56) 22.09(3.33)	NA	NA	DSM-IV MINI	HAMD-17	22.03(5.08) NA	Fecal samples	--	Metagenomic-Illumina NovaSeq	NA	MDD and Controls	Lefse: LDA > 2.5
Yang Y et al. 2021 ¹⁰¹	Chinese	Cross-sectional associations	METH abuser (N=16) Control (N=14)	36(7.8) 36(9.4)	16/0 14/0	--	NA	Methamphetamine	DSM-5	PANSS	--	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina NovaSeq platform	V4	Cross-sectional associations with depression symptom measures	Spearman's rank-correlation analysis: p < 0.05
Ye X et al. 2021 ¹⁰²	Chinese	Case-control	MDD (N=26) Control (N=28)	26.04(7.83) 26.04(7.83)	5/21 7/21	19.78(2.12) 21.59(3.48)	NA	NA	DSM-IV HAMD-17:24	HAMD-17	27.92(2.77) 1.29(1.3)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina HiSeq 2500 platform	V3-V4	MDD and Controls (baseline)	LEfSe: p < 0.05 and LDA > 3.5
Zhang Q et al. 2021 ¹⁰³	Chinese	Case-control	MDD (N=36) Control (N=45)	36.81(13.52) 39.29(11.44)	12/15 19/26	24.47(4.16) 23.94(3.05)	NA	NA	ICD-10 HAMD-D >17	HAMD-17	5.36(6.24) 0.51(1.01)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina NovaSeq 6000 platform	V4-V5	MDD and Controls	LEfSe: p < 0.05 and LDA ≥ 2.0
Zhao H et al. 2021 ¹⁰⁴	Chinese	Case-control	MDD (N=24) Control (N=26)	29.96(8.554) 31.31(9.707)	7/17 8/18	--	NA	NA	DSM-5, HAMD-17:17	HAMD-17	24.83(3.116) 2.12(2.776)	Fecal samples	-80°C	Metagenomics sequencing-Illumina Novaseq 6000 platform	--	MDD and Controls	LEfSe: p < 0.05 and LDA > 2.0 meta stat analysis
Zheng P et al. 2016 ⁹¹	Chinese	Case-control	MDD (N=58) Control (N=63)	40.6(11.7) 41.8(12.3)	22/36 23/40	22.0(2.4) 22.6(2.5)	NA	In MDD: 19 Antidepressants (e.g., Citalopram, Venlafaxine)	DSM-IV-TR	HAMD-17	22.8(4.4) 0.3(0.7)	Fecal samples	-80°C	16S rRNA gene sequencing-Roche 454 sequencing	V3-V5	MDD and Controls	Random Forests
Zheng P et al. 2020 ¹⁰⁵	Chinese	Case-control	MDD (N=122) BD (N=169) Control (N=171)	26.54(4.07) 25.59(8.41) 26.85(5.48)	45/77 85/84 71/100	22.41(3.63) 21.77(3.68) 22.07(3.38)	NA	NA	DSM-IV	HAMD	22.65(5.50) NA	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MDD and Controls	Kruskal-Wallis test: p < 0.05 LEfSe: fold change >2.0 and LDA > 2.5
Zheng S et al. 2021 ¹⁰⁶	Chinese	Case-control	Depression (N=30) Control (N=30)	30.80 (10.85) 33.77 (7.02)	12/18 13/17	--	NA	NA	ICD-10	HAMD-24	20.17 (7.92) 0.30 (0.79)	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	Unspecified	Depression and Controls	LEfSe: p < 0.05 and LDA > 2.0 and other methods unspecified
Zhou Y et al. 2020 ¹⁰⁷	Chinese	Case-control	PPD (N=28) Control (N=16)	33.64(4.27) [†] 32.57(3.98) [†]	0/28 0/16	21.50 (2.87) [†] 20.90 (2.24) [†]	NA	NA	DSM-IV HAMD-17:7	HAMD-17	13.46 (3.51) [†] 3.83(1.98) [†]	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	PPD and Controls	LEfSe: p < 0.05 and LDA > 2.0
Zhu J et al. 2021 ¹⁰⁸	Chinese	Case-control	Depression (N=25) Control (N=46)	55.30(8.20) 55.63(7.78)	13/10 21/25	24.43(3.21) 25.51(3.47)	Anxiety	--	--	PHQ-9:5	PHQ-9	--	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	Depression with anxiety and Controls	LEfSe: p < 0.05 and LDA > 2.032
Zhuang Z et al. 2020 ¹⁰⁹	European	Cross-sectional associations	MDD (N=135458) Control (N=344901)	--	--	--	--	--	DSM-IV,DSM-III, ICD-9 or ICD-10	--	--	Fecal samples	--	Microbiota-related gene set enrichment analysis (GSEA)-	--	Cross-sectional associations between MDD and gut	Unspecified

Note:

^aData from 56 OI patients with or without depression (Ref.22)

^bData from all 2737 individuals (Ref.23)

^cData from all 17 patients with irritable bowel syndrome (Ref.29)

^dData from 38 patients with depression and 18 controls (Ref.54)

^eData from total 48 patients (Ref.56)

^fData from 39 patients with postpartum depressive disorder and 18 controls (Ref.68)

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Table S2. Characteristics of studies investigating gut microbiota composition in animal models of depression.

Study	Object	Country	Study design	housed	Depression model	groups	Age	Sex	Definition of depression-like behaviors	Time point of sample collection	Sample	Storage	Gut microbiome estimation	Sequencing region	Microbial biomarkers from comparisons	Microbial biomarkers selection
Abildgaard A et al. 2021 ^[1]	Flinders sensitive line rats Flinders resistant line rats	Denmark	case-control	pair-housed	FSL-depression	FSL (N=12) FSL-HFD (N=12) FSL+Probiotics (N=11) FSL-HFD+Probiotics (N=11) FRL-Control (N=12)	5-week-old	male	FST: No data (immobility) OFT: No data (locomotor activity)	Fresh faecal samples were collected at study initiation and study end	Faecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V4	FSL-depression and FRL-control	Two-way ANOVA followed by Bonferroni correction: $p < 0.05$
Aithal Y et al. 2018 ^[2]	Swiss mice	Morocco	case-control	-	GBH-depression	Acute GBH low-dose (N=6) Subchronic GBH low-dose (N=6) Chronic GBH low-dose (N=6) Acute GBH high-dose (N=6) Subchronic GBH high-dose (N=6) Chronic GBH high-dose (N=6) Acute control (N=6) Subchronic control (N=6) Chronic control (N=6)	1-month-old	male	OFT: center time] EPM: anxiety index] TST: immobility time] Splash test: grooming time]	After subchronic and chronic groups were treated daily for 6 and 12 weeks	Intestinal samples	-	Bacterial strain-dilution/spreading method	-	GBH-depression and control	Two-way ANOVA followed by Holm-Sidak post hoc test: $p < 0.05$
Amini-Khoei H et al. 2019 ^[3]	NMRI mice	Iran	case-control	4 mice/cage	MS-depression	MS (N=9-12) Adrenalectomized MS (N=9-12) Control (N=9-12) Adrenalectomized control (N=9-12)	pnd 50-52	male	FST: immobility time] Splash test: grooming activity time] OFT: horizontal activity and rearing] EPM: open arm time and entries]	Fresh feces were collected from male mice at PNDS2 after having carried out valid behavioral tests	Colon contents	-80°C	Real-time RT-PCR	-	MS-depression and control	Two-way ANOVA followed by Bonferroni post hoc test: $p < 0.05$
As Q et al. 2020 ^[4]	C57BL/6J mice	China	case-control	5 mice/cage	CUMS-depression	CUMS (N=12) CUMS+AGO (N=12) CUMS+NMDEA low-dosage (N=12) CUMS+NMDEA high-dosage (N=12) Control (N=12)	8-week-old	male	Body weight] SPT: sucrose preference] FST: immobility time] TST: immobility time]	After 1 week of acclimatization and 8 weeks of CUMS (the last 4 weeks received drugs treatment)	Faecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	Mann-Whitney test followed by multiple comparisons using Benjamini & Hochberg's false discovery rate: FDR < 0.05
Arslanova A et al. 2021 ^[5]	mice	Russia	case-control	4-5 mice/cage	Antibiotic-depression	Antibiotic (N=25) Antibiotic+lactobacilli (N=25) Control (N=25)	25-day-old	male	Mortality rate? Body weight] SFT: sucrose preference] OFT: crossing number, defecation, grooming]; rearing number, head dips, latency to exit from central zone] Rotarod test: Latency to falls] PaGE: time to spent on the grip] T maze: alternation] Novel Object Recognition: time index]	Cecum content samples were collected on the 15th day of the experiment	Caecum contents	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	Antibiotic-depression and control	Nonparametric ANOVA Kruskal-Wallis test: $p < 0.05$
Bharwani A et al. 2017 ^[6]	C57BL/6 mice	Canada	case-control	Single	CSDS-depression	CSDS (N=24) CSDS-L. rhamnosus JB-1 (N=17) Control (N=18) Control+L. rhamnosus JB-1 (N=13)	8-week-old	male	SIT: social interaction ratios] OFT: rearing number] LDT: light zone entries]	Faecal pellets were collected before the first defeat session (at 18th day of L. rhamnosus JB-1 treatment), the final defeat session (at the final day of JB-1	Faecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3	CSDS-depression and control	Kruskal-Wallis one-way ANOVA or the Mann Whitney U test, followed by the Benjamini-Hochberg correction

						UCMS (N=8) UCMS+L. reuteri (N=8) Control (N=8)										
Chen T et al. 2021 ^[71]	C57BL/6N mice	China	case-control	3-4 mice/cage	CRS-depression FMT CRS-depression	Experiment 1: CRS (N=8) DSS (N=8) DSS+CRS (N=8) Control (N=8) Experiment 2: donor Control (N=10) donor CRS (N=20) recipient Control (N=6) recipient CRS (N=6) recipient CRS+A. muciniphila (N=6) recipient Control+DSS(N=8) recipient CRS+DSS(N=8) recipient CRS+A. muciniphila+DSS (N=8)	18-20 g	male	OFT: total distance↓ TST: immobility time↑ FST: immobility time↑	After 7 days of acclimatization and 30 days of CRS, followed by 7 days of DSS treatment	Cecal contents	-	16S rRNA gene sequencing- Illumina HiSeq platform	V3-V4	CRS-depression and control FMT-CRS-depression and FMT-control	Two-way ANOVA with Bonferroni's post-hoc test for multiple comparisons: p < 0.05.
Chen X et al. 2021 ^[72]	Sprague-Dawley rats	China	case-control	-	Lead exposure-depression	Lead exposure (N=15) Control (N=15)	Adult 200 ± 10 g	male	SPT: sacrose preference↓ FST: immobility time↑ OFT: total distance↑, center distance↑ EPM: open arms entries↑, open arms time↓	After 1 week of acclimatization and 24 weeks of lead exposure	Fecal samples	-	16S rRNA gene sequencing-	V4	Lead exposure-depression and control	Anosim: p < 0.05 LEISE: p < 0.05 and LDA > 3.0
Chen X et al. 2022 ^[73]	Sprague-Dawley rats	China	case-control	-	Lead exposure-depression	Lead exposure (N=15) Lead exposure+Probiotics (N=15) Control (N=15)	Adult 200 ± 10 g	male	SPT: sacrose preference↓ FST: immobility time↑ TST: immobility time↑	After 1 week of acclimatization and 24 weeks of lead exposure	Fecal samples	-	16S rRNA gene sequencing-	V4	Lead exposure-depression and control	Anosim: p < 0.05 LEISE: p < 0.05 and LDA > 3.0
Chen Y et al. 2021a ^[74]	C57BL/6 mice	China	case-control	-	CUMS-depression	Prevention trial: CUMS (N=6) CUMS+Fluoxetine (N=6) CUMS+PHGG (N=6) CUMS+PHGG+Fluoxetine (N=6) Control (N=6) Intervention trial: CUMS (N=7) CUMS+Fluoxetine (N=7) CUMS+PHGG (N=7) CUMS+PHGG+Fluoxetine (N=7)	5-week-old	male	Body weight↓ SPT: sacrose preference↓ FST: immobility time↑ OFT: center time↓, rearing number and crossing number↓	After 1 week of acclimatization, mice feces were collected every week during 4 weeks of CUMS and drugs treatment	Fecal samples	-80-C	16S rRNA gene sequencing- Illumina HiSeq platform	V3-V4	CUMS-depression and control	Student's t-test: p < 0.05
Chen Y et al. 2021b ^[75]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+ Semen Sojoe Praeparatum (N=10) Control (N=10)	Adult 180-220 g	male	SPT: sugar preference↓ FST: immobility time↑ LDT: dark time↑	After 15 days of acclimatization, 3 weeks of CUMS and 4 weeks of Semen Sojoe Praeparatum treatment	Cecum contents	-80-C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISE: p < 0.05 and LDA > 3.0 one-way ANOVA and Welch's t-test: p < 0.05

Cheng D et al. 2018 ⁽⁷⁶⁾	Sprague-Dawley rat	China	case-control	single	Hydrocortisone-depression	Hydrocortisone (N=10) Hydrocortisone+Tiansi (N=10) Control (N=10)	250-280 g	male	OFF: total distance↓ SPT: sucrose preference↓	After 1 week of acclimatization and 21 days of drugs	Feces from the colon samples and small intestinal mucosa	~80 °C	16S rRNA gene sequencing-MiSeq (Illumina) platform	V3-V4	Hydrocortisone-depression and control	A Kruskal-Wallis test: $p < 0.05$ Metastats: FDR-adjust $p \leq 0.1$
Cheng R et al. 2021 ⁽⁷⁷⁾	C57BL/6 mice	China	case-control	-	CUMS-depression	CUMS (N=7-8) CUMS+Amuc_1100 (N=7-8) CUMS+Fluoxetine (N=7-8) Control (N=7-8)	5-6 weeks old	male	LDT: light time↓	After 6 weeks of CUMS and treatment	Fecal samples	-	16S rRNA gene sequencing-	V3-V4	CUMS-depression and control	One-way ANOVA and Fisher's least significant difference (LSD) tests for multiple comparisons: $p < 0.05$
Chevalier G et al. 2020 ⁽⁷⁸⁾	C57BL/6J mice	France	case-control	-	UCMS-depression	UCMS (N=4) Control (N=4) FMT-UCMS (N=4) FMT-Control (N=4)	8-10-week-old	male	NSFT: latency to eat↓ Splash test: grooming latency↓, self-grooming behavior↓ FST:immobility time↓ TST:immobility time↓	After 1 week of acclimatization and 8 weeks of UCMS 8 weeks post FMT	Fecal samples	-	16S rRNA metagenomic-Illumina MiSeq instrument	V3-V4	UCMS-depression and control FMT-UCMS and FMT-control	Mann-Whitney test: $p < 0.05$
Chi L et al. 2020 ⁽⁷⁹⁾	Sprague-Dawley rats	China	case-control	4-6 rats/cage for control, single for CUMS mice	CUMS-depression	CUMS (N=12) CUMS+FOS (N=12) CUMS+Flx (N=12) CUMS+DP5 (N=10) Control (N=8) Control+FOS (N=8)	6-week-old	male	Body weight↓ SPT: sucrose preference↓ OFF: total distance↓, immobility time↑, travel velocity↓	After 1 week of acclimatization and 7 weeks of CUMS, the last 3 weeks received drugs treatment, fecal samples were collected at day 0, 15, and 22 during the drug treatment period	Fecal samples	~80 °C	16S rRNA gene pyrosequencing-Illumina MiSeq system	V3-V4	CUMS-depression and control	LEISe: $p < 0.05$ and LDA > 1.0
Choi J et al. 2020 ⁽²²⁾	C57BL/6J mice	Korea	case-control	-	CRS-depression	CRS (N=12) CRS+Lac-EV (N=8) CRS+Bac-EV (N=12) CRS+Akk-EV (N=11) Control (N=12) Control+Lac-EV (N=6) Control+Bac-EV (N=12) Control+Akk-EV (N=12)	7-week-old	male	FST: immobility time↑ TST: immobility time↑	After 5 days of acclimatization, stools were collected at day 1 (before stress), day 14 (after stress), and post-stress day 14	Fecal samples	~80 °C	16S rRNA gene sequencing-Roche 454 sequencing	V1-V2	CRS-depression and control (post-stress day 14)	Two-way ANOVA: $p < 0.05$
Daugé V et al. 2020 ⁽²³⁾	Long Evans Rats	China	case-control	-	MD-depression	Experiment for Fischer rats: Probiotics (N=12) Control (N=12) Experiment for Long Evans rats: MD (N=12) MD+Probiotics (N=12) Control (N=12) Control+Probiotics (N=12)	6-week-old	male	OFF: center visits number↓, rearings number↓	After receiving 0.5 mL of the probiotics for 5 weeks for Fischer rats and 9 weeks for Long Evans rats (until euthanasia)	Cecal content	~80 °C	16S rRNA sequencing analysis-Illumina MiSeq platform	V3-V4	MD-depression and control	ANOVA: $p < 0.05$
Deng Y et al. 2021 ⁽²⁴⁾	C57BL/6J mice	China	case-control	5 mice/cage	CRS-depression	CRS+PBS (N=8) CRS+CITA (N=8) Control+PBS (N=8) Control+CITA (N=8)	6-week-old	male	FST: immobility time↑ SPT: sucrose preference↓ PFT: center time↓ EPM: open arms time↓	After 2 week of acclimatization and 5 weeks of CRS (the last 3 weeks received drugs)	Fecal samples	~80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CRS-depression and control (PBS)	Two-way ANOVA followed by Fisher's LSD test or Dunn's correction: $p < 0.05$

Dhalwaj J et al. 2018 ²⁹	Swiss albino LACA mice	India	case-control	-	CUMS-depression SD-depression	CUMS (N=8) CUMS+L. plantarum MTCC 9510 (N=8) Control (N=8) Control+L. plantarum MTCC 9510 (N=8) SD (N=8) SD+L. plantarum MTCC 9510 (N=8) Control (N=6) Control+L. plantarum MTCC 9510 (N=6)	25-30 g	male	Locomotor activity EZM: open arm time MCT: mirror chamber time Stereotypic behaviour: stereotypy scores MWM: transfer latency , target quadrant time and frequency of appearance PAR: number of mistakes FST: immobility time TST: immobility time	After 4 weeks of CUMS (and L. plantarum MTCC 9510) After 21 days of L. plantarum MTCC 9510 (day 7-10 received sleep deprivation)	Caecal contents	-	qPCR	-	CUMS-depression and control SD-depression and control	One-way ANOVA followed by Tukey's multiple comparison test: p < 0.05
Ding Y et al. 2021 ²⁹¹	C57BL/6 mice	China	case-control	-	CRS-depression	CRS (N=6) CRS+A. muciniphila (N=6) A. muciniphila (N=6) CRS+ Lactobacillus low-dose (N=6) CRS+ Lactobacillus high-dose (N=6) Control (N=6)	6-8-week-old	male	OFT: total distance FST: immobility time TST: immobility time	After 1 week of acclimatization and 3 weeks of CRS and Akkermansia muciniphila treatment	Cecal contents and fecal samples	-80°C	16S rRNA gene sequencing-Illumina platform	V3-V4	CRS-depression and control	Welch's t-test: p < 0.05
Diviccaro S et al. 2019 ⁷³	Sprague-Dawley rats	Italy	case-control	-	Finasteride-depression	Finasteride after treatment (N=10) Control after treatment (N=10) Finasteride after withdrawal (N=10) Control after withdrawal (N=10)	250-275g	male	FST: immobility time	After 1 week of acclimatization and 20 days of finasteride treatment and 1 month after withdrawal	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Finasteride-depression and control (withdrawal)	Mann-Whitney test: p < 0.05
Donoso F et al. 2020 ²⁹²	Sprague-Dawley rats	Ireland	case-control	2-4 rats/cage	MS-depression	MS (N=12) MS+Phlorotannins (N=10) MS+Xanthohumol (N=10) MS+Quercetin (N=10) Control (N=12)	16-week-old	male	FST: immobility time , swimming time OFT: center time and entries	After maternal separation (PND2-12) and dietary intervention of polyphenols (week 9-16)	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MS-depression and control	Pairwise implementation of the α diversity function followed by Benjamini-Hochberg correction: q < 0.1
Du HX et al. 2020 ²⁹³	NOD/ShiLJ mice	China	case-control	-	EAP-depression ABX FMT-EAP-depression	EAP treatment (N=8) Control (N=8) ABX FMT-EAP (N=8) ABX FMT-Control (N=8) ABX FMT-PBS (N=8) Na Ve (N=8)	4-week-old	male	OFT: center distance , center time , rearing number SPT: sucrose preference FST: immobility time TST: immobility time	After 1 week of acclimatization and 24 days of immunization After 1 week of acclimatization, 14 days of antibiotics treatment and 14 days fecal transplantation	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	EAP-depression and control ABX FMT-EAP and ABX FMT-Control	Independent sample t test: p < 0.05 One-way ANOVA followed by post hoc Tukey tests: p < 0.05
Duan J et al. 2021 ²⁹⁴	C57BL/6 mice	China	case-control	Single	CUMS-depression	CUMS (N=7) CUMS+escitalopram response (N=7) CUMS+escitalopram non-response (N=9) Control (N=8)	4-6 weeks of age	male	Body weight SPT: sucrose preference FST: immobility time	After 4 weeks of CUMS then fecal samples were collected prior to ESC administration (day 0) and at 4 weeks post administration (end of study)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	Wilcoxon rank-sum test: p < 0.05
Egerton S et al. 2020 ²⁹⁵	Sprague-Dawley rats	Ireland	case-control	2-4 mice/cage	MS-depression	MS (N=12) MS+Flaxetine (N=12) MS+Fish oil (N=10) MS+Flaxetine+Fish oil (N=12) Control (N=12)	16-week-old	male	OFT: center time and entries FST: immobility time , swimming time	After maternally separated stress (PND2-12), and drugs intervention (week 8-16), fecal samples were collected at 16 weeks	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	MS-depression and control	Student's t-test: p < 0.05

El Aidy S et al. 2017 ⁷²	mice	Netherlands	case-control	-	MS	MS-5-HTT ^{-/-} (N=8) Control-5-HTT ^{-/-} (N=8) MS-5-HTT ^{+/-} (N=8) Control-5-HTT ^{+/-} (N=8) MS-5-HTT ^{+/+} (N=8) Control-5-HTT ^{+/+} (N=8)	pnd21	male/female	NA	Fecal samples were collected at PND 21.	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	Unspecified	MS and control	The rank test-Kruskal-Wallis test: p < 0.05
Fan L et al. 2021 ⁷³	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=9) CUMS+TG (N=9) CUMS+CTE (N=9) CUMS+Fluoxetine (N=9) CUMS+TG+PhG (N=9) CUMS+TG+IG (N=9) CUMS+HT (N=9) Control (N=9)	6-week-old	male	SPT: sucrose preference↓ OFT: total distance traveled↓, rearing number↓ FST: total immobility time↑	After 1 week of acclimatization and 4 weeks of CUMS	Cecum content samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq PE300 system	V3-V4	CUMS-depression and control	LetSe: p < 0.05 and LDA > 2.5 Kruskal-Wallis H-test: p < 0.05
Farshim P et al. 2016 ⁷⁴	Wistar albino rats	UK	case-control	6 rats/cage	Non-weaned-depression	S-Weaned (N=6) S-Non-weaned (N=6) NS-Weaned (N=6) NS-Non-weaned (N=6)	PND25	male	FST: immobility time↑, limbing time↓, swimming time↓	Fecal samples were collected at PND25	Contents of duodenum, jejunum, ileum, cecum and colon	-	Fluorescence in situ Hybridization (FISH) analysis for Lactobacillus—Enterococcus, Bifidobacterium spp. and Clostridium histolyticum group	-	Non-weaned-depression and weaned	Two-way ANOVA followed by Bonferroni-adjusted: p < 0.05
Feng Y et al. 2020 ⁷⁵	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+Bupleuri Radix (N=6) CUMS+Venlafaxine (N=6) Control (N=6)	200 ± 20 g	male	Body weight↓ SPT: sucrose preference↓ OFT: crossing and rearing number↓	After 1 week of acclimatization and 4 weeks of CSDS	Cecum contents	-80 °C	16S rRNA sequencing analysis-Illumina MiSeq platform	V3-V4	CUMS-depression and control	one-way ANOVA followed by Dunnett's test: p < 0.05 LEISe: p < 0.05 and LDA > 3.0
Feng Z et al. 2020 ⁷⁶	Sprague Dawley rats	China	case-control	single	CMS-depression	CMS (N=6) CMS-low-dose WYJYD (N=6) CMS+medium-dose WYJYD (N=6) CMS-high-dose WYJYD (N=6) CMS+Fluoxetine (N=6) Control (N=6)	8-week-old	male	FST: immobility time↑	After 1 week of acclimatization and 4 weeks of CMS with drugs treatment	Colon contents	-	16S rRNA gene sequencing-	Unspecified	CMS-depression and control	One-way ANOVA: p < 0.05
Forouzan S et al. 2021 ⁷⁷	Sprague-Dawley rats	USA	case-control	2 rats/cage	METH-depression	METH (N=8) Control (N=8)	60-90 days old	male	OFT: total distance↓ FST: immobility time↑	Fecal samples were collected at the following time points: saline day 5, day 7, and day 14 of METH administration, and at 24, 48, and 96 h, and days 7, 14, and 30 of withdrawal or cessation	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	METH-depression and control	Non-parametric Mann-Whitney test or the Kruskal-Wallis test: p < 0.05
Gao K et al. 2022 ⁷⁸	BALB/c mice	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+L.c. lactis WHH2078 (N=10) CUMS+Fluoxetine (N=10) Control (N=10)	6-8 weeks old	male	SPT: sugar preference↓ FST: immobility time↑ TST: immobility time↑ OFT: total distance↓, center time↓	After 1 week of adaptation and 5 weeks of WHH2078 or fluoxetine treatment (4 weeks of CUMS after adaptation)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	One-way ANOVA (or Kruskal-Wallis test): p < 0.05 LEISe: p < 0.05 and LDA > 3.0

Gao X et al. 2020 ^[93]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+TPC (N=6) CUMS+Venlafaxine (N=6) Control (N=6)	200 ± 20 g	male	Body weight SPT: sucrose preference OFT:crossing number , rearing number	After 1 week of acclimatization and 4 weeks of CUMS	Cecal contents	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	One-way ANOVA followed by Dunnett's test: p < 0.05
Gong X et al. 2021 ^[94]	C57BL/6J mice	China	case-control	5 mice/cage	CSDS-depression	CSDS (N=10) Control (N=10)	6-8-week-old	male	SFT: SI ratio OFT: total and central distance , central time and entries FST: immobility time	After 1 week of acclimatization and 10 days of CSDS	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CSDS-depression and control	LEISe: p < 0.05 and LDA > 3.0
Gu F et al. 2020 ^[91]	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	CUMS (N=6) CUMS+L. casei (N=6) CUMS+Paroxetine (N=6) Control (N=5)	5-week-old	male	Body weight SPT: sucrose consumption FST: immobility time OFT: moving distance , velocity	After 1 week of acclimatization and 7 weeks of CUMS (the last 4 weeks received drugs treatment)	Fecal samples	-	16S rRNA gene sequencing-Illumina HiSeq 250 platform	V3-V4	CUMS-depression and control	LEISe: Unspecified
Gu X et al. 2022 ^[92]	Wistar rats	China	case-control	4 rats/cage	PSD-depression	PSD (N=8) PSD+Conventional coffee (N=8) PSD+Decaffeinated coffee (N=8) Control (N=8)	240 ± 10g	male	OFT: total behavioral score SPT: sucrose preference FST: immobility time SFT: sucrose preference	After 1 week of acclimatization and 7 days of paradoxical sleep deprivation	Fecal samples	-80 °C	16S rRNA sequencing analysis-Illumina MiSeq platformNovaSeq platform	V3-V4	PSD-depression and control	One-way ANOVA test and two tailed Student's t-test: p < 0.05
Guida F et al. 2018 ^[95]	C57/bl6 mice	Italy	case-control	-	Antibiotic-depression	Antibiotics (N=10-12) Antibiotics+L. casei (N=10-12) Antibiotics+Saline (N=10-12) Control (N=10-12) Antibiotics+Recovery (N=10-12)	6-week-old	male	TST: immobility time FST: immobility time	After 1 week of acclimatization, 14 days of antibiotics treatment, and 7 days of probiotics treatment	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Antibiotic-depression and control	Kruskal-Wallis and pairwise Wilcoxon tests: p < 0.05
Guo Y et al. 2018 ^[96]	ICR mice	China	case-control	5 mice/cage	CRS-depression	CRS (N=12) CRS+Rosemary extracts (N=12) Control (N=12)	Adult	male	OFT: center time TST: immobility time FST: immobility time	After 1 week of acclimatization and 3 weeks of CRS	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V1-V3	CRS-depression and control	One-way ANOVA: p < 0.05
Guo Y et al. 2019 ^[97]	ICR mice	China	case-control	4-5/cage	CRS-depression	Experiment 1: Amiripryline (N=10) Low-dose B. adolescentis (N=10) Middle-dose B. adolescentis (N=10) High-dose B. adolescentis (N=10) Control (N=10) Experiment 2: CRS (N=12) CRS+B. adolescentis (N=12) Control (N=12)	6-week-old	male	OFT: center time EPM: open arms time and entries FST: immobility time TST: immobility time	After 1 week of acclimatization and 21 days of CRS	Cecal contents	-	16S rRNA gene sequencing-Illumina MiSeq platform	V1-V3	CRS-depression and control	One-way ANOVA followed by the Student-Newman-Keuls test: p < 0.05
Han SK et al. 2019 ^[98]	C57BL/6 mice	Republic of Korea	case-control	-	IS-depression	IS (N=8) IS-NK41 (N=8) IS-NK46 (N=8) IS-NK41+NK46 (N=8) IS-fluoxetine (N=8) Control (N=8)	6-week-old	male	EPM: open arms time and entries FST: immobility time TST: immobility time	After 2 days of IS	Fecal samples	-	qPCR	-	IS-depression and control	One-way ANOVA followed by a Duncan multiple range test: p < 0.05

Han SK et al. 2020a ⁴⁷³	C57BL/6 mice	Korea	case-control	-	IS-depression EC-depression	<p>Experiment 1: IS (N=6) IS+Red ginseng low-dose (N=6) IS+Red ginseng middle-dose (N=6) IS+Red ginseng high-dose (N=6) IS+Fermented red ginseng low-dose (N=6) IS+Fermented red ginseng middle-dose (N=6) IS+Fermented red ginseng high-dose (N=6) Control (N=6)</p> <p>Experiment 2: IS (N=6) IS+Fluoxetine (N=6) IS+Red ginseng low-dose (N=6) IS+Red ginseng middle-dose (N=6) IS+Fermented red ginseng low-dose (N=6) IS+Fermented red ginseng middle-dose (N=6) Control (N=6)</p> <p>Experiment 3: EC (N=6) EC+Buspirone (N=6) IS+Red ginseng low-dose (N=6) IS+Red ginseng middle-dose (N=6) IS+Fermented red ginseng low-dose (N=6) IS+Fermented red ginseng middle-dose (N=6) Control (N=6)</p> <p>Experiment 4: EC (N=6) EC+Ginsenoside Rd (N=6) EC+Protopanaxatriol (N=6) Control (N=6)</p>	6-week-old	male	EPM: open arm time and entries ↓ TST: immobility time ↑ FST: immobility time ↑ LDT: light box time ↓	After 1 week of acclimatization, 5 days of <i>Escherichia coli</i> exposed and 5 days of drugs treatment	Colon contents	~80-C	16S rRNA gene sequencing-Illumina iSeq 100 platform	V4	EC-depression and control	One-way ANOVA followed by Tukey's multiple range test: $p < 0.05$ LEIS: $p < 0.05$ and LDA > 3.5
Han SK et al. 2020b ⁴⁸¹	C57BL/6 mice	Korea	case-control	-	EC-depression	<p>EC (N=5) EC+<i>Lactobacillus reuteri</i> NK33 (N=5) EC+<i>Bifidobacterium adolescentis</i> NK98</p>	5-week-old	male	TST: immobility time ↑ FST: immobility time ↑	After 1 week of acclimatization, 5 days of <i>Escherichia coli</i>	Fecal samples	-	16S rRNA gene sequencing-Illumina iSeq 100 platform	V4	EC-depression and control	One-way ANOVA followed by Tukey's multiple range test: $p <$

					(N=5) EC+ <i>NK33/NK98</i> (1:1) (N=5) EC+ <i>NK33/NK98</i> (4:1) (N=5) EC+ <i>NK33/NK98</i> (9:1) (N=5) Control (N=5)				exposed and 5 days of drugs treatment						0.05 LEISe: $p < 0.05$ and LDA > 3.5
Han SK et al. 2021 ^[91]	C57BL/6 mice	Korea	case-control	3 mice/cage	RS-depression FMT-RS-depression Experiment 1: RS (N=6) RS+CSS low-dose (N=6) RS+CSS middle-dose (N=6) RS+CSS high-dose (N=6) Control (N=6) Experiment 2: RS (N=6) RS+CSS middle-dose (N=6) RS+Busiprone (N=6) Control (N=6) Experiment 3: Control (N=6) FMT-RS (N=6) FMT-Control (N=6) Experiment 4: FMT-RS (N=6) Control (N=6) FMT-RS+CSS to RS (N=6) FMT-Control to RS (N=6)	6-week-old	male	EPM: open arm time and entries] TST: immobility time] FST: immobility time] LDT: light box time and entries]	After 1 week of acclimatization, 2 days of RS exposed and 5 days of drugs treatment	Fecal samples	-	16S rRNA gene sequencing-Illumina iSeq platform	V4	RS-depression and control FMT-RS-depression and control	Kruskal-Wallis test with Dunn's post-hoc test: $p < 0.05$
Hao W et al. 2021 ^[92]	C57BL/6 mice	China	case-control	-	Antibiotic-depression Ampicillin (N=10) Ampicillin+Xiaoyaosan (N=10) Ampicillin+Probiotics (N=10) Control (N=10)	8-week-old	male	Body weight] TST: immobility time] OFT: total distance] EPM: open arms time and distance]	After 1 week of acclimatization and 2 weeks of ampicillin administration	Cecal contents	20 °C	16S rRNA gene sequencing-	V3-V4	Antibiotic-depression and control	Kruskal-Wallis multi-sample rank sum test: $p < 0.05$
Hao WZ et al. 2021 ^[93]	C57BL/6 mice	China	case-control	-	CUMS-depression CUMS (N=10) CUMS+Comiferyl ferulate (N=10) Control (N=10)	8-week-old	male	Body weight] SPT: sugar preference] FST: immobility time] TST: immobility time] OFT: total distance], center frequency] EPM: open arms time and entries]	After 1 week of acclimatization and 8 weeks of CUMS (the last 4 weeks received comiferyl ferulate treatment)	Colon contents	-	16S rRNA gene sequencing-	V3-V4	CUMS-depression and control	LEISe: $p < 0.05$ and LDA > 4.0 Repeated ANOVA: $p < 0.05$
Hassan AM et al. 2019 ^[93]	C57BL/6J mice	Austria	case-control	2-3 mice/cage	HFD-depression HFD (N=12) Control (N=12)	8-week-old	male	SIT: mouse comparison preference], mouse near vicinity preference] Hair coat index:] SPT: sucrose preference]	caecal contents were collected from each rat at the end of the HFD experiment (8 weeks)	Caecal contents	-	16S rDNA sequencing-Ion PGM Sequencer and an Ion Sequencing 400 Kit	Unspecified	HFD-depression and control	LEISe: $p < 0.05$ and LDA > 2.0

