

# Effects of estrogen supplementation for patients with thin endometrial lining receiving oral clomiphene citrate

<b>Submission date</b> 26/01/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
<b>Registration date</b> 28/01/2021	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Protocol <input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 04/02/2021	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Subfertility is defined as the inability to conceive after 1 year of regular unprotected intercourse. It can be treated with fertility treatments such as intrauterine insemination (IUI) or timed sexual intercourse (TSI). This study aims to find out whether estrogen supplementation improves the thickness of the endometrial lining (the lining of the uterus) in patients with thin lining as a result of clomiphene citrate, which is used for ovulation induction (release of an egg from the ovary) in fertility treatment. Oral estradiol supplements have been used in fertility treatment for a long time but the duration of use may vary according to the clinician's preference as there are no standard protocols with regards to the duration of use.

### Who can participate?

Women with primary or secondary subfertility planned for intrauterine insemination (IUI) or timed sexual intercourse (TSI)

### What does the study involve?

Participants are randomly allocated to take no treatment or to take oral estradiol valerate 8 mg once a day for 4 days. Participants will be required to visit the reproductive medicine unit for serial transvaginal sonogram (ultrasound) assessment of endometrial thickness.

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

Oral estradiol is a safe drug used in fertility treatment and there have been no reported cases of serious side effects from this drug besides occasional nausea or vomiting that a small number may experience. Oral estradiol supplementation may improve the endometrial thickness and therefore may improve pregnancy rates.

### Where is the study run from?

University Malaya Medical Centre (Malaysia)

### When is the study starting and how long is it expected to run for?

December 2019 to December 2022

Who is funding the study?  
University Malaya Medical Centre (Malaysia)

Who is the main contact?  
Dr Rajeev Kumar Rajaratnam  
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## Contact information

**Type(s)**  
Public

**Contact name**  
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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**Protocol serial number**  
MREC ID NO: 20191227-8112

## Study information

**Scientific Title**  
Estrogen supplementation for thin endometrium in patients undergoing ovulation induction with clomiphene citrate: a randomized controlled trial

**Acronym**  
ESTE

**Study objectives**  
Estrogen supplementation increases endometrial thickness among patients with thin endometrium who were on clomiphene citrate for ovulation induction.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

Approved 29/04/2020, Medical Research Ethics Committee, University Malaya Medical Centre (Lembah Pantai, 59100 Kuala Lumpur, Malaysia; +60 (0)3-79493209/2251; rosmawatib@ummc.edu.my), ref: 20191227-8112

**Study design**

Multicentre randomized control trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Primary or secondary subfertility

**Interventions**

Patients diagnosed with either primary or secondary subfertility undergoing ovulation induction with clomiphene citrate in preparation for IUI (intrauterine insemination) or TSI (timed sexual intercourse) will be randomly allocated to receive either oral estradiol valerate 8 mg OD for 4 days or a control group (no treatment). Those eligible will be approached by the attending clinician and the research investigator. An explanation will be given regarding the study and its flow. They will be given sufficient time to consider their participation in the trial. Written, informed consent will be obtained by the attending clinician from patients agreeing to participate in the study. A patient information sheet will be provided to outline the study, procedures performed for assessment and treatment given. There will be a sealed opaque envelope containing the randomization ticket that will be opened in front of the patient.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Estradiol valerate (Progynova)

**Primary outcome(s)**

Endometrial thickness measured using transvaginal sonogram at initial visit (baseline), between days 8-10 of the current cycle and 4 days later

**Key secondary outcome(s)**

1. Pregnancy rate measured using the urinary pregnancy test or serum B-HCG when the patient misses her period the subsequent month
2. Miscarriage rate measured using the transabdominal/transvaginal sonogram and clinical assessment if the patient experiences early pregnancy complications such as bleeding or passing out of products of conception
3. Nausea and vomiting assessed where the patient records having any of these symptoms during her visit 4 days after being randomised

**Completion date**

31/12/2022

## Eligibility

**Key inclusion criteria**

Women diagnosed with primary or secondary subfertility undergoing ovulation induction using clomiphene citrate in preparation for intrauterine insemination (IUI) or timed sexual intercourse (TSI)

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

Female

**Key exclusion criteria**

1. Planned IVF
2. Diagnosed with an endometrial polyp
3. Using GnRH Agonist
4. Systemic diseases (e.g. autoimmune, cardiac, liver, thyroid disease or malignancy)

**Date of first enrolment**

31/01/2021

**Date of final enrolment**

31/05/2022

## Locations

**Countries of recruitment**

Malaysia

**Study participating centre**

**University Malaya Medical Centre**

Lembah Pantai

Kuala Lumpur

Malaysia

59100

**Study participating centre**  
**Hospital Tengku Ampuan Rahimah Klang**  
Jalan Langat, Klang  
Selangor  
Malaysia  
41200

## Sponsor information

**Organisation**  
University Malaya Medical Centre

**ROR**  
<https://ror.org/00vkrxq08>

## Funder(s)

**Funder type**  
Hospital/treatment centre

**Funder Name**  
University Malaya Medical Centre

## Results and Publications

### Individual participant data (IPD) sharing plan

All data obtained will be kept private and confidential within the Reproductive Medicine Unit. Data will be charted in a data collection form as well as into the clinical notes during which the patient undergoes ovulation induction. Patients consent will be obtained with regards to the use and storage of the data on the online electronic medical record system as well as the clinical notes. Data will be tabulated and stored by the primary investigator as soft copy material. The treating physicians, primary investigator and the embryologist of the reproductive medicine unit will have access to the data for tabulation and storage purpose. All data will be kept confidential and only investigators and treating clinicians will have access. All records will be stored for 2 years after completion of the study.

### IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>			04/02/2021	No	No

