

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	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 30/08/2018	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 06/09/2023	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data

Plain English Summary

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?

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Contact information

Type(s)

Scientific

Contact name

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Netherlands

3015 CD

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 hypothesis

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

Condition

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

Overall study end date

01/12/2018

Eligibility

Participant 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

Participant 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

Recruitment start date

02/06/2015

Recruitment end date

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