									LabMaster system: horizontal and vertical locomotor activity] MPT: morphine preference], saccharin solution intake]							
Huang F et al. 2021 ^[71]	C57BL/6 mice	China	case-control	pair-housed	Ovariectomy-depression	Ovariectomy (N=7-8) Ovariectomy+P. histicola (N=7-8) Ovariectomy+Cohousing (N=7-8) Control (N=7-8)	10-12-week-old	female	OF: center time and frequency] EPM: open arms time and frequency] FST: immobility] TST: immobility]	14 weeks after ovariectomy	Fecal samples	-80 °C	16S rRNA sequencing analysis-Illumina MiSeq platform	Unspecified	Ovariectomy-depression and control	Kruskal-Wallis H test: p < 0.05 LEIS: p < 0.05 and LDA > 3.0
Huang N et al. 2019 ^[55]	C57BL/6 mice	China	case-control	-	LPS-depression	LPS (N=8) LPS+ketamine (N=8) Control (N=8)	2-month-old	male	FST: immobility time]	After 1 week of acclimatization, fecal samples were collected after LPS and ketamine treatment	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V5	LPS-depression and control	Fisher's exact test: p < 0.05 LEIS: p < 0.05 and LDA > 2.0
Huang YJ et al. 2021 ^[70]	C57BL/6J mice	China	case-control	single	sCSDS-depression	sCSDS (N=7) sCSDS + WGE (N=7) Control (N=7)	5-week-old	male	Water and food intake] SIT: social interaction ratio], total distance] OFT: total distance], crossings number], center bouts proportion] SPT: sucrose preference]	After 1 week of acclimatization and 10 days of sCSDS	Fecal samples	-	16S rRNA gene sequencing-Illumina NextSeq platform	V4	sCSDS-depression and control	Kruskal-Wallis test: p < 0.01
Huang YY et al. 2022 ^[68]	C57BL/6N mice	China	case-control	-	DSS-depression	DSS (N=8) DSS+low-dose L. plantarum(N=8) DSS+high-dose L. plantarum (N=8) DSS+Fluoxetine(N=8) Control (N=8)	4-5 weeks	male	OFT: total distance], center distance] LD: light area distance] SPT: sugar preference.] FST: immobility time]	After 7 days of adaption and 7 days of DSS treatment	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina platform	V3-V4	DSS-depression and control	LEIS: p < 0.05 and LDA > 2.0 One-way ANOVA: p < 0.05
Insera A et al. 2019 ^[73]	C57BL/6J mice	Australia	case-control	Single	(Casp1, Ifng, Nos2) KO anti-depression CUS-depression	(Casp1, Ifng, Nos2) KO CUS (N=20) (Casp1, Ifng, Nos2) KO (N=20) Wild-type CUS(N=16) Wild-type (N=16)	60 days	male	(Casp1, Ifng, Nos2) KO: FST: floating time], swimming and climbing time] SPT: sucrose preference] EPM: open arms time] CUS: FST: floating time], climbing time] EPM: open arms time] OF: center time]	After 1 week of acclimatization and 4 weeks of CUS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq	V4	(Casp1, Ifng, Nos2) KO anti-depression and wild-type CUS-depression and control	LEIS: p < 0.05 and LDA > 3.0
Jang HM et al. 2019 ^[69]	C57BL/6 mice	Korea	case-control	-	IS-depression	IS (N=7) PC-Bupirofen (N=7) IS-NK13 (N=7) IS-NK98 (N=7) IS-NK13+NK98 (N=7) Control (N=7)	5-week-old	male	EPM: open arm time and entries] TST: immobility time] FST: immobility time] LDT: light box time], transition number.]	After 1 week of acclimatization, 2 days of immobilization stress and 5 days of drugs treatment	Fecal samples	-	qPCR for Firmicutes, Bacteroidetes, Actinobacteria and δγ-Proteobacteria	-	IS-depression and control	One-way ANOVA followed by a Duncan multiple range test: p < 0.05
Ji S et al. 2022 ^[69]	C57BL/6 mice	China	case-control	-	CRS-depression	CRS (N=15) CRS-high-dose JWXY (N=10) CRS-middle-dose JWXY (N=14) CRS-low-dose JWXY (N=12)	8-week-old	-	SPT: sucrose preference] FST: floating time] OF: total distance], center distance and time]	After 1 week of acclimatization, the fecal samples were collected after 8 weeks of CRS	Cecal contents	-80 °C	Full-length 16S rRNA sequencing-PacBio platform	-	CRS-depression and control	LEIS: p < 0.05 and LDA > 4.0 Metastats: p < 0.05 or FDR < 0.05

						CRS-Sertraline (N=14) Control (N=10)			Y-Maze: alternation LDT: Time (count) and time (percent)							
Jiang W et al. 2021 ^[90]	Sprague-Dawley rats	China	case-control	5 rat/cage	Post-stroke depression	Post-stroke depression (N=30) Stroke (N=21) Control (N=14)	180-200g	male	Body weight SPT: sucrose preference OFT: center time FST: immobility time	After 1 week of acclimatization, 3 days after IR surgery and 4 weeks of CUMS	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	Post-stroke depression and control	LEISe: p < 0.05 and LDA ≥ 2.0
Jiang Y et al. 2020 ^[91]	C57BL/6J mice	China	case-control	Single	Alcohol-depression	Alcohol (N=7) Alcohol-NR (N=7) Control (N=7) ABX FMT-alcohol (N=6) ABX FMT-alcohol-NR (N=6) ABX FMT-control (N=6)	7-week-old	male	Body weight SPT: sucrose preference FST: immobility time EMP: open arms time and entries Y-maze test: novel arm time , start arm time	After 3 weeks of group housed and 10 weeks of alcohol exposure	Colonic contents	-80 °C	16S rRNA gene sequencing- Illumina HiSeq PE250 platform	V3-V4	Alcohol-depression and control	LEISe: p < 0.05 and LDA > 2.0
Jianguo L et al. 2019 ^[92]	Sprague-Dawley rats	China	case-control	single	CUMS-depression	CUMS (N=6) Control (N=6)	8-week-old	male	SPT: sugar preference OFT: immobility time , grooming time , crossing count , rearing counts FST: immobility time TST: immobility time	After 1 week of acclimatization and 4 weeks of CUMS	Fecal samples	-	16S rRNA gene sequencing- Illumina MiSeq system	V4	CUMS-depression and control	LEISe: adjusted p < 0.05 and LDA > 3.0
Kamimura Y et al. 2021 ^[93]	C57BL/6J mice	Japan	case-control	single	CSDS-depression Modified CSDS-depression	CSDS (N=5) Control (N=7) Modified CSDS (N=5) Control (N=6)	6-week-old	male	Body weights food consumption SIT: social interaction ratio FST: immobility time	After 1 week of acclimatization and 10 days of CSDS	Colon contents	-	16S rRNA gene sequencing- Illumina MiSeq platform RT-PCR for Bifidobacterium spp.	V3-V4	CSDS-depression and control Modified CSDS-depression and control	Student's t-test: p < 0.05
Karen C et al. 2021 ^[94]	Wistar rats	India	case-control	-	MS-depression	Experiment 1: MS (N=6) M+P+S (N=6) MS+S+M (N=6) Control (N=6) Experiment 2: MS+Probiotics (N=6) M+P+S+Probiotics (N=6) MS+S+M+Probiotics (N=6) Control-Probiotics (N=6)	PND34	-	OFT: cross squares number , center time and entries FST: immobility time , swimming time	After maternal separation (PND5-10) and probiotics treatment (PND2-16), fecal samples were collected at PND27	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	MS-depression and control	One-way ANOVA and post hoc comparisons were performed with the Bonferroni test: p < 0.05
Kelly JR et al. 2016 ^[95]	Sprague-Dawley rats	Ireland	case-control	-	ABX FMT-depression	ABX FMT-MDD (N=13) ABX FMT-HC (N=15)	Adult 350 g	male	SPT: sucrose preference EPM: open arms visits OFT: center time	After 14 days of acclimatization, 28 days of antibiotic , 3 days of FMT and 7 days of recolonization	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	Unspecified	FMT-MDD and FMT-HC	Main-Whitney U test and Benjamini-Hochberg FDR-adjusted p-value ≤ 0.1
Kemp KM et al. 2021 ^[96]	C57BL/6J mice	USA	case-control	-	MS	MS+Early weaning (N=37) Control (N=31)	PND28	male:female (1:1)	NA	Colon contents were collected at PND2, PND10 and PND28	Colon contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V4	MS and control	Analysis of composition of microbiomes (ANCOM)

Kim JK et al. 2020 ^[97]	C57BL/6J mice	South Korea	case-control	3-4 mice/cage	EC-depression	Escherichia coli K1 (N=7) EC K1+L. mucosae NK41 (N=7) Control (N=7)	5-week-old	male	EPM: open arms time; FST: immobility time [†]	After 1 week of acclimatization and 5 days of Escherichia coli K1 treatment and 5 days of Lactobacillus mucosae NK41 treatment	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina iSeq 100 platform	V4	EC-depression and control	LEIS: p < 0.05 and LDA > 2.0 one-way ANOVA followed by a Duncan multiple range test: p < 0.05
Kim JK et al. 2021 ^[98]	C57BL/6N mice	South Korean	case-control	3 mice/cage	IS-depression EC-depression	IS (N=6) IS+Buspiroline orally gavaged (N=6) IS+Buspiroline intraperitoneally injected (N=6) Control (N=6) EC (N=6) EC+Buspiroline orally gavaged (N=6) EC+Buspiroline intraperitoneally injected (N=6) Control (N=6)	6-week-old	male	EPM: open arms time and entries; LDT: light time and transition; FST: immobility time [†] TST: immobility time [†]	After 2 days of immobilization stress (or Escherichia coli K1) and 5 days of buspiroline treatment	Fecal samples	-	16S rRNA gene sequencing- Illumina iSeq 100 platform	V4	IS-depression and control EC-depression and control	LEIS: p < 0.05 and LDA > 3.5
Kaudsen JK et al. 2021 ^[99]	Flinders sensitive line rats Flinders resistant line rats	Denmark	case-control	pair-housed	FMT-MDD-depression	FSL-FMT-MDD (N=10) FSL-FMT-Healthy (N=10) FSL-CON-Auto (N=10) FSL-CON-H2O (N=10) FRL-FMT-MDD (N=10) FRL-FMT-MDD-Ser (N=10) FRL-FMT-Healthy (N=10) FRL-CON-Auto (N=10) FRL-CON-H2O (N=10)	6-8-week-old	male	FST: struggling [‡] , immobility [†]	After 1 week of acclimatization, faecal samples were collected before transplantation (pre-FMT) and after transplantation (post-FMT)	Fecal samples	-80 °C	16S rRNA sequencing analysis- Illumina MiSeq platform	V4	FRL-FMT-MDD and FMT-Healthy	Kruskal-Wallis test followed by Dunn's post hoc test: p < 0.05
Kosuge A et al. 2021 ^[78]	C57BL/6J mice	Japan	case-control	-	CSDS-depression	Experiment 1: CSDS (N=11) Control (N=22) Experiment 2: CSDS+M-16V (N=12) CSDS (N=21) Control+M-16V (N=12) Control (N=28)	7-week-old	male	SIT: interaction zone time [‡] , corner areas time [†]	The fecal samples were collected 1 day before exposure of CSDS and after 5 days of CSDS	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CSDS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Kati D et al. 2020 ^[71]	C57BL/6J mice	Hungary	case-control	2-3 mice/cage	MS+CVS-depression	MS+CVS+Rifaximin (N=14) MS+CVS (N=12) Control+Rifaximin (N=10) Control (N=9)	PND80	male	OFT: velocity and total distance [‡] , center time [‡] , first latency in border [‡] EPM: Open arm preference [‡] SPT: Sugar consumption [‡]	Colon contents were collected after 12 days of MS (PND1-12) and 4 weeks of CVS (PND50-78)	Colon contents	-70°C	RT-qPCR	-	MS+CVS-depression and control	Two-way ANOVA followed by Sidak's multiple comparison test: p < 0.05
Lai WD et al. 2022 ^[72]	Wistar rats	China	case-control	-	SD-depression	SD (N=8) SD+Fish oil-riched diet (N=8) Control (N=8)	6-week-old	-	Body weight [‡] OFT: total distance [‡] , center time and entries [‡]	After a 6-week dietary intervention and followed by 4-week chronic sleep deprivation	Colon contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	SD-depression and control	LEIS: p < 0.05 and LDA > 3.0

									SPT: sugar preference; FST: immobility time [†]							
Leclercq S et al. 2020 ⁷³	C57BL/6J mice	Belgium	case-control	3 mice/cage	FMT-AD-depression	Experiment 1: ABX FMT-AD (N=12) ABX FMT-Control (N=12) Experiment 2: Ketogenic diet (N=21) Control (N=21)	3-week-old	male	Three-chamber sociability test: chamber time [†] , sociability index [†] FST: latency to immobility [†]	After 10 days of antibiotic treatment, feces were collected at three time points (23, 35 and 45 days after FMT) and caecal content obtained at necropsy	Fecal samples Caecal contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform qPCR for Faecalibacterium prausnitzii	V5-V6	FMT-AD-depression and FMT-control	Wilcoxon test with FDR correction: q < 0.05
Lee HC et al. 2020 ⁷⁴	BALB/c mice	China	case-control	5-6 mice/cage	Lard diet-depression	Normal diet+Flaxetine (N=6) Fish oil-based diet (N=10) Lard-based diet (N=10) Normal diet control (N=6)	8-week-old	-	OF: central zone visit number [†] FST: immobility time [†]	After 4 weeks of acclimatization and 12 weeks of dietary intervention	Fecal samples	-	16S rRNA gene sequencing- Illumina HiSeq 2500 platform	V1-V3	Lard diet-depression and normal diet control	LEIS: p < 0.05 and LDA > 3.0
Li H et al. 2019 ⁷⁵	Wistar rats	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+FOS-GOS (N=10) CUMS+B. longum (N=10) CUMS+L. rhamnosus (N=10) Control (N=10)	200 ~ 220 g	male	Body weights [†] FST: immobility time [†] SPT: sucrose ingestion [†]	After 7 days of acclimatization and 4 weeks of CUMS	Cecal contents	-80°C	16S rRNA gene sequencing- Illumina HiSeq2500 platform	V4	CUMS-depression and control	Metastats analysis followed by Benjamini and Hochberg false discovery rate: q < 0.05
Li H et al. 2021 ⁷⁶	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=14) CUMS+Rifaximin (N=14) Control (N=14) Control+Rifaximin (N=14)	3-week-old	male	SPT: sucrose preference [†] OF: crossing number [†] , rearing number [†] , center time [†]	After 1 week of acclimatization and 28 days of CUMS and rifaximin treatment	Fecal samples	-	16S rRNA sequencing analysis- Shanghai Majorbio Bio-pharm Technology (Shanghai, China)	V3-V4	CUMS-depression and control	Two-way ANOVA followed by Benjamini and Hochberg correction post hoc test: q < 0.05
Li N et al. 2018 ⁷⁷	C57BL/6 mice	China	case-control	3-4 mice/cage	CMS-depression	CMS (N=8) CMS+Flaxetine (N=8) CMS+Probiotics (N=8) Control (N=8) Control+Flaxetine (N=8) Control+Probiotics (N=8)	6-8-week-old	male	SPT: sucrose preference [†] EPM: open arms time [†] FST: immobility time [†]	After 2 weeks of acclimatization and 4 weeks of CMS	Cecal contents	-80°C	16S rDNA gene sequencing- Illumina HiSeq PE250 platform	V3-V4	CMS-depression and control	Non-parametric Kruskal-Wallis test: p < 0.05
Li N et al. 2019 ⁷⁸	C57BL/6J mice	China	case-control	Single	CUMS-depression	CUMS (N=8) Control (N=8) CUMS-donor (N=8) Control-donor (N=8) ABX FMT-CUMS (N=8) ABX FMT-Control (N=8)	7-week-old	male	Body weights [†] SPT: sucrose preference [†] OF: center time [†] EPM: open arms time [†] FST: immobility time [†]	After 1 week of acclimatization and 4 weeks of UCMS 2 weeks post FMT	Cecum content	-80 °C	16S rRNA gene sequencing- Illumina HiSeq platform	V3-V4	CUMS-depression and control FMT-CUMS and FMT-control	Wilcoxon rank sum tests: p < 0.05
Li P et al. 2021 ⁷⁹	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	CUMS (N=8) CUMS+Acupuncture (N=8) CUMS+Flaxetine (N=8) Control (N=8)	5-week-old	male	Body weight [†] OF: total distance [†] EPM: open arms time [†] SPT: sucrose preference [†]	After 1 week of acclimatization and 6 weeks of CUMS	Fecal samples	-	16S rDNA gene sequencing- Illumina platform	V3-V4	CUMS-depression and control	One-way ANOVA followed by Games-Howell test: p < 0.05
Li Q et al. 2021 ⁸⁰	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	CUMS (N=6) CUMS+Paroxetine (N=6)	6-8-week-old	male	Body weights [†] FST: immovability time [†]	After 1 week of acclimatization and 4 weeks of CUMS	Cecal contents	-	RT-PCR for Lactobacillus, Bifidobacteria, Enterococcus faecalis and Escherichia coli	-	CUMS-depression and control	One-way ANOVA followed by the least significant difference test: p < 0.05

						CUMS+Probiotic (N=6) Control (N=6)			OFF: total distance , center time SPT: sucrose preference							
Li Y et al. 2018 ^[61]	Sprague-Dawley rats	China	case-control	in groups	CUS-depression	CUS+Saline (N=8) CUS+high-dose CTE (N=8) CUS+low-dose CTE (N=8) CUS+Fluoxetine (N=8) Control+Saline (N=8)	200 ± 20 g	male	SPT: sucrose preference OFF: total distance NSF: latency to eat	After 1 week of acclimatization and 4 weeks of CUS	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUS-depression and control	Metastats: p < 0.05
Lim EY et al. 2021 ^[52]	Sprague Dawley rats	Korea	case-control	10-11 rats/cage	Ovariectomy-depression	Experiment 1: Ovariectomy (N=11) Control (N=11) Experiment 2: Ovariectomy (N=10) Ovariectomy+17β-oestradiol (N=10) Ovariectomy+vSL#3 (N=10) Ovariectomy+L. intestinalis (N=11) Ovariectomy+L. intestinalis YT2 (N=11) Control (N=10)	10-week-old	female	Body weight FST: immobility time	Faecal samples (0.5 g) were collected at 0, 1, 3, 6, 10, 14, 18 week after ovariectomy	Fecal samples	-	16S rRNA gene sequencing- high-sensitivity DNA chips and the Biosanalyzer 2100 (Agilent Technologies, Santa Clara, CA, USA)	V1-V2	Ovariectomy-depression and control	Wilcoxon rank-based test: p < 0.05 LEISe: p < 0.05 and LDA > 3.0
Liu S et al. 2021 ^[53]	ICR mice	China	case-control	5 mice/cage	CRS-depression	CRS (N=10) CRS+low-dose crocetin (N=10) CRS+middle-dose crocetin (N=10) CRS+high-dose crocetin (N=10) CRS+fluoxetine (N=10) Control (N=10)	2-week-old	male	Body weights TST: latency time , immobility time OFF: crossing number , fecal number	After 28 days of CRS (before the behavioral tests)	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq 16S Metagenomic Sequencing Library Preparation protocol	V3-V4	CRS-depression and control	Student's t test: p < 0.05
Liu QF et al. 2020 ^[54]	ICR mice	Korea	case-control	-	IS-depression	IS (N=10) IS+Fluoxetine (N=10) IS+Probiotic (N=10) Control (N=10)	6-week-old	male	FST: immobility time , swimming time TST: immobility time OFF: total distance , periphery and center distance EPM: closed arms time , open arms time	After 1 week of acclimatization, fecal samples were collected on day 60 after immobilization stress and fluoxetine or probiotic treatment	Fecal samples	-70 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V4-V5	IS-depression and control	Student's t test: p < 0.05
Liu X et al. 2021a ^[55]	C57BL/6 mice	China	case-control	Single	CUMS-depression	CUMS+inosine (N=30) CUMS (N=30) Control (N=15)	PND21	male	Body weights SPT: sucrose preference OFF: total distance EPM: open arms time , closed arms time	After 1 week of acclimatization and 4 weeks of CUMS and inosine treatment	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 2.0
Liu XJ et al. 2021b ^[56]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+Venlafaxine (N=6) CUMS+Xiaryassan (N=6) CUMS+Shugan (N=6) CUMS+Jiampi (N=6) Control (N=6)	6-week-old	male	Body weights SPT: sucrose preference FST: immobility time	After 1 week of acclimatization and 4 weeks of CUMS and drugs treatment	Cecal contents	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	One-way ANOVA followed by Tukey's post hoc test: p < 0.05 LEISe: p < 0.05 and LDA > 2.0
Liu Z et al. 2020 ^[57]	C57BL/6J mice	China	case-control	4 mice/cage	HFD-postpartum depression	HFD (N=12) HFD+Inulin (N=12)	2-month-old	female	MWM: escape time , target quadrant distance	Once the 21-day lactation was over	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq	V3-V4	HFD-postpartum depression and control	LDISe: p < 0.05 and LDA > 3.0

						Control (N=12) Control-Inulin (N=12)				TST: immobility time† OFT: crossing number ‡							
Lao X et al. 2021 ^[91]	C57BL/6J mice	China	case-control	-	EMF-induced-depression	Electromagnetic field exposure (EMF) (N=10) EMF+Heat acclimation (N=10) Heat acclimation (N=10) Control (N=10)	8-week-old	male		FST: immobility time† TST: immobility time†	After 28 days of ambient temperature, the fecal samples were collected after 5 weeks of EMF	Fecal samples	-80 °C	16S rRNA sequencing analysis-Illumina MiSeq platform	V4	EMF-depression and control	LEISe: p < 0.05 and LDA > 2.0
Lv M et al. 2021 ^[92]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+Venlafaxine (N=6) CUMS+Xiaoyaoan (N=6) Control (N=6)	200 ± 20 g	male		Body weights‡ SPT: sucrose preference‡ OFT: total distances and rearings number ‡ FST: immobility time†	After 1 week of acclimatization and 4 weeks of CUMS	Cecal contents	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 2.0 Random Forests
Lv WJ et al. 2019 ^[93]	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	CUMS (N=6) Control (N=6) ABX FMT-CUMS (N=6) ABX FMT-Control (N=6)	8-week-old	male		Body weight‡ SPT: sucrose preference‡ OFT: center time‡ TST: immobility time†	After 1 week of acclimatization and 4 weeks of CUMS -	Fecal samples	-80 °C	16S rRNA gene sequencing-Unspecified	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 3.0
Lv WJ et al. 2020 ^[94]	Sprague-Dawley rats	China	case-control	-	DSS-depression	DSS (N=5) DSS+Melatonin (N=6) Control (N=7)	6-week-old	male		SPT: sucrose preference rates‡ OFT: center time‡ FST: immobility time†	The fecal samples were collected after 7 weeks of DSS and 2 weeks of recovery	Fecal samples	-80°C	16S rRNA gene sequencing-	V4-V5	DSS-depression and control	One-way ANOVA followed by Bonferroni's post hoc test: p < 0.05
Mu W et al. 2019 ^[95]	Wistar rats	China	case-control	Single	PSD-depression	7d-PSD (N=10) Control (N=10)	240 ± 10 g	male		OFT: total behavioral score‡ FST: immobility time† TST: immobility time† SPT: sucrose preference‡	After 1 week of acclimatization and 7 days of paradoxical sleep deprivation	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	PSD-depression and control	Nonparametric Mann-Whitney U test: p < 0.05
Marin IA et al. 2017 ^[96]	C57BL/6 mice	USA	case-control	2-3 mice/cage	UCMS-depression	UCMS (N=12) Control (N=11)	8-week-old	male		FST: escape behavior‡	After 1 week of acclimatization and 5 weeks of UCMS	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform qPCR	V3-V4	UCMS-depression and control	Two-tailed t-test with Welch's correction: p < 0.05
Martin-Hernandez D et al. 2016 ^[97]	Wistar rats	Spain	case-control	Single	CMS-depression	CMS (N=9) CMS+Antibiotics (N=10) Control (N=8)	200-225g	male		Weight gain‡ FST: immobility time† SPT: sucrose consumption‡ Splash test: latency time‡ EPM: open arms time percentage‡	After 2 week of acclimatization and 3 weeks of CMS and antibiotics treatment	Blood, mesenteric lymph nodes (MLN), liver, spleen	-	Bacterial ecosystems analysis,	-	CMS-depression and control	-
Matoudu Y et al. 2020 ^[98]	Sprague-Dawley rats	Japan	case-control	Single	CSDS-depression	CSDS (N=6) Control (N=6)	8-week-old	male		SIT: social target‡	Fresh fecal samples were collected before the first SDS application (before), 1 day (stress 2d), 4 days (stress 5d), and 10 days (stress 11d) after the first SDS application, and 1 day (after stress), 7 days (1 W), and 1 month (1 M) after the last SDS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CSDS-depression and control (after stress)	Two-way ANOVA followed by Sidak's multiple comparisons test: p < 0.05

McGaughy KD et al. 2019 ^[91]	C57BL/6J mice	USA	case-control	Single	CSDS-depression	CSDS (N=20) Control (N=19)	6-week-old	male	OFF: total distance ↓, vertical activity ↓, center time ↓, corner time ↑ SPT: sucrose preference ↓ FST: immobility time ↑	24hr before the start of the social defeat trials and 24hr after the social interaction testing (after 7 days of acclimatization and 7 days of CSDS)	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CSDS-depression and control	Wilcoxon Rank Sum and Kruskal-Wallis tests followed by a Dunn's post-test: p < 0.05
Medina-Rodriguez EM et al. 2020 ^[71]	C57BL/6 mice	USA	case-control	-	LH-depression	LH (N=5) Non-LH (N=5) Control (N=3)	6-12-week-old	male	Escape failures ↑ Learned helplessness: ↑	Stools immediately after exposure to escapable foot shocks	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq instrument	V4	LH-depression and control	Kruskal-Wallis rank sum test with Bonferroni correction: p < 0.05
Meng C et al. 2022 ^[91]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=20) CUMS+Antibiotics (N=20) Control (N=20)	6-week-old	male	FST: immobility time ↑, swimming time ↓	After 1 week of acclimatization and 4 weeks of CUMS, fresh feces samples were collected at end of short-term antibiotics exposure period (at week 5) and long-term antibiotics exposure period (at week 9)	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina NovaSeq platform	V3-V4	CUMS-depression and control (short-term antibiotics exposure)	One-way ANOVA with a Duncan's test: p < 0.05
Moya-Pérez A et al. 2017 ^[91]	C57BL/6J mice	Spain	case-control	-	MS-depression	MS (N=18) MS+Bifidobacterium (N=18) Control (N=18) Control+Bifidobacterium (N=18)	PND21 PND40	male	EPM: open arms time ↓	After maternal separation (PND2: 21), stool samples were collected at PND21 and PND40	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V4-V5	MS-depression and control (PND21)	Wilcoxon Ranks Sum test with post hoc Bonferroni test: p < 0.05
Murray E et al. 2019 ^[91]	CD-1 mice	Canada	case-control	2 mice/cage	LPS-depression	Acute effect for both male and female: LPS (N=10) LPS+Probiotic (N=10) Control (N=10) Control+Probiotic (N=10) Long term effect for both male and female: LPS (N=10) LPS+Probiotic (N=10) Control (N=10) Control+Probiotic (N=10)	3-week-old	male/female	FST: immobility time ↑ OFF: center time ↓ EPM: open arms time ↓	Fecal samples were collected at five time points; 5 weeks of age (before probiotic treatment), 6 weeks of age (after 1 week of probiotics and just before LPS injection), 24 h after LPS injection, 7 weeks of age (at the end of two-week course of probiotic treatment), 10 weeks of age (adulthood)	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V6-V8	LPS-depression and control	Three-way mixed ANOVA: p < 0.05
O'Mahony SM et al. 2020 ^[91]	Sprague-Dawley rats	Ireland	case-control	3 rats/cage	MS-depression	MS (N=12) MS+MFGM (N=12) MS+Probiotic (N=12) MS+MFGM+Probiotic (N=12) Control (N=12) Control+MFGM (N=12) Control+Probiotic (N=12) Control+MFGM+Probiotic (N=12)	14-week-old	male	NOR: discriminate ability ↓	After maternal separation (PND2: 12), stool samples were collected at the end of the study (weeks 14)	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	MS-depression and control	Rank Kruskal-Wallis test followed by Dunn's test with false discovery rate adjustment: q < 0.05

Osman A et al. 2021 ^[106]	Wistar albino rats	USA	case-control	8 rats/cage	Casein-depression A1/A2 β -casein-depression	Casein experiment: Weaned-Casein-rich milk (N=8) Weaned-Casein-free milk (N=8) Weaned-Control (N=8) A1/A2 milk experiment: Weaned+A1/A2 β -casein milk (N=8) Weaned+A2 β -casein milk (N=8) Weaned-Control (N=8)	PND25	male	FST: immobility time [†]	Fecal samples were collected at PND25	Contents of duodenum, jejunum, ileum, cecum and colon	-	Fluorescence in situ Hybridization (FISH) analysis for Bifidobacterium spp., Clostridium_histolyticum_group, Lactobacilli Enterococci spp.	-	Casein-rich-depression and Casein-free control	Wilcoxon test followed by Benjamini-Hochberg: $p < 0.05$
Partrick KA et al. 2021 ^[107]	Syrian hamsters (Mesocricetus auratus)	USA	case-control	Single	CSDS-depression	Acute CSDS+Placebo (N=20) Acute CSDS-low probiotic (N=10) Acute CSDS-high probiotic (N=20) Repeat CSDS+Placebo (N=20) Repeat CSDS+low probiotic (N=10) Repeat CSDS+high probiotic (N=20) Control+Placebo (N=20) Control+low probiotic (N=10) Control+high probiotic (N=20)	3-month-old	male	SBT: Avoidance behavior [†] , Interaction [†]	Prior to the initial defeat (baseline samples), 24 h after the acute defeat (acute defeat samples), and 24 h after the final defeat (repeated defeat sample)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform qPCR	V3-V4	CSDS-depression and control	Nonparametric Kruskal-Wallis with Dunn's multiple comparisons test: $p < 0.05$ LEIS: $p < 0.05$ and LDA > 2.0
Patterson E et al. 2019 ^[94]	C57BL/6J mice	Ireland	case-control	3-4 mice/cage	HFD-depression	HFD (N=14) HFD+ L. brevis DPC6108 (N=14) HFD+L. brevis DSM32386 (N=14) LFD (N=14)	3-week-old	male	Body weight [†] FST: immobility time [†]	After 5 week of acclimatization, 24 weeks of high fat feeding (the last 12 weeks received L. brevis intervention)	Caecal contents	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	HFD-depression and LFD-control	One-way ANOVA: $p < 0.05$
Pearson-Leary J et al. 2020 ^[105]	Sprague-Dawley rats	USA	case-control	Single	CSDS-depression	CSDS-vulnerable (N=9) CSDS-resilient (N=10) Control (N=8) FMT-CSDS-vulnerable (N=13) FMT-CSDS-resilient (N=13) FMT-Control (N=14) Control (N=15)	275-300g	male	Rats exhibiting passive behavior and shortlatencies (SL/vulnerable) to defeat exhibit increased anxiety- and depressive-like behaviors FST: latency to immobility [†] , immobility time [†] , swimming time [†]	At 24 h before the first social defeat (day 0) and 24 h after the 7th episode of social defeat (30 min/day)(day 8)	Fecal samples	-80 °C	Shotgun metagenome sequencing-Illumina HiSeq 2500 16S rRNA gene sequencing-Illumina MiSeq	- V1-V2	CSDS-depression vulnerable and control	Wilcoxon rank sum test: adjust $p < 0.05$
Pu Y et al. 2021 ^[106]	C57BL/6 mice	Japan	case-control	4-5/cage	Chrm7 KO-depression FMT-Chrm7 KO-depression	Chrm7 KO (N=10) Wild-type (N=10) ABX FMT-Chrm7 KO (N=10) ABX FMT-wild-type (N=10)	8-week-old	male	FST: immobility time [†] TST: immobility time [†] SPT: sacrose preference [†]	At around 10:00 for KO mice After 14 days of antibiotics treatment and 14 days of FMT	Fecal samples	-80 °C	16S rRNA sequencing analysis-MyMetagenome Co., Ltd. (Tokyo, Japan)	Unspecified	Chrm7 KO-depression and wild-type FMT-Chrm7 KO-depression and FMT-wild-type	LEIS: $p < 0.05$ and LDA > 2.0
Puscoddu MM et al. 2015 ^[97]	Sprague-Dawley rats	Ireland	case-control	5 rats/cage	MS	MS (N=10) MS+EPA/DHA low-dose (N=10) MS+EPA/DHA high-dose (N=10) Control (N=10)	17-week-old	female	NA	After maternally separation stress (PND2-12) and EPA/DHA treatment (weeks 5-17), faecal pellets were collected at weeks 17 from female rats	Fecal samples	-80 °C	16S rDNA gene sequencing-Illumina MiSeq platform	Unspecified	MS and control	Wilcoxon rank test: $p < 0.05$

						Control+EPADHA low-dose (N=10) Control+EPADHA high-dose (N=10)											
Qiao Y et al. 2020 ^[106]	Kunming mice	China	case-control	-	CRS-depression CUMS-depression CRS+CUMS-depression	CRS (N=10) CUMS (N=10) CRS+CUMS (N=10) Control (N=10)	8-week-old	male	Body weight Food consumption SPT: sucrose preference FST: immobility time TST: immobility time OFT: rest time , move time , center time and distance	After 1 week of acclimatization and 3 weeks of stress	Rectal contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CRS-depression and control CUMS-depression and control CRS+CUMS-depression and control	Multiple t-test: p <0.05 LEISr: p < 0.05 and LDA > 2.0	
Qiu X et al. 2021 ^[109]	C57BL/6J mice	China	case-control	Single	LPS-depression	LPS (N=8) LPS+Lactobacillus (N=8) Control (N=8) Control+Lactobacillus (N=8)	8-week-old	-	SPT: sucrose preference FST: immobility time	After 7 days of acclimatization, followed by LPS and 7 days of Lactobacillus treatment	Fecal samples	-	qPCR	-	LPS-depression and control	Two-way ANOVA followed by least significant difference (LSD) post-hoc test: p < 0.05	
Qu W et al. 2019 ^[108]	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	CUMS-susceptible (N=6) CUMS-susceptible+TCM (N=19) Control (N=12)	adult 180-220 g	male	SPT: sucrose preference OFT: rearing and crossing numbers LDT: dark zone time	At least 2 fecal pellets were obtained from each rat in Week 9 and 15.	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina HiSeq 2500 platform Shotgun metagenomic analysis- Illumina HiSeq 4000 platform	V4-V5	CUMS-depression and control	One-way ANOVA followed by the LSD test: p < 0.05	
Qu Y et al. 2017 ^[111]	C57BL/6 mice	Japan	case-control	Single	CSDS-depression	CSDS susceptible+Saline (N=6) CSDS susceptible+(R)-ketamine (N=6) CSDS susceptible+Lanicemine (N=6) Control (N=6)	8-week-old	male	FST: immobility time TST: immobility time SPT: sucrose preference	After 10 days of CSDS and 3 days after a single dose of drugs	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq 16S Metagenomic Sequencing	V4	CSDS-depression susceptible and control	One-way ANOVA followed by post-hoc Tukey test: p < 0.05	
Qu Y et al. 2020 ^[112]	C57BL/6 mice	Japan	case-control	-	CSDS-depression	CSDS (N=9) CSDS+Betaine (N=9) Control (N=11) Control+Betaine (N=11)	8-week-old	male	SPT: sucrose preference	After 24 days of betaine treatment (day1-24) and 10 days of CSDS (day15-24), fecal samples were collected at day25	Fecal samples	-80°C	16S rRNA gene sequencing-	V3-V4	CSDS-depression and control	Two-way ANOVA followed by post-hoc Fisher's Least Significant Difference (LSD) test: p < 0.05	
Qu Y et al. 2022 ^[113]	ICR mice	China	case-control	Single	CUMS-depression	CUMS (N=12) Control (N=12)	7 weeks old	male	Body weight SPT: sugar preference FST: immobility time TST: immobility time	After 1 week of acclimatization and 8 weeks of CUMS	Intestinal contents	-80 °C	16S rDNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	Pearson's correlation analysis: p < 0.05	
Rao J et al. 2021 ^[114]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+FMT-control (N=6) Control (N=6)	180 ± 20 g	male	SPT: sucrose preference FST: immobility time	After 1 week of acclimatization, 4 weeks of CUMS and 2 weeks of fecal microbiota transplantation treatment	Colonic contents	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	Kruskal-Wallis test: p < 0.05	
Ray P et al. 2021 ^[115]	C57BL/6 mice BALB/c mice	India	case-control	-	Vancomycin-depression	Vancomycin (N=6) Control (N=6)	6-8-week-old	male	EPM: closed arms time OFT: center time FST: immobility time	Fresh cecal samples were collected everyday till 6th day (total of six time points) during perturbation and four time points of restoration (on 15th, 30th, 45th, and 60th day)	Cecal contents	-	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	Vancomycin-depression and control	ANOVA: p < 0.05	

