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Determining the optimum strategy for the detection of advanced liver disease in primary care interface

Submission date
19/10/2022

Recruitment status
No longer recruiting

Registration date
21/12/2022

Overall study status
Completed

Last Edited
28/08/2024

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Undiagnosed significant liver disease is highly prevalent in the community, primarily due to high rates of harmful alcohol consumption and obesity. Obesity and harmful alcohol consumption cause fatty liver disease, which can progress to cirrhosis and complications including liver cancer and liver failure. Because liver disease is usually asymptomatic at early stages, patients frequently present once advanced liver disease has developed when they are at high risk of complications. Early identification of liver disease before cirrhosis and earlier initiation of lifestyle
changes and treatment may prevent progression to cirrhosis. The overall aim of this study is to develop an effective primary care fibrosis biomarker pathway to identify patients with advanced liver fibrosis in individuals with risk factors for liver disease. The study will use a clinical care pathway that incorporates a 'liver assessment' within primary care annual chronic disease reviews to identify patients with significant liver disease. This pathway will be a platform to evaluate the performance of non-invasive liver fibrosis biomarkers. In the pathway, individuals with obesity, Type 2 diabetes or harmful alcohol consumption will have a 'liver assessment' using established non-invasive fibrosis biomarkers including FIB-4, ELF and transient elastography (TE; Fibroscan). Blood samples will be taken for novel biomarkers, including ProC3, to evaluate their performance. Individuals with suspected significant/advanced liver fibrosis will be reviewed in a secondary care liver clinic to confirm their stage of liver fibrosis and institute specific treatment and/or enhanced lifestyle management within routine NHS clinical services. This pathway will allow us to evaluate the diagnostic accuracy of the FIB-4, ELF and ProC3 alone or in combination, as well as collect samples to assess future novel blood-based biomarkers of liver disease. Patients will also be followed longitudinally via their electronic health records and NHS digital to assess long-term clinical outcomes.

Who can participate?
Individuals aged 18-80 years old attending for an 'annual review of care', 'chronic disease review' or 'health check' with one or more of the following risk factors:

1. Obesity (BMI >30kg/m2)
2. Type 2 diabetes
3. Potentially hazardous/harmful alcohol consumption (AUDIT score > 8)

What does the study involve?
Patients attending for their 'annual year of care review', 'chronic disease review' or 'health check' in primary care will be invited to participate in this study if they have risk factors for liver disease. These individuals will be offered a 'liver assessment' to identify or exclude advanced liver disease. This will include blood tests for liver enzymes, blood fibrosis markers (FIB-4, ELF, PRO-C3 and CTX3 and blood for storage to analyse
future biomarkers), and Transient elastography (TE; Fibroscan). All participants will be given relevant lifestyle advice and an information booklet with advice on how to reduce their risk of liver disease progression. We will evaluate two pathways to determine which is most clinically and cost-effective. In pathway one, all patients will be offered TE and have blood tests for liver fibrosis biomarkers. In pathway two, patients with blood fibrosis tests indicating possible advanced fibrosis/cirrhosis (FIB-4 >1.3 or ELF >9.8) have TE to stage their fibrosis. Individuals whose investigations indicate possible moderate to advanced liver fibrosis (TE > 8kPa) will be offered referral to secondary care for further assessment and treatment. These individuals may have further investigations if needed, and/or treatment for their liver disease as per usual NHS care. Some may require ongoing treatment and follow-up in secondary care. Patients with low TE readings will remain in primary care. We will collect blood to analyse for new liver fibrosis markers to assess their performance in diagnosing advanced liver fibrosis and we hope to develop more efficient pathways to identify patients with liver disease in primary care.

What are the possible benefits and risks of participating?
By taking part in the study and having the liver fibrosis assessment we may identify undiagnosed liver disease, which you can then have treatment for. We will also provide information about lifestyle changes that you can make to reduce your risk of liver fibrosis in the future. In addition, the outcome of the research could help to improve the care of other patients. You will not personally receive any financial benefit from taking part in the research. In most cases, we do not anticipate any disadvantages of taking part. Being diagnosed with liver disease could cause you to worry about the diagnosis, but it does also potentially lead to you being able to have treatment to reduce your risk of progressive liver disease if this were diagnosed. The risks of participation are very low, but having a blood sample collected can be uncomfortable for a short time or may leave a small bruise.

