The exploration of an online intervention to prevent weight gain in new kidney transplant recipients

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THE EXPLORATION OF AN ONLINE INTERVENTION TO PREVENT WEIGHT GAIN IN NEW KIDNEY TRANSPLANT RECIPIENTS

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Abstract

Although kidney transplantation is cost-effective and is the gold standard treatment for end-stage kidney disease, it is not without risk. Particularly in the first-year post transplantation, kidney transplant recipients (KTRs) are at risk of weight gain, which has been associated with adverse health outcomes. Weight gain appears to be a multifactorial problem for KTRs. The lifting of dialysis dietary interventions, the increase in appetite from anti-rejection medications, reduced physical activity and impaired physical function contribute to this clinical issue. Recent clinical guidelines stipulate KTRs should have access to specialist healthcare professionals (HCPs) to address weight gain in kidney transplant care. However, there are no recognised interventions to address weight gain prevention in the first-year post kidney transplantation.

A narrative systematic review (including16 studies) and meta-analysis (including ten randomised controlled trials (RCTs) (study 1, chapter 2) was conducted to examine the effect of exercise, physical activity, dietary and/or combined interventions on body weight and body mass index (BMI) within the first year of kidney transplantation. The results suggest limited research in this field, with variable study quality, variation in intervention design and delivery, making a pooled effect analysis challenging. Post-hoc exploratory analysis suggests combined complex interventions, with physical activity, dietary advice and behaviour change techniques (BCT's) warrant further research in future RCTs.

The research fellow led a multi-professional research team, including KTRs, and input from a software company to create a bespoke online intervention to address weight gain in new KTRs, called the ExeRTiOn online intervention. A combined intervention design

was used, with the person-based approach at the centre. This ensured the target end user of the product (new KTRs) was at the centre of the design, development and evaluation of the online intervention.

A qualitative study (study 2, chapters 3 and 4) was conducted in a purposive sample of 11 new KTRs and 6 transplant HCPs to capture the usability (functionality, navigation and engagement) and experience of using the ExeRTiOn prototype online intervention. Results from this published study (chapter 4) facilitated iterative and person-based revisions of the ExeRTiOn online intervention using a recognised digital intervention prioritisation tool.

A mixed methods feasibility RCT (studies 3 and 4, chapter 6) recruited a new sample of seventeen acute KTRs to assess the feasibility of conducting a RCT using the revised ExeRTiOn online intervention, compared with usual care. The primary outcomes addressed the feasibility of conducting the study (screening, recruitment, adherence, retention, hospitalisations etc) and using the revised ExeRTiOn online intervention. Quantitative data captured secondary outcomes including body weight, BMI, physical function, self-reported physical activity, self-efficacy, fatigue and quality of life (study 3) at baseline, 3-months and 12-months. A nested qualitative study (study 4, chapter 6) captured the experiences of trial participation, and using the online intervention. A convergent integrated mixed methods analysis (chapter 6) was performed on quantitative (study 3) and qualitative (study 4) datasets. The overall feasibility was assessed against pre-set progression criteria. The results of this study suggest the trial was feasible, the intervention was acceptable to our sample of KTR participants, and a post-PhD multicentre pilot RCT is warranted. Secondary outcome data suggest the online IG

appeared to maintain median body weight across the study; 94.5kg, (IQR 63.0, 102.0) at baseline, 95.0kg, (IQR 66.7, 105.3) at 3-months and 94.7kg (IQR 77,2, 117.3) at 12-months. Whereas usual care participants increased body weight, 81.3kg, (IQR 73.6,94.6) at baseline, 86.2kg (75.4, 96.5) at 3-months and 93.3kg (70.3, 101.9) at 12-months. The IG increased six-minute walk distance (6MWD) over the three timepoints (450m, (IQR 450, 540), 525m (IQR 472.5, 615) and 495m (IQR 465, 615). The usual care group decreased 6MWD (517.5m (IQR 436, 570), 507.5m (IQR 442.5, 605) and 435m (IQR 435, 555)). All other outcomes were comparable across the sample.

The results and work presented in this thesis provide novel contributions to the evidence base. The systematic review (study 1) is the first to include combined interventions, as well as single arm interventions such as dietary or exercise interventions. Studies 2, 3 and 4 provide transparent reporting of the design, development, usability testing, and feasibility evaluation of a new online intervention to address weight gain in new KTRs. A follow-up multi-centre pilot RCT is planned. Future research is required to explore the effectiveness and cost-effectiveness of weight gain prevention interventions for new KTRs.

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Personal contributions and declaration of originality

The work presented in this thesis was conducting during the PhD fellowship by the research fellow (EC). The fellowship was funded by Kidney Research UK (AHPF_001_20171122). The views expressed in this thesis are those of the research fellow, not necessarily those of the NHS, Kidney Research UK, or the Department of Health and Social Care. The funders did not have any role in study design; collection, analysis, and interpretation of data; writing the thesis or the publication manuscript.

The data collection, data analysis, study management, and drafting of the thesis were conducted by EC. Supervision was provided by SG, JC and KB. A small portion of the qualitative interviews from study 4 were conducted by a master's student (PD). However, EC completed training of PD, and completed all of the analysis. External qualitative support, and support to complete the meta-analysis was sought and obtained from an external researcher (JG). Discussions on the statical plan proposed by EC was discussed with the supervisory team (SG, JC and KB) and an external statistician (RP).
The contributions for each of the four studies included in the thesis is summarised below.

Contributions to the systematic review and meta-analysis (study 1, chapter 2):
The research protocol was created by EC with input from the supervisors (SG, JC and KB), JG and EMc. The primary search and data extraction was conducted by EC. JG acted as a second searcher and checked data. Quality assessments were independently conducted by EC and EMc on each of the individual papers. EMc aided as the secondary assessor of all included studies.

The research fellow acknowledge Leorita Joseph Henry, Clinical Support Librarian, King's College Hospital London (for her invaluable professional advice and support in revising the search strategy). The research fellow acknowledge Karen Poole and John Woodcock, Library & Collections, King's College London (for their professional assistance via the Advanced Searching for systematic reviews discussion forum for their feedback on refining the search strategy).

Contributions to study 2 (chapters 3 and 4):

EC with support from SG and JC designed the study. EC completed all study management, data acquisition and data analysis with supervision and further interpretation from JG, SG, and JC. SG, JC, and JG supervised and mentored the research fellow. Each author contributed important intellectual content presented in the published manuscript (chapter 4), drafting of revisions and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. EC and SG take responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

The research fellow would like to acknowledge the King's College Hospital Clinical Research Facility and the assistance from SPIKA Ltd in the software development. The authors would like to acknowledge Dr Helen MacLaughlin and Giulia Dijk for their assistance with creating the ExeRTiOn online intervention, alongside our kidney transplant recipient's expert patients who contributed to the intervention design.

Design and refinement of the online intervention presented throughout the thesis:

The design and refinement of the online intervention in the thesis was led by the research fellow. Expert input was sought from the supervisory team (SG, JC and KB). Expert dietetic content for modules were sought by HM and GD as outlined above. Expert kidney transplant recipients contributed to content of the intervention through quotes, videos and examples. Refinement of the online intervention after study 2 was led by the research fellow, with input from the supervisory team, trial management group (including patient representation) and a software company (SPIKA LTD).

Contributions to studies 3 and 4 (chapters 3 and 6):

EC with supervision from SG, JC and KB conceived and designed the study. EC were involved in data acquisition. A small portion of the qualitative interviews in the nested qualitative study (study 4) were undertaken by a master's student (PD) with training, supervision by EC. All data was initially analysed and interpreted by EC with input from an external statistician (RP). SG, JC and KB reviewed and commented on all analysis and interpretation as supervisors. Coding of the online intervention to the behaviour change technique taxonomy (version 1) was completed by the research fellow, with supervision by JC. Qualitative findings were discussed and validated with an external researcher (JG) who mentored the research fellow over the PhD fellowship. SG, JC, and JG supervised and mentored the research fellow throughout the study.

Abbreviations

Abbreviation	Meaning
AI	Augmentation index
Ax	Assessment
BC	Body composition
BCT's	Behavioural Change Techniques
BCTTv1	Behaviour Change Technique Taxonomy version 1
BCW	The Behaviour Change Wheel
BIA	Bioimpedance Analysis
BMI	Body mass index, measured by kg/m^2
BP	Blood pressure measured in millimetres mercury (mmHg)
BRS	British Renal Society is a multi-professional organisation for renal multi-professionals in the UK
BTS	British Transplant Society
CFS	Chalder fatigue scale, a self-reported scale of fatigue
CKD	Chronic Kidney Disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration creatine equation is a specific method for measuring eGFR and is (measured in ml/ min/1.73m^2)
CMV	Cytomegalovirus, a post-transplant complication
COM-B	The Capability Opportunity Motivation-Behaviour model, central to the Behaviour Change Wheel
CONSORT	Consolidated Standards of Reporting Trials is a framework to encourage transparent reporting of research
COVID-19	Coronavirus disease 2019
CRF	Clinical Research Facility
CVD	Cardiovascular disease
CVE	Cardiovascular event e.g., stroke or heart attack
CVR	Cardiovascular risk
CVS	Cardiovascular system
eGFR	Estimated glomerular filtration rate
EQ-5D-5L	The EuroQol 5 Dimension 5 Level is a self-reported questionnaire reporting health-related quality of life and includes three subcomponents
EQ-5D-5L health state	The EuroQol 5 Dimension 5 Level health state includes mobility, self-care, usual activities, pain/discomfort and anxiety/depression

EQ-5D-5L index value	The EuroQol 5 Dimension 5 Level index value is a single number with 1 indicating full health, and 0 indicating a state as bad as being dead
EQ-5D-5L VAS	The EuroQol 5 Dimension 5 Level visual analogue scale, a subcomponent of the EQ-5D-5L questionnaire
ESKD	End-stage kidney disease, ultimately kidney failure
EuroQoL	European Quality of Life group
ExeRTiOn	Exercise and weight in renal transplant online study
FM	Fat mass, a measure from body composition
GFR	Glomerular filtration rate
GPPAQ	General Practice Physical Activity Questionnaire
GSTT	Guy's at St Thomas' Hospital
HbA1c	Haemoglobin A1C, glycated haemoglobin
HCPs	Healthcare Professionals including all members of the multi-professional transplant team
HR	Heart rate measured in beats per minute
HRA	Health Research Authority
IG	Intervention group
ITU	Intensive Care Unit
IQR	Interquartile range
KCH	King's College Hospital
KDIGO	Kidney Disease: Improving Global Outcomes
KTRs	Kidney transplant recipients
KTx	Kidney transplant
LTM	Lean tissue mas, a measure from body composition
MMR	Mixed Methods research
MoSCoW method	M represents 'Must have' changes, S is the 'Should have' changes, C is 'Could have' changes and W is the 'Would have' changes
MRC	Medical Research Council
MS	Metabolic syndrome
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute of Health Research
Non-RCT	Non-RCT, e.g., a quasi-experimental study
PA	Physical activity

PAI	Physical Activity Index- The categorisation of physical activity levels from the GPPAQ
PI	Principle Investigator
PICO	Population, Intervention, Controls, Outcome' framework
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PROSPERO	The international prospective register for systematic reviews
PTDM	Post-transplant diabetes mellitus, which was previously referred to as new onset of diabetes after transplantation (NODAT)
PWV	Pulse wave velocity is a non-invasive measure of arterial stiffness and is measured in meters per second
QUALI	Qualitative research
QUANT	Quantitative research
RA	The renal Association is a UK renal organisation for members of the renal community
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RRT	Renal replacement therapy
R&I	Research and Innovation team
Rx	Intervention
SD	Standard deviation
SOT	Solid-organ transplant (includes kidney, liver, heart and lung transplant recipients)
TMG	Trial management group refers to a multi professional group designed to oversee a stud
UC	Usual care group i.e., the comparator group
UKKRC	UK Kidney Research Consortium
VAS	Visual analogue scale
6MWD	Refers to six-minute walk test (in metres) which is the results of the 6MWT
6MWT	Refers to the six-minute walk test. A standardised self-paced walking test used to assess functional capacity

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Most importantly, **thank you to all the kidney transplant recipients who helped along the way with this research project**. Thank you for volunteering your time to contribute to the online intervention design, trial management meetings, and participating in the studies outlined in this thesis. I am continuing to learn about the kidney transplant experience, and I am so very grateful to capture your unique and important experiences and insights.

I would not be able to complete this PhD without my funding and I am extremely grateful for my **Kidney Research UK Allied health PhD fellowship**.

Publications, presentations and awards arising from the PhD

Publications arising during PhD Fellowship

Castle, E.M., Greenwood, J., Chilcot, J., & Greenwood, S.A. (2020). *"Usability and experience testing to refine an online intervention to prevent weight gain in new kidney transplant recipients"*. *British Journal of Health Psychology,* 26 (1),p232-255. DOI:10.1111/bjhp.12471
https://bpspsychub.onlinelibrary.wiley.com/doi/10.1111/bjhp.12471

Castle, E.M., McBride, E., Greenwood, J., Bramham, K., Chilcot, J., & Greenwood, S.A. (2021). "*Do exercise, physical activity, dietetic or combined interventions improve body weight in new kidney transplant recipients: a narrative systematic review and meta-analysis"*. (In press, submitted).

Conference presentations during PhD Fellowship

Date	Presentation	Organisation and location
September 2018	Motivational interviewing for supporting physical activity behaviour for people living with kidney disease *(Invited speaker and conference lead organiser)*	British Renal Society Rehabilitation Network training day, York, UK
November 2018	Motivational interviewing principles for physical activity and kidney transplant recipients *(Invited speaker)*	The European Transplant Allied Healthcare Professionals (ETAHP) presentation at the European Society for organ transplant (ESOT) conference, Munich, Germany
June 2019	The Exercise in Renal Transplant Online and weight study (ExeRTiOn) *(Poster presentation of study 2 findings)*	UK Kidney Week (UKKW), Brighton, UK
September 2019	The Exercise in Renal Transplant Online weight gain prevention (ExeRTiOn) study	Kidney Research UK Fellows Day, Leicester, UK

	(Abstract selected for a rapid talk presentation of study 2)	
February 2020	Motivational interview training workshop to support physical activity in transplant recipients *(Invited speaker)*	Transplantoux Symposium Leuven, Belgium
February 2020	An online intervention to prevent weight gain in new Kidney Transplant Recipients *(Invited speaker, discussing PhD project)*	King's College London Rehabilitation showcase, London, UK
March 2021	Keeping fit on dialysis *(invited speaker)*	International Society of Peritoneal Dialysis, virtual webinar
May 2021	How can we support kidney transplant recipients to control their weight? *(Invited speaker, invited chair)*	Royal Society of Medicine, Living Well with Chronic Kidney Disease Event, London, UK

Awards during the PhD fellowship

Date	Award	Organisation
September 2020	The Trevor Cook award recipient. This award is voted by a panel of clinicians and people living with kidney disease. It is awarded for the presentation that has the best clarity from a lay perspective	Kidney Research UK Fellows Day https://kidneyresearchuk.org/2019/09/20/research-highlights-at-fellows-day-2019/

Chapter 1 General introduction

1.1 Chapter overview

The focus of this thesis is to explore the creation, usability, acceptability and feasibility of an online intervention designed specifically to prevent weight gain in new kidney transplant recipients (KTRs). Therefore, the purpose of this chapter is:

- To introduce and define the key terms of this thesis
- To present the background to the thesis
- To provide a rational for the thesis by stating the key aims and objectives
- To outline the structure of this thesis

1.2 Definition of key terms

1.2.1 Chronic Kidney Disease

Chronic Kidney Disease (CKD) is a growing global issue (NHS Digital, 2017). The management of CKD is a challenge for healthcare systems (Kerr, Bray, Medcalf, O'Donoghue, & Matthews, 2012). The Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group defines CKD as: Abnormalities of the kidney structure or function, present for >3-months, with implications for health (KDIGO CKD Work Group, 2013a, p. 5). CKD is classified by the cause of kidney disease, the functioning of the kidney as depicted by the glomerular filtration rate (GFR), and the level of albumin in the urine (KDIGO CKD Work Group, 2013b). Elevated levels of albumin in the urine (albuminuria) is one of the signs of CKD is associated with the progression of CKD and cardiovascular risk (CVR) (KDIGO CKD Work Group, 2013b). As CKD is progressive,

one of the main focuses of management includes the prevention or slowing of the disease progression to end-stage kidney disease (ESKD), i.e., kidney failure.