Robertson RC et al. 2017 ¹¹⁴	C57BL/6J mice	Ireland	case-control	3-4 mice/cage	n-3 PUFA deficiency-depression	n-3 PUFA supplement (N=10) n-3 PUFA deficiency (N=10) Control (N=10)	13-week-old	male	FST: immobility time [†] Three chamber test: time interaction with object [†] , time interaction with mouse [†]	Fecal samples were collected after 13 weeks of dietary treatment	Fecal samples	~20°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	n-3 PUFA deficiency-depression and control (adult only)	Kruskal-Wallis tests followed by Mann-Whitney tests: p < 0.05 LEISe: p < 0.05 and LDA > 2.0
Rosa JM et al. 2020 ¹¹⁷	Swiss mice	Brazil	case-control	10 mice/cage	Aβ1-40-depression	Aβ1-40 (N=8) Aβ1-40+Exercise (N=8) Control (N=8) Control+Exercise (N=8)	30-40 g, 45-55 days	male	FST: immobility time [†] FUST: sniffing time [†]	After 1 week of acclimatization and 28 days of treadmill exercise (Aβ1-40 injection at day 18)	Colon contents	~80°C	RT-qPCR for Firmicutes and Bacteroidetes	-	Aβ1-40-depression and control	Two-way ANOVA followed by Duncan's multiple range post hoc test: p < 0.05
Schmidner AK et al. 2019 ¹¹⁶	NAB/HAB rats	Germany	case-control	3-4 rats/cage	HAB-depression	HAB (N= no data) HAB-Mnocyline (N= no data) HAB+Escitalopram (N= no data) HAB-Mnocyline+Escitalopram (N= no data) NAB (N= no data) NAB-Mnocyline (N= no data) NAB+Escitalopram (N= no data) NAB-Mnocyline+Escitalopram (N= no data)	11-12-week-old	male/female	FST: struggling score [†] , immobility score [†] LDT: light box time [†] , distance traveled [†] EPM: open arms time [†]	After 14 days of drugs injection	Cecum contents	~80°C	16S rDNA gene sequencing-454 pyrosequencing	V3-V6	HAB-depression and NAB control	ANOVA with a subsequent Tukey's test: p < 0.05
Shan B et al. 2021 ¹¹⁸	Sprague-Dawley rats	China	case-control	-	CUS-depression	Experiment 1: CUS (N=15) Control (N=10) Experiment 2: ABX (N=8-10) ABX FMT-CUS (N=8-10) ABX FMT-Control (N=8-10) D-lactic acid (N=8-10) L-lactic acid (N=8-10) Control (N=8-10)	180-220 g	male	OFT: center time [†] EPM: open arms time [†] , closed arms time [†] TST: immobility time [†] FST: immobility time [†]	After 1 week of acclimatization and 5 weeks of CUS	Fecal samples	~80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUS-depression and control	Wilcoxon rank-sum test: p < 0.05 LEISe: p < 0.05 and LDA > 2.0
Shao S et al. 2021 ¹²⁰	C57BL/6 J mice	China	case-control	Single	CRS-depression	CRS+CRS xenografts (N=5) CRS+Fluoxetine+CRS xenografts (N=5) CRS+XCHT-low+CRS xenografts (N=5) CRS+XCHT-high+CRS xenografts (N=5) Control+CRS xenografts (N=5)	6-7-week-old	male	SFP: sucrose preference [†] TST: immobility time [†]	After 7 days of acclimatization, 14 days of CRS, 25 days of behavioural tests, tumour cell injection, and fluoxetine or XCHT treatment	Fecal samples	~80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CRS-depression and control	ANOVA test: p < 0.05
Sheng L et al. 2021 ¹²¹	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+Fluoxetine (N=10) CUMS+Exercise (N=10) Control (N=10)	180 g	female	FST: swimming time [†] , resting time [†] TST: resting time [†] OFT: total distance [†] , peripheral distance [†] EPM: open arms time [†] , closed arms time [†]	Fecal samples were collected after 60 days of exercise	Fecal samples	~70°C	16S rRNA gene sequencing-Illumina MiSeq platform	V4-V5	CUMS-depression and control	Mann-Whitney nonparametric test: p < 0.05
Stopi E et al. 2020 ¹²²	C57BL/6J mice	France	case-control	5 mice/cage	UCMS-depression	Experiment 1: UCMS (N=10) Control (N=10) ABX FMT-UCMS (N=10)	8-week-old	male	TST: immobility time [†] FST: immobility time [†]	After 9 week of UCMS (the last week were received behavioral testing)	Fecal samples	~80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	UCMS-depression and control	ANOVA test: p < 0.05 FMT-UCMS-

					FMT-UCMS-depression	<p>ABX FMT-Control (N=10)</p> <p>Experiment 2: UCMS (N=10) UCMS+Fluoxetine (N=12) Control (N=10)</p> <p>Experiment 3: ABX FMT-UCMS (N=15) ABX FMT-Control (N=13) ABX FMT-UCMS+Fluoxetine (N=10) ABX FMT-UCMS+5-HTP (N=10) ABX FMT-UCMS+Fluoxetine+5-HTP (N=10)</p>				After 1 week of ABX treatment, 4 days of microbiota transplantation, and 8 weeks of colonization (the last week were received behavioral testing)					depression and FMT-control	
Song J et al. 2019a ^[27]	Wistar rats	China	case-control	-	ACTH-depression	ACTH-treatment (N=10) Control (N=10)	10-week-old	male	FST: immobility time [†] TST: immobility time [†]	After 14 days of ACTH treatment	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	ACTH-depression and control	LEIS: p < 0.05 and LDA > 3.0
Song J et al. 2019b ^[28]	Wistar rats	China	case-control	-	ACTH-depression	ACTH (N=10) ACTH+CGA (N=10) control (N=10)	10-week-old	male	SPT: sugar preference [‡] FST: immobility time [†] TST: immobility time [†] OFT: total distance [‡] , rearing number [‡]	After 7 days of acclimatization and 14 days of ACTH treatment	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	ACTH-depression and control	LEIS: p < 0.05 and LDA > 3.0
Song X et al. 2021 ^[25]	ICR mice	China	case-control	Single	CUMS-depression	CUMS (N=8) CUMS+Fluoxetine (N=8) CUMS+Puerarin low-dose (N=8) CUMS+Puerarin high-dose (N=8) Control (N=8) Control+Fluoxetine (N=8) Control+Puerarin high-dos (N=8)	20.0 ± 2.0 g	male	SPT: sucrose preference [‡] FST: immobility time [†]	After 1 week of acclimatization and 4 weeks of CUMS with drugs treatment	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	Kruskal-Wallis test with Bonferroni correction: p < 0.05 LEIS: p < 0.05 and LDA > 2.0
Soviji WN et al. 2019 ^[29]	C57BL/6J mice	Japan	case-control	-	Ovariectomy-depression	Experiment 1: Ovariectomy (N=15) Ovariectomy+Progesterone (N=15)	6-week-old	female	OFT: center time and entries [‡] FST: immobility time [†]	After 2 weeks of recovery from ovariectomy (at 8-week-old of age) and 2 weeks of progesterone treatment	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Ovariectomy-depression and ovariectomy+progesterone control	LEIS: p < 0.05 and LDA > 2.0
Sun L. et al. 2019a ^[27]	C57/6 mice	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+Fluoxetine (N=10) Control (N=10)	8-week-old	male	Body weight [‡] SPT: sucrose preference [‡] TST: immobility time [†] EPM: open arms time [‡]	After 1 week of acclimatization and 5 weeks of CUMS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	Unspecified	CUMS-depression and control	LEIS: Unspecified
Sun L. et al. 2019b ^[28]	C57BL/6 mice	China	case-control	-	Fto-KO anti-depression	Fto-KO (N=8) Wild-type (N=8)	3-month-old	male	EPM: open arms time [‡] OFT: central time [‡] FST: floating time [‡]	Unspecified	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Fto-KO anti-depression and wild-type	Wilcoxon rank sum test: p < 0.05

						Pto-KO (N=7) wild-type (N=7)							Metagenomic-Illumina Hiseq2500 Microbiome Profiling setup	-		
Sun X et al. 2021 ^[170]	C57BL/6 mice	China	case-control	3-4 mice/cage	CRS-depression	CRS (N=10) CRS-WLPLD4 (N=10) Control (N=10)	4-week-old	male	OF1: center time EPM: open arms time and entries FST: immobility time	After 4 weeks of CRS	Fecal samples	-	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CRS-depression and control	One-way ANOVA: p < 0.05
Sun Y et al. 2019 ^[170]	Kunming mice	China	case-control	-	CUMS-depression	CUMS (N=8) CUMS+Fluoxetine (N=8) CUMS+low-dose L.kefirnofaciens ZW3 (N=8) CUMS+middle-dose L.kefirnofaciens ZW3 (N=8) CUMS+high-dose L.kefirnofaciens ZW3 (N=8) Control (N=8)	14-20 g	male	SPT: sucrose preference FST: immobility time OF1: vertical movements , crossings number	After 1 week of acclimatization and 6 weeks of CUMS (the last 2 weeks received drugs treatment)	Fecal samples	-	16S rRNA gene sequencing- Illumina HiSeq platform	V4	CUMS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Sun Y et al. 2020 ^[171]	C57BL/6 mice	China	case-control	4 mice/cage	LPS-depression	LPS (N=12) LPS+Schizandrin (N=12) Control (N=12)	20 ± 2 g	male	FST: immobility time TST: immobility time	After 1 week of acclimatization and 2 weeks of vehicle or SCH treatment	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	LPS-depression and control	One-way ANOVA followed by Tukey multiple comparison test : p < 0.05
Suzuki K et al. 2021 ^[172]	C57BL/6 J (B6) mice	Japan	case-control	-	CSDS-depression	CSDS (N=6) CSDS-Crp4 (N=6) Control (N=6)	7-week-old	male	SIT: social interaction time , distance traveled	We sampled at three time points on day 1, 9, and 14 in the first experiment and at two time points on day 0 and 32 in the second experiment	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	After CSDS- depression and pre-CSDS control	Pairs student's t test: p < 0.05
Szyszkowicz JK et al. 2021 ^[173]	C57BL/6 mice	Canada	case-control	Single	CSDS-depression	CSDS-susceptible (N=10) CSDS-resilient (N=8) Control (N=6)	7-9-week-old	male	SIT: social interaction ratios , contact time , Corner zones time	After 1 week of acclimatization and 3 weeks of CSDS	Cecum contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq Sequencing	V3-V4	CSDS-depression and control	One-way ANOVA followed by Bonferroni correction: p < 0.05
Takahashi E et al. 2021a ^[174]	C57BL/6Jc1 (B6) mice	Japan	case-control	group	AIN-93G-depression	AIN-93G young (N=10) CRF-1 young (N=10) AIN-93G old (N=10) CRF-1 old (N=10)	3-week-old	male	TST: immobility time FST: immobility time	After 5 weeks of AIN-93G diet for young and 85 weeks of AIN-93G diet for old mice	Small intestinal contents	-80 °C	Terminal restriction fragment length polymorphism (T-RFLP) method	-	AIN-93G-depression and CRF-1 control (in old mice)	ANOVA followed by the Bonferroni correction post hoc test: p < 0.05
Takahashi E et al. 2021b ^[175]	C57BL/6Jc1 (B6) mice	Japan	case-control	group	CRS-depression	Cohort 1 CRS-AIN-93G short (N=10) CRS-CRF-1 short (N=10) Control-AIN-93G short (N=10) Control-CRF-1 short (N=10) Cohort 2 CRS-AIN-93G long (N=10) CRS-CRF-1 long (N=10) Control-AIN-93G long (N=10) Control-CRF-1 long (N=10)	3-week-old	male	Body weight FST: struggling time , immobility time SPT: sucrose preference	After 3 weeks of CRS and 1 week of AIN-93G diet for cohort 1 or 5 weeks of AIN-93G diet for cohort 2	cecum contents	-80 °C	Terminal restriction fragment length polymorphism (T-RFLP) method	-	CRS-AIN-93G long-depression and Control-AIN-93G long control	Unpaired t-test with Welch's correction: p < 0.05

Teng Y et al. 2021 ^[156]	Macaca fascicularis monkeys	China	case-control	Single	CUMS-depression	CUMS-depression (N=5) Control (N=5)	1-4 year-old	male	Frequency and duration of huddle posture [†] Frequency and duration of locomotion [†] AAT: attempts for the apple [†] HT: anxiety-like behaviors [†]	Fresh feces were collected from mice of each group over 55 days after the model was built	Lumen and mucosa of cecum, ascending colon, transverse colon, and descending colon	~80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 2.0
Tian P et al. 2019 ^[177]	C57BL/6J mice	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+Fluoxetine (N=6) CUMS+CCFM687 (N=6) Control (N=6)	6-week-old	-	FST: immobile time [†] TST: immobile time [†] SDT: latent time [†] EMP: open arms time [†] LDT: light box time [†]	After 1 week of acclimatization and 5 weeks of CUMS	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	One-way ANOVA followed by Fisher's LSD multiple comparison test: p < 0.05
Tian P et al. 2019 ^[178]	C57BL/6J mice	China	case-control	-	CUMS-depression	CUMS (N=6) CUMS+Fluoxetine (N=6) CUMS+Probiotics (N=6) Control (N=6)	6-week-old	male	FST: swimming time [†] SPT: sucrose preference [†] EPM: open arms time [†] OFT: center time [†] LDT: light chamber entries [†] SDT: latency (s) of jumping [†]	After 5 weeks of CUMS	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 2.0
Tian P et al. 2020 ^[179]	C57BL/6J mice	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+Fluoxetine (N=10) CUMS+CCFM1025 (N=10) Control (N=10)	6-week-old	male	FST: immobility time [†] TST: immobility time [†] OFT: center time [†] SPT: sucrose preference [†] EPM: open arms time [†]	After 1 week of acclimatization and 5 weeks of CUMS (and drugs)	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEISe: p < 0.05 and LDA > 3.0
Tian P et al. 2021 ^[148]	mice	China	case-control	-	CRS-depression	CRS (N=6) CRS+Acetylated starch (N=8) CRS+Propionylated starch (N=8) CRS+Butyrylated starch (N=8) CRS+Isobutyrylated starch (N=8) Control (N=10)	-	-	OFT: active time [†] , open field time [†] FST: immobility time [†]	After 1 week of acclimatization and 2 weeks of CRS	Fecal samples	-	16S rRNA gene sequencing-	V3-V4	CRS-depression and control	LEISe: p < 0.05 and LDA > 2.0
Tian XY et al. 2021 ^[141]	BALB/c mice	China	case-control	Single	IS-postpartum depression	IS-PPD (N=10) IS-PPD+919 syrup (N=10) Control (N=10)	7-week-old	female	FST: immobility time [†] TST: immobility time [†]	On PND2, PND9, PND16, and PND23, fecal samples were collected from each mouse at 12 a.m. and quickly frozen in liquid nitrogen.	Fecal samples	Liquid nitrogen	16S rRNA gene sequencing-Illumina HiSeq2500 platform Metagenomic Sequencing-Illumina HiSeq platform	V3-V4 -	IS-postpartum depression and control	LEISe: p < 0.05 and LDA > 3.0
Tillmann S et al. 2019 ^[62]	Flinders sensitive line rats Flinders resistant line rats	Danish	case-control	pair-housed	FSL-depression	FSL-saline (N=8) FSL-FMT-FSL (N=8) FSL-FMT-FRL (N=8) FRL-saline (N=8) FRL-FMT-FSL (N=8) FRL-FMT-FRL (N=8)	10.6 ±1.1 weeks old	male	Body weight [†] OFT: No data FST: No data	After 2 weeks of acclimatization and 16 days of fecal suspensions transplantation	Fecal samples	~80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	FSL-depression and FRL-control	DESeq2: adjusted p (Benjamini-Hochberg) < 0.05

Tung TH et al. 2019 ^[41]	Sprague-Dawley rats	China Taiwan	case-control	-	CMS-depression	CMS (N=5) CMS-Imipramine (N=5) CMS-Fish oil (N=5) CMS-Olive oil (N=5) Control (N=5)	6-week-old	male	Body weights; OFT: total distances; SPT: sucrose preference; FST: immobile time†	After 2 weeks of acclimatization and 12 weeks of CMS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq system	V3-V4	CMS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Wang L et al. 2020 ^[44]	Kummung mice	China	case-control	Single	CUMS-depression	CUMS (N=8) CUMS+low-dose TIV (N=8) CUMS+medium-dose TIV (N=8) CUMS+high-dose TIV (N=8) CUMS+Fluoxetine (N=8) Control (N=8)	6-week-old	male	Body weight; FST: immobility time; SPT: sucrose preference;	After 1 week of acclimatization and 4 weeks CUMS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina HiSeq platform	V4	CUMS-depression and control	One-way ANOVA followed by LSD tests: p < 0.05
Wang L et al. 2021 ^[45]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=10) CUMS+Fluoxetine (N=10) CUMS+low-dose SI (N=10) CUMS+middle-dose SI (N=10) CUMS+high-dose SI (N=10) Control (N=10)	200-220g	female and male	Body weight; SPT: sucrose preference; OFT: horizontal and vertical movements score; LDT: dark area time†	After 2 weeks of acclimatization, 10 weeks of CUMS and 8 weeks of drugs	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CUMS-depression and control	LEIS: p < 0.05
Wang P et al. 2021 ^[46]	C57BL/6J mice	China	case-control	-	Antibiotic-depression	Antibiotic (N=9) Antibiotic+Saline (N=9) Antibiotic+Probiotics (N=9) Control (N=9)	6-week-old	male	EPM: total crossing[, open arms time, velocity]; OFT: total distance[, center time and distance]; TST: immobility time† Splash test: grooming latency;	After 1 week of acclimatization, fecal samples were collected after 3 weeks of ASC antibiotics treatment, and 2 weeks of probiotics treatment	Fecal samples	-	qPCR	-	Antibiotic-depression and control	One-way ANOVA followed by Tukey's multiple comparisons test: p < 0.05
Wang Q et al. 2019 ^[47]	CD-1 mice	China	case-control	single	CMS-depression	CMS (N=8) CMS+SE (N=8) Control (N=8)	3-month-old	male	SPT: sucrose preference; FST: immobility time† MBT: number of marbles buried; LDT: light zone duration;	After 2 weeks of acclimatization and 10 weeks of CMS	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CMS-depression and control	LEIS: p < 0.05 and LDA > 3.0
Wang R et al. 2021 ^[48]	C57BL/6J mice	China	case-control	-	CRS-depression	CRS (N=5) CRS+TFA low-dosage (N=5) CRS+TFA high-dosage (N=5) Control (N=5)	6-week-old	male	OFT: total distance; FST: immobility time† TST: immobility time†	After 7 days of acclimatization and 30 days of CRS	Cecum contents	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CRS-depression and control	One-way ANOVA: p < 0.05
Wang S et al. 2020b ^[49]	C57BL/6 mice	Japan	case-control	Single	FMT CSDS-depression Microbe-depression	ABX FMT CSDS-susceptible (N=7) Water FMT CSDS-susceptible (N=7) ABX FMT control (N=7) Water FMT control (N=7) ABX-Microbe (N=10) ABX+Water (N=10) Water (N=10)	8-week-old	male	SPT: sucrose preference; FST: immobility time† TST: immobile time†	After 14 days of antibiotic cocktail treatment and 14 days of FMT from CSDS-susceptible mice or control	Fecal samples	-	16S rRNA gene sequencing-MiSeq according to the Illumina protocol	V1-V2	FMT CSDS-depression and FMT control	Two-way ANOVA followed by post hoc Fisher's LSD test: p < 0.05
Wang S et al. 2020b ^[50]	C57BL/6 mice	Japan	case-control	-	CSDS-depression	CSDS (N=10) CSDS+Antibiotics (N=10)	8-week-old	male	SPT: sucrose preference;	Fresh fecal samples were collected on day 15 before CSDS	Fecal samples	-80-C	16S rRNA gene sequencing-Illumina MiSeq platform	V1-V2	CSDS-depression and control	Two-way ANOVA followed by post hoc Tukey test: p < 0.05

						Control (N=10) Control+Antibiotics (N=10)				and 24 hours after CSDS (day15-24)						
Wang S et al. 2021 ^[151]	C57BL/6 mice	Japan	case-control	Single	FMT CSDS-depression	ABX FMT CSDS-susceptible Eplax2 KO (N=10) ABX FMT CSDS-susceptible WT (N=10) ABX FMT control Eplax2 KO (N=10) ABX FMT control WT (N=10)	8-week-old	male	SPT: sucrose preference ↓	After 14 days for antibiotic cocktail treatment and 14 days for FMT procedure	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V1-V2	FMT CSDS-depression and control (in both Eplax2 KO mice and WT mice)	Kruskal-Wallis test: p < 0.05
Wang Y et al. 2021 ^[152]	C57BL/6 mice	China	case-control	4 mice/cage	LPS-depression	LPS (N=20) LPS+(S)-norketamine (N=15) LPS+(R)-norketamine (N=15) Control (N=8)	2-month-old	male	FST: immobility time ↑ TST: immobility time ↑	After 1 week of acclimatization and a single injection of LPS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V5	LPS-depression and control	Kruskal-Wallis test: p < 0.05
Ward AK et al. 2019 ^[153]	C57BL/6 mice	Ireland	case-control	4 mice/cage	ADR-159-depression	ADR-159 (N=12) Control (N=12)	8-week-old	male	OFT: center time ↓, total distance ↓ 3CT: interaction time ↓, chamber time ↑ TST: immobility time ↑	After 1 week of acclimatization, faecal samples were collected weekly during the 8 weeks of designated diet	Fecal samples	-80 °C	16S rRNA gene sequencing-MiSeq sequencing (Germany)	V3-V4	ADR-159-depression and control	DESeq2 with Wald test: p < 0.05
Wei CL et al. 2019 ^[154]	C57BL/6J mice	China-Taiwan	case-control	4 mice/cage	Corticosterone-depression	Corticosterone (N=8) Corticosterone+Fluoxetine (N=8) Corticosterone+Live L. paracasei PS23 (N=8) Corticosterone+Heat-killed L. paracasei PS23 (N=8) Control (N=8)	6-8 weeks old	male	OFT: total distance ↓, center time and entries ↓ SPT: sugar preference ↓ FST: immobility time ↑	Three or four fecal pellets were collected on day 38	Fecal samples	-20 °C	qPCR for Bifidobacterium, Clostridium coccoides group, Enterobacteriaceae, Enterococcus, and Lactobacillus	-	Corticosterone-depression and control	One-way ANOVA followed by Newman-Keuls multiple comparison test: p < 0.05
Wei LN et al. 2019 ^[155]	Wistar rats	China	case-control	Single	CUMS-depression	CUMS (N=9) Control (N=9)	180-210 g	male	SPT: sucrose preference ↓ FST: swimming time ↓, immobility time ↓	After 1 week of acclimatization and 5 weeks of CUMS	Rectal contents	-80 °C	16S rRNA gene sequencing-Illumina HiSeq2500 platform	V4	CUMS-depression and control	LEISc: p < 0.05 and LDA > 4.0
Westfall S et al. 2021 ^[156]	C57BL/6J mice	USA	case-control	group	CUMS-depression CUMS+US-depression	Stress (N=16) Stress+BDPP (N=16) Stress+Probiotics (N=16) Stress+Synbiotics (N=16) Control (N=16) Control+BDPP (N=16) Control+Probiotics (N=16) Control+Synbiotics (N=16)	8-week-old	male	FST: freezing time ↑ OFT: center time ↓	After 2 week of acclimatization and 11 weeks of respective treatment (fecal pellets were collected after 4 weeks of CUMS and after 7 days of US)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	CUMS-depression and control CUMS+US-depression and control	One-way ANOVA and Tukey's post-hoc analysis: p < 0.05
Wong ML et al. 2016 ^[157]	C57BL/6J mice	Australia	case-control	group	CRS-depression	CRS (N=15) CRS+Minocycline (N=15) Minocycline (N=12) Control (N=12)	60-90 days	male	Body weight ↓ FST: floating time ↑, swimming and climbing behaviors ↓ EPM: open arms time ↓, open/close arms time ↓ OFT: defecations number ↑	After 21 days of CRS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	CRS-depression and control	Mann-Whitney U-test: p < 0.05
Wu F et al. 2020 ^[158]	C57BL/6 mice	China	case-control	-	HFD-depression	HFD (N=10) HFD+A. muciniphila (N=10) Control (N=10) Control+A. muciniphila (N=10)	8-week-old	female	SPT: sugar preference ↓ YMT: the error times ↑	After 2 week of acclimatization and 10 months of high-fat diet plus A. muciniphilus gavage	Fecal samples	-	16S rDNA gene sequencing-Illumina MiSeq platform	V4	HFD-depression and control	One-way ANOVA: p < 0.05

Wu J et al. 2021 ^[159]	C57BL/6 mice	China	case-control	Single	CUMS-depression Dexamethasone-depression	CUMS (N=15) Dexamethasone (N=15) Control (N=15)	4 to 6-week-old	female	OFF: total distance ₁ , speed ₁ , crossing and rearing number ₁ EPM: open arms time ₁ FST: immobility time ₁ TST: immobility time ₁ SPT: sucrose preference ₁	After 1 week of acclimatization, the fecal samples were collected after 35 days of CUMS or dexamethasone treatment	Fecal samples	-80 °C	16S rRNA sequencing analysis- Illumina MiSeq platform	V3-V4	CUMS-depression and control Dexamethasone-depression and control	LEIS: p < 0.05 and LDA > 3.0 Kruskal-Wallis tests with multiple comparison correction: p < 0.05
Wu J et al. 2022 ^[160]	Macaca fascicularis monkeys	China	case-control	group	Naturally-occurring depression	Depression (N=6) Control (N=6)	Adult	female	Duration of huddle and sit alone behaviors ₁ Duration of amicable and locomotion activities ₁	After behavioral tests	Cecum contents	-80 °C	Metagenomic-Illumina HiSeq X platform	-	Naturally-occurring depression and control	LEIS: p < 0.05 and LDA > 2.0
Wu M et al. 2020 ^[161]	C57BL/6 mice	China	case-control	Single	CRS-depression	CRS (N=20) Control (N=20)	8-16 week-old	male	OFF: center time ₁ , center distance ₁ FST: immobility time ₁ SPT: sucrose preference ₁ Body weight ₁	After 4 weeks of CRS	Fecal samples	-80 °C	16S rRNA gene sequencing- Roche 454 sequencing	V3-V5	CRS-depression and control	LEIS: p < 0.05 and LDA > 3.0
Xiu J et al. 2021 ^[162]	C57BL/6 mice	China	case-control	Single	LPS-depression	LPS (N=6) CAP (N=6) LPS+CAP (N=6) Control (N=6)	4-week-old	male	SPT: sucrose preference ₁ OFF: rearing and crossing number ₁ FST: immobility time ₁ TST: immobility time ₁	After 4 months of CAP treatment. During the last 5 days, mice in LPS and CAP+LPS groups received lipopolysaccharide	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	LPS-depression and control	LEIS: p < 0.05 and LDA > 3.0
Xiao Q et al. 2020 ^[163]	C57BL/6 mice	China	case-control	Single	CRS-depression	CRS (N=10) CRS+Crocin-1 (N=10) Control (N=10)	6-week-old	male	SPT: sucrose preference ₁ FST: immobility time ₁ TST: immobility time ₁	After 1 week of acclimatization and 10 weeks of CRS (the last 6 weeks received crocin-1 and duration of CRS is halved)	Cecal contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CRS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Xie R et al. 2020a ^[164]	C57BL/6 mice	China	case-control	Single	CSDS-depression	CSDS-susceptible (N=7) CSDS-resistant (N=7) Control (N=7)	7-week-old	male	SIT: interaction ratio ₁ , interaction time ₁ SPT: sucrose preference ₁ OFF: total distance ₁ , center time ₁ , center entries ₁	After 1 week of acclimatization and 10 days of CSDS	Peyer's patches-gut-associated lymphoid tissue	-	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CSDS-depression susceptible and control	One-way ANOVA: p < 0.05
Xie R et al. 2020b ^[165]	C57BL/6 mice	China	case-control	4 mice/cage	CSDS-depression	CSDS-susceptible (N=10) CSDS-susceptible+L. reuteri 3 (N=10) Control (N=10) Control+L. reuteri 3 (N=10)	8-week-old	male	SIT: interaction ratio ₁ SPT: sucrose preference ₁ TST: immobility time ₁ OFF: center time and entries ₁ , total distance ₁	After 1 week of acclimatization, 10 days of CSDS and 4 weeks of microbial treatment	Colonic contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq sequencing	V3-V4	CSDS-depression and control	One-way ANOVA test followed by Tukey's test: p < 0.05
Xie Y et al. 2021 ^[166]	C57BL/6 mice	China	case-control	Single	SIMT-anti-depression	Small intestinal microbiota transplantation (N=6) Large intestinal microbiota transplantation (N=6) Control (N=6)	PND56	male	SPT: sucrose preference ₁ FST: immobility time ₁ TST: immobility time ₁	Before microbiota transplantation (PND7) and after 14 days of microbiota transplantation (PND92)	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	SIMT-anti-depression and control	Kruskal-Wallis H test followed by the Bonferroni post hoc test: p < 0.05
Xu J et al. 2022 ^[167]	C57BL/6 mice	China	case-control	Single	CUMS-depression	CUMS (N=12) CUMS+high-dose L. rhamnosus zz-1 (N=12) CUMS+middle-dose L. rhamnosus zz-1	4-week-old	male	Body weight ₁ SPT: sugar preference ₁ FST: immobility time ₁ OFF: total distance ₁ , center time ₁	After 1 week of acclimatization and 5 weeks of CUMS	Cecal contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	one-way analyses of variance (ANOVAs) followed by Tukey's post hoc test: p < 0.05 LEIS

						(N=12) CUMS+low-dose <i>L. rhamnosus</i> zz-1 (N=12) Control (N=12)										
Xu M et al. 2022 ^[166]	C57BL/6J mice	China	case-control	-	CUS-depression	CUS (N=9) CUMS+ <i>Lactobacillus</i> for each strain (N=7) Control (N=8)	6 weeks	male	OF1: center time; MBT: number of buried beads; LDT: open chamber time; FST: immobility time; TST: immobility time	After 1 week of acclimatization and 6 weeks of CUS	Colon contents	-	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUS-depression and control	-
Xu Z et al. 2019 ^[166]	C57BL/6 mice	China	case-control	4 mice/cage	CAE-depression	CAE (N=6) Control (N=6)	4-week-old	male	OF1: center time and distance; EPM: open arms time; FST: mobility time; TST: immobility time	After 1 week of acclimatization and fecal samples were collected at the twentieth day of the drinking session	Fecal samples	-80 °C	16S rRNA metagenomic sequencing- 16S metagenomic sequencing library protocol (Illumina)	V3-V5	CAE-depression and control	Unpaired Student's t-test; p < 0.05
Xue M et al. 2021 ^[170]	C57BL/6J mice	China	case-control	Single	Alcohol-depression	Alcohol (N=8) Alcohol+Facoidan (N=8) Control (N=8)	8-week-old	male	Body weight; Food intake; SPT: sucrose preference; FST: immobility time; Y-maze test: novel arms time; OF1: total distance, center time and entries	After 3 weeks of acclimatization and 10 weeks of alcohol exposure (and facoidan treatment)	Colon contents	-	16S rRNA gene sequencing- Illumina HiSeq platform	V3-V4	Alcohol-depression and control	One-way ANOVA followed by Tukey's test or Kruskal-Wallis test followed by Bonferroni test; p < 0.05
Yan T et al. 2020 ^[171]	C57BL/6 mice	China	case-control	4 mice/cage	CUMS-depression	CUMS (N=10) CUMS+Polysaccharide (N=10) Control (N=10) CUMS-donor (N=10) CUMS+Polysaccharide-donor (N=10) Control-donor (N=10) ABX FMT-CUMS (N=10) ABX FMT-CUMS+Polysaccharide (N=10) ABX FMT-Control (N=10)	18-22 g	male	OF1: center distance; EPM: open arms time and entries; TST: immobility time; FST: immobility time	After 1 week of acclimatization and 4 weeks of CUMS	Cecum contents	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	One-way ANOVA followed by Tukey multiple comparison tests; p < 0.05
Yan T et al. 2021 ^[172]	C57BL/6 mice	China	case-control	4 mice/cage	LPS-depression	LPS (N=10) LPS+SCE (N=10) LPS+SCL (N=10) LPS+SCPS (N=10) LPS+SCVO (N=10) Control (N=10)	18-22 g	male	FST: immobility time; TST: immobility time	After 7 days of acclimatization and 14 days of drugs	Fecal samples	-	16S rRNA gene pyrosequencing- Illumina MiSeq platform	V3-V4	LPS-depression and control	One-way ANOVA followed by Tukey multiple comparison tests; p < 0.05
Yang C et al. 2017a ^[173]	C57BL/6 mice	Japan	case-control	Single	CSDS-depression	CSDS-susceptible (N=8) CSDS-resistant (N=6) Control (N=8)	8-week-old	male	SIT: interaction time	After 10 days of CSDS	Fecal samples	-80 °C	16S rRNA analysis-Terminal restriction fragment length polymorphism (T-RFLP) analysis	-	CSDS-depression susceptible and control	Fisher's exact test; p < 0.05

Yang C et al. 2017 ⁹¹⁷⁴	C57BL/6 mice	Japan	case-control	Single	CSDS-depression	CSDS (N=6) CSDS+(R)-ketamine (N=6) CSDS+(S)-ketamine (N=6) Control (N=6)	8-week-old	male	FST: immobility↓ TST: immobility↑ SPT: sucrose preference↓	The fecal samples were collected 10 days of CSDS and 4 days (day 16) after a single dose of drugs	Fecal samples	-80 °C	16S rRNA sequencing analysis-Illumina MiSeq platform	V4	CSDS-depression and control	One-way ANOVA: p < 0.05
Yang C et al. 2019 ¹⁷⁷⁵	Sprague-Dawley rats C57BL/6 mice	China	case-control	-	SNI-depression FMT SNI susceptible-depression	SNI anhedonia susceptible (N=8) SNI anhedonia resilient (N=8) Control (N=8) ABX FMT-SNI susceptible (N=10) ABX FMT-SNI resilient (N=10) ABX PBS (N=10) Control (N=10)	2-month-old	male	Body weight↓ MWt: withdraw threshold↓ SPT: sucrose preference↓ TFT: tail flick latency↓ FST: immobility time↑ TST: immobility time↑	After 7 days of acclimation, then 23 days after spared nerve injury (day 0) After 7 days of acclimation, 14 days of antibiotics treatment and 14 days of feces transplantation	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq system	V3-V4	SNI-depression susceptible and control ABX FMT SNI susceptible-depression and ABX PBS-control	One-way ANOVA followed by post-hoc Tukey's test: p < 0.05
Yang HL et al. 2021 ¹⁷⁷⁶	C57BL/6J mice	China	case-control	-	CRS-depression	CRS (N=15) CRS+Dexamethasone (N=15) Control (N=15) Control+Dexamethasone (N=15)	7-week-old	male	SPT: sucrose preference↓ FST: immobility time↑ OFT: center time↓ EPM: closed arms time↑	After 1 week of acclimatization and 5 weeks of CRS along with dexamethasone	Fecal samples	-	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CRS-depression and control	One-way ANOVA followed by Dunnett's multiple comparison test: p < 0.05
Yang J et al. 2021 ¹⁷⁷⁷	Sprague-Dawley rats	China	case-control	-	PSD-depression	PSD (N=15) PSD+Exercise Training (N=15) Control (n=15)	230-250 g	male	-	After 7 days of acclimatization and 30 consecutive days of UCS	-	-	-	-	PSD-depression and control	LEIS: p < 0.05 and LDA > 3.0
Yang Q et al. 2020 ¹⁷⁷⁸	C57BL/6 mice	China	case-control	5 mice/cage	CUMS-depression	CUMS (N=8) CUMS+Imipramine (N=8) CUMS+chronic minocycline (N=8) CUMS+acute minocycline (N=8) Control (N=8)	6-8 week-old	male	OFT: total distance↓, center time↓ TST: immobility time↑ FST: immobility time↑	After 1 week of acclimatization and 6 weeks of CUMS (the last 4 weeks received drugs treatment)	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4-V5	CUMS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Yang Y et al. 2022 ¹⁷⁷⁹	Sprague-Dawley rats	China	case-control	-	MS-postpartum depression	MS (N=8) MS+Lactobacillus casei (N=8) MS+Paroxetine (N=8) Control (N=8)	Postpartum PND28	female	SPT: sugar preference↓ EPM: open arms time and entries↓ FST: immobility time↑ TST: immobility time↑	PND 28 (PND2-PND21 for MS)	Cecal contents	-	qPCR for <i>Enterococcus faecalis</i> , <i>Bifidobacterium</i> , <i>Lactobacillus</i> , <i>Escherichia coli</i>	-	MS-postpartum depression and control	ANOVA: p < 0.05
Yu JB et al. 2019 ¹⁷⁸⁰	Sprague-Dawley rats	China	case-control	-	CUS-depression	CUS (N=8) CUS+Fluoxetine (N=8) CUS+Paclitaxel low-dosage (N=8) CUS+Paclitaxel high-dosage (N=8) Control (N=8)	180-200 g	male	SPT: sucrose preference↓	After 8 weeks of CUMS (the last 2 weeks received drugs treatment)	Fecal samples	-	16S rRNA gene sequencing-Barcoded pyro sequencing	V3-V4	CUMS-depression and control	Student's t-test: p < 0.05
Yu M et al. 2017 ¹⁷⁸¹	Wistar rats	China	case-control	-	CVS-depression	CVS (N=8) Control (N=8)	8-week-old	male	Body weight↓ OFT: rearing and crossing numbers↓ SPT: sucrose preference↓	After 4 weeks of CVS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina HiSeq platform	V3-V4	CVS-depression and control	Student's t-test: p < 0.05
Yu M et al. 2020 ¹⁷⁸²	Wistar rats	China	case-control	-	CVS-depression	CVS (N=8) CVS+Antibiotic (N=8) CVS+CSGS (N=8) CVS+Antibiotic+CSGS (N=8) Control (N=8)	200 ± 20 g	male	Body weight↓ SPT: sucrose preference↓ OFT: rearing number↓, crossing number↓	After 28 days of CVS experiment	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	CVS-depression and control	One-way ANOVA: p < 0.05

