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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

Crance

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 glucagonlike 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) \geq 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 metaanalysis. 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/1 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

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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.

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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 \pm 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.

Solution

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 -2 nd 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

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

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

 $\dagger BMI > 30 \text{ AND fasting glucose} \geq 5.6 \text{ mmol/L AND} \geq 2 \text{ of the following criteria: triglyceride levels} \geq 1.7 \text{ mmol/L}; \text{ high-density lipoprotein}$

cholesterol <1.0 mmol/L; blood pressure ${\geq}130/85$ mm Hg; waist circumference ${\geq}102$ cm

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

‡ assessed by hyperinsulinemic euglycemic clamp

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

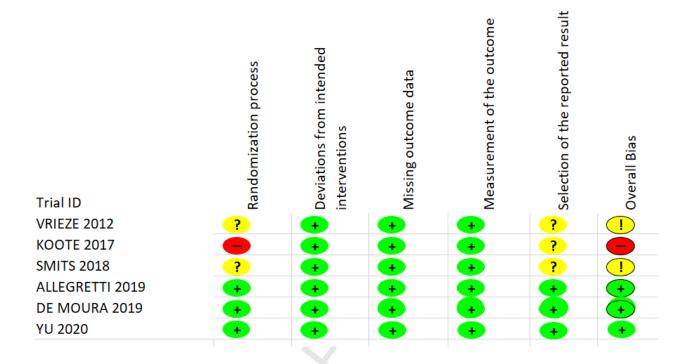


Table 3: Quality of evidence by Grading of Recommendations Assessment, Development and Evaluation (GRADE)

			Certainty as	sessment			N	⁰ of patients	Ef	fect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO/SHAM (2-6 weeks)	Relative (95% Cl)	Absolute (95% CI)	Certainty	Importance
HbA1c												
6	randomised trials	serious	not serious	not serious	serious	none	80	67	-	MD 1.69 lower (2.81 lower to 0.56 lower)		IMPORTANT
HDL Cho	lesterol											
6	randomised trials	serious	not serious	not serious	serious	none	80	66	-	MD 0.09 higher (0.02 higher to 0.15 higher)		IMPORTANT
LDL Cho	lesterol											
6	randomised trials	serious	serious	serious	not serious	none	80	66	-	MD 0.19 higher (0.05 higher to 0.34 higher)		IMPORTANT
fasting g	lucose							•		•		
6	randomised trials	serious	not serious	not serious	serious	none	78	66	-	MD 0.09 lower (0.22 lower to 0.04 higher)		IMPORTANT
Triglycer	ides							1				
6	randomised trials	serious	very serious	serious	not serious	none	66	54	-	MD 0.02 lower (0.52 lower to 0.49 higher)		IMPORTANT
Total Ch	olesterol			-	•	÷		÷	•	•	-	•
5	randomised trials	serious	not serious	serious	not serious	none	69	55	-	MD 0 (0.17 lower to 0.16 higher)		IMPORTANT
BMI												
3	randomised trials	serious	serious	not serious	serious	none	46	32	-	MD 0.85 lower (2.9 lower to 1.2 higher)		IMPORTANT

Early (2-6 weeks) clinically significant parameters

Weight

			Certainty as	sessment			N	of patients	Eff	fect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO/SHAM (2-6 weeks)	Relative (95% Cl)	Absolute (95% CI)	Certainty	Importance
4	randomised trials	serious	serious	not serious	not serious	none	56	44	-	MD 1.67 higher (9.5 lower to 12.84 higher)		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)		IMPORTANT	
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CI: Confidence interval; MD: Mean difference

4. Late (12 weeks) clinically significant parameters

			Certainty ass	sessment			N≌ o	of patients	Ef	fect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO (reduction 12 weeks)	Relative (95% CI)	Absolute (95% Cl)	Certainty	Importance
BMI redu	ction											
2	randomised trials	not serious	serious	not serious	serious	none	23	15	-	MD 0.34 lower (1.81 lower to 1.13 higher)		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)		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)		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)		IMPORTANT

LDL cholesterol

			Certainty ass	sessment			N≌ c	of patients	Efi	fect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FMT	PLACEBO (reduction 12 weeks)	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
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)		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)		IMPORTANT	
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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)		IMPORTANT
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Fasting glucose

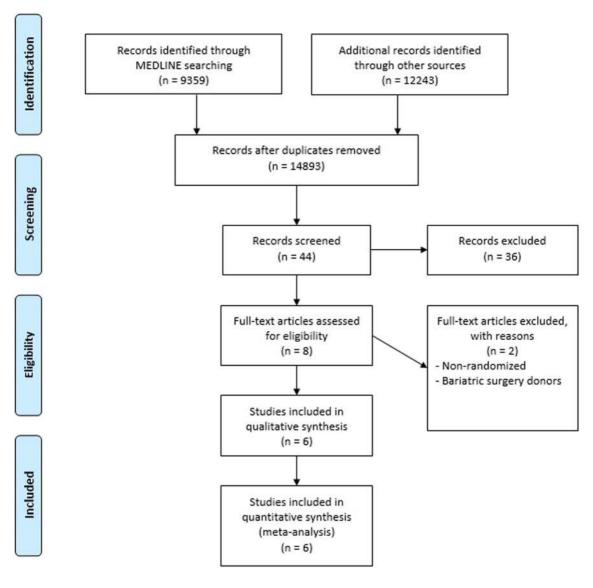
2	randomised trials	not serious	not serious	not serious	very serious	none	22	21	-	MD 0.17 lower (0.49 lower to 0.16 higher)	IMPORTANT
CI: Confic	dence interval;	MD: Mean	difference								

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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

