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PII: S0271-5317(20)30488-7

DOI: https://doi.org/10.1016/j.nutres.2020.06.018

Reference: NTR 8145

To appear in: *Nutrition Research*

Received date: 21 January 2020

Revised date: 2 May 2020

Accepted date: 26 June 2020

Please cite this article as: I.M. Proença, J.R. Allegretti, W.M. Bernardo, et al., Fecal Microbiota Transplantation Improves Metabolic Syndrome Parameters: Systematic Review with Meta-analysis Based on Randomized Clinical Trials, *Nutrition Research* (2020), https://doi.org/10.1016/j.nutres.2020.06.018

Fecal Microbiota Transplantation Improves Metabolic Syndrome Parameters: Systematic Review with Meta-analysis Based on Randomized Clinical Trials

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ABREVIATIONS

AACE: American Association of Clinical Endocrinologists

BMI: Body Mass Index

CI: Confidence Interval

EGIR: European Group for the Study of Insulin Resistance

FMT: Fecal Microbiota Transplantation

GI: gastrointestinal

GLP-1: Glucagon-Like Peptide 1

GRADE: Grading of Recommendations Assessment, Development and Evaluation

HbA1c: Hemoglobin A1c (glycated hemoglobin)

HDL: High Density Lipoprotein

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance

IDF: International Diabetes Federation

LDL: Low Density Lipoprotein

MD: Mean Difference

NAFLD: Non-Alcoholic Fatty Liver Disease

NCEP ATP: National Cholesterol Education Program Adult Treatment Panel

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: Prospective Register of Systematic Reviews

RCT: Randomized Clinical Trial

RoB-2: Revised Cochrane Risk-of-Bias tool for randomized trials

SCFA: Short Chain Fatty Acids

TMAO: Trimethylamine-N-oxide

UC: ulcerative colitis

WHO: World Health Organization

ABSTRACT

Obesity and metabolic syndrome are important health problems that can lead to significant morbidity/mortality as well as subsequent health concerns. Alterations in the gut microbiota have been implicated in both obesity and metabolic syndrome. Fecal Microbiota Transplantation (FMT) has emerged as a new promising therapeutic approach aimed at manipulating the gut microbiota in various chronic diseases. Randomized clinical trials assessing the use of FMT in obese and metabolic syndrome patients have been reported. The purpose of this systematic review with meta-analysis using randomized clinical trials (RCT) is to evaluate the role of FMT for the treatment of obesity and metabolic syndrome and its impact on clinically relevant parameters. We searched the main databases, as well as the gray literature, to identify RCTs comparing FMT from lean donor(s) vs placebo for obese/metabolic syndrome patients. We included all studies that utilized any form of placebo (sham, saline, autologous FMT or placebo capsules). Six studies met the inclusion criteria and were included for final analysis with a total of 154 patients. We looked for clinically significant parameters related to obesity and metabolic syndrome and organized the findings into early (2-6 weeks after intervention) and late (12 weeks after intervention) outcomes. Two to six weeks after intervention, mean HbA1c was lower in the FMT group (MD=-1,69 mmol/mol, CI [-2.88, -0.56], p=0,003) and mean HDL cholesterol was higher in the FMT group (MD=0,09 mmol/l, CI [0,02, 0,15], p=0,008). There was no difference in obesity parameters six to twelve weeks after intervention. No serious adverse events were reported. The findings for this meta-analysis show that FMT may have a role for the treatment of metabolic syndrome, but there is currently not enough evidence to

support its use in clinical practice. High quality well powered RCTS with longer follow up are necessary to clarify the role of FMT in this patient cohort.

Keywords: Fecal Microbiota Transplantation; Gastrointestinal Microbiome; Obesity; Metabolic Syndrome; Systematic Review.

1. INTRODUCTION

1.1.Condition: Obesity and metabolic syndrome.

Obesity and metabolic syndrome are important health problems worldwide. The incidence of both have been increasing over the last decades [1],[2]. A retrospective study that analyzed data from 68.5 million people showed that the prevalence of obesity has doubled in more than 70 countries since 1980 [3], and with it the development of atherosclerotic cardiovascular disease, non-alcoholic fatty liver disease (NAFLD) and other related complications [4],[5].

Although there are many treatment modalities for obesity and the various components of metabolic syndrome (abdominal obesity, dyslipidemia, hypertension, and insulin resistance), optimal management is still a challenge as multiple factors are involved in its pathophysiology, such as genetic predisposition, lack of exercise, and body fat distribution [6],[7].

1.2.*Intervention: Fecal Microbiota Transplantation*

The gut microbiota is a complex community with microorganisms estimated in the trillions that might influence humans health. Alterations have been linked to many diseases and conditions, including obesity and metabolic syndrome [8],[9],[10],[11],[12],[13]. Therapeutic approaches targeting dysbiosis and manipulation of the gut microbiome have been trialed, including probiotics, antibiotics, and more recently fecal microbiota transplantation (FMT). FMT

can be delivered via the upper gastrointestinal (GI) tract – enteroscopy and nasoenteric tube – or the lower GI tract – colonoscopy, sigmoidoscopy or enema. Oral capsules have also been developed and have been used as a non-invasive way to perform FMT. Two trials demonstrated similar efficacy rates of capsules to colonoscopy [14],[15]. FMT is thought to alter the gut microbiota, increase its diversity, modulate bacterial ratios, increase the release of glucagon-like peptide 1 (GLP-1), modulate bile acid pathways and interfere with production of short-chain fatty acid (SCFA), among other possible mechanisms. Those mechanisms have be hypothesized to possibly assist with treatment of metabolic syndrome/obesity by improving insulin sensitivity, decreasing fat body and modulating lipids and cholesterol (HDL, LDL) metabolism. [8],[11],[16],[17].

1.3. Objective

Although there is evidence showing a relationship between an altered gut microbiome and metabolic syndrome, especially in animal models, translating these findings to humans showed low reproducibility and causality has been hard to prove [18],[19],[20]. It is unclear whether it is possible to change the microbiome by FMT and improve clinically significant parameters.

We performed a systematic review and meta-analysis of randomized clinical trials (RCT) to assess the role of FMT for the treatment of obesity with or without metabolic syndrome and its impact on clinically significant parameters.

2. Approach

2.1. Protocol and registration

This study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and registered in International Prospective Register of Systematic Reviews (PROSPERO) under the register number CRD42019137446.

2.2.Eligibility criteria

Types of studies: Only randomized clinical trials (RCT) were included, irrespective of language, date of publication, or publication status.

Patients: Adults diagnosed with metabolic syndrome by any valid definition (NCEP ATP3 2005, IDF 2006, EGIR 1999, WHO 1999, AACE 2003) and/or obesity - defined as Body Mass Index (BMI) ≥ 30.

Exclusion criteria: Patients who underwent bariatric surgery.

Intervention and control: FMT from lean donor(s) versus placebo. We considered sham, saline or autologous stool as placebo when FMT was performed by an endoscopic technique, and identical placebo capsules when FMT was performed via oral capsules. All routes for FMT were accepted - including colonoscopy, enteroscopy, enema, nasoenteral tube, and oral capsules. Studies were required to have at least two weeks of follow-up to be included.

Outcomes: Clinically significant parameters of metabolic syndrome and obesity. Other outcomes noted in the literature including FMT engraftment, change in GLP-1, and vascular injury were not analyzed as these factors are not felt to have a direct clinical impact.