Yu M et al. 2021 ^[103]	Wistar rats	China	case-control	-	CVS-depression	CVS (N=8) Antibiotic (N=8) CVS+Antibiotic (N=8) Control (N=8)	200 ± 20 g	male	OFF: number of rearing and crossing ↓ SPT: sucrose preference ↓	After 4 weeks of CVS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina HiSeq platform	V3-V4	CVS-depression and control	One-way ANOVA: p < 0.05
Yun SW et al. 2020 ^[104]	C57BL/6J mice	Korea	case-control	-	EC-depression	EC (N=6) EC+L. gasseri NK109 (N=6) Control (N=6)	5-week-old	male	TST: immobility time ↑ FST: immobility time ↑	After 1 week of acclimatization and 5 days of Escherichia coli K1 treatment and 5 days of Lactobacillus gasseri NK109 treatment	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina iSeq 100 platform	V4	EC-depression and control	Unpaired t-test: p < 0.05
Yun SW et al. 2021 ^[105]	C57BL/6J mice	Korea	case-control	3 mice/cage	EC-depression	EC (N=6) EC+L. paracasei NK112 (N=6) Control (N=6)	5-week-old	male	EPM: open arms time and entries ↓ TST: immobility time ↑ FST: immobility time ↑	After 1 week of acclimatization and 5 days of Escherichia coli K1 treatment and 5 days of Lactobacillus paracasei NK112 treatment	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina iSeq 100 platform	V4	EC-depression and control	one-way ANOVA with Tukey's multiple comparison test: p < 0.05 LEIS: p < 0.05 and LDA > 4.0
Zhang F et al. 2020 ^[106]	Sprague-Dawley rats	China	case-control	5 rats/cage	5-Fu-depression	5-Fu treatment (N=10) Control (N=10)	5-week-old	male	Body weight and food intake ↓ TST: sedentary time ↑ SPT: sugar preference rate ↓	After 1 week of adaption and 4 days of 5-Fu treatment	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina NovaSeq platform	V3-V4	5-Fu-depression and control	Wilcoxon's rank-sum test: p < 0.05
Zhang J et al. 2020 ^[107]	C57BL/6 mice	Japan	case-control	-	LPS-depression	LPS (N=10) LPS+SDV (N=10) SDV (N=10) Control (N=10)	8-week-old	male	FST: immobility time ↑	After 14 days of recovery and LPS intraperitoneally (i.p.) injected	Fecal samples	-80 °C	16S rRNA gene sequencing-MiSeq according to the Illumina protocol	V1-V2	LPS-depression and control	Two-way ANOVA followed by post-hoc Tukey's multiple comparison tests: p < 0.05
Zhang JC et al. 2017 ^[108]	C57BL/6 mice	Japan	case-control	Single	CSDS-depression	CSDS (N=5) CSDS+MR16-1 (N=5) Control (N=5)	8-week-old	male	SIT: No data SPT: sucrose preference ↓ FST: immobility time ↑ TST: immobility time ↑	After 10 days of CSDS	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V4	CSDS-depression and control	One-way ANOVA followed by the post hoc LSD test: p < 0.05
Zhang K et al. 2019 ^[109]	Sprague-Dawley rats	Japan	case-control	-	LH-depression	LH (N=6) non-LH (N=7) Control (N=7)	7-week-old	male	Post-shock test: numbers of escape failures ↑	Fresh fecal samples were collected in a blind manner before post-shock stress on day 4	Fecal samples	-80°C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	LH-depression and control	One-way analysis of variance, followed by post hoc Fisher's LSD test: p < 0.05
Zhang L et al. 2021 ^[110]	Kunming mice	China	case-control	Single	CUMS-depression	CUMS (N=12) CUMS+Fluoxetine (N=12) CUMS+TIV low-dosage (N=12) CUMS+TIV middle-dosage (N=12) CUMS+TIV high-dosage (N=12) Control (N=12)	Adult 16-20 g	male	Body weight ↓ TST: immobility time ↑ SPT: sucrose preference ↓	After 1 week of acclimatization and 4 weeks of CUMS (the last 2 weeks received drugs treatment)	Colon contents	-20°C	16S rRNA gene sequencing-Rhoinia's MiSeq platform	V4	CUMS-depression and control	One-way ANOVA: p < 0.05
Zhang M et al. 2021 ^[111]	ICR mice	China	case-control	Single	CUMS-depression	CUMS (N=10) CUMS+Imipramine (N=10) CUMS+Alkaloids (N=10) Control (N=10)	20-25 g	male	SPT: sucrose preference ↓ FST: immobility time ↑ OFF: crossings and rearings number ↓, modifications number ↓	After 1 week of acclimatization and 7 weeks of CUMS (the last 4 weeks received drugs treatment)	Cecum contents	-20°C	16S rRNA gene sequencing-Illumina NovaSeq platform	V3-V4	Depression-like behaviors correlate with gut microbes	LEIS: p < 0.05 and LDA > 2.0 Spearman correlation test: p < 0.05
Zhang W et al. 2021 ^[112]	Sprague-Dawley rats	China	case-control	Single	CUMS-depression	At weeks 9: CUMS (N=36) Control (N=12)	180-220 g	male	Body weight ↓ SPT: sucrose preference ↓ OFF: rearing and crossing numbers ↓ LDT: dark time ↑	After 1 week of acclimatization, 8 weeks of CUMS and 6 weeks of treatment period. Fecal samples were collected at weeks 9 and 15.	Fecal samples	-	At weeks 9: 16S rRNA gene sequencing-Illumina HiSeq 2500 platform	V4-V5	CUMS-depression and control at weeks 9 and 15	Kruskal-Wallis H test with Tukey's posthoc tests: p < 0.05 LEIS: p < 0.05 and LDA > 2.0

					At weeks 15: CUMS (N=6) CUMS+Amiripryline (N=6) CUMS+Fluoxetine (N=7) Control (N=12)							At weeks 15: Shotgun metagenomics- Illumina HiSeq 4000 platform	NA		
Zhang Y et al. 2021 ^[39]	Sprague-Dawley rats	China	case-control	-	CUMS-depression CUMS (N=9) CUMS+Fluoxetine (N=9) CUMS+Green tea (N=9) CUMS+low-dose jasmine tea (N=9) CUMS+middle-dose jasmine tea (N=9) CUMS+high-dose jasmine tea (N=9) Control (N=9)	4 weeks	male	Body weight SPT: sugar preference FST: immobility time OFT: inner/outer/staging number	After 1 week of acclimatization, feces of rats in each group at day 29 were collected	Fecal samples	-80 °C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CUMS-depression and control	ANOVA followed by Bonferroni's test: p < 0.05
Zhang Y et al. 2019 ^[39]	C57BL/6 mice	China	case-control	-	NLRP3-KO anti-depression NLRP3-KO (N=14) Wild-type (N=14) CUS-depression ABX FMT-NLRP3-KO CUS (N=16) ABX FMT-NLRP3-KO Control (N=15) ABX FMT-WT CUS (N=14) ABX FMT-WT Control (N=15)	6-8-week-old	male	NLRP3-KO: FST: immobility time TST: immobility time OFT: total distance , center time , center distance CUS: SPT: sucrose preference FST: immobility time TST: immobility time	Unspecified	Fecal samples	-	16S rRNA gene sequencing- -	V4-V5	NLRP3-KO anti-depression and wild-type FMT-WT CUS and FMT-WT Control	Mann-Whitney test: p < 0.05
Zhang Z et al. 2021 ^[39]	C57BL/6 mice	China	case-control	-	Offspring of prenatal IS-depression Prenatal IS (N=12) Control (N=12)	6-8 week-old	female	EPM: open arm time , closed arm time LDT: dark area time SPT: sucrose preference FST: immobility time	Fecal samples were collected from F1 adult female mice at 6-8 weeks old	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	Prenatal IS-depression and control	LEIS: p < 0.05 and LDA > 2.0
Zhang Z et al. 2020 ^[39]	athymic nude mice (NCR-nu)	China	case-control	5 mice/cage	CRS-depression CRS-CRC xenografts (N=15) CRS-Fluoxetine-CRC xenografts (N=15) CRS-Xiaoyaosan-low-CRC xenografts (N=15) CRS-Xiaoyaosan-high-CRC xenografts (N=15) Control-CRC xenografts (N=15)	6-7 week-old	male	SPT: sucrose preference TST: immobility time	After 7 days of acclimatization, 14 days of CRS, 42 days of behavioural tests, tumour cell injection, and fluoxetine or xiaoyaosan treatment	Fecal samples	-	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	CRS-depression and control	LEIS: p < 0.05 and LDA ≥ 2.0
Zhang Z et al. 2022 ^[39]	C57BL/6 mice	China	case-control	Single	CRS-depression CRS (N=7) CRS-Hyperforin (N=7) Control (N=7)	7-9 weeks	male	SPT: sucrose preference	After 1 week of acclimatization and 10 days of CRS and hyperforin treatment	Fecal samples	Dry ice	Full-length 16S rRNA gene sequencing-PacBio platform	-	CRS-depression and control	Metastat analysis: p < 0.05
Zhao B et al. 2020 ^[39]	C57BL/6 mice	China	case-control	-	DSS-depression DSS (N=12) DSS+Lycopene (N=12) Control (N=12)	8-week-old	male	OFT: path length , dwell time BMT: marbles buried TST: immobility time EPM: percentage of open arm entries	After 35 days of corresponding diet and 7 days of DSS treatment	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	DSS-depression and control	Kruskal-Wallis test or Wilcoxon rank-sum test: p < 0.05 LEIS: p < 0.05 and LDA > 3.0
Zhao F et al. 2021 ^[39]	Sprague-Dawley rats	China	case-control	single	CUMS-depression Pregnant rat CUMS (N=8) CUMS+LBP (N=8)	200 ± 20 g	female	SPT: sucrose preference OFT: horizontal and vertical movements	Fresh feces were collected from female rats at 21 days after CUMS procedure, feces of the	Fecal samples	-80°C	16S rRNA gene sequencing- Illumina MiSeq platform	V3-V4	Pregnant rat CUMS-depression and control	One-way ANOVA followed by Bonferroni multiple comparison test: p < 0.05

				4 rats/cage	Offspring of prenatal CUMS-depression	Control (N=8) Offspring of Prenatal CUMS (N=16) Prenatal CUMS+LBP (N=16) Control (N=16)	PND 20	female : male (1:1)	Offspring Body weight SPT: sucrose preference OFT: horizontal and vertical movements TST: immobility time	offspring were collected at PND 20					Offspring of Prenatal CUMS-depression and control	
Zhao W et al. 2019 ^[200]	C57BL/6J mice	China	case-control	-	ABX FMT-Alc depression	ABX FMT-Alc (N=14) ABX FMT-Con (N=14) Control (N=12)	6 week-old	male	OFT: center time , center distance EPM: open arms time and entries TST: immobility time	After 21 days of antibiotics administration and 13 days of FMT	Fecal samples	-80 °C	16S rRNA gene sequencing-	V3-V5	ABX FMT-Alc depression and ABX FMT-control	Student's unpaired t-test and Mann-Whitney test: p < 0.05
Zhao Z et al. 2020 ^[201]	BALB/c mice	China	case-control	10 mice/cage	Antibiotic-depression	Ceftriaxone (N=20) Control (N=20)	6-8 week-old	male	Body weight OFT: center time , center distance , peripheral time , peripheral distance TST: activity phase , quiescence phase	After 1 week of acclimatization and 11 weeks of ceftriaxone sodium solution intragastrically	Fecal samples	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform	V3-V4	Antibiotic-depression and control	One-way ANOVA or Wilcoxon rank sum test: p < 0.05
Zheng P et al. 2016 ^[202]	Kunming mice	China	case-control	5 mice/cage	GF FMT-depression	GF FMT-MDD (N=63) GF FMT-HC (N=69)	6-8 week-old	male	OFT: proportion of center motion distance FST: duration of immobility TST: duration of immobility	2 weeks post FMT	Fecal samples Cecum samples	-80 °C	16S rRNA gene sequencing-Roche 454 sequencing Shotgun metagenomic-Illumina HiSeq2500	V3-V5 -	FMT-MDD and FMT-HC	Random Forests
Zheng P et al. 2020 ^[203]	Macaca fascicularis monkeys	China	case-control	group	Naturally-occurring depression	Depression (N=6) Control (N=6)	Adult	female	Duration of huddle and sit-alone behaviors Duration of amicable and locomotion activities	After behavioral tests	Cecum contents	-80 °C	16S rRNA gene sequencing-Illumina MiSeq platform Metagenomic-Illumina HiSeq X platform	V3-V4 -	Naturally-occurring depression and control	LEIS: p < 0.05 and LDA > 2.0
Zhou H et al. 2022 ^[204]	C57BL/6 mice	China	case-control	-	Dcf1 KO-depression	Dcf1 KO (N=5) Dcf1 KO+ B. longum (N=5) Dcf1 KO+ L. marinus (N=5) Dcf1 KO+ L. reuteri (N=5) WT (N=5) WT+Fecal of Dcf1 KO mice (N=5)	Adult, 20-25 g	male	SPT: sucrose preference FST: immobility time TST: immobility time	-	Fecal samples	-	16S rRNA gene sequencing-	Unspecified	Dcf1 KO depression and wild-type	-
Zhu HZ et al. 2019 ^[205]	Sprague-Dawley rats	China	case-control	-	CRS-depression	CRS (N=13) CRS+Xiaoyaosan (N=13) CRS+Flaxosine (N=13) Control (N=13)	200 ± 20 g	male	Body weight SPT: sugar preference OFT: residence time , total distance , number of entries	After 7 days of acclimatization and 21 days of CRS	Fecal samples	-20 °C	16S rRNA gene sequencing-Illumina-MiSeq high-throughput sequencing platform	V3-V4	CRS-depression and control	Metastats: p < 0.05 LEIS: p < 0.05 and LDA > 2.0
Zhu JP et al. 2021 ^[206]	Sprague-Dawley rats	China	case-control	-	CUMS-depression	CUMS (N=12) CUMS+Flaxosine (N=12) CUMS+low-dose BHT (N=12) CUMS+middle-dose BHT (N=12) CUMS+high-dose BHT (N=12) Control (N=12)	230-250 g	male	SPT: sucrose preference OFT: horizontal crossings , vertical erections	After 5 days of acclimatization and 30 consecutive days of CUMS	Rectum contents	Liquid nitrogen	16S rRNA sequencing analysis-Shanghai Biotech Biotechnology Co., Ltd.	Unspecified	CUMS-depression and control	One-way ANOVA or Kruskal-Wallis H test: p < 0.05

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Table S3. Microbiota β -diversity in patients with depression.

Study	Metric	Analysis	Significance
Bai S et al. 2021	–	PCoA	Sig. difference
Bai S et al. 2022	–	OPLS-DA	Sig. difference
Caso JR et al. 2021	Bray–Curtis Jaccard	PCoA, PERMANOVA	No sig. difference No sig. difference
Chahwan B et al. 2019	Weighted Unifrac	PCoA, PERMANOVA	No sig. difference
Chen JJ et al. 2018	UniFrac	PCoA, PLS-DA	Sig. difference
Chen JJ et al. 2020	–	OPLS-DA	Sig. difference
Chen T et al. 2021	Unweighted UniFrac	PCoA, ANOSIM	Sig. difference
Chen YH et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Chung YE et al. 2019	Weighted Unifrac Unweighted UniFrac	PERMANOVA	Sig. difference Sig. difference
Ciocan D et al. 2021	Weighted Unifrac Unweighted UniFrac	ANOSIM	No sig. difference Sig. difference
Dong Z et al. 2021	Bray–Curtis	PCA	No sig. difference
Huang Y et al. 2018	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference No sig. difference
Huang Y et al. 2021	Bray–Curtis	PLS-DA, PCA, PCoA, NMDS	Sig. difference
Jiang H et al. 2015	Unweighted UniFrac	PCoA	No sig. difference
Jiang HY et al. 2020	Bray–Curtis Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference No sig. difference No sig. difference
Kelly JR et al. 2016	Bray–Curtis Weighted Unifrac Unweighted UniFrac	PCoA, Adonis PERMANOVA	Sig. difference Sig. difference Sig. difference
Kleiman SC et al. 2015	Weighted Unifrac Unweighted UniFrac	–	No sig. difference Sig. difference
Kurokawa S et al. 2018	Weighted UniFrac Unweighted UniFrac	PCoA	No sig. difference Sig. difference
Lai WT et al. 2021	Bray–Curtis	PCoA, PERMANOVA	Sig. difference
Lin P et al. 2017	Weighted Unifrac	PCoA	Sig. difference
Ling Y et al. 2020	Bray–Curtis	PCoA, ANOSIM	No sig. difference
Liśkiewicz P et al. 2021	Bray–Curtis Unweighted UniFrac	PCoA, PERMANOVA	– No sig. difference
Liu P et al. 2021	Jaccard	PCoA	Sig. difference
Liu RT et al. 2020	Bray–Curtis Weighted Unifrac Unweighted UniFrac	PCoA, Adonis	Sig. difference Sig. difference Sig. difference
Liu T et al. 2020	Bray–Curtis	PCoA, ANOSIM	No sig. difference
Liu Y et al. 2016	–	PCA	Sig. difference
Madan A et al. 2020	Jaccard similarity index	–	Sig. difference
Mason BL et al. 2020	Weighted UniFrac	PERMANOVA	No sig. difference
Minichino A et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Naseribafrouei A et al. 2014	–	PLS-DA	Sig. difference
P érez-Santiago J et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA, PERMANOVA	Sig. difference Sig. difference
Qin Q et al. 2021	–	PCA, NMDS	No sig. difference

Rhee SJ et al. 2020	Bray-Curtis Weighted Unifrac Unweighted UniFrac	PCoA, PERMANOVA	Sig. difference No sig. difference Sig. difference
Rhee SJ et al. 2021	Bray-Curtis Weighted Unifrac Unweighted UniFrac	PERMANOVA	No sig. difference Sig. difference No sig. difference
Shen Y et al. 2021	Binary jaccard algorithm	PCoA	Sig. difference
Simpson CA et al. 2020	Weighted Unifrac Unweighted UniFrac	PCoA, PERMANOVA	No sig. difference No sig. difference
Stevens BR et al. 2020	Bray-Curtis (unfiltered data) Bray-Curtis (filtered data)	PERMANOVA	No sig. difference Sig. difference
Stevens BR et al. 2021	Bray-Curtis	PCoA	Sig. difference
Taylor AM et al. 2020	Weighted UniFrac	–	–
Taylor BC et al. 2020	Unweighted Unifrac	PERMANOVA	Sig. difference
Wingfield B et al. 2021	Bray-Curtis	–	Sig. difference
Yang J et al. 2020	Bray-Curtis	PCoA, PERMANOVA	Sig. difference
Yang Y et al. 2021	Bray-Curtis Weighted Unifrac Unweighted UniFrac	PCoA, NMDS, ADONIS	Sig. difference Sig. difference Sig. difference
Ye X et al. 2021	Unweighted UniFrac	PCoA	Sig. difference
Zhang Q et al. 2021	Bray-Curtis Jaccard Weighted Unifrac Unweighted UniFrac	PCoA, ANOSIM	Sig. difference Sig. difference Sig. difference Sig. difference
Zhao H et al. 2021	–	PCA	Sig. difference
Zheng P et al. 2016	Bray-Curtis Unweighted UniFrac	PCoA	Sig. difference
Zheng P et al. 2020	–	PLS-DA, PERMANOVA	Sig. difference
Zhou Y et al. 2020	Weighted UniFrac	PCoA, Wilcoxon rank-sum test	Sig. difference
Zhu J et al. 2021	Bary-Curtis Jaccard Weighted Unifrac Unweighted UniFrac	PCoA, PERMANOVA	No sig. difference Sig. difference No sig. difference No sig. difference

Table S4. Microbial β -diversity in animal models of depression.

Study	Metric	Analysis	Significance
Abildgaard A et al. 2021	Bray-Curtis Jaccard	PCoA, PERMANOVA	Sig. difference Sig. difference
An Q et al. 2020	Unweighted UniFrac	PCA, ANOSIM	Sig. difference
Arslanova A et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA	–
Bharwani A et al. 2017	Bray-Curtis	PCoA	Sig. difference
Bridgewater LC et al. 2017	Bray-Curtis	PCoA	Sig. difference
Burokas A et al. 2017	Unweighted UniFrac	PCoA	Sig. difference
Chakraborti A et al. 2021	Weighted Unifrac Unweighted UniFrac Bray-Curtis	PCoA, PERMANOVA	Sig. difference Sig. difference Sig. difference
Chen L et al. 2021	–	PCA	Sig. difference
Chen P et al. 2019	Bray-Curtis Jaccard	PCoA, NMDS	Sig. difference Sig. difference
Chen T et al. 2021	Unweighted UniFrac	PCoA, ANOSIM	Sig. difference
Chen X et al. 2021	Weighted UniFrac	PCA	Sig. difference
Chen X et al. 2022	Weighted Unifrac	PCoA	Sig. difference
Chen Y et al. 2021b	Weighted Unifrac Bray-Curtis	PCoA, PERMANOVA	Sig. difference Sig. difference
Cheng D et al. 2018	Morisita-Horn dissimilarity	PCA	Sig. difference
Cheng R et al. 2021	UniFrac	PCoA	Sig. difference
Chevalier G et al. 2020	Bray-Curtis	PCoA	–
Chi L et al. 2020	–	PLS-DA	Sig. difference
Daug�V et al. 2020	Bray-Curtis	MDS	Sig. difference
Deng Y et al. 2021	–	PCoA	Sig. difference
Ding Y et al. 2021	–	PCA, ANOSIM	Sig. difference
Diviccaro S et al. 2019	Weighted Unifrac Unweighted UniFrac Bray-Curtis	PCoA, PEMANOVA	Sig. difference Sig. difference Not mention
Donoso F et al. 2020	Aitchison	PCA, PERMANOVA	Sig. difference
Du HX et al. 2020	Bray-Curtis	NMDS	Sig. difference
Duan J et al. 2021	Unweighted UniFrac	PCoA, PLS-DA, ANOSIM	Sig. difference
Egerton S et al. 2020	Bray-Curtis	PCoA, Adonis PERMANOVA	Sig. difference
El Aidy S et al. 2017	Weighted UniFrac	PCoA, PEMANOVA	Sig. difference
Fan L et al. 2021	–	PCoA	Sig. difference
Feng Y et al. 2020	–	PLS-DA	Sig. difference
Feng Z et al. 2020	UniFrac	PCA, NMDS	Sig. difference
Forouzan S et al. 2021	Weighted UniFrac	PCoA	Sig. difference
Gao K et al. 2022	Bray-Curtis	PCoA, PERMANOVA	Sig. difference
Gao X et al. 2020	–	PLS-DA	Sig. difference
Gong X et al. 2021	Weighted UniFrac	PCoA	Sig. difference
Gu F et al. 2020	Weighted UniFrac	PCoA	Sig. difference
Gu X et al. 2022	Weighted UniFrac	PLS-DA, ANOSIM	Sig. difference
Guida F et al. 2018	Bray-Curtis Jaccard	PEMANOVA	Sig. difference Sig. difference
Guo Y et al. 2018	–	NMDS	Sig. difference
Guo Y et al. 2019	–	PCA, Adonis	No sig. difference
Han SK et al. 2020a	Jensen-Shannon	PCoA	Sig. difference

Han SK et al. 2020b	Jensen-Shannon	PCoA	Sig. difference
Han SK et al. 2021	Weighted UniFrac	PCoA	Sig. difference
Hao W et al. 2021	–	PCA	Sig. difference
Hao WZ et al. 2021	Weighted Unifrac Unweighted UniFrac Bray-Curtis	PCoA	Sig. difference Sig. difference Sig. difference
Hassan AM et al. 2019	Weighted UniFrac	PCoA, Adonis	Sig. difference
Huang F et al. 2021	UniFrac	PCA	Sig. difference
Huang N et al. 2019	Euclidean Bray-Curtis	PCoA	Sig. difference Sig. difference
Huang YJ et al. 2021	Bray-Curtis	PCoA	Sig. difference
Huang YY et al. 2022	Bray-Curtis	PcoA	Sig. difference
Inserra A et al. 2019	Weighted UniFrac	PERMANOVA	Sig. difference
Ji S et al. 2022	Weighted Unifrac Unweighted UniFrac Bray-Curtis	PCoA, PERMANOVA	No sig. difference Sig. difference Sig. difference
Jiang W et al. 2021	–	PCoA, Adonis	Sig. difference
Jiang Y et al. 2020	Unweighted UniFrac	PCoA, ANOSIM	Sig. difference
Jianguo L et al. 2019	Bray-Curtis	PERMANOVA	Sig. difference
Kamimura Y et al. 2021	Weighted UniFrac	PCoA	Sig. difference
Kemp KM et al. 2021	Aitchison	PCA, Adonis PERMANOVA	Sig. difference
Kim JK et al. 2020	Weighted Unifrac	PcoA	Sig. difference
Kim JK et al. 2021	Generalized UniFrac	PCoA	Sig. difference
Knudsen JK et al. 2021	–	PCA	Sig. difference
Kosuge A et al. 2021	Bray-Curtis Jaccard	PCoA, Adonis PERMANOVA	Sig. difference Sig. difference
Lai WD et al. 2022	–	PCA, PcoA, NMDS	Sig. difference
Leclercq S et al. 2020	Bray-Curtis Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Lee HC et al. 2020	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Li H et al. 2021	Bray-Curtis	PCoA	Sig. difference
Li N et al. 2018	Weighted Unifrac Unweighted UniFrac	PCoA, ANOSIM	Sig. difference Sig. difference
Li N et al. 2019	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Li P et al. 2021	Unweighted UniFrac	PCoA	Sig. difference
Li Y et al. 2018	Weighted Unifrac	PCoA	Sig. difference
Lim EY et al. 2021	Weighted Unifrac	PCoA	Sig. difference
Lin S et al. 2021	–	PCA, NMDS	Sig. difference
Liu QF et al. 2020	Unweighted UniFrac	PCoA	Sig. difference
Liu X et al. 2021a	Bray-Curtis	PCoA, PLS-DA	Sig. difference
Liu X et al. 2021b	Bray-Curtis	PCoA, NMDS, Adonis, Permdisp	Sig. difference
Liu Z et al. 2020	Unweighted UniFrac	PCoA	Sig. difference
Luo X et al. 2021	Bray-Curtis	NMDS, ANOSIM	Sig. difference
Lv M et al. 2021	Weighted Unifrac	PCoA, NMDS	Sig. difference
Lv WJ et al. 2019	Weighted Unifrac	PCA, PCoA, PLS-DA	Sig. difference
Lv WJ et al. 2020	Unweighted UniFrac	PCA, PCoA, NMDS, PERMANOVA, ANOSIM	Sig. difference
Ma W et al. 2019	Bray-Curtis	PCA	Sig. difference

Matsuda Y et al. 2020	Bray-Curtis	PcoA	Sig. difference
McGaughey KD et al. 2019	Unweighted UniFrac	PCoA, ANOSIM	Sig. difference
Meng C et al. 2022	–	CPCoA, PcoA	Sig. difference
Moya-Pérez A et al. 2017	Bray-Curtis	PCoA, Permanova	Sig. difference
O'Mahony SM et al. 2020	Bray-Curtis	PCoA, Adonis	Sig. difference
Partrick KA et al. 2021	Unweighted UniFrac	PCoA, PERMANOVA	Sig. difference
Patterson E et al. 2019	Bray-Curtis	PCoA	Sig. difference
Pearson-Leary J et al. 2020	Bray-Curtis Weighted UniFrac	PCoA	Sig. difference Sig. difference
Pu Y et al. 2021	–	PCA, ANOSIM	No sig. difference
Pusceddu MM et al. 2015	–	RDA	Sig. difference
Qiao Y et al. 2020	Bray-Curtis Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference Sig. difference
Qu W et al. 2019	Bray-Curtis	PCoA	Sig. difference
Qu Y et al. 2017	Bray-Curtis	PCoA	Sig. difference
Qu Y et al. 2020	Weighted Unifrac	PCoA	Sig. difference
Rao J et al. 2021	Bray-Curtis Jaccard	PCoA	Sig. difference
Robertson RC et al. 2017	Unweighted UniFrac	PCoA	Sig. difference
Schmidtner AK et al. 2019	Bray-Curtis	PCoA	Sig. difference
Shan B et al. 2021	Bray-Curtis	PCoA	Sig. difference
Shao S et al. 2021	–	PCoA	No sig. difference
Sheng L et al. 2021	Unweighted UniFrac	PCoA	Sig. difference
Siopi E et al. 2020	Bray-Curtis	PCoA	Sig. difference
Song J et al. 2019a	–	PLS-DA	Sig. difference
Song J et al. 2019b	–	PLS-DA	Sig. difference
Song X et al. 2021	Bray-Curtis Unweighted UniFrac	PLS-DA, ANOSIM	Sig. difference Sig. difference
Sovijit WN et al. 2019	Bray-Curtis	PCoA, PERMANOVA	Sig. difference
Sun L et al. 2019a	Bray-Curtis	PCoA	Sig. difference
Sun L et al. 2019b	Unweighted UniFrac	PCoA	Sig. difference
Sun Y et al. 2019	Unweighted UniFrac	PCA, PCoA	Sig. difference
Sun Y et al. 2020	Weighted Unifrac	PCoA	Sig. difference
Suzuki K et al. 2021	Unweighted UniFrac	PCoA, PERMANOVA	Sig. difference
Szyszkowicz JK et al. 2017	–	PCA	Sig. difference
Teng T et al. 2021	Bray-Curtis	PCoA, PLS-DA, sparse PLS-DA	Sig. difference
Tian P et al. 2019a	–	PCoA	Sig. difference
Tian P et al. 2019b	–	PCA	Sig. difference
Tian P et al. 2020	Unweighted UniFrac	PCA, PCoA, PERMANOVA	Sig. difference
Tian P et al. 2021	Aitchison	PCA, PERMANOVA	Sig. difference
Tian XY et al. 2021	–	PCA, PCoA, ANOSIM, Adonis	Sig. difference
Tillmann S et al. 2019	–	PCA, PLS-DA	Sig. difference
Tung TH et al. 2019	Bray-Curtis	NMDS	Sig. difference
Wang L et al. 2020	Unweighted UniFrac	PCoA	Sig. difference
Wang L et al. 2021	–	PCoA	Sig. difference
Wang Q et al. 2019	Unweighted UniFrac	PCoA, PERMANOVA	Sig. difference
Wang R et al. 2021	Bray-Curtis	PCoA	Sig. difference

Wang S et al. 2020a	Unweighted UniFrac	PCoA	Sig. difference
Wang S et al. 2020b	Unweighted UniFrac	PCoA	Sig. difference
Wang S et al. 2021	–	PCA, ANOSIM	Sig. difference
Wang Y et al. 2021	Weighted Unifrac Jaccard	PCoA	Sig. difference Sig. difference
Warda AK et al. 2019	Bray-Curtis	PCoA, PERMANOVA	Sig. difference
Wei LN et al. 2019	Bray-Curtis	PCoA, NMDS	Sig. difference
Westfall S et al. 2021	Weighted Unifrac	PCoA, PERMANOVA	Sig. difference
Wong ML et al. 2016	Bray-Curtis	PERMANOVA	Sig. difference
Wu F et al. 2020	Unweighted UniFrac	PcoA	Sig. difference
Wu J et al. 2021	Unweighted UniFrac	PCoA	Sig. difference
Wu M et al. 2020	–	PCoA	Sig. difference
Xia J et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA, OPLS-DA	Sig. difference Sig. difference
Xiao Q et al. 2020	Unweighted UniFrac	PCoA, NMDS	Sig. difference
Xie R et al. 2020a	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Xie R et al. 2020b	–	PCA	Sig. difference
Xie Y et al. 2021	Bray-Curtis	PCoA	Sig. difference
Xu M et al. 2022	–	PCoA	Sig. difference
Xu Z et al. 2019	Bray-Curtis Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Xue M et al. 2021	Unweighted UniFrac	PCoA, Adonis	Sig. difference
Yang C et al. 2017b	Bray-Curtis Euclidean	PCoA	Not mention Not mention
Yang C et al. 2019	–	PCoA	Sig. difference
Yang HL et al. 2021	Unweighted UniFrac	PCoA	No sig. difference
Yang Q et al. 2020	Bray-Curtis Weighted Unifrac Unweighted UniFrac	PCoA	Not mention
Yu M et al. 2017	Bray-Curtis	PCoA	Sig. difference
Yu M et al. 2020	–	PCoA	Sig. difference
Yu M et al. 2021	Bray-Curtis	PCoA	Sig. difference
Yun SW et al. 2020	Jansen-Shannon	PCoA	Sig. difference
Yun SW et al. 2021	Bray-Curtis	PCoA	Sig. difference
Zhang F et al. 2020	–	PCoA	Sig. difference
Zhang J et al. 2020	Bray-Curtis	PCoA	Sig. difference
Zhang K et al. 2019	–	PCoA	Sig. difference
Zhang L et al. 2021	Bray-Curtis	PCoA, NMDS	Sig. difference
Zhang M et al. 2021	Bray-Curtis	PCoA, PERMANOVA, ANOSIM	Sig. difference
Zhang W et al. 2021	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Zhang Y et al. 2019	Unweighted UniFrac	PCoA	Sig. difference
Zhang Y et al. 2021	Bray-Curtis	PLS-DA	Sig. difference
Zhang Z et al. 2020	–	PLS-DA	No sig. difference
Zhang Z et al. 2021	Unweighted UniFrac	PCoA, NMDS, ANOSIM	Sig. difference
Zhang Z et al. 2022	Unweighted UniFrac	PCoA, PERMANOVA, ANOSIM	No sig. difference
Zhao B et al. 2020	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference

Zhao F et al. 2021	Bray-Curtis	PCoA	Not mention
Zhao Z et al. 2020	Weighted Unifrac	PCA, PCoA, MDS	Sig. difference
Zheng P et al. 2016	Weighted Unifrac Unweighted UniFrac	PCoA	Sig. difference Sig. difference
Zheng P et al. 2020	–	PLS-DA	Sig. difference
Zhou H et al. 2022	–	PCoA	Sig. difference
Zhu HZ et al. 2019	Weighted Unifrac Unweighted UniFrac	PCA, PCoA, NMDS	Sig. difference Sig. difference

Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	7	6	1	5	5	0				4	4	0	4	4	0				
		Bifidobacteriales	Bifidobacteriaceae	8	6	2	8	6	2					7	6	1	7	6	1			
		Corynebacteriales	Corynebacteriaceae	2	1	1	2	1	1					2	1	1	2	1	1			
		Micrococcales	Micrococcaceae	3	1	2	2	1	1					2	1	1	2	1	1			
Bacteroidetes	Coriobacteria	Coriobacteriales	Coriobacteriaceae	9	5	4	9	5	4	2	1	1	6	4	2	7	4	3	2	1	1	
	Bacteroidia	Bacteroidales	Bacteroidaceae	10	4	6	9	4	5				9	4	5	9	4	5				
			Barnesiellaceae	3	1	2	3	1	2					2	1	1	3	1	2			
			Porphyromonadaceae	5	5	0	5	5	0					5	5	0	5	5	0			
			Prevotellaceae	9	0	9	9	0	9					8	0	8	8	0	8			
			Rikenellaceae	10	6	4	10	6	4	3	0	3		7	6	1	7	5	2	3	1	2
			Tannerellaceae	3	3	0	3	3	0					3	3	0	3	3	0			
			Marinilabiales	Marinilabillaceae	2	1	1	2	1	1								2	1	1		
	Chitinophagia	Chitinophagales	Chitinophagaceae	2	0	2	2	0	2				2	0	2	2	0	2				
	Flavobacteria	Flavobacteriales	Flavobacteriaceae	3	1	2	2	1	1							2	1	1				
			Fusobacteriaceae	3	2	1	2	2	0					2	2	0	2	2	0			
	Firmicutes	Bacilli	Lactobacillales	Camobacteriaceae	2	1	1	2	1	1				2	1	1						
Enterococcaceae				5	3	2	4	3	1					3	2	1	4	3	1			
Erysipelotrichaceae				4	1	3	4	1	3					3	1	2	3	1	2			
Lactobacillaceae				4	1	3	4	1	3					3	1	2	3	1	2			
Leuconostocaceae				2	2	0	2	2	0					2	2	0						
Streptococcaceae				4	3	1	4	3	1					3	2	1	3	2	1			
Clostridia				Clostridiales	Clostridiaceae	9	3	6	9	3	6				9	3	6	8	2	6		
Eubacteriaceae		5	4		1	5	4	1					4	4	0	4	3	1				
Lachnospiraceae		20	8		12	19	7	12	3	0	3		14	5	9	13	6	7	6	1	5	
Oscillospiraceae		4	3		1	4	3	1					4	3	1	4	3	1				
Ruminococcaceae		15	6		9	15	6	9	4	1	3		10	5	5	11	4	7	4	2	2	
Erysipelotrichia		Erysipelotrichales	Turicibacteraceae	2	0	2	2	0	2													
Negativicutes		Acidaminococcales	Acidaminococcaceae	8	5	3	8	5	3				7	4	3	6	3	3	2	2	0	
		Veillonellales	Veillonellaceae	6	4	2	5	3	2				5	3	2	5	3	2				
Patescibacteria		Saccharimonadia	Saccharimonadales	Saccharimonadaceae	2	2	0	2	2	0									2	2	0	
Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	3	2	1	3	2	1				3	2	1	3	2	1				
			Oxalobacteraceae	2	0	2																
			Sutterellaceae	2	0	2	2	0	2					2	0	2	2	0	2			
			Campylobacteriales	Campylobacteraceae	2	2	0	2	2	0				2	2	0						

Gammaproteobacteria	Enterobacterales	Enterobacteriaceae	13	10	3	12	9	3	2	2	0	9	6	3	8	5	3	4	4	0
	Pasteurellales	Pasteurellaceae	3	1	2	3	1	2				3	1	2	3	1	2			

Table S6. Commensal microbiota alterations at Genus level in patients with depression.