Solution



Vlegretti 2019			Total Mean (mmo		[mmol/r		Mean Differen Weight IV, Fixed, 95% CI (m	mol/mol] IV, Fixed, 95% CI [mmol/m
e Moura	37.7 50	4.1	11 14	37.2 49		4.2 11 14 13		87, 3.97]
potte 2017	38 37.4	1.7	26	42		3.2 12	34.0% -4.00 (-5.	92,-2.08]
nits 2018 ieze 2012	38	3.5 1.2	10 9	38.3 39		3.9 10 3 9	28.3% -1.00 [-3	.15, 2.35]
2020	37	4	10	37		3 12		1.00, 3.00]
tal (95% Cl) terogeneity: Chi ^a = 9.20, df :	= 5 (P = 0.10); P = 46	%	80			67	100.0% -1.69 [-2.	81, -0.56]
st for overall effect Z = 2.94		20						-10 -5 Ó 5 Favours (FMT) Favours (P
HDL cholesterol	FMT		PLAC	EBO			Mean Difference	Mean Difference
udy or Subgroup Mean [r agretti 2019	nmol/L] SD [mmol		Mean [mmol/L]	SD [mmol/L			V, Fixed, 95% CI [mmol/L] 0.20 [-0.05, 0.45]	IV, Fixed, 95% CI [mmolil.]
Moura		3 11 3 14	1.2 1.5	0.3		6.3% 3.8%	-0.20 [-0.52, 0.12]	
otte 2017 nits 2018		1 26	1	0.3			0.10 [-0.02, 0.22] 0.00 [-0.18, 0.18]	
eze 2012	1 0	1 9	0.9	0.1	1 9	46.3%	0.10 [0.01, 0.19]	
2020	1.3 0	.5 10	1.1	0.3			0.20 (-0.15, 0.55)	
tal (95% CI) sterogeneity: Chi ² = 5.26, df =	5 (P = 0.39); I# = 5%	80			66	100.0%	0.09 [0.02, 0.15]	
st for overall effect Z = 2.66 (-0.5 -0.25 0 0.25 0.5 Favours [PLACEBO] Favours [FMT]
LDL cholesterol								
tudy or Subgroup Mean [FMT mmol/L] SD [mmol	L] Total	PLAC Mean [mmoi/L]] Tota	Weight	Mean Difference IV, Fixed, 95% CI [mmol/L]	Mean Difference IV, Fixed, 95% CI [mmol/L]
legretti 2019	2.9	1.2 11	2.8	0.	5 11	3.4%	0.10 [-0.67, 0.87]	
e Moura potte 2017	3.8	0.9 14 0.3 26	2.8 3.5	0.		47.9%	0.00 [-0.74, 0.74] 0.30 [0.09, 0.51]	
nits 2018 ieze 2012).8 10).3 9	3.2 2.9	0. 0.			0.30 [-0.28, 0.88] 0.10 [-0.14, 0.34]	
2020).9 10	3.3	1.			-0.30 [-1.18, 0.58]	
otal (95% Cl)		80			66	6 100.0%	0.19 [0.05, 0.34]	◆
eterogeneity: Chi ^a = 3.30, df = est for overall effect: Z = 2.67							-	-1 -0.5 0 0.5 1
Fasting glucose								Favours [FMT] Favours [PLACEBO]
	FMT		PLAC				Mean Difference	Mean Difference
udy or Subgroup Mean (n egretti 2019	nmol/L] \$D [mmol/ 5.3 0	.7 11	Mean [mmol/L] 5.3	D (mmol/L 0.3	Sector Se	Weight I 8.0%	V, Fixed, 95% CI [mmol/L] 0.00 [-0.45, 0.45]	IV, Fixed, 95% CI [mmol/L]
Moura	7.1 1	.9 12	6.2	1.6	3 12	0.7%	0.90 [-0.58, 2.38]	
otte 2017 nits 2018		4 26 .6 10	5.9 6	0.3			-0.30 [-0.53, -0.07] -0.10 [-0.63, 0.43]	
eze 2012 2020	5.7 0	2 9 .7 10	5.7 4.8	0.1	2 9	47.6%	0.00 [-0.18, 0.18] 0.00 [-0.49, 0.49]	+
	4.0 U		4.0	0.4		1000		
ital (95% CI) sterogeneity: Chi ² = 6.14, df =	5 (P = 0.29); I* = 199	78 %			06	100.0%	-0.09 [-0.22, 0.04]	105 .025 0 obe of
st for overall effect: Z = 1.42 (-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO)
Triglycerides								
	FMT mmol/L] SD [mmol	L] Totai	PLAC Mean [mmol/L]	CEBO SD [mmol/l	.] Tota	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Mean Difference IV, Random, 95% CI [mmol/L]
legretti 2019	2.7	0.9 11	3.4	1.	6 11	11.3%	-0.70 [-1.78, 0.38]	
e Moura ootte 2017	0 1.3	0 0 0.2 26	0 1.7	0.	0 0 3 12		Not estimable -0.40 (-0.59, -0.21)	
mits 2018 rieze 2012	1.3	0.4 10 0.4 9	1	0.	3 10	22.0%	0.30 [-0.01, 0.61] -0.30 [-0.67, 0.07]	
u 2020		0.4 10	1.2	0.			0.70 [0.40, 1.00]	
otal (95% CI)		66			54	100.0%	-0.02 [-0.52, 0.49]	· · · · ·
eterogeneity: Tau ^e = 0.27; Ch est for overall effect: Z = 0.06		< 0.00001)	, 1'= 91%					-2 -1 0 1 Favours (FMT) Favours (PLACEBO)
0101411 01001. A = 0.00								r monte parti i diomo particolo
				EBO		Wainht I	Mean Difference /, Fixed, 95% CI [mmol/L]	Mean Difference IV, Fixed, 95% CI [mmol/L]
Total cholesterol	FMT	1 Total	PLAC Moon (mmol/l)	(Illommolil)				
Total cholesterol udy or Subgroup Mean (n Moura	1.7 SD [mmol/ 4.7 0	9 14	Mean (mmol/L) S 5	D (mmol/L) 1.2	12	4.1%	-0.30 [-1.13, 0.53] +	
Total cholesterol udy or Subgroup Mean (n Moura otte 2017	nmol/L] SD (mmol/ 4.7 0 5.4 0	9 14 4 26	Mean [mmol/L] 5 5 5.3	1.2 0.3	2 12 3 12	4.1% 53.2%	-0.30 [-1 13, 0.53] + 0.10 [-0.13, 0.33]	
Total cholesterol udy or Subgroup Mean (n Moura othe 2017 nits 2018 leze 2012	nmol/L] SD [mmol/ 4.7 0 5.4 0 5.3 0 4.6 0	9 14 4 26 9 10 4 9	Mean [mmol/L] 5 5 5.3 5 4.8	1.2 0.3 0.7 0.2	2 12 3 12 7 10 2 9	4.1% 53.2% 5.6% 32.7%	-0.30 [-1.13, 0.53] 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09]	
Total cholesterol udy or Subgroup Mean (n Moura ootte 2017 nis 2018 eze 2012 2020	nmol/L] SD [mmol/ 4.7 0 5.4 0 5.3 0 4.6 0	9 14 4 26 9 10 4 9 8 10	Mean [mmol/L] 5 5 5.3 5	1.2 0.3 0.7	2 12 3 12 7 10 2 9 1 12	4.1% 53.2% 5.6% 32.7% 4.4%	-0.30 [-1.13, 0.53] 4- 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09] 0.10 [-0.70, 0.90]	
Total cholesterol udy or Subgroup Mean (n Moura Moie 2017 nits 2018 eze 2012 2020 2020	nmol/L] SD [mmol/ 4.7 0 5.4 0 5.3 0 4.6 0 5.2 0	9 14 4 26 9 10 4 9 8 10 69	Mean [mmol/L] 5 5 5.3 5 4.8	1.2 0.3 0.7 0.2	2 12 3 12 7 10 2 9 1 12	4.1% 53.2% 5.6% 32.7%	-0.30 [-1.13, 0.53] 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09]	
Total cholesterol whoura othe 2017 whis 2018 eze 2012 2020 tal (95% CI) terogeneity: Chi# = 3.79, df =	science science 4.7 0 5.4 0 5.3 0 4.6 0 5.2 0 4 (P = 0.44); P = 0%	9 14 4 26 9 10 4 9 8 10 69	Mean [mmol/L] 5 5 5.3 5 4.8	1.2 0.3 0.7 0.2	2 12 3 12 7 10 2 9 1 12	4.1% 53.2% 5.6% 32.7% 4.4%	-0.30 [-1.13, 0.53] 4- 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09] 0.10 [-0.70, 0.90]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO)
