

The GFR-Exercise feasibility study

Submission date 24/09/2018	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 01/10/2018	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 06/04/2021	Condition category Urological and Genital Diseases	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

There are many causes of Chronic Kidney Disease (CKD) and it has been recognised for many years that kidney dysfunction often progresses to total kidney failure. People with CKD have about 50% of the exercise capacity of normal sedentary individuals and are unable to participate in the same activities as healthy people. Physical inactivity doubles the risk of developing heart disease but, unlike people with other long-term conditions, people with kidney disease are not generally offered exercise rehabilitation. Physiotherapists are best placed to initiate prescribed exercise for this patient population. The main aim of this study is to determine if it feasible to recruit, randomise and retain participants in a study that uses the gold standard measure of kidney function (mGFR), to explore whether a 12-month exercise training intervention can slow down the progression of kidney disease for patients who haven't yet reached the stage where they require regular haemodialysis – which is very restrictive, debilitating and costly. If this study shows exercise results in improved or preserved kidney function, delaying or preventing progression to kidney failure, haemodialysis and kidney transplantation, this would give an additional treatment option that would have a major impact on individual's health, quality of life and long-term prognosis. This study team hopes to use the results of this study to plan a larger study examining the effectiveness of exercise training to slow CKD progression.

Who can participate?

CKD patients aged over 18 years

What does the study involve?

Participants are randomly allocated into the intervention group or the control group. Participants in the intervention group receive a 12-month supervised exercise intervention, provided by a physiotherapy assistant, in addition to usual care. The control group receives usual care, which includes 3 yearly attendances at hospital general nephrology clinics. The progression of kidney disease is assessed with measured glomerular filtration rate clearance (kidney function measurement). The main objective of this study is to determine if it is feasible to recruit, randomise and retain participants in this type of study.

What are the possible benefits and risks of participating?

The main benefit is to help improve care for future patients. The risk of a serious illness from

participating in this study is very low. There have been no cases reported of chromium-51 labeled ethylenediamine tetraacetic acid (51Cr-EDTA) causing kidney damage at the low dose which will be used in the study (this is used to measure mGFR).

Where is the study run from?

1. King's College Hospital NHS Foundation Trust (UK)
2. Betsi Cadwaladr University Health Board (UK)

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

September 2018 to April 2021 (updated 18/10/2019, previously: September 2019)

Who is funding the study?

National Institute for Health Research (NIHR) (UK)

Who is the main contact?

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

38499

Study information

Scientific Title

Exercise training and progression of chronic kidney disease: a randomised controlled feasibility study. The GFR-Exercise feasibility study (GFR-Ex)

Acronym

GFR-Ex

Study objectives

This trial is a feasibility study for a planned multi-centre randomised controlled trial that will examine the efficacy of exercise training as a means to retard progression of CKD in pre-dialysis patients with declining kidney function.

The main aim of this study is to determine if it is feasible to recruit, randomise and retain participants in a study that utilises the gold standard measured glomerular filtration rate (mGFR), with chromium-51 labeled ethylenediamine tetraacetic acid (51Cr-EDTA) or Inulin, to explore whether an exercise training intervention has the potential to retard kidney function decline in patients with progressive stage 3 to 4 CKD.

Ethics approval required

Old ethics approval format

Ethics approval(s)

London - Camden & Kings Cross Research Ethics Committee, 09/08/2018, ref: 18/LO/0852

Study design

Randomised; Both; Design type: Treatment, Process of Care, Psychological & Behavioural, Complex Intervention, Physical, Rehabilitation, Qualitative

Primary study design

Intentional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

See additional files

Health condition(s) or problem(s) studied

Chronic kidney disease

Interventions

STUDY DESIGN: A feasibility randomised controlled trial with a nested qualitative study to explore participants experiences.

ESTIMATED TRIAL DURATION PER PARTICIPANT: 12 months

SAMPLE AND RECRUITMENT JUSTIFICATION:

The aim is to recruit 50 participants at Kings and 40 participants at Betsi Cadwaladr University Health Board (BCUHB) to this feasibility RCT study. It isn't necessary to calculate a sample size for a feasibility study, although a justification of the chosen sample size is helpful. In total 90 participants with progressive CKD will be recruited over 12 months. This will allow the rate of potential participant recruitment, actual rate of recruitment, retention, and ease of data collection to be assessed adequately and efficiently, yet in a large enough sample to inform the definitive study power calculation.

Potential trial participants will be approached during routine nephrology clinic at King's College Hospital or Betsi Cadwaladr University Health Board (BCUHB). Members of the site staff will screen for potential eligible study participants using the inclusion/exclusion criteria. Patients who fulfil the inclusion criteria will have their eligibility confirmed by the research team. After confirming eligibility, eligible patients will be approached by an appropriately trained member of the clinic team to ascertain interest in entering the study. This individual (likely to be either the PI or research nurse) will give a comprehensive verbal explanation of the trial (explaining both the investigational and standard treatment options and highlighting any possible benefits or risks relating to participation). Time for questions throughout the discussion will be given and questions adequately addressed. Potential participants will also be given a written information sheet about the trial and be given sufficient time (providing they have received the patient information sheet and had at least 24 hours to read and fully understand the implications of the trial) to consider the study information prior to deciding whether to take part. Participants that agree to enter the study will then be asked to consent to undergo study assessments. If the participant is willing to take part then they will be asked to sign the consent form with a member of the research team countersigning.

