

# Investigating the risk of heart and blood vessel problems in mild overactive thyroid disorder

<b>Submission date</b> 02/03/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 03/03/2020	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Protocol
<b>Last Edited</b> 03/12/2021	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

An overactive thyroid, also known as hyperthyroidism or thyrotoxicosis, is where the thyroid gland produces too much of the thyroid hormones. Subjects with mild form of overactive thyroid gland (subclinical hyperthyroidism) have an increased risk of developing diseases affecting blood vessels and heart such as fast and irregular heart rhythms, heart failure and possibly death due to vascular conditions. The exact reason for this risk is not known. Traditional risk factors such as high blood pressure and abnormal lipid levels are usually not affected in this condition. Hence, we wished to study newer cardiovascular risk markers such as endothelial progenitor cells (EPC, one type of stem cells), circulating endothelial cells (CEC, which are shredded cells lining the blood vessels), C reactive protein (CRP, known vascular risk factor), in patients with mild form of overactive thyroid.

### Who can participate?

Adults aged 21 - 85 years, with diagnosis of subclinical hyperthyroidism confirmed at least on two occasions (low serum TSH with normal FT4).

### What does the study involve?

Participants will be randomly allocated to receive either thyroid drug carbimazole (drug used to treat overactive thyroid condition) or placebo pill for 6 months.

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

**Benefits:** There is no direct benefit for the participants taking part in this study. The researchers hope that the research outcomes may help to treat this condition in future.

**Risks and Side Effects:** Side effects related to the use of Carbimazole (if taking carbimazole tablet) include agranulocytosis (agranulocytosis means a failure of the bone marrow to make enough white blood cells, neutrophils and bone marrow is the soft tissue inside bones that helps form blood cells), liver function abnormalities such as cholestatic hepatitis and allergic reactions. They are quite rare in clinical practice (less than 0.5%), but this can not be prevented.

### Where is the study run from?

Tan Tock Seng Hospital (Singapore)

When is the study starting and how long is it expected to run for?  
December 2012 to January 2018

Who is funding the study?  
National Healthcare Group - Small Innovative Grant, SIG/12011 (Singapore)

Who is the main contact?  
Dr Shaikh Abdul Kader Kamaldeen Abdul Shakoor  
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## Contact information

### Type(s)

Public

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

Singapore health sciences authority (HSA) clinical trials ref; CTC 1200221

## Study information

### Scientific Title

The role of endothelial progenitor and circulating endothelial cells in cardiovascular risk of patients with sub clinical hyperthyroidism

### Acronym

EPISH

**Study objectives**

Increased cardiovascular risk in subclinical hyperthyroidism (SH) is contributed to by reduction in CEPC and increased circulating endothelial cells.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 12/04/2012, NHG Domain Specific Review Board (DSRB) Singapore (6 Commonwealth Lane, Level 6 GMTI building, Singapore, 149547, Singapore; +65 64968900; no email provided), ref: 2011/02144

**Study design**

Interventional single centre randomized controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Sub clinical hyperthyroidism

**Interventions**

Treatment with carbimazole or placebo for 6 months.

Randomisation process will be done electronically using randomization codes with the help of medical statistician at the CRU (TTSH) in blocks of 4 (for carbimazole or placebo pill).

Randomization will be done online (intranet access) in which only coordinators (unblinded) will be given access to the system.

**Intervention Type**

Drug

**Phase**

Phase IV

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

Carbimazole

**Primary outcome(s)**

Levels of circulating endothelial progenitor cells (EPC), circulating endothelial cells (CEC), Hs CRP, ADMA, lipoprotein-associated phospholipase A2 (Lp-PLA2) activity, Neutrophil lymphocyte ratio and monocyte lymphocyte ration in peripheral blood measured using an assay of blood sample at baseline and 6-months

**Key secondary outcome(s)**

At baseline and 6-months:

1. Anthropometry

- 1.1. Blood pressure (mmHg)
- 1.2. Weight (kg)
- 1.3. BMI (kg/m<sup>2</sup>)
2. Thyroid hormones, and endothelial markers such as EPC, CEC, ADMA measured by blood test
3. Cognitive assessments:
  - 3.1. Mini mental state examination (MMSE)
  - 3.2. Montreal cognitive assessment (MoCA)

**Completion date**

31/01/2018

## Eligibility

**Key inclusion criteria**

1. Diagnosis of subclinical hyperthyroidism confirmed at least on two occasions (low serum TSH with normal FT4) and one normal FT3 levels within three months prior to the recruitment
2. Aged 21-85 years
3. Written informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Total final enrolment**

40

**Key exclusion criteria**

1. Sick euthyroid syndrome
2. Recent radioiodine therapy (within 1 year of screening visit)
3. Pregnant or breastfeeding patients
4. Acute medical illnesses such as infections and active cancer

**Date of first enrolment**

19/12/2012

**Date of final enrolment**

31/01/2018

## Locations

**Countries of recruitment**

Singapore

**Study participating centre**  
**Tan Tock Seng Hospital**  
11 Jalan Tan Tock Seng  
Singapore  
Singapore  
308433

## Sponsor information

**Organisation**  
Tan Tock Seng Hospital

**ROR**  
<https://ror.org/032d59j24>

## Funder(s)

**Funder type**  
Government

**Funder Name**  
National Healthcare Group-Small Innovative Grant, SIG/12011

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request available for up to 6 years after completion of the study.

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		26/11/2021	03/12/2021	Yes	No
<a href="#">Protocol file</a>	version v12	05/12/2019	06/03/2020	No	No