

# Testing for liver scarring at the diabetes annual review

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<b>Registration date</b> 27/04/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 04/11/2025	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Changes in the liver are common among people with diabetes and are mostly due to fat buildup. This condition is called non-alcoholic fatty liver disease (NAFLD) and is found in up to two-thirds of people living with type 2 diabetes (T2D). In some cases patients with NAFLD are not at particularly increased risk of developing serious liver disease, but in some patients NAFLD can take a more progressive form that involves inflammation and scarring in the liver (non-alcoholic steatohepatitis or NASH) that can progress to cirrhosis, liver failure and liver cancer. Sadly people with diabetes are at increased risk of developing NASH and scarring in the liver. Researchers want to identify people who will develop serious liver disease in the earlier stages, when something can be done to stop progression.

For most people, there are no symptoms of fatty liver, scarring or even cirrhosis until the latest stages of disease when treatment is less effective. Routine blood tests do not diagnose scarring or cirrhosis, but it is possible to calculate scores from these tests, such as the Fib-4 used in this study to accurately rule out significant disease. If Fib-4 is negative, we can be fairly confident that patients do not have significant fibrosis. If Fib-4 is positive, then patients should have further specialist investigations.

This study will focus on people in GP practices with T2D because they have an annual review that includes blood tests, to which a Fib-4 test will be added. Patients who have positive test results will be referred for a liver fibrosis scan either at their local hospital or GP practice. If Fib-4 testing in the annual review identifies more patients with fibrosis and is cost-effective, this test could be introduced across the NHS to target treatment and reduce the number of people who develop liver cancer or liver failure.

### Who can participate?

Patients aged 18 years and over with type 2 diabetes who are registered at the GP practices participating in the study

### What does the study involve?

Participants will not experience anything different at their annual review and blood samples will be taken in the normal way – only one blood draw is needed as normal for the annual review. Depending on the blood tests the practice does as standard, participants may not need to give any extra blood. If the Fib-4 blood test cannot exclude significant liver scarring, participants will

be told and invited to have a special scan of the liver called a Fibroscan. This is a quick test (10 minutes) that involves applying jelly to the abdomen and running a probe over the liver. It is not painful and there are no needles involved. This might take place at a local hospital or at a location in or near the GP practice.

A small number of people will be asked to take part in an optional interview and/or focus group to explore people's thoughts about liver screening alongside the diabetes annual review and the experience of being involved in this study. This interview and/or focus group would take place either in person at the GP practice, other NHS sites, or alternatively online/by telephone. This should take less than 90 minutes. The researchers wish to audio or video record this interview /focus group to record what is said. These recordings will then be destroyed after transcription to a written record. Transcription of interviews will be undertaken by the study team in an anonymised format. Afterwards the researchers may wish to contact participants to ask follow up questions based on comments from other patient interviews before completion of the study. Direct quotes from interviews may be published alongside the results of this study without any details that could identify participants.

What are the possible benefits and risks of participating?

If the results of the examinations performed in this study identify any abnormalities with the liver then participants will be referred to their local hospital liver clinic for routine clinical care.

Where is the study run from?

Barts Health NHS Trust (UK)

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

January 2020 to September 2024

Who is funding the study?

Gilead Sciences (USA)

Who is the main contact?

bartshealth.rlhprelude1@nhs.net

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## Contact information

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Scientific

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## **Additional identifiers**

**Clinical Trials Information System (CTIS)**  
Nil known

**Integrated Research Application System (IRAS)**  
299934

**Protocol serial number**  
CPMS 51136, IRAS 299934

## **Study information**

**Scientific Title**  
Feasibility and acceptability of a primary care liver fibrosis testing pathway centred on the diabetes annual review

**Acronym**  
PRELUDE-1

**Study objectives**  
Liver fibrosis screening using FIB-4 and Fibroscan will prove feasible in primary care as a component of the diabetes annual review.