STUDY SCHEDULE:

Testing will occur at the same time of day (early morning) for each study visit at baseline, 6 and 12 months. Blinded randomisation will be done via direct web randomisation hosted at the King's Clinical Trials Unit (KCTU). Participants will be allocated into intervention or control group using a 1:1 allocation ratio. The study nurse and the fellow collecting other outcome measures will be blinded to treatment allocation. Participants will be asked to not reveal their group allocation. For full details on outcome collection please refer to study protocol.

a) Baseline /randomisation visit

The baseline/randomisation visit must occur no more than 4 weeks after the patient has successfully passed a screening visit. These assessments may be split over 2 visits if the participant prefers.

Data to be collected: informed consent and registration, medical history, height, weight, blood pressure, pulse rate, medications, waist and hip circumference, blood test for kidney function using chromium-51 labeled ethylenediamine tetraacetic acid (51Cr-EDTA) or inulin, urine test (albumin to creatinine ratio and protein to creatinine ratio), pulse wave velocity, flow mediated dilatation, carotid intima-media thickness, bioelectrical impedance analysis, peak and submaximal cardiorespiratory fitness, International Physical Activity Questionnaire and GTX accelerometer, short-form 12 questionnaire, knee extension muscle strength assessment, contrast enhanced ultrasound of the kidneys.

b) 6-month visit

The 6-month visit must occur within the period of time 2 weeks either side of the scheduled 6-month assessment date. These assessments may be split over 2 visits if the participant prefers. The data must be collected for all required procedures performed during the baseline

/randomisation visit, with the exception of the contrast enhanced ultrasound of the kidney which will be performed at 12 months only.

d) 12-month visit

The 12-month visit must occur within the period of time 2 weeks either side of the scheduled 12-month assessment date. These assessments may be split over 2 visits if the participant prefers. The data must be collected for all required procedures performed during the baseline /randomisation visit.

In addition to these outcomes, a selection of participants (up to 20) will be invited to individual semi-structured interviews to record qualitative data of their experiences during the study.

THE INTERVENTION GROUP:

Participants randomised to the active treatment arm of the study will receive a 12-month supervised exercise intervention, provided by a physiotherapy assistant, in addition to usual care. The individualised exercise plan will be based on objective assessment of cardiorespiratory fitness during an incremental cycling exercise protocol. The exercise plan will consist of aerobic and strength training components as per established physical activity guidelines. Exercise intensity for the aerobic training will be set at moderate intensity 40-70% of VO₂ reserve (VO₂R) or heart rate reserve (HRR) and will be delivered in 10 minute bouts. The aim for patients will be to accumulate 40 minutes of moderate intensity exercise 4 x/week (3 supervised, 1 unsupervised) (160 min/week) after 6 months of training and to sustain this level for the final 6 months. Duration of aerobic training component will range from 20-40 minutes, depending on individual fitness and exercise plan. The strength training will consist of a range of 6-8 exercises targeting large multi-joint muscle groups in order to improve core strength and balance, as well as functional mobility and strength. Initial level of external load will be maximum weight that will still allow patients to perform 10 to 15 repetitions with correct technique. The strength training will last between 10-20 minutes and will be performed in between or at the end of the aerobic training bouts. The intervention will be delivered by physiotherapy assistants in a hospital-gym setting, in groups of up to 6 participants.

THE USUAL CARE GROUP:

Usual care for patients with stages 3-4 CKD includes 3 yearly attendances at hospital general nephrology clinics. They receive a number of management interventions, including blood pressure control, treatment of anaemia, phosphate control, and cardiovascular risk mitigation strategies. They may also receive dietary advice, counselling, input from social workers, and other forms of educational support. Many of the patients take renin angiotensin blockers, aspirin and/or lipid lowering agents in an attempt to reduce cardiovascular risk. Patients do not receive formal physical activity or exercise recommendations as part of usual care. They will be assessed at 0, 6, and 12 months.

STATISTICAL ANALYSIS:

This will be conducted by the Principal Investigator and collaborators, supported by Fiona Reid, Senior Statistician, King's College London.

a) Number and percentages of potential participants identified for screening for recruitment, recruited and retained in the study for up to 12 months:

- Number screened per month
- Number recruited per month (aim > 15% of invitees)
- Number retained per month (aim > 80% at 6 and 12 months)
- Percentage of study visits / intervention sessions completed in full and mean duration of baseline and follow up visits
- Proportion of planned data collection visits that are completed in full

