ISRCTN11121053 https://doi.org/10.1186/ISRCTN11121053

Effect of triiodothyronine (T3) in heart failure with reduced ejection (HFrEF)

Submission date 19/03/2026	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol
Registration date 21/05/2026	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 21/05/2026	**Condition category** Circulatory System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Heart failure (HF) affects around one million people in the UK. The thyroid gland produces hormones, including Triiodothyronine (T3) which helps the heart to pump normally. Some people with HF have low levels of T3. Three small studies have shown that it is safe to give HF patients T3 supplements, and that T3 supplements may help the heart to pump better after 6 weeks.
Aim: To compare the effect of T3 supplements with a placebo (dummy capsule) on exercise capacity, health-related quality of life (HRQoL) and heart function over 24- weeks in people with HF.
Research question: What is the effect of T3 supplements on exercise capacity in people with HF and low T3 levels?

Who can participate?
Participant population: 258 patients with moderate to severe HF with reduced ejection fraction and low blood T3 levels will be identified from 14 NHS hospitals.

What does the study involve?
Treatment schedule: 10 mcg oral liothyronine sodium (a synthetic T3 supplement) or matched dummy capsule (placebo) taken twice daily for 24 weeks. Randomisation/enrolment procedures: Participants who provide their consent will have a blood test to measure their T3 levels. Participants with low T3 will be randomly allocated to receive either 10 mcg of oral liothyronine sodium or placebo in addition to their usual HF treatment. Participants will have an equal (50/50) chance of receiving either the oral liothyronine sodium or placebo. Methods: This trial is 'blinded' (the research team and participant group will not know which group they are in until the end of the trial). Exercise capacity (the distance walked in metres during a 6-minute walk test), HRQoL and HF questionnaires, and heart function (echocardiograms) will be measured at Baseline and after 24-weeks of treatment. We will compare the change in exercise capacity from Baseline to 24 weeks between the two groups. If T3 is found to improve exercise capacity in people with HF and low T3 we will plan a bigger trial to find out if T3 is effective for other HF patients.

What are the possible benefits and risks of participating?
Everyone who joins will be asked to give up some of their time at the start of the trial (Baseline visit). If participants are eligible to take one of the trial treatments (T3 or placebo) they will need

to give some more of their time at 10 weeks and 24 weeks (6 months) after they start the trial treatment. The major burden on participants is the time taken to complete EQ-5D-5L and the Minnesota HF questionnaires, and complete the six minute walking test at Baseline and 6 months. Participants will also have to remember to take their trial medication twice daily for 6 months. Blood samples will be taken by health care professionals who are trained to take blood (phlebotomists or clinicians) at the Screening visit, Baseline visit (if required) and 6 months visits (if participant provides consent for this). This will be similar to a regular blood test at a GP surgery or hospital. Some people feel mild discomfort when giving a blood sample. Sometimes there is mild bruising afterwards.
The amount of blood that we will take should not cause anaemia and we will keep a record of this in order to minimise this risk. Participants should tell their local research team if they have given blood (any amount) for any reason anywhere else in the past month. We will minimise the risks associated with the IMP by routine review by a trial steering committee, which will look at complication rates while the trial is running and can call a halt to the trial if unexpected complications arise.

Where is the study run from?
Centre for Trials Research, Cardiff University (UK)

When is the study starting and how long is it expected to run for?
May 2026 to April 2028

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
1013521

Sponsor's protocol code number
016529 10889

Study information

Scientific Title
A randomised, double-blind, placebo-controlled trial to evaluate the efficacy of orally administered Triiodothyronine (T3) for 24 weeks in patients with heart failure with reduced ejection (HFrEF)

Acronym
The T3-HF Trial

Study objectives
Our primary objective is to compare exercise tolerance, defined as the change in distance walked (metres) during a 6-minute walk test from baseline to 24 weeks, in participants randomised to oral liothyronine sodium with participants receiving a placebo.

Secondary objectives include assessing the effect of oral liothyronine use on:
• Thyroid function
• Serum markers of HF and inflammation
• Functional classification for HF
• Health-related QoL
• LV function
• Cardiac function
• HR and new onset AF
• Major adverse cardiovascular events (MACE)
• Length of stay for any HF hospitalisation
• Non-cardiovascular mortality
• Mechanism(s) affecting exercise tolerance i.e. cardiac function

Ethics approval required
Ethics approval required

Ethics approval(s)

submitted 18/03/2026, Wales REC 1 (Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; no telephone number provided; Wales.REC1@wales.nhs.uk), ref: 26/WA/0098

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Single

Purpose
Treatment, Safety

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Heart failure with reduced ejection fraction and low serum T3 levels

Interventions
Intervention: 10 mcg oral liothyronine sodium capsule taken orally twice daily for 24 weeks.

Control: Matched placebo capsule, taken orally twice daily for 24 weeks.