**Ethics approval required**  
Old ethics approval format

## **Ethics approval(s)**

Approved 15/02/2022, East of England - Cambridge East Research Ethics Committee (The Old Chapel Royal Standard Place Nottingham NG1 6FS, UK; +44 (0)207 104 8102, +44 (0)2071048265; CambridgeEast.REC@hra.nhs.uk), ref: 21/EE/0269

## **Study design**

Non-randomized; Both; Design type: Screening, Diagnosis, Process of Care, Management of Care, Cohort study

## **Primary study design**

Interventional

## **Study type(s)**

Diagnostic

## **Health condition(s) or problem(s) studied**

Liver fibrosis

## **Interventions**

This is a prospective cohort study of automated fibrosis testing in patients with type 2 diabetes linked to a trial of hospital-based versus community-based second-tier testing. The overall strategy is to determine whether focussing on at-risk type 2 diabetes patients, without a priori recognition or suspicion of nonalcoholic fatty liver disease (NAFLD), is a feasible and acceptable approach to fibrosis testing in the community. This study takes advantage of the mature nationwide programme of annual diabetes review and the performance-based remuneration system in UK primary care.

Blood requests will be automatically generated at the review and the Fib-4 automatically calculated from these results and an action plan recommended based on the threshold of 1.3. Practices allocated to the hospital arm will send the referral to hospital as per existing local referral pathways. Practices in the community arm send electronic referrals to a dedicated NHS address and a member of the NHS care team will arrange an appointment for the patient at the community centre. Results from Fibroscans will be returned to the GP practice for coding in primary care records and clinical action.

## **Study procedures:**

1. Practice-wide consent to take part in PRELUDE-1
2. Adoption and agreement to include Fib-4 test at diabetes annual review alongside standard biochemistry tests
3. Patients with indeterminate/high risk (Fib-4 >1.3) scores proceed to either community or hospital Fibroscan (pre-determined for each practice in this feasibility study)
4. Patients with Fibroscan >7.9 kPa referred to local hepatology services
5. Data extraction from EMIS 2021-22
6. Data extraction from EMIS 2022-23

The intervention builds on existing infrastructure and data extraction/audit tools that are already built into the routine care software packages that are in use in >90% of UK GP practices. This means that anonymised data can be extracted using Read codes (version CTV3) for "Diabetes Annual Review" or "Diabetes Type 2 Review" as the primary handle. The researchers will extract demographic and clinicopathological data to include ethnicity, social deprivation, partial postcode, medical history including alcohol consumption, medication use, blood and

imaging results including liver aetiology screen. They will work with data using a remote secure server under the guidance of the the QMUL Research data access and management policy.

#### **Cost-effectiveness**

The researchers will undertake an exploratory cost-utility analysis of protocolled versus historic opportunistic testing for fibrosis in order to construct a Markov model of lifetime costs from a health and social care perspective and quality-adjusted life expectancy, considering current and potential novel drug therapies. The structure will be informed by a conceptual modelling phase, but is likely to include health states representing cirrhosis, decompensation and transplantation. The model will be parameterised following a structured literature search. Parameters on prevalence of fibrosis will be informed by the trial. The model will be probabilistic and results will be reported in the form of cost-effectiveness acceptability curves.

#### **Identifying attitudes**

The qualitative arm will comprise a semi-structured interview/focus group with primary care staff (GPs and practice nurses), and a semi-structured interview with patients taking part in the wider study. Purposive sampling across relevant key characteristics (e.g., job role, length of time in role, ethnicity, age, and gender) will be used to capture varying levels of staff clinical experience and knowledge, as well as diversity in sociodemographic factors. No sample size has been set as the target is saturation of themes. However, based on previous studies and to facilitate adequate purposive sampling, a minimum of 30 participants (15 staff and 15 patients) is a reasonable approximation. Interviews/focus groups will be scheduled to take place at the most convenient time for participants. Relevant routine departmental or practice meetings will be utilised where possible for staff focus groups to reduce burden on resources. Flexibility will be provided in cases where group participation is not possible, offering individual semi-structured interviews where preferred. Participation will involve a single session interview or focus group of approximately 60 minutes in duration.

