

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

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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, MFI oocytes, germinal vesicles.
- Poor ovarian response defined as the growth of less than 3 follicles of > 14 mm. under maximal ovarian stimulation of 225 IU 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 transfer
- 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 asked 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

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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 (testicular 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: NTR
Title:

In other registers

Register	ID
CCMO	NL42977.018.15
OMON	NL-OMON26052