Microorganisms					Commensal microbiota			Gut microbiota																	
								Total			American			Chinese			MDD			Depression					
					Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased			
Phylum	Class	Order	Family	Genus																					
Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces	6	5	1	4	4	0				4	4	0	4	4	0						
			Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	11	4	7	11	4	7				9	4	5	8	4	4	3	0	3		
	Coriobacteria	Coriobacteriales	Coriobacteriaceae	Collinsella	Collinsella	4	3	1	4	3	1				3	2	1	2	2	0	2	1	1		
				Atopobiaceae	Atopobium	2	2	0	2	2	0				2	2	0	2	2	0					
				Olsenella	Olsenella	4	3	1	4	3	1				4	3	1	3	3	0					
				Adlercreutzia	Adlercreutzia	2	2	0	2	2	0				2	2	0	2	2	0					
				Eggerthellales	Eggerthellaceae	Eggerthella	7	7	0	7	7	0				6	6	0	7	7	0				
			Granulicatella	Granulicatella	2	2	0	2	2	0				2	2	0				2	2	0			
Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	18	8	10	17	8	9	2	1	1	11	5	6	12	7	5	5	1	4			
				Barnesiella	6	1	5	6	1	5				3	1	2	2	1	1	4	0	4			
			Odoribacteraceae	Butyricimonas	2	1	1	2	1	1				2	1	1									
				Odoribacter	3	1	2	3	1	2				3	1	2	2	1	1						
			Prevotellaceae	Alloprevotella	2	1	1	2	1	1				2	1	1									
				Paraprevotella	6	6	0	6	6	0				3	3	0	3	3	0	3	3	0	3	3	0
				Prevotella	10	5	5	9	4	5				7	3	4	7	3	4	3	2	1			
				Prevotella-2	3	1	2	2	0	2				2	0	2	2	0	2						
				Prevotella-9	3	2	1	2	1	1				2	1	1	3	2	1						
			Tannerellaceae	Alistipes	12	7	5	11	6	5				8	4	4	7	5	2	4	1	3			
			Parabacteroides	Parabacteroides	9	8	1	9	8	1				8	7	1	7	7	0	2	1	1			
Firmicutes	Bacilli	Bacillales	Bacillales_incertae_se_dis	Gemella	2	2	0																		
			Enterococcaceae	Enterococcus	5	4	1	4	4	0				3	3	0	3	3	0						
		Lactobacillales	Lactobacillaceae	Lactobacillus	9	5	4	9	5	4				5	4	1	6	4	2	3	1	2			
			Weissella	Weissella	2	0	2	2	0	2				2	0	2									
			Streptococcaceae	Streptococcus	11	9	2	9	7	2				8	7	1	7	5	2	2	2	0			

				Anaerotruncus	2	2	0	2	2	0				2	2	0	3	3	0			
				Clostridium_IV	2	1	1	2	1	1												
				Faecalibacterium	19	3	16	18	2	16	3	0	3	12	2	10	10	2	8	8	0	8
				Flavonifractor	5	5	0	5	5	0	2	2	0	3	3	0	4	4	0			
				Oscillospira	2	2	0	2	2	0							2	2	0			
				Ruminococcaceae_UCG-002	2	1	1															
				Ruminococcaceae_UCG-014	2	2	0	2	2	0												
				Ruminococcus	9	1	8	9	1	8	3	0	3	4	1	3	3	1	2	6	0	6
				Ruminococcus-1	3	1	2	3	1	2	2	1	1				2	0	2			
				Ruminococcus-2	2	0	2	2	0	2				2	0	2	2	0	2			
				Subdoligranulum	3	0	3	3	0	3				2	0	2	2	0	2			
				Clostridium_XVIII	2	1	1	2	1	1												
				Faecalitalea	3	2	1	3	2	1				3	2	1	3	2	1			
				Holdemania	2	0	2	2	0	2										2	0	2
				Holdemania	5	5	0	5	5	0				3	3	0	4	4	0			
				Turicibacter	4	2	2	4	2	2				2	1	1	3	2	1			
				Acidaminococcus	3	3	0	3	3	0				2	2	0	2	2	0			
				Phascolarctobacterium	7	2	5	7	2	5				6	1	5	6	1	5			
				Megamonas	6	1	5	6	1	5				6	1	5	5	1	4			
				Mitsuokella	3	1	2	2	0	2				2	0	2				2	0	2
				Dialister	12	5	7	11	4	7	2	2	0	5	2	3	5	2	3	6	2	4
				Megasphaera	4	1	3	4	1	3				4	1	3	4	1	3			
				Veillonella	8	7	1	7	6	1				6	5	1	2	2	0	5	4	1
				Parvimonas	4	3	1	3	2	1				3	2	1	2	2	0			
				Fusobacterium	5	2	3	3	1	2				3	1	2	2	1	1			
				Gemmiger	3	0	3	3	0	3				2	0	2				3	0	3
				Parasutterella	2	1	1	2	1	1				2	1	1	2	1	1			
				Sutterella	8	1	7	8	1	7				7	0	7	6	1	5	2	0	2
				Desulfovibrio	5	4	1	5	4	1				2	2	0	4	3	1			
				Campylobacter	2	1	1	2	1	1				2	1	1						
				Enterobacter	2	1	1	2	1	1				2	1	1	2	1	1			
				Escherichia	2	2	0	2	2	0				2	2	0	2	2	0			
				Escherichia-Shigella	7	5	2	6	4	2				5	3	2	3	2	1	3	2	1
				Klebsiella	2	1	1	2	1	1				2	1	1	2	1	1			

		Pasteurellales	Pasteurellaceae	Haemophilus	4	1	3	4	1	3				4	1	3	3	0	3			
		Pseudomonadales	Pseudomonadaceae	Pseudomonas	2	1	1															
Streptophyta	Magnoliopsida	Fabales	Fabaceae	Rothia	3	2	1	3	2	1				3	2	1	3	2	1			
Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Akkermansiaceae	Akkermansia	3	2	1	3	2	1				2	2	0				2	1	1

Table S7. Commensal microbiota alterations at Species level in patients with depression.

Microorganisms						Commensal microbiota			Gut microbiota														
									Total			American			Chines			MDD			Depression		
						Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased
Phylum	Class	Order	Family	Genus	Species																		
Actinobacteria	Actinomycetia	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	Bifidobacterium_adolescentis	3	3	0	3	3	0				2	2	0	2	2	0			
					Bifidobacterium_bifidum	2	2	0	2	2	0				2	2	0	2	2	0			
					Bifidobacterium_breve	2	2	0	2	2	0				2	2	0	2	2	0			
					Bifidobacterium_dentium	2	2	0	2	2	0				2	2	0	2	2	0			
					Bifidobacterium_longum	6	4	2	6	4	2				4	3	1	4	3	1	2	1	1
	Coriobacteria	Micrococcales	Micrococcaceae	Rothia	Rothia_mucilaginosa	3	2	1	2	2	0				2	2	0	2	2	0			
					Lancefieldella	2	2	0	2	2	0				2	2	0	2	2	0			
		Coriobacteriales	Atopobiaceae	Olsenella	Olsenella_uli	2	2	0	2	2	0				2	2	0	2	2	0			
					Coriobacteriaceae	Coriobacterium	Coriobacterium_glomerans	2	2	0	2	2	0				2	2	0	2	2	0	
			Eggerthellales	Eggerthellaceae	Adlercreutzia	Adlercreutzia_équoficiens	3	2	1	3	2	1				2	1	1	2	1	1		
Eggerthella	Eggerthella_lenta	3			3	0	3	3	0				3	3	0	3	3	0					
Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Bacteroides_caccae	3	2	1	3	2	1	2	1	1				2	2	0			
					Bacteroides_dorei	2	2	0	2	2	0												
					Bacteroides_fragilis	3	3	0	3	3	0				2	2	0	2	2	0			
					Bacteroides_massiliensis	3	2	1	3	2	1				2	1	1	2	1	1			
					Bacteroides_nordii	2	2	0	2	2	0												
					Bacteroides_plebeius	2	1	1	2	1	1				2	1	1						
					Bacteroides_stercoris	3	2	1	3	2	1	2	1	1							2	1	1
					Bacteroides_thetaiotaomicron	4	4	0	4	4	0				3	3	0	2	2	0	2	2	0
					Bacteroides_uniformis	2	2	0	2	2	0												
					Bacteroides_vulgatus	2	1	1	2	1	1												
					Prevotellaceae	Paraprevotella	Paraprevotella_xylaniphila	2	2	0	2	2	0				2	2	0	2	2	0	
							Prevotella	Prevotella_copri	2	2	0	2	2	0									
						Prevotella_melaninogenica	2	2	0	2	2	0				2	2	0	2	2	0		
					Rikenellaceae	Alistipes	Alistipes_finegoldii	2	2	0	2	2	0										
							Alistipes_onderdonkii	3	3	0	3	3	0	2	2	0				2	2	0	

	Negativicutes	Acidaminococcales	Acidaminococcaceae	Acidaminococcus	Acidaminococcus_fermentans	2	2	0	2	2	0				2	2	0	2	2	0					
					Acidaminococcus_intestini	2	2	0	2	2	0				2	2	0	2	2	0					
		Veillonellales	Veillonellaceae	Megasphaera	Megasphaera_elsdenii	2	2	0	2	2	0				2	2	0	2	2	0					
Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Bilophila	Bilophila_wadsworthia	2	2	0	2	2	0														
					Desulfovibrio	Desulfovibrio_desulfuricans	2	2	0	2	2	0													
						Desulfovibrio_vulgaris	2	2	0	2	2	0					2	2	0	2	2	0			
	Gammaproteobacteria	Enterobacterales	Enterobacteriaceae	Enterobacter	Enterobacter_cloacae	2	2	0	2	2	0				2	2	0	2	2	0					
					Enterococcus_faecalis	2	1	1	2	1	1				2	1	1	2	1	1					
					Escherichia	Escherichia_coli	4	4	0	4	4	0				4	4	0	3	3	0				
			Klebsiella	Klebsiella_pneumoniae	2	1	1	2	1	1							2	1	1						
			Pasteurellales	Pasteurellaceae	Haemophilus	Haemophilus_parainfluenzae	5	0	5	4	0	4				3	0	3	4	0	4				
Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Akkermanssiaceae	Akkermansia	Akkermansia_muciniphila	5	3	2	5	3	2	2	1	1	3	2	1	3	2	1	2	1	1		

Table S8. Commensal microbiota alterations at Phylum, Class, Order, and Family levels in animal models of depression.

Microorganisms	Commensal microbiota	Total																				
		Total			Mice			Rats			Fecal samples			Cecum contents			Colon contents					
		Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased	Total no. of frequency	No. of increased	No. of decreased
	Phylum																					
	Actinobacteria	35	14	21	35	14	21	27	9	18	8	5	3	30	11	19	5	3	2			
	Bacteroidetes	73	40	33	73	40	33	49	25	24	22	15	7	51	29	22	17	9	8	5	2	3
	Cyanobacteria	11	3	8	11	3	8	8	3	5	3	0	3	9	2	7	2	1	1			
	Deferribacteres	12	7	5	12	7	5	11	7	4				11	7	4						
	Firmicutes	78	28	50	78	28	50	55	18	37	23	10	13	58	20	38	15	6	9	5	2	3
	Proteobacteria	48	37	11	48	37	11	41	31	10	7	6	1	34	26	8	10	6	4	6	5	1
	Tenericutes	15	5	10	15	5	10	13	4	9	2	1	1	14	5	9						
	TM7	5	2	3	5	2	3	4	2	2				4	1	3						
	Verrucomicrobia	30	14	16	30	14	16	23	11	12	7	3	4	18	7	11	8	5	3	4	2	2
	Phylum																					
	Class																					
	Actinobacteria	9	7	2	9	7	2	3	2	1	5	4	1	4	2	2	3	3	0			
	Coriobacteria	4	1	3	4	1	3	3	1	2				4	1	3						
	Bacteroidetes	15	7	8	15	7	8	12	6	6	3	1	2	11	6	5	3	1	2			
	Cyanobacteria	3	2	1	3	2	1	3	2	1							2	1	1			
	Deferribacteres	5	4	1	5	4	1	4	3	1				5	4	1						
	Bacilli	15	7	8	15	7	8	9	4	5	6	3	3	8	3	5	5	3	2			
	Clostridia	17	11	6	17	11	6	12	7	5	5	4	1	11	7	4	3	1	2	2	2	0
	Erysipelotrichia	10	3	7	10	3	7	9	3	6				8	2	6						
	Negativicutes	2	1	1	2	1	1							2	1	1						
	Alphaproteobacteria	6	0	6	6	0	6	5	0	5				4	0	4	2	0	2			
	Betaproteobacteria	7	5	2	7	5	2	2	1	1	5	4	1	3	2	1	3	3	0			
	Deltaproteobacteria	9	7	2	9	7	2	4	4	0	5	3	2	6	6	0						
	Epsilonproteobacteria	7	7	0	7	7	0	6	6	0				4	4	0	2	2	0			
	Gammaproteobacteria	8	8	0	8	8	0	7	7	0				6	6	0						
	Spirochaetes	3	2	1	3	2	1	3	2	1				3	2	1						
	Tenericutes	7	4	3	7	4	3	6	4	2				6	4	2						

			Peptostreptococcaceae	12	7	5	12	7	5	7	6	1	5	1	4	7	3	4	2	2	0	2	1	1
			Ruminococcaceae	45	27	18	45	27	18	31	19	12	13	7	6	34	19	15	7	5	2	3	3	0
	Erysipelotrichia	Erysipelotrichales	Erysipelotrichaceae	19	7	12	19	7	12	16	5	11	2	1	1	13	4	9	3	2	1			
	Negativicutes	Acidaminococcales	Acidaminococcaceae	2	0	2	2	0	2															
	Negativicutes	Veillonellales	Veillonellaceae	3	2	1	3	2	1				2	1	1	3	2	1						
			Anaerovoracaceae	3	2	1	3	2	1							2	1	1						
			Monoglobaceae	2	2	0	2	2	0															
Patescibacteria	Saccharimonadia	Saccharimonadales	Saccharimonadaceae	3	3	0	3	3	0	3	3	0				2	2	0						
		Hyphomicrobiales	Devosiaceae	2	0	2	2	0	2	2	0	2												
		Rhizobiales	Brucellaceae	2	2	0	2	2	0							2	2	0						
		Rhodospirillales	Rhodospirillaceae	2	1	1	2	1	1	2	1	1				2	1	1						
		Sphingomonadales	Sphingomonadaceae	4	3	1	4	3	1	3	3	0				2	2	0	2	1	1			
			Alcaligenaceae	6	2	4	6	2	4	5	2	3				5	2	3						
			Burkholderiaceae	3	0	3	3	0	3															
			Comamonadaceae	3	3	0	3	3	0							2	2	0						
			Oxalobacteraceae	5	4	1	5	4	1	2	1	1	2	2	0				3	3	0			
			Sutterellaceae	6	1	5	6	1	5	5	1	4				4	0	4	2	1	1			
Proteobacteria	Deltaproteobacteria	Desulfiovibrionales	Desulfiovibrionaceae	27	20	7	27	20	7	20	15	5	7	5	2	19	16	3	6	3	3			
			Campylobacteraceae	2	0	2	2	0	2															
			Helicobacteraceae	15	12	3	15	12	3	12	9	3	2	2	0	12	9	3						
			Enterobacteriales	14	12	2	14	12	2	13	11	2				11	10	1	2	1	1			
			Pasteurellales	3	2	1	3	2	1							2	2	0						
			Moraxellaceae	5	3	2	5	3	2	2	1	1	3	2	1	2	1	1	2	2	0			
			Pseudomonadaceae	2	0	2	2	0	2															
Spirochaetes	Spirochaetia	Spirochaetales	Spirochaetaceae	3	2	1	3	2	1	2	1	1				2	1	1						
		Brachyspirales	Brachyspiraceae	2	2	0	2	2	0															
			Anaeroplasmatales	8	3	5	8	3	5	7	2	5				6	3	3	2	0	2			
			Mycoplasmatales	3	1	2	3	1	2	3	1	2				2	1	1						
			Akkermansiaceae	5	0	5	5	0	5	5	0	5				3	0	3						
Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	10	9	1	10	9	1	8	8	0	2	1	1	4	3	1	4	4	0	2	2	0
			AC160630	3	1	2	3	1	2	3	1	2				3	1	2						

Table S11. Characteristics of studies investigating the efficiency of gut microbiota-based therapeutics in patients with depression.

Study	Depression model	Microbiota-based therapies	Genus	Species	Intervention method	Depression alleviation	Gut-brain axis mechanism	OCEBM evidence level
Kilin çarşlan S et al. 2020 ^[1]	IBD patients with depression symptoms	Fecal microbiota transplantation	–	–	The fresh stool from healthy donors was diluted with saline before transplantation, and the suspension was prepared by mixing with a spatula. The stool suspension was infused into the patient through colonoscopy	The severity of anxiety, depression and obsession in IBD patients decreased after FMT	–	3
Kurokawa S et al. 2018 ^[2]	IBS patients with depression symptoms	Fecal microbiota transplantation	–	–	Approximately 100 g of feces were collected from the pack, dissolved in 200 mL of saline	Depression and anxiety symptoms were improved by FMT regardless of gastrointestinal symptom change in patients with IBS	FMT altered disordered fecal microbiota	3
Lin H et al. 2021 ^[3]	IBS patients with depression symptoms	Fecal microbiota transplantation	–	–	The donor is a healthy 36-year-old male. Patients received FMT treatment (oral administration) from May 2019 to December 2019. The patients took the intestinal flora capsules 3 times in total, once every other day, 30 capsules each time	FMT treatment can effectively alleviate the anxiety and depression behaviors of IBS-D patients	FMT treatment regulated the gut microbiota	2
Guo Q et al. 2021 ^[4]	IBS patients with depression symptoms	Fecal microbiota transplantation with enterobacteria capsules	–	–	The FMT treatment was intervened by oral enteric capsules for 3 times (every 2 days one time and 30 capsules each time)	FMT therapy alleviated anxiety/depression symptom in IBS patients	FMT therapy restored the intestinal micro-ecology	2
Chinna Meyyappan A et al. 2022 ^[5]	Patients with MDD and GAD	Multispecies probiotics	–	Microbial Ecosystem Therapeutic-2 (MET-2), which contained 40 strains of bacteria	During the 8 weeks of treatment, all participants consumed three MET-2 capsules per day orally; each 0.5-g MET-2 capsule contains 3.2×10^3 to 3.2×10^{11} CFU	Over the course of 10 weeks, MET-2 significantly decreased mean MADRS and GAD-7 scores	–	3
Dao VH et al. 2021 ^[6]	Chronic gastrointestinal disorders patients with depression symptoms	Multispecies probiotics	Lactobacillus, Bifidobacterium, Lactococcus	B.bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. lactis W19, Lc. lactis W58	The product consists of over 2.5×10^9 CFU per gram, patients would mix one sachet (2g of product) in 100mL of water for 8 weeks	After 2 months using the probiotic product, the symptoms of anxiety and depression improved significantly	–	3
Venkataraman R et al. 2021 ^[7]	Students facing examination stress	Multi-strain probiotics	Bacillus, Lactobacillus, Bifidobacterium	Bacillus coagulans Unique IS2, L. rhamnosus UBLR58, B. lactis UBBLa70, L. plantarum UBLP40, B. breve UBBR01, B. infantis UBBi01	Receiving the multi-strain probiotic (Bacillus coagulans Unique IS2, L. rhamnosus UBLR58, B. lactis UBBLa70, L. plantarum UBLP40 (each of 2 billion CFU); B. breve UBBR01, B. infantis UBBi01	Supplementation of multistrain probiotic significantly reduced the depressive symptoms in students facing examination	–	2

					(each of 1 billion CFU)) capsule with glutamine (250 mg) 2 times a day for 28 days			
Akkasheh G et al. 2016 ^[8]	Patients with MDD	Probiotics	Lactobacillus, Bifidobacterium	Lacidophilus, L. casei, B. bifidum	Patients in the probiotic group received daily one probiotic capsule containing L. acidophilus (2×10^9 CFU/g), L. casei (2×10^9 CFU/g), and B. bifidum (2×10^9 CFU/g) for 8 weeks	After 8 wk of intervention, patients who received probiotic supplements had significantly decreased Beck Depression Inventory total scores	Probiotic administration in patients with MDD for 8 wk had beneficial effects insulin, homeostasis model assessment of insulin resistance, hs-CRP concentrations, and glutathione concentrations	2
Bai & R et al. 2022 ^[9]	Patients with moderate depression	Probiotics	Bacillus, Bifidobacterium, Lactobacillus, Streptococcus	14 species: B. subtilis PXN@ 21, B. bifidum PXN@ 23, B. breve PXN@ 25, B. infantis PXN@ 27, B. longum PXN@ 30, L. acidophilus PXN@ 35, L. delbrueckii ssp. bulgaricus PXN@ 39, L. casei PXN@ 37, L. plantarum PXN@ 47, L. rhamnosus PXN@ 54, L. helveticus PXN@ 45, L. salivarius PXN@ 57, L. lactis ssp. lactis PXN@ 63, S. thermophilus PXN@ 66	Participants were asked to take four capsules (2×10^9 CFU) in the morning each day with food within 4 week	Probiotic intake significantly reduced depression scores on the Patient Health Questionnaire 9	-	2
Bambling M et al. 2017 ^[10]	Patients with SSRI treatment resistant depression	Probiotics	Lactobacillus, Bifidobacterium, Streptococcus	L. acidophilus, B. bifidum, S. thermophiles	Capsules administered pre meals as a combination of lyophilized probiotics (L. acidophilus, B. bifidum, S. thermophiles total CFU of 2×10^{10}) and magnesium orotate 1600 mg divided in two daily doses for 8 weeks	At the end of an 8-week intervention mean changes for depression scores and quality of life in the group was clinically significantly improved	-	3
Chen HM et al. 2021 ^[11]	Patients with MDD	Probiotics	Lactobacillus	L. plantarum PS128 (PS128)	One PS128 capsule twice a day was given to recruited patients, each PS128 capsule contains 300 mg of probiotics, equivalent to 3×10^{10} CFU of Lactobacillus plantarum PS128	After 8-week PS128 intervention, scores of Hamilton Depression Rating Scale-17 and Depression and Somatic symptoms Scale significantly decreased	-	3
Jamilian M et al. 2018 ^[12]	Women with polycystic ovary syndrome	Probiotics	Lactobacillus, Bifidobacterium	L. acidophilus, L. reuteri, L. fermentum, B. bifidum	Intaking 8×10^9 CFU/day probiotic containing L. acidophilus, L. reuteri, L. fermentum, B. bifidum (2×10^9 CFU/g each) plus 200 µg/day selenium for 12 weeks	Probiotic and selenium co-supplementation resulted in a significant improvement in beck depression inventory and depression anxiety and stress scale scores compared with the placebo	Co-administration of probiotic and selenium for 12 weeks to women with PCOS had beneficial effects on mental health parameters, serum total testosterone, hirsutism, hs-CRP, TAC, GSH and MDA levels	2
Kazem YI et al. 2021 ^[13]	Healthy female volunteers	Probiotics	Bifidobacterium	Yogurt enriched with Bifidobacterium spp.	All volunteers were given seven cups of yogurt every week (as one cup daily) fortified with the strain specific probiotic which was Bifidobacterium spp. for 8 weeks provided that each cup of yogurt was weighing 100 g	Bifidobacterium spp. supplementation combined with improvement in dietary intake resulted in improvement of depressive mood and well-being	Bifidobacterium spp. supplementation reduced kynurenine blood level	3

					and each gram contained not less than 10^8 cells of <i>Bifidobacterium</i> spp.			
Kim CS et al. 2019 ^[14]	Nationwide individuals	Probiotics	–	–	The types of probiotic food included fermented vegetables (kimchi) and fermented milk products	Compared with the lowest tertile of probiotic food consumption, the highest tertile had significantly lower odds in PHQ-9 depression severity and self-reported clinical depression, particularly in men	–	4
Lee HJ et al. 2021 ^[15]	Healthy adults	Probiotics	<i>Lactobacillus</i> , <i>Bifidobacterium</i>	Probiotic NVP-1704, a mixture of <i>L. reuteri</i> NK33 and <i>B. adolescentis</i> NK98	Each 500 mg capsule of NVP-1704 contained 2.5×10^9 CFU of microorganisms (2.0×10^9 CFU for <i>L. reuteri</i> NK33 and 0.5×10^9 CFU for <i>B. adolescentis</i> NK98), two capsules with water were taken once a day, daily, for eight weeks	NVP-1704 group had a more significant reduction in depressive symptoms at four and eight weeks of treatment, and anxiety symptoms at four weeks compared to the placebo group	NVP-1704 treatment decreased serum interleukin-6 levels, and regulated the gut microbiota composition	2
Majeed M et al. 2018 ^[16]	MDD patients with IBS	Probiotics	<i>Bacillus</i>	<i>Bacillus coagulans</i> MTCC 5856	Receiving <i>B. coagulans</i> MTCC 5856 at a daily dose of 2×10^9 CFU (2 billion spores) for 90 days	<i>B. coagulans</i> MTCC 5856 reduced the depression symptoms in MDD patients with IBS (HAM-D, MADRS)	<i>B. coagulans</i> MTCC 5856 reduced the level of serum myeloperoxidase	2
Messaoudi M et al. 2011 ^[17]	Healthy human volunteers	Probiotics	<i>Lactobacillus</i> , <i>Bifidobacterium</i>	<i>L. helveticus</i> R0052, <i>B. longum</i> R0175	During or just after breakfast, all volunteers took one stick of 1.5 g/day of probiotics containing <i>L. helveticus</i> R0052 and <i>B. longum</i> R0175 (3×10^9 CFU/stick) for 30 days	Administration of probiotics significantly alleviated depression and anxiety in volunteers, as measured by the HSCL-90 scale	–	2
Mi GL et al. 2015 ^[18]	Infantile colic and colicky induced maternal depression	Probiotics	<i>Lactobacillus</i>	<i>L. reuteri</i> (DSM 17938)	Participants received <i>L. reuteri</i> at a dose 10^8 CFU for 28 days and they were followed for 4 weeks	<i>L. reuteri</i> (DSM 17938) reduces daily crying time and maternal depression during infantile colic	–	2
Miyaoka T et al. 2018 ^[19]	Patients with treatment-resistant MDD	Probiotics	<i>Clostridium</i>	<i>C. butyricum</i> MIYAIRI 588 (CBM588)	20 mg orally twice daily for the first week and 20 mg orally three times daily from weeks 2 to 8	CBM588 in combination with antidepressants is effective and well tolerated in the treatment of treatment-resistant MDD	–	2
Mohammadi AA et al. 2016 ^[20]	Petrochemical workers	Probiotics	<i>Lactobacillus</i> , <i>Bifidobacterium</i>	<i>L. lactis</i> , <i>L. acidophilus</i> , <i>Bifidobacterium</i>	Probiotic and conventional yogurts or multispecies probiotic supplements were provided for participants every day for 6 weeks	After 6 weeks of intervention, a significant improvement of DASS scores was observed in the probiotic yogurt and in the probiotic capsule group	–	2
Moludi J et al. 2019 ^[21]	Myocardial infarction patients with depression symptoms	Probiotics	<i>Lactobacillus</i>	<i>L. rhamnosus</i>	Patients in the probiotic group received one probiotic capsule daily containing 1.6×10^9 CFU of <i>L. rhamnosus</i> with their lunch for 12 weeks	The total BDI-II score decreased significantly in patients who received probiotic supplements compared with the placebo group	Markers of inflammatory and oxidative stress were influenced favorably by probiotic supplements	2

Okubo R et al. 2019 ^[22]	Schizophrenia patients with depression symptoms	Probiotics	Bifidobacterium	B. breve A-1	All participants received B. breve strain A-1 (10^{11} CFU/day) for 4 weeks followed by 4 weeks of observation	B. breve A-1 in improved anxiety and depressive symptoms in patients with schizophrenia	B. breve A-1 administration changed the function of the gut epithelial barrier function related to TRANCE and IL-22	3
Otaka M et al. 2021 ^[23]	Patients with MDD or BD	Probiotics	Lactobacillus	L. casei strain Shirota (LcS)	Daily intake of 8.0×10^{10} CFU for 12 weeks	Depression severity, evaluated by the Hamilton Depression Rating Scale, was significantly alleviated after LcS treatment	LcS was beneficial to alleviate depressive symptoms, partly through its association with abundance of Actinobacteria in the gut microbiota	3
Pinto-Sanchez MI et al. 2017 ^[24]	IBS patients with depression symptoms	Probiotics	Bifidobacterium	B. longum NCC3001	Receiving 42 sachets of spray dried B. longum NCC3001 ($1.0E+10$ CFU/1gram powder with maltodextrin)	Probiotic B. longum NCC3001 reduced depression scores and increased quality of life in patients with IBS	The probiotic reduced limbic reactivity	2
Qin Q et al. 2021 ^[25]	Patients with test anxiety	Probiotics	Lactobacillus, Bifidobacterium, Streptococcus	1.2×10^{10} CFU of B. longum subsp. Longum BAMA-B05/BauB1024, 1.9×10^{10} CFU of B. lactis BAMA-B06/Bau-B0111, 1.5×10^{10} CFU of B. adolescentis, 3.2×10^9 CFU of S. thermophilus, 4.6×10^9 CFU of L. acidophilus, 3.0×10^9 CFU of L. delbrueckii subsp. bulgaricus	Taking probiotic supplement preparation for 15 consecutive days (twice per day, and approximately 12-hour set time between two intakes)	Administration of the PSP markedly alleviated students' depression	-	3
Raygan F et al. 2018 ^[26]	Type 2 diabetic patients with depression symptoms	Probiotics	Lactobacillus, Bifidobacterium	L. acidophilus, B. bifidum, L. reuteri, L. fermentum	Intaking 50,000 IU vitamin D3 every 2 weeks plus 8×10^9 CFU/g probiotic, containing L. acidophilus, B. bifidum, L. reuteri, and L. fermentum (each 2×10^9) for 12 weeks	Vitamin D and probiotic co-supplementation resulted in significant improvements in beck depression inventory total scores	Vitamin D and probiotic co-supplementation regulated serum hs-CRP, plasma NO, TAC, glycemic control and HDL-cholesterol levels	2
Raygan F et al. 2019 ^[27]	Type 2 diabetic patients with depression symptoms	Probiotics	Lactobacillus, Bifidobacterium	L. acidophilus, B. bifidum, L. reuteri, L. fermentum	Receiving 200 mg/day selenium as selenium yeast plus 8×10^9 CFU/day probiotic containing L. acidophilus, L. reuteri, L. fermentum and B. bifidum (2×10^9 CFU/g each) for 12 weeks	Probiotic and selenium co-supplementation significantly decreased Beck Depression Inventory index	Probiotic and selenium co-supplementation improved metabolic profiles	2
Sanchez M et al. 2017 ^[28]	Obese individuals	Probiotics	Lactobacillus	L. rhamnosus CGMCC1.3724	Participants received two capsules per day , corresponding to an average of 3.24×10^8 CFU/day for 24 weeks	The LPR female group displayed a more pronounced decrease in the Beck Depression Inventory score	-	2
Slykerman RF et al. 2017 ^[29]	Postpartum depression	Probiotics	Lactobacillus	L. rhamnosus HN001	Women were randomised to receive either HN001 at a dose of 6×10^9 CFU, to be taken daily from enrolment until birth and, from birth up till six months post-birth whilst breastfeeding.	Women who received HN001 had significantly lower depression and anxiety scores in the postpartum period	-	2

Tian P et al. 2022 ^[36]	Patients with MDD	Probiotics	Bifidobacterium	B. breve CCFM1025	The freeze-dried CCFM1025 in a dose of viable bacteria of 10^{10} CFU was given to MDD patients daily for four weeks	B. breve CCFM1025 showed a better antidepressant-like effect than placebo, based on the HDRS-24 and MADRS evaluation	B. breve CCFM1025 changed in the gut microbiome and tryptophan metabolism	2
Wallace CJK et al. 2021 ^[31]	Patients with MDD	Probiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052 and B. longum R0175 (CEREBIOME®)	Participants consumed a probiotic supplement containing Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 (CEREBIOME®) at a dose of 3×10^9 CFU once per day for 8 weeks	Significant improvements in depressive symptoms were observed at week 4 and were sustained at week 8	–	3
Wu SI et al. 2021 ^[32]	Information technology specialists	Probiotics	Lactobacillus	Lactobacillus plantarum PS128TM (PS128TM)	Participants were asked to take two capsules containing PS128TM powder, equivalent to 20 billion CFU, daily for 8 weeks	After 8-week-intervention, participants showed significant decreases in the levels of depression (PHQ-9)	–	3
Yamamura R et al. 2021 ^[33]	Schizophrenic patients with depression symptoms	Probiotics	Bifidobacterium	B. breve A-1 (synonym B. breve MCC1274)	For the first 4 weeks, the participants consumed two 2-g sachets of freeze-dried Bifidobacterium breve A-1 (synonym B. breve MCC1274) per day, each containing 5.0×10^{10} CFU	Probiotic treatment with B. breve A-1 alleviated anxiety and depressive symptoms in patients with schizophrenia	It is suggested that an elevated lipid and energy metabolism at baseline might be associated with the effects of probiotics on anxiety and depressive symptoms	3
Zhang X et al. 2021 ^[34]	Patients with depression and constipation	Probiotics	Lactobacillus	Fermented Milk Containing L. paracasei Strain Shirota (LcS)	The subjects consumed 100 mL of a LcS beverage (10^8 CFU/mL) every day for 9 weeks.	Daily consumption of LcS for 9 weeks appeared to relieve constipation and improve the potentially depressive symptoms in patients	LcS supplementation significantly decreased the IL-6 levels, and appeared to regulate the intestinal microbiota related to mental illness	2
Kavyani M et al. 2021 ^[35]	NAFLD patients with depression symptoms	Prebiotics	–	Resistant dextrin	The intervention group received 15% of the total daily intake of fat (~20 g) as Camelina sativa oil with 10 g/day of resistant dextrin, 5 g at breakfast and 5 g at dinner for 12 weeks	Supplementation of Camelina sativa oil + resistant dextrin for 12 weeks improved depression symptoms (DASS scores) in patients with NAFLD	Prebiotic and CSO co-supplementation improved glycemic status, metabolic endotoxemia, inflammation, oxidant/antioxidant biomarkers	2
Miki T et al. 2016 ^[36]	Japanese employees	Prebiotics	–	Dietary fiber	Dietary intake for 58 food and beverage items, energy, and selected nutrients were estimated using an ad hoc computer algorithm for the BDHQ	Dietary fiber intake from vegetables and fruits was significantly inversely associated with depressive symptoms	–	4
Park M et al. 2020 ^[37]	Patients with depression	Prebiotics	–	Flavonoids	Participants consumed flavonoid-rich orange juice (serving a daily 380 mL, 600 ± 5.4 mg flavonoids) for 8 weeks	Flavonoid-rich orange juice treatment significantly decreased the depression symptoms (CES-D)	Flavonoid-rich orange juice treatment regulated the gut microbiome	2
Heidarzadeh-Rad N et al. 2020 ^[38]	Patients with MDD	Probiotics, prebiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052, B. longum R0175, and galactooligosaccharide (GOS)	The probiotic sachet containing 10 billion ($\geq 10 \times 10^9$) CFU of freeze-dried L. helveticus R0052 and B. longum R0175, the prebiotic sachets contained 80% GOS powder per sachet. Participants were instructed to consume 1 sachet at the same time daily for 8 weeks	Eight-week supplementation with B. longum and L. helveticus in depressive patients improved depression symptoms	Probiotics supplementation resulted in significantly higher serum BDNF levels	2

Karbownik MS et al. 2022 ^[39]	Psychiatrically healthy medical students	Probiotics, prebiotics	–	Fermented food and food-derived prebiotics	An electronic open-ended form of the Food Record was constructed to gather information regarding consumption of 34 selected food items categorized in five classes	High intake of fermented food was associated with more severe depressive and anxiety symptoms under stress; however, no such link was observed for food-derived prebiotics	–	3
Kazemi A et al. 2019 ^[40]	Patients with MDD	Probiotics, prebiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052, B. longum R0175, and galactooligosaccharide	The probiotic product contains freeze-dried L. helveticus R0052 and B. longum R0175 bacteria at a dosage 10 × 10 ⁹ CFU/per 5 g sachet for 8 weeks, and the prebiotic product was composed of galactooligosaccharide and 0.2% Plum flavor	8 weeks of probiotic supplements to subjects with MDD resulted in an improvement in BDI score compared with placebo whereas no significant effect of prebiotic supplementation was seen	The probiotic may exert at least part of its effects on depression through the kynurenine to tryptophan ratio	2
Moludi J et al. 2021 ^[41]	Coronary artery disease (CAD) patients with depression symptoms	Probiotics, prebiotics	Lactobacillus	L. rhamnosus G	Receiving one capsule contained 1.9 × 10 ⁹ CFU of L. rhamnosus per day, or one sachet containing 15 g inulin per day, or both for 8 weeks	Probiotic-Inulin Co-supplementation significantly decreased depression symptoms (BDI)	Probiotic plus prebiotic may exert their effects on depression through the inflammatory cytokines and LPS	2
Perez-Cornago A et al. 2016 ^[42]	Spanish university graduates	Probiotics, prebiotics	–	Yogurt (total, wholefat, and low-fat) and prebiotic ((fructans and galacto-oligosaccharide))	Participants were allocated into 4 categories according to servings (1 serving = 125 g) of yogurt (total, whole-fat (3% fat), and low-fat (0.1% fat)) consumed per week: <0.5 servings (<63 g), ≥0.5 to <3 servings (≥63 to <250 g), ≥3 to <7 servings (≥250 to <875 g), and ≥7 servings (≥875 g)	High consumption of whole-fat yogurt was related to a lower risk of depression in women of the SUN cohort	–	3
Hadi A et al. 2019 ^[43]	Obese or overweight adults	Synbiotics	Lactobacillus, Bifidobacterium	Synbiotics containing L. acidophilus, L. casei, B. bifidum plus inulin	Synbiotic supplements in form of a 500 mg capsule contained L. acidophilus, L. casei and B. bifidum (2 × 10 ⁹ CFU/g each) plus 0.8 g inulin for 8 weeks	A significant between-group decrease in depression was found in the synbiotic group compared to the placebo.	Synbiotic supplementation decreased the TG, TC, LDL-C levels	2
Haghighat N et al. 2021a ^[44]	Hemodialysis patients	Synbiotics, probiotics	Lactobacillus, Bifidobacterium	Synbiotic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10 ⁷ CFU/g each)) or probiotics (5 g fructo-oligosaccharides (FOS), 5 g galacto-oligosaccharides (GOS), 5 g of inulin)	Receiving the synbiotic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10 ⁷ CFU/g each)) or probiotics (5 g probiotics as in synbiotic group) for 12 weeks	Synbiotic supplementation resulted in greater improvement in depression symptoms compared to the probiotic supplementation in HD patients especially in the subgroup of patients with depression symptoms	Synbiotic supplementation increased the serum BDNF level	2
Haghighat N et al. 2021b ^[45]	Hemodialysis patients	Synbiotics, probiotics	Lactobacillus, Bifidobacterium	Synbiotic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10 ⁷ CFU/g each)) or probiotics (5 g fructo-oligosaccharides (FOS), 5 g galacto-oligosaccharides (GOS), 5 g of inulin)	Receiving the synbiotic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10 ⁷ CFU/g each)) or probiotics (5 g probiotics as in synbiotic group) for 12 weeks	From baseline to 12 weeks, synbiotic and probiotic supplementation resulted in a significant decrease in BDI and BAI score in comparison to the placebo	Synbiotic and probiotic supplementation increased the serum Hb level	2

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Table S12. Characteristics of studies investigating the efficiency of gut microbiota-based therapeutics in animal models of depression.

