ISRCTN83157250 https://doi.org/10.1186/ISRCTN83157250

# Validation test ("ReceptIVFity-test") to predict the chance of pregnancy with IVF or IVF-ICSI treatment based on bacteria composition

**Submission date**
17/08/2018

**Recruitment status**
No longer recruiting

**Registration date**
30/08/2018

**Overall study status**
Completed

**Last Edited**
06/09/2023

**Condition category**
Pregnancy and Childbirth

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
In the last decade, research has shown that microorganisms may have an impact on the outcome of assisted reproductive procedures such as IVF or IVF-ICSI. Microorganisms, together with their genetic information and the environment in which they live and interact is called the microbiome. One common type of bacteria that lives in the vagina is Lactobacillus. Studies have shown that the presence of Lactobacillus during assisted reproductive procedures can have a positive impact on the outcome. However, using the microbiome as a way of predicting the outcome of these procedures has not yet been investigated. This study aims to develop a method of using the microbiome to identify women with low, mid and high chances of becoming pregnant prior to the start of IVF or IVF-ICSI treatment. Having the ability to predict this may help couples to make decisions about whether to continue these treatments.

Who can participate?
Females aged 20-44 with a male partner, who have been indicated for IVF or IVF-ICSI

What does the study involve?
Participants will be asked to
Participants will receive a sampling protocol and collect a vaginal swab and urine sample by themselves in the IVF centre. The swab and the urine sample will take place once and have to be taken within the two months prior to the embryo transfer.
The urine sample collection will be obtained according to a standard 'clean catch' protocol, including washing hands thoroughly, cleaning the urinary opening with towelettes and collecting a midstream specimen in a sterile container. Vaginal samples will be taken with FLOQSwabs™. The participants will be instructed to insert the swab 3-5 centimetres beyond the vaginal orifice, and move the swab around along the vaginal wall for 10-15 seconds.

What are the possible benefits and risks of participating?
This research may not directly benefit the participants, since the test result is not shared with the participants during the study. However, the participants may help us to develop a predictive test based on the urogenital microbiome and hopefully this will contribute to a personalised

medicine approach in the future. There are no known risks to participants taking part in this study.

Where is the study run from?
Division Reproductive Endocrinology and Infertility, Department Obstetrics and Gynaecology, Erasmus University Medical Centre, Rotterdam (The Netherlands) (lead centre) and 7 other centres in The Netherlands

When is the study starting and how long is it expected to run for?
July 2014 to December 2018

Who is funding this study?
1. NGI Pre-Seed (The Netherlands)
2. RedMedTech (The Netherlands)
3. STW (The Netherlands)
4. Eurostars VALBIOME (Belgium)

Who is the main contact?
Dr Rivka Koedooder
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# Contact information

### Type(s)
Scientific

### Contact name
Miss Rivka Koedooder

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
METC 2014-455

# Study information

## Scientific Title
Analysis of the microbiome to determine the predictive accuracy of the urogenital microbiome for IVF/IVF-ICSI outcome prediction in IVF/IVF-ICSI patients

## Acronym
ReceptIVFity

## Study objectives
The urogenital microbiome can be used as predictor for IVF/IVF-ICSI outcome.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
The protocol was approved by the Institutional Medical Ethical Review Board of all participating centres, the coordinating centre was Erasmus University Medical Centre, Rotterdam, The Netherlands (MEC-2014-455). Date of approval: 15/08/2014

## Study design
Observational prospective multi-centre cohort study

## Primary study design
Observational

## Secondary study design
Cohort study

## Study setting(s)
Hospital

## Study type(s)
Diagnostic

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

## Health condition(s) or problem(s) studied
In vitro fertilisation (IVF) and intracytoplasmic sperm injection (IVF-ICSI)

## Interventions
A microbiome profiling intervention based on a urinary sample and a vaginal swab obtained prior to the start of the IVF or IVF/ICSI treatment. The ultimate goal will be to develop a predictive algorithm that enables identification of the group of women with a low, mid and high chance to become pregnant prior to the start of the IVF or IVF-ICSI treatment. Predictive knowledge of the microbiome profile may enable couples to make a more substantiated decision on whether to continue treatment or not. Hence, the unnecessary physical and emotional burden of a failed IVF or IVF-ICSI treatment can be avoided.
Participants will receive a sampling protocol and collect the samples by themselves in the IVF centre.

The urine sample collection will be obtained according to a standard ‘clean catch’ protocol, including washing hands thoroughly, cleaning the urinary opening with towelettes and collecting a midstream specimen in a sterile container. Vaginal samples will be taken with FLOQSwabs™. The participants will be instructed to insert the swab 3-5 centimetres beyond the vaginal orifice, and move the swab around along the vaginal wall for 10-15 seconds.
The sampling will take place once and the swab and the urine sample have to be taken within the 2 months prior to the embryo transfer.

