Multimodal effects of Thyroid hormone Replacement for Untreated older adults with Subclinical hypothyroidism* a randomised placebo controlled Trial

Published: 04-10-2012
Last updated: 26-04-2024

Main objective: To test the efficacy of thyroxine replacement for subclinical hypothyroidism (SCH) in older adults. Primary Objective: To determine multi-modal effects (quality of life; cognitive; musculoskeletal and cardiovascular) of levo-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Thyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON43858

Source
ToetsingOnline

Brief title
TRUST

Condition

- Thyroid gland disorders

Synonym
mildly underactive thyroid

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,European Commission; FP7-HEALTH-2011-twostage;Proposal No: 2781482,Merck

Intervention

Keyword: Levothyroxine, Older adults, Randomized placebo-controlled trial, Subclinical hypothyroidism

Outcome measures

Primary outcome

Change in disease specific QOL and symptom burden

Secondary outcome

1) General QOL

2) Handgrip strength

3) Cognitive function

4) Total mortality

5) Functional ability (basic and extended activities of daily living)

6) Haemoglobin

7) Depressive symptoms

8) Fatal and non-fatal cardiovascular events

Study description

Background summary

Subclinical hypothyroidism (SCH) is a common condition (8-18%) among older men and women. Although by definition SCH comprises biochemically mild thyroid hormone deficiency, it is a possible contributor to multiple problems in older age. Thyroid hormone has effects on numerous physiological systems, including the vascular tree, heart, skeletal muscle and brain. Therefore, thyroxine substitution to overcome thyroid hormone deficiency has the potential to give multisystem benefits to older people with SCH. Small studies have reported reduced atherosclerosis and improved heart function with thyroxine replacement,

but no large clinical trials have been performed. Therefore the available evidence is limited, leading to major variations in guidelines and clinical practice, with uncertainty regarding the indications for screening and treatment. Therefore, the aim of this study is to test the efficacy of thyroxine replacement for subclinical hypothyroidism (SCH) in older adults to provide the necessary evidence to properly inform best practice for treatment of SCH in older people.

Study objective

Main objective: To test the efficacy of thyroxine replacement for subclinical hypothyroidism (SCH) in older adults.

Primary Objective:
To determine multi-modal effects (quality of life; cognitive; musculoskeletal and cardiovascular) of levo-thyroxine treatment for SCH in older adults.

Secondary objectives:
1) To determine effects of SCH treatment in various subgroups
2) To determine adverse effects associated with SCH treatment with particular focus on arrhythmia and heart failure
3) To establish a blood bio-bank, to be used in future research into causes and mechanisms of health, disease and disability in later life

Study design

Randomised double-blind placebo-controlled parallel group trial of Levothyroxine for older people with subclinical hypothyroidism

Intervention

Oral Levothyroxine starting dose 50 µg daily (reduced to 25 µg daily in subjects <50Kg body weight, or if known coronary heart disease) versus matching placebo.
The dose will be changed according to the serum TSH level measured at 6-8 weeks after starting medication and after each dose change. Dose titration will be according to a predefined dosing schedule.

Study burden and risks

Adverse events (atrial fibrillation, heart failure and fractures in particular) are likely to occur only in the context of over replacement of Levothyroxine. Our dose titration scheme and study processes of careful monitoring of thyroid function tests are designed to ensure we avoid prolonged periods of thyroid hormone excess.
For the group allocated to placebo, there is risk of developing overt clinical

hypothyroidism* however, our study processes of careful monitoring of thyroid function tests are designed to avoid this scenario.

Contacts

Public
Leids Universitair Medisch Centrum

Hippocratespad 21
Leiden 2333 ZD
NL
Scientific
Leids Universitair Medisch Centrum

Hippocratespad 21
Leiden 2333 ZD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Community-dwelling patients aged 65 years and over with subclinical hypothyroidism.
-Subclinical hypothyroidism is defined as persistently elevated TSH levels (><=4.6 and *19.9 mU/L) and free thyroxine (fT4) in reference range measured on a minimum of two occasions at least 3 months apart.

Exclusion criteria

-Subjects currently on Levothyroxine, antithyroid drugs, amiodarone or lithium.
-Recent thyroid surgery or radio-iodine therapy (within 12 months).
-Grade IV NYHA heart failure.
-Prior clinical diagnosis of dementia.
-Recent hospitalisation for major illness or elective surgery (within 4 weeks).
-Recent acute coronary syndrome, including myocardial infarction or unstable angina (within 4 weeks).
-Acute myocarditis or acute pancarditis
-Untreated adrenal insufficiency and adrenal disorder
-Terminal illness.
-Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption
-Subjects who are participating in ongoing RCTs of therapeutic interventions (including clinical trials of investigational medicinal products [CTIMPs])
-Plan to move out of the region in which the trial is being conducted within the next 2 years (proposed minimum follow-up period).

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-04-2013
Enrollment:	188
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Euthyrox
Generic name:	Levothyroxine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-10-2012
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-11-2012
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-01-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	13-03-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-03-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-04-2013
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-04-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-10-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-12-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	30-04-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-05-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-06-2014
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	17-07-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-09-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-12-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-03-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-07-2015
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-07-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-06-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-004554-26-NL
ClinicalTrials.gov	NCT01660126
CCMO	NL42067.058.12