Study	Object	Depression model	Microbiota-based therapies	Genus	Species	Intervention method	Depression alleviation	Gut-brain axis mechanism
Rao J et al. 2021a ^[1]	Sprague-Dawley rats	CUMS-depression	Fecal microbiota transplantation	–	–	FMT group was administered a gavage of fecal supernatant with 2×10^8 fecal microbiota for 14 consecutive days	Fecal microbiota transplantation improved the CUMS-induced depressive-like behavior	Fecal microbiota transplantation altered the gut microbiota imbalance, and alleviated the intestinal tract inflammation, intestinal mucosa disruption, and neuroinflammation
Rao J et al. 2021b ^[2]	Sprague-Dawley rats	CUMS-depression	Fecal microbiota transplantatio	–	–	For each rat, 1 ml of bacterial suspension (2×10^8 CFU/ml) was transplanted to each of the recipient rat by gavage each day for consecutive 14 days	Treatment with fecal microbiota transplantation ameliorated depression-like behaviors	Treatment with fecal microbiota transplantation suppressed activation of glial cells and NLRP3 inflammasome in the brain
Han SK et al. 2021 ^[3]	C57BL/6 mice	RS-depression FMT-RS-depression	Fecal microbiota transplantation	–	–	0.2 mL of the fecal microbiota suspension were orally gavaged in (the stomach of) mice once a day for 5 days	Fecal transplantation of vehicle-treated control or RS/CSS-treated mice into RS-exposed mice significantly mitigated RS-induced anxiety- and depressive-like behaviors	Fecal transplantation treatment suppressed the NF- κ B activation in the hippocampus and colon, reduced the IL-6 and corticosterone levels in the blood, and regulated gut microbiota composition
Marcondes Ávila PR et al. 2020 ^[4]	Wistar rats	CMS-depression	Fecal microbiota transplantation	–	–	An equivalent of 3×10^8 cells in a 100- μ L solution was given to each rat for five consecutive days by gavage	FMT treatment improved depressive-related (open-field) behavior	Manipulation of the microbiota reversed the behavioral and biochemical changes induced by the CMS protocol, and the vagus nerve influenced the gut-brain axis response
Xu Z et al. 2018 ^[5]	C57BL/6 mice	Alcohol-induced depression	Fecal microbiota transplantation	–	–	Mice in FMT group received 200 μ L suspensions with a minimum dose of approximately 10^{10} bacteria at each oral gavage (from 3 male healthy volunteers)	FMT significantly decreased anxiety- and depressive-like behaviors	–
Zhang Y et al. 2019 ^[6]	C57BL/6 mice	CUS-depression	Fecal microbiota transplantation	–	–	Antibiotic-treated mice were orally challenged with 300 μ l fecal transplants (approximately 2×10^8 viable probiotic bacteria dissolved in sterile PBS) by gavaging on 3 consecutive days	Transplantation of the NLRP3 KO microbiota alleviated the CUS-induced depressive-like behaviors	FMT significantly ameliorated astrocyte dysfunction in recipient mice treated with CUS via inhibition of circHIPK2 expression
Zhou H et al. 2022 ^[7]	C57BL/6 mice	Dcf1 KO-depression	Fecal microbiota transplantation and probiotics treatment	Lactobacillus, Bifidobacterium	L. reuteri, L. murinus, B. longum	Microbial transplantation was performed at 9:00 a.m. each day for 14 days. L. murinus, L. reuteri, and B. longum were diluted using 0.9% NaCl to a density of 10^9 CFU/mL.	Depression-like behavior of KO group was relieved following transplantation with L. reuteri, L. murinus, B. longum	Lactobacillus rescued depressive symptoms by restoring GABA levels
Wu Z et al. 2021 ^[8]	C57/B6	CSDS-depression	Fermentate of bacteria	Lactobacillus, Streptococcus	Adzuki bean sprout fermented milk generated by L. bulgaricus, S. thermophilus, L. plantarum 15953, and L. brevis J1	Administration of full dose of adzuki bean sprout fermented milk (high, 0.4 mL per day), half dose of adzuki bean sprout fermented milk (medium, 0.2 mL of per day), and a low dose of adzuki bean sprout fermented milk (low, 0.1 mL per day) for 10 days	GABA-enriched adzuki bean sprout fermented milk alleviated the depression-like	GABA-enriched adzuki bean sprout fermented milk treatment regulated the GABA _B -cAMP-PKA-CREB) signaling pathway and increased the monoamine transmitters (5-hydroxytryptamine, norepinephrine, and dopamine) in the hippocampus of mice

Han SK et al. 2020a ^[9]	C57BL/6 mice	IS-depression EC-depression	Fermentate of Bifidobacteria	Bifidobacteria	Bifidobacteria-Fermented Red Ginseng and Its Constituents Ginsenoside Rd and Protopanaxatriol	10 mg/kg/day of RG; 25 mg/kg/day of RG; 50 mg/kg/day of RG; 10 mg/kg/day of fRG; 25 mg/kg/day of fRG; and 50 mg/kg/day of fRG dissolved in 1% maltose were orally gavaged once a day for 5 days	Treatment with RG and fRG significantly mitigated the stress-induced anxiety/depression-like behaviors	fRG and its constituents Rd and protopanaxatriol mitigated anxiety/depression and colitis by regulating NF- κ B-mediated BDNF expression and gut dysbiosis
Ko CY et al. 2013 ^[50]	Sprague-Dawley rats	FST-depression	Fermentate of probiotics	Lactobacillus	Fermented black soybean milk by <i>L. brevis</i> FPA 3709	Feeding with 48-h fermented black soybean milk at a dosage of 35 mg/kg b.w. including 2.5 mg GABA/kg b.w., and a double-dosage sample group (70 mg/kg b.w. including 5.0 mg GABA/kg b.w.) for 28 days	Oral feeding of 48-h fermented product significantly reduced the duration of immobility in a dose dependent manner	The underlying mechanism for the antidepressant effect of this fermented product merits further research into the changes in the profile of monoamines, such as serotonin, dopamine, and norepinephrine, in rat brains
Warda AK et al. 2019 ^[11]	C57BL/6 mice	ADR-159-depression	Heat-killed fermentate of bacteria	Lactobacillus	ADR-159, a heat-killed fermentate generated by <i>L. fermentum</i> and <i>L. delbrueckii</i>	ADR-159 was incorporated into standard mice chow to a final concentration of 5%, equivalent to approximately 3×10^9 cell bodies per gram of chow	ADR-159 fed animals exhibited depressive- and anxiety like behaviors	ADR-159 fed animals had significantly lower base line corticosterone levels and disturbed microbial community
Xu N et al. 2018 ^[12]	ICR mice	Constipation-depression	Multispecies probiotics	bifidobacteria, lactobacillus, lactococcus and yeast	No data	The probiotic group was given probiotic (10 mg/kg daily by gavage), for 14 consecutive days	Administration of a probiotic ameliorated depressive behaviors	Probiotics alleviated depression through protecting neuronal health via activation of the AKT signaling pathway
Abildgaard A et al. 2021 ^[13]	Flinders sensitive line rats Flinders resistant line rats	FSL-depression	Multi-species probiotics	Bifidobacterium, Lactococcus and Lactobacillus	9 strains: <i>B. bifidum</i> W23, <i>B. lactis</i> W51, <i>B. lactis</i> W52, <i>L. acidophilus</i> W37, <i>L. brevis</i> W63, <i>L. casei</i> W56, <i>L. salivarius</i> W24, <i>Lc. lactis</i> W19 and <i>Lc. lactis</i> W58	Receiving a bottle of 4.5 g (2.5×10^9 CFU/g) freeze-dried probiotics dissolved in 30 mL of tap water for 12 weeks. The treatments were administered daily between 4 and 6 pm and completely emptied by the animals during the night.	Probiotics has effects on the gut microbiota composition associated with depressive-like behaviour	-
Li N et al. 2018 ^[14]	C57BL/6 mice	CMS-depression	Multistrain probiotics	Bifidobacterium, Lactobacillus	<i>L. helveticus</i> R0052, <i>L. plantarum</i> R1012, <i>B. longum</i> R0175	The bacterial solution (200 μ l or 2×10^9 CFU) was administered by oral gavage daily for 4 weeks during the experimental procedure	Probiotics attenuated CMS-induced anxiety- and depressive-like behaviors	Probiotics treatment modulated the gut microbiota-inflammation-brain axis, characterized by regulated gut microbiota, decreased hippocampal levels of proinflammatory cytokines (IFN- γ and TNF- α), and direct or inflammatory-mediated inhibition of IDO1 activity
Liu QF et al. 2020 ^[15]	ICR mice	IS-depression	Multi-strains probiotics	Bifidobacterium, Lactobacillus, Pediococcus	<i>L. plantarum</i> LP3, <i>L. rhamnosus</i> LR5, <i>B. lactis</i> BL3, <i>B. breve</i> BR3, <i>P. pentosaceus</i> PP1	Probiotic formulation (500 μ l; 2×10^9 CFU/mL) was subsequently administered to mice subjected to stress conditions over a 4-week period	Probiotic administration alleviated depressive-like behaviors	Ingested probiotics altered the composition of gut microbiota and decreased corticosterone level in serum

Ding Y et al. 2021 ^[16]	C57BL/6 mice	CRS-depression	Next-generation probiotics	Akkermansia, Lactobacillus	A. muciniphila ATCC® BAA-835™, L. plantarum CICC® 23,133	200 µl (5 × 10 ⁸ CFU/mL) of A. muciniphila was administered via gavage for 3 weeks 200 µl (5 × 10 ⁸ CFU/mL or 5 × 10 ⁹ CFU/mL) of L. plantarum was administered via gavage for 3 weeks	A. muciniphila and high-dose Lactobacillus plantarum treatments ameliorated CRS-induced depressive-like behaviors in mice	A. muciniphila treatment regulated abnormal variations in hormone (corticosterone), neurotransmitter (dopamine and serotonin), and BDNF expression levels in CRS-induced mice, and regulated gut microbiota
Abildgaard A et al 2017a ^[17]	Sprague-Dawley rats	Fed with a control or high-fat diet	Probiotics	Lactobacillus, Bifidobacterium	8 bacterial strains: B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19, Lc. Lactis W58	Each cage received a bottle containing 4.5 g(2.5 × 10 ⁹ CFU/g) of freeze-dried powder dissolved in 30 mL of tap water, the bottles were administered daily between four and six pm for 5 weeks	Probiotic treatment markedly reduced depressive-like behaviour in the forced swim test	Probiotic treatment regulated the HPA axis, immune system and microbial tryptophan metabolism
Abildgaard A et al. 2017b ^[18]	Flinders Sensitive Line rats	HFD-depression	Probiotics	Lactobacillus, Bifidobacterium	8 bacterial strains: B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19, Lc. Lactis W58	Each cage received a bottle containing 4.5 g(2.5 × 10 ⁹ CFU/g) of freeze-dried powder dissolved in 30 mL of tap water, the bottles were administered daily between four and six pm for 5 weeks	Probiotic treatment protects against the pro-depressant-like effect of high-fat diet in Flinders Sensitive Line rats	Probiotic treatment regulated cerebral T cell populations demonstrating that lymphocyte-brain interactions as a promising future research area in the field of psychoneuroimmunology
Abildgaard A et al. 2019 ^[19]	Sprague-Dawley rats	-	Probiotics	Bifidobacterium, Lactococcus, Lactobacillus	B. bifidum W23, B. lactis W51, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19 and Lc. lactis W58	Each probiotics cage of two rats was administered a bottle of 4.5 g (2.5 × 10 ⁹ CFU/g) freeze-dried PRO in a carrier matrix (maize starch, maltodextrins and vegetable protein) dissolved in 30 mL of tap water for 8 weeks	Probiotics had antidepressant-like effect	The cohabiting microbiota and the faecal abundance of probiotics may modulate the antidepressant-like effect of probiotics in rats
Agusti A et al. 2018 ^[20]	C57BL/6 mice	HFD-depression	Probiotics	Bifidobacterium	B. pseudocatenulatum CECT 7765	Receiving a daily dose of 1 × 10 ⁹ CFU B. pseudocatenulatum CECT 7765 by gavage for 14 weeks	B. pseudocatenulatum CECT 7765 ameliorated depressive-like behaviors	B. pseudocatenulatum CECT 7765 regulated the endocrine and immune mediators of the gut-brain axis.
Arseneault-Bre & J et al. 2012 ^[21]	Sprague-Dawley rats	Post-myocardial infarction depression	Probiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052, B. longum R0175	For 7 d before MI and between the 7th post-MI day and euthanasia, half the MI and sham rats were given one billion live bacterial cells of L. helveticus R0052 and B. longum R0175 per d dissolved in water	L. helveticus R0052 and B. longum R0175 combination interfered with the development of post-MI depressive behaviour	The beneficial impact of probiotics combination also includes the maintenance of intestinal barrier integrity, which may contribute to the inflammatory state observed after MI
Arslanov A et al. 2021 ^[22]	mice	Antibiotic-depression	Probiotics	Lactobacillus	Two strains: L. rhamnosus B-8238, L. plantarum 8PA3	Receiving 1 mL drinking water contained 2 × 10 ⁵ CFU/mL of a lactobacilli mixture (1:1) once a day for 14 days	Lactobacillus treatments decrease the anxiety level, increase the muscle endurance and motor coordination, and improve cognitive functions of mice	Lactobacillus treatments decreased the inflammation and oxidative stress, and improved microbiota content

Aygun H et al. 2022 ^[23]	WAG/Rij rats	Depressive-like behavior in WAG/Rij rat	Probiotics	Lactobacillus, Bifidobacterium, Streptococcus	VSL#3 contains 4 strains of Lactobacillus (<i>L. plantarum</i> , <i>L. acidophilus</i> , <i>L. delbrueckii</i> subsp. <i>bulgaricus</i> and <i>L. casei</i>), 3 strains of Bifidobacterium (<i>B. longum</i> , <i>B. breve</i> , <i>B. infantis</i>) and Streptococcus <i>salivarius</i> subsp. <i>Thermophilus</i>	VSL#3 at the doses of 12.86 bn living bacteria/kg/day in 0.5 ml for 30 day by gavage	VSL#3 supplementation exhibited anxiolytic and anti-depressive effect	VSL#3 supplement also increased the NGF immunoreactivity while decreasing IL-6, TNF- α and NO levels in WAG/Rij rat brain
Barros-Santos T et al. 2020 ^[24]	Swiss mice		Probiotics	Lactobacillus	<i>L. plantarum</i> 286 (Lp 286), <i>L. plantarum</i> 81 (Lp 81)	Mice were treated daily for 30 days with single doses of 0.1 ml vehicle solution supplemented with Lp 286 ($10^9/0.1$ ml CFU) or Lp 81 ($10^9/0.1$ ml CFU)	The <i>L. plantarum</i> 286 strain exerted antidepressant- effects under our experimental conditions	-
Bharwani A et al. 2017 ^[25]	C57BL/6 mice	CDSDS-depression	Probiotics	Lactobacillus	<i>L. rhamnosus</i> JB-1	Gavaging with 200 μ l (1.67×10^9 CFU) of <i>L. rhamnosus</i> (JB-1) TM for 28 days	JB-1 treatment partially corrected the adverse effects of stress on social preference, exploration, and anxiety-like behaviours	JB-1 treatment promoted systemic changes in the immunoregulatory phenotype and influenced the effects of chronic stress on host immunity
Birmann PT et al. 2021 ^[26]	Swiss mice	LPS-depression	Probiotics	Komagataella	<i>K. pastoris</i> KM71H	Mice were treated with <i>K. pastoris</i> KM71H in the concentration of 8 log UFC/g/per animal by intragastric route (i.g.) for a period of 14 consecutive days for CRS stress and 7 days for LPS stress	<i>K. pastoris</i> KM71H prevented depression-like behavior induced by stress	<i>K. pastoris</i> KM71H modulated the permeability of the blood-brain barrier, prevented an inflammatory response and oxidative stress, and decreased the plasma corticosterone levels
Bravo JA et al. 2011 ^[27]	BALB/c mice	Healthy status	Probiotics	Lactobacillus	<i>L. rhamnosus</i> (JB-1)	Animals were orally gavaged with broth with <i>L. rhamnosus</i> (JB-1) 10^9 CFU daily between 8:00 and 9:00 for a period of 28 continuous days	<i>L. rhamnosus</i> (JB-1) reduced stress-induced anxiety- and depression-related behavior	<i>L. rhamnosus</i> (JB-1) modulated the GABAergic system in mice and therefore may have beneficial effects in the treatment of depression and anxiety
Chen P et al. 2019 ^[28]	BALB/c mice	UCMS-depression	Probiotics	Lactobacillus	Three strains: <i>L. reuteri</i> , <i>L. murinus</i> , <i>L. johnsonii</i>	Gavaging with 200 μ l bacterial suspension of <i>L. reuteri</i> (3×10^9 CFU/mL in pre-reduced PBS) for another 30 days	<i>Lactobacillus reuteri</i> has a significant therapeutic effect on depression	Oral administration of <i>Lactobacillus reuteri</i> increased brain serotonin levels and serotonin-positive cells in the dorsal raphe nucleus, and modulated microbiota
Chen T et al. 2021 ^[29]	C57BL/6N mice	CRS-depression FMT CRS-depression	Probiotics	Akkermansia	<i>A. muciniphila</i>	Orally administration of another 100 μ l of <i>A. muciniphila</i> containing 1×10^9 bacteria for 14 days	<i>A. muciniphila</i> supplementation alleviated depression-like behaviors	<i>A. muciniphila</i> supplementation prevented mucosal barrier defects and aggravation of colitis, and modified the gut microbiota
Chen X et al. 2022 ^[30]	Sprague-Dawley rats	Lead exposure-depression	Probiotics	Lactobacillus, Bifidobacterium	-	Probiotics (6 billion live bacteria/2 g) were administered to the rats by gavage 5 times a week, at least 1.2×10^9 CFU combined strains were given to each rat, and doses as high as 4.8×10^{10} CFU were administered	Probiotic intervention relieved the depression-like behavior of lead-exposed rats	Probiotic intervention altered the gut microbiome, while the fecal SCFAs could be a possible adjuvant therapy of depression

Chen Y et al. 2021b ^[31]	Sprague-Dawley rats	CUMS-depression	Probiotics	Rhizopus, Bacillus	Semen Sojiae Praeparatum, a fermented food by <i>R. chinensis</i> 12 and <i>Bacillus</i> sp. DU-106	The rats were given a daily dose of 0.97 g/kg Semen Sojiae Praeparatum (dissolved in 10 mL of normal saline) for 4 weeks	Semen Sojiae Praeparatum fermented by <i>R. chinensis</i> 12 and <i>Bacillus</i> sp. DU-106 could ameliorate depressive behaviors.	Semen Sojiae Praeparatum regulated the metabolite levels in the serum and hippocampus tissue, reversed the cell morphology and mitochondrial function of hippocampal neurons through improving the imbalance in gut microbiota and inhibiting the excessive SCFAs accumulation
Chevalier G et al. 2020 ^[32]	C57BL/6J mice	UCMS-depression	Probiotics	Lactobacillus	<i>L. plantarum</i> ^{WLI}	Supplementing with oral feeding 5 days a week with 2×10^8 CFU of <i>L. plantarum</i> ^{WLI} diluted in 200 μ l of PBS	Complementation with <i>L. plantarum</i> ^{WLI} normalized depression-like behaviors	Complementation with <i>L. plantarum</i> ^{WLI} : improved lipid metabolism and the generation of eCBs, leading to increased signaling in the eCB system and adult neurogenesis in the hippocampus
Choi J et al. 2019 ^[33]	C57BL/6J mice	CRS-depression	Probiotics	Lactobacillus	Extracellular vesicles (EV) from <i>L. plantarum</i>	L-EVs at a dose of 0.1 μ g/kg were intraperitoneally injected into a mouse at a volume of 100 μ l 30 min prior to restraint treatment for 14 days: for the post-stress period, L-EVs were intraperitoneally injected at a volume of 100 μ l containing increasingly higher doses; 0.1 μ g/kg for the first 5 days, 0.18 μ g/kg for the following 2 days, and 0.27 μ g/kg for the final 7 days	L-EV treatment in CRST-treated mice rescued stress-induced depressive-like behaviors	L-EV treatment in CRST-treated mice rescued the reduced expression of Bdnf
Choi J et al. 2022 ^[34]	C57BL/6J mice	CRS-depression	Probiotics	Lactobacillus, Bacillus, Akkermansia	Extracellular vesicles (EV) from <i>L. plantarum</i> , <i>Bacillus subtilis</i> , and <i>A. muciniphila</i>	Lac-EV, Bac-EV, or Akk-EV were administered, each with 6 μ g in 100 μ l of injection volume, for 14 days	Injection of EV isolated from culture media of <i>L. plantarum</i> , <i>Bacillus subtilis</i> and <i>A. muciniphila</i> are sufficient to ameliorate stress-induced depressive-like behavior	Injection of EV from the three selected probiotics restored the expression of McCP2, Sirt1, and/or neurotrophic factors in the hippocampus
Daug \acute{e} V et al. 2020 ^[35]	Fischer/Long Evans Rats	MD-depression	Probiotics	Lactobacillus, Bifidobacterium, Lactococcus, Streptococcus	<i>L. helveticus</i> LA 102, <i>B. longum</i> LA 101, <i>L. lactis</i> LA 103, and <i>S. thermophilus</i> LA 104	Rats received 0.5 mL of the probiotics (1×10^9 CFU) by gavage with probes 5 days a week for 5 weeks for Fischer rats and 9 weeks for Long Evans rats (until euthanasia)	A probiotic mixture induces anxiolytic- and antidepressive-Like effects	Probiotic mixture treatment changed the levels of certain metabolites, such as 21-deoxycortisol, and changed brain monoamines
Desbonnet L et al. 2010 ^[36]	Sprague-Dawley rats	MS-depression	Probiotics	Bifidobacterium	<i>B. infantis</i> 35624	<i>B. infantis</i> 35624 was administered by dissolving a powdered preparation, containing a dose of 1×10^{10} live bacterial cells, in 100 ml of the rats drinking water every morning from P50 to the day of sacrifice	<i>B. infantis</i> 35624 treatment alleviated depressive-like behaviors	Probiotic treatment resulted in normalization of the immune response and restoration of basal NA concentrations in the brainstem.
Dhaliwal J et al. 2018 ^[37]	Swiss albino LACA mice	CUMS-depression SD-depression	Probiotics	Lactobacillus	<i>L. plantarum</i> MTCC 9510	<i>L. plantarum</i> MTCC 9510 (2×10^{10} CFU per mice) was supplemented to male Swiss albino mice either subjected to chronic unpredictable mild stress (28 days) or sleep deprivation stress (21 days)	<i>L. plantarum</i> MTCC 9510 supplementation prevented stress-induced behavioural despair (depression, anxiety, learning and memory, stereotypic behaviour)	<i>L. plantarum</i> MTCC 9510 supplementation prevented the oxidative stress and inflammatory response in brain and serum, and prevented intestinal permeability and selected gut microbial aberrations

Gao K et al. 2022 ^[36]	BALB/c mice	CUMS-depression	Probiotics	Lactococcus	Lc. lactis strain WHH2078	Orally administered with 200 μ L pre-warmed WHH2078 preparation (1×10^9 CFU/mL) for 5 consecutive weeks	Lc. lactis strain WHH2078 alleviated depressive and anxiety-like behaviors	Lc. lactis strain WHH2078 improved the 5-HT metabolism along the GBA and modulation of the gut microbiome composition
Gu F et al. 2020 ^[39]	Sprague-Dawley rats	CUMS-depression	Probiotics	Lactobacillus	L. casei	Administration with L. casei (8×10^8 CFU/kg/day) for 4 weeks from 4th to 7th week of CUMS	L. casei treatment relieved the depressive-like behaviors of rats induced by CUMS	L. casei treatment up-regulated the expression levels of monoamines 5-HT, DA and NE, activated the BDNF-TrkB signaling, inhibited the phosphorylation of EK1/2 and P38 in frontal cortex, and regulated the gut microbiota composition
Guida F et al. 2018 ^[40]	C57/bl6 mice	Antibiotic-depression	Probiotics	Lactobacillus	L. casei DG	Oral gavage with the probiotic (L. casei DG, 10^9 cells in saline, 100 μ l) up to 7 days.	L. casei treatment relieved the depressive-like behaviors induced by antibiotics	Administration of L. casei adjusted gut inflammation, normalized the hippocampal BDNF-TrkB signaling, improved hippocampal and cortical electrophysiological neuronal activity, and reduced microglia and astrocyte activation
Guo Y et al. 2019 ^[41]	ICR mice	CRS-depression	Probiotics	Bifidobacterium	B. adolescentis	Receiving 0.25 $\times 10^9$ CFU/kg B. adolescentis by gavage for 21 days	B. adolescentis treatment prevented the development of anxiety- and depressive-like behaviors caused by CRS	B. adolescentis treatment are related to reducing inflammatory cytokines and rebalancing the gut microbiota
Han SK et al. 2019 ^[42]	C57BL/6 mice	IS-depression	Probiotics	Lactobacillus, Bifidobacterium	L. mucosae NK41, B. longum NK46	1×10^9 CFU of NK41/mouse/day; 1×10^9 CFU of NK46/mouse/day; 1×10^9 CFU of NK41 and NK46 mixture (1:1) mix/mouse/day	Oral administration of NK41, NK46, or their mixture synergistically alleviated immobilization stress-induced anxiety- and depressive-like behaviors in mice	Oral administration of NK41, NK46, or their mixture inhibited gut inflammation through the inhibition of gut bacterial LPS production, and prevented gut dysbiosis
Han SK et al. 2020b ^[43]	C57BL/6 mice	EC-depression	Probiotics	Lactobacillus, Bifidobacterium	L. reuteri NK33, B. adolescentis NK98	1×10^9 CFU/mouse/day of NK33; 1×10^9 CFU/mouse/day of NK98; EN1:1, 1×10^9 CFU/mouse/day of the NK33 and NK98 (1:1)(4:1)(9:1) mixture were orally gavaged once a day for 5 days from 24 h after the final K1 treatment	Oral gavage of NK33 and/or NK98 alleviated Escherichia coli K1-induced depression-like behaviors in mice	Oral gavage of NK33 and/or NK98 shifted Escherichia coli K1-induced gut microbiota alteration in mice
Hao W et al. 2021 ^[44]	C57BL/6 mice	Antibiotic-depression	Probiotics	Bifidobacterium, Lactococcus, Lactobacillus and Streptococcus	Sixteen strains: B. longum, L. acidophilus, B. bifidum, B. breve, B. lactis, L. brevis, L. bulgaricus, L. casei, L. helveticus, L. plantarum, L. reuteri, L. rhamnosus, L. salivarius, Lc. lactis, S. thermophilus, and B. infantis	Receiving probiotics solution (0.15 ml/d) for 14 consecutive days	Probiotics treatment mitigated antibiotic-induced anxiety- and depressive-like behaviors	Probiotics treatment modulated the gut microbiota, corrected excessive LPS release, and inhibited the immoderate activation of the NLRP3 inflammasome in the colon

Hao Z et al. 2019 ^[45]	Sprague-Dawley rats	CUMS-depression	Probiotics	Faecalibacterium	<i>F. prausnitzii</i> (ATCC 27766)	Rats were fed at the same time each day by oral gavaged with 200 μ L of resuspended <i>F. prausnitzii</i> , 1×10^9 CFU (from the eighth week to the eleventh week) daily.	Administration of <i>F. prausnitzii</i> had preventive and therapeutic effects on CUMS-induced depression-like and anxiety-like behavior	<i>F. prausnitzii</i> administration led to higher levels of SCFAs in the cecum and higher levels of cytokines interleukin-10 (IL-10) in the plasma, prevented the effects on corticosterone, C-reaction protein and cytokines interleukin-6 (IL-6) release induced by CUMS
Huang F et al. 2021 ^[46]	C57BL/6 mice	Ovariectomy-depression	Probiotics	Prevotella	<i>P. histicola</i> DSM19854	Receiving <i>P. histicola</i> (10 ml/kg) per second day for 12 weeks	<i>P. histicola</i> alleviated depressive behaviors caused by estrogen deficiency	<i>P. histicola</i> regulated disorder microbiota to attenuate central inflammation, which might be involved in TLR4/Myd88/JNK MAPK pathway (Figure 9) and further upregulate BDNF expression for hippocampal neurogenesis
Huang YY et al. 2022 ^[47]	C57BL/6N mice	DSS-depression	Probiotics	Lactobacillus	<i>L. plantarum</i> DMDL 9010 (LP9010)	Mice administered orally with 0.2 mL/10 g weight per day LP9010 at a dose of 10^7 CFU/mL and 10^9 CFU/mL for 7 days	LP9010 intake lightened depression-like behavior	LP9010 promoted anti-inflammatory cytokines, reduced proinflammatory cytokines, enhanced SCFAs production, and reorganized the gut microbiome
Jang HM et al. 2019 ^[48]	C57BL/6 mice	IS-depression	Probiotics	Lactobacillus, Bifidobacterium	<i>L. reuteri</i> NK33, <i>B. adolescentis</i> NK98	Orally gavaged NK3 or NK49 at a dose of 1×10^9 CFU/mouse/day for 5 days in IS-treated mice	Treatment with NK33 and/or NK98, which were orally gavaged in mice before or after IS treatment, significantly suppressed the occurrence and development of anxiety/depression	NK33 and NK98 synergistically regulated of gut immune responses (inhibited NF- κ B activation, attenuated colitis and hippocampal inflammation) and microbiota composition
Kambe J et al. 2020 ^[49]	C57BL/6J mice	Healthy status	Probiotics	Enterococcus	Heat-killed <i>E. faecalis</i> strain EC-12 (EC-12)	The EC-12 group was fed on AIN-93 M diet with heat-killed EC-12 at a concentration of 0.125 % for 4 weeks	EC-12 supplementation reduced anxiety- and depressive-like behaviors	EC-12 supplementation regulated the gut microbiota
Karen C et al. 2021 ^[50]	Wistar rats	MS-depression	Probiotics	Lactobacillus	<i>L. paracasei</i> HT6	Supplementing with <i>L. paracasei</i> HT6 (per orally, p.o. by oral gavage; from PND-2 to 16)	<i>L. paracasei</i> supplementation prevented early life stress-induced anxiety and depressive-Like behavior	<i>L. paracasei</i> supplementation potentially mediated stress hormones, neurotransmitters, and expression of miRNAs, glutamate receptors, and the microbiota-gut-brain axis
Kim JK et al. 2020 ^[51]	C57BL/6J mice	Escherichia coli K1-depression	Probiotics	Lactobacillus	<i>L. mucosae</i> NK41	Mice were orally gavaged with the NK41 (1×10^9 CFU/mouse/day) once a day for 5 days from 24 h after treatment with K1 suspension	NK41 treatment reduced K1-induced cognitive decline and anxiety/depression	The superiority of anti-inflammatory bacteria such as <i>L. mucosae</i> can alleviate psychiatric disorders with the attenuation of altered microbiota
Kochalska K et al. 2020 ^[52]	Wistar rats	CUMS-depression	Probiotics	Lactobacillus	<i>L. rhamnosus</i> JB-1	The JB-1 group was fed a microbiotic diet with LR-JB1 TM daily for 4 weeks	Dietary supplement of LR-JB1 TM resulted in a reduction of stress-induced behavior in a rat model of depressive-like disorder	A microbiotic diet with LR-JB1 TM brought improvements in neurochemical balance in the course of depressive-like disorder
Kosuge A et al. 2021 ^[53]	C57BL/6J mice	CSDS-depression	Probiotics	Bifidobacterium	<i>B. breve</i> M-16V	M-16V-treated groups were fed the AIN-93G diet which containing 5.0×10^9 nonviable cells/0.5 g	Heat-sterilized <i>B. breve</i> M-16V supplementation significantly prevented depressive-like behavior (social interaction impairment)	Heat-sterilized <i>B. breve</i> M-16V supplementation suppressed CSDS-induced neuroinflammation and modulated the gut microbiota composition

