(NMDA) receptor antagonists, and tricyclic antidepressants (TCAs), exhibit antibacterial activities. Hence, this systematic review explores the impact of antidepressants on gut microbiota and potential strategies to alleviate antidepressant-associated dysbiosis.

**Methods** This systematic review was conducted based on the PRISMA guidelines. Predefined MeSH terms ‘antidepressants AND gut microbiome’; ‘antidepressants AND antimicrobial activity’ were used in three databases (Pubmed, Embase, ProQuest; from database inception to June 2021). Studies reporting on the gut microbiota variation and antidepressants action were included. Studies without antidepressants and/or gut microbiome data were excluded, including conference proceedings, reviews, systematic reviews, meta-analyses, and commentaries.

**Results** According to the study’s inclusion criteria, twelve studies out of 300 articles were selected for the qualitative analysis. In the in-vivo studies, animals administered with SSRIs had a decreased abundance of Firmicutes, Alphaproteobacteria, Bacteroides, Ruminococcus, Adlercreutzia, Turicibacter, and alpha diversity but an increase in Prevotella, Parabacteroides, Butyricimonas, and Alistipes. Besides, antidepressants were shown to exhibit significant in vitro antimicrobial activity against Akkermansia muciniphila, Bifidobacterium animalis, and Bacteroides fragilis, suggesting that the chronic use of antidepressants potentially causes adverse effects due to their antimicrobial effects and dysbiosis (IDDF2021-ABS-0164 Figure 1. Illustration of gut microbiota dysbiosis in response to antidepressants). Probiotics, prebiotics and fecal microbiota transplantation are shown to be promising strategies to ameliorate antidepressant-associated dysbiosis.

**Conclusions** Understanding the interaction between antidepressants and gut microbiota, including dysbiosis as a consequence of treatment and potential side effects, is vital for the future development of better and personalized treatment. Supplementing the gut microbiome with prebiotics/probiotics could be an adjuvant treatment to improve the clinical efficacy of the current antidepressant therapies.
features (i.e., Streptococcus, Erysipelotrichaceae UCG-003, Sutterella and Parabacteroides) were found to be positively associated with severe distress, of which Erysipelotrichaceae UCG-003 was more abundant in both distressed and stressed donors (DESeq2, p<0.05; (IDDF2021-ABS-0165 Figure C). Bar plot showing differentially abundant genera identified between individuals falling under (i) severe (red) vs. well (blue) category of distress and (ii) high (pink) vs. low (light blue - not detected) stress). Besides, the abundance of Megamonas in the gut was negatively correlated with PSQI after covariates (i.e., age and BMI) adjustment (IDDF2021-ABS-0165 Figure D. Correlation matrix showing the association between differentially abundant bacterial genera and K10, PSS and PSQI categories after covariates adjustment (based on Pearson’s correlation; p<0.05)), suggesting the lowered abundance of Megamonas observed in distressed individuals may be related to their sleep quality.

Conclusions One-third of the participants exhibited high stress/distress levels and almost half poor sleep. In this study, we identified several bacterial genera that are significantly altered in the gut microbiome of stressed individuals, with Erysipelotrichaceae UCG-003 being consistently increased across people with high stress and severe distress levels. Erysipelotrichaceae UCG-003 was previously reported to be elevated in individuals with sleep deprivation. Our findings also suggest the need to factor for stress and sleep quality when studying the gut microbiome of healthy individuals.

Background Epidemiological evidence supports a relationship between adiposity and elevated risk of colorectal cancer (CRC). Nevertheless, the role of gut microbiota in mediating the carcinogenic effect of adiposity is unknown. In this study, we transplanted stool from obese patients to mice to evaluate its effects and mechanisms on intestinal carcinogenesis.

Methods Azoxyemthane (AOM)-treated mice, ApcMin/+ and germ-free mice were gavaged with feces from obese patients and control subjects respectively. The colonic tumor load and number were recorded at endpoint. The gut microbiota composition was assessed by metagenomic sequencing and colonic transcriptome was assessed by total RNA sequencing.

Results The colonic tumor load and number were significantly higher in mice receiving feces from obese patients (OB), compared with those from control subjects (NB, normal BMI), in both AOM-induced and ApcMin/+ mice (IDDF2021-ABS-0166 Figure 1A-C). Histological assessments showed increased dysplasia proportions and Ki-67 positive cells (IDDF2021-ABS-0166 Figure 1D) in mice receiving feces from obese patients in both murine cancer models. Metagenomic analysis showed an altered microbiota composition (IDDF2021-ABS-0166 Figure 2A), with a lower alpha diversity (IDDF2021-ABS-0166 Figure 2B), decreased abundance of Faecalibaculum, Bifidobacterium and Lactobacillus, as well as increased abundance of Akkermansia in recipients of feces from obese patients (IDDF2021-ABS-0166 Figure 2C). Transcriptomic analysis on colon tissue showed upregulation of oncogenic (Wnt signaling pathway, MAPK signaling pathway and Rap1 signaling pathway) and pro-inflammatory pathways (TNF signaling pathway and chemokine signaling pathway). Mice received feces from obese patients showed impaired murine barrier function evidenced by decreased mucus layer thickness, loosened tight junction and over-expression of epithelial leaky protein Claudin-2 in the colonic crypt.

Conclusions Feces from obese patients promoted colorectal carcinogenesis in mice. Such action was associated with the

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