Causes of CKD include diabetes, cardiovascular disease (CVD), obesity, genetic kidney disorders, the process of ageing, toxicity from medication (Centers for Disease Control and Prevention, 2021) and also structural damage to the kidney and its associated structures (NICE, 2015). According to data from the Health Survey for England National Survey, rates of obesity (Hounkpatin et al., 2020; NHS Digital, 2020) and diabetes (Hounkpatin et al., 2020) are on the rise in the United Kingdom (UK), which are main contributors to the development of CKD. Adding to the complexity of CKD management, is the fact that CKD is often present with other co-morbidities such as CVD, and diabetes (NICE, 2015). The National Institute for Health and Care Excellence (NICE) recommend people with a history of hypertension, diabetes, acute kidney injury, CVD, structural renal tract disease, multisystem diseases that could impact the kidney (e.g. lupus), family history of heredity kidney disease, family history of ESKD, and those with a presence of blood in the urine (haematuria) should be tested for CKD (NICE, 2015).

CKD leads to multi-system disfunction, therefore, it can produce wide reaching symptoms such as anaemia and associated fatigue, endocrine dysfunction, bone and metabolic disorders and hypertension (KDIGO CKD Work Group, 2013b). As symptoms often present later in the disease trajectory, CKD is often diagnosed late (NICE, 2015).

The recent years have seen a shift from traditional paternalistic medical models of care to that of self-management and empowering our healthcare service users. The National Health Service (NHS) five year forward view (2017) stipulates the need to harness

technology, and to ensure patients are supported to take an 'active role' in their health and wellbeing (NHS England, 2017). The NHS England Long Term Plan (2019) focuses on facilitating the healthcare service users to take ownership of healthcare, well-being and ensure care across the NHS care is co-ordinated and collaborative (NHS England, 2019). Patient-centred care is becoming more frequent, and is encouraged in the NICE guidelines for the assessment and management of CKD (NICE, 2015). Patient-centred care focuses on individualising care pathways and allows clinicians to support those living with CKD to make informed healthcare decisions to manage CKD and its associated symptoms.

1.2.1.1 Stages of CKD and medical management

There are five stages of CKD, ranging from normal/mild to the most severe stage (ESKD, stage 5), which is kidney failure. The first stages of CKD are often silent or symptom free (NICE, 2015). Stages 3 to 5 of CKD have been associated with acute kidney injury, frailty, falls and mortality (NICE, 2015). As people living with CKD approach stage 5, lifesaving renal replacement therapy (RRT) is needed as the kidneys can no longer manage independently in filtering the toxins in the body. RRT includes either haemodialysis that can be presented in-centre or at home, peritoneal dialysis which can be provided at home, or transplantation (British Medical Journal Best Practice, 2021). Extensive, individualised pre-ESKD education is needed to allow people living with CKD to choose either forms of RRT, or symptom management (known as conservative care) (Cassidy et al., 2018; Shukla et al., 2019). Preparation and speciality services are required to prepare for RRT such as preparing access points to deliver both haemodialysis and peritoneal dialysis to the body, or extensive assessment and work up to be waitlisted for a transplant if appropriate. Complications and symptom management increase as people

progress through the stages of CKD. Patients may need management of the associated complications such as hypertension, anaemia, secondary hyperthyroidism, bone mineral disorders, calcium and vitamin D deficiencies, and metabolic acidosis (British Medical Journal Best Practice, 2021). Table 1.1 below summarises the stages of CKD based on GFR levels from the KDIGO guidelines (KDIGO CKD Work Group, 2013b) and the associated management strategies from best practice recommendations from the British Medical Journal (BMJ) (British Medical Journal Best Practice, 2021). In addition to GFR, stages of CKD can be categories by albuminuria and the cause of CKD (KDIGO CKD Work Group, 2013b; NICE, 2015); for simplicity, categories of CKD will be shown for GFR. Whilst GFR is the gold standard for kidney function, estimated Glomerular Filtration Rate (eGFR) is often used in clinical practice. It is important to note that age, sex, race-ethnicity and other clinical factors can influence eGFR (KDIGO CKD Work Group, 2013b).

Table 1-1 CKD categories for adults

Category based on GFR from KDIGO guidelines (2013b)	Associated GFR level (ml/min/1.73m2)	Terms of Category and severity	Management strategies from BMJ best practice (2021)
1	≥90	Normal or high kidney function	• Prevent/delay progression of CKD • Address co-morbidities • Addressing CVD and CKD risk factors • Education to address physical activity, healthy weight and smoking cessation • Optimising blood pressure (ACE inhibitors or angiotensin-II receptor antagonist medications) • Reduce lipids (e.g., statins) • Reduce proteinuria • Optimise glycaemic control (aim haemoglobin HbA1c <7%) • Education
2	60-89	Mildly reduced	• Continue with CVD and CVR risk management and reduction • Continue with education • Addressing symptoms of CKD if present/appropriate • Estimate the rate of CKD progression, and prepare for RRT
3a	45-59	Mild to moderately reduced	• Education is key to prepare for ESKD using shared decision making • Continue with CVD and CKD risk management • Identification and management of CKD complications (anaemia and secondary hyperthyroidism if present)
3b	30-44	Moderately to severely reduced	
4	15-29	Severely reduced	• As above risk management and symptom management (anaemia, hyperparathyroidism and metabolic acidosis management if appropriate) • Education and preparation for ESKD and RRT is crucial • Referral to specialist ESKD teams such as dialysis access, transplant work-up or conservative care depending on patient preference
5	<15	Kidney Failure	• Transplant, dialysis or conservative management • Symptom management

• Risk management

Note. This table was modified based on the KDIGO guidelines (KDIGO CKD Work Group, 2013b) and the BMJ best practice guidance for Chronic Kidney Disease (British Medical Journal Best Practice, 2021). Stage 3 is divided into groups 3a and 3b due to different risks. BMJ= British medical journal, GFR= glomerular filtration rate (measured in ml/min/1.73m^2), CVD=cardiovascular disease, CKD= Chronic Kidney Disease, ACE inhibitors=Angiotensin-converting-enzyme inhibitors, HbA1c=Haemoglobin A1c refers to the amount of glucose attached to haemoglobin, ESKD= end stage kidney disease, and RRT= renal replacement therapy (dialysis or transplant)

The UK Renal Registry collate data from adult (n=71) and paediatric (n=13) renal units across the UK (The UK Renal Registry, 2020). In 2018 there was an incidence of 8,000 new cases of RRT, and 67,000 total cases of RRT in the UK (UK Renal Registry, 2019). Health Survey for England data (2017) report that 2 % of adults aged 16 and over had been diagnosed with CKD. However, exploration of the eGFR and albumin levels suggest these rates are higher, with 15% of adults over 35 years of age having CKD (stages 3 to 5), and 34% of adults aged 75 and over having CKD (NHS Digital, 2017). Similar rates of CKD are reported in the United States (US), with 15% of adults estimated to have CKD (Centers for Disease Control and Prevention, 2021).

Economic modelling has estimated that the cost to the NHS each year to be approximately 1.44 to 1.45 billion pounds, with the majority of the costs being associated with RRT (Kerr et al., 2012). Furthermore, people living with CKD have a 35% longer hospital stay when compared with people of the same age without CKD (Kerr et al., 2012). The estimated additional cost to the NHS for bed-days for people living with CKD was estimated to be 46 million pounds from 2009 to 2010 (Kerr et al., 2012).

1.2.1.2 Risks associated with CKD progression and cardiovascular risk

The presence of CVD, protein in the urine (proteinuria), acute kidney injury, hypertension, diabetes, smoking history, being of African, African-Caribbean or Asian

family origin, chronic use of NSAIDS and untreated urinary outflow tract obstruction are identified in the NICE guidance as risk factors for the progression of CKD (NICE, 2015).

There is a strong association with CKD and cardiovascular risk (CVR). CVD such as hypertension can cause CKD, and CKD is a strong risk factor for the development of CVD (Jankowski, Floege, Fliser, Böhm, & Marx, 2021). As CVD is the leading cause of death in people living with CKD, the management of CKD includes the management of 'traditional' CVR factors including blood pressure control, correction of hyperlipidaemia, reducing protein in the urine (proteinuria), and optimising glycaemic control (British Medical Journal Best Practice, 2021). When compared with age-and gender matched controls, from 2009 to 2010 it was estimated that people living with CKD had an additional 7,000 strokes and 12, 000 myocardial infarctions (heart attacks), with an estimated cost of 174-178 million pounds (Kerr et al., 2012). Therefore, the focus on reducing CVR for people living with CKD, and addressing the CVR factors is of clinical importance.

In addition to the 'traditional' CVR factors, people living with CKD often experience additional (non-traditional) risk factors associated with CKD processes (Jankowski et al., 2021) and kidney transplantation (Devine, Courtney, & Maxwell, 2019). The processes of CKD can lead to the accumulation of toxins which can influence cholesterol. There can be calcification of blood vessels, increased arterial stiffness and hemodynamic changes associated with haemodialysis therapy and fluid imbalances due to the kidney no longer functioning (Jankowski et al., 2021). The maladaptive changes to the cardiovascular system (CVS) that occur with CKD progression and ESKD, and haemodialysis therapy prior to transplantation remain present in KTRs. KTRs have a three to five times higher

risk for CVD compared with age-matched controls (Devine et al., 2019). Furthermore the British Transplant Society (BTS) report (2017) the leading cause of transplant graft loss is due to death with a functioning graft, with CVD being reported as one of the leading causes of death in KTRs. Therefore, the management of CVR is imperative for KTRs. Transplant specific factors such as rejection of the transplant kidney, and anti-rejection immunosuppressant medications can contribute further to CVR in KTRs (Devine et al., 2019). Table 1.2 summarises the 'traditional' CVR factors, and the CVR factors associated with CKD and kidney transplantation.

Table 1-2 Cardiovascular risk factors in CKD and kidney transplant

	Factors contributing to CVR in people with CKD	Comments
Traditional risk factors [a]	• Age > 50 • Hypertension • Smoking history • HDL • Total cholesterol • History of diabetes • LVH • Insulin resistance • Dyslipidaemias • Obesity • Family history of CVD	• Contribute to atherosclerotic vascular disease • Contribute to CKD progression by affecting the large and small vessels of the kidneys • Contribute to CVR and CVE • Often present in people living with CKD • Hypertension and diabetes are causes of CKD
Non-traditional (CKD specific) [b]	• Can be in addition to traditional risk factors above • CKD is a strong risk factor for CVD • Changes to HDL cholesterol levels based on the progression of CKD and the accumulation of urea • Reduced eGFR • Albuminuria • Proteinuria • Hemodynamic changes to from CKD leading to LVH and myocardial fibrosis • Systematic inflammation process associated with CKD • Haemodialysis history • Anaemia • malnutrition	• The progression of CKD can lead to the accumulation of toxins (e.g., urea) and changes to structures such as fatty deposits • Calcification of blood vasculature, hypertension, increased arterial stiffness and resistance associated with CKD can lead to LVH • Haemodialysis causes adverse effects on the CVS
Non-traditional (kidney transplant specific) factors [c]	• In addition to traditional and CKD risk factors • Immunosuppressant use • Metabolic syndrome • Adverse weight gain • Reduced graft function • Episodes of acute rejection and dysfunction • Episodes of transplant renal artery stenosis • Reduced eGFR • Anaemia	• Maladaptive changes from ESKD and dialysis still present in KTRs • Additional changes specific to transplantation such as medications to prevent rejection (immunosuppressant use) and graft rejection. • Immunosuppressant medications can lead to weight gain, PTDM and exacerbate hypertension in KTRs

	• PTDM • Dyslipidaemia common in KTRs

Note. This table has been created with evidence for traditional CVR factors [a](Anderson, Wolson, Odell, & Kannel, 1991; Wilson et al., 1998), [b] CKD risk factors (Jankowski et al., 2021; Sarnak et al., 2003) and [c] transplant specific risk factors (Devine et al., 2019)
HDL= high-density lipoprotein (HDL) cholesterol levels, LVH= left ventricular hypertrophy, CVD= cardiovascular disease, CKD= Chronic kidney disease, CVR= cardiovascular risk, Cardiovascular event (e.g., stroke, heart attack), eGFR= estimated glomerular filtration rate, CVS= cardiovascular system, ESKD=end stage kidney disease (stage 5), PTDM= post-transplant diabetes mellitus and KTRs= kidney transplant recipients

1.2.2 Kidney transplantation

As previously described, RRT includes both dialysis (haemodialysis and peritoneal dialysis) and transplantation. People living with CKD, who choose transplantation as their modality of treatment require extensive assessment including age (usually less than 80 years of age is recommended) and co-morbidities to assess the appropriateness for transplantation by a specialist team (British Medical Journal Best Practice, 2021). Transplantation can occur by a deceased donor, or a living donor (related or unrelated) (Barnett & Mamode, 2011). Pre-emptive transplants (those occurring before ESKD and RRT) and living donor transplants are associated with better outcomes (Barnett & Mamode, 2011). However, there is still a lengthily wait to receive either a living or deceased kidney transplant (Barclay & Burnapp, 2013).

During the transplant surgery, the new kidney is usually placed in the left or right groin (iliac fossa) and is connected to the pre-existing renal blood supply and the bladder (Barnett & Mamode, 2011). Therefore, due to the superficial location in the groin, it is unsurprising that KTRs have reported fear of harming the new kidney, which is associated with physical activity (Zelle et al., 2016).

1.2.2.1 Kidney transplants in the UK

In the UK Renal Registry Report, there were 3,644 adult and children kidney and combined kidney transplants performed from the 31st of December 2017 to the 31st of December 2018 (UK Renal Registry, 2019). The prevalence of adult KTRs was 55.7% of all of the UK RRT population, with a median age of 55.2 years and 60.8% were male (UK Renal Registry, 2019). The leading cause of death for KTRs from 2017-2018 was infection (23.6%) and malignancy (21.0%) (UK Renal Registry, 2019). Cardiac disease accounted for 17.5% of all transplant deaths, however, cause of death was not reported in 35% of the cases, and 20.6% of deaths were coded as 'other causes' (UK Renal Registry, 2019). Looking at cause of death for all RRT patients in the UK (including KTRs), cardiac disease was responsible for 20.7% of deaths occurring from 2017-2018 (UK Renal Registry, 2019).

1.2.2.2 Kidney transplant management and complications

Kidney transplantation is the gold standard treatment for ESKD (Barclay & Burnapp, 2013). It has favourable cost implications (Kerr et al., 2012) and health outcomes such as survival (British Medical Journal Best Practice, 2021) when compared to dialysis therapy. However, kidney transplantation is not without risk. There is a high prevalence of diabetes, CVD and obesity in KTRs (Friedman, Miskulin, Rosenburg, & Levey, 2003; Gordon, Prohaska, Siminoff, Minch, & Sehgal, 2005). Anti-rejection (immunosuppressant) medication is required for life for KTRs to prevent the body rejecting the new kidney (Barnett & Mamode, 2011). Whilst immunosuppressant medications are essential to preventing rejection, they have been found to increase both the severity and incidence of CVR factors in KTRs (Hricik, 2011). Refer to Table 1.2 which displays the transplant specific CVR factors experienced by KTRs.

Current post kidney transplant immunosuppressant medication includes 'triple therapy' including corticosteroids (e.g., prednisolone), calcineurin inhibitors (e.g., Tacrolimus) and anti-proliferative agents (e.g., mycophenolate mofetil), which has been shown to reduce the risk of the kidney transplant graft failing (Baker et al., 2017; KDIGO Transplant Work Group, 2009). However, these immunosuppressant medications have side effects on bone health, weight gain, CVR, hypertension, abnormal glucose mechanisms, and the development of post-transplant diabetes mellitus (PTDM) (Baker et al., 2017).

PTDM, previously referred to as new onset of diabetes after transplant, is a specific form of type two diabetes experienced after solid-organ (kidney, liver, lung and heart) transplant (SOT), and is associated with adverse clinical outcomes (Chowdhury et al., 2021). PTDM develops due to a combination of reduced insulin secretion and increased insulin resistance (Chowdhury et al., 2021). Recent guidelines from the British Clinical Diabetologists and Renal Association recommend that due to the influence of both transplant-specific and traditional risk factors, PTDM is

> Considered a distinct pathophysiological entity (Chowdhury et al., 2021, p. 2).