Li Q et al. 2021 ^[54]	Sprague-Dawley rats	CUMS-depression	Probiotics	Bifidobacterium, Lactobacillus	L. helveticus, L. rhamnosus, L. casei, B. longum	Giving 2 ml of probiotics at a concentration of 4×10^8 CFU/kg once daily for 4 weeks	Probiotics alleviated CUMS-induced depressive-like behaviors	Probiotics treatment remodeled intestinal flora, increased the monoamine neurotransmitters (norepinephrine and 5-hydroxytryptamine), and inhibited hypothalamic-pituitary-adrenal neuroendocrine system (ACTH and corticosterone)
Liang S et al. 2015 ^[55]	Sprague-Dawley rats	CRS-depression	Probiotics	Lactobacillus	L. helveticus NS8	The strain was resuspended in drinking water at a concentration of 10^9 CFU/ml, and was administered for 26 days until the termination of the experiment	Treatment with probiotic L. helveticus NS8 had anxiolytic and antidepressant effects, promoted cognition	Treatment with probiotic L. helveticus NS8 decreased plasma CORT and ACTH levels, modulated pro-inflammatory and anti-inflammatory balance, and restored 5-HT, NE, and BDNF content in the hippocampus
Liao JF et al. 2019 ^[56]	C57BL/6J mice	MS-depression	Probiotics	Lactobacillus	L. paracasei PS23 (PS23)	The live (live cells of PS23 at 1×10^9 CFU/mouse/day) and heat-killed cells (heat-killed cells of PS23 at 1×10^9 cells/mouse/day) were administered by oral gavage for 4 weeks starting from PD 29	L. paracasei PS23 alleviated stress, anxiety, and depressive traits in maternal separated mice	PS23 modulated stress responses via immunomodulatory effects along the dopaminergic systems of the brain, illustrating the potential of PS23 as a psychobiotic
Lim EY et al. 2021 ^[57]	Sprague Dawley rats	Ovariectomy-depression	Probiotics	Lactobacillus	L. intestinalis YT2	Treatment (10^9 CFU/ml) started one week after surgery and lasted for 18 weeks	Treatment with L. intestinalis YT2 significantly alleviated menopausal symptoms including depression-like behaviour	Administration of L. intestinalis YT2 restored the intestinal microbial composition, promoted gut barrier integrity by increasing the mRNA levels of tight junction-related markers
Liu Y et al. 2020 ^[58]	BALB/c mice	Healthy status	Probiotics	Lactobacillus	L. rhamnosus JB-1	The bacteria were delivered in drinking water at 1×10^8 CFU per day for 28 days prior to behavioural testing and continued throughout the testing period for a total of 39 days treatment	L. rhamnosus JB-1 treatment reduced depressive- and anxiety-like behavior	CD4+CD25+ cells, most likely regulatory T cells, are both necessary and sufficient for L. rhamnosus JB-1 induced antidepressant and anxiolytic-like effects
Liu YW et al. 2015 ^[59]	C57BL/6J mice	MS-depression	Probiotics	Lactobacillus	L. plantarum PS128	Giving saline re-suspended PS128 daily (10^9 CFU/mouse/day) by gavage for 4 weeks from PND 29 to 8 weeks old	Chronic ingestion of PS128 could ameliorate anxiety- and depression-like behaviors	PS128 reduced inflammatory cytokines and increased anti-inflammatory cytokines in the serum, and increased the dopamine level in the prefrontal cortex
Maehata H et al. 2019 ^[60]	C57BL/6J mice	sCSDS-depression	Probiotics	Lactobacillus	Heat-killed L. helveticus MCC1848	Heat-killed MCC1848 was added to AIN93G at 3.3×10^8 organisms/g, resulting in the consumption of approximately 1.0×10^8 organisms/day for 24 days	MCC1848 improved anxiety- or depressive-like behaviors in sCSDS mice	MCC1848 ameliorated sCSDS-induced gene expression alterations in signal transduction or nervous system development
McVey Neufeld KA et al. 2018 ^[61]	BALB/c mice	Healthy status	Probiotics	Lactobacillus	L. rhamnosus JB-1	JB-1 was delivered via the drinking water at a dose of 10^8 CFU/day for 28 days	Feeding L. rhamnosus JB-1 to BALB/c mice reduced depressive-like behavior	Feeding L. rhamnosus JB-1 to BALB/c mice attenuated plasma corticosterone and hastens recovery
Moya-Pérez A et al. 2017 ^[62]	C57BL/6J mice	MS-depression	Probiotics	Bifidobacterium	B. pseudocatenulatum CECT 7765	Receiving a daily oral dose of 1×10^8 CFU B. pseudocatenulatum CECT 7765 from P2 until P21	B. pseudocatenulatum CECT 7765 treatment reduced MS-induced anxiety- and depressive-like behaviors in adulthood	B. pseudocatenulatum CECT 7765 treatment modulated the consequences of chronic stress on the HPA response via modulation of the intestinal neurotransmitter, cytokine network, and gut microbiota composition

Murray E et al. 2019 ^[63]	CD-1 mice	LPS-depression	Probiotics	Lactobacillus	<i>L. lactis</i> , <i>L. cremoris</i> , <i>L. diacetylactis</i> , <i>L. acidophilus</i>	5 g of dry kefir probiotic culture (3.0×10^8 CFU/g) into 1L of skim milk, mice had <i>ad libitum</i> access to kefir	Probiotic consumption during puberty protected against LPS-induced depression- and anxiety-like behaviors in adulthood	Probiotic consumption during puberty mitigated inflammation, and prevented LPS-induced changes to the gut microbiome
Natale NR et al. 2021 ^[64]	Long-Evans rats	CUS-depression	Probiotics	Lactobacillus	<i>L. helveticus</i> R0052, <i>L. rhamnosus</i> R0011	The PB-infused water was prepared by rehydrating 2.87 g of powder (mixed with maltodextrin and milk powder) in 75 mL of distilled water for a final concentration of 10^8 CFU/ml for 2 weeks	Probiotics prevented the anxiety and depressive behavior	Probiotics reduced microglia immunoreactivity in the basolateral amygdala, possibly indicating a neuroprotective effect of PB supplements in this rodent model
Partrick KA et al. 2021 ^[65]	Syrian hamsters (Mesocricetus auratus)	CSDS-depression	Probiotics	Lactobacillus, Bifidobacterium	<i>L. helveticus</i> R0052, <i>B. longum</i> R0175	Probiotic at a low dose of 10^8 CUF per day, or probiotic high dose of 10^{10} CUF per day for 14 days	Surprisingly, probiotic administration at the low dose significantly increased social avoidance and decreased social interaction	Probiotic administration altered gut microbial composition and promoted an anti-inflammatory profile
Patterson E et al. 2019 ^[66]	C57BL/6J mice	HFD-depression	Probiotics	Lactobacillus	<i>L. brevis</i> DPC6108, <i>L. brevis</i> DSM32386	Water containing either <i>L. brevis</i> DPC6108 (1×10^{10} CFU/day) or <i>L. brevis</i> DSM32386 (1×10^{10} CFU/day) was supplied to the mice in these groups for the 12 week intervention period and bottles were replaced daily	Probiotics treatment improved depression-like behaviour	Probiotics treatment improved metabolic syndrome in mice (reduced the accumulation of mesenteric adipose tissue, increased insulin secretion, improved plasma cholesterol clearance and reduced basal corticosterone)
Qiu X et al. 2021 ^[67]	C57BL/6J mice	LPS-depression	Probiotics	Lactobacillus	<i>L. delbrueckii</i>	Giving 10^8 CFU Lac intragastrically daily for 7 days	<i>L. delbrueckii</i> treatment effectively inhibited the occurrence of depressive-like behavior	<i>L. delbrueckii</i> treatment inhibited intestinal inflammation and subsequent neuroinflammation (through inhibiting toll-like receptor 4 (TLR4) signaling), and microbiota dysbiosis
Ramalho JB et al. 2019 ^[68]	C57BL/6 mice	Healthy status	Probiotics	Lactococcus	<i>Lc. lactis</i> subsp. <i>cremoris</i> LL95	Female C57BL/6 mice received LL95 orally at a dose of 10^8 UFC/day for 28 days	Oral supplementation of <i>L. lactis</i> LL95 improved depressive- and anxiety-like behaviour	Oral supplementation of <i>L. lactis</i> LL95 improved the antioxidant parameters in the hippocampus, and increased the faecal contents of lactic acid bacteria
Ramalho JB et al. 2022 ^[69]	C57BL/6 mice	LPS-depression	Probiotics	Lactococcus	<i>Lc. lactis</i> subsp. <i>cremoris</i> LL95	Oral administration of LL95 for one week with a daily oral dose of 1×10^8 CFU/100 μ L.	LL95 intervention improved LPS-induced depression-like behaviors in mice	LL95 intervention modulated the oxidative status and pro-inflammatory cytokine expression in the hippocampus and alteration in the LAB content of the gut microbiota
Sandes S et al. 2020 ^[70]	C57BL/6J mice	CRS-depression	Probiotics	Weissella	<i>W. paramesenteroides</i> WpK4	Mice were pretreated, receiving 10^8 CFU of <i>W. paramesenteroides</i> WpK4 during 10 days, followed by 21 days of challenge, being restrained daily	Bacterial consumption was associated with a reduced anxiety-like and depressive-like behaviors	<i>W. paramesenteroides</i> WpK4 exerted their beneficial roles in gut-brain axis through their immunomodulatory effects with consequences in several metabolic pathways related to intestinal permeability and hippocampal physiology
Savignac HM et al. 2014 ^[71]	BALB/c mice	-	Probiotics	Bifidobacterium	<i>B. longum</i> 1714, <i>B. breve</i> 1205	Bacteria were daily reconstituted in sterile phosphate buffered saline (PBS) to a final concentration of 1×10^8 CFU/mL ingested by mice for 6 weeks	Both Bifidobacteria reduced anxiety and <i>B. longum</i> 1714 induced antidepressant-like behavior	-
Silva LC et al. 2021 ^[72]	Swiss Webster mice	Light-dark box and tail suspension test	Probiotics	Saccharomyces, Lactobacillus	<i>S. cerevisiae</i> var boulardii 17, <i>L. paracasei</i> DTA 81, <i>S. cerevisiae</i> S-04	Daily treated with probiotic-containing functional wheat beer (PWB) or probiotic-containing functional sour beer (PSB) (100 μ L) for 7 days	<i>S. boulardii</i> 17 and <i>L. paracasei</i> DTA 81 withstood at sufficient doses to promote antidepressant effects in the mice group	-

Soltanmoradi H et al. 2021 ^[73]	BALB/c mice		Probiotics	Lactobacillus	L. rhamnosus GG, and kefir, a probiotic supplement	–	Kefir, L. rhamnosus GG, and the investigated probiotic supplement have antidepressant-like properties	–
Sovijit WN et al. 2019 ^[74]	C57BL/6J mice	Ovariectomy-depression	Probiotics	Lactobacillus	L. reuteri	Feeding with food pellets that were pulverized in a blender and kneaded with L. reuteri (2 billion CFU/mouse/day) at 10 weeks of age, and lasting for 2 weeks	L. reuteri supplementation improves depressive behaviors in OVX mice	Supplementation of L. reuteri upregulated hippocampal brain-derived neurotrophic factor (BDNF) gene expression
Stenman LK et al. 2020 ^[75]	Swiss mice	CRS-depression	Probiotics	Bifidobacterium, Lactobacillus	12 candidate probiotics: B. longum BG0014, B. longum ssp. infantis B111471, B. animalis BL0005, B. animalis ssp. lactis 420, L. paracasei Lpc-37, L. salivarius Ls-33, L. plantarum LP12418, L. plantarum LP12151, L. plantarum LP12407, L. acidophilus LA11873, L. rhamnosus LX11881, L. helveticus LH0138	Mice were administered a daily oral gavage containing 1×10^8 CFU of selected candidate probiotic solution for one week prior to and for three weeks during daily chronic restraint stress.	Of the twelve candidate probiotics, L. paracasei Lpc-37, L. plantarum LP12407, L. plantarum LP12418 and L. plantarum LP12151 prevented stress-associated anxiety and depression-related behaviours	Each of these strains had a unique profile in terms of mechanistic biomarkers related to the HPA axis and prefrontal cortex GABA receptor expression
Sun J et al. 2018 ^[76]	C57BL/6 mice	CUMS-depression	Probiotics	Clostridium	C. butyricum WZMC1018	The bacterial solution was prepared every day in sterile milk and treated orally at a concentration of 5×10^8 CFU/0.5 mL/day/mice for 28 consecutive days.	C. butyricum WZMC1018 treatment effectively improved depressive-like behavior	C. butyricum WZMC1018 treatment stimulated the GLP-1 secretion and increased the 5-HT and BDNF through the gut-brain axis
Sun X et al. 2021 ^[77]	C57BL/6 mice	CRS-depression	Probiotics	Lactobacillus	L. plantarum WLPL04	The final concentration of the L. plantarum WLPL04 in drinking water was 10^8 CFU/mL for 28 days	L. plantarum WLPL04 treatment alleviated CRS-induced anxiety/depressive-like behaviors and cognitive deficits	L. plantarum WLPL04 treatment reversed the abnormal change in intestinal microbiota, and alleviated the reduced levels of 5-HT, BDNF, and TrkB induced by CRS in mice
Sun Y et al. 2019 ^[78]	Kunming mice	CUMS-depression	Probiotics	Lactobacillus	L. kefirifaciens ZW3	Treated with L. kefirifaciens ZW3 at different doses (10^7 CFU, 10^8 CFU, 10^9 CFU)/mouse/day for 6 weeks	Supplementation with Lactobacillus kefirifaciens ZW3 improved depressive-like behavior	L. kefirifaciens ZW3 regulated disorder of tryptophan metabolism, protected the HPA axis, inhibited inflammation, and reshaped the structure of the gut microbiota caused by CUMS
Takahashi K et al. 2019 ^[79]	ddY mice	DSS-depression	Probiotics	Enterococcus	E. faecalis 2001 (EF-2001)	EF-2001 was administered orally (250mg/kg per os [p.o.]) from 14 days before the beginning of DSS	EF-2001 attenuated IBD-like symptoms and depressive-like behavior in DSS-treated mice	EF-2001 decreased rectal and hippocampal inflammatory cytokines and facilitated the NFκB p65/XIAP pathway in the hippocampus

						administration until the day prior to the last DSS treatment for 20 days		
Takahashi K et al. 2022 ^[60]	ddY mice	Olfactory bulbectomized-depression	Probiotics	Enterococcus	E. faecalis 2001 (EF-2001)	EF-2001 (250 mg/kg) was dissolved in drinking water and administered orally (per os [p.o.]) once a day in a volume of 0.1 mL/10 g mouse body weight using a 1 mL syringe with an oral probe, from 6 days before the OBX operation for 28 days.	EF-2001 administration prevented depressive-like behaviors	EF-2001 administration regulated prefrontal cortical myelination via the enhancement of CREB/BDNF and NFκB p65/LIF/STAT3 pathways
Tian P et al. 2019a ^[61]	C57BL/6J mice	CUMS-depression	Probiotics	Bifidobacterium	B. longum subspecies infantis strain CCFM687	Lyophilized bacteria powder was re-suspended in 10% skimmed milk solution, and administered at a dose of 10 ⁹ CFU/mL viable bacteria for 6 weeks	B. longum subsp. infantis strain CCFM687 showed a good anti-depressive effect	B. longum subsp. infantis strain CCFM687 increased the 5-hydroxytryptamine, serotonin and BDNF, alleviated the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis response and accordingly reversed the peripheral inflammation status, and reshaped the gut microbiome
Tian P et al. 2019b ^[62]	C57BL/6J mice	CUMS-depression	Probiotics	Bifidobacterium	B. longum subsp. infantis E41, B. breve M2CF22M7	Lactic acid bacteria treatment group was gavaged at a dose of 10 ⁹ CFU/mL body weight daily for 5 weeks	Administration of several Lactic acid bacteria strains alleviated depressive behaviors of mice	Lactic acid bacteria strains alleviated depression possibly via a 5-HTP-dependent mechanism, gut microbiota structure modulation
Tian P et al. 2020 ^[63]	C57BL/6J mice	CUMS-depression	Probiotics	Bifidobacterium	B. breve CCFM1025	The CCFM1025 treatment group was gavaged at a volume of 0.1 mL/10g (10 ⁹ CFU/mL) body weight daily for 6 weeks	CCFM1025 treatment significantly reduced depression- and anxiety-like behaviors	CCFM1025 treatment significantly alleviated hyperactive hypothalamic-pituitary-adrenal response, as well as inflammation, down-regulated the pCREB-c-Fos pathway, increased BDNF, SCFA and 5-HTP, and restored gut microbial abnormalities
Tian P et al. 2021a ^[64]	C57BL/6J mice	UCMS-depression	Probiotics	Lactobacillus, Bifidobacterium, Pediococcus	30 strains: B. adolescentis, 3 strains of B. breve, 4 strains of B. bifidum, 2 strains of B. longum subsp. infantis, 5 strains of B. longum subsp. Longum, 4 strains of B. longum, 3 strains of L. fermentum, 2 strains of L. helveticus, 3 strains of L. plantarum, 2 strains of L. rhamnosus, Pediococcus acidilactici	Giving viable bacteria (10 ⁹ CFU/day) by oral gavage via 10% skim milk for 6 weeks	16 strains show anti-depression and anti-anxiety like effect in at least three behavioral tests	Intestinal 5-HTP supplementary on the biosynthesis of brain serotonin is the possible mechanism of the candidate probiotics

Tian P et al. 2021b ^[85]	C57BL/6 mice	CUMS-depression	Probiotics	Bifidobacterium	B. breve CCFM1025 and FHLJDQ3M5	Probiotic treatment persisted for 6 weeks by daily oral gavage. Lyophilized bacteria powder were re-suspended in 10% skim cow milk and administered at a dose of 10 ⁹ CFU/mL viable bacteria.	CCFM1025 significantly decreases the chronically stressed mice's depressive-like behaviors	CCFM1025 altered genomic and metabolic features involving glycoside hydrolases and neuromodulatory metabolites
Tian T et al. 2019 ^[86]	C57BL/6 mice	CSDS-depression	Probiotics	Clostridium	C. butyricum Miyairi 588 (CBM588)	SPF mice were provided sterile water containing Miyairi 588 (>5 × 10 ⁶ CFU) for 4 weeks ad libitum	CBM588 pre-feeding attenuates social avoidance and depressive-like behaviours in CSDS mice	CBM588 may be involved in the regulation of microglia-mediated immune responses in the brain, and regulated gut microbiota composition
Tillmann S et al. 2019 ^[87]	Flinders Sensitive Line rats Flinders resistant line rats	FSL-depression	Probiotics	Bifidobacterium, Lactobacillus, Lactococcus	Ecologic® Barrier + 4: B. breve W25, B. longum W108, L. helveticus W74, and L. rhamnosus W71 Ecologic® Barrier: B. bifidum W23, B. lactis W51, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. lactis W19, and Lc. lactis W58	Rats received a daily dose of 5 × 10 ⁹ CFU/2 g for Ecologic® Barrier and a daily dose of 5 × 10 ⁹ CFU/1.25 g for Ecologic® Barrier + 4, administered in water bottles at a volume of 60 mL.	Probiotics exhibited risk-reducing properties (depressive-related behavior)	-
Trudeau F et al. 2019 ^[88]	Sprague-Dawley rats	Post-myocardial infarction-depression	Probiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052; B. longum R0175; L. salivarius HA-118	Each rat in the probiotic groups received a daily dose of 10 ⁹ CFU for 14 days	B. longum mitigated the depressive-like symptoms	B. longum reduced the Caspase-3 activity and plasma C-reactive protein concentrations in the lateral and medial amygdala
Wang P et al. 2021 ^[89]	C57BL/6J mice	Antibiotic-depression	Probiotics	Bifidobacterium, Lactobacillus	Unspecific	Probiotics (Live Combined Bifidobacterium and Lactobacillus Tablets, Inner Mongolia Shuang Qi Pharmaceutical Co., Ltd. PRC, Inner Mongolia, China) for another 2 weeks	Probiotics treatment alleviated anxiety behaviors, depressive-like behaviors and recognitive performance	Probiotics treatment improved neuronal activation in different brain regions, characterized by increased expression of Fos protein
Wang S et al. 2020a ^[90]	C57BL/6 mice	FMT CSDS-depression Microbe-depression	Probiotics	Lactobacillus	L. intestinalis, L. reuteri	Mice were orally administered water containing the microbes (approximately 1 × 10 ⁸ CFU/day) for 14 days (days 15–28) using gastric gavage	Ingestion of L. intestinalis and L. reuteri causes depression- and anhedonia-like phenotypes	Ingestion of L. intestinalis and L. reuteri caused biochemical abnormalities in antibiotic-treated mice via the subdiaphragmatic vagus nerve
Wei CL et al. 2019 ^[91]	C57BL/6J mice	Corticosterone-depression	Probiotics	Lactobacillus	Live and heat-killed L. paracasei PS23	The L-PS23 group received a daily oral gavage of L-PS23 (108 cells/0.2 ml/day) from days 1 to 41, and the H-PS23 group received a daily gavage of H-PS23 at the same dose and duration.	PS23 reverses corticosterone treatment-induced anxiety-like and depression-like behaviors	The effects of chronic PS23 treatment are due to (1) increases in the hippocampal GR, MR, and BDNF proteins; (2) increases in serotonergic and dopaminergic activities in the hippocampus, prefrontal cortex, and striatum; and (3) improvement of the gut microbiota

Xie R et al. 2020 ^[92]	C57BL/6 mice	CSDS-depression	Probiotics	Lactobacillus	<i>L. reuteri</i> 3	Treating for 4 weeks with <i>L. reuteri</i> 3 (10^{10} CFU/ml of per mouse in 0.1 ml phosphate-buffered saline [PBS]) after 10 days of CSDS	Treatment with <i>L. reuteri</i> 3 ameliorated depressive-like behaviors	Treatment with <i>L. reuteri</i> 3 regulated the gut microbiota, SCFAs, and serotonin metabolism
Xu J et al. 2022 ^[93]	C57BL/6 mice	CUMS-depression	Probiotics	Lactobacillus	<i>L. rhamnosus</i> zz-1	Mice received <i>L. rhamnosus</i> zz-1 at a dose of 2×10^8 CFU per kg bw, 2×10^8 CFU per kg bw or 2×10^7 CFU per kg bw for 6 weeks. The volume of the daily gavage liquid was adjusted to 0.1 mL.	<i>L. rhamnosus</i> zz-1 intervention ameliorated CUMS-induced depression-like behaviors	<i>L. rhamnosus</i> zz-1 improved stress-induced physiological problems in model mice, including HPA axis hyperactivity, neurotransmitter deficiency, and impairments in the BDNF-TrkB signaling, and regulated gut microbiota
Xu M et al. 2022 ^[94]	C57BL/6J mice	CUS-depression	Probiotics	Lactobacillus	<i>L. paracasei</i> 126L6, CCFM1229, 29L1, 4L3, <i>L. helveticus</i> 132M1, 8G3, Q7M66, 10M6, <i>L. rhamnosus</i> CCFM1131, CCFM1130, CCFM1228, <i>L. reuteri</i> CCFM1132, 11M59	The freeze-dried bacterial powder was suspended in sterile skimmed milk. The concentration of surviving bacteria was 5×10^8 CFU/mL. The gavage volume of each mouse is 200 μ L for 6 weeks	<i>L. paracasei</i> CCFM1229 and <i>L. rhamnosus</i> CCFM1228 significantly reduced anxiety- and depression-related behaviour	The strains CCFM1229 and CCFM1228 regulated the gut microbiota and xanthine oxidase activity in the brain
Yang Y et al. 2022 ^[95]	Sprague-Dawley rats	MS-postpartum depression	Probiotics	Lactobacillus	<i>L. casei</i>	From postnatal day 2 to day 28, rats were gavage-fed with <i>Lactobacillus casei</i> (8×10^8 CFU/kg/day)	Administration of <i>L. casei</i> improved depressive-like behaviors	Administration of <i>L. casei</i> altered gut microbiota composition, brain monoamines and oxidative stress, which may be associated with the regulation of the BDNF-ERK1/2 pathway
Yun SW et al. 2020 ^[96]	C57BL/6J mice	EC-depression	Probiotics	Lactobacillus	<i>L. gasseri</i> NK109	NK109 at a dosage of 1×10^8 CFUs/mouse/day was orally gavage once a day for 5 days in the mice with <i>Escherichia coli</i> K1 (1×10^8 CFUs/mouse/day)-induced depression	NK109 significantly alleviated <i>Escherichia coli</i> K1-induced cognitive impairment- and depression-like behaviors	NK109 regulated the immune response through NF- κ B-involved BDNF expression, IL-1 β expression, and vagus nerve-mediated gut-brain signaling, and mitigated <i>Escherichia coli</i> -induced colitis and gut dysbiosis
Yun SW et al. 2021 ^[97]	C57BL/6J mice	EC-depression	Probiotics	Lactobacillus	<i>L. paracasei</i> NK112	Receiving NK112 (1×10^8 CFU/mouse/day) daily for 5 days	Oral gavage of NK112 significantly alleviated K1-induced anxious, depressive, and memory-impaired behaviours	NK112 treatment suppressed IL-6, TNF- α , and BDNF expression through the regulation of gut microbiota and NF- κ B activation
Yunes RA et al. 2020 ^[98]	BALB/c mice	Healthy status	Probiotics	Lactobacillus, Bifidobacterium	<i>L. plantarum</i> 90sk, <i>B. adolescentis</i> 150	One dose (0.5 ml) of the mixture of strains contained 10^8 CFU <i>L. plantarum</i> 90sk and 10^7 CFU <i>B. adolescentis</i> 150 for 14 days	Administration of the probiotic composition decreased the duration of immobility of mice	-
Zhao Y et al. 2020 ^[99]	Sprague-Dawley rats	Corticosterone-depression	Probiotics	Lactobacillus	<i>Lactobacillus plantarum</i> DP189	Administration of DP189 (1.0×10^9 CFU/d) suspension by gavage for 21 days	<i>L. plantarum</i> DP189 treatment prevented and/or alleviated depression-like behaviors	<i>L. plantarum</i> DP189 treatment increased neurotransmitters in brain tissue, reduced serum levels of inflammatory factors, and regulated hippocampal neural apoptosis
Burokas A et al. 2017 ^[100]	C57BL/6J mice	Prebiotics-anti-depression CSDS-depression	Prebiotics	-	Fructo-oligosaccharides (FOS), Galacto-oligosaccharides (GOS)	Administering the prebiotics FOS, GOS, a combination of FOS and GOS (dissolved in drinking water for 0.3-0.4 g/mouse/day) for 3 weeks	FOS+GOS administration significantly improved the depressive- and anxiety-like behaviors	Prebiotic administration significantly decreased the hypothalamic-pituitary-adrenal axis (corticosterone levels), influenced hippocampal and hypothalamic gene expression,

								improved the tryptophan and monoamines metabolism, and normalized the effects of stress on the microbiota
Chen Y et al. 2021a ^[101]	C57BL/6 mice	CUMS-depression	Prebiotics	–	Partially hydrolyzed guar gum (PHGG)	After 28 days of CUMS, mice received 600 mg/kg PHGG	PHGG significantly inhibited the loss of body weight, and prevented CUMS-induced depressive-like behavior in mice	PHGG modulated the gut microbiota structure and then increased the levels of short-chain fatty acids in mice feces and the levels of 5-hydroxytryptamine and dopamine in serum, striatum, and hippocampus
Cheng D et al. 2018 ^[102]	Sprague-Dawley rats	Hydrocortisone-depression	Prebiotics	–	Tiansi Liquid	The dose of Tiansi Liquid was 0.45 g/kg once a day for 21 days	Tiansi Liquid ameliorated depressive symptoms in rats	Tiansi Liquid modulated the gut microbiota composition and metabolites in the tryptophan-kynurenine pathway
Chi L et al. 2020 ^[103]	Sprague-Dawley rats	CUMS-depression	Prebiotics	–	Fructo-oligosaccharides (FOS)	Administration with FOS (50 mg/kg) via oral gavage for 3 weeks from the fifth week onward	FOS administration alleviated depressive-like behaviors	FOS administration repaired intestinal epithelia damages, decreased the hypothalamic-pituitary-adrenal axis (corticosterone levels), and modified the gut microbiota
Davis DJ et al. 2017 ^[104]	C57BL/6J mice	Social isolation-depression	Prebiotics	–	N-3 polyunsaturated fatty acid docosahexaenoic acid (DHA)	The mice were then treated with either 0.1% by weight or 1.0% by weight DHA	A DHA diet, regardless of dose, exhibited reduced anxiety and depressive-like behaviors only in male mice	DHA altered the commensal community composition
Donoso F et al. 2020 ^[105]	Sprague-Dawley rats	MS-depression	Prebiotics	–	Polyphenols: phlorotannins, xanthohumol, quercetin	Dietary intervention of polyphenols (Phlorotannins 0.03%; Xanthohumol 0.015%; Quercetin 0.03%), delivered ad libitum in food, began once the animals were eight weeks old and continued for eight weeks.	Polyphenols reversed MS-induced depressive- and anxiety-like behaviours	Polyphenols treatment prevented exacerbated production of corticosterone after acute stress in MS animals, reversed MS-induced plasma BDNF depletion and changes in diversity
Egerton S et al. 2020 ^[106]	Sprague-Dawley rats	MS-depression	Prebiotics	–	Fish oil (containing polyunsaturated fatty acid)	Fish oil (composition fatty acid profile and vitamins & minerals) was added to the diets in the place of soybean oil in the standard chow, at 7% of total feed from 9 to 16 weeks of age	Fish oil dietary supplementation partly prevented the depressive-like behaviours	Fish oil dietary supplementation altered brain fatty acids, significantly decreased plasma corticosterone levels and reduced brain stem serotonin turnover, and regulated the gut microbial composition
Fan L et al. 2021 ^[107]	Sprague-Dawley rats	CUMS-depression	Prebiotics	–	Cistanche tubulosa extracts: total glycosides, Cistanche tubulosa aqueous extract, phenylethanoid and iridoid glycosides	Receiving different dose of extracts for 4 weeks	Cistanche tubulosa extracts prevented the depressive-like behaviours	Cistanche tubulosa extracts regulated the hyperactivation of the HPA axis, severe peripheral and neural inflammation, and deficiencies in 5-HT and BDNF in the hippocampus
Gao X et al. 2020 ^[108]	Sprague-Dawley rats	CUMS-depression	Prebiotics	–	Triterpenoids extracts from Poria cocos (TPC)	Receiving TPC at 15 g herb/kg 30 min before stressing exposure lasting 28 days	TPC significantly ameliorated depression-like behaviors in CUMS rats	TPC treatment restored the level of the neurotrophic factor system and regulated the gut microbiota composition, and regulated metabolic system, including primary bile acid biosynthesis, taurine and hypotaurine metabolism, arginine and proline metabolism
Gong MJ et al. 2016 ^[109]	Sprague-Dawley rats	Corticosterone-depression	Prebiotics	–	Icariin	The treatment group was treated with icariin (60 mg/kg, suspended in saline) by gastric instillation 1 h prior to CORT injection once a day for 21 days	Icariin produced an antidepressant-like effect in CORT-induced depressive rats	Icariin increased the BDNF expression in the hippocampus, regulated the energy metabolism, lipid metabolism, amino acid metabolism and gut microbe metabolism

Guo Y et al. 2018 ^[100]	ICR mice	CRS-depression	Prebiotics	–	Rosemary extracts	Receiving rosemary extracts (100 mg/kg) for 21 days during CRS stress	Pretreatment with rosemary extracts prevented the depressive- and anxiety-like behaviors	Rosemary extracts improved antiinflammatory effects in hippocampus, serum and BV-2 microglia as well as rebalanced the gut microbiota
Hao WZ et al. 2021 ^[111]	C57BL/6 mice	CUMS-depression	Prebiotics	–	Coniferyl ferulate	The mice received coniferyl ferulate at a dose of 50 mg/kg once daily via gavage for 4 weeks	Oral administration of coniferyl ferulate attenuated weight loss and depression-like and anxiety-like behaviors induced by CUMS in mice	Coniferyl ferulate administration significantly ameliorated colonic inflammation, lowered the levels of IL-6, IL-1 β , and TNF- α , and restructured the gut microbiome, and microbial metabolism
Huang YJ et al. 2021 ^[112]	C57BL/6J mice	sCSDS-depression	Prebiotics	–	Water extract of <i>Gastrodia elata</i> (WGE)	WGE was administered at an optimal dose of 500 mg/kg bw via gavage once a day for 30 successive days	Oral treatment with WGE resulted in reversal of depression-like behavior	WGE exerts antidepressant-like effects mediated by the serotonergic and KYN pathways in the prefrontal cortex and colon, and altered the gut microbiota composition
Lai WD et al. 2022 ^[113]	Wistar rats	SD-depression	Prebiotics	–	Fish oil	Feeding with a fish oil-rich diet for 10 weeks	A fish oil-based diet reduced anxiety- and depressive-like behaviors, and improved cognitive function under chronic SD.	A fish oil-based diet increased the probiotics production, increased the SCFA content, improved the intestinal barrier, increased SCFA receptor expression, and decreased blood circulation proinflammatory status
Lax NC et al. 2018 ^[114]	C57BL/6J mice	–	Prebiotics	–	Cyanobacterial extract DUQ0002I	For all injections, fraction DUQ0002I and subfractions DUQ0002I-1A-C, DUQ0002-2-4 were administered at a dose of 40 μ g per cannula	DUQ0002I induced robust antidepressant and anxiolytic-effects	This extract blocked the 5-HT7R
Lee HC et al. 2020 ^[115]	BALB/c mice	Lard diet-depression	Prebiotics	–	Fish oil (containing polyunsaturated fatty acid)-based diet	Treatment with fish oil concentrated with 50% EPA and 20% DHA triacylglycerol form for 12 weeks	Treatment with fish oil prevented depressive-like behavior	Treatment with fish oil regulated gut microbiota composition, and the prefrontal cortex fatty acid profile
Li Y et al. 2018 ^[116]	Sprague-Dawley rats	CUS-depression	Prebiotics	–	<i>Cistanche tubulosa</i> extract (CTE)	CTE at high dose (CTEH) (400 mg/kg) and low dose (CTEL) (200 mg/kg) were intragastrically administered 1 h before the CUS procedure (8:00 a.m. to 9:00 a.m.) over the course of 4 weeks	CTE significantly improved depression-like behaviors in rats under CUS	CTE restored the level of neurotransmitters and neurotrophic factors in CUS rats, regulated the gut microbial composition, and modulated SCFAs concentrations
Lin S et al. 2021 ^[117]	ICR mice	CRS-depression	Prebiotics	–	Crocetin	Receiving crocetin-L (20 mg/kg), crocetin-M (40 mg/kg), crocetin-H (80 mg/kg) for 28 days	Crocetin ameliorated CRS-induced depression-like behaviors in mice	Crocetin regulated MKP-1/ERK1/2/CREB pathway and gut microbiota
Liu Z et al. 2020 ^[118]	C57BL/6J mice	HFD-postpartum depression	Prebiotics	–	Inulin	Taking standard diet with 37 g inulin/1000 kcal for 8–10 weeks	Inulin intake significantly attenuated cognitive deficits and depressive-like behaviors	Inulin intake upregulated the monoamine neurotransmitters (5-hydroxytryptamine and norepinephrine) and suppressed neuroinflammation
Mika A et al. 2017 ^[119]	F344 rats	LH-depression	Prebiotics	–	Galactooligosaccharide (GOS), polydextrose (PDX)	Rats began diets on postnatal day 24 (PND 24) with GOS and PDX (7.0 g/kg each) for 4 weeks	Prebiotics differentially attenuated stress-induced learned helplessness	Prebiotics diets reduced stress-evoked <i>cfos</i> mRNA in the dorsal raphe nucleus (DRN), attenuated stress-evoked decreases in mRNA for the 5-HT1A autoreceptor in the DRN. GOS and PDX diet increased basal BDNF mRNA within the prefrontal cortex