Total cholesterol idy or Subgroup Mean [n Moura othe 2017 this 2018 eze 2012 2020 tata (95% CI) tata (95% CI) terogeneity. Chi# = 3.79, df = st for overall effect. Z = 0.04 (dt)	science science 4.7 0 5.4 0 5.3 0 4.6 0 5.2 0 4 (P = 0.44); P = 0%	9 14 4 26 9 10 4 9 8 10 69	Mean [mmol/L] 5 5 5.3 5 4.8	1.2 0.3 0.7 0.2	2 12 3 12 7 10 2 9 1 12	4.1% 53.2% 5.6% 32.7% 4.4%	-0.30 [+1,3,0.53] ← 0.10 [+0.13,0.33] 0.30 [+0.41,1.01] -0.20 [+0.49,0.09] 0.10 [+0.70,0.90] -0.00 [-0.17,0.16]	-0'5 -0'25 0 0'25 0'5
Total cholesterol udy or Subgroup Mean (m Moura otte 2017 otte 2017 szez 2012 2020 tal (95% CI) terogeneity: Chil* = 3.79, df = st for overall effect: Z = 0.04 (c BMI	nmol/L] SD [mmol/ 4,7 0 5,4 0 5,3 0 4,6 0 5,2 0 4 (P = 0.44); I [#] = 0% P = 0.97) FMT	9 14 4 26 9 10 4 9 8 10 69	Mean [mmol/L] 5 5 5,3 5 4,8 5,1 5,1 9 LACEB	1.2 0.3 0.7 0.2 1.1	2 12 3 12 7 10 2 9 1 12 55	4.1% 53.2% 5.6% 32.7% 4.4%	-0.30 [-1 13, 0.53] ← 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09] 0.10 [-0.70, 0.90] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference
Total cholesterol idy or Subgroup Mean [m Moura Mean [m onte 2017 Mean [m ids 2018 Sez 2012 2020 Mean [m al (95% CI) Serrogeneiky Chi# = 3.79, df = st for overall effect: Z = 0.04 (BMI udy or Subgroup Mean [n udy or Subgroup Mean [n eyeretti 2019 Mean [n	Immolil SD [mmolil 4.7 0 5.4 0 5.3 0 4.6 0 5.2 0 4 (P = 0.44); IP = 0% P = 0.97) FMT kg/m2] SD [kg/m2] 41.6 5	9 14 4 26 9 10 4 9 8 10 69 <u>Total N</u>	Mean (mmolt.) 5 5 5 4.8 5.1 PLACEB lean (kg/m2] 5D j 40.4	1.2 0.3 0.7 0.2 1.1 0 <u>(kg/m2] Tc</u> 4.6	2 12 3 12 7 10 2 9 1 12 55 55 0tal We 11 17	4.1% 53.2% 5.6% 32.7% 4.4% 100.0%	-0.30 [+1,13, 0.53] ← 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09] 0.10 [-0.70, 0.90] -0.00 [-0.17, 0.16] -0.00	-0.5 -0.25 0.5 Favours (FMT) Favours (PLACEBO)
Total cholesterol udy or Subgroup Mean [m Moura Mean [m otte 2017 Mean [m wis 2018 2020 tal (95% CI) Errogeneity: Chi# = 3.79, df = st for overall effect: Z = 0.04 (BMI wdy or Subgroup Mean [n wdy or Subgroup Mean [n udy or Subgroup Mean [n legretti 2019 2017	sD [mmol/] SD [mmol/ 4.7 0 5.4 0 5.3 0 6.6 0 5.2 0 4 (P = 0.44); I*= 0% P = 0.97) FMT kg/m2] SD [kg/m2] 3.6 0.8	9 14 4 26 9 10 4 9 8 10 69 <u>Total N</u> 11 26	Mean [mmolt] 5 5.3 5.3 4.8 5.1 PLACEB lean [kg/m2] 5D] 40.4 36.1	1.2 0.3 0.7 0.2 1.1 <u>kg/m2] Tc</u> <u>4.6</u> 2.6	2 12 3 12 7 10 2 9 1 12 55 55 0tal We 11 17 12 40	4.1% 53.2% 5.6% 32.7% 4.4% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.10, 0.10] -2.50 [+4.00, -1.00]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference
Total cholesterol ady or Subgroup Mean [n] Moura Mean [n] ofte 2017 Mean [n] his 2018 2020 tata (95% C) Mean [n] terogeneity, Chil* = 3.79, df = st for overall effect: Z = 0.04 (BMI Mean [n] tady or Subgroup Mean [n] legrefit 2019 ootte 2017 ieze 2012 2020	Immolil SD [mmolil 4.7 0 5.4 0 5.3 0 4.6 0 5.2 0 4 (P = 0.44); IP = 0% P = 0.97) FMT kg/m2] SD [kg/m2] 41.6 5	9 14 4 26 9 10 4 9 8 10 69 <u>Total N</u> 11 26 9	Mean (mmolt.) 5 5 5 4.8 5.1 PLACEB lean (kg/m2] 5D j 40.4	1.2 0.3 0.7 0.2 1.1 (kg/m2) TC 4.6 2.6 1.6	2 12 3 12 7 10 2 9 1 12 55 55 55 0tal We 11 17 12 40 9 42	4.1% 53.2% 5.6% 32.7% 4.4% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.20 [+0.49, 1.29] -0.10 [+1.49, 1.29]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference
Total cholesterol ady or Subgroup Mean [m] Moura Mean [m] ofte 2017 Mean [m] hs 2018 2020 tati (95% Cl) Mean [m] terogeneity: Chi# = 3.79, df = 1.79, df = st for overall effect: Z = 0.04 (BMI tudy or Subgroup Mean [n] legretti 2019 ootha 2017 storal 2012 othal (95% Cl) eterogeneity: Tau* = 2,11; Ch Ch	$\begin{array}{c} \mbox{mmoll} \underline{I} \ \ \mbox{SD} \ (mmoll) \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 9.0 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	9 14 4 26 9 10 4 9 8 10 69 <u>Total 1</u> 11 26 9 46	Mean (mmolt) 5 53 55 4.8 5.1 PLACEB lean (kg/m2) 5D 40.4 36.1 35.7	1.2 0.3 0.7 0.2 1.1 (kg/m2) TC 4.6 2.6 1.6	2 12 3 12 7 10 2 9 1 12 55 55 0tal We 11 17 12 40	4.1% 53.2% 5.6% 32.7% 4.4% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.20 [+0.0, 1.00] -2.50 [+4.00, -1.00]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference
Total cholesterol idy or Subgroup Mean [m Moura Moura otte 2017 Mean [m its 2018 2020 atal (95% C) Etrogeneity: Chi# = 3.79, df = st for overall effect: Z = 0.04 (BMI Mean [legrett] 2019 obte 2017 Mean [legrett] 2019 iste 2012 Mail (95% C) isterogeneity: Tau* = 2.11; Ch Ch	$\begin{array}{c} \mbox{mmoll} \underline{I} \ \ \mbox{SD} \ (mmoll) \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 9.0 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	9 14 4 26 9 10 4 9 8 10 69 <u>Total 1</u> 11 26 9 46	Mean (mmolt) 5 53 55 4.8 5.1 PLACEB lean (kg/m2) 5D 40.4 36.1 35.7	1.2 0.3 0.7 0.2 1.1 (kg/m2) TC 4.6 2.6 1.6	2 12 3 12 7 10 2 9 1 12 55 55 55 0tal We 11 17 12 40 9 42	4.1% 53.2% 5.6% 32.7% 4.4% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -1.20 [+2.81, 5.21] -2.50 [+4.00, -1.00] -0.10 [+1.49, 1.29]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference
Total cholesterol udy or Subgroup Mean [m Moura Mean [m onte 2017 Mean [m his 2018 2020 tati (95% Cl) Mean [m rerogeneity Chi#= 3.79, df = 3.79, df = st for overall effect: Z = 0.04 (d BMI tudy or Subgroup Mean [m leagreth 2019 ootte 2017 ricez 2012 otal (95% Cl) eterogeneity: Tau*= 2.11; Ch ch	$\begin{array}{c} \text{so} \mbox{ (mmod)} \\ 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 9 & 0.97 \\ \hline \\ FMT \\ \hline \\ FMT \\ \frac{kg/m2!}{33.6} & 0.8 \\ 35.6 & 1.4 \\ 33.6 & 0.8 \\ 35.6 & 1.4 \\ 10^{2} = 6.58, df = 2 \ (P = 0.42) \\ \hline \end{array}$	9 14 4 26 9 10 8 10 69 <u>Total 8</u> 11 26 9 46 0.04), I ^p =	Mean [mmolt] S 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 1 9 LACEB 1 9 6 0.1 35.7 70%	1.2 0.3 0.7 0.2 1.1 (kg/m2) TC 4.6 2.6 1.6	2 12 3 12 7 10 2 9 1 12 55 55 55 55 11 17 12 40 9 42 32 10	4,1% 53,2% 5,6% 32,7% 4,4% 100.0% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -1.20 [+2.81, 521] -2.50 [+4.00, -1.00] -0.10 [+1.49, 1.29] -0.85 [+2.90, 1.20]	-0.5 -0.25 0.0.25 0.5 Favours (FMT) Favours (FMT) Wean Difference IV, Random, 95% CI (kg/m2)