PTDM occurs in 5-20% of KTRs and is thought to impact on survival through its contribution to CVR and CVD (Baker et al., 2017). Risk factors include immunosuppressant medications (calcineurin inhibitors and corticosteroids), older age, obesity, metabolic syndrome, glucose intolerance, hepatitis C, rejection episodes, reduced GFR, cytomegalovirus (CMV) and a family history of diabetes (Baker et al., 2017; Chowdhury et al., 2021). It is often diagnosed using oral glucose tolerance tests after six weeks post transplantation as KTRs can experience episodes of transient hyperglycaemia acutely post transplantation (Chowdhury et al., 2021). Significant weight gain post

transplantation, and obesity, are risk factors for PTDM (Devine et al., 2019). Furthermore, those without a history of diabetes, and those who have a diabetes diagnosis, are both at risk of PTDM, an elevated CVR and a risk of a Cardiovascular event (CVE) such as stroke (Devine et al., 2019). Current national guidelines for PTDM in KTRs suggest the monitoring of hyperglycaemia, diagnosis, structured education, diabetic pharmacology if required, blood pressure control and statin therapy (Chowdhury et al., 2021). In addition to medical management, modifiable risk factors such as obesity and metabolic syndrome could be influenced by diet and physical activity interventions and are recommended for KTRs (Chowdhury et al., 2021).

Higher doses of calcineurin inhibitors (e.g., Tacrolimus) has been found to lead to abnormal glucose mechanisms and PTDM in KTRs, more so than corticosteroids (Baker et al., 2017). Whilst corticosteroids such as prednisolone have been known to contribute to osteoporosis, avascular necrosis, weight gain, cataracts, diabetes, hypertension and dyslipidaemia, a lower maintenance dose (approximately 5mg prednisolone per day) is recommended in national and international kidney transplant guidelines (Baker et al., 2017; KDIGO Transplant Work Group, 2009). The withdrawal of corticosteroids in the acute post-operative kidney transplant period (weeks to months post-surgery), is associated with higher rates of acute rejection (KDIGO Transplant Work Group, 2009). Acute post-transplant medical management often involves careful and frequent monitoring and titration of immunosuppressant medications to balance the risk of complications such as CVD, and the risk of rejection of the new kidney graft.

Metabolic syndrome (MS) is a composition of symptoms such as insulin resistance and inflammation, obesity, hyperlipidaemia and hypertension, and is thought to have a

prevalence of 20 to 65% in KTRs (Pedrollo et al., 2016). A systematic review found that KTRs with MS had a 3 times greater risk of graft loss, and 3 and a half times greater risk of death by CVD than those without MS (Pedrollo et al., 2016). A history of MS is associated with an increased risk of developing both diabetes and hypertension (KDIGO CKD Work Group, 2013b). The association between all-cause mortality and MS remains unclear. As MS is associated with a reduced GFR, proteinuria, PTDM, CVD and reduced graft function and graft loss, its management is of clinical and research interest for KTRs (Pedrollo et al., 2016).

1.2.3 Weight gain in KTRs

In the dialysis population, there is evidence to suggest that the presence of obesity has been associated with survival benefits known as the 'obesity paradox' (Baker et al., 2021; Herselman, Esau, Kruger, Labadarios, & Moosa, 2010). This is not the case for KTRs. A systematic review demonstrated that obesity is associated with mortality in KTRs (Ahmadi et al., 2014). In addition to this, an analysis of the UK Transplant Registry data revealed that 78.3% of transplant recipients who had died during follow-up did so with a functioning kidney (Kostakis et al., 2020). Therefore, addressing modifiable CVR factors, such as obesity, and weight gain are important to optimise clinical care for KTRs.

Weight gain is a common complication for KTRs, and as previously discussed, is linked to CVR, PTDM and MS. The work presented in this thesis will focus on adverse significant weight gain post kidney transplantation, rather than the weight gain that may be beneficial for those who suffer from being underweight. However, it is important to define and differentiate between beneficial weight gain in those who may be underweight

and suffer from sarcopenia, and those who may experience adverse weight gain that is associated with poor clinical outcomes.

Sarcopenia is defined as muscle failure including a reduction in muscle strength, function and mass (Cruz-Jentoft et al., 2019). Sarcopenia has been associated with reduced ability to perform activities of daily living, increased health care costs, falls, physical disability, frailty and mortality (Cruz-Jentoft et al., 2019). Whilst it is primarily caused by the processes of aging, it can also occur due to systemic chronic diseases and inflammation (Cruz-Jentoft et al., 2019), and occurs in ESKD (Bellafronte, Sizoto, Vega-Piris, Chiarello, & Cuadrado, 2020; Hanna, Ghobry, Wassef, Rhee, & Kalantar-Zadeh, 2020). The uraemic toxicity, inflammation associated with CKD, loss of protein intake, and energy stores are thought to contribute to this pattern (Hanna et al., 2020). A recent study by Bellafronte et al (2020) evaluated 'bedside measures' of body composition (BC), and anthropometric measures in a sample of 265 CKD participants (including 48 KTRs). The authors report that whilst nutritional status and impaired muscle function occurred in KTRs, it was worse in haemodialysis participants (Bellafronte et al., 2020).

The NICE guidelines distinguish between overweight and obesity using body mass index (BMI), measured by dividing body weight (in kilograms) by height (in meters) squared (NICE, 2014b). BMI cut-offs for the overweight category (in adults) is a BMI between 25 and 29.9 kg/m^2, whereas obesity is categorised by a BMI of 30 kg/m^2 or more (NICE, 2014b). Of concern, is the fact that obesity rates have almost doubled in recent years in the UK, and are associated with a number of co-morbidities (NICE, 2014b). Sarcopenic obesity is defined as the presence of both obesity and sarcopenia, is associated with worse outcomes than sarcopenia or obesity alone and can occur in ESKD and KTRs (Bellafronte

et al., 2020). NICE guidelines for the assessment and management of obesity recommend that whilst BMI can assess adiposity, interpretation requires caution (NICE, 2014b). Clinicians need to consider the addition of waist circumference measurement in people with a BMI of less than 35kg/m^2 and the impact of highly muscular individuals on BMI recordings (NICE, 2014b). In addition to body weight, BMI and waist circumference, Bioimpedance Analysis (BIA), which measures BC such as fat, muscle and fluid, may provide an additional useful tool pre and post intervention to assess fat and fat free mass (NICE, 2017b).

A recent single centre observational study from the USA reported that body weight significantly increased at 3-months after kidney transplant (KTx) by 2.2kg ($p<0.03$), and then increased further at 12-months after KTx (6.6kg, $p< 0.001$) (Workeneh et al., 2019). BC results suggested that the distribution of this weight gain was largely due to increase of adipose tissue around the truncal region (Workeneh et al., 2019). Therefore, when assessing body weight, and its impact in KTRs, other measures such as BMI, and BC may be of importance to evaluate if participants are experiencing beneficial weight gain such as muscle mass, or adverse weight gain such as the increase of adipose tissue.

1.2.3.1 Adverse weight gain in KTRs

Weight gain within the first year of SOT has been associated with adverse clinical events, and poor transplant outcomes (Kugler et al., 2015; Saigi-Morgui et al., 2016). Whilst weight gain presents as a clinical issue for all SOT recipients, the experiences of weight gain vary across the SOT groups. Liver transplant recipients tend to have a reduction in body weight in the first six months associated with the removal of ascites, followed by a period of weight gain (Beckmann et al., 2017). In contrast, kidney, heart, and lung

transplant recipients demonstrate rapid weight gain in the acute-post operative period (Beckmann et al., 2017).

Increased body weight and BMI is associated with poor transplant outcomes. A retrospective analysis of 25,539 adult KTRs in the UK reported a BMI of greater than 25 kg/m^2 was an independent risk factor for both delayed graft function, and primary graft non-function (Kostakis et al., 2020). In addition, KTR who were underweight and KTRs living with obesity were reported to have poorer graft survival (Kostakis et al., 2020).

Weight gain within the first year of receiving a kidney is a critical health issue (Glicklich & Mustafa, 2019). KTRs who gain more than 15% of their body weight within the first year of transplant surgery are at an increased risk of death with a functioning kidney (Vega, Huidobro, De La Barra, & Haro, 2015). When referring to weight gain throughout the thesis, the research fellow will be referring to the adverse rapid weight gain that occurs within the first twelve months of receiving a kidney transplant and is associated with adverse health outcomes.

New KTRs experience unique challenges with regards to performing physical activity behaviours and following a balanced diet, which could contribute to post-transplant weight gain. These challenges experienced by KTRs acutely post kidney-transplant include:

- The fear of injuring the new transplant kidney (Stanfill, Bloodworth, & Cashion, 2012; Zelle et al., 2016)

- The burden of other health problems have also been reported as barriers to achieving a healthy weight and being physically active after a kidney transplant (Stanfill et al., 2012)
- KTRs have identified an unmet need for early support services to address diet and physical activity behaviours (Stanfill et al., 2012)
- Reduced functional capacity due to preceding uremic myopathy and the effects of haemodialysis therapy (Koufaki, Greenwood, Macdougall, & Mercer, 2013)
- Muscle atrophy and wasting (Van Den Ham et al., 2005)
- Reduced PA (Nielens et al., 2001)
- Cravings and an increased appetite (Cashion et al., 2014)
- Complications associated with immunosuppressant medications (Devine et al., 2019), (refer to table 1.2, chapter 1)
- The lifting of of dietary restrictions compared to heamodialysi results in increased freedom of food choices (Stanfill et al., 2012).

1.2.3.2 Interventions to address adverse weight gain in KTRs

A qualitative study of KTRs who gained 12% of their body weight within the first year of transplantation identified medications use, fear of injuring the new kidney, and burden of other health problems as barriers to achieving a healthy weight and being physical active after transplantation (Stanfill et al., 2012). KTRs identified a need for early support services to address diet and physical activity after kidney transplantation (Stanfill et al., 2012). A systematic review by Jamieson et al (2016) explored the challenges and motivations experienced by KTRs towards self-management. The study included a sample of 1238 participants from 50 studies from 19 different countries. The authors

reported that there is inconsistent and vague education from clinical teams, which presents as a key barrier to self-management (Jamieson et al., 2016). This systematic review highlights an unmet educational need, and that interventions to address individualised education, self-monitoring of behaviour and self-management are warranted for new KTRs.

The BTS guidelines (2017) recommend KTRs follow a healthy diet, perform physical activity, are referred to weight management services for support, and aim for a BMI equal to or less than 25kg/m^2. UK guidelines for clinical practice and the renal workforce, recommend access to weight management services for KTRs, and that transplant teams should be multi-disciplinary and include dietitians and physiotherapists (Baker et al., 2021; The British Renal Society, 2020). However, access to specialist weight management pathways and specialist clinicians are variable and scarce across the UK (Kostakis et al., 2020).

Physical activity (PA) is defined as any habitual or planned activity of the body such as occupational, transportation, domestic and social (Caspersen, Powell, & Christenson, 1985). In contrast, exercise interventions are defined as any planned, structured, prescriptive activity designed to improve a specific aspect of physical fitness (American College of Sports Medicine, 2013; Caspersen et al., 1985). Despite PA levels increasing in KTRs after transplantation, they remain lower than age and gender matched controls (Nielens et al., 2001).

Previous systematic reviews and literature reviews have shown exercise and PA interventions to have had a positive effect on various outcomes such as cardiorespiratory

fitness and exercise tolerance (Calella et al., 2019; Chen, Gao, & Li, 2019; Oguchi et al., 2019; Takahashi, Hu, & Bostom, 2018), muscle strength and function (Chen et al., 2019; Oguchi et al., 2019), health related quality of life, (Calella et al., 2019; Oguchi et al., 2019; Takahashi et al., 2018) maximum heart rate (Calella et al., 2019), and arterial stiffness (Chen et al., 2019). Expert clinical guidance documents (Baker et al., 2021; Baker et al., 2017), and international guidelines for KTRs (KDIGO Transplant Work Group, 2009) and people living with CKD (KDIGO CKD Work Group, 2013b) recommend regular PA. Examples of renal specific face-to-face rehabilitation (renal rehabilitation) led by expert renal physiotherapists exist in the UK, and have shown benefit to various functional measures and survival (Greenwood et al., 2018; Greenwood et al., 2012). Despite the evidence suggesting the benefits of exercise training for people living with CKD and KTRs (Heiwe & Jacobson, 2014; Koufaki et al., 2013; Koufaki, Greenwood, Painter, & Mercer, 2015) , renal rehabilitation services are not common practice, and are not offered to all people living with CKD (Castle, Wilkinson, Ancliffe, & Young, 2020; Greenwood, Koufaki, Rush, Macdougall, & Mercer, 2014; The British Renal Society, 2020). Multi professional national (KRUK, 2021; The British Renal Society, 2018), and international groups (GREX, 2021) are focused on bridging the gaps with evidence and implementation of exercise and wellbeing services for people living with CKD, including KTRs.

Although weight gain and maintaining positive PA behaviours are real concerns for KTRs, they are not routinely offered formal weight management or weight gain prevention interventions. Results from a recent UK survey of all transplant centres revealed clinicians believed that kidney transplant outcomes were adversely affected by obesity (Kostakis et al., 2020). Despite this recognised clinical need, dedicated pathways

to address weight management for KTRs were sparse with variable access (Kostakis et al., 2020).

There is also a difference between weight management services, i.e., services designed to reduce body weight, and those designed specifically to prevent weight gain from occurring. Whilst there are some general community schemes for exercise and weight management available, KTRs report that these community schemes are not always understanding of the specific issues surrounding kidney transplantation. There are some existing renal-specific face-to-face services available for weight loss for people living with CKD that report significant weight loss and improvement in functional outcome measures (Cook, MacLaughlin, & Macdougall, 2008; MacLaughlin et al., 2010; MacLaughlin et al., 2012). However, these specialist services are sparse, and not available throughout the country. In addition, the KTRs who access the weight management services have to have gained significant weight to be referred to these services.

In addition to the unique challenges faced by new KTRs, the medical management of acute KTRs results in a high frequency of kidney transplant clinic specialist outpatient appointments in the first year of receiving a kidney transplant. The BTS Clinical Practice Guidelines for post-operative care in KTRs (2017) recommend transplant clinic appointment frequencies of; 2-3 times a week in the first month, 1-2 times a week in the 2nd and 3rd month post-transplant, biweekly- monthly for 4 to 6 months post-transplant, and every 4 to 6 weeks for six months to 12-months post-transplant. Attendance for additional face-to-face rehabilitation services may be challenging for new KTRs (Greenwood et al., 2015). Furthermore, KTRs often attend these specialist transplant

outpatient clinics from a wide geographical catchment area and return to work in the first three months after transplant, exacerbating the burdens of time and travel. These unique challenges could be addressed by the exploration of online interventions to support weight gain prevention following kidney transplantation.

The popularity and use of online interventions in healthcare is growing. In Great Britain, 93% of households have access to the internet (The Office for National Statistics, 2019). Furthermore, people living with CKD in the UK readily use online platforms to monitor their CKD health such using 'renal patient view' (The Renal Association, 2020a). Evidence regarding the use of online interventions to support people living with CKD is growing. A recent Cochrane review by Stevenson et al (2019) evaluated the risks and benefits of online health interventions for people living with kidney disease. A small number of the included studies in this systematic review (15%) included KTRs, and none focused on weight gain prevention. The quality of evidence was low, and further research of interventions using theoretical frameworks, self-monitoring and personalised education were recommended (Stevenson et al., 2019). Published literature from studies involving participants living with excess weight and obesity suggest that online behaviour change interventions are acceptable, feasible and can provide clinical and statistically significant weight reduction (Bradbury, Dennison, Little, & Yardley, 2015; Little et al., 2016; Yardley et al., 2014; Yardley et al., 2012).Therefore, the exploration of an online intervention to provide KTRs with the information and skills to address PA, and healthy eating post KTx warrant further exploration, and will be addressed in this thesis.

1.3 Aims and objectives of this thesis

The thesis is structured around four empirical studies that serve to address the following aims and objectives. The aims and objectives are summarised below.

