ISRCTN12900952 https://doi.org/10.1186/ISRCTN12900952

LiFT: Liver fibrosis after low-energy treatment in steatohepatitis

Submission date 08/02/2020	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/02/2020	**Overall study status** Completed	
Last Edited 30/09/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
The building up of fat in the liver can cause inflammation and scarring. This serious condition is called non-alcoholic steatohepatitis (NASH). NASH can lead to liver problems and heart disease. It affects almost 4 million people in Britain and about 80-90% of them have obesity. No drug is currently available to treat NASH. Weight loss programmes might improve NASH, but only if they lead to large weight loss. One programme that could achieve this on a large scale is a low-calorie diet with one-to-one support. In this programme, people only eat soups and shakes for 12 weeks (about 810 calories per day). Then, slowly over the next 12 weeks, they swap some soups and shakes for regular food. The support helps people stick to the programme and develop healthier eating habits. People lose weight rapidly and lower their risk of heart disease and type 2 diabetes. About half of the people with type 2 diabetes stop their medication. This may also be a good treatment for NASH, but there is some evidence that rapid weight loss may worsen scarring in the liver. Here the researchers will test the programme in a small group of people with detailed monitoring of the health of their liver.

Aims: To measure the changes in the liver fibrosis and inflammation with non-invasive procedures in people with NASH after a total diet replacement programme.

Who can participate?
Patients with BMI >= 30 and liver fibrosis.

What does the study involve?
Participants will be asked to follow the weight loss programme. The researchers will do blood tests after 4 weeks to check for an early changes. At the start and after 3 and 6 months, participants will have a magnetic resonance imaging (MRI) scan and an ultrasound of their liver to see if there has been any further change in the health of their liver.

What are the possible benefits and risks of participating?
The liver disease may improve, remain stable, or worsen. We will monitor the liver frequently and carefully, so that participants can stop the programme if necessary. This means that the likelihood of suffering an adverse event is very low. Most people do not experience side effects due to the programme. Participants may experience side effects (e.g. constipation) during the

programme, but most side effects are only mild and temporary. We will check these regularly. The weight loss can reduce the risk of heart disease and diabetes. If participants are taking medication for blood pressure or diabetes, their doctor may advise you to stop them completely or reduce the dose as part of their standard clinical care.

Where is the study run from?
John Radcliffe Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2020 to August 2022

Who is funding the study?
NIHR Oxford Biomedical Research Centre (UK)

Who is the main contact?
Dr Dimitrios Koutoukidis
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
269633

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

Study information

Scientific Title
Changes in liver fibrosis and inflammation estimated non-invasively after treatment with a low-energy total diet replacement programme in people with non-alcoholic steatohepatitis: a single-arm trial

Acronym
LiFT

Study objectives
The aim of the current study is to examine the changes in liver fibrosis and inflammation assessed non-invasively in people with non-alcoholic steatohepatitis following a total diet replacement programme with behavioural support

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/01/2020, London - Surrey Borders Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 104 8134; NRESCommittee.London-SurreyBorders@nhs.net), Ref: 19/LO/1856

Study design
Single-arm trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Nonalcoholic steatohepatitis [NASH]

Interventions
The intervention is a low-energy total diet replacement programme with behavioural support (TDR) and has three phases. Phase 1 starts with sole source TDR for up to 12 weeks. Participants will consume about 810kcal/day in a nutritionally complete package of soups and shakes. The exact treatment durations will depend upon response and aim to achieve 20kg weight loss at 3 months. Participants may choose to move to phase 2 as soon as they have achieved their target weight loss or they can continue in Phase 1 for the whole period of 12 weeks, whichever is earlier. In such a case, the next phase will be extended accordingly, so that all participants receive the intervention for 24 weeks. Between weeks 12-16 (phase 2), products will be gradually reduced and replaced with food-based meals. During the weight maintenance phase 3 (weeks 16-24), participants will consume one product a day. Depending on the weight changes, it

may be recommended to participants to return to Phase 1 for a short period of time. Participants will have regular contact with the dietitian for behavioural support over the phone or via an app.

