# Cost-effectiveness of IVF for unexplained, or mild male, subfertility in women from 38 years up.
# A multi-centre randomized controlled trial

Published: 19-08-2015
Last updated: 15-05-2024

In view of this uncertainty in which current practice in IVF is applied in *older* women, we propose a nationwide randomized trial comparing IVF with natural conception.

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Sexual function and fertility disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50639

**Source**
ToetsingOnline

**Brief title**
IVF38+ study

### Condition

- Sexual function and fertility disorders

**Synonym**
unexplained subfertility and mild male subfertility

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,ZonMw

## Intervention

**Keyword:** expectant management, IVF, milde male subfertility, older women, unexplained subfertility

## Outcome measures

### Primary outcome

Ongoing pregnancy rate leading to live birth

### Secondary outcome

- IVF outcome parameters, such as the total number of follicles, oocytes, MFII

oocytes, germinal vesicles.

- Poor ovarian response defined as the growth of less than 3 follicles of > 14

mm. under maximal ovarian stimulation of 225 EH FSH.

- Total number of embryo*s and embryo quality.

- Clinical pregnancy; defined as the presence of a gestational sac seen by

transvaginal sonography 5-7 weeks after embryo tranfer

- Ongoing pregnancy; defined as the presence of positive heart beat as seen by

transvaginal sonography 10 weeks after embryo transfer.

- Multiple pregnancy; defined as two or more gestational sacs seen by

transvaginal sonography 5-7 weeks after embryo transfer

- Ongoing multiple pregnancy; defined as two or more positive heart beats seen

by transvaginal sonography 10 weeks after embryo transfer

- Miscarriage; defined as the loss of a pregnancy prior to 16 weeks gestation

- Ectopic pregnancy, defined as the ectopic nidation of a pregnancy, confirmed

with sonography or laparoscopy

- Couples* preference, measured by means of a DCE (discrete choice experiment)

(100 patients)

- Generic quality of life measured by questionnaires (SF36 and fertiQoL) (100

patients), women in the expectant arm will be ask to keep a diary.

- Financial Costs

# Study description

### Background summary

Currently, 8,750 IVF and 8,250 IVF/ICSI cycles are performed in the Netherlands every year for an average cost of approximately ¤3,000 per cycle. This number of cycles is strongly growing, and has almost doubled in the last decade. In approximately 1 in 4 couples with unfulfilled child wish no causal reason for their fertility problem can be found, but for the fact the woman is reproductively old, i.e. above the age of 38. Nevertheless, such couples are usually treated with IVF. This is worrisome, as in these women IVF, which was originally developed for women with obstructed tubes, has never been compared with natural conception over a longer period of time. It may well be that IVF does not at all counteract the natural decline in female fertility. Cohort studies indicate that increased female age is the single most negative prognostic factor in IVF. Moreover, there is emerging evidence that the IVF children have lower birth weight, higher blood pressure and impaired glucose metabolism.

### Study objective

In view of this uncertainty in which current practice in IVF is applied in *older* women, we propose a nationwide randomized trial comparing IVF with natural conception.

### Study design

Multicenter randomised clinical trial with an economic analysis alongside it.

### Intervention

A maximum of three cycles of IVF treatment versus natural conception within a

time horizon of 8 months.

**Study burden and risks**

As we compare strategies that are already applied in current practice, no additional risks or burdens are expected from the study.

# Contacts

**Public**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1104 AZ
NL
**Scientific**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1104 AZ
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

-- Age at least 38 and younger than 42.
- Had unprotected regular intercourse during at least 12 months without conception.

- Normal regular ovulatory cycle between 26 and 34 days as confirmed by either history, basal temperature curve, ultrasound monitoring or serum progesterone
- tubal patency of at least one tube as established with either hysterosalpingography, contrastsonography, or diagnostic laparoscopy, or a confirmed earlier intra-uterine pregnancy (miscarriage or ongoing) not through IVF, or a negative history of tubal damage in combination with a negative CAT result.
- partners with normal or mildly impaired semen quality (TMSC * 3 million).

### Exclusion criteria

- Age <38 or > 41 at the time of inclusion
- Irregular cycle, defined as < 25 days or >34 days.
- Double sided tubal occlusion
- Poor semen quality (TMSC <3 million)
- Couples undergoing IVF combined with Pre-implantation Genetic Diagnosis
- Couples undergoing ICSI combined with TESE (testiculair spermextraction)
- Couples undergoing IVF or ICSI with donor sperm

## Study design

### Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Treatment

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 09-10-2015 |
| Enrollment: | 150 |
| Type: | Actual |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 19-08-2015 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-10-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 13-10-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-11-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-12-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-12-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-12-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-01-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 01-02-2016 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 14-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-04-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-04-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-05-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-09-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-11-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-12-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 14-12-2016 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-02-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

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

No registrations found.

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

ID: 26052
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL42977.018.15 |
| OMON | NL-OMON26052 |