O'Mahony SM et al. 2020 ^[120]	Sprague-Dawley rats	MS-depression	Prebiotics	–	Polydextrose/galactooligosaccharide prebiotic blend	Test diets differed from control diet by the inclusion of (a) GOS 20.86 g/kg and PDX 6.44 g/kg (Prebiotic)	Dietary interventions altered stress-induced spatial learning and memory	Dietary interventions regulated the hypothalamic-pituitary-adrenal axis, reduced the long-term impact of MS on myelination, and influenced the gut microbiota composition
Pusceddu MM et al. 2015 ^[121]	Sprague-Dawley rats	MS	Prebiotics	–	N-3 Polyunsaturated Fatty Acids (PUFAs)	Oral administration of an eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) (80% EPA, 20% DHA) (0.4 g/kg/day or 1 g/kg/day) n-3 PUFAs mixture was administered by gavage when animals reached 5 weeks of age	No data	Long-term supplementation of EPA/DHA restored the microbiota composition
Qu Y et al. 2020 ^[122]	C57BL/6 mice	CSDS-depression	Prebiotics	–	Betaine	Betaine (2.5% as monohydrate in drinking water) was given to mice for 24 days from day 1 to day 24	Betaine supplementation contributed to resilience to anhedonia in mice subjected to CSDS	Betaine had prophylactic effects for abnormal composition of gut microbiota in mice after CSDS and anti-inflammation action
Robertson RC et al. 2017 ^[123]	C57BL/6J mice	n-3 PUFA deficiency-depression	Prebiotics	–	N-3 Polyunsaturated Fatty Acids (PUFAs)	Fed with n-3 PUFAs supplemented diet (1 g Eicosapentaenoic acid (EPA) + Docosahexaenoic acid (DHA)/100 g diet) or n-3 PUFAs deficient diet from gestational day 0	N-3 PUFAs supplementation prevented depressive-like behaviors and memory defect	N-3 PUFAs supplementation comprehensively altered the gut microbiota composition, HPA-axis activity and inflammation
Song J et al. 2019b ^[124]	Wistar rats	ACTH-depression	Prebiotics	–	Polyphenols: chlorogenic acid (CGA)	CGA pretreatment (500 mg/kg) by intragastric administration 1 h prior to ACTH injection once a day for 14 days	CGA pretreatment ameliorated depressive-like behavior	CGA pretreatment increased the level of monoamine neurotransmitters and reduced the levels of inflammatory cytokines, and modified gut microbial community structure
Song X et al. 2021 ^[125]	ICR mice	CUMS-depression	Prebiotics	–	Puerarin	Low and high doses of Puerarin were 30 and 100 mg/kg, respectively, and these were administered intragastrically in the model	Puerarin (100 mg/kg) treatment was found to alleviate the CUMS-induced depression-like behaviors	Puerarin treatment reversed the gut microbial changes induced by CUMS
Sun Y et al. 2020 ^[126]	C57BL/6 mice	LPS-depression	Prebiotics	–	Schisandrin	Mice were treated with schisandrin (30 mg/kg, i.p.) for 14 days	Schisandrin pre-treatment attenuated LPS-induced depressive-like behaviors in mice	Schisandrin might recover the gut microbial disorder of depressive mice through suppressing the expression of TLR4/NF- κ B signaling pathway
Tian P et al. 2021 ^[127]	mice	CRS-depression	Prebiotics	–	SCFA-Acylated Starches	Feeding with 15% acylated starch for 2 weeks during chronic restraint stress	Consumption of SCFA-acylated starches alleviated the depressive symptoms of stressed mice	SCFA-Acylated Starches significantly reduced the colonic permeability via increasing the tight junction proteins (including ZO-1, Claudin, and Occludin) gene expression and reduced the level of the inflammatory cytokines, and modified gut microbiome
Tung TH et al. 2019 ^[128]	Sprague-Dawley rats	CMS-depression	Prebiotics	–	Fish oil (containing polyunsaturated fatty acid) and olive oil	Male rats were fed fish oil-rich (contained 20.5% (w/w) EPA and 11.2% DHA) or olive oil-rich diets for 14 weeks	Fish oil intervention reversed the stress-induced abnormal depressive-like behavior	Fish oil and olive oil exerted part of a prebiotic-like effect to ameliorate dysbiosis induced by CMS
Vald�-Sustaita B et al. 2021 ^[129]	Wistar rats	Ovariectomized-depression	Prebiotics	–	Aqueous extract of pomegranate (AE-PG)	The pomegranate extract (AE-PG) was dissolved in saline solution 0.9% and given by intraperitoneal route.	AE-PG administered by intraperitoneal route induced antidepressant-like effects	AE-PG given intraperitoneally activated the ER β and the serotonergic system

Wang L et al. 2020 ^[130]	Kummig mice	CUMS-depression	Prebiotics	–	Total iridoids of Valeriana jatamansi (TIV)	Treated with lowdose, medium-dose, or high-dose TIV (5.7, 11.4, and 22.9 mg/kg/d, respectively) at a volume of 10 mL/kg by the intragastric route once per day for 2 successive weeks	Administration of TIV increased body weight, sucrose solution consumption, and ameliorated depression-like behaviors	It is concluded that the antidepressant effects of TIV may be related to gut flora structures and regulation of 5-HT, NE, SP, and CRF in the brain and intestine
Wang L et al. 2021 ^[131]	Sprague-Dawley rats	CUMS-depression	Prebiotics	–	Soy isoflavones	The SI low dose, SI middle dose, and SI high dose groups were given SI at a dose of 40 mg/kg, 80 mg/kg, and 160 mg/kg per group per rat per day by oral gavage for 8 weeks	Soy isoflavones supplements significantly improved the CUMS-induced depression-like behaviour	Soy isoflavones supplements increased monoamine neurotransmitters of CUMS rats by reshaping the structure of the gut microbiota
Wang P et al. 2022 ^[132]	C57BL/6J mice	Alcohol-depression	Prebiotics	–	Propolis	Propolis group was given 120 mg/kg of propolis by gavage daily for 10 weeks	Propolis exerted an improving effect on alcohol-induced depressive symptoms	Propolis dietary supplementation repaired the intestinal mucosal barrier and hippocampal injury, and further improved brain gut dysfunction.
Wang Q et al. 2019 ^[133]	CD-1 mice	CMS-depression	Prebiotics	–	Sesamin	Orally administered with sesamin (50 mg/kg/day, dissolved in olive oil) for 10 weeks	Oral sesamin administration (50 mg/kg bodyweight/day) significantly attenuated depressive, aversive, repetitive, and anxiety-like behaviors	Sesamin inhibited stress-induced gut barrier integrity damage, reduced circulating lipopolysaccharide levels, suppressed neuroinflammatory responses, and restructured the gut microbiome
Wang R et al. 2021 ^[134]	C57BL/6J mice	CRS-depression	Prebiotics	–	Total Flavone of Abelmoschus manihot (TFA)	TFA was suspended in 1% carboxymethyl cellulose solution at different concentrations for oral administration (62.5 and 125 mg/kg) for 37 days	TFA treatment improved the depressive-like phenotype	TFA treatment improved the disturbed gut microbiota, and the intestinal barrier function
Xia J et al. 2021 ^[135]	C57BL/6J mice	LPS-depression	Prebiotics	–	Capsaicin	The mice were fed standard laboratory chow plus 0.005% capsaicin for 4 months	Dietary capsaicin improved depressive-like behavior	Dietary CAP regulated the structure of gut microbiota, increased the levels of the monoamine neurotransmitter 5-HT, and reduced the levels of inflammatory cytokine TNF- α in LPS-induced mice
Xiao Q et al. 2020 ^[136]	C57BL/6 mice	CRS-depression	Prebiotics	–	Crocin-I	Mice were daily supplied with crocin-I at a dose of 40 mg/kg by gavage for six weeks	Administration of crocin-I mitigated depression-like behaviors	Oral administration of crocin-I improved the structure of gut microbiota to restore SCFAs levels and intestinal barrier function, thereby decreasing the neuroinflammation and increasing BDNF protein to effectively alleviated depression-like behavior in depressed mice
Xue M et al. 2021 ^[137]	C57BL/6J mice	Alcohol-depression	Prebiotics	–	Fucoidan extracted from Fucus vesiculosus	Receiving 300 mg/kg body weight of fucoidan at 12:00 a.m. during the 10 weeks' experiment.	Oral administration of fucoidan alleviated alcohol withdrawal-induced depressionlike behaviors of mice	Oral administration of fucoidan regulated the gut flora of mice and reduced endotoxemia, down-regulated the TLR4/MyD88/NF- κ B p65 pathway, inhibited alcohol-induced microglia cell activation and inflammation
Yan T et al. 2020 ^[138]	C57BL/6 mice	CUMS-depression	Prebiotics	–	Polysaccharide from okra (Abelmoschus esculentus (L) Moench)	Mice were treated with polysaccharide (400 mg/kg, i.g.) for 14 days	Polysaccharide treatment alleviated depressive-like behaviors in CUMS-induced mice	Polysaccharide treatment inhibited the inactivation of inflammatory reactions in the colon, serum, hippocampus as well as BV2 cells, down-regulated the TLR4/ NF- κ B

								pathway and MAPKs signaling, and rebalanced the intestinal flora
Yan T et al. 2021 ^[139]	C57BL/6 mice	LPS-depression	Prebiotics	–	Schisandra chinensis fractions: total extracts (SCE), lignans (SCL), polysaccharides (SCPS), and essential oil (SCVO)	Mice were treated with fractions (SCE treatment [1.2 g/kg], SCL treatment [500 mg/kg], SCPS treatment [300 mg/kg] , SCVO treatment [150 mg/kg]) (i.g.) for 14 days	Fractions treatment alleviated depressive-like behaviors in LPS-induced mice	Fractions treatment regulated the neuroinflammation via the TLR4/NF- κ B/IKK α signaling pathway, and recovered the gut microbiota
Yu JB et al. 2019 ^[140]	Sprague-Dawley rats	CUS-depression	Prebiotics	–	Paeoniflorin	Mice were treated with paeoniflorin at a dose of 10 mg/kg or 20 mg/kg for 8 weeks	Paeoniflorin treatment alleviated depressive-like behaviors in CUS-induced mice	Paeoniflorin regulated the composition of the gut microbiota by increasing the abundance of probiotics. And benzoic acid, the gut characteristic metabolite of paeoniflorin, was absorbed into blood and penetrated the BBB and entered the central nervous system relieving depressive behaviors
Zhang L et al. 2021 ^[141]	Kunming mice	CUMS-depression	Prebiotics	–	Total iridoids of Valeriana jatamansi (TIV)	Treated with lowdose, medium-dose, or high-dose TIV (5.7, 11.4, and 22.9 mg/kg/d, respectively) at a volume of 10 mL/kg by the intragastric route once per day for 2 successive weeks	Administration of TIV increased body weight, sucrose solution consumption, and ameliorated depression-like behaviors	TIV may modulate the intestinal flora, thereby inducing the expression of ZO-1 and occludin, protecting the blood-brain barrier
Zhang M et al. 2021 ^[142]	ICR mice	CUMS-depression	Prebiotics	–	Sophora alopecuroides L.-derived alkaloids	Alkaloids were dissolved in 0.9% saline at a stock concentration of 3 mg/ml, and the mice received 30 mg/kg alkaloids for 4 weeks	Sophora alopecuroides L.-derived alkaloids improved depression-like behaviors and depression-related indicators in mice.	Alkaloids improved depression in mice through modulating gut microbiota
Zhang Z et al. 2022 ^[143]	C57BL/6 mice	CRS-depression	Prebiotics	–	Hyperforin	Hyperforin is dissolved in DMSO and the dosage of hyperforin is 0.38mg/kg.Mice in hyperforin treated group were intraperitoneally injected with hyperforin solution before daily restraint	Hyperforin prevented anhedonia induced by CRS in mice	Hyperforin prevented altered the richness and evenness of bacteria populations
Zhao B et al. 2020 ^[144]	C57BL/6 mice	DSS-depression	Prebiotics	–	Lycopene	Treating with distilled water and lycopene (50 mg/kg body weight/day) mixed in standard diet (AIN-93M) for 35 days	Lycopene improved DSS-induced depression and anxiety-like behavioral disorders	Lycopene suppressed neuroinflammation and prevented synaptic ultrastructure damages by upregulating the expressions of neurotrophic factor and postsynaptic-density protein, and reshaped the gut microbiome and improved the gut barrier integrity
Zhao F et al. 2021 ^[145]	Sprague-Dawley rats	Prenatal CUMS-depression in offsprings	Prebiotics	–	Lycium barbarum polysaccharide (LBP)	Gavaging with LBP at 14:00 daily, the concentration of gavage is 40 mg/kg, for 14 days	LBP treatment improved the body weight, changed the emotional function	LBP treatment reduced offspring's plasma corticosterone level and increased the diversity of gut microbiota

Zhao ZX et al. 2018 ^[146]	Sprague-Dawley rats	CUS-depression	Prebiotics	-	Albiflorin	Treating with benzoic acid (14 mg/kg)(albiflorin metabolites),albiflorin (7 mg/kg),albiflorin (14 mg/kg)for 2 weeks	Benzoic acid, a therapeutic mediator of albiflorin generated by the gut microbiota, after crossing the blood-brain barrier, entered the central nervous system to exert antidepressant effects	Albiflorin treatment regulated the gut microbiota and inhibited D-amino acid oxidase in the brain
Li H et al. 2019 ^[147]	Wistar rats	CUMS-depression	Probiotics, prebiotics	Bifidobacterium, Lactobacillus	Fructo-oligosaccharides (FOS), Galacto-oligosaccharides (GOS), B. longum, L. rhamnosus	Orally gavaged with with FOS and GOS (8%, 1 mL per 100g weight; FOS/GOS) or with B. longum (1 × 10 ⁹ CFU per 100 g weight) or with L. rhamnosus (1 × 10 ⁹ CFU per 100 g weight) during the CUMS molding for 4 weeks	Prebiotics (FOS/GOS) and probiotics (B. longum and L. rhamnosus) alleviated CUMS-induced depressive-like behaviors	Prebiotics and probiotics treatment has a considerable impact on the modulation of tryptophan metabolism and the composition of gut microbiota
Gilbert K et al. 2012 ^[148]	Sprague-Dawley rats	Post-myocardial infarction depression	Probiotics, prebiotics	Lactobacillus, Bifidobacterium	L. helveticus R0052, B. longum R0175, and PUFA n-3 diets	Each rat in the probiotics group received a daily dose of 10 ⁹ CFU for 2 weeks	Depressive-like behaviour was attenuated with the high-PUFA n-3 diet or/and probiotics	A high-PUFA n-3 diet or the administration of probiotics were beneficial to attenuate apoptosis in the limbic system in the rat
Zhu X et al. 2017 ^[149]	Sprague-Dawley rats	CUS-depression	Probiotics, prebiotics	Bifidobacterium	Bifidobacterium, Berberine	Prior to modeling with each chronic unpredictable stress method, the rats were treated with either 2 ml of a low concentration of berberine (40 mg/kg/day), a high concentration of berberine (200 mg/kg/day), bifidobacterium (140 mg/kg/day)	Berberine and bifidobacterium treatment alleviated depressive behaviors caused by CUS	Berberine and bifidobacterium appeared to reverse the physical damage brought about by stress within the gastric mucosa and intestinal microvilli of the stomach, ileum, cecum and colon
Westfall S et al. 2021a ^[150]	C57BL/6J mice	CUMS-depression CUMS+US-depression	Probiotics, prebiotics, and synbiotics		L. plantarum ATCC 793, B. longum ATCC 15707, Bioactive Dietary Polyphenol Preparation (BDPP)	The bacteria were incorporated into the animals' drinking water at a final dosage of 1.0x10 ⁹ CFU/day per bacterium; BDPP was comprised of 1% w/v grape seed polyphenol extract, 1% w/v resveratrol and a 5% w/v concord grape extract made in sterile water during the experiment	The probiotic and synbiotic attenuated depressive-like behavior following CUS, while the synbiotic rescued the phenotype following CUS and CUS+US; only BDPP and the synbiotic improved anxiety-like behavior	Microbiota-targeted treatment normalized gut microbiota populations and promoted regulatory T cell (Treg) expansion through modulation of ileal innate lymphoid cell (ILC)3 activity, an impact reflecting behavioral responses better than limbic brain region neuroinflammation
Westfall S et al. 2021b ^[151]	C57BL/6J mice	CUS-depression	Probiotics, prebiotics, and synbiotics	Lactobacillus, Bifidobacterium	L. plantarum ATCC 793, B. longum ATCC 15707, Bioactive Dietary Polyphenol Preparation (BDPP)	The bacteria were incorporated into the animals' drinking water at a final dosage of 1.0x10 ⁹ CFU/day per bacterium; BDPP was comprised of 1% w/v grape seed polyphenol extract, 1% w/v resveratrol and a 5% w/v concord grape extract made in sterile water during the experiment	The probiotic and synbiotic attenuated stress-induced depressive- and anxiety-like behaviors	A synbiotic rescued stress-induced reduction in serotonin through inflammatory and kynurenine pathway regulation, attenuated peripheral and neuroinflammatory responses, and ameliorated the stress-induced increase of the T helper 17 to regulatory T cell ratio
Mesripour A et al. 2021 ^[152]	albino mice	Dexamethasone or water avoidance stress induced depression	Synbiotics	Lactobacillus, Bifidobacterium, Streptococcus	Syn cocktail containing L. casei, L. acidophilus, L. rhamnosus, L. bulgaricus, B. breve, B. infantis, S.	The synbiotic regimen (12.5 × 10 ⁹ CFU) was supplemented in drinking water for 7 days	Synbiotic mixture prevented the effects of WAS, acute or sub-acute Dex-induced depression in mice	-

					thermophiles, and Fructooligosaccharides			
Leo A et al. 2021 ^[153]	C57BL/6J mice	CUMS-depression	Prebiotics, Postbiotics	–	α -lactalbumin (ALAC) Sodium butyrate (NaB)	ALAC (125, 250 and 500 mg/kg), NaB (30, 100, 300 mg/kg) and the co-administration of ALAC (125, 250 and 500 mg/kg) with a fixed NaB dose (100 mg/kg) were administered in drinking water for 15 days	ALAC, NaB and their combination reduced depressive- and anxiety-like behaviour in CUMS mice	–
Cheng R et al. 2021 ^[154]	C57BL/6 mice	CUMS-depression	Postbiotics	Akkermansia	Outer membrane protein Amuc_1100 of <i>A. muciniphila</i>	Mice were gavaged daily with 80 mg of Amuc_1100 in sterile PBS with a volume of 200 μ l	Amuc_1100 intervention ameliorated CUMS-induced depression-like behavior	Amuc_1100 intervention improved the gut microbiota, up-regulated the BDNF level, and inhibited the neuroinflammatory response
Kochanowska AJ et al. 2008 ^[155]	Swiss Webster mice	Healthy status	Postbiotics	–	Secondary metabolites from sponges (brominated compounds, sesquiterpene quinones, hydroquinones)	Each group was injected ip with the compound at a dose of 1–20 mg/kg	5,6-Dibromo-N,N-dimethyltryptamin possessed significant antidepressant-like activity	–
Li J et al. 2018 ^[156]	Sprague-Dawley rats	CUMS-depression	Postbiotics	–	Sodium propionate (NaP, the salt form of propionic acid)	1 mL of NaP (200 mmol/L) was administered intrarectally every day for 1 week from the beginning of the 5th week	Administration of NaP induced antidepressant-like effects	Administration of NaP rebalanced the plasma metabolome, and rescued the neurotransmitters in the prefrontal cortex, which may be achieved through the reduction of catabolism of noradrenaline, tryptophan and dopamine, rather than serotonin
Matsuda Y et al. 2020 ^[157]	Sprague-Dawley rats	CSDS-depression	Postbiotics	–	Ergothioneine, a metabolite of <i>Lactobacillus reuteri</i>	Oral administration of L-ergothioneine (0.25 mg/ml) aqueous solution was conducted from 1 week prior to SDS initiation (day -7) to the end SDS application (day 14)	Oral administration of ergothioneine prior to and during the SDS paradigm had a preventative effect on SDS-induced depressive behaviors	–
Yu M et al. 2021 ^[158]	Wistar rats	CVS-depression	A broad-spectrum β -lactam antibiotics	–	Tienam (imipenem/cilastatin sodium with equal quantities)	Imipenem/cilastatin sodium was administered at a daily dose of 75 mg/kg of body weight from day 25 to day 28 during 28 days' CVS	Antibiotic treatment reversed the depression-like behaviors	Antibiotic treatment regulated the purine metabolism and fatty acid metabolism that are impacted by gut bacteria
Suzuki K et al. 2021 ^[159]	C57BL/6 J (B6J) mice	CSDS-depression	Antibacterial active peptides	–	α -defensin (Cryptdin-4)	Recombinant Cryptdin-4 (mouse α -defensin) were dissolved in ultrapure water and administered orally at 250 μ g/mouse once daily from day 1 to day 32	No data	Administration of α -defensin recovered dysbiosis and significant microbial composition changes in the intestinal metabolites
Martin-Hernandez D et al. 2016 ^[160]	Wistar rats	CMS-depression	Antibiotics	–	Streptomycin, Penicillin G	Giving drinking water ad libitum containing streptomycin sulfate (2 mg/mL) and penicillin G (1500 U/mL) for 21 days	Antibiotics treatment reversed the CMS-induced a depressive-like phenotype	Antibiotics treatment inhibited bacteria translocation that play a role in the pathophysiology of depression through the p38 MAPK pathway which could aggravate the neuroinflammation and the oxidative/nitrosative damage

Meng C et al. 2022 ^[161]	Sprague-Dawley rats	CUMS-depression	Antibiotics	–	Metronidazole, ciprofloxacin	Treating with metronidazole (1 g/L) and ciprofloxacin (0.2 g) in drinking water for 5 weeks	Antibiotics exposure reduced anxiety-like and depression-like behavior of rat	Antibiotics regulated neurotransmitter and inflammatory response through gut microbiota
Schmidner AK et al. 2019 ^[162]	NAB/HAB rats	HAB-depression	Antibiotics	–	Minocycline	In the first set of experiments, 40 mg/kg/day minocycline, while in the second set, 80 mg/kg/day minocycline alone, all dissolved in tap water, was applied for 22 days	Three weeks of minocycline treatment alleviated the depressive-like phenotype	Minocycline treatment promoted an anti-inflammatory state by control of microglial activation and/or modulation of the gut microbiome and metabolome
Wang S et al. 2020b ^[163]	C57BL/6 mice	CSDS-depression	Antibiotics	–	Ampicillin, Neomycin sulfate, Metronidazole	Broad-spectrum antibiotics (ampicillin 1 g/L, neomycin sulfate 1 g/L, and metronidazole 1 g/L) dissolved in drinking water were provided ad libitum to male C57BL/6 mice for 14 consecutive days	CSDS did not produce an anhedonia-like phenotype in the antibiotic-treated mice	Antibiotic-treated reduced the diversity of gut microbiota, and changed their composition
Wong ML et al. 2016 ^[164]	C57BL/6J mice	CRS-depression	Antibiotics	–	Minocycline	Treating with minocycline (LKT Laboratories, St Paul, MN, USA; 5 mg/kg per day in 10 ml/kg saline, intraperitoneally) for 21 days	Minocycline treatment decreased depressive- and anxiety-like behaviors	Minocycline treatment regulated the gut microbiota–inflammation–brain axis, characterized by attenuated inflammation and rebalanced the gut microbiota
Yang Q et al. 2020 ^[165]	C57BL/6 mice	CUMS-depression	Antibiotics	–	Minocycline	Minocycline (40 mg/kg, Cayman Chemical) was administered intraperitoneally daily for 4 weeks starting 2 weeks after CUMS	Minocycline treatment for 4 weeks, not acute treatment, exerted antidepressant effect in mice exposed to CUMS	Chronic minocycline treatment inhibited neuroinflammation of hippocampus and altered species abundance and metabolites of gut microbiota, and ameliorated intestinal barrier disruption and reduced the bacteriological indexes

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Table S13. A summary of probiotics that alleviate depression symptoms.

Probiotics	objects	Probiotics	objects
Akkermansia_muciniphila	Animal models	Lactobacillus_diacetylactis	Animal models
Akkermansia_muciniphila ATCC® BAA-835™	Animal models	Lactobacillus_fermentum	Human beings,Animal models
Bacillus_coagulans MTCC 5856	Human beings	Lactobacillus_gasseri NK109	Animal models
Bacillus_coagulans Unique IS2	Human beings	Lactobacillus_helveticus	Animal models
Bacillus_sp.DU-106	Animal models	Lactobacillus_helveticus 132M1	Animal models
Bacillus_subtilis	Animal models	Lactobacillus_helveticus LA 102	Animal models
Bifidobacteria	Animal models	Lactobacillus_helveticus LH0138	Animal models
Bifidobacterium	Human beings,Animal models	Lactobacillus_helveticus MCC1848	Animal models
Bifidobacterium spp.	Human beings	Lactobacillus_helveticus NS8	Animal models
Bifidobacterium_adolescentis	Human beings,Animal models	Lactobacillus_helveticus PXN® 45	Human beings
Bifidobacterium_adolescentis 150	Animal models	Lactobacillus_helveticus R0052	Human beings,Animal models
Bifidobacterium_adolescentis NK98	Human beings,Animal models	Lactobacillus_helveticus W74	Animal models
Bifidobacterium_animalis BL0005	Animal models	Lactobacillus_intestinalis	Animal models
Bifidobacterium_animalis ssp.lactis 420	Animal models	Lactobacillus_intestinalis YT2	Animal models
Bifidobacterium_bifidum	Human beings,Animal models	Lactobacillus_johnsonii	Animal models
Bifidobacterium_bifidum BIA-6	Human beings	Lactobacillus_kefiranofaciens ZW3	Animal models
Bifidobacterium_bifidum plus inulin	Human beings	Lactobacillus_lactis	Human beings,Animal models
Bifidobacterium_bifidum PXN® 23	Human beings	Lactobacillus_lactis ssp. lactis PXN® 63	Human beings
Bifidobacterium_bifidum W23	Human beings,Animal models	Lactobacillus_mucosae NK41	Animal models
Bifidobacterium_breve	Animal models	Lactobacillus_murinus	Animal models
Bifidobacterium_breve 1205	Animal models	Lactobacillus_paracasei 126L6	Animal models
Bifidobacterium_breve A-1 (synonym Bifidobacterium_breve MCC1274)	Human beings	Lactobacillus_paracasei DTA 81	Animal models
Bifidobacterium_breve CCFM1025	Human beings,Animal models	Lactobacillus_paracasei HT6	Animal models
Bifidobacterium_breve FHLJDQ3M5	Animal models	Lactobacillus_paracasei Lpc-37	Animal models
Bifidobacterium_breve M-16V	Animal models	Lactobacillus_paracasei NK112	Animal models
Bifidobacterium_breve M2CF22M7	Animal models	Lactobacillus_paracasei PS23	Animal models
Bifidobacterium_breve PXN® 25	Human beings	Lactobacillus_paracasei PS23 (PS23)	Animal models
Bifidobacterium_breve UBBr01	Human beings	Lactobacillus_plantarum	Animal models
Bifidobacterium_breve W25	Animal models	Lactobacillus_plantarum 15953 (strain CGMCC15953)	Animal models
Bifidobacterium_infantis	Animal models	Lactobacillus_plantarum 286 (Lp 286)	Animal models
Bifidobacterium_infantis 35624	Animal models	Lactobacillus_plantarum 81 (Lp 81)	Animal models
Bifidobacterium_infantis PXN® 27	Human beings	Lactobacillus_plantarum 8PA3	Animal models
Bifidobacterium_infantis UBB101	Human beings	Lactobacillus_plantarum 90sk	Animal models
Bifidobacterium_lactis	Animal models	Lactobacillus_plantarum ATCC 793	Animal models
Bifidobacterium_lactis BAMA-B06/Bau-B0111	Human beings	Lactobacillus_plantarum DMDL 9010 (LP9010)	Animal models
Bifidobacterium_lactis BIA-7	Human beings	Lactobacillus_plantarum LP12151	Animal models
Bifidobacterium_lactis UBBLa70	Human beings	Lactobacillus_plantarum LP12407	Animal models
Bifidobacterium_lactis W51	Animal models	Lactobacillus_plantarum LP12418	Animal models
Bifidobacterium_lactis W52	Human beings,Animal models	Lactobacillus_plantarum LP3	Animal models
Bifidobacterium_longum	Animal models	Lactobacillus_plantarum MTCC 9510	Animal models
Bifidobacterium_longum NK46	Animal models	Lactobacillus_plantarum PS128	Animal models
Bifidobacterium_longum R0175	Human beings	Lactobacillus_plantarum PS128 (PS128)	Human beings
Bifidobacterium_longum 1714	Animal models	Lactobacillus_plantarum PXN® 47	Human beings
Bifidobacterium_longum ATCC 15707	Animal models	Lactobacillus_plantarum R1012	Animal models
Bifidobacterium_longum BG0014	Animal models	Lactobacillus_plantarum UBLP40	Human beings
Bifidobacterium_longum BIA-8	Human beings	Lactobacillus_plantarum WLPL04	Animal models
Bifidobacterium_longum LA 101	Animal models	Lactobacillus_plantarumWJL	Animal models
Bifidobacterium_longum NCC3001	Human beings	Lactobacillus_reuteri	Human beings,Animal models
Bifidobacterium_longum PXN® 30	Human beings	Lactobacillus_reuteri (DSM 17938)	Human beings
Bifidobacterium_longum R0175	Human beings,Animal models	Lactobacillus_reuteri 3	Animal models
Bifidobacterium_longum ssp. infantis B111471	Animal models	Lactobacillus_reuteri CCFM1132	Animal models
Bifidobacterium_longum subsp. Infantis	Animal models	Lactobacillus_reuteri NK33	Human beings,Animal models
Bifidobacterium_longum subsp. infantis E41	Animal models	Lactobacillus_rhamnosus	Human beings,Animal models
Bifidobacterium_longum subsp. Longum	Animal models	Lactobacillus_rhamnosus (JB-1)	Animal models

Bifidobacterium_longum subsp. Longum BAMA-B05/BauB1024	Human beings		Lactobacillus_rhamnosus B-8238	Animal models
Bifidobacterium_longum subsp.infantis CCFM687	Animal models		Lactobacillus_rhamnosus CCFM1131	Animal models
Bifidobacterium_longum W108	Animal models		Lactobacillus_rhamnosus CGMCC1.3724	Human beings
Bifidobacterium_pseudocatenulatum CECT 7765	Animal models		Lactobacillus_rhamnosus G	Human beings
Bifidobacterium_subtilis PXN® 21	Human beings		Lactobacillus_rhamnosus GG	Animal models
Clostridium_butyricum MIY AIRI 588 (CBM588)	Human beings,Animal models		Lactobacillus_rhamnosus HN001	Human beings
Clostridium_butyricum WZMC1018	Animal models		Lactobacillus_rhamnosus JB-1	Animal models
Enterococcus_faecalis 2001 (EF-2001)	Animal models		Lactobacillus_rhamnosus LR5	Animal models
Enterococcus_faecalis strain EC-12 (EC-12)	Animal models		Lactobacillus_rhamnosus LX11881	Animal models
Faecalibacterium_prausnitzii (ATCC 27766)	Animal models		Lactobacillus_rhamnosus PXN® 54	Human beings
Fermented Milk Containing Lactobacillus_paracasei Strain Shirota (LcS)	Human beings		Lactobacillus_rhamnosus R0011	Animal models
Komagataella_pastoris KM71H	Animal models		Lactobacillus_rhamnosus UBLR58	Human beings
Lactobacillus_plantarum DP189	Animal models		Lactobacillus_rhamnosus W71	Animal models
Lactobacillus_plantarum PS128TM	Human beings		Lactobacillus_rhamnosus zz-1	Animal models
Lactobacillus_acidophilus	Human beings,Animal models		Lactobacillus_salivarius	Animal models
Lactobacillus_acidophilus LA11873	Animal models		Lactobacillus_salivarius HA-118	Animal models
Lactobacillus_acidophilus PXN® 35	Human beings		Lactobacillus_salivarius Ls-33	Animal models
Lactobacillus_acidophilus T16	Human beings		Lactobacillus_salivarius PXN® 57	Human beings
Lactobacillus_acidophilus W37	Human beings,Animal models		Lactobacillus_salivarius W24	Human beings,Animal models
Lactobacillus_brevis	Animal models		Lactococcus_lactis	Animal models
Lactobacillus_brevis DPC6108	Animal models		Lactococcus_lactis LA 103	Animal models
Lactobacillus_brevis DSM32386	Animal models		Lactococcus_lactis strain WHH2078	Animal models
Lactobacillus_brevis FPA 3709	Animal models		Lactococcus_lactis subsp. cremoris LL95	Animal models
Lactobacillus_brevis J1	Animal models		Lactococcus_lactis W19	Human beings,Animal models
Lactobacillus_brevis W63	Human beings,Animal models		Lactococcus_lactis W58	Human beings,Animal models
Lactobacillus_bulgaricus	Animal models		Pediococcus_acidilactici	Animal models
Lactobacillus_casei	Human beings,Animal models		Prevotella_histicola DSM19854	Animal models
Lactobacillus_casei DG	Animal models		Probiotic NVP-1704	Human beings
Lactobacillus_casei PXN® 37	Human beings		Rhizopus_chinensis 12	Animal models
Lactobacillus_casei strain Shirota (LcS)	Human beings		Streptococcus_cerevisiae S-04	Animal models
Lactobacillus_casei W56	Human beings,Animal models		Streptococcus_cerevisiae var boulardii 17	Animal models
Lactobacillus_cremoris	Animal models		Streptococcus_thermophilus	Human beings,Animal models
Lactobacillus_delbrueckii	Animal models		Streptococcus_thermophilus LA 104	Animal models
Lactobacillus_delbrueckii ssp. bulgaricus PXN® 39	Human beings		Streptococcus_thermophilus PXN® 66	Human beings
Lactobacillus_delbrueckii subsp. Bulgaricus	Human beings,Animal models		Weissella_parmesenteroides WpK4	Animal models

Table S14. Search strategy for electronic databases.

Search strategy for PubMed		Hits
#1	(depress*[Title/Abstract] OR dysthymi*[Title/Abstract] OR mood disorder*[Title/Abstract] OR affective disorder*[Title/Abstract] OR antidepress*[Title/Abstract])	556,593
#2	(microb*[Title/Abstract] OR bacteria*[Title/Abstract] OR metaproteom*[Title/Abstract] OR metagenom*[Title/Abstract] OR "16S rRNA"[Title/Abstract] OR flora[Title/Abstract])	1,075,172
#3	#1 AND #2	5,634
Search strategy for Web of Science		
#1	TS=(depress* OR dysthymi* OR mood disorder* OR affective disorder* OR antidepress*)	502,875
#2	Topic=(microb* OR bacteria* OR metaproteom* OR metagenom* OR "16S rRNA" OR flora)	1,209,922
#3	#1 AND #2	6,594
Search strategy for Cochrane Library		
#1	(depress*):ti OR (dysthymi*):ti OR (mood disorder*):ti OR (affective disorder*):ti OR (antidepress*):ti	36,107
#2	(microb*):ti,ab,kw OR (bacteria*):ti,ab,kw OR (metaproteom*):ti,ab,kw OR (metagenom*):ti,ab,kw OR ("16S rRNA"):ti,ab,kw OR (flora):ti,ab,kw	56,167
#3	#1 AND #2	129
Search strategy for EMBASE-MEDLINE-PsycINFO		
#1	depress*:ab,ti OR dysthymi*:ab,ti OR "mood disorder*":ab,ti OR "affective disorder*":ab,ti OR antidepress*:ab,ti	1,063,823
#2	microb*:ab,ti OR bacteria*:ab,ti OR metaproteom*:ab,ti OR metagenom*:ab,ti OR "16S rRNA":ab,ti OR flora: ab,ti	1,300,339
#3	#1 AND #2	7,992

Table S15. Search strategy for microbiota-based interventions of depression from PubMed.

Search strategy for PubMed	Hits
#1 (depress*[Title/Abstract] OR dysthymi*[Title/Abstract] OR mood disorder*[Title/Abstract] OR affective disorder*[Title/Abstract] OR antidepress*[Title/Abstract])	474,410
#2 (microb*[Title/Abstract] OR flora[Title/Abstract] OR probiotic*[Title/Abstract] OR prebiotic*[Title/Abstract] OR synbiotic*[Title/Abstract] OR psychobiotic*[Title/Abstract] OR postbiotic*[Title/Abstract] OR "fecal microbiota transplantation"[Title/Abstract] OR "fecal transplantation"[Title/Abstract])	639,026
#3 #1 AND #2	3,633