Intervention Type
Behavioural

Primary outcome(s)
At baseline, 12 weeks, and 24 weeks:
1. Iron-corrected relaxation time (cT1) values by magnetic resonance imaging (MRI)
2. Liver stiffness by transient elastography (added 16/11/2020: and magnetic resonance elastography)
3. Proton density fat fraction (PDFF)
4. Controlled attenuation parameter
5. Glucose regulation biomarker (HbA1c)
6. Total body fat on bioelectrical impedance
7. Visceral fat on MRI
8. Subcutaneous fat on MRI
9. Number and dose of medication
10. Diversity and abundance of the gut microbiome

At baseline, 4 weeks, 12 weeks, and 24 weeks:
11. Liver blood biomarkers (ALT, AST, ALP, bilirubin, FIB-4, Apo-F)
12. Renal blood biomarkers (U&E)

At 4 weeks, 12 weeks, and 24 weeks:
13. Adverse events

Key secondary outcome(s))
Before baseline
1. Number of potentially eligible participants
2. Proportion of eligible participants enrolled
3. Reasons for non-enrolment

At baseline, 4 weeks, 12 weeks, and 24 weeks:
4. Weight
5. Proportion of sessions attended
6. Reasons for non-adherence
7. Proportion of participants attending their follow-ups out of all enrolled
8. Alcohol intake

At 4 weeks, 12 weeks, and 24 weeks:
9. Reasons for dropout

At 24 weeks:
10. Feedback questionnaire on intervention

Completion date
31/08/2022

Eligibility

Key inclusion criteria
BMI >=30 kg/m² and histological evidence of NASH and fibrosis stage 1a to 3

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
16

Key exclusion criteria
1. ALT 10x upper limit of normal or above
2. Total bilirubin > 25.5 µmol/l
3. Evidence of other known forms of known chronic liver disease such as alcoholic liver disease, hepatitis B, hepatitis C, primary biliary cholangitis, primary sclerosing cholangitis, autoimmune hepatitis, Wilson disease, iron overload, alpha-1-antitrypsin deficiency, drug-induced liver injury, known or suspected hepatocellular carcinoma (HCC)
4. Previous liver transplant or current placement on a liver transplant list
5. High risk of alcohol dependence defined as a score of 8 and above in the alcohol screening tool (AUDIT-C)
6. Consumption of more than 14 units of alcohol over the last week
7. Previous or planned bariatric surgery or ileal resection
8. History of biliary diversion
9. Acute cholecystitis or acute biliary obstruction
10. Contraindication to MRI
11. Currently attending or having attended within 3 months prior to study enrolment a weight management programme including behavioural programmes and weight loss medication
12. Weight loss of 5% or more since biopsy
13. Current insulin use
14. HbA1c > 9% (>75mmol/mol)
15. Diagnosed with type 2 diabetes with substantial changes in medication within the past 3 months
16. If taking GLP-1 agonists or SGLT2 inhibitors, changes in dosage during the past 6 months
17. Taking medication known to have potential activity against NASH (pioglitazone, Vitamin E)
18. Documented arrhythmia, except atrial fibrillation, or prolonged QT syndrome
19. Taking warfarin
20. Chronic renal failure of stage 4 or 5
21. Scheduled for surgery within 6 months
22. People having active treatment for cancer other than skin cancer treated with curative intent by local treatment only or people taking hormonal or other long-term secondary prevention treatment after initial cancer treatment
23. Currently taking part in other clinical trials

24. Pregnant, breastfeeding, or planning to become pregnant during the course of the study
25. Those that the clinician judges not able to meet the demands of either treatment programme or measurement schedule. This may include severe medical problems not listed above or severe psychiatric problems including substance misuse that make following the treatment programme or adhering to the protocol unlikely

Date of first enrolment
01/03/2020

Date of final enrolment
15/12/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
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OX3 9DU

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name

NIHR Oxford Biomedical Research Centre

Alternative Name(s)
NIHR Biomedical Research Centre, Oxford, OxfordBRC, OxBRC

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
De-identified datasets generated during and/or analysed during the current study will be available upon request from the chief investigator (Dr Dimitrios Koutoukidis dimitrios.koutoukidis@phc.ox.ac.uk) following publication of the results. All proposals requesting data access will need to complete a data request form with details of the research question and analysis plan. Participants have consented to their de-identified data being shared for future research.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/07/2023	27/07/2023	Yes	No
Results article		28/09/2024	30/09/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results		03/07/2023	27/07/2023	No	Yes