2.3. Information sources and search

We searched the following electronic databases: Medline (via Pubmed), Embase, Central Cochrane and Latin-American and Caribbean Health Sciences Literature (LILACS). We also performed a "gray literature" search on ongoing RCT (by emailing the authors) and on unpublished theses. We requested additional information from authors when a study was not yet published or if the published data was insufficient for meta-analysis. We updated our search until September 2019 and performed a last review in April 2020.

The search strategy for Medline was: (((Fecal OR Faecal OR faeces OR stool OR microbiota OR microbiome) AND (Transfer OR Transplantation OR Transplantations OR transplant OR transplants)) OR FMT))). We used simplified strategies derived from the one above for the remaining databases.

2.4.Study selection and data collection process

Two independent authors accessed all records in the aforementioned sources by titles. Potentially relevant studies were screened for eligibility by abstracts. If an abstract matched the eligibility criteria, or if it was unclear, the full text was accessed. Duplicates were removed. The

reference lists of studies of interest were then manually reviewed for additional articles by cross checking bibliographies. Any differences were resolved by mutual agreement and in consultation with a third reviewer. The researchers used Excel spreadsheets to extract the data and relevant results.

2.5. Data items

After selection for final analysis we looked for: author, year of publication, patients' characteristics, number of patients, how FMT/placebo was performed, follow-up, adverse events, primary outcome and clinically significant parameters related to metabolic syndrome/obesity. We considered clinically significant parameters: hemoglobin A1C (HbA1c), fasting glucose, HOMA-IR, cholesterol (total/LDL/HDL), triglyceride, hip width, weight, and body mass index (BMI). We considered early outcomes to be those that occurred between two to six weeks after intervention. Late outcomes were those that occurred twelve weeks or later after intervention.

2.6. Risk of bias in individual studies

The risk of bias of the selected RCTs was assessed by the Revised Cochrane Risk-of-Bias tool for randomized trials (RoB-2) [21]. We performed a complete analysis for each outcome in each study. In order to simplify the analyses, we also evaluated the global risk of bias for each study using the same domains suggested on RoB-2: Randomization process, Deviations from intended interventions, Missing outcome data, Measurement of outcome, and Selection of the reported result.

2.7. Statistical analyses

We identified means and standard deviations to calculate the means differences. If a study published data using medians and interquartile ranges, we used Hozo´s formula [22] to estimate the standard deviation and used medians as means in order to make data suitable for meta-analysis. For statistical significance, we considered results with a 95% confidence interval (CI) and $p< 0.05$. Results of the meta-analysis were expressed as a forest plot. Heterogeneity was assessed using the Higgins test (I^2). We used the fixed effect for $I^2 < 50\%$ (low heterogeneity). If $I^2 > 50\%$ (high heterogeneity), we used the random effect to reduce the impact of heterogeneity on the result.

2.8.Summary measures and synthesis of results

All outcomes were continuous variables. We used Review Manager software (version Revman 5.3) for the meta-analysis, calculation of the Means Differences (MD), and confidence intervals (CI).

2.9. Risk of bias across studies and quality of evidence

We assess the risk of bias across the studies using RoB-2 as guidance and the quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADEpro Guideline Development Tool). Evaluated items to access quality of evidence are:

Study design, risk of bias, inconsistency, indirectness and imprecision. Evidence quality can be classified as *Very low, Low, Moderate* or *High.*

3. RESULTS

3.1. Study selection

A total of 21,602 records were identified through a search in the databases and gray search. After adjusting for duplicates, 14,893 records remained and were evaluated by title. Forty-four were evaluated by abstract. Eight were accessed for eligibility and two were rejected: one was a case series [23] and one compared FMT from donors that underwent Roux-en-Y Gastric by-pass versus FMT from metabolic syndrome donors [24]. We received full data tables with all information about all patients from two studies [25],[26] by e-mailing the authors. Thus, we included 6 studies for the final analysis [27],[28],[29],[25],[26][30] (Figure 1).

3.2. Study characteristics

Six RCTs with a total of 154 participants were included. The main study characteristics are shown in Table 1. Five studies [27],[28],[29],[26],[30] assessed the role of FMT for metabolic syndrome and obese patients while one [25] assessed for obese patients without metabolic syndrome. Three [27],[28],[29] were conducted in the Netherlands, two [25],[30] in the USA, and one in Brazil [26]. All studies used stool from lean donors for FMT, but in one [29] donor was also vegan. Lean donor was defined by BMI differently in each study, ranging

from BMI = 17,5 to BMI < 25. Two studies [25], [26] were designed as a proof of concept study with no sample size calculation due to lack of similar studies in literature. Four studies [27],[28],[29],[30] calculated the sample size for 80% statistic power using a hypothesis based on animals studies, previous similar studies and experience of the authors, according to the primary outcome selected. Three studies [27],[28],[29] administered FMT by nasoduodenal tube, one [26] by anterograde enteroscopy, and two [25],[30] by oral capsules. Three [27],[29],[26] administered a single FMT induction dose, one [28] administered a second dose on week six – but main analysis occurred before second dose -, one [25] administered an induction dose followed by maintenance doses at weeks 4 and 8 and one [30] administered weekly doses for 6 weeks. Three studies [27],[28],[29] used autologous stool as placebo, one [26] used saline as placebo, and two [25],[30] used placebo capsules.

The primary outcome was change in insulin sensitivity in four studies [27],[28],[26],[30]. Three [27],[28],[30] assessed insulin sensitivity by hyperinsulinemic euglycemic clamps to calculate the rate of glucose disappearance (Rd) and its variation in percentage after intervention measuring insulin-mediated peripheral glucose uptake (mmol/kg/min). One [26] assessed insulin sensitivity by HOMA-IR. The primary outcome was change in GLP-1 assed by the area under the curve of GLP-1 in one study[25]. Vascular injury was the primary outcome in one study [29], assessed by the area under the curve of plasma Trimethylamine-N-oxide (TMAO) levels (mmol/l) and by F-fluorodeoxyglucose uptake on PET-CT of the aorta. Although each study had different primary outcomes, we extracted clinically significant parameters from each study for final analysis.

All six studies reported clinically significant parameters in each group (FMT and placebo), but only two studies [31],[26] reported changes in significant parameters after intervention. No related adverse events were reported in any study.

The time point and primary endpoint assessed varied among studies, including 2 weeks [29], 6 weeks [27], 12 weeks [25],[30] and 18 weeks [28]. One study [26] is still ongoing to assess data at one year, but data is available for 12 weeks post intervention. Although one study [28] had 18 weeks follow-up, no clinically significant parameters were reported at week 18. One study [25] had 26 weeks of follow-up for safety.

3.3. Risk of bias in included studies

The risk of bias for each study was performed by Cochrane Risk of Bias tool for randomized trial (RoB-2) [21] and it is summarized by study in Table 2. The overall risk of bias was *low* for three studies [25],[26],[30] , *high* for one study [28], and there were *some concerns* for two studies [27],[29]. The high risk of bias in Kootte [32] was mainly due to imbalance in important baseline characteristics, which can be attributed to problems in randomization, selection bias and/or causality. Vrieze [27] and Smits [29] had *some concerns* in two domains: randomization process, since it was not clear how it was performed, and in selection of reported results.

3.4. Synthesis of results and quality of evidence

To analyze the effects of the intervention, we divided outcomes into early effects - between two and six weeks after intervention - and late effects -twelve weeks after intervention. Thus, we ended up with two groups for analysis: Early (2-6 weeks) Mean differences of clinically significant parameters, and Late (12 weeks) Mean differences of clinically significant parameters.

