

# ORCHARD: Study to prevent progression of kidney disease in pregnancy

<b>Submission date</b> 09/11/2019	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 29/01/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 20/05/2024	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Pregnancy can worsen chronic kidney disease (CKD). Low nitric oxide may stop kidneys coping with pregnancy and by replacing nitrate in the form of a dietary supplement (beetroot juice) we may be able to protect kidney function in pregnancy.

### Who can participate?

Pregnant women aged 18 years or above with CKD Stages 2-5

### What does the study involve?

This study will recruit pregnant women with CKD to monitor their health during pregnancy and look for any possible associations between those women in whom kidney function worsens during pregnancy and those in who do not have a reduction in kidney function.

Some participants will be asked to drink a beetroot juice supplement daily for the duration of their pregnancy. The study will tell us how many women are willing to take part, how women felt about the trial and whether they were happy to take treatment. We will also look at treatment effects on kidney function and babies' growth and wellbeing. These measurements will be used to plan a bigger study to test whether treatments can protect kidney function in pregnancy.

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

Participating in the observational study may benefit pregnant women with kidney disease in the future. The risks of participating in the observational arm are minimal and relate to time and mild discomfort that may be experienced when taking samples (blood, saliva, tongue scraping). Possible benefits of Orchard Beet include lowering of blood pressure and possible reduction in pregnancy associated kidney function decline and pregnancy complications. The risks are that this treatment may lead to hypotension (low blood pressure), may be unpleasant to take and may have unanticipated side effects. The dietary nitrate has been studied in other pregnant and non-pregnant populations and has been well tolerated and associated with very little risk to participants.

### Where is the study run from?

King's College Hospital NHS Foundation Trust (UK)

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

Who is funding the study?

1. Kidney Research UK
2. National Institute for Health Research (NIHR) (UK)

Who is the main contact?

Dr Kate Bramham  
kate.bramham@kcl.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Dr Kate Bramham

### Contact details

Department of Nephrology  
King's College Hospital NHS Foundation Trust  
Denmark Hill  
London  
United Kingdom  
SE5 9RS  
+44 (0)20 3299 9000  
kate.bramham@kcl.ac.uk

## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

JFS\_RP\_008\_20170915, CPMS 44456

## Study information

### Scientific Title

Observational cohort with embedded randomised controlled feasibility trial to study pregnancy-associated progression of renal disease

### Acronym

ORCHARD

## **Study objectives**

### **Primary Aim:**

To establish a cohort of pregnant women with CKD including longitudinal blood, urine, saliva, tongue scraping samples to enable future embedded randomised controlled trials

### **Secondary Aim:**

To determine the relationship between maternal factors and rates of change in maternal renal function, maternal complications and neonatal adverse outcomes

### **Sub study (ORCHARD-BEET):**

The aim of this investigation is to determine the feasibility and acceptability of recruiting pregnant women with chronic kidney disease (CKD) to a trial of an intervention to prevent progression of the disease

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

1. Approved 10/01/2020, West of Scotland Research Ethics Service, REC 3 (Ground Floor, Ward 11, Dykebar Hospital, Grahamston Road, Paisley PA2 7DE, UK; +44 (0)1413140211; WOSREC3@ggc.scot.nhs.uk), REC ref: 19/WS/0197 (ORCHARD Observational study)
2. Approved 13/02/2020, London City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead Bristol. BS1 2NT, UK; +44 (0)207 104 8171; nrescommittee.london-cityandeast@nhs.net), REC ref: 20/LO/0009 (ORCHARD BEET study)

## **Study design**

Trial within a cohort (embedded randomized controlled feasibility trial)

## **Primary study design**

Other

## **Secondary study design**

## **Study setting(s)**

Hospital

## **Study type(s)**

Prevention

## **Participant information sheet**

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

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

Progression of chronic kidney disease in pregnancy

## **Interventions**

Eligible women will be identified from GP referral letters, antenatal or outpatient clinic visits and from health professionals on antenatal wards.

During pregnancy, a blood and urine test will be done at the same time as other blood and urine tests required as part of routine antenatal care (a maximum 3 visits in pregnancy and 2 post-

partum visits at 6 weeks and 6 months after delivery). There will be at least one blood and urine test in pregnancy from the time informed consent is given.

