Innovation for small-scale experiments: ReceptIVFity test.

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1. Evaluation of the efficiency of Shared Decision Making compared to Physician Decision in terms ofa) the success probability of an IVF cycle, b) the proportion of women with a successful pregnancyc) the number of unsuccessful IVF cycles.2....

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON54318

Source
ToetsingOnline

Brief title
ReceptIVFity test.

Condition

- Other condition

Synonym
chance to conceive., vaginal microbiome

Health condition

Periconceptie zorg en onderzoek; microbiële dys-/balans - fysiologie.

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: NZa (Nederlandse Zorgautoriteit)

Intervention

Keyword: ART- IVF/IVF-ICSI, Microbiome, ReceptIVFity, Shared decision making

Outcome measures

Primary outcome

- Successful pregnancy (dichotomous), i.e., a pregnancy with a positive

heartbeat at 12 weeks of gestation,

- The number of the successful IVF or IVF/ICSI cycle

- The total number of IVF or IVF/ICSI treatment cycles per patient.

Secondary outcome

- Scores of the SDM-Q-9 (questionnaire for patient satisfaction), which

consists of nine statements that can be rated on a six-point scale from 0=

completely disagree to 5= *completely agree*.

- The total costs of all received treatments within the study period.

-The primary endpoints given above for the women of non-European origin

included in the observational part of this study.

- The primary endpoints given above for women with endometriosis grade III and

IV.

Study description

Background summary

Currently, approximately 35% of all IVF/IVF-ICSI treatments result in a

pregnancy and a subsequent live birth (1). Since an IVF/IVF-ICSI treatment is a mentally as well as physically incriminating process, there is a great need for accurate prediction of pregnancy success. The first step has recently been made in a prospective cohort study in which the composition of the vaginal microbiome two months prior to the embryo transfer was predictive for pregnancy outcome in a specific defined set of patients. In patients harboring the most favorable composition of the vaginal microbiome as determined by use of the ReceptIVFity test, 53% became pregnant during that cycle. In contrast, in those with an unfavorable ReceptIVFity test profile only 6% became pregnant (2). Determination of the vaginal microbiome and its related predictive profile prior to the start of IVF/IVF-ICSI is now possible by the use of the ReceptIVFity test, which is now standard of care at the department of Reproductive Endocrinology and Infertility at the Erasmus MC, Rotterdam. Patients receive the test prior to start of hormonal treatment. Subsequently, their attending physician will discuss the reported vaginal microbiome profile and a decision regarding whether or not to continue with hormonal treatment is made in a shared decision between the couple and their doctor (3).
In 2019 and 2020, the ReceptIVFity test was introduced to all IVF/IVF-ICSI patients in both aforementioned hospitals, which was made possible by a grant received from health insurance company *CZ-groep*. CZ-groep wanted to investigate how introduction of the test would be received by clinicians and their patients, as well as how different predictive vaginal microbiome profiles might impact on the decision to continue with the IVF/IVF-ICSI treatment or postpone it until a more favorable vaginal profile at a later stage.
Recent data shows that there is a new and better predictive algorithm that can predict the chance of not conceiving and is independent of the obstetric history. The prediction is thus predictive for both nulligravida and those who have been pregnant before. In addition, the algorithm is based on data from a larger patient cohort of n=527 patients. The new percentages for the RecepIVFity profiles are: low 3.3%, medium 32.3% and high 66.7% chance of pregnancy. Data is not published yet.

More recently (January 2023), analyses of the current data showed that the predictive value of the algorithm for the RecepIVFity test seems to be optimal for women of European origin, and not predictive for women of non-European origin. This is in line with reported differences in vaginal microbiome attributed to ethnicity (4, 5). Moreover, women suffering from severe endometriosis (grade III or IV) are confronted with a significantly impact on their fertility by affecting ovarian function, egg quality, and implantation rates. Recent study shows that the composition of the vaginal microbiome is significantly difference at genus level between women with stage 3-4 endometriosis and healthy controls. Analyzing the vaginal microbiome composition of these women will provide valuable insights in the effects of endometriosis on fertility and vaginal health. In order to develop a predictive algorithm for women of non-European origin and women suffering from endometriosis, collection of more data for input is essential. As part of an observational sub-cohort, we intend to collect and analyse their vaginal

microbiome composition, to optimize their fertility treatment and improve their chance of achieving a successful pregnancy.

