

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

**Dr Andrew Nixon**<sup>1,2</sup>, Dr Theodoros Bampouras<sup>3,4</sup>, Mrs Helen Gooch<sup>5</sup>, Mrs Hannah Young<sup>6,7</sup>, Mr Kenneth Finlayson<sup>8</sup>, Professor Neil Pendleton<sup>9</sup>, Professor Sandip Mitra<sup>10,11</sup>, Dr Mark Brady<sup>1</sup>, Dr Ajay Dhaygude<sup>1</sup>

<sup>1</sup>Department of Renal Medicine, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom,

<sup>2</sup>Division of Cardiovascular Sciences, University of Manchester, Manchester, United Kingdom, <sup>3</sup>Lancaster Medical School, Lancaster University, Lancaster, United Kingdom, <sup>4</sup>Centre for Ageing Research, Lancaster University, Lancaster, United Kingdom, <sup>5</sup>Core Therapies Department, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom,

<sup>6</sup>Department of Respiratory Sciences, University of Leicester, Leicester, United Kingdom, <sup>7</sup>John Walls Renal Unit, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom, <sup>8</sup>Research in Childbirth and Health Unit, University of Central Lancashire, Preston, United Kingdom, <sup>9</sup>Division of Neuroscience and Experimental Psychology, University of Manchester, Manchester, United Kingdom, <sup>10</sup>Manchester Academy of Health Sciences Centre, University of Manchester, Manchester, United Kingdom, <sup>11</sup>NIHR Devices for Dignity MedTech & In-vitro Diagnostics Co-operative, , United Kingdom

**Introduction:** Frailty is highly prevalent in adults with chronic kidney disease (CKD) and is associated with adverse health outcomes. However, exercise training may improve physical function leading to associated improvements in outcomes. The EX-FRAIL CKD trial (ISRCTN87708989) aimed to inform the design of a randomised controlled trial (RCT) that investigates the efficacy of a progressive home-based exercise programme in pre-frail and frail older adults with CKD.

**Methods:** Patients aged 65 years with CKD G3b-5 and a Clinical Frailty Scale score  $\geq 4$  were eligible for participation. Participants categorised as pre-frail or frail, following Frailty Phenotype (FP) assessment, were randomised to receive a tailored 12-week home-based exercise programme or usual care. Primary outcome measures included recruitment, intervention adherence, outcome measure completion and participant attrition rate. Secondary outcome measures included frailty status (FP), physical function (walking speed, handgrip strength and Short Physical Performance Battery [SPPB]), fall concern (Falls Efficacy Scale-International tool [FESI]), symptom-burden (Palliative Care Outcome Scale-Symptoms RENAL [POS-S RENAL]) and health-related quality of life (Short Form-12v2 [SF-12]). Outcome measures are reported descriptively with 95% confidence intervals (CI) as recommended for pilot trials. Progression criteria to RCT stage were defined as: (1) eligibility  $>10\%$ ; (2) recruitment  $>30\%$ ; (3) exercise adherence  $>70\%$ ; (4) outcome measure completion  $>80\%$ ; and (5) loss to follow-up  $<25\%$ .

**Results:** Six hundred and sixty-five participants had an eligibility assessment with 201 (30% [95% CI 27-34]) patients eligible for enrolment. Thirty-five (17% [95% CI 12-23]) participants were recruited. Six participants were categorised as robust and therefore were withdrawn prior to randomisation. Fifteen participants were randomised to exercise (mean age  $77.0 \pm 8.3$  years; mean eGFR  $18.9 \pm 7.0$  ml/min/1.73m<sup>2</sup>) and 14 to usual care (mean age  $78.8 \pm 7.0$  years; mean eGFR  $20.4 \pm 7.2$  ml/min/1.73m<sup>2</sup>). Exercise adherence (average of  $\geq 2$  exercise sessions/week) was achieved by 73% (95% CI 45-92). Eight (28% [95% CI 13-47]) participants were lost to follow-up. Retained participants (n=21, 100% [95% CI 84-100]) completed all outcome measures. The odds ratio for improvement in frailty status with exercise was 5.50 (95% CI 0.46-65.16) and for deterioration in frailty status was 0.63 (95% CI 0.05-8.20). The adjusted mean group differences in walking speed, grip strength and SPPB score between exercise and usual care groups were: 0.01 metres/second (95% CI -0.07-0.10), 3.6 kg (95% CI -0.6-7.9) and 0.5 (95% CI -0.9-1.8), respectively. The adjusted mean group differences in POS-S RENAL, FESI, SF-12 Physical Component Summary and SF-12 Mental Component Summary scores

were: -1.4 (95% CI -6.6-3.7), 3.4 (95% CI -3.5-10.3), -3.9 (95% CI -9.3-1.5) and 0.2 (95% CI -6.2-6.6), respectively.

Discussion: Eligibility, adherence and outcome measure progression criteria thresholds were exceeded; however, recruitment and loss to follow-up progression criteria thresholds were not achieved. Analysis of a nested qualitative study will explore perceived barriers to participation and retention. The EX-FRAIL CKD trial demonstrates that it is possible to progress to a definitive RCT with adaptations that address the barriers described. It has also provided preliminary evidence that frailty status and physical function may be improved with a home-based exercise programme in patients living with frailty and CKD.