

# Controlled ovarian stimulation and intrauterine insemination or in vitro-fertilisation for the first line treatment of unexplained infertility

<b>Submission date</b> 15/06/2013	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 08/08/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 17/05/2017	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Both intrauterine insemination (IUI) and in vitro fertilization (IVF) are accepted treatment options for unexplained infertility. The recent National Institute for Health and Care Excellence (NICE) guideline proposes to offer IVF as a first-line treatment to these couples excluding IUI. There is no strong evidence on which this recommendation is made, so we aim to conduct this trial of IUI compared to IVF as the first-line management for unexplained infertility. If the live birth rates in both the groups are found to be same, then these couples should not be denied IUI, which is less invasive and more acceptable to patients.

### Who can participate?

Couples (with female partner <37 years), trying to conceive for at least a year of unprotected intercourse, in the presence of normal semen analysis, evidence of regular ovulation, open fallopian tubes, and who had no previous fertility treatment other than clomiphene citrate.

### What does the study involve?

Couples are randomly allocated to either receive controlled ovarian hyperstimulation (COH) + IUI (50% of women) or IVF (50% of women) as the first offered treatment. The medicines used in the cycles are the same as usual. One cycle of treatment to which the couple is allocated is given in a 12-month period. If they are in the COH + IUI group and fail to conceive in the three cycles then they are automatically recommended for IVF treatment outside of this study. If they are in the IVF group, then after three cycles they are not offered IUI. This is the normal unit policy. The results in the two groups are compared in order to see which group has a better outcome in terms of ongoing pregnancy rate/live birth rate.

### What are the possible benefits and risks of participating?

The results of this study will help improve the treatment of people with unexplained infertility in future. There are no added disadvantages and risks over and above the routine treatment.

### Where is the study run from?

The study will be carried out in Homerton fertility unit.

When is the study starting and how long is it expected to run for?  
The study started in July 2013 and will run for a year or 18 months.

Who is funding the study?  
No extra funding is required for this study. Patients' IVF treatment is usually funded by their primary care trust irrespective of their involvement in the study. No extra funding is available.

Who is the main contact?  
Dr Anupa Nandi

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Anupa Nandi

**Contact details**  
Homerton Fertility Unit  
Homerton Hospital  
London  
United Kingdom  
E9 6SR

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
Version no. 2.0

## Study information

**Scientific Title**  
Controlled ovarian stimulation and intrauterine insemination or in vitro fertilization for the first line treatment of unexplained infertility: a randomised controlled trial

**Study objectives**  
What should be the first line treatment option for couples with unexplained infertility: intrauterine insemination (IUI) or in vitro fertilization (IVF)?

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

**Study design**

Single-centre randomised controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

See additional files

**Health condition(s) or problem(s) studied**

Best first line treatment options for unexplained infertility

**Interventions**

Randomisation will be performed by an independent worker in blocks of 10 and distributed in individual consecutively numbered opaque envelopes. Participants will be randomised into two groups:

**Group 1: Controlled ovarian hyperstimulation (COH)+ IUI**

In COH + IUI group the controlled ovarian hyperstimulation can be performed with daily subcutaneous injections of 75 IU FSH (Fostimon) starting from day 3-4 of menstrual cycle onwards. Dose might be altered according to the response of the patient to be decided by the attending clinician. The follicular growth is strictly monitored by transvaginal ultrasound. When at least 1-2 follicles with diameter 17-18mm is present, final oocyte maturation is induced by administration of recombinant chorionic gonadotropin (hCG) (Ovitrelle) and 24-36 hours later IUI would be performed. If  $\geq 3$  follicles of  $> 16$ mm develop then the cycle would be cancelled by withholding hCG and IUI and avoiding sexual intercourse due to risk of multiple pregnancies. Semen samples would be processed within one hour of ejaculation using density gradient centrifugation followed by washing with culture medium and then used for insemination. Single insemination will be done

**Group 2: IVF**

In IVF group women will undergo controlled ovarian hyperstimulation after down-regulation with GnRH agonist in a long protocol starting on day 2. COH is started with FSH (either Menopur or Gonal F) with dose ranging from 150-450 IU depending on initial AMH level decided by the attending clinician. Follicular tracking by transvaginal ultrasound will be performed. Treatment will be continued until follicles are  $> 18$  mm. Ovulation is induced by hCG (Ovitrelle) and cumulus-oocyte complexes will be retrieved by transvaginal ultrasound guided oocyte retrieval 36 hours after hCG trigger. Embryos will be assessed daily for their morphological grading according to our laboratory's protocol until the time of transfer. Day of embryo transfer will be decided by the embryologist based on the embryo quality. One embryo will be transferred on either day 2

or 3 or 5 if one or more good quality embryos are available. If no good quality embryos are available then two embryos will be transferred. Luteal phase support will be provided with progesterone vaginal pessaries (Cyclogest). Non-transferred good quality embryos will be cryo-preserved. In case of unsuccessful cycle or early miscarriage, frozen embryos will be thawed and transferred and this will be counted as another cycle.

**Intervention Type**

Other

**Phase**

Not Applicable

**Primary outcome measure**

Singleton live birth rate is assessed using medical record review

**Secondary outcome measures**

1. Clinical pregnancy rate is assessed using medical record review
2. Multiple pregnancy rates is assessed using medical record review

**Overall study start date**

01/10/2012

**Completion date**

04/08/2016

**Eligibility****Key inclusion criteria**

1. Couples with female partner's age between 23- 37 years
2. Diagnosed with unexplained infertility at the time of first treatment
3. Inability to conceive following a minimum of one year of unprotected intercourse
4. In the presence of normal semen analysis, proof of regular ovulatory cycles with a day 3 follicle stimulating hormone (FSH)<10IU/L
5. Two patent tubes and a normal uterine cavity on hysterosalpingography (HSG)

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Female

**Target number of participants**

160 in each group.

**Key exclusion criteria**

1. Female partner aged 37 years or more
2. People with physical disability or psychosexual problems who find difficulty in achieving

vaginal intercourse

3. Couples in a same sex relationship (as these do not fall into the definition of unexplained infertility)

4. Couples where the male/female is HIV positive, as they would need specific consideration to methods of conception

5. Couples who have had no previous IUI or IVF treatment for infertility

**Date of first enrolment**

10/08/2013

**Date of final enrolment**

15/07/2015

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Homerton Fertility Unit**

London

United Kingdom

E9 6SR

## **Sponsor information**

**Organisation**

Homerton University Hospital (UK)

**Sponsor details**

c/o Mr Narendra Aladangady

R&D Department

London

England

United Kingdom

E9 6SR

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/00x444s43>

# Funder(s)

## Funder type

Hospital/treatment centre

## Funder Name

Patients IVF treatment is usually funded by their primary care trust irrespective of their involvement in the study.

# Results and Publications

## Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal.

## Intention to publish date

31/12/2017

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from [anupa.nandi@gmail.com](mailto:anupa.nandi@gmail.com)

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version V4	10/08/2013	15/12/2016	No	Yes
<a href="#">Results article</a>	results	01/06/2017		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No