1.3.1 Aims

1. To create on online intervention to address weight gain prevention in new kidney transplant recipients
2. To explore the feasibility and acceptability of the online intervention for new kidney transplant recipients

1.3.2 Objectives

1. To review and synthesise the current evidence regarding weight gain prevention interventions for new kidney transplant recipients
2. To construct a prototype of a bespoke online intervention to assist with weight gain prevention in new kidney transplant recipients using a person-based approach
3. To test the usability, functionality and experience of using the prototype online intervention to aid refinement and acceptability
4. To refine the prototype of the online intervention using patient and health care professional feedback
5. To conduct a feasibility mixed methods randomised controlled trial:
    a. To assess the feasibility to screen and recruit participants, measure adherence to study visits and the intervention, and capture safety outcomes (quantitative outcomes)

b. To capture and report the experience of using the online intervention over 12 weeks, and the experience of taking part in the feasibility study (qualitative outcomes)

1.4 Structure of the thesis

To achieve these aims and objectives, this thesis will include four empirical studies: a systematic review and meta-analysis (study 1), a qualitative evaluation of the prototype of the bespoke online intervention (study 2), and a mixed methods feasibility trial (study 3) with a nested qualitative evaluation (study 4) using the refined online intervention. These studies resided within an iterative complex intervention development process. Figure 1.1 demonstrates the main processes of this thesis that will be expanded upon in the following chapters:

- Chapter 2 (study 1) will provide a critical review and synthesis of the existing literature relating to the effect of either PA, dietary or combined interventions on body weight and BMI in new KTRs
- Chapter 3 will outline the methodological principles of studies 2, 3 and 4, including data collection, creation of the online interventions, the theories influencing the design of the online intervention and the initial refinement
- Chapter 4 will present a peer-review publication summarising the main results of study 2 (the usability and functionality of the prototype online intervention)
- Chapter 5 briefly summarises the context and the implications of COVID-19 on the target population of interest, clinical services, and subsequent adaptions to studies 3 and 4

- Chapter 6 will present studies 3 and 4, the feasibility, qualitative, quantitative and mixed methods analysis from the feasibility RCT utilising the revised online intervention
- Chapter 7 will provide a general thesis discussion
- Chapter 8 will offer conclusions, which will be followed by references and related appendices.

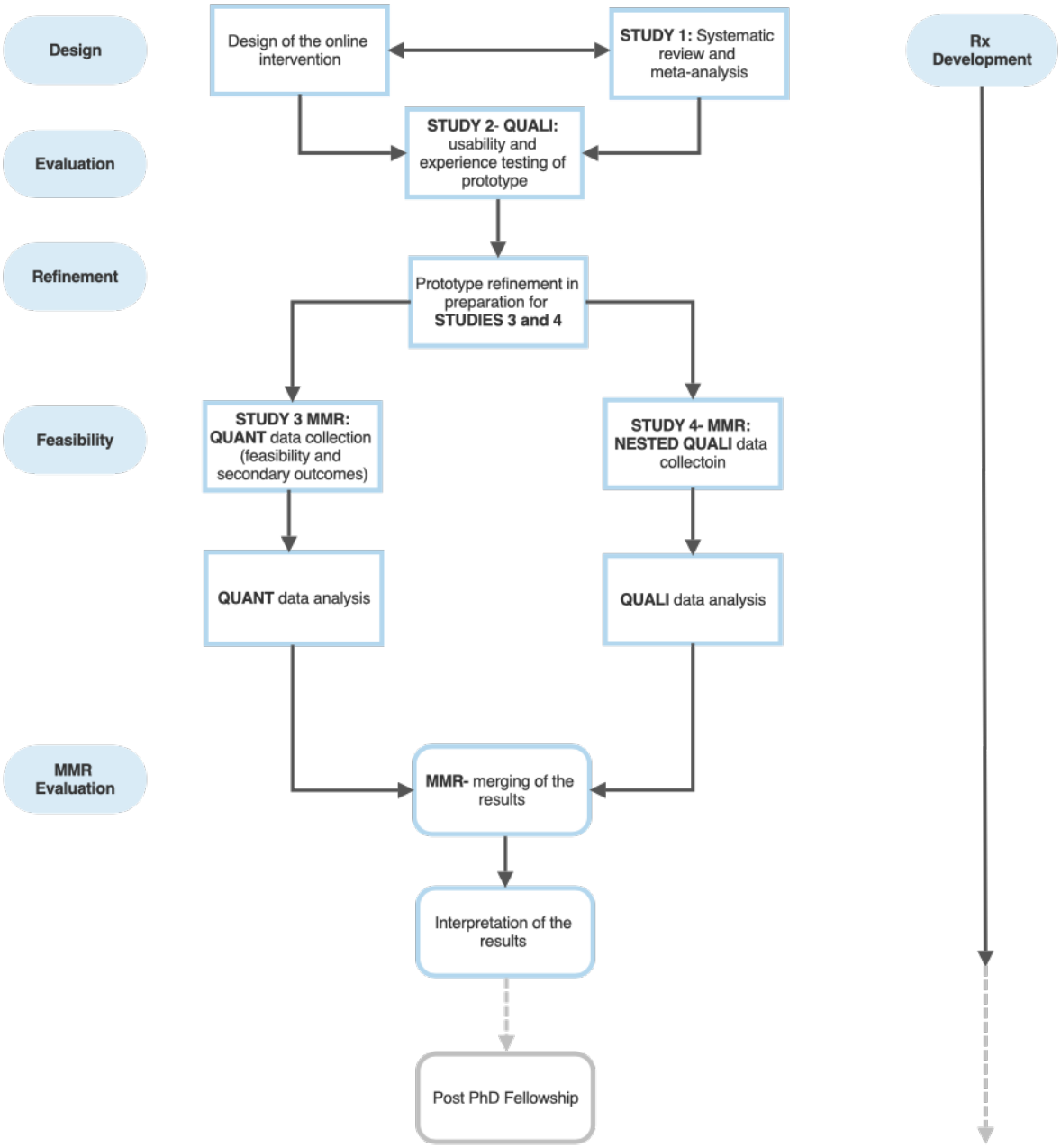


Figure 1-1 Thesis processes diagram

Note. The figure above presents the mixed methods design that will be expanded throughout the thesis chapters. The blue boxes on the far left indicate the medical research council (MRC) framework. The central boxes show the four studies included in this PhD. As indicated by the box on the far right, intervention development is iterative, and will occur throughout the thesis and beyond.

This figure was designed based on a combination of the convergent mixes-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

QUALI= qualitative, QUANT=quantitative, MMR= mixed methods research and Rx=intervention

1.5 Chapter summary

This chapter has provided the background, aims and objectives of the thesis. CKD affects multiple systems of the body and has wide reaching symptoms. However, it is often only symptomatic in end stages. ESKD requires either transplantation or dialysis for survival and management of kidney failure. Whilst transplantation is the most effective and cost-effective option for people with ESKD, it is not without risk. In addition to the traditional and CKD related risk factors for CVD, KTRs experience additional unique risk factors for CVD and CVE such as immunosuppressant medication effects, abnormal glucose mechanisms, PTDM, MS and adverse weight gain. KTRs have requested support with weight gain, and this is encouraged by clinical guidelines. However, there is no routine treatment to prevent weight gain for new KTRs. The aims and objectives of this thesis relate to the creation, acceptability, usability and feasibility evaulation of a bespoke online intervention designed to prevent weight gain in acute KTRs. The following chapter will outline study 1, the meta-analysis and systematic review.

Chapter 2 Study 1- Synthesis of the existing evidence regarding exercise, physical activity, dietary or combined interventions and body weight in new kidney transplant recipients.

2.1 Abstract

Weight gain within the first year of kidney transplantation is associated with adverse outcomes. This narrative systematic review and meta-analysis examines the effect of exercise, PA, dietary and/or combined interventions on body weight and BMI within the first year of kidney transplantation.

Seven databases were searched from January 1985 to April 2021 (Prospero ID: CRD42019140865) by two reviewers using a 'Population, Intervention, Controls, Outcome' (PICO) framework. Risk-of-bias was assessed by two reviewers. A random-effects meta-analysis was conducted on randomised controlled trials (RCT's) that included post-intervention body weight or BMI values.

Of 1198 articles screened, sixteen met the search criteria. Ten were RCT's, and six were quasi-experimental studies (non-RCTs), including a total of 1821 KTRs within the first year of transplantation. Sample sizes ranged from 8 to 452. Interventions (duration and type) were variable. Random-effect meta-analysis revealed no significant differences in post-intervention body weight (-2.5 kg, 95% CI -5.22 to 0.22) or BMI (-0.4 kg/m^2, 95% CI -1.33 to 0.54). Despite methodological variance, statistical heterogeneity was not significant. Sensitivity analysis suggest combined interventions warrant further investigation. Five RCT's were classified as 'high-risk', one as 'some-concerns' and four as 'low-risk' for bias.

We did not find evidence that dietary, exercise, or combined interventions led to significant changes in body weight or BMI post kidney transplantation. The number and quality of intervention studies are low. Higher quality RCT's are needed to evaluate the immediate and longer-term effects of combined interventions on body weight in new KTRs.

2.2 Background

As described in the previous chapter, adverse weight gain is an important clinical issue for new KTRs and is associated with poor health outcomes. Previous literature reviews (Stefanović & Milojković, 2005; Takahashi et al., 2018), systematic reviews (Calella et al., 2019; O'Brien & Hathaway, 2016), and meta-analyses (Chen et al., 2019; Oguchi et al., 2019) that examine the effects of exercise (Calella et al., 2019; Chen et al., 2019; Oguchi et al., 2019; Stefanović & Milojković, 2005) or PA interventions (O'Brien & Hathaway, 2016; Takahashi et al., 2018) for KTRs have shown a favourable effect on multiple outcomes. These outcomes include; cardiorespiratory fitness and exercise tolerance (Calella et al., 2019; Chen et al., 2019; Oguchi et al., 2019; Takahashi et al., 2018), muscle strength and function (Chen et al., 2019; Oguchi et al., 2019), health related quality of life, (Calella et al., 2019; Oguchi et al., 2019; Takahashi et al., 2018) maximum heart rate (Calella et al., 2019), and arterial stiffness (Chen et al., 2019). Exercise studies have failed to show significant effects on body weight or composition (Calella et al., 2019). However, combined interventions that included any combination of either exercise, PA and/or dietary interventions were excluded in these reviews.

A Cochrane review of dietary interventions for adults with ESKD (including KTRs), concluded clinical dietary care recommendations could not be made for KTRs due to insufficient evidence (Palmer et al., 2017a). However, this review excluded studies with interventions that involved 'implementation strategies for dietary or lifestyle management' (Palmer et al., 2017b, p. 6).

Currently, there are no systematic reviews and meta-analyses that consider the impact of either exercise, PA, dietary, or combined interventions on body weight and BMI in KTRs within the first year of receiving a kidney transplant. The research question for this systematic review (study 1 of the thesis) was 'do exercise, PA, dietetic or combined interventions improve body weight in new KTRs?' By improvement in body weight, we were interested in either the maintenance and/or reduction of body weight within the first year of kidney transplantation. The aim of this narrative systematic review and meta-analysis was to provide a synthesis and pooled effect of post-transplant interventions on body weight and BMI within the first year of kidney transplantation and suggest recommendations for future research.

2.3 Methods and materials

A pre-specified protocol was published on the 9th of September 2019 (www.crd.york.ac.uk/PROSPERO, id: CRD42019140865). This narrative systematic review and meta-analysis was undertaken as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (PRISMA, 2009). A copy of a completed PRISMA checklist can be found in Appendix A. Eligibility criteria were based on the PICO framework (Richardson, Wilson, Nishikawa, & Hayward, 1995; Thomas, Kneale D, McKenzie JE, Brennan SE, & S., 2019), and are summarised in table

2.1 below. The population of interest was new KTRs within the first year of kidney transplantation. Post-transplant interventions consisted of either exercise, PA, dietary interventions, or a combination thereof. PA was defined as any habitual or planned activity of the body such as occupational, transportation, domestic and social (Caspersen et al., 1985). In contrast, exercise interventions were defined as any planned, structured, prescriptive activity designed to improve a specific aspect of physical fitness (American College of Sports Medicine, 2013; Caspersen et al., 1985). Dietary interventions included dietary modifications, advice, nutritional counselling, and education regarding food-based interventions (Palmer et al., 2017a). Combined interventions refer to any combination of exercise, PA and/or dietary interventions. They may also include behaviour change techniques (BCT's) designed to address PA, and/or healthy eating behaviour(s) (Michie, Ashford, et al., 2011).

Table 2-1 Eligibility criteria based on the PICO framework

PICO(s)	Inclusion	Exclusion	Reasons for exclusion
Population	KTRs within the first 12 months of transplantation	• >12 months post-transplant • <18 years of age • Mixed samples (e.g., dialysis and transplant patients)	• WG occurs within first year • Different populations (adults vs paediatric) • Difficult to isolate effects to just KTR in mixed sample unless information provided by authors
Intervention	Complex interventions involving; either exercise, activity, nutrition, diet, behaviour change, or combined interventions designed to prevent WG occurring	• Treatments including pharmacological intervention	• Difficult to isolate effects of the other components of the treatment
Comparator	Usual care or standard care or no intervention	• No comparator available	• Difficult to determine the treatment effect(s)
Outcomes-Primary outcome	WG from baseline to short term (3-months) baseline to long term (6-12 months)	• No reported BW or BMI at baseline or follow-up (3-12 months)	• Unable to determine change in BW or BMI
Study Types	RCT's, non-RCT's (quasi-experimental)	• Exclude literature reviews • Exclude trials with no control group	• Outside scope of this review
Language	English		• Limited resources for this project
Year	Published after 1985		• Changes to standards of care

Note. KTR indicates kidney transplant recipient, BW= body weight, WG= weight gain, CKD= chronic kidney disease, RCT's= randomised controlled trials, non-RCT's= nonrandomised controlled trial

As weight gain is of clinical concern, particularly within the first year of receiving a kidney transplant, interventions were included if they were offered within the first year of receiving the kidney transplant. A copy of the search strategy can be found in Appendix A. RCT's and non-RCT's with a comparator group were included. The primary outcome

of interest was post-intervention measures of body weight or BMI. No upper limit for body weight or BMI was set for this review, as weight gain has been reported to occur in KTR's both living with and without obesity (Chan et al., 2014). Long-term follow-up of body weight and BMI were included if available. Secondary outcomes included BC, physical function, PA levels, self-efficacy towards PA and mood. This systematic review will focus on body weight and BMI from the RCT's. Secondary outcomes and non-RCT's will be presented briefly.

2.3.1 Study identification

MEDLINE, Embase, Psychinfo, CINAHL, SCOPUS, The Cochrane Library, and Web of Science were searched from the 1st of January 1985 to the 6th of April 2021. Grey literature was searched using OpenGrey. A combination of free text searching, subject headings, and Boolean operators were used. This search strategy was piloted and refined by authors and subject matter experts, with assistance from librarians. Search terms were adapted to each database. The final search was conducted by two authors (EC and JG). Conference abstracts were searched for full text publications, and reference lists were hand-searched.

2.3.2 Study selection, data extraction and risk-of-bias

All stages of the review were recorded on an Excel spreadsheet and Endnote software. Duplicate citations were removed. The remaining citations were assessed against the pre-defined eligibility criteria. Title and abstracts that did not meet the search criteria were excluded. The remaining full text articles were assessed for eligibility (EC and JG). See Appendix A for a copy of the screening form and search strategy.

Data were extracted from the full text publications and tabulated, based on the 'characteristics included in studies table' in the Cochrane Handbook for Systematic Reviews of Interventions (McKenzie, Brennan, Ryan, Thomson, & Johnston, 2019). In addition, ten percent of titles and abstracts, and ten percent of the full text citations were selected using a random number generator and assessed for eligibility by two subject matter experts (JC and SG). When missing data were encountered, the corresponding author was contacted via email. If no response was received, this was repeated with secondary and senior manuscript authors.

Two reviewers (EC and EMc) independently assessed the final full text publications using version two of the Cochrane risk-of-bias tool for randomized studies (Sterne et al., 2019) and the risk-of-bias in non-randomised studies of interventions tool (Sterne et al., 2016). If disagreements occurred, both reviewers would discuss until consensus was achieved. Where consensus could not be achieved, a third reviewer (SG) would resolve disagreements.