Build State Mean (m udy or Subgroup Mean (m Moura offe 2017 nits 2018 de 2017 nits 2018 de 2012 2020 tal (95% CI) terogeneity. Chi# = 3.79, df = st for overall effect: Z = 0.04 (BMI tudy or Subgroup Mean [n tudy or Subgroup Mean [n legretit 2019 oothe 2017 teze 2012 otal (95% CI) eterogeneity. Tau# = 2.11; Ch eterogeneity. Tau# = 2.11; Ch weight	$\begin{array}{c} \mbox{mmoll} \underline{I} \ \ \mbox{SD} \ (mmoll) \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 4.6 & 0 \\ 5.2 & 0 \\ 9.0 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	9 14 4 26 9 10 4 9 8 10 69 <u>Total M</u> 11 26 9 46 0.04); I ^a =	Mean [mmolt] 5 5 5 5 4.8 5.1 PLACEB0 PLACEBO	1.2 0.3 0.7 0.2 1.1 kg/m2] TC 4.6 1.6	2 12 3 12 12 9 9 9 12 55 55 55 55 55 55 55 55 55 5	4 1% 53.2% 5.6% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 0.0% 0.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.90] -0.00 [-0.17, 0.16] -0.00 [-0.1	-0.5 -0.25 0.5 0.5 Favours (FMT) Favours (PLACEBO) Mean Difference IV, Random, 95% CI (kg/m2)
Total cholesterol dy or Subgroup Mean [m Moura Mean [m ste 2017 Mean [m its 2018 2020 al (95% Cl) Terogeneity: Chi# = 3.79, df = tf toroverall effect: Z = 0.04 (BMI udy or Subgroup Mean [l operatil 2019 tota 2017 tota 2017 terogeneity: Tsu* = 2.11; Ch tef for overall effect: Z = 0.81 Weight Weight Weight 2019 udy or Subgroup Mean [l gerefti 2019 11	$\begin{array}{c} \text{nmoll} & \text{SD} [\text{nmmoll} \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 6.6 & 0 \\ 5.2 & 0 \\ \hline 4.6 & 0 \\ 5.2 & 0 \\ \hline 4.6 & 0 \\ 5.2 & 0 \\ \hline 9.0.37 \\ \hline \\ FMT \\ \hline \\ \frac{\text{FMT}}{\text{SD}[\text{Kg}(\text{m2})]} \\ \hline 5.0 \\ \frac{\text{Kg}(\text{m2})}{33.6} \\ 0.8 \\ 33.6 & 0.8 \\ 35.6 & 1.4 \\ \hline \\ \mu^{\text{e}} = 6.58, \ \text{df} = 2 \ (\text{P} = 0.42) \\ \hline \\ \hline \\ FMT \\ \hline \\ \frac{\text{Kg}}{\text{KM}} \\ \hline \\ \frac{\text{Kg}}{\text{SD}[\text{Kg}]} \\ \hline \\ \text{Total} \\ 3.8 & 22.8 & 11 \\ \hline \end{array}$	9 14 4 26 9 10 4 9 8 10 69 <u>Total 8</u> 11 26 9 46 0.04); P = F <u>Mean [k</u> 110	Mean [mmolt] 5 5 5 4.8 5.1 9 4.8 5.1 4.8 5.1 4.8 5.1 4.8 5.1 4.8 5.1 40.4 38.1 35.7 70% LACEBO 2] SD [kg] Total 1 19.1 11	1.2 0.3 0.7 0.2 1.1 0 <u>kgim2) Tc</u> 4.6 2.6 1.6 1.6 <u>Weight 1</u> 18.6%	2 12 3 12 12 12 12 12 12 12 12 55 55 55 55 55 55 55 55 55 5	4.1% 5.8% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 1000 1000	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.10 [+1.49, 1.29] -0.85 [-2.90, 1.20] -0.85 [-2.90, 1.20] -0.95 [-2.90, 1.20] -0.9	-0.5 -0.25 0.5 Favours (FMT) Favours (FLACEBO) Mean Difference IV, Random, 95% CI (kg/m2)
Total cholesterol udy or Subgroup Mean [m Moura Moura otle 2017 Mean [m tis 2018 2020 zal (95% CI) Terogeneity: Chi# = 3.79, df = terogeneity: Chi# = 3.79, df = St for overall effect: Z = 0.04 (BMI udy or Subgroup Mean [l udy or Subgroup Mean [l tote 2017 St for overall effect: Z = 0.14 (BKI udy or Subgroup Mean [l udy or Subgroup Mean [l St for overall effect: Z = 0.14 (Weight Verall Mean [l udy or Subgroup Mean [l Mean [l udy or Subgroup Mean [l Mean [l udy or Subgroup Mean [l St for overall effect Z = 0.11 (udy or Subgroup Mean [l St for overall effect Z = 0.11 (udy or Subgroup Mean [l St for overall effect Z = 0.11 (udy or Subgroup Mean [l St for overall effect Z = 0.11 (udy or Subgroup 1 St for overall effect Z = 0.11 ($\begin{array}{c} \text{nmoll} & \text{SD [nmoll}\\ \hline 4.7 & 0.0\\ 5.4 & 0.5\\ 5.3 & 0.0\\ 5.2 & 0.0\\ 5.2 & 0.0\\ 5.2 & 0.0\\ 5.2 & 0.0\\ 6.5 & 0.0\\ 7.0 & 0.0\\$	9 14 4 26 9 10 4 9 8 10 69 0.04), I ^a = 46 0.04), I ^a = <u>8</u> 46 0.04), I ^a = <u>11</u> 11 11 11 11 11 11 11 11 11 11 11 11	Mean [mmolt] 5 5 5 4.8 5.1 PLACEB0 10.1 3.57 70%	1.2 0.3 0.7 0.2 1.1 0 kg/m2] Tc 4.6 2.6 1.6 1.6 3.4% 3.3,3%	2 12 3 12 2 9 12 55 55 55 55 55 55 55 55 55 5	4 1% 53.2% 5.6% 32.7% 4.4% 100.0% 100.0% eight IV. Ri 7.4% 0.0% 0.0% 0.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.120] -0.00 [+0.120] -0.05 [+0.20] -0.85 [+0.20	-0.5 -0.25 0.5 Favours (FMT) Favours (FLACEBO) Mean Difference IV, Random, 95% CI (kg/m2)
Total cholesterol idy or Subgroup Mean [m Moura Moura otte 2017 Mean [m ibs 2018 2020 z020 Z020 tal (95% CI) Errogeneity: Chi# = 3.79, df = terogeneity: Chi# = 3.79, df = Stor overall effect: Z = 0.04 (C BMI Moura tudy or Subgroup Mean [l tody or Subgroup Mean [l tody or Subgroup Mean [l terogeneity: Tau* = 2.11; Ch Stof for overail effect: Z = 0.81 Weight Weight Mean [l day or Subgroup Mean [l egretti 2019 11 offec 2017 1 zez 2012 1 2020 1	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	9 14 4 26 9 10 4 9 8 10 69 <u>Total 8</u> 11 26 9 46 0.04); I ^a = F <u>Mean (k</u> 110 110	Mean [mmolt] 5 53 53 53 5 5 4.8 5.1 4.8 5.1 40.4 36.1 35.7 70% LACEBO 2) SD[kg] Total 1 19.1 11 1 5.2 12 3 7 9 1 20 12	1.2 0.3 0.7 0.2 1.1 0 <u>kg/m2] Tc</u> 4.6 1.6 1.6 3.3.4% 3.3.4% 3.1.3%	2 12 3 12 1 10 2 9 1 2 55 55 55 55 55 55 55 55 55 5	4 1% 53 2% 5.6% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.17, 0.16] -0.00 [+0.120] -0.00 [+0.120] -0.05 [+0.20] -0.85 [+0.20	-0.5 -0.25 0.5 Favours (FMT) Favours (FLACEBO) Mean Difference IV, Random, 95% CI (kg/m2)