3.4.1. Early (2-6 weeks) Means Differences of clinically significant parameters

All six studies reported HbA1c, fasting glucose, and cholesterols/triglycerides two or six weeks after intervention. For HbA1c there were a total of 80 participants in the FMT group and 67 in the Placebo group. Patients in the FMT group had lower mean HbA1c than the placebo group (MD = -1,69 mmol/mol CI [-2.81, -0,56], p=0,003) 2-6 weeks after intervention (figure 2.A). The quality of evidence is *low* for this outcome (Table 3).

For HDL cholesterol there were a total of 80 patients in the FMT group and 66 in the Placebo group. Patients in the FMT group had higher mean HDL cholesterol than the placebo group (MD = 0,09 mmol/l CI [0,02, 0,15], p=0,008) 2-6 weeks after intervention (Figure 2.B). The quality of evidence is *low* for this outcome (Table 3).

For LDL cholesterol there were a total of 80 patients in the FMT group and 66 in the placebo group. The placebo group had lower mean LDL cholesterol than the FMT group (MD = 0.19 mmol/l CI [0,05, 0,34], p=0,008) 2-6 weeks after intervention (figure 2.C). The quality of evidence is *very low* for this outcome (Table 3).

Fasting glucose, triglycerides, and total cholesterol did not differ between the two groups after 2-6 weeks (figure 2.D-F). The quality of evidence is *low* for fasting glucose and total cholesterol and *very low* for triglycerides (Table 3).

Four studies with a total of 105 patients [25],[26],[28],[30] reported HOMA-IR 6 weeks after intervention. There was no difference between groups (figure 2.1). The quality of evidence is *low* for this outcome (Table 3).

Three studies [28],[27],[25] reported BMI and four studies reported weight [25],[27],[28],[30] six weeks after intervention. There was no difference between groups for these parameters (fig. 2.G-H). The quality of evidence is *low* for weight and *very low* for BMI (Table 3).

3.4.2. Late (12 weeks) Mean differences of clinically significant parameters

Two studies [25],[26] reported BMI reduction (figure 3.A), and hip width reduction (figure 3.B) and three studies [25],[26],[30] reported weight (figure 3.C) 12 weeks after intervention. There was no statistically significant difference between the two groups. The quality of evidence is *moderate* for weight and hip reduction and *low* for BMI reduction (Table 4).

Two studies [25],[30] reported HbA1c, fasting glucose, LDLc, HDLc and triglycerides 12 weeks after intervention (Figure 3.D-G). There was no statistically significant difference

between the two groups for any of those outcomes. The quality of evidence is *moderate* for HbA1c and *low* for fasting glucose, LDLc, HDLc and triglycerides (Table 4).

4. DISCUSSION

4.1. The role of fecal microbiota transplantation for the treatment of metabolic syndrome and obesity

This is the first systematic review with meta-analysis to evaluate the role of FMT for treatment of obesity and metabolic syndrome. There is one previous systematic review [33] that included only three studies [27],[28],[29] and the authors did not have enough data to perform a meta-analysis. Thus, they performed a systematic review with only descriptive summaries of selected outcomes.

FMT was safe in this patient cohort. No study reported any serious related adverse events during follow-up. FMT may have a role in metabolic syndrome by improving some clinically significant parameters. Mean HbA1c was lower in the FMT group than the placebo group two to six weeks after intervention, although it was a small mean difference (MD = -1,69 mmol/mol CI [-2.81, -0,56], p=0,003) and the quality of evidence is *low* due to high risk of bias and imprecision . Two studies [27],[28] reported improvement in peripheral insulin sensitivity six weeks after FMT using a hyperinsulinemic euglycemic clamp to calculate rate of glucose disappearance (Rd). Also, two studies even showed a small reduction in HbA1c in the FMT

group [28],[30]. Thus, those findings are in accordance with current knowledge and previous animal and human studies, although the impact seems to be modest.

Mean HDL was higher in the FMT group than placebo group two to six weeks after intervention. Although there was statically significant difference in HDL between the FMT and the placebo groups, the mean difference was small (MD = 0,09 mmol/l CI [0,02, 0,15], p=0,008) and the quality of evidence was *low,* also due to high risk of bias and imprecision. Despite the low quality of evidence of this finding, the accumulating evidence from intervention studies using FMT indicate the possibility of a connection between FMT and changes in cholesterol metabolism. No previous studies have shown HDL increases after FMT, this is a new finding that should be better evaluated and studied. Although FMT apparently improved HbA1c and HDLc, its use cannot yet be supported by this meta-analysis, due to the low quality of evidence and the small impact on those parameters.

There was also a small, but statistically significant difference in LDL cholesterol favoring the placebo group (MD = 0.19 mmol/l CI [0,05, 0,34], p=0,008). The placebo group had a lower LDLc level than the FMT group 6 weeks after intervention. This difference was not seen on 12 weeks follow-up. Despite this finding, there was nothing in the literature to support that FMT could increase LDL cholesterol. Instead, there is some data suggesting that FMT may decrease LDL cholesterol levels in animal models [34]. Notably, none of the studies reported strict diet control, which could also interfere with this outcome. Therefore, we attribute this difference in LDL cholesterol to the *very low* quality of evidence for this outcome, the lack of diet control and

casualty. Moreover, more studies to assess and understand the role of microbiota in cholesterol metabolism should be done as discussed above.

Only two studies reported clinically significant metabolic parameters 12 weeks after intervention and there was no difference in any parameters between the two groups. The small number of studies and patients – only 46 in total – is probably the reason that no difference was found. Besides, it´s unknow for how long possibly metabolic benefits would remain after FMT [28],[30].

For significant obesity parameters (e.g.: weight, BMI, hip width), no differences were appreciated between the FMT and placebo groups in the short and long term. Besides, only three studies with a total of 78 patients reported weight and BMI 6 weeks after intervention. Two studies with a total of 38 patients reported BMI reduction and hip width reduction 12 weeks after intervention and three studies with a total of 75 patients reported weigh on 12 weeks follow-up. Such small numbers of patients may be one reason why we did not find a difference between groups for these parameters. Besides, these studies did not report important lifestyle changes – including diet and exercise – that are fundamental to promote improvement in obesity parameters regardless the treatment modality [35].

It is uncertain for how long engraftment profiles from FMT will remain in this population, but it has been shown that the gut microbiota in other chronic diseases, such as ulcerative colitis (UC) will trend back to a baseline state. In this obese patient population this may be especially relevant if there is no change in life style (e.g.: dietary habits and physical

activity) [36]. Kootte [28] demonstrated that improvement in insulin sensitivity observed at week six was not seen eighteen weeks after intervention. Yu [30] showed that engraftment was sustained 12 weeks after FMT. Thus, to keep the microbiome changes and their possible benefits for the long-term, more than one FMT may be required, and this has been shown to be necessary in UC as well [37]. We still do not understand the mechanism by which FMT works or may work in this patient population.

4.2. Limitations

There were some limitations in this systematic review. The small number of studies and patients is an important limitation, which leads to imprecision and inconsistency in results and large confidence intervals. The risk of bias was *high* for the largest study with 38 patients, which also contributed to the poor quality of evidence for some outcomes Follow-up was not long enough in some studies, especially for obesity parameters (e.g.: weight, BMI, hip width) and HbA1c. Our institution is still conducting an RCT [26] with one-year follow-up to assess the long term FMT effects on clinically significant parameters. Some studies reported not clinically significant outcomes as primary outcomes, which is another important limitation.

