ISRCTN87708989 https://doi.org/10.1186/ISRCTN87708989

The EX-FRAIL CKD Trial

Submission date
20/08/2018

Recruitment status
No longer recruiting

Registration date
30/08/2018

Overall study status
Completed

Last Edited
06/09/2023

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
Frailty is very common in people with chronic kidney disease. It is linked with disability, poorer quality of life and an increased risk of death. Despite knowing this, the best way to care for those that are frail with chronic kidney disease is not known. Studies have demonstrated that exercise appears to be helpful for frail older people. However, frail people with chronic kidney disease have health problems that are different to older people with normal kidneys. Muscle wasting appears to be more severe as kidney failure worsens. Exercise may decrease the muscle wasting that occurs and improve the overall health and quality of life of frail patients with chronic kidney disease. Most research studies of exercise programmes are performed under close supervision outside a person's own home. They are difficult to set up as they are expensive and require a lot of time from busy staff. They may also be demanding for frail older people as they need to travel to take part in exercise. Research is needed to explore the benefits of a home-based exercise programme for frail older people with chronic kidney disease. The aim of this small study is to find out whether it would be possible to perform a larger study that examines the benefits of a home-based exercise programme for frail older people with chronic kidney disease. The researchers have received feedback from members of a local kidney charity, a group of older patients with chronic kidney disease and members of the public, and have modified the study based upon this feedback. If they can successfully perform this small study and participants find the study acceptable, they will use the information gathered to design a larger study that examines the benefits of a home-based exercise programme for frail older people with chronic kidney disease.

Who can participate?
Patients aged 65 and older with chronic kidney disease

What does the study involve?
Participants are randomly allocated into two groups. The first group is taught by a physiotherapist how to perform the exercise programme. They are asked to perform the exercises at home three times a week for 12 weeks. The second group do not receive the exercise teaching. The researchers assess the physical ability and quality of life of participants in both groups at the beginning and end of the 12 weeks. They also ask some participants to take part in interviews that explore their experience of the study.

What are the possible benefits and risks of participating?
To the researchers' knowledge, this is the first study that tests the feasibility of a home-based exercise programme for pre-frail and frail older patients with chronic kidney disease. Frail older adults with chronic kidney disease are vulnerable to falls, though exercise programmes have been performed safely by those with chronic kidney disease and by frail, older adults. Thus, the researchers believe that an exercise programme can be safely performed by frail, older patients with chronic kidney disease provided appropriate precautions are followed. Several measures have been taken to minimise risks for participants in the exercise group. High-risk patients are not recruited to this study and potential participants are assessed by a medical practitioner and physiotherapist to ensure their suitability. Thereafter, participants are telephoned on a weekly basis to provide ongoing support and guidance and to ask about side effects. Participants are encouraged to contact the research team if they are experiencing any problems and guidance is provided within the exercise guidebook detailing when they should seek medical attention. The information obtained from study participants will further inform the design of a larger study that investigates the effects of a home-based exercise programme on the physical function, quality of life and hospitalisation risk of pre-frail and frail older patients with chronic kidney disease. Positive findings from a large study will provide evidence to support the provision of home-based exercise services for pre-frail and frail older adults with chronic kidney disease as part of routine care. It is hoped that such a service would be associated with increased functional independence and improved health-related quality of life of older adults with chronic kidney disease, reducing social care demand and falls-related hospital admissions.

Where is the study run from?
Royal Preston Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2018 to December 2019

Who is funding the study?
Kidney Research UK

Who is the main contact?
Dr Andrew Nixon
andrew.nixon3@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Andrew Nixon

ORCID ID
https://orcid.org/0000-0002-4093-6204

Contact details
Department of Renal Medicine
Lancashire Teaching Hospitals NHS Foundation Trust
Royal Preston Hospital
Sharoe Green Lane

Fulwood
Preston
United Kingdom
PR2 9HT
+44 (0)1772 522031
andrew.nixon3@nhs.net

Additional identifiers

Protocol serial number
37980

Study information

Scientific Title
The EX-FRAIL CKD Trial: a pilot mixed methods randomised controlled trial of a home-based EXercise programme for pre-FRAIL and FRAIL, older adults with Chronic Kidney Disease

Acronym
The EX-FRAIL CKD Trial

Study objectives
Frailty, the increased state of vulnerability to physical stressors, is a devastating complication of CKD. It is associated with progressive renal impairment and is independently linked with adverse clinical outcomes in all stages of CKD, including an increased risk of worse quality of life, falls, hospitalisation and mortality. Preliminary studies have demonstrated that exercise training is beneficial for frail older adults. However, the evolving literature from the elderly population on exercise programmes cannot be generalised to those with CKD, as there are notable differences between those who are frail with CKD and those who are frail with normal kidney function. Specifically, a) patients with CKD are more likely to be frail at a younger age, b) the trajectory of robustness to frailty associates with worsening kidney function, with significant muscle wasting, a major contributor to physical frailty in CKD patients, occurring prior to the commencement of dialysis, c) patients with CKD have a considerable symptom burden, d) patients with CKD have higher healthcare utilisation. Consequently, exercise interventions that are feasible in the older population may not meet the needs of those with advanced CKD.

