

# A trial of different treatments on livers before transplantation

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<b>Registration date</b> 07/09/2021	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/01/2025	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

A recent innovation in liver transplantation is the ability to store livers outside the body for a period of time before implantation. This involves restoring an artificial blood supply to the livers (perfusion), which typically includes red cells in a plasma substitute with some additional chemicals which either help the liver during this period of storage or are believed to improve the way the liver will work after transplantation.

The aim of this study is to explore variations in both the plasma substitute and the additional chemicals to see which is associated with a better outcome. Outcome in this study will be determined by the expression of genes related to liver function and the immune response.

### Who can participate?

Any adult at our centre undergoing a liver transplant.

### What does the study involve?

The study involves altering the composition of the perfusate and measuring the outcomes in terms of gene expression, but also other markers such as the perfusion parameters, and chemical markers of looking at the injury occurring in the livers when the perfusion begins

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

The possible benefits are an improvement in the quality and initial function of the liver following transplantation. Conversely, the risks are that it may be worse.

### Where is the study run from?

Cambridge University Hospitals NHS Foundation Trust (UK)

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

June 2021 to December 2026

### Who is funding the study?

Investigator initiated and funded

Who is the main contact?  
Prof Chris Watson, cjew2@cam.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Prof Chris Watson

### ORCID ID

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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

295373

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

IRAS 295373

## Study information

### Scientific Title

A study to evaluate the effects of different perfusion conditions during ex situ liver perfusion

### Study objectives

Transcriptomics will differentiate between the effects of different perfusates during ex situ perfusion

### Ethics approval required

Old ethics approval format

**Ethics approval(s)**

Approved 17/09/2021, Cambridge South REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8104; cambridgesouth.rec@hra.nhs.uk), ref: 21/EE/0177

**Study design**

Interventional randomized single-centre study

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Liver transplantation

**Interventions**

This is a study of isolated livers undergoing normothermic perfusion ex situ (ex vivo). There are additional readouts for some groups)

Study groups (n=6 to 10) will undergo incremental changes before proceeding to the next group.

Intervention arms include:

1. Comparing starting perfusate pHs of 7.2 and 7.6
2. Addition of a leucocyte filter into the circuit vs. none
3. Addition of a cytokine filter into the circuit vs. none
4. Addition of a thrombolytic agent (TPA) into the perfusate
5. Use of Gelofusin, human albumin, or fresh frozen plasma as plasma substitute
6. Use of an amino acid (Aminoven) infusion, or L-arginine infusion, vs a one off loading dose at the start of perfusion (additional readout: perfusate amino acid concentrations)
7. Exclusion of insulin from the perfusate vs its inclusion
8. Addition of 100mg hydrocortisone vs 3.3mg dexamethasone vs no steroid in perfusate
9. Addition of 4mg ciclosporin to perfusate vs no ciclosporin
10. Addition of allopurinol to perfusate vs none
11. Addition of vitamins C and E to perfusate vs none

**Intervention Type**

Device

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Organox metra liver perfusion device, alteplase, Gelofusine, human albumin solution, fresh frozen plasma

**Primary outcome(s)**

Transcriptomic profile measured using liver biopsies collected into RNA Later before and after 4 hours and at the end of liver perfusion and after reperfusion in the recipient

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

1. Transcriptomic signature measured using DESeq on biopsies of the liver taken pre-perfusion and after 4h, and at the end of perfusion and following reperfusion
2. Post transplant function:
  - 2.1. Post reperfusion syndrome measured using mean blood pressure measured using an invasive arterial pressure monitor recording for the five minutes before and after reperfusion of the liver
  - 2.2. Early allograft function measured using the model for early allograft function score which looks at recipient biochemical and haematological variables over the first 3 days post transplant
  - 2.3. Early allograft function measured using L-GraFT7 score which looks at recipient biochemical and haematological variables over the first 7 days post transplant
  - 2.4. Early allograft function measured using Olthoff score which looks at recipient biochemical and haematological variables over the first 7 days post transplant
  - 2.5. Incidence of anastomotic and non-anastomotic structures in DCD livers measured using MRCP in the first 6 months post transplant
  - 2.6. Peak creatinine d1-7 measured using serum creatinine measurements at baseline and the first 7 days post transplant
3. Perfusate chemistry:
  - 3.1. TBARS measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
  - 3.2. HMGB-1 measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
  - 3.3. Hyaluronic acid levels measured using perfusate from the liver machine taken after 30mins and 4 hours of perfusion will be measured using a commercial kit
  - 3.4. Uric acid measured using the Piccolo Express near patient analyser at 1, 2 and 4 hours
  - 3.5. D-dimer concentration (thrombolysis group) measured on perfusate taken after 30mins and 4 hours of perfusion using a commercial assay kit

Early allograft function and cholangiopathy are based on tests in the recipient post transplant; one post transplant biopsy for transcriptomics will be done post transplant

### **Completion date**

31/12/2026

## **Eligibility**

### **Key inclusion criteria**

1. Aged  $\geq 18$  years
2. Requiring a liver transplant

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Lack of consent
2. Inability to comprehend the information

**Date of first enrolment**

01/08/2021

**Date of final enrolment**

01/07/2024

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Addenbrooke's Hospital**

Cambridge University Hospitals NHS Foundation Trust  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

## **Sponsor information**

**Organisation**

University of Cambridge

**ROR**

<https://ror.org/013meh722>

**Organisation**

Cambridge University Hospitals NHS Foundation Trust

**ROR**

<https://ror.org/04v54gj93>

# Funder(s)

## Funder type

Other

## Funder Name

Investigator initiated and funded

# Results and Publications

## Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

## IPD sharing plan summary

Other

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 3.1	07/03/2023	31/07/2023	No	No