All randomised participants will be followed-up at 10 weeks to assess compliance and 24-weeks to assess primary outcome measure (distance walked in metres during 6-minute walking test) and secondary outcomes measures, including Thyroid function assessed by TSH, FT4 and FT3 tests; Serum markers of heart failure (assessed by plasma levels of NT pro-BNP) and inflammation (assessed by high sensitivity CRP), Functional classification for HF (assessed by NYHA class); HRQoL assessed using EQ-5D-5L, and Minnesota Living with Heart Failure; LV function measured by LVEF assessed by 2D echocardiography; Cardiac function measured by GLS and GCS, assessed by 2D echocardiography; Heart rate and new-onset atrial fibrillation (assessed by ECG); MACE (defined as: cardiovascular mortality; AMI; hospitalisation for HF; stroke; hospitalisation for unstable angina or coronary revascularisation procedure); Length of stay for any HF hospitalisation assessed by clinical notes review; Non-cardiovascular mortality; and Mechanism(s) affecting exercise tolerance i.e. cardiac function.

Eligible participants will be randomised 1:1 using a minimisation algorithm with a random element to either active treatment (10 mcg oral liothyronine sodium) or control (placebo).

Allocations will be balanced by site, sex, age category (≤65 years/>65 years), and ischaemic cause of HFrEF (yes/no). The online randomisation program will be developed by the Cardiff CTR and will be embedded within the trial database with controlled access.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Liothyronine sodium

Primary outcome(s)
1. The distance covered by the participant in 6 minutes measured using the 6 minute walking test at baseline and the end of the intervention at 24 weeks

Key secondary outcome(s))
1. Thyroid function measured using TSH, FT4 and FT3 tests at Screening and 24 weeks

2. Serum markers of heart failure measured using plasma levels of NT pro-BNP and inflammation by high-sensitivity CRP at baseline and 24 weeks

3. Functional classification for HF measured using the NYHA class at screening and 24 weeks

4. Health-related QoL measured using EQ-5D-5L, and Minnesota Living with Heart Failure, at baseline and 24 weeks

5. LV function measured using LVEF by 2D echocardiography at screening (most recent LVEF from previous 24 months used) and 24 weeks

6. Cardiac function measured using GLS and GCS by 2D echocardiography at baseline (most recent GLS and GCS from previous 24 months) and 24 weeks

7. Heart rate and new-onset atrial fibrillation measured using ECG at baseline and 24 weeks

8. MACE, defined as: cardiovascular mortality; AMI; hospitalisation for HF; stroke; hospitalisation for unstable angina or coronary revascularisation procedure, measured using a clinical notes review at 24 weeks

9. Length of stay for any HF hospitalisation measured using a clinical notes review at 24 weeks

10. Non-cardiovascular mortality measured using a clinical notes review at 24 weeks

11. Mechanism(s) affecting exercise tolerance i.e. cardiac function measured using 2D echocardiography at 24 weeks

Completion date
30/04/2028

Eligibility

Key inclusion criteria
1. Adults aged 18 years or older who are able to provide informed consent
2. Those with moderate to severe HFrEF (defined as LVEF ≤40% on the most recent echocardiogram)
3. Participants with chronic and stable HF (diagnosed ≥3 months before recruitment and no inpatient admission to hospital for HF exacerbations <1 month before recruitment)
4. Those with serum free T3 levels ≤4.0 pmol/L
5. Those on maximally tolerated guideline-directed medical therapies for HFrEF

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
120 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Taking medications affecting thyroid function (including levothyroxine, antithyroid drugs, amiodarone, lithium and sodium valproate)
2. Participating in another interventional trial if it is deemed to interfere with the assessment of the primary outcome by the local investigator
3. Unable to attempt the 6MWT (as it would be unethical to include a person in an intervention trial where they would not be contributing to the primary outcome)
4. Currently pregnant or are planning to become pregnant in the next 24 weeks
5. Newly diagnosed with overt hypothyroidism (serum TSH higher than the upper limit of the reference range and a low serum free T4 level) or hyperthyroidism (low TSH with normal or elevated FT4 levels)
6. Any current comorbidity expected to reduce life expectancy to ≤6 months

Date of first enrolment
25/05/2026

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
England
NE9 6SX

Study participating centre
North Tees and Hartlepool NHS Foundation Trust
University Hospital of Hartlepool
Holdforth Road
Hartlepool
England
TS24 9AH

Study participating centre
Liverpool Heart & Chest Hospital
Broadgreen Hospital
Thomas Drive
Liverpool
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L14 3PE

Study participating centre
Hull University Teaching Hospitals NHS Trust
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Anlaby Road

Hull
England
HU3 2JZ

Study participating centre
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St. James's University Hospital
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LS9 7TF

Study participating centre
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NE29 8NH

Study participating centre
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TS4 3BW

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

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 the Centre for Trials Research, Cardiff University.

IPD sharing plan summary
Available on request