At the out-patient clinic, non-naïve patients also request and want to benefit from the RecepIVFity-test to enhance their chance of achieving a successful pregnancy. Not only do non-naïve patients request inclusion in the study, from an ethical point of view we want to respect the principles of autonomy, beneficence and justice: excluding them would not be fair. Recent data indicates that hormonal changes during IVF/IVF-ICSI treatment do not significantly affect the vaginal microbiome of infertile women. By also offering non-naïve patients the effectiveness of the shared decision and physician decision-making can be investigated to ensure the broad applicability of this test when implemented as standard care. The CZ-trial has shown that couples with a low ReceptIVFity test profile often decide to temporarily refrain from starting an IVF/IVF-ICSI cycle. In 2019, an interim analysis showed that 63.9% of the couples decided to temporarily postpone continuation of treatment in case of a low ReceptIVFity test profile. Moreover, couples who have a previous failed attempt seem more inclined to postpone treatment: in the first IVF/IVF-ICSI cycle 57.8%, which increased to 75% in the second cycle, and till 100% in the third cycle (which is also generally the last treatment to be reimbursed by the health insurance companies).
The ReceptIVFity acts as a timing-tool for prediction of optimal pregnancy chances and provides insight in the patient*s current (two months after sampling) success rate of an IVF/IVF-ICSI treatment. Benefits of postponing treatment in case of an unfavourable vaginal profile and a low chance of achieving a pregnancy include reducing unnecessary morbidity and treatment burden, stress and disappointment, while increasing efficiency of actual treatment. In order to be able to offer this innovative standard of care without additional costs for the patient for the coming three years, the Dutch Healthcare Authority (NZa) has authorized funding within the context of "Innovation for small-scale experiments".

Study objective

1. Evaluation of the efficiency of Shared Decision Making compared to Physician Decision in terms of
a) the success probability of an IVF cycle,
b) the proportion of women with a successful pregnancy
c) the number of unsuccessful IVF cycles.
2. Determine the accuracy (positive and negative predictive value) of the ReceptIVFity test to predict success of an IVF/IVF-ICSI treatment cycle.
3. Evaluation of patient satisfaction and cost effectiveness for SDM and physician decision
4. Gain experience with the use of the ReceptIVFity test for all IVF/IVF-ICSI indications and patients to facilitate the embedding of the test in the reimbursement system of health care.
5. Observational cohort: Develop and evaluate a success-rate stratification

based on the ReceptIVFity test for 1. women of non-European origin and
2. Women with 3rd and 4th grade of endometriosis.
6. Evaluation of the effectiveness of Shared Decision Making compared to Physician Decision in non-naïve women.

Study design

A prospective, clinical non-invasive randomized controlled study with an additional observational study arm (for women of non-European origin), will be performed in women visiting the outpatient clinic of the Department of Reproductive Endocrinology and Infertility (and collaborating intake-/transport-clinics) and eligible for IVF/IVF-ICSI who use the standard of care vaginal swab (ReceptIVFity test) for determination of the vaginal microbiome.

Randomization component (for naïve and non-naïve patients):
Women of European origin will be randomized 1:1 to either the shared decision group or the physician decision group. All women of European origin may undergo one to three cycles of IVF/IVF-ICSI reimbursed by the health insurance. The follow-up ends after the outcome of the last of these cycles has been determined. The desired outcome of the IVF or IVF/ICSI treatment is a successful pregnancy, i.e., a pregnancy with a heart-beat at 12 weeks of gestation.

Observational component:
Women of non-European origin are invited to take part in an observational component of this study. Without further evaluation of the results of their vaginal microbiome, they will continue with the IVF/IVF-ICSI cycle. Women eligible for participation are naïve and non-naïve patients and the follow-up ends after the outcome of the IVF/IVF-ICSI cycle has been determined. Women diagnosed with stage III and IV of endometriosis are also invited to take part in an observational component of this study.

Intervention

A vaginal self-swab is performed by the patient.

For women of European origin randomization in one of the following groups:
SDM group: Using Shared-Decision-Making according to the ReceptIVFity microbiome profile with its predicted chance of achieving a pregnancy in the current cycle.
Physician decision group: Postponing treatment until a switch to a favorable ReceptIVFity microbiome profile.

For women of non-European origin and for women with endometriosis grade 3-4:
A vaginal self-swab is performed by the patient. The results of the vaginal

microbiome composition will be used for the development of an algorithm with a predictive value of the ReceptIVFity test in women of non-European origin and for women with endometriosis grade 3-4.

Study burden and risks

The risk associated with this study is minimal. The use of the commercially available ReceptIVFity test is safe. No adverse events have been reported since the introduction of the ReceptIVFity test in 2015 (4).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Naïve and non-naïve IVF or IVF/ICSI patients.

2. 18 years < age < 43 years.
3. Willing to provide a vaginal swab with the ReceptIVFity test.
4. Willing to provide informed consent.

Exclusion criteria

1. The use of hormonal contraceptives at the time of taking the test.
2. The use of antibiotic treatment at the time of taking the test.
3. Emergency IVF for cancer or other reasons.
4. Women having IVF for egg preservation reasons.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-09-2023
Enrollment:	994
Type:	Actual

Medical products/devices used

Generic name:	The ReceptIVFity test
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	10-08-2023

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-03-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-12-2024
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
CCMO	NL75810.078.23