# The relationship between age at menopause loci and the response of controlled ovarian hyperstimulation in women undergoing IVF: a candidate gene study.

No registrations found.

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| **Ethical review** | Positive opinion |
| **Status** | Pending |
| **Health condition type** | - |
| **Study type** | - |

## Summary

### ID

NL-OMON28369

**Source**
Nationaal Trial Register

**Brief title**
RiSPONS

**Health condition**

Subfertile women who will undergo IVF treatment.

### Sponsors and support

**Primary sponsor:** Ferring
**Source(s) of monetary or material Support:** Ferring

### Intervention

### Outcome measures

**Primary outcome**

The primary outcome parameter is the responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment, i.e. number of retrieved oocytes.

### Secondary outcome

Secondary study parameters are other outcomes of the IVF treatment, described by the number of follicles after stimulation, quality of retrieved oocytes, quality of embryo’s as well as pregnancy rate and live-birth rate.

## Study description

### Background summary

Rationale: Over the last decade genome-wide association studies (GWAS) have identified hundreds of common genetic variants (Single Nucleotide Polymorphisms, SNPs) associated with age of natural menopause (ANM). The peri-menopausal stage is preceded by a decrease in fertility eventually leading to sterility in the 10 years before menopause. Poor response to controlled ovarian hyperstimulation (COH) during IVF treatment is a reasonable predictor of diminished ovarian reserve. Therefore, we hypothesize that presence of genetic variants associated with earlier age of natural menopause might also be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment. In other words, patients that carry more SNPs associated with early age of menopause might as well have a poor response to COH treatment. Consequently, if that is the case, these SNPs might be used as a predictor for ovarian response during IVF treatment using polygenic risk scores.

Objective: In this project, we hypothesize that presence of genetic variants associated with earlier age of natural menopause might be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment. Furthermore, we aim to investigate whether polygenic risk scores of genetic variants associated with age at natural menopause based on the large-scale GWAS are predictive of the response to IVF stimulation in patients starting their first IVF treatment cycle leading to a more patient-tailored care-setting.

Study design: This candidate gene study will be conducted in a retrospective as well as prospective cohort study.

Study population: Patients will be recruited at the IVF outpatient clinic of the Division of Reproductive Medicine at the Erasmus MC, University Medical Center, Rotterdam. All women with a regular menstrual cycle undergoing their first cycle of IVF because of male infertility or unexplained infertility will be asked to participate in this study.

Study protocol: Baseline characteristics, including medical history, age, BMI, smoking, SES, and endocrine parameters such as FSH, LH, progesterone, estradiol, AMH will be determined. Extra blood samples will be taken during standard blood sampling. DNA will be extracted

from peripheral blood, and genotyping shall be executed using Illumina arrays. Standard quality-control procedures are performed. SNPs were selected to be included in the Polygenic Risk Score calculation based on their p-values in the original GWAS. Patients will undergo hormonal stimulation according to a standard protocol in our clinic. Response to the IVF stimulation in terms of dose of exogenous FSH, number of follicles and number and quality of obtained oocytes as well as pregnancy will be monitored.

Main study parameters: The primary outcome parameter is the responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment, i.e. number of retrieved oocytes. Secondary study parameters are other outcomes of the IVF treatment, described by the number of follicles after stimulation, quality of retrieved oocytes, quality of embryo's as well as pregnancy rate and live-birth rate.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Single blood sampling is needed to execute this candidate gene study, although this will be combined with standard blood sampling women will need to visit the hospital one extra time.

### Study objective

We hypothesize that presence of genetic variants associated with earlier age of natural menopause might be involved in diminished responsiveness of the ovaries to exogenous FSH stimulation during IVF treatment.

### Study design

Before IVF treatment the extra blood samples will be taken.

### Intervention

Extra blood samples will be taken during standard blood sampling.

## Contacts

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**Scientific**
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# Eligibility criteria

## Inclusion criteria

- A regular menstrual cycle
- Undergoing IVF because of male infertility or unexplained infertility
- First cycle IVF treatment
- Age between 18 and 45 years at the time of the IVF treatment

## Exclusion criteria

- A history of ovarian surgery, chemotherapy of radiation therapy
- Non Northern European ethnicity

# Study design

## Design

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| Intervention model: | Other |
| Allocation: | Non controlled trial |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

## Recruitment

NL

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| Recruitment status: | Pending |
| Start date (anticipated): | 01-01-2021 |
| Enrollment: | 500 |
| Type: | Anticipated |

## IPD sharing statement

**Plan to share IPD:** No

# Ethics review

Positive opinion
Date: 06-01-2021
Application type: First submission

# Study registrations

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

ID: 54409
Bron: ToetsingOnline
Titel:

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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| NTR-new | NL9173 |
| CCMO | NL75062.078.20 |
| OMON | NL-OMON54409 |

# Study results