- Blood and urine samples will be taken by a research midwife/practitioner, processed immediately and then stored at -80°C for future measurements (e.g. plasma nitrate/nitrite concentrations).

Optional samples will be collected for future research projects including:

- Tongue scrapings placed into a sterile sealed container and stored at -80°C for bacterial community profiling using Next-Generation sequencing for future assessment of relationship with oral nitrate conversion to nitrite.

- Salivary samples (x2) will be collected into sterile tubes, and either processed immediately or stored at -80°C for future measurements (e.g. nitrate/nitrite concentrations and enzymatic activity assays).

If a woman delivers at another hospital the research team will attempt to get the relevant information from the maternity unit used with the permission of the woman.

Following delivery, participants will be asked if they can be contacted to give additional blood and urine samples at 6 weeks and 6 months postpartum. This visit can be coordinated with other postnatal appointments or booked separately after delivery.

If the woman is unable or unwilling to give all samples at each visit she will not be excluded from the main study.

**Sub study (ORCHARD-BEET):**

Women with CKD will be randomised to take dietary nitrate supplement or no treatment and kidney function at 6 months after delivery will be assessed.

Randomisation to Orchard Beet will take place once patient is recruited to the main ORCHARD study. Minimisation randomisation will immediately be performed electronically after data entry to ORCHARD observational study by the local site team with confirmation emails automatically generated to relevant individuals detailing the allocation by King's Clinical Trials Unit.

Minimisation will be used to ensure balance between the groups with respect to study centre (8 centres), highest serum creatinine concentration prior to randomisation ( $\leq 90 \mu\text{mol/L}$ , 91-120 or  $>120 \mu\text{mol/L}$ ) and gestation at recruitment ( $<12$  weeks, 12-15+6 weeks, 16-19+6 weeks,  $\geq 20$  weeks).

Dietary nitrate: 70 mls 'Beet It Sport shot'; <http://beet-it.com/sport>

Active ingredient: 400 mg nitrate/ 6.45 mmol nitrate)

Suppliers Name: James White

## **Intervention Type**

Supplement

## **Primary outcome measure**

ORCHARD: Recruitment per centre per month (determined from screening /enrolment logs)

Sub-study (ORCHARD-BEET): Recruitment rate of pregnant women with CKD per site per month (determined from screening /enrolment logs)

## **Secondary outcome measures**

ORCHARD study:

1. Maternal factors will be measured using demographic and clinical data obtained from medical notes, patient interview, examination and blood/urine tests at baseline
2. Maternal renal function will be measured using serum creatinine and urine protein measurement (albumin creatinine ratio, protein creatinine ratio OR 24 hour urine protein) at

baseline, each trimester, 6 weeks post-partum and 6 months post-partum

3. Maternal complications will be measured using maternal outcomes (mode, timing, indications for and complications of delivery) and adverse events as defined by the protocol and identified with medical notes and patient interview at each trimester visit, 6 weeks post-partum and 6 months post-partum

4. Neonatal adverse outcomes will be measured using review of medical notes at 6 weeks post-partum to assess mode and outcome of delivery, Apgar scores, measures of size and weight, admission to Neonatal ICU or Special Care Unit

Sub study (ORCHARD-BEET):

5. Number of eligible women with CKD will be assessed from recruitment logs

6. Feasibility and acceptability of the intervention to clinicians and women (including reasons for declining, retention during study and participant attitudes) will be measured using by short semi-structured interviews of local principal investigators (face-to-face or by telephone) and acceptability of women will be assessed with "Survey Monkey" questionnaire sent 2-4 weeks after recruitment, 32+0-35+6 weeks' gestation, 6-12 weeks after delivery asking whether they enjoyed taking their beetroot juice, whether they would be willing to take it in future pregnancies and whether they would recommend it to other pregnant women with chronic kidney disease

7. Adherence and reasons for non-adherence will be measured using daily diaries of participants which are reviewed and entered into an adherence log on the Orchard database at each trimester and 6 weeks post-partum

8. Mean and SD for primary outcome will be estimated to inform sample size for a definitive trial

### **Overall study start date**

01/09/2017

### **Completion date**

30/04/2024

## **Eligibility**

### **Key inclusion criteria**

ORCHARD study:

1. Pregnant women with CKD Stages 2-5 including those with renal transplants i.e. pre-pregnancy eGFR  $<90\text{mls/min/1.73m}^2$  OR pregnancy creatinine  $>70\text{ }\mu\text{mol/l}$  (or  $>80\text{ }\mu\text{mol/l}$  if Black) with no clinical suspicion of acute kidney injury
2.  $<24+6$  weeks' gestation
3.  $\geq 18$  years old
4. Willing and able to provide written informed consent

Sub study (ORCHARD-BEET):

5. Consented to observational ORCHARD study
6. Agreed to be contacted about future research studies

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

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

**Sex**

Female

**Target number of participants**

114

**Key exclusion criteria**

ORCHARD study:

1. Already established on haemodialysis or peritoneal dialysis
2. Multifetal pregnancy
3. Major life-threatening congenital abnormality

Sub study (ORCHARD-BEET):

4. Known allergy to beetroot

**Date of first enrolment**

01/02/2020

**Date of final enrolment**

30/04/2023

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**King's College Hospital NHS Foundation Trust**

Denmark Hill

London

United Kingdom

SE5 9RS

**Study participating centre**

**Guy's and St Thomas' NHS Foundation Trust**

Trust Offices, Guys Hospital

Great Maze Pond

London

United Kingdom

SE1 9RT

**Study participating centre**

**Barts Health NHS Trust**

The Royal London Hospital  
Whitechapel  
London  
United Kingdom  
E1 1BB

**Study participating centre**

**Manchester University NHS Foundation Trust**

Cobbett House  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Nottingham University Hospital NHS Trust**

Trust Headquarters  
Queens Medical Centre  
Derby Road  
Nottingham  
United Kingdom  
NG7 2UH

**Study participating centre**

**University Hospitals Birmingham NHS Trust**

Trust HQ, PO Box 9551  
Queen Elizabeth Medical Centre  
Edgbaston  
Birmingham West  
United Kingdom  
B15 2TH

**Study participating centre**

**Imperial College Healthcare NHS Trust**

St Mary's Hospital  
Praed Street  
London  
United Kingdom  
W2 1NY

**Study participating centre**  
**University Hospitals of Leicester NHS Trust**  
Leicester Royal Infirmary  
Infirmary Square  
Leicester  
United Kingdom  
LE1 5WW

## **Sponsor information**

**Organisation**  
King's College Hospital NHS Foundation Trust

**Sponsor details**  
The R&I Office  
161 Denmark Hill  
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England  
United Kingdom  
SE5 9RS  
+44 (0)20 3299 1980  
kch-tr.research@nhs.net

**Sponsor type**  
Hospital/treatment centre

## **Funder(s)**

**Funder type**  
Charity

**Funder Name**  
Kidney Research UK

**Alternative Name(s)**

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Other non-profit organizations

**Location**



United Kingdom

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

The research team plans to disseminate the study research findings in the following settings:

- Conference presentation of study process and results at UK Kidney Week, American Society of Nephrology Conference or the European Renal Association conference and related Obstetric Conferences including British Maternal and Fetal Medicine Society and International Society of Nephrology.
- Publication of results in a renal or obstetric specific recognised impact journal

The protocol and SAP will be available on request from the study contact below.

**Intention to publish date**

01/10/2024

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request from the Chief Investigator, Dr Kate Bramham (kate.bramham@kcl.ac.uk).

- Type of data: Fully anonymised individual patient demographic and clinical data
- Suitable for all types of analyses conditional on ethics approval and approval by the Orchard Trial Group
- Mechanism: Obtain REC approval for study, contact Dr Bramham, request considered by Orchard Trial Group and if deemed appropriate then data sharing agreement drafted and requested data transferred
- Consent: Will be sought from Orchard participants at recruitment for their data to be used in future studies subject to ethics approval

**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
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>		17/05/2024	20/05/2024	Yes	No