With regards to FMT, in these studies, the authors used heterogeneous techniques. Dose, delivery modality and donor microbiome profile are important variables that may affect FMT success. The differences between the techniques used to perform FMT in each study is another important limitation difficult to overcome when conducting a meta-analysis. There are also donor variables and recipient characteristics, such as genetic and immunological characteristics,

and their microbiome that are not well understood and that may affect FMT success and may be another confounding factor [38].

4.3. Future directions

Besides the limitations and uncertainties, there is enough evidence to encourage further investigations into the use of FMT as adjuvant therapy for metabolic syndrome. Although there were statistically significant differences in HbA1c and HDLc after FMT, the impact in both parameters were modest. Two studies [28],[30] suggested that lower gut microbiota diversity at baseline could predict better metabolic responses to FMT. Future studies could incorporate this into their investigation in order to clarify the role of host characteristics in FMT efficacy. In order to increase the quality of future RCTs, FMT should be considered for patients with known poor diversity gut microbiota that could have a better metabolic response[32],[30]. Study designs should incorporate short as well as long-term follow-up. Moreover, study design and the selection of primary endpoint influence the results. Thus, in order to verify FMT´s clinical relevance, RCTs should be designed to assess clinically significant parameters for metabolic syndrome/obesity as primary outcomes with appropriate follow-up and associate lifestyle changes – diet and physical activity. Lifestyle changes are essential to any treatment for metabolic syndrome and/or obesity and they may even help to promote and prolong microbiota changes after FMT [19]. Finally, more studies to investigate the relation between gut microbiota and cholesterol metabolism are needed in order to clarify the findings from this meta-analysis regarding HDLc and LDLc.

5. CONCLUSION

FMT may have a role for the treatment of metabolic syndrome as an adjuvant therapy, especially with regards to improvement in HbA1c as well as HDL cholesterol, although the clinical impact is modest. However, the quality of evidence is still low and more study is needed. For obesity , FMT did not improve clinically relevant parameters compared to placebo. More trials that are appropriately powered for clinical significant outcomes, and that incorporate diet and lifestyle changes into the design must be done to clarify FMT role for this population.

Acknowledgments: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors declare no conflict of interest.

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Figures Legends

Figure 1: Flow diagram of included and excluded clinical trials

Figure 2: FMT vs. Placebo - 2-6 weeks after intervention

Figure 3: FMT vs. Placebo – 12 weeks after intervention

Figures Footnotes

Figure 2: Means ± Standard Deviation are presented in each study and each group. Column "Total" refers to number of patients in each study and each group. Means Differences (MD) are

presented with the 95% Confidence Interval (CI) for each study and for the combined results. Test for overall effect Z demonstrate the *p* value. The forest plot illustrated the MD and their CI.

Figure 3: Means ± Standard Deviation are presented in each study and each group. Column "Total" refers to number of patients in each study and each group. Means Differences (MD) are presented with the 95% Confidence Interval (CI) for each study and for the combined results. Test for overall effect Z demonstrate the *p* value. The forest plot illustrated the MD and their CI.

Table 1: Characteristics of included studies.

Author (year)	Study design	Participants	Number	Intervention	Control	Primary outcome	Clinically significant parameters reported	Follow up primary outcome
Yu (2020)	RCT	Obese (BMI>30) and insulin resistance patients form 25-60 yo	24: 12 FMT 12 Placebo	FMT from lean donors (BMI 19.5-21.8) by oral capsules weekly for 6 weeks.	Identical placebo capsules. Same doses.	Insulin Sensitivity‡	HOMA-IR, HbA1c, fasting glucose, cholesterols/triglycerides, weight	12 weeks
De Moura	RCT	Obese (BMI 30-40) metabolic syndrome women from 18-70 yo	32: 16 FMT 16 Sham	Single dose FMT from single lean donor (IMC=18,9) by anterograde enteroscopy	Saline 0,9% by anterograde enteroscopy	Insulin sensitivity (HOMA-IR)	Fasting glucose, HbA1c, HOMA-IR, cholesterols/triglycerides, weight, BMI, hip	12 weeks (on going)
Allegretti (2019)	RCT	Obese (BMI>35) and no metabolic syndrome, manly women (20 of 22)	22: 11 FMT 11 Placebo	FMT from single lean donor (BMI=17,5) by capsules (0.75 grams stool) -Induction dose: 30 capsules once -Maintenance: 12 capsules at week 4 and week 8	Identical placebo capsules (saline and glycerol). Same doses.	Increase of GLP-1 (area under the curve)	Fasting glucose, HbA1c, HOMA-IR, cholesterols/triglycerides, weight, BMI, hip	12 weeks
Smits (2018)	RCT	Male metabolic syndrome patients from 21-69 yo†	20: 10 FMT 10 Sham	Single dose FMT from lean vegan donors (BMI 20-25) by nasoduodenal tube	autologous FMT, visually identical to intervention	Vascular injury§	Fasting glucose, HbA1c, cholesterols/triglycerides	2 weeks
Kootte (2017)	RCT	Male metabolic syndrome patients from 21-69 yo†	38: -1st step: 26 FMT 12 Sham -2nd step: 13 single FMT 13 two doses FMT	Single or double dose FMT from lean donors (BMI<25) by nasoduodenal tube	First step: autologous FMT Second step: sham	Insulin Sensitivity‡	Fasting glucose, HbA1c, HOMA-IR, cholesterols/triglycerides, weight, BMI	18 weeks
Vrieze (2012)	RCT	Male metabolic syndrome	18: 9 FMT	Single dose FMT from lean donors	autologous FMT, visually	Insulin sensitivity‡	Fasting glucose, HbA1c, cholesterols/triglycerides,	6 weeks

		patients†	9 Sham	(BMI<23) by nasoduodenal tube	identical to intervention		weight, BMI	

RCT = Randomized Clinica Trial / BMI = Body Mass Index / FMT = Fecal Microbiota Transplantation / yo = years old

†BMI>30 AND fasting glucose ≥5.6 mmol/L AND ≥2 of the following criteria: triglyceride levels ≥1.7 mmol/L; high-density lipoprotein cholesterol <1.0 mmol/L; blood pressure ≥130/85 mm Hg; waist circumference ≥102 cm

§ assessed by choline and carnitine challenge test (CCCT) and PET-CT of the aorta

‡ assessed by hyperinsulinemic euglycemic clamp

Table 2: Summarized risk of bias by RoB-2 tool

Table 3: Quality of evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Early (2-6 weeks) clinically significant parameters

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO/SHAM (2-6 weeks)	Relative (95% CI)	Absolute (95% CI)		
HbA1c												
6	randomised trials	serious	not serious	not serious	serious	none	80	67	-	MD **1.69 lower** (2.81 lower to 0.56 lower)	⨁⨁◯◯ LOW	IMPORTANT
HDL Cholesterol												
6	randomised trials	serious	not serious	not serious	serious	none	80	66	-	MD **0.09 higher** (0.02 higher to 0.15 higher)	⨁⨁◯◯ LOW	IMPORTANT
LDL Cholesterol												
6	randomised trials	serious	serious	serious	not serious	none	80	66	-	MD **0.19 higher** (0.05 higher to 0.34 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
fasting glucose												
6	randomised trials	serious	not serious	not serious	serious	none	78	66	-	MD **0.09 lower** (0.22 lower to 0.04 higher)	⨁⨁◯◯ LOW	IMPORTANT
Triglycerides												
6	randomised trials	serious	very serious	serious	not serious	none	66	54	-	MD **0.02 lower** (0.52 lower to 0.49 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
Total Cholesterol												
5	randomised trials	serious	not serious	serious	not serious	none	69	55	-	MD **0** (0.17 lower to 0.16 higher)	⨁⨁◯◯ LOW	IMPORTANT
BMI												
3	randomised trials	serious	serious	not serious	serious	none	46	32	-	MD **0.85 lower** (2.9 lower to 1.2 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
Weight												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO/SHAM (2-6 weeks)	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	serious	serious	not serious	not serious	none	56	44	-	MD **1.67 higher** (9.5 lower to 12.84 higher)	⨁⨁◯◯ LOW	IMPORTANT
HOMA-IR												
4	randomised trials	serious	serious	not serious	not serious	none	59	46	-	MD **0.35 lower** (1.56 lower to 0.86 higher)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

