# The promote study, a pilot: The characterization of the microbiome in pregnancy and prediction of pregnancy outcomes.

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Research question: Is maternal microbiome dysbiosis in MOB an underlying mechanism in the pathophysiology of adverse maternal pregnancy and offspring outcome?Objectives: Analyse the differences between the gut and vaginal microbiome, maternal and...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON51666

**Source**
ToetsingOnline

**Brief title**
PROMOTE

### Condition

- Other condition
- Pregnancy, labour, delivery and postpartum conditions
- Vascular hypertensive disorders

**Synonym**
ongunstige samenstelling van darmmicroben., zwangerschapssuikerziekte, Zwangerschapsvergiftiging

**Health condition**

Darmdysbiose: ongunstige verstoring van het microbioom van de darmen.

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** ZonMw

## Intervention

**Keyword:** BMI, Microbiome, Pregnancy, Pregnancy outcomes

## Outcome measures

### Primary outcome

The composition of the maternal gut and vaginal microbiome (in obese women (BMI >30 kg/m2) and non-obese women (BMI 18-25 kg/m2)).

### Secondary outcome

The associations between the composition of the microbiome and:

1) Clinical maternal outcomes (e.g. pregnancy outcome, gestational age at delivery, preeclampsia, hypertension, gestational diabetes)

2) Clinical fetal outcomes (e.g. fetal growth trajectories in first, second and third trimester, birthweight)

3) Maternal (and fetal) immune response and one-carbon metabolism (e.g. inflammatory and biomarkers)

4) Placental function (e.g. placental vascular architecture and volume during the 1st trimester, placental weight, inflammatory status)

# Study description

### Background summary

Our research aims to elucidate an underlying mechanism of maternal obesity (MOB)-induced pregnancy and long-term health complications for mothers and their offspring. With the rising global prevalence of obesity, MOB-related pregnancy problems are increasingly occurring. Microbial gut symbiosis plays an important role in health, where dysbiosis is associated with diseases as obesity. Of interest, pregnancy, dietary patterns and pre- or probiotics affect the composition of the gut microbiome. The microbiome itself can influence many physiological processes, such as immune responses (production of microbial products) and the nutrient dependent one-carbon metabolism. We hypothesize that gut dysbiosis in MOB can be regarded as an endogenous chronic stressor inducing deranged immune responses and one-carbon metabolism. Both processes result in excessive oxidative stress, detrimental for cell multiplication, differentiation and epigenetic programming of maternal and offspring tissues. Together, these biological derangements contribute to placental and vascular dysfunction resulting in increased risks of preeclampsia or gestational diabetes mellitus. Vertical (during pregnancy) and horizontal (during delivery) transfer of gut dysbiosis from mother to new-born, and epigenetic placental and fetal changes can ultimately accumulate in macrosomia and childhood obesity.

## Study objective

Research question: Is maternal microbiome dysbiosis in MOB an underlying mechanism in the pathophysiology of adverse maternal pregnancy and offspring outcome?

Objectives:
Analyse the differences between the gut and vaginal microbiome, maternal and fetal immune response and one-carbon metabolism in obese vs normal weight pregnant women.

## Study design

A single center prospective longitudinal observational cohort pilot study embedded in the Rotterdam periconception cohort (Predict study, METC 2004-227) will be performed periconceptional/early in the first trimester and continue until the delivery/postpartum at the Erasmus MC.

## Study burden and risks

For all cases, the risks involve primarily the burden of participating in a study, which usually means additional hospital visits and assessments. There will be a maximum of 6 hospital visits, which will take approximately 30-45 minutes each. There will be two/three first trimester vaginal ultrasound examinations, two abdominal ultrasound examinations during the second and third trimester and 1 postpartum visit (all part of the Predict study, METC 2004-227). At a maximum of 5 of the appointments (periconceptional, in the

first, second, third trimester, postpartum) blood draws and rectal swabs will be obtained. The first blood draw is combined with the blood draw of the Predict study, the three/four consecutive blood draws are additional for the PROMOTE study, as are the rectal swabs. Maternal anthropometrics, including weight, height and blood pressure will be measured preconceptionally or during the first trimester (as part of the Predict study). The risks of participation are considered to be nil and the potential benefit outweighs the risks. From the above explanations, it is clear that there are no obvious risks associated with participation in the study. After each visit, the patient will receive a picture of their fetus obtained by 3D or 2D ultrasound, if it is possible to generate one. In a subgroup of 20 extra included women we will collect a fecal (stool) sample, one time, in the third trimester of pregnancy. This subgroup of 20 inclusions will only have one visit for signing the informed consent forms and receiving the fecal collection package and one visit for handing over the collected fecal sample to the researchers. They therefore do not follow the regular PROMOTE study protocol.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Newborns

## Inclusion criteria

• Participation in Predict study
• Preconceptional women who wish to become pregnant or pregnancy <13 weeks of gestational age.
• BMI > 30 kg/m2 or 18-25 kg/m2
• Understanding of Dutch in speaking and reading
• Willingness to give written informed consent

For participants included for maternal fecal collection only the following criteria apply:
• BMI > 30 kg/m2 or 18,5-25 kg/m2
• > 28 weeks of gestational age
• Understanding of Dutch in speaking and reading
• Willingness to give written informed consent

## Exclusion criteria

• Age < 18 years and > 45 years.
• >=13 weeks of gestational age
• Multiple pregnancy
• Smoking
• Gastro-intestinal diseases, heart diseases, liver, pancreas and kidney diseases.
• Use of antibiotics < 2 weeks before sampling
• Pre-existent diabetes mellitus
• Unable or unwilling to give informed consent

For participants included for maternal fecal collection only the following exclusion criteria apply:
• Age < 18 years and > 45 years.
• < 28 weeks of gestational age
• Multiple pregnancy
• Smoking
• Gastro-intestinal diseases, heart diseases, liver, pancreas and kidney diseases.
• Use of antibiotics < 2 weeks before sampling
• Pre-existent diabetes mellitus
• Unable or unwilling to give informed consent

# Study design

## Design

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|---|---|
| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Basic science |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 21-07-2022 |
| Enrollment: | 240 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 04-07-2022 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 28-11-2023 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 |
|---|---|
| Other | ClinicalTrials gov 0925-0586 |
| CCMO | NL80155.078.22 |