### Intervention Type
Procedure/Surgery

### Primary outcome measure
To assess the specificity and sensitivity of the urinary and vaginal microbiome composition for the prediction of embryo implantation failure of a consecutive IVF or IVF-ICSI procedure.
1. The composition of the urinary and vaginal samples, assessed by Next Generation Sequencing and the IS-pro technique within the 2 months prior to the embryo transfer
2. Ongoing pregnancy (defined as an intrauterine embryo/foetus with detection of cardiac activity on transvaginal ultrasound between 7-9 weeks of gestation after fresh embryo transfer)
3. Sensitivity - the proportion of women who become pregnant who test mid or high chance to become pregnant based on microbiome analysis using urinary and vaginal samples (true positive (TP) / (TP + false negative (FN)))
4. Specificity - the proportion of women who do not become pregnant who test low chance to become pregnant based on microbiome analysis using urinary and vaginal samples (true negative (TN) / (TN + false positive (FP)))

### Secondary outcome measures
There are no secondary outcome measures

### Overall study start date
08/07/2014

### Completion date
01/12/2018

## Eligibility

### Key inclusion criteria
1. Female
2. Indication for an IVF or IVF-ICSI procedure
3. Aged 20-44 years
4. Willing to provide a urine sample and a vaginal swab
5. Willing to provide informed consent
6. Male partner

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
20 Years

### Upper age limit
44 Years

### Sex
Female

### Target number of participants
300

### Total final enrolment
192

### Key exclusion criteria
1. No transferable embryos after IVF or IVF-ICSI
2. Indication for emergency IVF because of cancer or other reasons
3. AFS (American Fertility Society) III/IV classified endometriosis and pre-treatment with a GnRH (gonadotropin-releasing hormone) analogue
4. >3 weeks use of hormonal contraceptives 3 months prior to start IVF or IVF-ICSI
5. Pregnant previously to the start of the IVF or IVF-ICSI (including miscarriage)
6. Hormonal treatments 3 months prior to start IVF or IVF-ICSI
7. Use of sperm donation

### Date of first enrolment
02/06/2015

### Date of final enrolment
09/04/2016

## Locations

### Countries of recruitment
Netherlands

### Study participating centre
**Erasmus University Medical Centre**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Erasmus University Medical Centre
Wytemaweg 80
Rotterdam
Netherlands
3015 CN

### Study participating centre

**Radboud University Medical Centre**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6525 GA

**Study participating centre**
**Isala Kliniek**
Isala Voortplantingscentrum
Dokter Spanjaardweg 29
Zwolle
Netherlands
8025 BT

**Study participating centre**
**VU University Medical Centre**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
De Boelelaan 1117
Amsterdam
Netherlands
1081 HV

**Study participating centre**
**Sint Elisabeth Ziekenhuis**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Hilvarenbeekseweg 60
Tilburg
Netherlands
5022 GC

**Study participating centre**
**VivaNeo Medisch Centrum Kinderwens**
Simon Smitweg 16
Leiderdorp
Netherlands
2353 GA

**Study participating centre**
**University Medical Centre Utrecht**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
Heidelberglaan 100
Utrecht
Netherlands
3584 CX

**Study participating centre**
**Maastricht Universitair Medisch Centrum+**
Division of Reproductive Medicine
Department of Obstetrics and Gynaecology
P. Debyelaan 25
Maastricht
Netherlands
6229 HX

# Sponsor information

**Organisation**
Erasmus University Medical Centre

**Sponsor details**
Dr. Molewaterplein 40
Rotterdam
Netherlands
3015 CD

**Sponsor type**
Hospital/treatment centre

**ROR**
https://ror.org/018906e22

# Funder(s)

**Funder type**
Not defined

**Funder Name**
Netherlands Genomics Initiative

**Funder Name**
RedMedTech

**Funder Name**
Stichting voor de Technische Wetenschappen

**Alternative Name(s)**
Technology Foundation STW, Technologiestichting STW, Dutch Technology Foundation, Dutch Technology Foundation STW, STW

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Trusts, charities, foundations (both public and private)

**Location**
Netherlands

**Funder Name**
Eurostars

**Alternative Name(s)**
EUREKA Eurostars

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
Belgium

# Results and Publications

**Publication and dissemination plan**
The results of the determination of the urinary microbiome and vaginal microbiome using NGS and IS-pro will be published in a scientific journal in 2018.
The results of the predictive accuracy of the urogenital microbiome as predictor for IVF/IVF-ICSI outcome will be published in a scientific journal in 2018.

## Intention to publish date
01/09/2018

## Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from r.koedooder@erasmusmc.nl. This will contain anonymised data after our primary data are published, but only if formally requested so we can control the nature of the analyses.

## IPD sharing plan summary
Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 04/06/2019 | 17/07/2020 | Yes | No |
| Protocol article | | 07/12/2018 | 06/09/2023 | Yes | No |