4. Late (12 weeks) clinically significant parameters

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO (reduction 12 weeks)	Relative (95% CI)	Absolute (95% CI)		
BMI reduction												
2	randomised trials	not serious	serious	not serious	serious	none	23	15	-	MD **0.34 lower** (1.81 lower to 1.13 higher)	⨁⨁◯◯ LOW	IMPORTANT
Hip width reduction												
2	randomised trials	not serious	not serious	not serious	serious	none	23	15	-	MD **0.83 lower** (4.68 lower to 3.03 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
Weight												
3	randomised trials	not serious	not serious	not serious	serious	none	35	30	-	MD **0.32 higher** (6.81 lower to 7.45 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
HbA1c												
2	randomised trials	not serious	not serious	not serious	serious	none	22	21	-	MD **0.05 lower** (2.17 lower to 2.06 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
LDL cholesterol												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO (reduction 12 weeks)	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	not serious	not serious	not serious	very serious	none	22	21	-	MD **0.32 lower** (0.92 lower to 0.29 higher)	⨁⨁◯◯ LOW	IMPORTANT
HDL cholesterol												
2	randomised trials	not serious	not serious	not serious	very serious	none	22	21	-	MD **0.22 higher** (0.04 lower to 0.48 higher)	⨁⨁◯◯ LOW	IMPORTANT
Triglycerides												
2	randomised trials	not serious	not serious	not serious	very serious	none	22	21	-	MD **0.09 higher** (0.24 lower to 0.42 higher)	⨁⨁◯◯ LOW	IMPORTANT
Fasting glucose												
2	randomised trials	not serious	not serious	not serious	very serious	none	22	21	-	MD **0.17 lower** (0.49 lower to 0.16 higher)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

Highlights

- Fecal Microbiota Transplantation may have a role for treatment of metabolic syndrome

- Fecal Microbiota Transplantation improves HbA1c and HDLc

- Fecal Microbiota Transplantation does not improve obesity parameters

- Fecal Microbiota Transplantation may affect cholesterol metabolism

- Fecal Microbiota Transplantation is safe in short term for obesity and metabolic syndrome

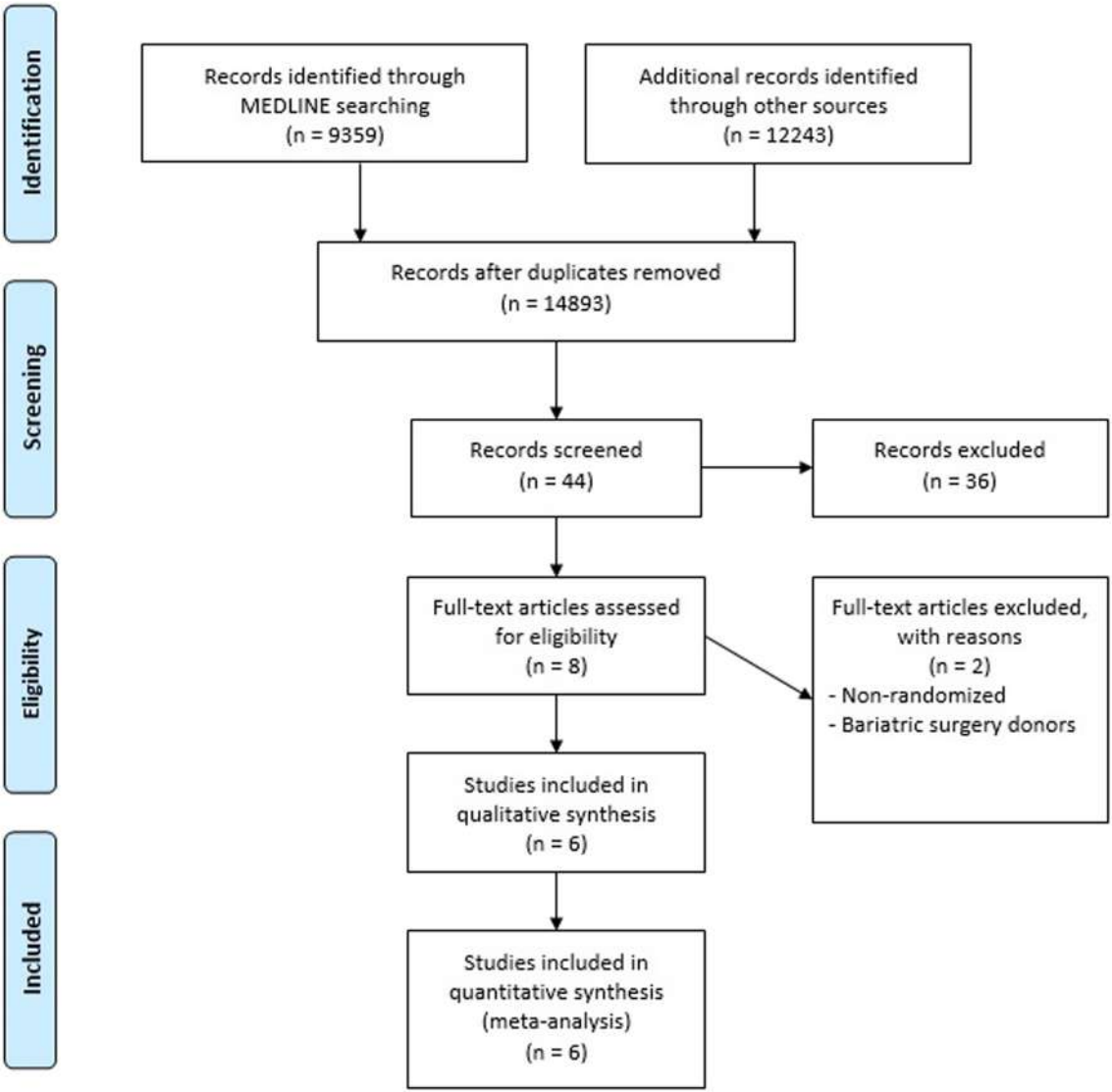
Identification
Screening
Eligibility
Included
Records identified through MEDLINE searching (n = 9359)
Additional records identified through other sources (n = 12243)
Records after duplicates removed (n = 14893)
Records screened (n = 44)
Records excluded (n = 36)
Full-text articles assessed for eligibility (n = 8)
Full-text articles excluded, with reasons (n = 2)
- Non-randomized
- Bariatric surgery donors
Studies included in qualitative synthesis (n = 6)
Studies included in quantitative synthesis (meta-analysis) (n = 6)