2.3.3 Statistical analysis

The Cochrane handbook was utilised to calculate standard deviations (SD) based on the available data reported (Higgins, Li, & Deeks, 2019). RCT's that reported post-intervention body weight (n=8) and post-intervention BMI (n=8) for an intervention group (either diet, PA, exercise, or combined interventions), and a comparator group (usual care or no intervention) were included in the meta-analysis. This allowed for calculation of an estimate of pooled effect of the interventions on body weight and BMI, with associated confidence intervals to demonstrate precision. Meta-analysis was not

completed for secondary outcomes in this systematic review due to the variation in measurement scales.

Post-intervention values (body weight and BMI) were used rather than change scores for the meta-analysis. There was inadequate data from the studies to calculate confidence intervals for change-scores in body weight and BMI values in all of the RCT's. Secondly, meta-analyses with post-intervention values have been shown to have more conservative estimate of effect than change scores (Fu & Holmer, 2016). For the studies with more than one treatment arm, guidance was used to combine means and SDs to form an intervention group mean with SD (Cochrane UK, 2015; Rücker, Cates, & Schwarzer, 2017).

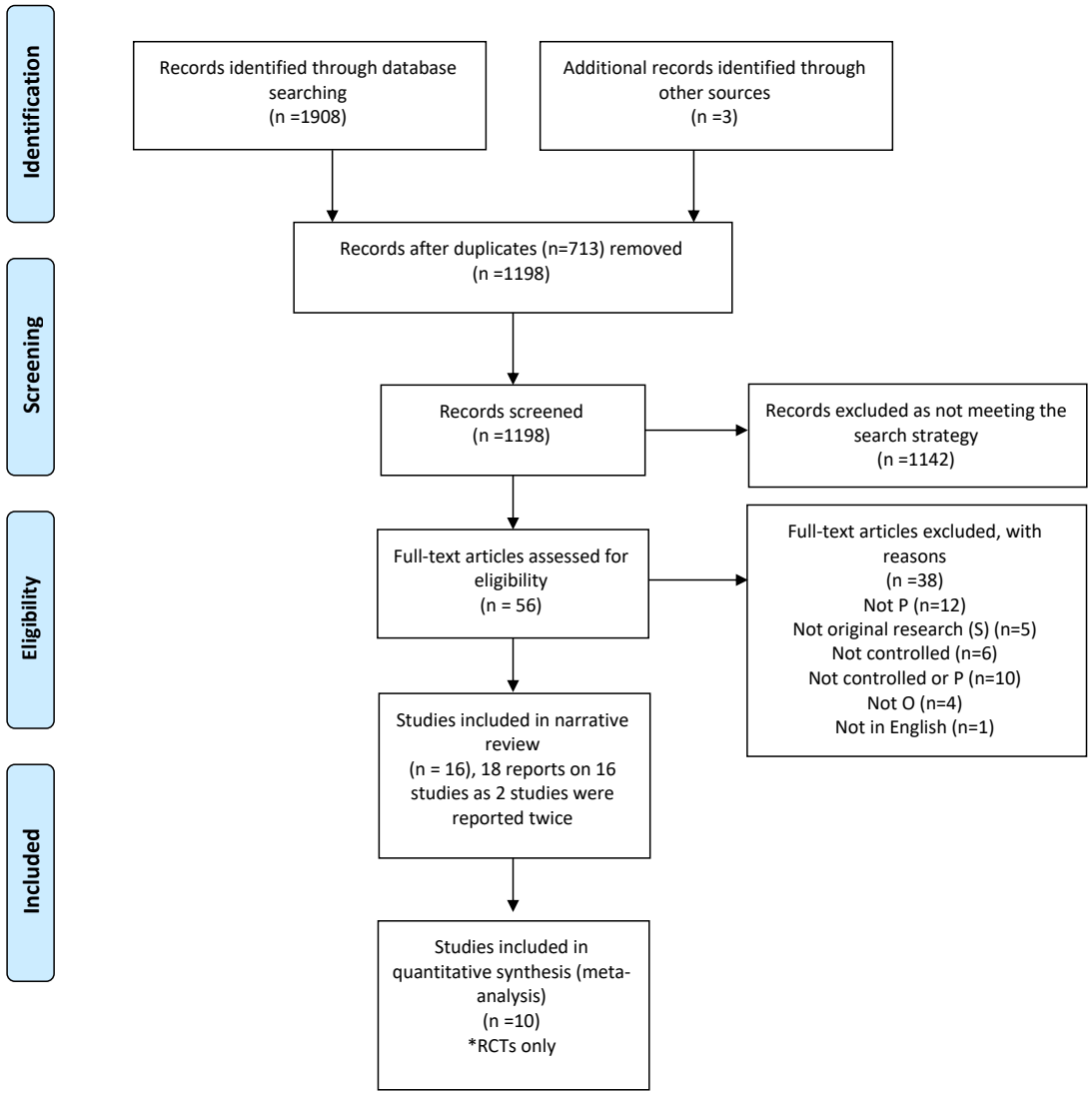
Meta-analyses were conducted using RevMan software (The Cochrane Collaboration, 2020). The inverse model for continuous data and the Der Simonian and Laird (1986) random-effects model were used to produce a pooled estimate of effect. A random-effects model was selected due to the anticipated heterogeneity caused by clinical and methodological differences between the RCT's (Sterne et al., 2011).

Forrest plots, with chi squared and I^2 statistics were used to assess heterogeneity before proceeding with the meta-analysis as per the Cochrane handbook (Deeks, Higgins, & Altman, 2020). Due to the small number of RCT's included in each meta-analysis, and the methodological variation in trial designs, sub-group analysis was not completed. Heterogeneity, and publication bias were explored using funnel plots (Sterne et al., 2011). A Post-hoc exploratory sensitivity analysis was performed to examine the potential influence of different intervention types on body weight and BMI values.

2.4 Results

2.4.1 Search Results and study characteristics

After removal of duplicates, 1198 citations were reviewed for eligibility. This systematic review revealed eighteen publications, from sixteen studies that met the search inclusion criteria. Four publications (Greenwood et al., 2015; O'Connor et al., 2017; Painter et al., 2002; Painter et al., 2003) were from two studies. O'Connor et al (2017) reported long-term follow-up of the same participants of the original study by Greenwood et al (2015). Therefore, these two studies (Greenwood et al., 2015; O'Connor et al., 2017) were considered as one intervention for the purpose of this systematic review and meta-analysis. Painter et al (2002; 2003) were publications from the same trial and were also considered as one intervention. Figure 2.1 below summarises the study selection process utilising a PRISMA diagram (Moher, Liberati, Tetzlaff, & Altman, 2010).



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 2-1 Flow chart of study selection process with reasons for exclusion
Note. Where n= number of studies, P=population of interest, S= study design, O=outcome of interest. Randomised Controlled Trials (RCTs) only were included in the meta-analysis

From the sixteen final studies, ten were RCT's, and six non-RCT's (quasi-experimental studies) with a total of 1821 KTR participants within the first year of kidney transplantation. Individual study sample sizes ranged from eight (Leasure, Belknap, Burks, & Schlegel, 1995) to 452 participants (Jezior et al., 2007). Two studies include other transplant populations (Schmid-Mohler et al., 2019; Serper et al., 2020), however one author was able to provide data for the KTR sub-group on request (Schmid-Mohler et al., 2019). The included studies were all from developed countries; one study was from Canada (Karelis, Hébert, Rabasa-Lhoret, & Räkel, 2016), six studies were from the United States of America (Gibson et al., 2020; Leasure et al., 1995; Lorenz et al., 2015; Painter et al., 2002; Serper et al., 2020; Tzvetanov et al., 2014), five studies were from the United Kingdom (Kuningas et al., 2020; Lawrence et al., 1995; O'Connor et al., 2017; Patel, 1998; Sharif, Moore, & Baboolal, 2008), three studies were from Europe (Jezior et al., 2007; Schmid-Mohler et al., 2019; Teplan et al., 2014) and one study was from New Zealand (Henggeler et al., 2018).

There was variation across sample characteristics which could limit generalisability (see tables 2.2 and 2.3). Some trials excluded KTRs with diagnosed diabetes (Karelis et al., 2016; Kuningas et al., 2019; Lawrence et al., 1995; Sharif et al., 2008), another study included hyperlipidaemic KTRs (Lawrence et al., 1995), and two studies included only KTRs living with excess weight or obesity (Jezior et al., 2007; Tzvetanov et al., 2014). See Appendix A for a detailed summary of the study sample characteristics (n=16).

Six studies reported body weight only (Kuningas et al., 2019; Leasure et al., 1995; Lorenz et al., 2015; O'Connor et al., 2017; Serper et al., 2020; Sharif et al., 2008), four reported BMI (Lawrence et al., 1995; Schmid-Mohler et al., 2019; Teplan et al., 2014; Tzvetanov

et al., 2014), and six reported both body weight and BMI post-intervention (Gibson et al., 2020; Jezior et al., 2007; Karelis et al., 2016; Painter et al., 2002; Patel, 1998; Schmid-Mohler et al., 2019). Seven out of the sixteen studies recorded body weight or BMI at an interim time point of three to six months, and at one year follow-up (Henggeler et al., 2018; Lawrence et al., 1995; Lorenz et al., 2015; O'Connor et al., 2017; Painter et al., 2002; Patel, 1998; Tzvetanov et al., 2014). Only one RCT included long-term follow-up of body weight after intervention cessation (O'Connor et al., 2017), making it difficult to determine longer-term intervention effects. Tables 2.2 summarise the study characteristics of the included RCT studies (n=10). The non-RCT's (n=6) are summarised in Appendix A.

Table 2-2 Summary of characteristics of included in RCTs (n=10)

First author, year (country of origin)	Study duration (months)	Sample	Groups	Outcomes (primary and secondary)	Results (for primary and secondary outcomes)	Comments
Lawrence et al (1995) **(UK)**	12	n=38, KTRs with hyperlipidaemia	**IG:** Dietitian only for 12 months **CG:** Usual care, no dietary intervention	**Primary:** Dietary intake (24-hour recall assessed for total energy intake, fibre intake, protein, carbohydrate, fat and distribution of fat intake) and fasting lipids **Secondary:** BW, BMI, medications, Renal function	**Primary:** • No significant difference between groups in total cholesterol, HDL cholesterol or plasma triglyceride levels • LDL cholesterol was significantly lower in the IG at 1 month after Tx • Significant improvement in polyunsaturated-to-unsaturated fat ratio in the IG • Change in dietary intake not associated with changes in serum lipid levels • Fibre intake significantly higher at 3-months in the IG **Secondary:** • No difference in BMI, medication, or kidney function between groups at any time • Both groups reduced average consumption of cigarettes and alcohol	• AEs not reported • Limited reporting of; blinding, allocation, analysis plan, treatment, protocol deviations and statistical plan
Painter et al (2002)	12	n=167	**IG:**	**Primary:** Not stated	**Primary/ Secondary:**	• AEs not reported • High dropout rate

(USA)			12-months ET, home based AT **CG:** no ET	**Secondary:** VO_2peak, Muscle strength, BC (DEXA), QoL (SF-36), PA reporting (active or inactive)	• No difference in BW, BMI or BC, all participants increased BW, BMI, FM, LTM, % FM • IG had greater gains in VO_2peak and muscle strength • IG had higher % classified as active at follow-up • No difference in QoL	• 42% did not complete assessment at all three timepoints • Painter 2003 duplicate paper from this study
Tzvetanov et al (2014) **(USA)**	12	n=17, KTs living with obesity	**IG:** 12-month combined Rx (Exercise, behaviour and nutrition guidance) **CG:** Nutritional guidance only	**Primary:** Not stated? feasibility **Secondary:** Physical (weightlifting capacity) and vascular function (PWV and CiMT), BC, QoL (SF-36), kidney function, blood lipid markers, and adherence	**Primary/ Secondary:** • No significant difference in BMI at 12 months • Greater adherence to follow-up in IG (100%) vs CG (25%) • Improved weightlifting and PWV (IG only) • significant difference in CiMT (IG only) • Improvement in QoL (P=0.008) and employment rate (P=0.02) in IG vs CG • No significant differences between groups in kidney function or lipids	• AEs not reported • Small sample • t-tests used, not ITT • High dropouts in CG vs IG • Missing data (BC, PWV, CiMT) in CG
Karelis et al (2016) **(Canada)**	≈4	n=24, KTRs without diabetes, excluded smoking history	**IG:** Exercise only for 16 weeks (RT) **CG:** Instructed not to perform any structured exercise	**Primary:** Feasibility outcomes (adherence, injuries, drop-outs) **Secondary:** BC (DEXA), OGTT, Lipid profile, BP, QoL, Anthropometrics,	**Primary:** • 47% consent rate • 80% compliance IG • 17% dropout IG **Secondary:** • No difference in BW or BMI, BC, VO_2peak, lipids, OGTT or QoL	• No AE's or injuries reported • Short study duration (16 weeks) • Small sample size

				Muscle strength (leg press), VO_2peak	• Both groups increased FM (BC) • IG associated with increase in muscle strength (P=0.003)	
O'Connor et al (2017) **(UK)**	12	n=47 of the original 60 ExeRT cohort (Greenwood et al., 2015)	**IG1:** Supervised AT for 12 weeks **IG2:** Supervised RT for 12 weeks **CG:** No ET for 12 weeks	**Primary:** PWV and VO_2 peak **Secondary:** Anthropometrics, BP	**Primary:** • Significant difference in PWV in IG2 (RT) vs CG (P=0.03) • Favourable difference in VO_2 peak IG1 (AT) vs CG (P=0.02) **Secondary:** • No difference between-groups in BW or BP • BMI not reported • No difference in BMI reported in original study manuscript (Greenwood et al., 2015)	• No AE's • Long-term follow-up data from the ExeRT cohort (Greenwood et al., 2015) • Dropouts • ANCOVA used
Henggeler et al (2018) **(NZ)**	12	N=37 KTRs with a BMI of > 18.5 and <40kg/m^2	**IG:** 12-month combined Rx including standard care + dietitian appointments (12 sessions in total) and exercise sessions **CG:** Standard care (4 sessions in 12-months) with renal dietitian	**Primary:** BW at 6 months adjusted for baseline weight, obesity, and gender **Secondary:** Change in Anthropometrics and BC (DEXA), resting energy expenditure, physical function (grip, 25-feet gait speed, STS), PA (NZ PA questionnaire), serum biochem, QoL (SF-36)	**Primary:** • No significant difference in BW or BC between groups at 6 months **Secondary:** • No between-group difference in BC or energy expenditure • Both groups increased total body fat and % body fat • No significant difference in biochemistry • Whole sample HbA1c and fasting glucose increased, cholesterol decreased	• No AE's • CG greater than clinical practice in the UK • May require formal ET/ PA to elicit training response • ANCOVA used

					• Whole sample improved physical function, body protein and QoL	
Kuningas et al 2019 (2019) **(UK)**	6	n=130 KTRs without diabetes	**IG:** 6-month exercise and nutrition education +BCT's **CG:** Passive education (booklet) on healthy eating, exercise, and risks of PTDM	**Primary:** 6-month change in insulin sensitivity, secretion, and disposition index (OGTT) **Secondary:** PA (GPPAQ), Physical function (DASI), QoL (EQ-5D), Beck depression inventory, situational motivational score, safety issues, BW, BC (skinfolds and bioimpedance)	**Primary:** • No between-group difference in 6-month glucose metabolism **Secondary:** • Significant between-group difference in BW favouring IG vs. UC (*P*=0.02) • Significant between-group difference in FM IG vs CG (*P*=0.03) • Clinically significant reduction in PTDM, halved in IG vs CG • No between-group difference in any questionnaires	• No safety concerns • Dropout out rate 20.8% • Pre-post study design with no long-term follow up • Excluded KTRs with diabetes • Single centre study • No reporting of BMI at 6 months
Schmid-Mohler et al (2019) **(Switzerland)**	12	n=123 KTR and Kidney-pancreas Tx (120 KTR)	**IG:** Control + 8-month nurse-led intervention including dietary and PA counselling with motivational interviewing and action planning **CG:** A single nurse-led education session with booklet	**Primary:** Difference in BMI (baseline to 8 months) in patients with a BMI of ≥18.5kg/m^2 **Secondary:** change in BMI baseline to 12 months, Rx adherence, satisfaction with counselling, BC (bioimpedance), PA (IPAQ), patient assessment of chronic illness care PACIC)	**Primary:** • No signficiant between-group difference in change in BMI or BC from baseline to 8 months, or Baseline to 12 months **Secondary:** • No significant differences between-group in BC, steps or IPAQ • IG more chronic care related activities (PACIC) • High acceptability IG • 88.5% IG received ≥7 sessions • Singificant difference in PACIC in all but one score IG vs CG	• AEs not reported • Sample includes kidney-pancreas Tx • Means and SD for KTR (n=120) provided on request. • There was no significant between-group in BW or BMI at any timepoint in KTRs

