

Optimal prescribing of levothyroxine for underactive thyroid gland treatment

Submission date 23/06/2022	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 18/10/2022	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 31/12/2024	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Levothyroxine is the third most commonly prescribed medication in the UK and at 4 pence per 100-µg tablet is amongst the cheapest. The general assumption has been that when patients are prescribed levothyroxine for a diagnosis of hypothyroidism (thyroid underactivity), the treatment is life-long. However, the commonest cause of hypothyroidism is Hashimoto's (autoimmune) thyroiditis, which may result in a variable degree of mild hypothyroidism or even have a relapsing/remitting course in some patients. In addition, levels in the blood of thyroid stimulating hormone (TSH) may rise for a short period following any 'non-thyroidal illness' and this physiological phenomenon may easily be mistaken for mild hypothyroidism in someone who doesn't feel well following an intercurrent infection or other health issues. Therefore, guidelines suggest observing such patients for 3 to 6 months to see if the elevation of TSH is persistent and then considering a trial of levothyroxine treatment in younger patients with compatible hypothyroid symptoms. Unfortunately, not all short-duration, variable or mild hypothyroidism is recognised as such, leading to overtreatment.

Recent evidence both from the US and the UK suggests that many patients with only mildly abnormal or even normal thyroid blood tests are being prescribed levothyroxine in primary care settings. A complementary meta-analysis of 11 studies showed that if levothyroxine therapy is withdrawn, 30-50% of patients remain euthyroid (with normal TSH levels). Thus, overprescribing levothyroxine is a potentially detrimental situation, not only because of wasted resources in medication prescriptions and monitoring blood tests but also because out-of-range thyroid tests are found in around 50% of people taking levothyroxine, which are associated with several undesirable health outcomes, including fractures, heart problems and increased mortality. Because levothyroxine is taken by around 3 million people in the UK, overprescribing could be adversely affecting the health of around half a million people. This study aims to address how this important public health issue can be best addressed.

Who can participate?

Patients identified from GP databases as taking levothyroxine for more than 6 months

What does the study involve?

Patients will be asked to temporarily stop taking their levothyroxine for 6 weeks. Thyroid blood

tests will be done at the end of 6 weeks and quality of life will be measured at the start and end of the study. Patients will be asked what they thought about stopping their medication, how they felt during the period off levothyroxine and whether they would recommend trying off thyroid medications to a friend. After 6 weeks, patients will have the option of staying on medication if they prefer, but if their thyroid tests are suitable, they will be offered the chance to remain off levothyroxine.

What are the possible benefits and risks of participating?

Benefits and risks not provided at time of registration

Where is the study run from?

Newcastle University (UK)

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

December 2021 to December 2024

Who is funding the study?

Newcastle University (Policy) (UK)

Who is the main contact?

Dr Simon Pearce

simon.pearce@ncl.ac.uk

Contact information

Type(s)

Principal investigator

Contact name

Prof Simon Pearce

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

313119

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

10156, IRAS 313119, CPMS 52796

Study information

Scientific Title

Optimal prescribing of levothyroxine study (OPAL)

Acronym

OPAL

Study objectives

A proportion of patients taking levothyroxine medication without documented overt hypothyroidism or serum thyroid-stimulating hormone (TSH) >10 mU/l will be able to discontinue thyroid hormone replacement with no detriment to health

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 01/06/2022, West of Scotland 4 (Research Ethics, Ward 11, Dykebar Hospital, Grahamston Road, Paisley, Scotland, PA2 7DE, United Kingdom; +44 (0)141 314 0213; WoSREC4@ggc.scot.nhs.uk), ref: 22/WS/0067

Study design

Single-group 6-week temporary-withdrawal interventional study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Hypothyroidism

Interventions

Withdrawal of levothyroxine from patients taking levothyroxine medication without documented overt hypothyroidism or serum thyroid-stimulating hormone (TSH) >10 mU/l

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Levothyroxine

Primary outcome(s)

1. Serum thyroid stimulating hormone levels measured using chemiluminescent assay at 6 weeks after levothyroxine treatment withdrawal
2. Serum free thyroxine (FT4) levels measured using chemiluminescent assay at 6 weeks after levothyroxine treatment withdrawal

Key secondary outcome(s)

1. Change from baseline in quality of life measured using thyroid-specific patient-reported outcome 39-item (ThyPRO-39) scoring at 6 weeks after levothyroxine treatment withdrawal
2. Proportion of recruitments versus patients invited at the start of the study measured using signed consent forms versus letters of invitation sent
3. Friends and family test measured using a subjective questionnaire at end of the study
4. Multivariate analysis of baseline demographics (sex, age), thyroid clinical features (prior TSH, duration of LT4 treatment) and biochemical parameters at 6 weeks (TSH, FT4)
5. Serum TSH measurements measured using electronic health records over 1 year
6. Number of levothyroxine prescriptions measured using electronic health records over 1 year

Completion date

06/12/2024

Eligibility

Key inclusion criteria

1. Patients taking levothyroxine for more than 6 months
2. Aged 18 years and over
3. No documented serum TSH ≥ 10 mU/l recorded in electronic health records
4. Pregnancy, breastfeeding or with a plan for pregnancy within 6 months
5. No history of thyroidectomy, pituitary disease or thyroid cancer
6. No active ischaemic heart disease, arrhythmia or other condition that in the opinion of the principal investigator would render the withdrawal of thyroid hormone unsafe
7. No dementia, active psychotic or serious mental health condition
8. Ability to give written informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

102

Key exclusion criteria

Does not meet the inclusion criteria

Date of first enrolment

20/06/2022

Date of final enrolment

01/11/2024

Locations**Countries of recruitment**

United Kingdom

England

Study participating centre**Forest Hall Medical Group**

Station Road

Forest Hall

Newcastle upon Tyne

United Kingdom

NE12 9BQ

Sponsor information**Organisation**

Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR

<https://ror.org/05p40t847>

Funder(s)**Funder type**

University/education

Funder Name

Newcastle University

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Universities (academic only)

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Simon Pearce, simon.pearce@ncl.ac.uk. These anonymised data will be made available to bona fide researchers following an initial publication.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet			27/06/2022	No	Yes