Figure 1

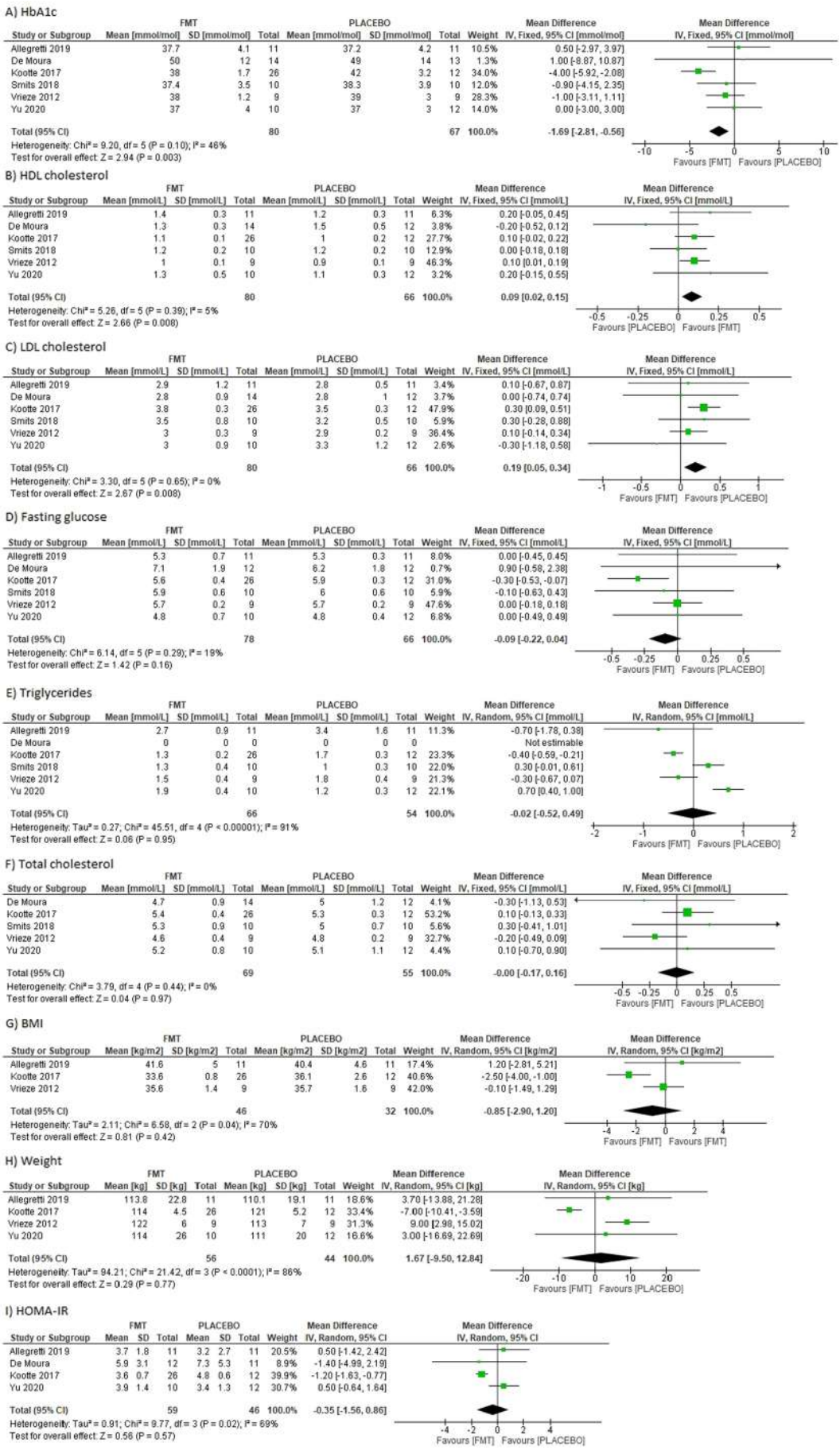
A) HbA1c
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/mol] | SD [mmol/mol] | Total | Mean [mmol/mol] | SD [mmol/mol] | Total | Weight | IV, Fixed, 95% CI [mmol/mol]
Allegretti 2019 37.7 4.1 11 37.2 4.2 11 10.5% 0.50 [-2.97, 3.97]
De Moura 50 12 14 49 14 13 1.3% 1.00 [-8.87, 10.87]
Kootte 2017 38 1.7 26 42 3.2 12 34.0% -4.00 [-5.92, -2.08]
Smits 2018 37.4 3.5 10 38.3 3.9 10 12.0% -0.90 [-4.15, 2.35]
Vrieze 2012 38 1.2 9 39 3 9 28.3% -1.00 [-3.11, 1.11]
Yu 2020 37 4 10 37 3 12 14.0% 0.00 [-3.00, 3.00]
Total (95% CI) 80 67 100.0% -1.69 [-2.81, -0.56]
Heterogeneity: Chi² = 9.20, df = 5 (P = 0.10); I² = 46%
Test for overall effect: Z = 2.94 (P = 0.003)
-10 -5 0 5 10
Favours [FMT] Favours [PLACEBO]
B) HDL cholesterol
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/L] | SD [mmol/L] | Total | Mean [mmol/L] | SD [mmol/L] | Total | Weight | IV, Fixed, 95% CI [mmol/L]
Allegretti 2019 1.4 0.3 11 1.2 0.3 11 6.3% 0.20 [-0.05, 0.45]
De Moura 1.3 0.3 14 1.5 0.5 12 3.8% -0.20 [-0.52, 0.12]
Kootte 2017 1.1 0.1 26 1 0.2 12 27.7% 0.10 [-0.02, 0.22]
Smits 2018 1.2 0.2 10 1.2 0.2 10 12.9% 0.00 [-0.18, 0.18]
Vrieze 2012 1 0.1 9 0.9 0.1 9 46.3% 0.10 [0.01, 0.19]
Yu 2020 1.3 0.5 10 1.1 0.3 12 3.2% 0.20 [-0.15, 0.55]
Total (95% CI) 80 66 100.0% 0.09 [0.02, 0.15]
Heterogeneity: Chi² = 5.26, df = 5 (P = 0.39); I² = 5%
Test for overall effect: Z = 2.66 (P = 0.008)
-0.5 -0.25 0 0.25 0.5
Favours [PLACEBO] Favours [FMT]
C) LDL cholesterol
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/L] | SD [mmol/L] | Total | Mean [mmol/L] | SD [mmol/L] | Total | Weight | IV, Fixed, 95% CI [mmol/L]
Allegretti 2019 2.9 1.2 11 2.8 0.5 11 3.4% 0.10 [-0.67, 0.87]
De Moura 2.8 0.9 14 2.8 1 12 3.7% 0.00 [-0.74, 0.74]
Kootte 2017 3.8 0.3 26 3.5 0.3 12 47.9% 0.30 [0.09, 0.51]
Smits 2018 3.5 0.8 10 3.2 0.5 10 5.9% 0.30 [-0.28, 0.88]
Vrieze 2012 3 0.3 9 2.9 0.2 9 36.4% 0.10 [-0.14, 0.34]
Yu 2020 3 0.9 10 3.3 1.2 12 2.6% -0.30 [-1.18, 0.58]
Total (95% CI) 80 66 100.0% 0.19 [0.05, 0.34]
Heterogeneity: Chi² = 3.30, df = 5 (P = 0.65); I² = 0%
Test for overall effect: Z = 2.67 (P = 0.008)
-1 -0.5 0 0.5 1
Favours [FMT] Favours [PLACEBO]
D) Fasting glucose
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/L] | SD [mmol/L] | Total | Mean [mmol/L] | SD [mmol/L] | Total | Weight | IV, Fixed, 95% CI [mmol/L]
Allegretti 2019 5.3 0.7 11 5.3 0.3 11 8.0% 0.00 [-0.45, 0.45]
De Moura 7.1 1.9 12 6.2 1.8 12 0.7% 0.90 [-0.58, 2.38]
Kootte 2017 5.6 0.4 26 5.9 0.3 12 31.0% -0.30 [-0.53, -0.07]
Smits 2018 5.9 0.6 10 6 0.6 10 5.9% -0.10 [-0.63, 0.43]
Vrieze 2012 5.7 0.2 9 5.7 0.2 9 47.6% 0.00 [-0.18, 0.18]
Yu 2020 4.8 0.7 10 4.8 0.4 12 6.8% 0.00 [-0.49, 0.49]
Total (95% CI) 78 66 100.0% -0.09 [-0.22, 0.04]
Heterogeneity: Chi² = 6.14, df = 5 (P = 0.29); I² = 19%
Test for overall effect: Z = 1.42 (P = 0.16)
-0.5 -0.25 0 0.25 0.5
Favours [FMT] Favours [PLACEBO]
E) Triglycerides