The topic guides are devised from the study aims and from background literature on liver screening in primary care. PPI groups have also reviewed the study materials and methodologies and feedback has been incorporated accordingly. Topic guides will be used flexibly to facilitate the process of qualitative data collection, with scope for discussion of other topics that participants find salient. The staff topic guide focuses on attitudes towards non-alcoholic steatohepatitis (NASH) and liver fibrosis in diabetes, typical experiences of testing for fibrosis in primary care, and assessment guidelines. Specifically, the interviews will explore experiences of perceived advantages and disadvantages of the assessment strategy and the barriers and facilitators to implementing protocolled screening for liver fibrosis beyond the trial context. For patients, the topic guide focuses on overall experiences of taking part in the study, comprehension and impact of assessment, and knowledge of risk factors and health behaviours for NASH and fibrosis pre and post-test.

This work will inform the implementation strategy for the subsequent trial phase and help us understand why previous guidance has not resonated with the community.

#### **Intervention Type**

Other

#### **Primary outcome(s)**

Proportion of individuals with type 2 diabetes with indeterminate or high-risk Fib-4 scores at the diabetes annual review

#### **Key secondary outcome(s)**

1. Proportion of patients referred for Fibroscan who attend in community vs hospital, measured at the end of the study
2. Exploratory cost-utility analysis of protocolled versus historic opportunistic testing for fibrosis, measured at the end of the study
3. Qualitative analysis of attitudes among primary care physicians towards NASH and liver fibrosis in diabetes, testing for fibrosis in primary care, and assessment guidelines, using structured interviews/focus groups at the end of the study
4. Proportion of individuals with indeterminate or high-risk Fib-4 who have raised fibroscan scores measured at the end of the study

**Completion date**

01/09/2024

## Eligibility

**Key inclusion criteria**

1. General practice with >4000 registered patients
2. Practice lead, or representative, confirms agreement to participate in the study after reading the practice information sheet
3. Practice lead, or representative, confirms practice support introduction of Fib-4 testing for all patients with type 2 diabetes attending for annual review
4. Track record of >85% of patients with type 2 diabetes attending for diabetes review
5. Practice uses EMIS computer system
6. Referral route for fibroscan based on primary care non-invasive score agreed

**Patient inclusion criteria:**

1. Type 2 diabetes
2. Serum biochemistry sample taken alongside diabetes annual review

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Key exclusion criteria**

1. Inclusion criteria not met
2. Practice participating in other screening or case-finding study related to liver fibrosis

**Date of first enrolment**

02/05/2022

**Date of final enrolment**

01/11/2023

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

### **Barts Health NHS Trust**

The Royal London Hospital

80 Newark Street

London

United Kingdom

E1 2ES

## Study participating centre

### **Queen Mary University of London**

Hepatology Blizard Institute

School of Medicine and Dentistry

Blizard Institute

4 Newark St

London

United Kingdom

E1 2AT

## Study participating centre

### **University of Bristol**

Public Health

Canynges Hall

Whatley Road

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United Kingdom

BS8 2PS

## Study participating centre

### **University Hospitals Bristol and Weston NHS Foundation Trust**

Trust Headquarters

Marlborough Street

Bristol

United Kingdom

BS1 3NU

**Study participating centre**  
**Bristol Royal Infirmary**  
Marlborough Street  
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United Kingdom  
BS2 8HW

**Study participating centre**  
**The Royal London Hospital**  
Whitechapel Road  
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E1 1FR

## Sponsor information

**Organisation**  
Queen Mary University of London

**ROR**  
<https://ror.org/026zzn846>

## Funder(s)

**Funder type**  
Industry

**Funder Name**  
Gilead Sciences

**Alternative Name(s)**  
Gilead, Gilead Sciences, Inc., Oligogen

**Funding Body Type**  
Government organisation

**Funding Body Subtype**  
For-profit companies (industry)

**Location**  
United States of America

# 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?
<a href="#">Protocol article</a>		19/05/2023	22/05/2023	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Baseline Data - conference Abstract	19/05/2023	25/11/2024	Yes	No
<a href="#">Other publications</a>	aseline Data - conference Abstract	19/05/2023	25/11/2024	Yes	No
<a href="#">Other publications</a>	qualitative process evaluation	13/10/2024	25/11/2024	Yes	No
<a href="#">Other publications</a>	qualitative process evaluation	13/10/2024	25/11/2024	Yes	No
<a href="#">Participant information sheet</a>	version 1.4	11/03/2022	22/04/2022	No	Yes