

## The role of gut-microbiome targeted therapies in the management of non-alcoholic fatty liver disease: a systematic review and meta-analysis

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### Background

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the Western world. Pre-clinical evidence suggests that gut microbiome-targeted therapies (MTTs) may represent a new therapeutic target for the condition. The aim of this research was to evaluate the current evidence supporting the role of MTTs in the management of NAFLD.

### Methods

The electronic databases MEDLINE, EMBASE and Web of Science were searched. Randomised controlled trials that compared MTTs with placebo or usual care in patients with NAFLD were eligible for inclusion. MTTs were defined as probiotics, prebiotics, synbiotics, antibiotics and faecal microbiota transplantation. A random effects meta-analysis was performed, and statistical heterogeneity was assessed using I<sup>2</sup>. If identified, this was explored using univariable meta-regression analysis.

### Results

12 studies were identified. 8 reported a significant reduction in hepatic steatosis following MTTs. MTTs were associated with a significant reduction in alanine aminotransferase (ALT) (WMD: -6.96 IU/L, 95% CIs: -11.78, -2.14) and aspartate aminotransferase (AST) (WMD: -6.52, 95% CIs: -12.05, -0.99) compared to control. However, significant heterogeneity between studies was reported (ALT: I<sup>2</sup> = 98.66%, AST: I<sup>2</sup> = 99.60%). For ALT, meta-regression revealed mean age at baseline was significantly associated with treatment effect estimate ( $p=0.010$ ). MTTs were not associated with a significant reduction in body mass index (BMI) (WMD: -0.27 kg/m<sup>2</sup>, 95% CIs: -0.62, 0.08 kg/m<sup>2</sup>).

### Key Messages

MTTs were associated with a significant reduction in hepatic steatosis and liver function markers, but not BMI. Although promising, significant heterogeneity between studies means the results are difficult to interpret.

