# Effect of Fecal microbiotA Transplantation combined with MEditerranean Diet on insulin sensitivity in subjects with metabolic syndrome

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To study the effect of a Mediterranean diet (MD) followed by lean donor fecal microbiota transplantation (FMT) versus the prescription of Mediterranean diet (MD) followed by autologous (own) FMT in male subjects with metabolic syndrome on peripheral...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Glucose metabolism disorders (incl diabetes mellitus) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42899

**Source**
ToetsingOnline

**Brief title**
FATMED

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Metabolism disorders NEC

**Synonym**
Metabolic syndrome, obesity

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** ZONMW

## Intervention

**Keyword:** Fecal transplantation, Gut microbiota, Mediterranean diet

## Outcome measures

### Primary outcome

Primary endpoints are changes in fecal, intestinal (biopsies) and oral microbiota composition and (the relation to) peripheral /hepatic insulin sensitivity (stable isotope based hyperinsulinemic euglycemic clamp and resting energy expenditure) at baseline and 6 weeks.

### Secondary outcome

Secondary endpoints are changes in postprandial plasma lipids (mixed meal test) and subcutaneous adipose tissue inflammation (biopt) at baseline and 6 weeks.
Finally, we will study effect on plasma and 24 feces and 24 urine metabolites at baseline, after 3 and 6 weeks

# Study description

### Background summary

The prevalence of obesity and type 2 diabetes mellitus (DM) is rising at an alarming pace. Although many factors have been identified as partakers in the development of these diseases, the complete pathophysiological pathway is still not completely understood and moreover, effective therapeutic options seem even harder to establish.
Mounting evidence links altered fecal intestinal microbiota composition to the development of obesity, insulin resistance/type 2 diabetes mellitus and even cardiovascular disease. Previous research has shown that faecal microbiota transplantation of lean healthy donors improves insulin sensitivity. Moreover,

we recently published that engraftment of these beneficial bacterial strains from lean donor feces is not equally efficient in all metabolic syndrome subjects, and that this is related to the level of improvement in insulin sensitivity upon allogenic fecal transplantation (LI-Nieuwdorp, Science 2016). It seems that especially the recipient microbiota composition determines whether engraftment of the benificial donor bacteria takes place. We know that diet is of pivotal importance in gutmicrobiota composition and changes is diet can rapidly alter gut micriobiota composition. In particular the mediterranean diet has shown many benificial effect on health in previous research.
Based on these data, we hypothesize that prescription of a beneficial (Mediterranean) diet will enhance engraftment of beneficial donor intestinal bacteria upon lean donor FMT and will thus have a synergistic beneficial effect on (peripheral) insulin sensitivity and intestinal microbiota composition in subjects with metabolic syndrome. Furthermore, this therapeutic intervention study will help us in understanding host-microbiota interactions in human (glucose) metabolism and will hopefully help to dissect progression from benign to malign (insulin resistant) obesity and eventually type 2 diabetes mellitus.

## Study objective

To study the effect of a Mediterranean diet (MD) followed by lean donor fecal microbiota transplantation (FMT) versus the prescription of Mediterranean diet (MD) followed by autologous (own) FMT in male subjects with metabolic syndrome on peripheral insulin sensitivity and (small) intestinal microbiota composition

## Study design

This is a double blind randomized single centre trial in which we will randomize 24 male metabolic syndrome patients in 2 treatment arms:
- Mediterranean diet followed by allogenic lean donor FMT (n = 12)
- Mediterranean diet followed by autologous FMT (n = 12)

12 healthy lean male donors will be uses for the allogenic donor FMT

## Intervention

All patient will adhere to the mediterranean for the total duration of the study with guidance of a dietitian and/or investigator.

Patients will be treated with infusion of either allogenic (lean healthy donor) or autologous (their own) feces transplantation:

1. Morning stool sample (150-250 gram) is collected by recipient & donor and brought to AMC for processing

2. Randomization met syndrom subject for either allogenic or autologous feces transplantation
2. Gastro-duodenoscopy will be perfomed for positioning of duodenal tube; during the procedure mucosal biopsies from small intestine will be taken. Correct position of the tube is checked with an abdominal X-ray.
3. Thereafter, bowel lavage with 2-3 liters of Clean Prep through the duodenal tube (according to standard protocols) will be performed to ensure complete bowel lavage (duration 2-3 hours)
4. Finally, feces mixed in ~ 500 cc saline (filtered, < 6 hours after processing) will be infused in the duodenum through positioned duodenal tube.

**Study burden and risks**

Total duration of study will be 14 weeks, during which patients will visit AMC 7 times (total 35 hours and 390 ml blood will be drawn) Moreover, subjects with metabolic syndrome will be asked to follow mediterranean diet for 8 weeks.

- Fecal transplantation: No side effects of faecal transplantation have been reported in our previous trials. Because a strict screening protocol is applied to faeces donors at the AMC, the risk of spreading potential pathogens during faecal transplantation seems negligible and no long term effects have been reported at our clinic since 2007 (>500 faecal transplantations performed).
- Gastroduodenoscopy: The risk of bleeding or perforation of the biopsy site during gastroscopy is regarded as small. The placing of the duodenal tube can be an unpleasant experience for the subjects, but there are no risks involved.
- Hyperinsulinemic clamp: This is regarded as a save test.The placing of the intravenous cannula in our study can be an unpleasant experience for the subjects and it can cause a minor hematoma, which will resolve spontanously.
- Discomfort: the participants could experience minor discomfort from placind of the intravenous cannula, blood withdrawal, injection with lidocaine during subcutaneous adipose tissue biopsies or placement of duodenal tube during gastroduodenoscopy.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Patients: Male obese (BMI > 30) subjects 21 to 65 years-old
With at least 3 out of 5 metabolic syndrome criteria (fasting plasma glucose * 5.6 mmol/l, triglycerides * 1.7 mmol/l, waist-circumference > 102 cm, HDL-cholesterol < 1.04 mmol/l, blood pressure * 130/85 mmHg). ;Donors: caucasian, age 18 - 65 years old, BMI 18.5 - 25 kg/m2

## Exclusion criteria

Patients:
- Use of any medication, including proton pomp inhibitors and antibiotics in the past three months
- Cholecystectomy
- A history of cardiovascular event (MI or pacemaker implantation)
- (expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240).
- Unmotivated or not able to adhere to a specific diet;Exclusion criteria for donors:
1. diarrhoea
2. cholecystectomy
3. HIV, HAV, HBV, HCV, active CMV, active EBV
4. Unsafe sex practice (questionnaire)
5. presence of fecal bacterial pathogens (salmonella, Shigella, Campylobacter, Yersinia) or parasites
6. positive C. difficile stool test

7. any medication use including PPI and antibiotics;Individuals with an increased risk for one of the above conditions (homosexual contacts, recent blood transfusions) will be excluded, and donors are not recruited amongst health care providers.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 31-10-2016 |
| Enrollment: | 36 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 20-07-2016 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-02-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL57871.018.16 |