Where is the study run from?
Recruitment is from primary care sites across North East England (UK)

When is the study starting and how long is it expected to run for?
September 2020 to December 2024

Who is funding the study?
The Medical Research Council (UK)

Who is the main contact?
Dr Stuart McPherson (Chief Investigator), stuart.mcpherson2@nhs.net (UK)

Contact information

Type(s)

Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
310086

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 52853, IRAS 310086

Study information

Scientific Title
Stratification Of LIver Disease (SOLID): Determining the optimum biomarker strategies for the detection of advanced liver disease at the primary-secondary care interface

Acronym
SOLID

Study objectives
We hypothesise that a pathway incorporating the use of liver fibrosis biomarkers will increase the diagnosis of patients with advanced liver fibrosis in primary care

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/06/2022, London - Chelsea Research Ethics Committee, Health Research Authority (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)20 7104 8064; chelsea.rec@hra.nhs.uk), ref: 22/PR/0535

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Diseases of the liver

Interventions
Patients attending for their ‘annual year of care review’, ‘chronic disease review’ or ‘health check’ in primary care will be invited to participate in this study if they have risk factors for liver disease (obesity [BMI >30 kg/m2], Type 2 diabetes or potentially harmful alcohol consumption [AUDIT score > 8]).
These individuals will be offered a 'liver assessment' to identify or exclude advanced liver disease. This will include blood tests for liver enzymes, blood fibrosis markers (FIB-4, ELF, PRO-C3 and CTX3 and blood for storage to analyse future biomarkers), Transient elastography (TE; Fibroscan) and a metabolic assessment.
All participants will be given relevant lifestyle advice and an information booklet with advice on how to reduce their risk of liver disease progression.
We will evaluate two pathways to determine which is most clinically and cost-effective. In pathway one (Northumberland GPs), all patients will be offered TE and have blood tests for liver fibrosis biomarkers. In pathway two (Newcastle GPs), patients with blood fibrosis tests indicating possible advanced fibrosis/cirrhosis (FIB-4 >1.3 or ELF >9.8) have TE to stage their fibrosis.
Individuals whose investigations indicate possible moderate to advanced liver fibrosis (TE >

8kPa) will be offered referral to secondary care for further assessment and treatment. These individuals may have further investigations if needed, and/or treatment for their liver disease as per usual NHS care. Some may require ongoing treatment and follow-up in secondary care. Patients with low TE readings will remain in primary care.
We will collect blood to analyse for new liver fibrosis markers to assess their performance in diagnosing advanced liver fibrosis and we hope to develop more efficient pathways to identify patients with liver disease in primary care.

Intervention Type
Other

Primary outcome(s)
Number of patients identified with advanced liver fibrosis/cirrhosis using each of the pathways based on an overall clinical evaluation by a panel of hepatologists measured using study records at a single time point

Key secondary outcome(s))
1. Usefulness of non-invasive testing/triage strategies to identify patients who have liver-related events (death, hepatic decompensation, transplantation) during longitudinal follow-up at 2, 5 and 10 years measured using electronic care records/NHS Digital
2. Performance of FIB-4, ELF, PRO-C3 and other novel blood-based biomarkers alone or in combination measured using overall clinical assessment or LSM to identify advanced fibrosis /cirrhosis at a single timepoint
3. Performance of the biomarkers to correctly exclude advanced fibrosis/cirrhosis as defined by overall clinical assessment or LSM at a single timepoint
4. Development of the optimum pathway (clinically and cost-effective and implementable)

Completion date
31/12/2024

Eligibility

Key inclusion criteria
Individuals aged 18-80 years attending for an ‘annual review of care’, ‘chronic disease review’ or ‘health check’ with one or more of the following risk factors for liver disease:
1. Obesity (BMI > 30),
2. Type 2 diabetes
3. Potentially harmful alcohol consumption (AUDIT score > 8)

We have included an upper cut-off for the age of 80 for inclusion in this study. This is because liver disease generally has a slow progression to liver-related complications even with compensated cirrhosis, and as a result, asymptomatic individuals > 80 years are unlikely to benefit from early detection of liver disease.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Life limiting disease on high risk or palliative care register
2. Known liver disease under secondary care follow up
3. Refusal or inability (lack of capacity) to provide informed consent
4. Unable to understand or speak English

Date of first enrolment
31/10/2022

Date of final enrolment
31/08/2024

Locations

Countries of recruitment
United Kingdom

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

Study participating centre
NIHR CRN: North East and North Cumbria
Regent Point
Regent Farm Road
Newcastle upon Tyne
United Kingdom
NE3 3HD

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
Medical Research Council; Grant Codes: MR/037331/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No