					• No difference between groups in satisfication with counselling	
Serper et al (2020) **(USA)**	4	n=127 KTR and Liver Transplants (65 KTR). Participants needed to own a smartphone compatible with wearable accelerometer	**IG1**: Device only group, access to online portal with education materials and questions + control education **IG2:** Control education + Intervention 1 + 2 plus bi-weekly texts, step goals and financial incentives **CG:** standard education on healthy diet, food hygiene and PA	**Primary:** Change in BW from baseline to 4 months **Secondary:** Daily steps- proportion of patients achieving > 7000 steps/ day, and continuous daily step data	**Primary:** • No significant difference in weight gain between all three groups (IG1, IG2 and CG) **Secondary:** • Singificantly higher step count reported in IG2 vs IG1 (P<0.001) • Retention rate 92.1% • Adherence final study weight assessment 88% • 74% IG2 adhered to their step targets • Study increased motivation to monitor weight and increase PA • Some participants dissapointed with randomisation • Some IG patients requested ability to track different activities, and have non-step related goals	• No AEs associated with study • Combined sample (KTR and Liver Transplant) • Unique approach with financial incentives • Diet education not designed for weight management • No longer-term follow-up • BMI not reported
Gibson et al (2020) **(USA)**	6	N=10 KTR, 6-12 months post-transplant, Mean age 44 years, BMI >22kg/$m^{2.}$	**IG:** 6-month combined Rx via telehealth (dietitian-led, 12 weeks of one-hour weekly calls and PA classes). Followed by 12 weeks of maintenance. Provided with tablet to track food and veg intake, whole grains intake, water	**Primary:** Primary outcomes relate to feasibility (recruitment, adherence, attendance) **Secondary:** Provide estimates of Rx effectiveness including changes to PA, food intake (fruit, veg, whole-grain and water).	**Primary:** • 78% attendance telehealth sessions (IG) • 86% adherence to weekly behaviour tracking via tablet • All patients attended week 12 study assessments	• Specific recruitment criteria included the ability to take part in six-month trial, ability to report data weekly (by phone, fax, email), access to the internet, English speaking,

	intake, steps and PA weekly **CG:** Standardised education to follow healthy eating and PA. Provided with tablet and tracking (as above). Did not receive weekly video calls or PA classes	Secondary outcomes included weight gain (baseline to six months), BW, BMI, BP, PA (accelerometer), QoL, Dietary intake (3-day food diary), qualitative interviews for strengths and weakness of intervention	• Tracking increased awareness but some had problems • All would recommend trial to others • Tailored education and the ability to complete Rx at home was valued **Secondary:** • Weight gain and BMI greater in IG versus CHG • QoL improvements greater in CG versus IG • No difference in BP and PA between groups • Improved diet quality in both groups	willingness to be randomised • One participant withdrew due to time commitments

Note. KTRs= kidney transplant recipient, IG= intervention Group, CG= control group, BW= body weight (kg), BMI= body mass index (kg/m2), HDL= high-density lipoprotein, LDL= low-density lipoprotein, Tx= transplant, AE= adverse event, AT= aerobic exercise training, Vo2peak= peak oxygen update, FM= fat mass, LTM= lean tissue mass, BC= body composition, DEXA=dual-energy x-ray absorptiometry, QoL= quality of life, SF-36= short form 36, PA= physical activity, PWV= pulse wave velocity, CiMT= carotid intima-media thickness via ultrasound, ITT= intention to treat analysis, KTx= kidney transplant, RT= resistance training, OGTT= oral glucose tolerance test, BP= blood pressure ET= exercise training, ANCOVA= analysis of covariance analysis, STS= sit to stand test, NZPA= New Zealand physical activity questionnaire, HbA1c=haemoglobin A1c, PTDM= post-transplant diabetes mellitus, GPPAQ= General Practice Physical Activity Questionnaire, DASI= Dukes Activity Status Index, EQ-5D= EuroQoL five dimension scale, BAME= black, Asian and minority ethnicity, IPAQ=international physical activity questionnaire, PACIC=patient assessment of chronic illness care questionnaire, SD=standard deviation, Rx= Intervention

2.4.2 Characteristics of interventions

Methodological variation was evident across the ten RCT's included in this systematic review and meta-analysis. One study included a 12-month diet only intervention (Lawrence et al., 1995), three studies (Karelis et al., 2016; O'Connor et al., 2017; Painter et al., 2002) included exercise only interventions ranging from three to twelve months, and six RCT's included combined interventions (Gibson et al., 2020; Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019; Serper et al., 2020; Tzvetanov et al., 2014). The RCT's with combined interventions varied significantly in duration between fourteen weeks (Serper et al., 2020), six months (Gibson et al., 2020; Kuningas et al., 2019), eight months (Schmid-Mohler et al., 2019) and one year (Henggeler et al., 2018; Tzvetanov et al., 2014). Two studies (Henggeler et al., 2018; Kuningas et al., 2019) did not report the specifics of the PA component of the combined intervention.

Two RCT's (O'Connor et al., 2017; Serper et al., 2020) included three treatment arms. O'Connor et al (2017) compared three months of either aerobic training or resistance training to usual care. Serper et al (2020) randomised kidney and liver transplant recipients into three groups; 1) education, 2) access to an online platform and a step tracking device, and 3) access to the online platform and step tracking device, plus text message support, automated step goals, and financial incentives. (Serper et al., 2020) However, limited information was provided on the education content within the treatment website.

The healthcare professionals (HCPs) providing interventions was variable. Some were dietitian-led face-to-face visits or telephone calls (Henggeler et al., 2018; Kuningas et

al., 2019; Lawrence et al., 1995), one was provided by a physiotherapist (O'Connor et al., 2017), two were provided by exercise professionals (Karelis et al., 2016; Tzvetanov et al., 2014) and one RCT did not specify the intervention provider (Painter et al., 2002). Two recent RCT's (Gibson et al., 2020; Schmid-Mohler et al., 2019) included combined interventions with a digital delivery component. Serper et al, (2020) provided both the two intervention groups with access to a combined online platform. Gibson et al (2020) provided both groups with a tablet to track healthy behaviours weekly. The intervention group were provided with dietary and PA interventions delivered by video teleconference calls (Gibson et al., 2020).

Whilst some interventions describe common strategies to promote behaviour change such as goal setting (Gibson et al., 2020; Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019) and motivational interviewing techniques (Henggeler et al., 2018; Schmid-Mohler et al., 2019), only three trials (Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019) explicitly described BCT's in reference to the BCT taxonomy (Michie et al., 2013). Self-monitoring, 'SMART goals' (Schut & Stam, 1994), action planning, social support, and revision of goals were the most common BCT's. Table 2.3 summarises the interventions of the RCT's. See Appendix A for tabulated descriptions of interventions for the non-RCT's.

Table 2-3 Detailed description of interventions RCT's (n=10)

Study	Rx type	Rx Description	Rx Behaviour components	Provider	Duration (months)	Frequency	Intensity	Type of ET	Time (minutes)
Lawrence et al (1995)	Diet	• Written and verbal edu to • reduce hyperlipidaemia • Diet: 30% total energy from fat and 50% from carbohydrates • Mode: NI, assume F2F	• NI	RD	12	NI	NA	NA	NA
Painter et al (2002)	Exercise	• Home ET (independent) • Fortnightly phone calls • Mode: Telephone	• Self-monitoring behaviour (diaries) • Phone calls for encouragement	NI	12	4x week	60-65% HRM, ⬆️ 75-80% HRM	AT	≥30
Tzvetanov et al (2014)	Combined	• Combination of 1:1 ET +CBT + nutrition • Topics include reduce sodium, emotional eating, increase protein, reduce cholesterol and balanced meals • Aims of Rx; build muscle tissue, change thoughts and empowerment • Mode: F2F	• CBT details not provided	P.Tr	12	ET 2x week	Not specified	RT	60
Karelis et al (2016)	Exercise	• ET programme of 7 exercises • Upper and lower limb RT • Mode: F2F supervised	• NI	Kinesiology student	16 weeks (≈3.68 months)	3x week (1x week supervised)	80% 1RM	RT	45-60

O'Connor et al (2017)	Exercise	• 2 intervention groups; AT and RT compared with UC • Mode: F2F	• Motivational interviewing	PT	3	3 x week (2x supervised group, 1x not supervised)	AT: 80% HRR RT: 80% 1RM 1-2 sets 10 reps, ⬆️ to 3 sets	AT or RT vs. UC	60 AT or RT 30 mins/week edu (AT and RT)
Henggeler et al (2018)	Combined	• Multi-professional and components • 12 sessions (4x UC sessions, plus 8 additional nutrition sessions) with RD • Exercise and PA component • Mode: NI, assume F2F	• SMART goal setting and revision of goals • Motivational interviewing • Action planning • Self-monitoring	RD Ex.Phys: ET and PA	12	12x RD follow-ups 3x ET with Ex.Phys	'Tailored PA advice', No further detail	NI	NI PA
Kuningas et al (2019)	Combined	• Combined Rx to prevent PTDM • Dietary habits • Personalised healthy eating edu based on diabetes UK and Public Health England • Graded ET • Exercise diary • Mode: F2F and phone follow-up	BCT's used: • Information on consequences • feedback on personal information • prompting intention formation • SMART goals • graded tasks • self-monitoring • revision of goals • social support	RD	6	4x F2F 1:1 with RD RD phone consultant between each F2F session	Specifics not Reported	AT	NI

Schmid-Mohler et al (2019)	Combined	• Developed brochure edu food types and hygiene, and encouraging PA • Initial 1:1 edu session with brochure as per UC group +8 APN-led sessions • Mode: F2F or phone	BCT's used: • goal setting • problem solving • action planning • review behaviour and outcome goals • feedback on behaviour • self-monitoring of behaviour • instruction on how to perform behaviour • information about health consequences • prompts/cues • habit formation and reversal • focus on past success • self-monitoring of behaviour • social support	APN (trained in motivational interviewing)	8	Combination of F2F and phone follow-up 9 sessions in total.	Specifics PA not reported	NI	35
Serper et al (2020)	Combined + online	**IG1:** Device only: • Step-counting device • Website with resources on healthy eating and PA • Health knowledge questionnaires • Mode: online **IG2.** Device and Rx: • As above	• prompts/ cues (text) • financial incentives (rewards)	1. Website 2. website and text messages (automated) by	14 weeks (≈3.22 months)	1. Online website, step-recording device 2. online website, step-recording	1. Device only- no prescription 2. Device and Rx: baseline steps increased 15% every	AT-steps	NI

		• + Financial incentives • + Automated step goals • + Bi-weekly text messages for health questionnaire • Mode: online and text		research team		device and text support	2 weeks until reached 7000 steps/day		
Gibson et al (2020)	Combined +tracking +video calls	• both groups given tablets for weekly tracking (fruit/veg, wholegrains, water, steps and PA) **IG:** 6-months video calls: • tracking • 12 weeks of diet Edu (DASH diet) • 12 weeks group PA • 12 weeks maintenance using tracking only • Mode: video calls	• Rx informed by the Social Cognitive Theory (Bandura, 1986) and self-efficacy (Bandura, 1977) • Self-monitoring • Goal setting	Tracking (not supervised) on tablet Diet Edu (RD), group PA (exercise professional)	6	Weekly	Moderate intensity (3-6 metabolic equivalent of task)	NI	Diet 1:1 and group PA 30mins/week (total 60 mins/week) Encouraged to do 10-15mins PA/day

Note. Rx indicates treatment, ET= exercise training, Edu=education, F2F=face-to-face, NI= no information, RD= renal dietitian, NA= not applicable, KTx= Kidney transplant, PT= Physiotherapist, Ax=assessment, AT= aerobic training, HR= hear rate, RT= resistance training, BCT= behaviour change techniques, HRM= heart rate max, Phys.= Physician, 1:1= one on one (individual treatment), CBT= cognitive behavioural therapy, P.Tr= Personal trainer, PA= physical activity, 1RM= one repetition maximum, UC= usual care, HRR- heart rate reserve, reps= repetitions, SMART goals= specific measurable achievable realistic and timed goals, Ex. Phys= Exercise Physiologist, PTDM= post-transplant diabetes mellitus, and APN= advanced practice nurse, IG= intervention group, DASH= dietary approaches to stop hypertension diet

2.4.3 Risk-of-bias

Minor disagreements between the two reviewers (EC and EMc) on quality assessments were resolved through discussion, with no need to involve a third reviewer. Four RCT's were classified as 'low-risk' (Gibson et al., 2020; Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019), one was classified as 'some concerns'(Serper et al., 2020) for risk of bias and five were classified as 'high-risk' overall (Karelis et al., 2016; Lawrence et al., 1995; O'Connor et al., 2017; Painter et al., 2002; Tzvetanov et al., 2014). 'High-risk' assessment was predominantly due to inadequate reporting on deviation from protocol and missing data. There was a wide variation in risk-of-bias for the non-RCT's (refer to Appendix A). Figure 2.2 demonstrate risk-of-bias plots created using the risk-of-bias visualisation tool (McGuinness & Higgins, 2020).

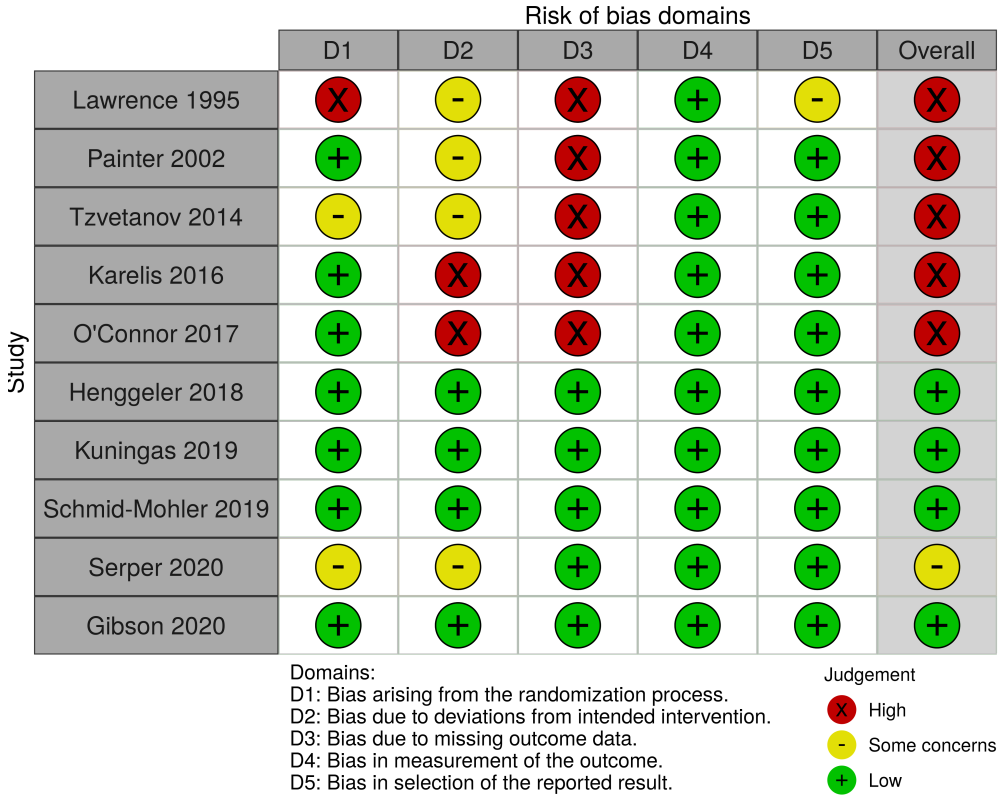


Figure 2-2 Risk-of-bias plot for RCT's (n=10)
Note. D=domain, scores based on the Cochrane review risk-of-bias tool

2.4.4 Body weight and BMI

Nine of the ten RCT's reported no effect of interventions on body weight or BMI values (Gibson et al., 2020; Henggeler et al., 2018; Karelis et al., 2016; Lawrence et al., 1995; O'Connor et al., 2017; Painter et al., 2002; Schmid-Mohler et al., 2019; Serper et al., 2020; Tzvetanov et al., 2014). However, Kuningas et al (2019) reported a change to these measures as a secondary outcome. 130 KTRs without diabetes were randomised to either a passive education booklet, or a dietitian-led six-month intervention involving dietary education, PA plans, and BCT's (Kuningas et al., 2019) (table 2.3). Whilst the study revealed no significant difference in its primary outcome of glucose metabolism, the authors report a significant difference in the change in body weight over the 6-month study of -2.47 kilograms (95% CI 0.401 to -0.92, P=0.002) (Kuningas et al., 2019). BMI post-intervention values were not presented by the authors. However, there was a significant mean difference in fat mass (FM) favouring the intervention group participants (Kuningas et al., 2019) . Risk-of-bias was categorised as 'low'.