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/L] | SD [mmol/L] | Total | Mean [mmol/L] | SD [mmol/L] | Total | Weight | IV, Random, 95% CI [mmol/L]
Allegretti 2019 2.7 0.9 11 3.4 1.6 11 11.3% -0.70 [-1.78, 0.38]
De Moura 0 0 0 0 0 0 Not estimable
Kootte 2017 1.3 0.2 26 1.7 0.3 12 23.3% -0.40 [-0.59, -0.21]
Smits 2018 1.3 0.4 10 1 0.3 10 22.0% 0.30 [-0.01, 0.61]
Vrieze 2012 1.5 0.4 9 1.8 0.4 9 21.3% -0.30 [-0.67, 0.07]
Yu 2020 1.9 0.4 10 1.2 0.3 12 22.1% 0.70 [0.40, 1.00]
Total (95% CI) 66 54 100.0% -0.02 [-0.52, 0.49]
Heterogeneity: Tau² = 0.27; Chi² = 45.51, df = 4 (P < 0.00001); I² = 91%
Test for overall effect: Z = 0.06 (P = 0.95)
-2 -1 0 1 2
Favours [FMT] Favours [PLACEBO]
F) Total cholesterol
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [mmol/L] | SD [mmol/L] | Total | Mean [mmol/L] | SD [mmol/L] | Total | Weight | IV, Fixed, 95% CI [mmol/L]
De Moura 4.7 0.9 14 5 1.2 12 4.1% -0.30 [-1.13, 0.53]
Kootte 2017 5.4 0.4 26 5.3 0.3 12 53.2% 0.10 [-0.13, 0.33]
Smits 2018 5.3 0.9 10 5 0.7 10 5.6% 0.30 [-0.41, 1.01]
Vrieze 2012 4.6 0.4 9 4.8 0.2 9 32.7% -0.20 [-0.49, 0.09]
Yu 2020 5.2 0.8 10 5.1 1.1 12 4.4% 0.10 [-0.70, 0.90]
Total (95% CI) 69 55 100.0% -0.00 [-0.17, 0.16]
Heterogeneity: Chi² = 3.79, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)
-0.5 -0.25 0 0.25 0.5
Favours [FMT] Favours [PLACEBO]
G) BMI
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [kg/m2] | SD [kg/m2] | Total | Mean [kg/m2] | SD [kg/m2] | Total | Weight | IV, Random, 95% CI [kg/m2]
Allegretti 2019 41.6 5 11 40.4 4.6 11 17.4% 1.20 [-2.81, 5.21]
Kootte 2017 33.6 0.8 26 36.1 2.6 12 40.6% -2.50 [-4.00, -1.00]
Vrieze 2012 35.6 1.4 9 35.7 1.6 9 42.0% -0.10 [-1.49, 1.29]
Total (95% CI) 46 32 100.0% -0.85 [-2.90, 1.20]
Heterogeneity: Tau² = 2.11; Chi² = 6.58, df = 2 (P = 0.04); I² = 70%
Test for overall effect: Z = 0.81 (P = 0.42)
-4 -2 0 2 4
Favours [FMT] Favours [FMT]
H) Weight
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean [kg] | SD [kg] | Total | Mean [kg] | SD [kg] | Total | Weight | IV, Random, 95% CI [kg]
Allegretti 2019 113.8 22.8 11 110.1 19.1 11 18.6% 3.70 [-13.88, 21.28]
Kootte 2017 114 4.5 26 121 5.2 12 33.4% -7.00 [-10.41, -3.59]
Vrieze 2012 122 6 9 113 7 9 31.3% 9.00 [2.98, 15.02]
Yu 2020 114 26 10 111 20 12 16.6% 3.00 [-16.69, 22.69]
Total (95% CI) 56 44 100.0% 1.67 [-9.50, 12.84]
Heterogeneity: Tau² = 94.21; Chi² = 21.42, df = 3 (P < 0.0001); I² = 86%
Test for overall effect: Z = 0.29 (P = 0.77)
-20 -10 0 10 20
Favours [FMT] Favours [PLACEBO]
I) HOMA-IR
FMT
PLACEBO
Mean Difference
Mean Difference
Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI
Allegretti 2019 3.7 1.8 11 3.2 2.7 11 20.5% 0.50 [-1.42, 2.42]
De Moura 5.9 3.1 12 7.3 5.3 11 8.9% -1.40 [-4.99, 2.19]
Kootte 2017 3.6 0.7 26 4.8 0.6 12 39.9% -1.20 [-1.63, -0.77]
Yu 2020 3.9 1.4 10 3.4 1.3 12 30.7% 0.50 [-0.64, 1.64]
Total (95% CI) 59 46 100.0% -0.35 [-1.56, 0.86]
Heterogeneity: Tau² = 0.91; Chi² = 9.77, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 0.56 (P = 0.57)
-4 -2 0 2 4
Favours [FMT] Favours [PLACEBO]