Prompt exercise rehabilitation may mitigate against the muscle wasting, and limit the propagation from robustness to frailty, that is associated with progressive decline in renal function. Though the prevalence of frailty is high within CKD groups, the reported prevalence of frailty within pre-dialysis CKD is not as high as within the dialysis-dependent CKD population. Furthermore, frail patients are typically poorly represented in interventional studies. Thus, the prevalence of frailty within exercise intervention studies in pre-dialysis CKD populations is likely low and accordingly existing evidence cannot be applied to this distinct patient group.

Most exercise programmes used in studies involving participants with CKD have been performed in intensively supervised environments, conditions that are challenging to implement in clinical practice considering financial constraints and staffing limitations. Such exercise programmes also confer significant travel demands that may be onerous for pre-frail and frail individuals with CKD. Research is needed to evaluate a more pragmatic home-based exercise programme for this patient cohort.

The researchers propose a pilot mixed-methods randomised controlled trial of a home-based exercise programme for pre-frail and frail older adults with CKD to be conducted over a 12-month period. The main objective is to evaluate the feasibility of performing a larger definitive randomised controlled trial that investigates the effect of a home-based exercise intervention on physical function, quality of life and risk of hospitalisation in pre-frail and frail older adults with CKD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
RES Committee North West Greater Manchester East Health Research Authority, 16/05/2018, ref: 18/NW/0211

Study design
Randomized; Interventional; Design type: Treatment, Education or Self-Management, Complex Intervention, Physical, Rehabilitation

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Frailty in people with chronic kidney disease

Interventions
Interventions as of 31/10/2018:
Eligible participants will initially have a Frailty Phenotype assessment performed. Only those meeting the definitions for pre-frailty and frailty when assessed by the Fried Phenotype will be eligible for randomisation. Those that are classified as robust (despite a Clinical Frailty Scale score ≥4) will receive advice on safe exercise practices but will not be eligible for randomisation and will be withdrawn from the study. Those eligible for randomisation will be randomly assigned to an exercise (plus standard care) or standard care alone group. Participants allocated to exercise will receive education on the exercise programme and provided with an exercise guidebook. The exercise intervention has been adapted from published studies that have examined the use of exercise in patients with CKD and studies that have investigated the benefits of exercise in frail, older patients. The exercises within the programme aim to improve and maintain functional independence, through developing balance, coordination and strength:

Exercise 1: Walking (Warm-Up/Aerobic Exercise)
Exercise 2: Lower Leg Extension (Lower Limb Strengthening)
Exercise 3: Bilateral Calf Raises (Lower Limb Strengthening and Balance)
Exercise 4: Sit to Stand (Lower Limb Strengthening and Balance)
Exercise 5: Wall/Table Push Ups (Upper Limb Strengthening)
Exercise 6: Marching/Stair Step (Lower Limb Strengthening and Balance)

Each exercise has 4 levels of difficulty. Participants meeting the Frailty Phenotype frailty criteria will initially perform each exercise at level 1. Participants meeting the Frailty Phenotype pre-frailty criteria will initially perform each exercise at level 2, unless the research team determine

that it would be unsafe for an individual participant to perform the exercises at this level. Participants will be asked to aim for three exercise sessions at home per week, with each session lasting approximately 30-45 minutes. The Borg Scale will be used to help participants rate their perceived exertion whilst performing the exercises. Participants should aim to perform exercise 1 at a light intensity (Borg scale score <12). Participants should aim to perform exercises 2-6 at a moderate intensity (Borg Scale Score 12-16). If participants can perform exercises 2-6 comfortably (Borg Scale Score <12), participants will be asked to progress to the next level for that exercise. Participants will be asked to record each exercise session in a personal exercise diary and will be telephoned on a weekly basis to monitor progress (including adherence and adverse events) and to provide ongoing guidance and support.

Participants will be offered additional educational sessions during the 12-week period as needed, for example, a participant may request a further educational session if they are progressing to a different exercise level. If a patient is not able to perform a specific exercise due to, for example, a functional impairment, an appropriate alternative will be agreed. This reflects exercise prescription in clinical practice. All adaptations will be recorded.

A Frailty Phenotype and Short Physical Performance Battery assessment will be performed at the beginning and end of the 12-week period. Participants will also be asked to complete questionnaires that evaluate activities of daily living, health-related quality of life, fear of falling and symptom-burden at the beginning and end of the 12-week period.

Semi-structured, individual interviews will be performed with a purposively selected group of participants at the end of the study period. A representative sample of participants (based on age, gender and frailty status) will be asked a series of open-ended questions relating to their experience of the trial and, where applicable, the intervention.

Previous interventions:
Participants will be randomly divided into two groups. The first group will be taught by physiotherapists how to perform the exercise programme. They will be asked to perform the exercises at home three times a week for 12 weeks. The second group will not receive the exercise teaching.