- Proportion of exercise sessions (supervised and unsupervised) completed in full
 - Length of time for study visits
- b) Calculate the dosage of exercise training delivered in the intervention (aerobic and resistance training) to assist with the production of a training manual (for intervention fidelity) for the future definitive study
- c) Mean differences and standard deviations between rate of change in kidney function (measured GFR, serum creatinine, eGFR, PCR, and ACR) values for exercising and non-exercising participants will be explored for the definitive study. The effect sizes of the difference in rate of change in measured GFR between the groups will be calculated for each variable
- d) The relationship between the rate of change in kidney function, exercise training, weight change and renal perfusion (measured with contrast enhanced ultrasound of the kidney) measures over time using simple linear regression (Pearson/Spearman correlation coefficient) and with exercise training as a categorical variable with ANOVA (note: not powered to detect statistical difference) will be described
- e) Interviews will be transcribed and analysed using inductive thematic analysis (Braun & Clarke, 2006), informed by techniques from grounded theory, including line-by-line open coding grounded in data and constant comparison of all instances of codes

Intervention Type

Behavioural

Primary outcome measure

Feasibility:

1. Number of participants screened per month, measured using a screening log monthly
2. Number recruited per month, measured using an enrolment log monthly
3. Proportions of eligible people unwilling to participate with reasons given (e.g. live too far away etc), measured using a screening log monthly
4. Number retained per month, measured using an enrolment log monthly
5. Proportion of planned data collection visits that are completed in full length of time for study visits
6. Adherence to planned supervised exercise training schedule (number of sessions attended) of >80%, measured using Trust Database (PiMS) Clinic Attendance Log
7. Completion of unsupervised exercise diaries of >80%

Secondary outcome measures

KIDNEY FUNCTION measured through blood tests and urine sample at baseline, 6-month and 12-month visits:

1. Measured glomerular filtration rate (mGFR) using chromium-51 labeled ethylenediamine tetraacetic acid (51Cr-EDTA) or Inulin
2. Estimated GFR (eGFR) by CKD-EPI equations; using lab determined serum creatinine and cystatin C
3. Urinary albuminuria (albumin to creatinine ratio) and proteinuria (protein to creatinine ratio)

KIDNEY VASCULAR HEALTH measured at baseline and 12-month visits:

1. Contrast enhanced kidney ultrasound at baseline and 12 months
2. Pulse Wave Velocity: arterial stiffness assessed at the systemic region (carotid-femoral PWV) using the Vicorder system (Skidmore Medical Ltd) - equipment already secured
3. Flow mediated dilatation
4. Carotid Intima-Media Thickness (CIMT)
5. Blood pressure
6. Heart rate

PHYSICAL FUNCTION OUTCOMES measured at baseline, 6-month and 12-month visits

1. Peak cardiorespiratory fitness: VO₂peak determined during an incremental recumbent cycling exercise tolerance protocol using the MetaLyzer 3B cardiopulmonary exercise testing system (Cortex)
2. Habitual physical activity, measured using long form International Physical Activity Questionnaire (IPAQ) and GTX accelerometers
3. Knee muscle strength measured by a Biodex dynamometer (3 times to the left and right leg)

BODY COMPOSITION and anthropometric measures, measured at baseline, 6-month and 12-month visits:

1. Body composition by bioelectrical impedance (Fresenius BCM)
2. Waist: hip ratio
3. Body mass (kg)
4. Body height (cm)
5. Body mass index

SAFETY measured at baseline, 6-month and 12-month visits:

1. No. of hospital admissions
2. Expected and unexpected harms

Overall study start date

11/09/2018

Completion date

30/11/2022

Eligibility

Key inclusion criteria

1. Stages 3-4 CKD patients defined by the following criteria:
 - 1.1. GFR 15-60mL/min from local lab CKD-EPI determined eGFR
 - 1.2. Minimum decline= 5mL/min/year over previous 12-24 months, as measured by linear regression analysis (minimum of 3 measurements of eGFR over 12 months)
2. Male or female
3. Age > 18 years
4. Declining CKD with no likelihood of reversibility

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 90; UK Sample Size: 90

Key exclusion criteria

1. Age < 18 years
2. Pregnancy
3. Have a history of untoward reactions to iodinated contrast media
4. Have a recent history (last six months) episode of acute kidney injury or have sickle cell disease
5. Requires support for ambulation less than 20 meters
6. Psychosis, bi-polar, eating disorders, any other cognitive/neurological related issues
7. Infection or course of antibiotics within the last month
8. Enrolled in supervised exercise training in previous 3 months

Date of first enrolment

14/09/2018

Date of final enrolment

30/11/2021

Locations

Countries of recruitment

England

United Kingdom

Wales

Study participating centre

King's College Hospital NHS Foundation Trust (lead site)

Denmark Hill

London

United Kingdom

SE5 9RS

Study participating centre

Betsi Cadwaladr University Health Board

Ysbyty Gwynedd

Penrhosgarnedd

Bangor

United Kingdom

LL57 2PW

Sponsor information

Organisation

King's College Hospital NHS Foundation Trust

Sponsor details

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United Kingdom
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kch-tr.research@nhs.net

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/01n0k5m85>

Funder(s)

Funder type

Government

Funder Name

NIHR Trainees Co-ordinating Centre (TCC); Grant Codes: ICA-CL-2017-03-020

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal.

Intention to publish date

31/03/2023

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study 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?
Participant information sheet	version V1	08/01/2018	01/10/2018	No	Yes