2.4.4.1 Meta-analyses body weight and BMI

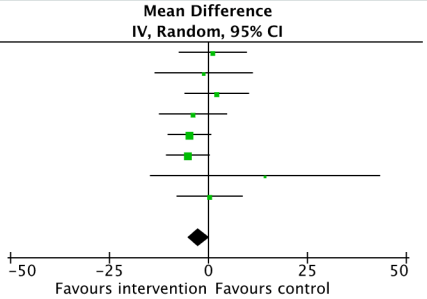
Eight out of the ten final RCT's reported post-intervention body weight values (Gibson et al., 2020; Henggeler et al., 2018; Karelis et al., 2016; Kuningas et al., 2019; O'Connor et al., 2017; Painter et al., 2002; Schmid-Mohler et al., 2019; Serper et al., 2020). Eight reported post-intervention BMI values and were included in the meta-analysis (Gibson et al., 2020; Greenwood et al., 2015; Henggeler et al., 2018; Karelis et al., 2016; Lawrence et al., 1995; Painter et al., 2002; Schmid-Mohler et al., 2019; Tzvetanov et al., 2014). Despite variation in methods and participant characteristics between included RCT's, measures of statistical heterogeneity were not significant for body weight (Chi^2 7, n=575, P=0.6 , I^2=0%) , or BMI (Chi^2 7, n=383, P=0.43, I^2=0%). Pooled data from 575 KTRs (table 2.4) revealed a non-significant mean difference in

body weight [effect size, -2.50kg, 95% confidence interval (95% CI) -5.22 to 0.22]. Pooled data from 383 KTRs revealed a non-significant mean difference in BMI (-0.4kg/m^2, 95% CI –1.33 to 0.53), see table 2.5.

Table 2-4 Meta-analysis body weight (post-intervention values)

Study or Subgroup	Intervention Mean [kilograms]	Intervention SD [kilograms]	Intervention Total	Control Mean [kilograms]	Control SD [kilograms]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Painter 2002 (12/12 ET)	78.1	22	54	77	20.4	43	10.3%	1.10 [-7.36, 9.56]	2002
Karelis 2016 (16/52 ET)	71.8	14	10	73	14	10	4.9%	-1.20 [-13.47, 11.07]	2016
O'Connor 2017 (3/12 ET)	79	15.6	26	76.9	12.1	20	11.5%	2.10 [-5.90, 10.10]	2017
Henggeler 2018 (12/12 Combined Rx)	79.7	12.5	18	83.6	13.4	18	10.3%	-3.90 [-12.37, 4.57]	2018
Kuningas 2019 (6/12 Combined Rx)	77.9	16.5	66	82.7	14.7	64	25.6%	-4.80 [-10.17, 0.57]	2019
Schmid-Mohler 2019 (8/12 Combined Rx)	71	13.2	60	76.2	16.7	60	25.5%	-5.20 [-10.59, 0.19]	2019
Gibson 2020 (6/12 Combined Digital Rx)	104.6	24.8	4	90.3	17.9	5	0.9%	14.30 [-14.63, 43.23]	2020
Serper 2020 (14/52 Combined Digital Rx)	86.3	20.7	76	86	22.1	41	11.0%	0.30 [-7.91, 8.51]	2020
Total (95% CI)			**314**			**261**	**100.0%**	**-2.50 [-5.22, 0.22]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.52$, df = 7 (P = 0.60); $I^2 = 0\%$
Test for overall effect: Z = 1.80 (P = 0.07)

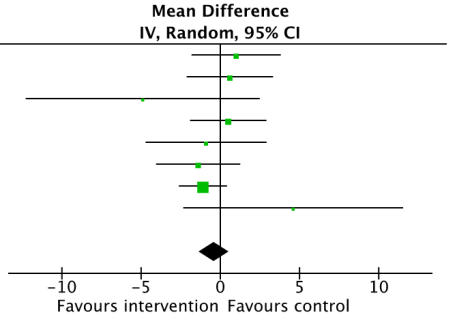


Note. Post-intervention values used for meta-analysis. Standard deviation calculated from SEM for Lawrence et al (1995) and Henggeler et al (2018). Schmid-Mohler et al (2019) provided BW and BMI data for KTR alone (n=120) on request. Studies with multiple intervention arms (O'Connor et al., 2017; Serper et al., 2020) were combined. Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx= intervention

Table 2-5 Meta-analysis BMI (post-intervention values)

Study or Subgroup	Intervention Mean [kg/m2]	Intervention SD [kg/m2]	Intervention Total	Control Mean [kg/m2]	Control SD [kg/m2]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Lawrence 1995 (12/12 Diet Rx)	26	4.7	22	25	4	16	11.2%	1.00 [-1.77, 3.77]	1995
Painter 2002 (12/12 ET)	27.7	7.4	54	27.1	6.1	43	12.0%	0.60 [-2.09, 3.29]	2002
Tzvetanov 2014 (12/12 Combined Rx)	41.4	5.4	9	46.3	9.3	8	1.6%	-4.90 [-12.25, 2.45]	2014
Greenwood 2015 (3/12 ET*)	27.7	4.6	26	27.2	3.6	20	15.4%	0.50 [-1.87, 2.87]	2015
Karelis 2016 (16/52 ET)	24.6	4	10	25.5	4.6	10	6.1%	-0.90 [-4.68, 2.88]	2016
Henggeler 2018 (12/12 Combined Rx)	26.9	3.8	18	28.3	4.2	18	12.6%	-1.40 [-4.02, 1.22]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	24.6	3.6	60	25.7	4.6	60	39.4%	-1.10 [-2.58, 0.38]	2019
Gibson 2020 (6/12 Combined Digital Rx)	36.3	2.4	4	31.7	7.4	5	1.8%	4.60 [-2.30, 11.50]	2020
Total (95% CI)			**203**			**180**	**100.0%**	**-0.40 [-1.33, 0.53]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 7.01$, df = 7 (P = 0.43); $I^2 = 0\%$
Test for overall effect: Z = 0.84 (P = 0.40)



Note. Post-intervention values used for meta-analysis. BMI was not reported in O'Connor et al (2017). Therefore, * indicates BMI from primary study manuscript (Greenwood et al., 2015). BMI values from Tzvetanov et al (2014) were calculated from mean change and baseline values. Standard deviations were calculated from SEM in Henggeler et al (2018). Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx= intervention

Exploratory post-hoc sensitivity analysis was performed on pooling the effects of the combined interventions, and the single modality interventions (exercise or diet alone) to further explore body weight and BMI values. Sensitivity analysis (Appendix A) revealed that combined interventions (Gibson et al., 2020; Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019; Serper et al., 2020) could have the potential to influence post-intervention body weight values. These findings were not echoed in the sensitivity analysis for post-intervention BMI values, refer to Appendix A. Funnel plots were completed to assess publication bias (Figures 2.3 and 2.4). These demonstrated the potential for publication bias.

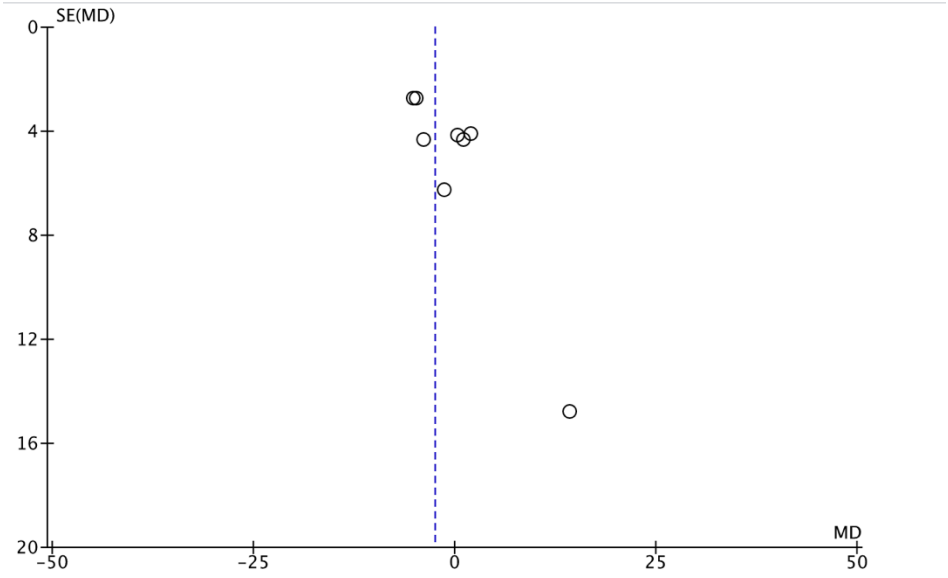


Figure 2-3 Funnel plot for post-intervention body weight
Note. Where SE= standard error, MD= mean difference

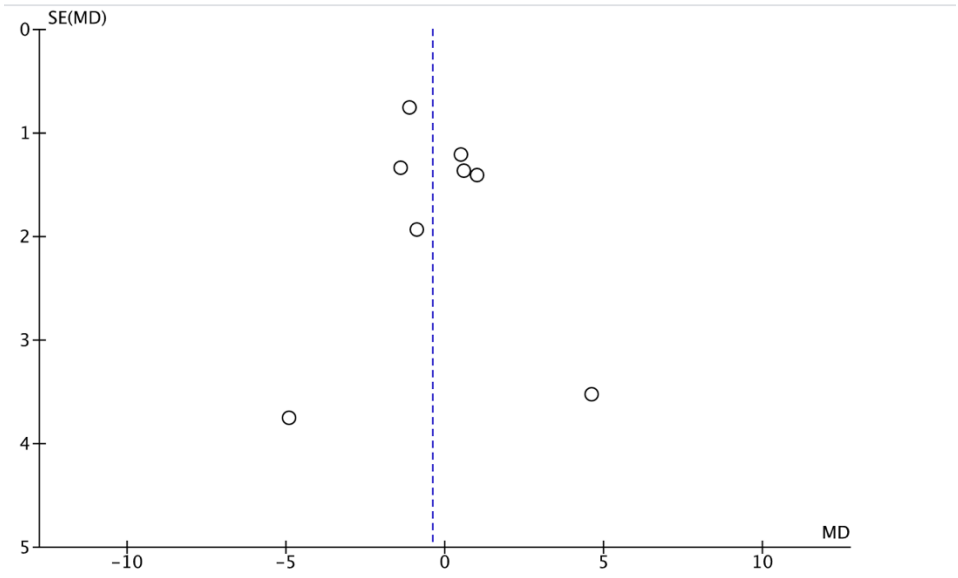


Figure 2-4 Funnel plot for post-intervention BMI
Note. Where SE= standard error, MD= mean difference

2.4.5 Secondary outcomes

Meta-analyses were not performed on secondary outcomes due to the large variation of measurement tools utilised (refer to tables 2.3 and 2.3), and the limited number of RCT's. Five RCT's assessed BC (Henggeler et al., 2018; Karelis et al., 2016; Kuningas et al., 2019; Painter et al., 2002; Schmid-Mohler et al., 2019). No studies reported a significant difference in LTM. Kuningas et al (2019) reported a significant mean difference in FM favouring the treatment group in their dietitian-led combined intervention (mean difference -1.54kg [-2.95 to -0.13], *P*=0.033). Another study reported a marginal decrease in the percentage FM; however, this outcome was only captured in the treatment group due to significant loss to follow-up (Tzvetanov et al., 2014). Four studies reported an increase in FM in all participants (Henggeler et al., 2018; Karelis et al., 2016; Leasure et al., 1995; Painter et al., 2002).

Four studies measured physical function using different measures (Henggeler et al., 2018; Kuningas et al., 2019; Teplan et al., 2014; Tzvetanov et al., 2014). One study

reported significant difference in physical function; however, data was only available for the intervention group (Tzvetanov et al., 2014).

Three studies used different questionnaires to measure PA (Henggeler et al., 2018; Kuningas et al., 2019; Schmid-Mohler et al., 2019). One study reported an increase in the PA of the treatment group but provided no further information (Patel, 1998). Another study reported a significant increase in percentage of participants achieving two hours or more of PA per-week (28% vs 71%, $p<0.001$); however data are not presented for the comparator group (Sharif et al., 2008). One study reported a higher proportion of self-reported PA levels at twelve months in the treatment group versus the usual care group (67% vs. 36%, $P=0.02$) (Painter et al., 2002). Three studies reported no significant between-group difference in PA (Gibson et al., 2020; Kuningas et al., 2019; Schmid-Mohler et al., 2019). One RCT demonstrated a high step count of over ten thousand steps-per-day in both groups (Schmid-Mohler et al., 2019). Serper et al (Serper et al., 2020) reported the group receiving the step tracker, website and online-intervention had a higher step count than the group receiving the device alone ($P<0.001$).

No studies assessed self-efficacy. One study reported no between-group difference in questionnaires assessing situational motivation scores and depression symptoms (Kuningas et al., 2019). Another study report motivation via the index of personality styles questionnaire in the intervention group only (Tzvetanov et al., 2014).

2.5 Discussion

2.5.1 Summary of findings

The current evidence evaluating interventions to address post-transplant weight gain are limited, with only ten RCT's consisting of mainly small samples, limited power, lack of long-term follow-up, variable sample characteristics, and variable intervention types and duration. This limits the ability to perform pooled estimates. Meta-analyses of post-intervention body weight and BMI values revealed no significant effect on body weight or BMI. Whilst the meta-analysis revealed no significant statistical heterogeneity, there was methodological heterogeneity across the included RCT's, including a variation in the baseline body weight reported. When performing exploratory post-hoc sensitivity analysis, combined interventions revealed the potential to reduce body weight (Appendix A), but not BMI in new KTRs.

Kuningas et al (2019) was the only RCT to show a significant difference in body weight following a six-month complex intervention involving dietetic education, PA plans, and BCT's. The authors reported a significant mean difference in change in weight of -2.47 kilograms at six months, and a significant mean difference in FM favouring the treatment group. Whilst this study was powered to for insulin sensitivity, its relatively large sample of 130 participants, and it's 'low risk' of bias provides some confidence in its findings. Whilst the study excluded KTRs with diabetes and did not include long-term follow-up, it provides a promising basis of intervention design for future research in this field.

Study design could have impacted the ability for RCT's using combined interventions (Gibson et al., 2020; Henggeler et al., 2018; Schmid-Mohler et al., 2019; Serper et al., 2020; Tzvetanov et al., 2014) to effect post-intervention body weight and BMI values.

Two RCT's included in this systematic review included enhanced usual care. In the trial by Henggeler et al (2018) usual care participants were given four sessions with a renal dietitian versus the twelve sessions in the intervention group. In the RCT by Schmid-Mohler et al (2019) usual care participants were given one session with an advanced practice nurse versus 8-months of combined intervention. Whilst these two RCT's with enhanced usual care fail to show an effect of their interventions over usual care, it does not mean that dietary counselling is not efficient to prevent weight gain. The lack of between-group treatment effect in Henggeler et al (2018) could have been further enhanced by the exercise component not being of sufficient dose to elicit change. Schmid-Mohler et al (2019) acknowledge that irrespective of the treatment groups, both groups had high levels of PA, which could have influenced their results.

Tzvetanov et al (2014) reported no significant between-group difference in BMI between the 12-month combined intervention group and the control group. Change in body weight was not reported. This study was assessed to have 'high risk' of bias due to its small sample size (n=12), large number of dropouts, particularly in the control group, impacting data collection on important outcomes such as BC.