Figure 2

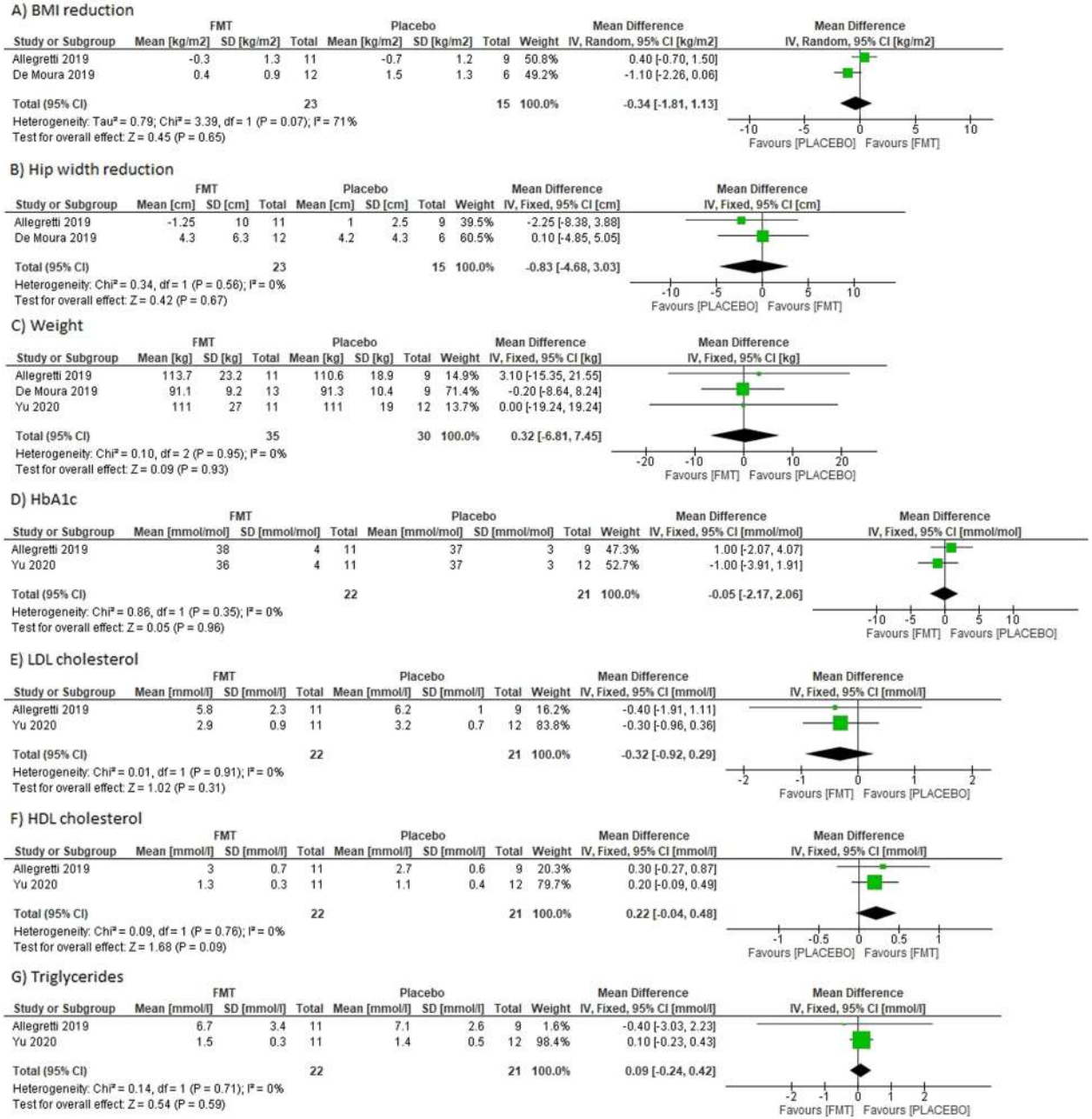
A) BMI reduction
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [kg/m2] SD [kg/m2] Total Mean [kg/m2] SD [kg/m2] Total Weight IV, Random, 95% CI [kg/m2]
IV, Random, 95% CI [kg/m2]
Allegretti 2019 -0.3 1.3 11 -0.7 1.2 9 50.8% 0.40 [-0.70, 1.50]
De Moura 2019 0.4 0.9 12 1.5 1.3 6 49.2% -1.10 [-2.26, 0.06]
Total (95% CI) 23 15 100.0% -0.34 [-1.81, 1.13]
Heterogeneity: Tau² = 0.79; Chi² = 3.39, df = 1 (P = 0.07); I² = 71%
Test for overall effect: Z = 0.45 (P = 0.65)
-10 -5 0 5 10
Favours [PLACEBO] Favours [FMT]
B) Hip width reduction
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [cm] SD [cm] Total Mean [cm] SD [cm] Total Weight IV, Fixed, 95% CI [cm]
IV, Fixed, 95% CI [cm]
Allegretti 2019 -1.25 10 11 1 2.5 9 39.5% -2.25 [-8.38, 3.88]
De Moura 2019 4.3 6.3 12 4.2 4.3 6 60.5% 0.10 [-4.85, 5.05]
Total (95% CI) 23 15 100.0% -0.83 [-4.68, 3.03]
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 0.42 (P = 0.67)
-10 -5 0 5 10
Favours [PLACEBO] Favours [FMT]
C) Weight
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [kg] SD [kg] Total Mean [kg] SD [kg] Total Weight IV, Fixed, 95% CI [kg]
IV, Fixed, 95% CI [kg]
Allegretti 2019 113.7 23.2 11 110.6 18.9 9 14.9% 3.10 [-15.35, 21.55]
De Moura 2019 91.1 9.2 13 91.3 10.4 9 71.4% -0.20 [-8.64, 8.24]
Yu 2020 111 27 11 111 19 12 13.7% 0.00 [-19.24, 19.24]
Total (95% CI) 35 30 100.0% 0.32 [-6.81, 7.45]
Heterogeneity: Chi² = 0.10, df = 2 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.09 (P = 0.93)
-20 -10 0 10 20
Favours [FMT] Favours [PLACEBO]
D) HbA1c
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [mmol/mol] SD [mmol/mol] Total Mean [mmol/mol] SD [mmol/mol] Total Weight IV, Fixed, 95% CI [mmol/mol]
IV, Fixed, 95% CI [mmol/mol]
Allegretti 2019 38 4 11 37 3 9 47.3% 1.00 [-2.07, 4.07]
Yu 2020 36 4 11 37 3 12 52.7% -1.00 [-3.91, 1.91]
Total (95% CI) 22 21 100.0% -0.05 [-2.17, 2.06]
Heterogeneity: Chi² = 0.86, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)
-10 -5 0 5 10
Favours [FMT] Favours [PLACEBO]
E) LDL cholesterol
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [mmol/l] SD [mmol/l] Total Mean [mmol/l] SD [mmol/l] Total Weight IV, Fixed, 95% CI [mmol/l]
IV, Fixed, 95% CI [mmol/l]
Allegretti 2019 5.8 2.3 11 6.2 1 9 16.2% -0.40 [-1.91, 1.11]
Yu 2020 2.9 0.9 11 3.2 0.7 12 83.8% -0.30 [-0.96, 0.36]
Total (95% CI) 22 21 100.0% -0.32 [-0.92, 0.29]
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.91); I² = 0%
Test for overall effect: Z = 1.02 (P = 0.31)
-2 -1 0 1 2
Favours [FMT] Favours [PLACEBO]
F) HDL cholesterol
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [mmol/l] SD [mmol/l] Total Mean [mmol/l] SD [mmol/l] Total Weight IV, Fixed, 95% CI [mmol/l]
IV, Fixed, 95% CI [mmol/l]
Allegretti 2019 3 0.7 11 2.7 0.6 9 20.3% 0.30 [-0.27, 0.87]
Yu 2020 1.3 0.3 11 1.1 0.4 12 79.7% 0.20 [-0.09, 0.49]
Total (95% CI) 22 21 100.0% 0.22 [-0.04, 0.48]
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.68 (P = 0.09)
-1 -0.5 0 0.5 1
Favours [PLACEBO] Favours [FMT]
G) Triglycerides
FMT
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean [mmol/l] SD [mmol/l] Total Mean [mmol/l] SD [mmol/l] Total Weight IV, Fixed, 95% CI [mmol/l]
IV, Fixed, 95% CI [mmol/l]
Allegretti 2019 6.7 3.4 11 7.1 2.6 9 1.6% -0.40 [-3.03, 2.23]
Yu 2020 1.5 0.3 11 1.4 0.5 12 98.4% 0.10 [-0.23, 0.43]
Total (95% CI) 22 21 100.0% 0.09 [-0.24, 0.42]
Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)
-2 -1 0 1 2
Favours [FMT] Favours [PLACEBO]

Figure 3