The exercise intervention has been adapted from published studies that have examined the use of exercise in patients with CKD and studies that have investigated the benefits of exercise in frail, older patients. The exercises within the programme aim to improve and maintain functional independence, through developing balance, coordination and strength:

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Each exercise has 4 levels of difficulty. Participants meeting the Frailty Phenotype frailty criteria will initially perform each exercise at level 1. Participants meeting the Frailty Phenotype pre-frailty criteria will initially perform each exercise at level 2, unless the research team determine that it would be unsafe for an individual participant to perform the exercises at this level. Participants will be asked to aim for three exercise sessions at home per week, with each session lasting approximately 30-45 minutes. The Borg Scale will be used to help participants rate their perceived exertion whilst performing the exercises. Participants should aim to perform exercise

1 at a light intensity (Borg scale score <12). Participants should aim to perform exercises 2-6 at a moderate intensity (Borg Scale Score between 12-16). If participants can perform exercises 2-6 comfortably (Borg Scale Score <12), participants will be asked to progress to the next level for that exercise. Participants will be asked to record each exercise session in a personal exercise diary and will be telephoned on a weekly basis to monitor progress (including adherence and adverse events) and to provide ongoing guidance and support.

The researchers will assess the frailty status and physical function of participants in both groups at the beginning and end of the 12 weeks. They will also ask participants to complete questionnaires that evaluate their exercise capacity, quality of life, symptom burden, fear of falling and anxiety/depression. They will ask some participants to take part in interviews that explore their experience of the study at the end of the study period.

Intervention Type
Behavioural

Primary outcome(s)
1. Proportion of patients attending General Nephrology Clinics eligible for Frailty Phenotype assessment
2. Proportion of participants randomised to the exercise programme who complete at least two exercise sessions per week during the 12-week exercise programme
3. Proportion of participants who adhere to the exercise programme that complete all outcome assessments
4. Semi-structured, individual interviews will be performed with a purposively selected group of participants from both groups. A representative sample (based on age, gender and frailty status) of participants will be asked a series of open-ended questions relating to their experience of the trial and, where applicable, the intervention

Key secondary outcome(s))
There were no secondary outcome measures

Completion date
23/12/2019

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 28/03/2019:
1. Participants must be able to give informed consent
2. Participants must be ≥65 years of age
3. Participants must have CKD stage 3b, 4 or 5 (not receiving dialysis or received a kidney transplant).
4. Participants are assessed as vulnerable or frail using the Clinical Frailty Scale (score ≥4)

Previous participant inclusion criteria:
1. Participants must be able to give informed consent
2. Participants must be ≥65 years of age
3. Participants must have CKD stage 4 or 5 (not receiving dialysis or received a kidney transplant)
4. Participants are assessed as vulnerable or frail using the Clinical Frailty Scale (score ≥4)

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
65 years

Sex
All

Total final enrolment
35

Key exclusion criteria
Current participant exclusion criteria as of 28/03/2019:
1. Unstable Angina or recent (within the last 3 months) myocardial infarction
2. Recent (within the last 3 months) stroke or transient ischaemic attacks
3. Uncontrolled arrhythmias
4. Persistent uncontrolled hypertension (systolic blood pressure >180 or diastolic blood pressure >110)
5. Registered blind
6. Unable to mobilise independently
7. Receiving palliative care for advanced terminal cancer
8. Recently (within the last 12 months) enrolled in a structured exercise programme (e.g. cardiac rehabilitation programme) prescribed by a health professional
9. Anticipated to commence dialysis or receive a renal transplant within the next 3 months
10. Insufficient understanding of English language to complete study questionnaires or follow advice within the EX-FRAIL CKD Trial Exercise Guidebook
11. Clinical and/or Research Team consider participation in the EX-FRAIL CKD Trial exercise programme unsafe.

Previous participant exclusion criteria as of 31/10/2018:
1. Unstable Angina or recent (within the last 3 months) myocardial infarction
2. Recent (within the last 3 months) stroke or transient ischaemic attacks
3. Uncontrolled arrhythmias
4. Persistent uncontrolled hypertension (systolic blood pressure >180 or diastolic blood pressure >110)
5. Registered blind
6. Unable to mobilise independently
7. Receiving palliative care
8. Recently (within the last 12 months) enrolled in a structured exercise programme (e.g. cardiac rehabilitation programme) prescribed by a health professional
9. Anticipated to commence dialysis or receive a renal transplant within the next 3 months
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10. Insufficient understanding of English language to complete study questionnaires or follow advice within the EX-FRAIL CKD Trial Exercise Guidebook

Date of first enrolment
03/09/2018

Date of final enrolment
31/07/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Sponsor information

Organisation
Lancashire Teaching Hospitals NHS Foundation Trust

ROR
https://ror.org/02j7n9748

Funder(s)

Funder type
Charity

Funder Name
Kidney Research UK; Grant Codes: IN_013_20180306

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

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?
Results article		01/07/2021	05/07/2021	Yes	No
Protocol article	protocol	22/06/2020	24/06/2020	Yes	No
Dataset		01/06/2021	06/09/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes