

# Stratify methotrexate: a study to investigate the liver function of patients taking methotrexate, and risk-stratify them accordingly

<b>Submission date</b> 28/10/2019	<b>Recruitment status</b> Suspended	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 18/11/2019	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 14/07/2020	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Methotrexate is a drug widely prescribed, however the most appropriate method of monitoring is debated and currently unclear, demonstrated by divergent guidelines across specialities. Historically concerns have been raised regarding methotrexate and the development of liver fibrosis; more recent publications have cast doubt upon this potential relationship.

The discovery of novel, non-invasive methods to assess liver fibrosis, such as transient elastography (e.g. FibroScan®) have allowed fresh consideration into this difficult area.

This study aims to assess the prevalence of liver fibrosis (by way of FibroScan®, blood tests and clinician review) in participants who are taking methotrexate, compared with those who have never taken this drug.

### Who can participate?

Patients aged over 18 who are have been taking methotrexate for six months or more, and age matched controls who have never taken methotrexate

### What does the study involve?

Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

### What are the possible benefits and risks of participating?

Possible benefits of taking part in this research include the health checks included as part of it, which you are informed at the time. For the majority of people, these health checks are very reassuring. Should any abnormalities be found then referral for appropriate assessment and investigations will be undertaken.

The culmination of this research should better inform clinicians about risk factors for potential liver injury in those individuals taking methotrexate, and help to shape future guidelines. There is a possibility that the health checks performed show up a problem. In this circumstance,

patients would be informed immediately and the next appropriate steps will be organised and made clear. We appreciate the discovery of health-related findings can cause worry and the staff are on hand to discuss any concerns

Where is the study run from?  
York Hospital (UK)

When is the study starting and how long is it expected to run for?  
From June 2019 to December 2021 (updated 14/07/2020, previously: September 2020)

Who is funding the study?  
LIVErNORTH (UK)

Who is the main contact?  
Dr Lucy Turner, [lucy.turner7@nhs.net](mailto:lucy.turner7@nhs.net)  
[lucy.turner7@nhs.net](mailto:lucy.turner7@nhs.net)

## Contact information

Type(s)  
Scientific

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## Additional identifiers

EudraCT/CTIS number  
Nil known

IRAS number

ClinicalTrials.gov number  
Nil known

Secondary identifying numbers  
42142

## Study information

**Scientific Title**

A study to investigate the liver function of patients taking methotrexate, and risk-stratify them accordingly

**Study objectives**

There is no difference in the prevalence of liver fibrosis between individuals taking methotrexate, compared with those who are not

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 18/06/2019, NHS HRA (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH), ref: 19/NE/0176

**Study design**

Non-randomized; Observational; Design type: Validation of investigation /therapeutic procedures

**Primary study design**

Observational

**Secondary study design**

Cohort study

**Study setting(s)**

Hospital

**Study type(s)**

Screening

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

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

Liver fibrosis

**Interventions**

Participants will be recruited largely from rheumatology and dermatology outpatient clinics in York and Scarborough Hospitals. Over the 12 month study period we will aim to recruit 698 patients. Controls will be matched by age and gender. Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

The following things will be undertaken for each study participant:

a) Electronic record

The PI will evaluate historical data from the patient electronic record; including blood test results, duration and cumulative dose of MTX prescribed (if relevant), patient demographic data such as postcode, age and gender. The data will be recorded in an EXCEL file, with no patient

identifiable factors. All information will be kept on an encrypted password protected York NHS Trust IT system.

**b) Participant questionnaire**

Participants will be asked to complete a lifestyle questionnaire. This will be anonymous; they will be given adequate time and assisted for any special needs as appropriate. The questionnaire focusses on patients' understanding and knowledge of methotrexate. The answers are in both qualitative and quantitative fashion. Answers will be compiled, cumulated and analysed.

**c) Participant history and special tests**

This part of the study will be largely completed by the PI. Participants will be reviewed in an outpatient environment. Participants will receive an Invite Letter and Participant Information Sheet through the post. Participants can either contact the research team in advance to make a mutually agreeable time to meet, or they can meet a member of the research team on the day of their existing outpatient appointment. The research member conducting the review will go through the questions detailed in the proforma. These questions are based on the participants' medical history, medications and alcohol intake - both historical and current. The research team member will go on to perform a liver Fibroscan® and body mass composite score. If blood tests have not been performed for the last three months, then the research member will request bloods (in keeping with current guidance). This information will be recorded onto an anonymised sheet.

Following the interview these sheets will be manually inserted onto a larger, anonymised database, also kept on an encrypted password-protected York NHS Trust IT system linked computer. When inserting the individuals' dataset onto the spreadsheet the information will be coded, for the ease of data analysis.

A patient group was involved in the compilation of the research methodology. Following their feedback alteration was undertaken to the consent form, participant information leaflet, invite letter, questionnaire, and posters for the research study.

The proposed sample size for this project is a total of 698 participants - 349 in each arm. This power calculation was calculated using existing data suggesting that the prevalence of liver fibrosis in patients taking methotrexate is reported as 5%, and the prevalence of liver fibrosis in patients not taking methotrexate as 1.3% in the UK population. This study uses a case control ratio of 1:1 and assumes a power of 80%.

**Participant Journey:**

From a participant point of view the following summarises their proposed progress through the study:

1) Receipt of a Participant Information Sheet and Invite Letter for study, with their pre-existing planned outpatient appointment.

2) Immediately after attendance at their planned outpatient appointment, they will have the opportunity to be recruited into the study which includes the following:

- Consent process
- Lifestyle questionnaire
- Medical history questions
- FibroScan®
- Body mass composition measurement

This will take approximately 30 minutes. Following this the participants' involvement in the study is complete. No additional visits or follow-up is required

**Intervention Type**

Other

**Primary outcome measure**

Presence of liver fibrosis (by liver Fibroscan®)

**Secondary outcome measures**

Risk factors for liver fibrosis will be assessed for each participant e.g. presence of diabetes mellitus, BMI and body mass composition, current and previous alcohol use, cumulative dose and duration of methotrexate use etc.

**Overall study start date**

03/09/2018

**Completion date**

31/12/2021

## Eligibility

**Key inclusion criteria**

1. Individuals in the methotrexate cohort must have taken this medication for at least 6 months
2. All participants must be over 18 years old

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 2,000; UK Sample Size:2,000

**Key exclusion criteria**

1. Pregnant females
2. Previously taken methotrexate, but are no longer currently taking it
3. Lack capacity to consent

**Date of first enrolment**

25/06/2019

**Date of final enrolment**

31/12/2021

## Locations

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**York Hospital**

Wigginton Road

York

United Kingdom

YO31 8HE

## **Sponsor information**

**Organisation**

York Teaching Hospital NHS Foundation Trust

**Sponsor details**

York Hospital

Wigginton Road

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YO31 8HE

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deborah.phillips@york.nhs.uk

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/027e4g787>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

LIVErNORTH

## **Results and Publications**

## Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal.

## Intention to publish date

31/12/2022

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Name: Lucy Turner

Email: [lucy.turner7@nhs.net](mailto:lucy.turner7@nhs.net)

Consent from participants was obtained for this sharing of data

All data will be completely anonymised

Data will be available from completion of study (25/06/20) for 1 year

Type of data:

1. Participant age
2. Height
3. Weight
4. BMI
5. Ethnicity
6. Gender
7. MTX cumulative dose (if appropriate)
8. other mediations
9. comorbidities
10. FibroScan result
11. Alcohol consumption (units per week)
12. Audit C score

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No