Total cholesterol udy or Subgroup Mean [m Moura Moura otte 2017 Mean [m Miss 2018 2220 2020 Tail (95% C) terogeneity: Chi#= 3.79, df = 3.79, df = st for overall effect: Z = 0.04 (BMI tudy or Subgroup Mean [n legretti 2019 Dotte 2017 botte 2017 Dotte 2017 botte 2017 Dotte 2017 bret orgeneity: Tau*= 2.11; Ch Setrogeneity: Tau*= 2.11; Ch terogeneity: Tau*= 2.11; Ch Setrogeneity: Tau*= 2.11; Ch veright udy or Subgroup Mean [n udy or Subgroup Mean [n Tote 2012 1 othe 2017 1 cudy or Subgroup Mean [n 2020 1 tot (95% Cl) 1	$\begin{array}{c} \mbox{model} \underline{I} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	9 14 4 26 9 10 4 9 8 10 69 700 46 9 46 46 46 8 9 8 46 10 11 11 12 11 11 11 11 11 11 11 11 11 11	Mean [mmolt] 5 5 5 4.8 5.1 PLACEB0 lean [kg]m2] 5D] 40.4 36.1 35.7 70% LACEBO 1 19.1 11 1 19.1 11 1 15.2 12 3 7 9 1 20 12 44	1.2 0.3 0.7 0.2 1.1 0 kg/m2] Tc 4.6 2.6 1.6 1.6 3.4% 3.3,3%	2 12 3 12 1 10 2 9 1 2 55 55 55 55 55 55 55 55 55 5	4 1% 53.2% 5.6% 32.7% 4.4% 100.0% 100.0% eight IV. Ri 7.4% 0.0% 0.0% 0.0%	-0.30 [-1 13, 0.53] ← 0.10 [-0.13, 0.33] 0.30 [-0.41, 1.01] -0.20 [-0.49, 0.09] 0.10 [-0.70, 0.80] -0.00 [-0.17, 0.16] Mean Difference Indom, 95% CI [kg/m2] 1.20 [-2.81, 5.21] -2.50 [-4.00, -1.00] -0.10 [-1.49, 1.29] -0.85 [-2.90, 1.20] Mean [kg] IV, Randou 1.28] -5.62] 2.69]	-0.5 -0.25 0 0.25 0.5 Favours (FMT] Favours (FLACEBO) Mean Difference IV, Random, 95% CI (kg/m2) -4 -2 0 2 4 Favours (FMT] Favours (FIMT) Difference m, 95% CI (kg)
Total cholesterol udy or Subgroup Mean [n] whoura Noura volte 2017 Noura his 2018 Image: Subgroup leze 2012 10202 vali (95% Cl) Image: Subgroup terogeneity: Chil* = 3.79, df = stor overall effect: Z = 0.04 (dr) BMI tudy or Subgroup Mean [l] tudy or Subgroup Mean [l] legrestic 2019 otal (95% Cl) Image: Subgroup Mean [l] legrestic 2012 1 stor overall effect: Z = 0.81 Weight tudy or Subgroup Mean [l] udy or Subgroup Mean [l] ieze 2012 total (95% Cl) 1 stor overall effect: Z = 0.81 Weight tudy or Subgroup Mean [l] total (95% Cl) 1 stor overall effect: Z = 0.7 total (95% Cl) tetor overall effect: Z = 0.7 1 tetor overall effect: Z = 0.7 1 stor overall effect: Z = 0.7	$\begin{array}{c} \text{nmoll} & \text{SD} [\text{nmoll} \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 6.5 & 0 \\ 5.2 & 0 \\ \hline 5.2 & 0 \\ \hline 6.5 & 0 \\ \hline 6.5 & 0 \\ \hline 7.5 & 0 \\ \hline $	9 14 4 26 9 10 4 9 8 10 69 700 46 9 46 46 46 8 9 8 46 10 11 11 12 11 11 11 11 11 11 11 11 11 11	Mean [mmolt] 5 5 5 4.8 5.1 PLACEB0 lean [kg]m2] 5D] 40.4 36.1 35.7 70% LACEBO 1 19.1 11 1 19.1 11 1 15.2 12 3 7 9 1 20 12 44	1.2 0.3 0.7 0.2 1.1 0 <u>kg/m2] Tc</u> 4.6 1.6 1.6 3.3.4% 3.3.4% 3.1.3%	2 12 3 12 1 10 2 9 1 2 55 55 55 55 55 55 55 55 55 5	4 1% 53 2% 5.6% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.90] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.10 [+1.49, 1.29] -0.85 [-2.90, 1.20] -0.85 [-2.90, 1.20] -0.95 [-2.9	-0.5 -0.25 0.0.25 0.5 Favours (FMT) Favours (FLACEBO) Mean Difference IV, Random, 95% CI (kg/m2) -4 -2 0.2 4 Favours (FMT) Favours (FLAT) Difference
Total cholesterol udy or Subgroup Mean [m whora Mean [n softe 2017 Mis 2018 leze 2012 1 12020 Nat (95% C) eterogeneity: Chill= 3.79, df = 3.79, df = staf (95% C) eterogeneity: Chill= 3.79, df = ital (95% C) eterogeneity: Tau? = 2.11; Chill itedrogeneity: Tau? = 2.11; Chill eterogeneity: Tau? = 2.11; Chill teterogeneity: Tau? = 2.11; Chill eterogeneity: Tau? = 2.11; Chill otal (95% C) eterogeneity: Tau? = 2.11; Chill tudy or Subgroup Mean [n u2020 11 otatic 12 otatic 12 otatic 12 otatic 12 otatic 1	$\begin{array}{c} \text{nmoll} & \text{SD} [\text{nmoll} \\ \hline 4.7 & 0 \\ 5.4 & 0 \\ 5.3 & 0 \\ 6.5 & 0 \\ 5.2 & 0 \\ \hline 5.2 & 0 \\ \hline 6.5 & 0 \\ \hline 6.5 & 0 \\ \hline 7.5 & 0 \\ \hline $	9 14 4 26 9 10 4 9 8 10 69 700 46 9 46 46 46 8 9 8 46 10 11 11 12 11 11 11 11 11 11 11 11 11 11	Mean [mmolt] 5 5 5 4.8 5.1 PLACEB0 lean [kg]m2] 5D] 40.4 36.1 35.7 70% LACEBO 1 19.1 11 1 19.1 11 1 15.2 12 3 7 9 1 20 12 44	1.2 0.3 0.7 0.2 1.1 0 <u>kg/m2] Tc</u> 4.6 1.6 1.6 3.3.4% 3.3.4% 3.1.3%	2 12 3 12 1 10 2 9 1 2 55 55 55 55 55 55 55 55 55 5	4 1% 53 2% 5.6% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.90] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.00 [-0.17, 0.16] -0.10 [+1.49, 1.29] -0.85 [-2.90, 1.20] -0.85 [-2.90, 1.20] -0.95 [-2.9	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (FMT) Mean Difference IV, Random, 95% CI (kg) 4 -2 0 2 4 Favours (FMT) Favours (FMT) Difference m, 95% CI (kg) 0 10 20
Total cholesterol udy or Subgroup Mean [m whora Moura vote 2017 Mean [m is 2018 Jack Jeze 2012 Jack Jobe Jack Jack Strain Merogeneity Chil# = 3.79, df = Jest for overall effect: Z = 0.04 (d) Mean [m Miggretti Mean [m Merogeneity Chil# = 2.11; Ch Jobt 2017 Integretti 2019 ootle 2017 Integretti 2019 Jobt 2018 Mean [m Merogenty Subgroup Mean [m Ilegretti 2019 Integretti 2019 Integretti 2019 Jobt 2017 1 Jack Jack VWeight Mean [m Integretti 2019 Integretti 2019 Jobt 2017 1 Jack Jack Jack Jobt 2017 1 Jack Jack Jack Jobt 2017 1 Jack Jack Jack Jack Jobt 105% Ch) Hotheeral effect: Z = 0.	$\begin{array}{c} \mbox{model} J $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $	9 14 26 9 10 4 26 9 10 4 9 6 10 69 6 9 6 9 11 12 26 9 9 46 0.04); * = * * * * * * * * * * * * * * * * * *	Mean [mmolt] S 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 9 104 35.7 70% LACEBO 1 2) SD [kg] 1 19.1 1 5.2 2 50 1 20 1 20 2 44 ; P= 88% Mean I	1.2 0.3 0.7 0.2 1.1 <u>kg/m2] Tc</u> 4.6 2.6 1.6 1.6 1.6 3.3,4% 31,3% 100.0%	2 12 3 12 3 12 5 10 2 9 1 12 55 55 55 55 55 55 55 55 55 5	4 1% 53.2% 56% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.33] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.30] -0.00 [-0.17, 0.16] -0.00 [-0.1	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (FMT) Mean Difference IV, Random, 95% CI (kg) 4 -2 0 2 4 Favours (FMT) Favours (FMT) Difference m, 95% CI (kg) 0 10 20
Total cholesterol udy or Subgroup Mean [n] volte Noura volte Noura volte 2017 his 2018 Image: Second Secon	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	9 14 26 9 10 4 26 9 10 6 9 10 6 9 10 6 9 10 6 9 4 11 25 9 46 0.004/, P = 110 11 11 12 11 12 11 12 11 12 12 12 10 12 11 12 12 12 12 12 12 12 12 12 12 12	Mean [mmoit] S S S S S S S S S S S S S S	0 weight 1 18.6% 33.4% 31.3% 100.0%	2 12 3 12 3 12 9 12 55 55 55 55 55 55 55 55 55 5	4 1% 53.2% 56% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.53] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.80] -0.00 [-0.17, 0.16] Mean Difference Indom, 95% CI [Kg/m2] 1.20 [+2.61, 5.21] -2.50 [+4.00, -1.00] -0.10 [+1.49, 1.29] -0.85 [-2.90, 1.20] Mean [Kg] V. Randol 1.28] -20 [-0 Favours [FM]	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (FMT) Difference m. 95% CI (kg) 0 10 20
Total cholesterol udy or Subgroup Mean [m volte 2017 Nota hs2018 12020 izez 2012 12020 variat (95% C) Stor overall effect: Z = 0.04 (d) PBMI 1000 tudy or Subgroup Mean [m liegrett 2019 0017 nicz 2012 0018 (d) oothe 2017 10000 nicz 2012 0019 oothe 2017 11 nicz 2012 11 tudy or Subgroup Mean [m nicz 2012 11 tudy or Subgroup Mean [m tudy or Subgroup Mean [m tudy or Subgroup Mean [m tudy or Subgroup 11 tudy or Subgroup 12 tudy or Subgroup 12 tudy or Subgroup	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	9 14 26 9 10 4 26 9 10 6 9 10 6 9 10 6 9 10 6 9 11 12 26 9 9 46 0.04), I ^a = 10 0.04), I ^a = 11 11 22 14 11 11 24 0.0001 25 00 50 Tota 2.7 11 1 2.5 3 11	Mean [mmolt] S 5 5 5 4.8 5.1 PLACEBI tean [kgim2] SD 40.4 35.7 70% LACEBO 2) SD [kg] Total 1 19.1 11 1 52.2 12 3 7 9 1 20 12 3 7 9 1 20 12 3 4 Kgi Rean [Weight IV, Ram 20.5% 0.50 8.9% -1.40	0 kg/m2] Tc 4.6 2.6 1.6 Weight 18.6% 33.4% 31.3% 16.6% 100.0% Mifference dom, 95% C [-1.42, 2.42 [-4.49, 2.14]	2 12 2 7 10 2 9 12 55 55 Mean 11 17 2 40 9 42 32 100 Mean 3.7 -7.0 9 3.0 3.0 1.0 1.0	4 1% 53.2% 56% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.33] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.30] -0.00 [-0.17, 0.16] -0.00 [-0.1	-0.5 -0.25 0 0.25 0.5 Favours (FMT) Favours (FMT) Difference m. 95% CI (kg) 0 10 20
Total cholesterol udy or Subgroup Mean [n udy or Subgroup Mean [n whora Note softe 2017 Note visco 2012 vicco 2012 vicco 2012 vicco 1000 victo 1000 victo 1000 Mall 195% CI) eterogeneity: Chi ^a = 3.79, df = victo 9 BMI tidudy or Subgroup Mean [l victo 1000 victo 2012 otal (95% CI) 10000 vieterogeneity: Tau ² = 2.11; Ch elf or overail effect: Z = 0.81 vieterogeneity: Tau ² = 2.11; Ch elf or overail effect: Z = 0.21 vieterogeneity: Tau ² = 94.21; C elf or overail effect: Z = 0.22 HOMA-IR Fi tudy or Subgroup Mean liegretti 2019 3.7	$\begin{array}{c} \underline{\text{mmoll}} & \underline{\text{SD}} [\text{mmoll}} \\ 4.7 & 0.0 \\ 5.4 & 0.0 \\ 5.3 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 1.6 & 0.0 \\$	9 14 26 9 10 4 26 9 10 4 9 69 10 69 69 11 26 9 46 0.04), P= F Mean [k0 10 11 12 26 0.04), P= F F Mean [k0 11 12 26 0.0001 12 11 12 26 0.0001 12 11 12 26 10 9 10 10 10 10 10 10 10 10 10 10 10 10 10	Mean [mmolt] S 5 5 5 5 4.8 5.1 40.4 36.1 35.7 70% LACEBO 20 2) SD [kg] Total 1 19.1 1 20 2 70 3 7 91 20 20 12 44 44 3,7 9 1 20 12 20 12 44 Weight IV, Ram 20.5 % 0.50 8.9 % -1.20	0 kg/m2) Tc kg/m2) Tc kg/m2) Tc 1.1 0 1.1 1.1 0 1.1 0 1.1 0 1.1 0 0 1.1 0 0 1.1 0 0 0 0 0 0 0 0 0 0 0 0 0	2 12 2 7 12 7 7 10 2 9 12 55 55 55 55 55 55 55 55 55 55 55 55 55	4 1% 53.2% 56% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.33] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.30] -0.00 [-0.17, 0.16] -0.00 [-0.1	-0.5 -0.25 0.5 0.5 Favours (FMT) Favours (FMT) Favours (FMT) -1 -2 -2 -4 -2 0 2 4 Favours (FMT) Favours (FMT) Favours (FMT) Difference m. 95% CI (kg)
Total cholesterol udy or Subgroup Mean [n vibura Noura vibura Noura vibura Noura vibura 1017 lisz 2010 1012 vibura Mean [n vibura Nean [n vibura	$\begin{array}{c} \underline{\text{mmoll}} & \underline{\text{SD}} [\text{mmoll}} \\ 4.7 & 0.0 \\ 5.4 & 0.0 \\ 5.3 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 4.6 & 0.0 \\ 5.2 & 0.0 \\ 1.6 & 0.0 \\$	9 14 26 9 10 4 26 9 10 4 9 69 69 69 7004 9 69 46 0.04), P= F Mean (ki 10 10 11 26 9 46 0.04), P= F F Mean (ki 10 11 12 12 12 11 12 12 12 11 12 12 12 12	Mean [mmolt] 5 53 53 53 53 5 4.8 5.1 PLACEB0 ean [kg]m2 5D] 40.4 36.1 35.7 70% LACEBO 2) 5D [kg] Total 1 19.1 11 1 5.2 12 3 7 9 1 20 12 1 20 12 1 20 12 44 ; F = 86% Mean 1 20.5% 0.50 8.9% -1.20 30.7% 0.50	0 kg/m2] Tc kg/m2] Tc kg/m2] Tc 4.6 2.6 1.6 18.6% 31.3% 18.6% 100.0% Mfference 6% 100.0%	2 12 2 7 12 7 7 10 2 9 12 55 55 55 55 55 55 55 55 55 55 55 55 55	4 1% 53.2% 56% 32.7% 4.4% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	-0.30 [+13, 0.33] ← 0.10 [+0.13, 0.33] 0.30 [+0.41, 1.01] -0.20 [+0.49, 0.09] 0.10 [+0.70, 0.30] -0.00 [-0.17, 0.16] -0.00 [-0.1	-0.5 -0.25 0.5 0.5 Favours (FMT) Favours (FMT) Favours (FMT) -1 -2 -2 -4 -2 0 2 4 Favours (FMT) Favours (FMT) Favours (FMT) Difference m. 95% CI (kg)

		FMT				Plac						ean Difference)ifference	
Study or Subgroup Allegretti 2019	Mean [kg/m] -0	and the second s	(g/m2] 1.3	Total 11		m2] : 0.7	- Contraction of the local division of the l	12] T		Veight 50.8%	IV, Rai	dom, 95% CI [kg/mi 0.40 (-0.70, 1.5)		IV, Random,	95% CI [kg	m2]
De Moura 2019	-0.		0.9	11		1.5		1.2		49.2%		-1.10 [-2.26, 0.0		-		
Total (95% CI)				23					15 1	00.0%		-0.34 [-1.81, 1.13	3]	-	-	
Heterogeneity: Tau² = Test for overall effect:			1 (P = 0	.07); I² =	= 71%								-10 Favou	-5 rs [PLACEBO	0] Favours	5 10 [FMT]
3) Hip width red		MT			Placebo	0			M	ean Diffe	rence		Mean Differ	ence		
Study or Subgroup	Mean [cm]] Total	Mean			Total \	Neigh		ixed, 95		m] P	V, Fixed, 95%			
Allegretti 2019 De Moura 2019	-1.25 4.3	10 6.3			1 4.2	2.5 4.3		39.59 60.59		-2.25 [-8 0.10 [-4				_		
Total (95% CI) Heterogeneity: Chi² = Test for overall effect:			23 I² = 0%				15	100.09	•	-0.83 [-4	1.68, 3.	-10	-5 0		l	
												Favours [Pl	LACEBO] Fa	vours [FMT]		
C) Weight	FI	π			Placebo				Mean	Differer	nce	M	ean Differenc	e		
Study or Subgroup	Mean [kg]	SD [kg]			kg] SD [k				IV, Fixe	ed, 95% (CI [kg]		ixed, 95% CI [
Allegretti 2019 De Moura 2019	113.7 91.1	23.2	11 13		0.6 18			.9%		[-15.35,						
De Moura 2019 Yu 2020	91.1	9.2 27	13					.4% .7%		20 (-8.64 (-19.24,						
Total (95% CI)			35				30 100	.0%	0.3	82 [-6.81	, 7.45]		-			
Heterogeneity: Chi [#] = Test for overall effect			l ^a = 0%									-20 -10 Favours	(FMT) Favou	10 20 rs [PLACEBO	1	
D) HbA1c		FM	т				P	laceb	0			Mean	Difference		M	ean Differend
Study or Subgroup	Mean [mmol	/mol] S		l/mol]		an (m	mol/mol] SD		_	otal	Weight IV, Fixed, 9				l, 95% CI [mn
Allegretti 2019		38														
				4	11		3			3	9	47.3%	1.00 [-2.07, 4			
/u 2020		36		4	11 11		3.			3			1.00 [-2.07, 4 -1.00 [-3.91, 1			-
/u 2020 Fotal (95% CI)		36		4							12	52.7%		.91]		-
/u 2020		36 = 0.35);	lª = 0%	4	11						12	52.7%	-1.00 (-3.91, 1	.91]	-10 Favours	5 0 5 [FMT] Favou
/u 2020 Fotal (95% CI) Heterogeneity: Chi ² =	Z = 0.05 (P = 0	36 = 0.35);).96)	lª = 0%	4	11		3				12 21	52.7%	-1.00 (-3.91, 1	.91] .06]	Favours	
ru 2020 Fotal (95% CI) Heterogeneity: Chi ² = Fest for overall effect: E) LDL cholester	Z= 0.05 (P= 0	36 = 0.35);).96) FMT		4 4	11 22		3	7	Total	3	12 21	52.7% 100.0% Jean Difference	-1.00 (-3.91, 1 -0.05 (-2.17, 2	.91] .06] Mean D	Favours	[FMT] Favou
ru 2020 Fotal (95% CI) Heterogeneity: Chi ^a = Fest for overall effect: E) LDL cholester Study or Subgroup	Z = 0.05 (P = 0 ol Mean [mmol	36 = 0.35);).96) FMT I/I] SD [I	mmol/I]		11 22	mol/IJ	3	7 nol/1]		3 Weight	12 21 <u>N</u>	52.7% 100.0% Jean Difference ixed, 95% CI [mmol/	-1.00 (-3.91, 1 -0.05 (-2.17, 2 I)	.91] .06]	Favours	[FMT] Favou
Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Child Cholestero Study or Subgroup Allegretti 2019 Yu 2020	Z = 0.05 (P = 0 ol Mean [mmo] 5	36 = 0.35);).96) FMT		11 11	11 22		3	7	9 12	3 Weight 16.2% 83.8%	12 21 <u>12</u>	52.7% 100.0% Iean Difference <u>ixed, 95% CI [mmol/</u> -0.40 [-1.91, 1.11 -0.30 [-0.96, 0.36	-1.00 [-3.91, 1 -0.05 [-2.17, 2 0 0)]	.91] .06] Mean D	Favours	[FMT] Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi ^a = Test for overall effect: E) LDL cholester Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI)	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2	36 = 0.35);).96) FMT I/I] SD [J i.8 2.9	<u>mmol/[]</u> 2.3 0.9	11	11 22	mol/I] 6.2	3	7 nol/l] 1	9 12	3 Weight 16.2%	12 21 <u>12</u>	52.7% 100.0% Iean Difference ixed, 95% CI [mmol/ -0.40 [-1.91, 1.11	-1.00 [-3.91, 1 -0.05 [-2.17, 2 0 0)]	.91] .06] Mean D	Favours	[FMT] Favou
Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Child Cholestero Study or Subgroup Allegretti 2019 Yu 2020	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P	36 = 0.35);).96) FMT I/I] SD [J i.8 2.9 = 0.91);	<u>mmol/[]</u> 2.3 0.9	11 11	11 22	mol/I] 6.2	3	7 nol/l] 1	9 12	3 Weight 16.2% 83.8%	12 21 <u>12</u>	52.7% 100.0% Iean Difference <u>ixed, 95% CI [mmol/</u> -0.40 [-1.91, 1.11 -0.30 [-0.96, 0.36	-1.00 [-3.91, 1 -0.05 [-2.17, 2 0 0 0 0 0 0 0 0 0 0 0 -2	.91] .06] Mean D	Favours hifference 5% CI (mmo	(FMT) Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi ² = Fest for overall effect: C) LDL cholester Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi ² =	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0	36 = 0.35);).96) FMT i.8 2.9 = 0.91);).31)	<u>mmol/[]</u> 2.3 0.9	11 11	11 22	mol/] 6.2 3.2	3. Icebo SD [mr	7 nol/l] 1	9 12	3 Weight 16.2% 83.8%	12 21	52.7% 100.0% 1ean Difference 1xed, 95% CI [mmol/ -0.40 [+1.91, 1.11 -0.30 [-0.96, 0.36 -0.32 [-0.92, 0.25	-1.00 [-3.91, 1 -0.05 [-2.17, 2 0 0 0 0 0 0 0 0 0 0 0 -2	.91] .06] .V, Fixed, 95 	Favours ifference 5% CI [mmo 0 0 Favours [(FMT) Favou
Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Child Cholestern Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity. Chi ² = Test for overall effect: Child Cholester	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol	36 = 0.35);).96) FMT M] SD [J i.8 2.9 = 0.91); 0.31) FMT	<u>mmol/I]</u> 2.3 0.9 I*= 0%	11 11 22	11 22 Mean [mr	mol/1] 6.2 3.2 Pla	3. Icebo <u>SD [mr</u>	7 <u>nol/i]</u> 1 0.7	9 12 21	3 Weight 16.2% 83.8% 100.0%	12 21	52.7% 100.0% Nean Difference <u>xed, 95% CI (mmol/</u> -0.40 [-1.91, 1.11 -0.30 [-0.96, 0.36 -0.32 [-0.92, 0.25 Nean Difference	-1.00 [3.91, 1 -0.05 [-2.17, 2 0 0 1] -2 1 1	.91] .06] IV, Fixed, 99 -1 -1 Favours [FMT] Mean D	Favours ifference 5% CI [mmo 0 0 Favours [bifference	(FMT) Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi ^a = Test for overall effect: E) LDL cholesteri Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi ^a = Test for overall effect:	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0	36 = 0.35);).96) FMT M] SD [J i.8 2.9 = 0.91); 0.31) FMT	<u>mmol/I]</u> 2.3 0.9 I*= 0%	11 11 22	11 22 Mean [mr	mol/1] 6.2 3.2 Pla	3. Icebo <u>SD [mr</u>	7 <u>nol/i]</u> 1 0.7	9 12 21	3 Weight 16.2% 83.8% 100.0% Weight	12 21 t IV, F	52.7% 100.0% 1ean Difference 1xed, 95% CI [mmol/ -0.40 [+1.91, 1.11 -0.30 [-0.96, 0.36 -0.32 [-0.92, 0.29 10.32 [-0.92, 0.29 Mean Difference 1xed, 95% CI [mmol/	-1.00 [3.91, 1 0.05 [-2.17, 2 0] 1] -2 1] 1] -2 1 1]	.91] .06] .V, Fixed, 95 	Favours ifference 5% CI [mmo 0 0 Favours [bifference	(FMT) Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi [#] = Test for overall effect: E) LDL cholestern Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi [#] = Test for overall effect: E) HDL cholester Study or Subgroup Allegretti 2019 Yu 2020	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol <u>Mean [mmo</u>	36 = 0.35); .0.96) FMT .0.9 = 0.91); 0.31) FMT .0.9 S.10 FMT .0.9 S.11	<u>mmol/I]</u> 2.3 0.9 * = 0% mmol/I]	11 11 22 Total 11 11	11 22 <u>Mean (mi</u> <u>Mean (mi</u>	mol/1] 6.2 3.2 Pla mol/1]	3. Icebo <u>SD [mr</u>	7 nol/i] 1 0.7 nol/i]	9 12 21 <u>Total</u> 9 12	3 Weight 16.2% 83.8% 100.0% Weight 20.3% 79.7%	12 21 t IV, F	52.7% 100.0%	-1.00 [3.91, 1 -0.05 [-2.17, 2)) -2) 1 -2) 1 -2) 1 -2) 1 -2) 1 -2)	.91] .06] IV, Fixed, 99 -1 -1 Favours [FMT] Mean D	Favours ifference 5% CI [mmo 0 0 Favours [bifference	(FMT) Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi ^a = Fest for overall effect: E) LDL cholester Study or Subgroup Allegretti 2019 Yu 2020 Fotal (95% CI) Heterogeneity: Chi ^a = Fest for overall effect: E) HDL cholester Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Total (95% CI)	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol <u>Mean [mmo</u> 1	36 = 0.35);).96) FMT <u>IU] SD [</u> i.8 2.9 = 0.91); 0.31) FMT IU] SD [3 3 .3	<u>mmol/1]</u> 2.3 0.9 I [#] = 0% <u>mmol/1]</u> 0.7 0.3	11 11 22 <u>Total</u> 11	11 22 <u>Mean (mi</u> <u>Mean (mi</u>	mol/1] 6.2 3.2 Pla mol/1] 2.7	3. Icebo <u>SD [mr</u>	7 nol/i] 1 0.7 <u>nol/i]</u> 0.6	9 12 21 <u>Total</u> 9 12	3 Weight 16.2% 83.8% 100.0% Weight 20.3%	12 21 t IV, F	52.7% 100.0% 1ean Difference ixed, 95% CI [mmol/ -0.40 [-1.91, 1.11 -0.30 [-0.96, 0.36 -0.32 [-0.92, 0.25 10.32 [-0.92, 0.25 10.30 [-0.27, 0.8]	-1.00 [3.91, 1 -0.05 [-2.17, 2)) -2) 1 -2) 1 -2) 1 -2) 1 -2) 1 -2)	.91] .06] IV, Fixed, 99 -1 -1 Favours [FMT] Mean D	Favours ifference 5% CI [mmo 0 0 Favours [bifference	(FMT) Favou
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Yu 2020 Fotal (95% CI) Heterogeneity: Chi ² = Test for overall effect: E) LDL cholestern Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Chi ² = Total (95% CI)	Z = 0.05 (P = 0 ol <u>Mean [mmol</u> 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol <u>Mean [mmo</u> 1 0.09, df = 1 (P Z = 1.68 (P = 0	36 = 0.35); .96) FMT <u>INJ SD [iv</u> .9 = 0.91); .9 = 0.91); .3 3 .3 = 0.91); .3 3 .3 = 0.76); .0.09) FMT	<u>mmol/1]</u> 2.3 0.9 ² = 0% <u>mmol/1]</u> 0.7 0.3 ² = 0%	11 11 22 <u>Total</u> 11 11 22	11 22 <u>Mean (mi</u>	mol/I] 6.2 3.2 Pla mol/I] 2.7 1.1	3: icebo <u>SD [mr</u> scebo <u>SD [mr</u>	7 <u>nol/1]</u> 1 0.7 <u>nol/1]</u> 0.6 0.4	9 12 21 <u>Total</u> 9 12 21	3 Weight 16.2% 83.8% 100.0% Weight 20.3% 79.7% 100.0%	12 21 t IV, F	52.7% 100.0%	-1.00 [3.91, 1 -0.05 [-2.17, 2 0 1 -2 1 -2 1 -2 1 Favou	.91] Mean D IV, Fixed, 95 Favours (FMT) Mean D IV, Fixed, 95 -0.5 s (PLACEBO Mean D	Favours ifference 5% CI [mmo 0 1 Favours [0 0 0 0 1 Favours [0 0 0 0 0 0 0 0 0 0 0 0 0	(FMT] Favou
Yu 2020 Fotal (95% CI) Heterogeneity: Chi [#] = Fest for overall effect: E) LDL cholester Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi [#] = Fest for overall effect: Chilegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi [#] = Test for overall effect: G) Triglycerides Study or Subgroup	Z = 0.05 (P = 0 ol Mean [mmol 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol 1 0.09, df = 1 (P Z = 1.68 (P = 0 Mean [mmol	36 = 0.35); .96) FMT mj SD [i .9 = 0.91); .9 = 0.91); .3 3 .3 = 0.76); 0.09) FMT mj SD [i .9 FMT sD [i .0 SD [i .0 S SD [i .0 SD [i .0 S SD [i .0 SD [i .0 S SD [i .0 S SD [] S SD [] S SD [] S SD [] S S SD [] S S SD [] S S SD []	<u>mmol/1]</u> 2.3 0.9 I ^P = 0% <u>mmol/1]</u> I ^P = 0% mmol/1]	11 11 22 <u>Total</u> 11 11 22 Total	11 22 <u>Mean (mi</u>	mol/I] 6.2 3.2 Pl/ mol/I] 2.7 1.1 Pl/ mol/I]	3: icebo <u>SD [mr</u> scebo <u>SD [mr</u>	7 <u>nol/1]</u> 1 0.7 0.6 0.4 0.4	9 12 21 <u>Total</u> 9 12 21 <u>Total</u>	3 Weight 16.2% 83.8% 100.0% Weight 100.0% Weight	12 21 <u>t IV, F</u>	52.7% 100.0%	-1.00 [3.91, 1 -0.05 [-2.17, 2 0 1]	Mean D IV, Fixed, 99 -1 -1 -1 Savours (FMT) Mean C IV, Fixed, 99 -0.5 s (PLACEBO	Favours ifference 5% CI [mmo 0 1 Favours [0 0 0 0 1 Favours [0 0 0 0 0 0 0 0 0 0 0 0 0	(FMT] Favou
Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Child Cholestern Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity. Chi ² = Test for overall effect: Child Cholestern Study or Subgroup Allegretti 2019 Yu 2020 Total (95% CI) Heterogeneity: Chi ² = Test for overall effect: Ci) Triglycerides Study or Subgroup Allegretti 2019 Yu 2020	Z = 0.05 (P = 0 ol Mean [mmoi 5 2 0.01, df = 1 (P Z = 1.02 (P = 0 rol 1 0.09, df = 1 (P Z = 1.68 (P = 0 2 1 0.09, df = 1 (P Z = 1.68 (P = 0 3 1 0.09, df = 1 (P Z = 1.68 (P = 0 3 1 0.09, df = 1 (P Z = 1.68 (P = 0 3 1 0.09, df = 1 (P Z = 1.68 (P = 0 3 1 0.09, df = 1 (P Z = 1.68 (P = 0 3 1 0.09, df = 1 (P Z = 1.02 (P = 0 3 1 0.09, df = 1 (P Z = 1.02 (P = 0 3 1 0.09, df = 1 (P Z = 1.02 (P = 0 3 1 0.09, df = 1 (P Z = 1.02 (P = 0 3 1 0.09, df = 1 (P Z = 1.02 (P = 0 3 1 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	36 = 0.35); .96) FMT <u>INJ SD [iv</u> .9 = 0.91); .9 = 0.91); .3 3 .3 = 0.91); .3 3 .3 = 0.76); .0.09) FMT	<u>mmol/1]</u> 2.3 0.9 ² = 0% <u>mmol/1]</u> 0.7 0.3 ² = 0%	11 11 22 <u>Total</u> 11 11 22 <u>Total</u> 11 11	11 22 <u>Mean (mi</u>	mol/I] 6.2 3.2 Pla mol/I] 2.7 1.1	3: icebo <u>SD [mr</u> scebo <u>SD [mr</u>	7 <u>nol/1]</u> 1 0.7 <u>nol/1]</u> 0.6 0.4	9 12 21 <u>Total</u> 9 12 21 <u>Total</u> 9 12	3 Weight 16.2% 83.8% 100.0% Weight 100.0% Weight 1.6% 98.4%	12 21 <u>t IV, F</u>	52.7% 100.0%	-1.00 [-3.91, 1 -0.05 [-2.17, 2 0 0 0 0 0 0 0 0 -2 1 7 1 3 1 7 1 3 1 7 1 3 1 7 1 3 1 7 1 3 1 7 1 9 1 7 1 9 1 7 1 9 1 7 1 9 1 9	.91] Mean D IV, Fixed, 95 Favours (FMT) Mean D IV, Fixed, 95 -0.5 s (PLACEBO Mean D	Favours ifference 5% CI [mmo 0 1 Favours [0 0 0 0 1 Favours [0 0 0 0 0 0 0 0 0 0 0 0 0	(FMT] Favou
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