Serper et al (2020) reported no significant between-group difference in change in body weight from baseline to four months. The authors acknowledge the dietary component of the online intervention was not designed for weight management, the intervention was relatively short in duration (14 weeks), and there was no long-term follow-up (Serper et al., 2020). In addition, there was the potential of contamination bias, with some of the control group participants purchasing wearable step trackers or using smart phone applications in response to randomisation (Serper et al., 2020). Participants randomised into the step tracker device with the text message and financial incentives

displayed a greater number of steps than those in the step tracking device group, suggesting a potential benefit of the text reminders and financial incentives on PA behaviour. This study was assessed as 'some concerns' for risk of bias. However, KTR data is not presented in isolation of the combined transplant sample, making it difficult to determine the effects of the intervention on KTRs alone.

Gibson et al (2020) reported the intervention group who received six months of combined intervention with video teleconference calls increased their body weight and BMI in comparison to the usual care group. Measures of BC were not included in this trial. This feasibility RCT had a small sample (n=10). It does however provide evidence of strong adherence rates in the intervention group, and qualitative findings to support further investigation into online interventions to support new KTRs.

Previous systematic reviews of exercise interventions in KTRs have shown favourable effects on exercise clinical outcomes but no consistent change in body weight (Calella et al., 2019; Chen et al., 2019). Therefore, it is unsurprising that our systematic review confirmed that exercise or PA interventions alone (Karelis et al., 2016; O'Connor et al., 2017; Painter et al., 2002) did not show favourable effects on body weight or BMI. This is likely due to the trial and intervention design, with exercise specific outcomes being selected to align with exercise intervention targets (Chiarotto, Ostelo, Turk, Buchbinder, & Boers, 2017), rather than targeting behaviour change. It is also unsurprising that the one RCT (Lawrence et al., 1995) included in this systematic review that compared 12-months of dietary intervention with usual care did not show significant impact in BMI (Lawrence et al., 1995). Combined interventions are likely to be needed to address the complex clinical problem of acute post-transplant weight gain.

A recent Cochrane review by Conley et al (2021) reviewed interventions for weight loss in people living with excess weight, obesity and CKD (including KTRs). The authors reported no difference in total weight loss when comparing weight loss interventions (dietary, PA, behavioural or combined) to usual care in KTRs (Conley et al., 2021). However, this systematic review focused on people living with excess weight and obesity, investigated weight loss rather than weight gain prevention, and included participants with older transplants, making it difficult to infer the effects on weight gain in the acute post-transplant period.

2.5.2 Implications for clinical practice

Fear of harming the new kidney transplant has been reported by KTRs (Gordon, Prohaska, Gallant, & Siminoff, 2009; Stanfill et al., 2012; Zelle et al., 2016). KTRs have reported receiving limited education from clinicians regarding the type and dose of recommended exercise after kidney transplant (Gordon et al., 2009). KTRs have expressed the need for early interventions that support PA behaviour change (O'Brien & Hathaway, 2016), and a healthy eating post-transplantation (Stanfill et al., 2012). Routine access to both physiotherapists and dietitians is not available for KTRs in the UK. A recent survey of the UK transplant units conducted by Kostakis et al (2020) revealed that despite clinicians agreeing that obesity and a high BMI negatively affects transplant outcomes, there was limited clinical support for weight control for new KTRs. Thus, data regarding the effect of interventions to prevent weight gain in new KTRs are limited and are urgently needed to inform clinical practice.

2.5.3 Implications for future research

This systematic review and meta-analysis suggest that there is insufficient evidence to advise clinical practice in this field, and that more research is warranted. Sufficiently

powered, RCT's, with clear reporting of complex multi-component interventions using recognised checklists such as the CReDECI criteria (Möhler, Köpke, & Meyer, 2015), the TiDieR checklist (Hoffmann et al., 2014), and reference to the BCT taxonomies (Michie et al., 2013) are required. It would be of particular interest for future studies to include combined interventions, with recognised BCT's, similar to those displayed in Kuningas et al (2019) to address both PA, and healthy eating behaviours. In addition, only one RCT in this review (O'Connor et al., 2017) reported twelve-month follow-up after a period of intervention cessation. There is therefore a need for RCT's to investigate longer-term outcomes.

There was significant variation in the methods utilised to assess BC, physical function, and PA in new KTRs, precluding the ability to perform a meta-analysis for these secondary outcomes. Whilst weight gain is a clinically important issue for new KTR's, future studies would benefit from including patient-centred outcomes, such as 'life participation' that has been listed as a core outcome measure by a group of international KTRs and HCPs from the Standardized Outcomes in Nephrology (SONG) Transplantation group (Ju et al., 2019).

Given there is no recognised intervention to prevent WG in new KTRs, exploration of other modes of delivery, such as online interventions would benefit from further research. Only two studies (Gibson et al., 2020; Serper et al., 2020) identified in this systematic review included an element of digital delivery to the intervention group. Despite both RCT's not revealing significant differences in body weight or BMI, they did demonstrate improved PA levels (Serper et al., 2020), acceptability and good adherence rates to the online interventions (Gibson et al., 2020; Serper et al., 2020).

A recent Cochrane systematic review evaluated the risks and benefits of online e-health interventions for people living with kidney disease (including KTRs) (Stevenson et al., 2019).The review concluded that there is low quality evidence for e-health interventions, and further research with interventions that utilise theoretical frameworks, self-monitoring and personalised education are warranted (Stevenson et al., 2019). Given the recent need for virtual clinics to support transplant patients during the COVID-19 pandemic (British Transplant Society, 2020), research exploring the use of online delivery of interventions to support KTRs requires further investigation.

2.5.4 Strengths and limitations

To our knowledge, this is the first systematic review and meta-analysis that included exercise, PA, dietary or combined interventions, and their effect on body weight in new KTRs. Previous reviews have focused on either exercise or PA alone (Calella et al., 2019; Chen et al., 2019; Oguchi et al., 2019), or excluded combined interventions (Palmer et al., 2017a). There is a need further research on dietary management for KTRs (Fry et al., 2009; Nolte Fong & Moore, 2018; Palmer et al., 2017a). This systematic review focused on body weight and BMI as primary outcomes. Therefore, it is possible that further studies reporting secondary outcomes, but not body weight or BMI were excluded in this search.

This systematic review focused on KTRs rather than all SOTs. However, KTRs have requested specific education and support (Castle, Greenwood, Chilcot, & Greenwood, 2020; Stanfill et al., 2012), experience a unique fear avoidance pattern associated with PA, (Zelle et al., 2016) and experience rapid weight gain in the acute post-operative period (Beckmann et al., 2017). Furthermore, this review focused on KTRs within the first year of transplant surgery. Studies that include participants with an older transplant

vintage were excluded which may have precluded additional insight into this research area. However, as weight gain within the first year is associated with adverse clinical outcomes (Ducloux, Kazory, Simula-Faivre, & Chalopin, 2005; Vega et al., 2015) the authors felt it was important to investigate the first-year post kidney transplantation.

The research fellow acknowledges the impact that the methodological variation between the final RCT's (sample characteristics, intervention type, dose, and duration) may have had on the validity of the pooled effects of interventions on body weight or BMI. Statistical heterogeneity was not significant. By performing the meta-analyses on body weight and BMI, and exploring this with sensitivity analysis, this systematic review provides novel implications for future research studies in this field.

2.6 Systematic review conclusions

This is the first systematic review and meta-analysis to examine the evidence on either dietetic, exercise or combined interventions on body weight and BMI within the first year of receiving a kidney transplant. There is limited evidence in the field, and we encourage further adequately powered theoretically informed RCT's, with pragmatic inclusion criteria, clear reporting of intervention components, and long-term follow-up, to further answer this important clinical question of acute weight gain post kidney transplantation.

2.7 Chapter summary

This chapter has presented the results of the first study, the systematic review and meta-analysis. Figure 2.5 below, shows how this study contributes to the overall thesis structure, and the online intervention development that will be revisited in the upcoming chapters. The products box summaries the key findings from study 1.

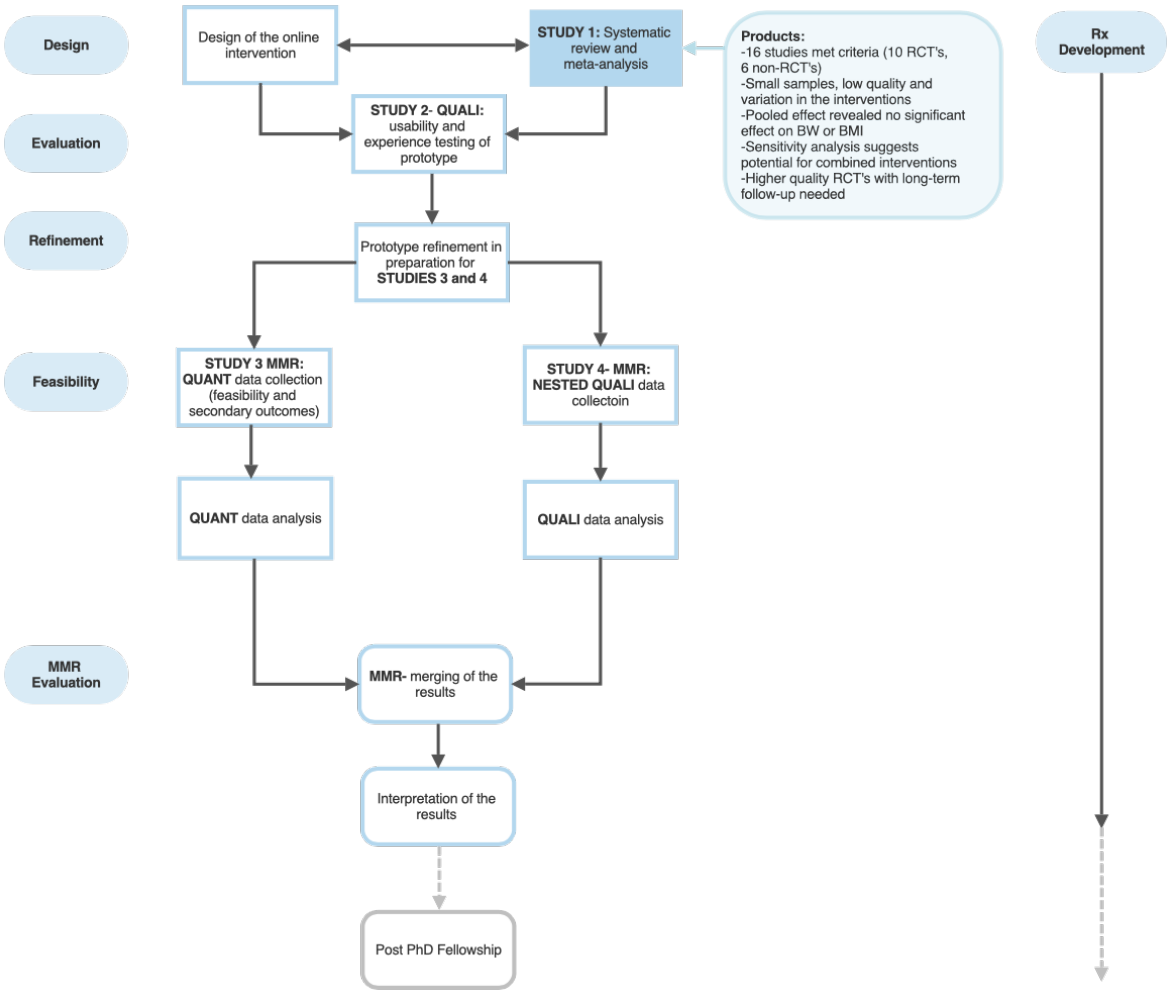


Figure 2-5 Thesis processes diagram updated to reflect study 1 (systematic review)

Note. The thesis processes diagram has been updated to reflect the results from the systematic review and meta-analysis (study 1) shown in the rounded edged blue rectangle 'product's box. Overall, there were a small number of trials, with low quality, variable interventions, and non-significant pooled effects.

This figure was designed based on a combination of the convergent mixes-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

RCT= randomised controlled trial, non-RCT= nonrandomised controlled trial (e.g., quasi experiential trial), BW= body weight, BMI= body mass index, QUALI= qualitative, QUANT=quantitative and MMR= mixed methods research

Chapter 3 General methods

3.1 Chapter overview

As presented in chapters 1 and 2, there is insufficient evidence to recommend either nutritional, and/or exercise interventions to prevent weight gain in new KTRs. The acceptability, feasibility and effectiveness of online interventions to prevent weight in new KTRs warrants investigation.

This chapter will summarise:

- The methodological approaches employed in this thesis
- The philosophical standpoint of the research fellow
- The rationale for the use of mixed methods research design
- The rationale for an online intervention
- The design, development and evaluation of an online intervention to address weight gain prevention in new KTRs
- The methodology utilised in study 2, a qualitative evaluation of the usability (function, navigation and interactivity) and experience of the ExeRTiOn online intervention prototype
- The methodology used to refine the online intervention between the completion of study 2, and before the commencement of studies 3 and 4
- The methodology that was utilised in a mixed methods feasibility RCT (which included study 3, the quantitative data, and study 4 a nested qualitative evaluation).

3.2 Philosophical worldview of the research fellow

Research does not occur in a vacuum, it is important to acknowledge the researchers perspective and beliefs that inform their actions and decisions (Creswell & Creswell, 2018). Qualitative analysis is not a passive process, and themes do not just emerge independently from the data, or the researchers perspective (Braun & Clarke, 2019a). Therefore, it is important to be transparent with the reporting of philosophical standpoints. The research fellow had prior experience in both clinical and research settings for supporting people living with kidney disease, (specifically KTRs) to adopt PA behaviours. The dual roles as a clinician, and a researcher, aligned with the pragmatic worldview. Pragmatism is not concerned with the search for reality, it is focused on researching the consequences of actions within a specific context, and practically choosing the best course of action (Cherryholmes, 1992). A pragmatic worldview was applied throughout this thesis as it involved problem-focused research, in 'real world' settings (Yardley & Bishop, 2012).

3.3 Justification for mixed methods thesis design

Pragmatism lends itself well to mixed methods research (MMR) (Yardley & Bishop, 2012). This PhD thesis included a mixed methods design, interpreted through a pragmatic lens. A mixed methods approach was utilised as it allowed for a richer exploration (Yardley & Bishop, 2012) of the usability, acceptability, feasibility and experience of using an online weight gain prevention intervention for new KTRs, in comparison to a single methods approach. Experiential qualitative (QUALI) data explored the experiences and acceptability from the target-user group perspective (new KTRs) to inform iterative refinements of the intervention. Quantitative (QUANT) data included the collection of feasibility outcomes, secondary outcomes, and engagement with the online intervention, which further explored feasibility and acceptability. Data

from this thesis was converged, and interpretated together, using mixed methods integrated analyses from a pragmatic standpoint.

3.4 The design, development, evaluation and refinement of bespoke online intervention for KTRs (ExeRTiOn)

3.4.1 Justification for an online intervention

Previous chapters (1 and 2) have presented the risk of adverse weight gain in new KTRs and synthesised the existing evidence base. As outlined in chapter 1, despite national guidance, and KTRs identifying a need for support, routine services to support KTRs with weight gain prevention do not exist. Whilst some face-to-face services exist such as renal weight management services for weight loss, routine access to support for weight management and prevention of weight gain is not provided for KTRs. Furthermore, whilst generic weight loss services do exist, they are not suited to the specific issues new KTRs face, and the context of acute care post kidney transplantation.

The interest in digital behaviour change interventions in health care is growing. Digital behaviour change online interventions, if acceptable and effective, have the potential to address behaviours (e.g. PA), and provide a wider reach of care at a low unit cost (West & Michie, 2016). An online intervention could be an appropriate mode to deliver support to KTRs remotely to prevent weight gain around their unique challenges experienced, therefore addressing the unmet clinical need. However, it would require research, and strong engagement with stakeholders and KTRs.

The appreciation of the context in which an intervention is delivered is a crucial (West & Michie, 2016). In the UK, KTR are engaged with online products such as renal 'PatientView' to monitor their renal bloods and medical management. It is used by 91% of the UK renal units (The Renal Association, 2020a). Collaborative discussions with members from the research team, clinical experts, and members of the trial management Group (TMG) (which included KTRs), resulted in the decision to use a reactive website to deliver the weight gain prevention intervention. A reactive website allowed participants to use any internet compatible device (e.g., laptop, personal computer, tablet or smart phone). A reactive website was chosen in preference to a mobile phone application as it had a greater reach, and prevented additional costs associated with the regular software upgrades of mobile phone applications.

3.4.2 Concepts and terms of intervention development

Complex healthcare interventions are comprised of multiple interactive components (O'Cathain, Croot, Duncan, et al., 2019). Due to this complexity, complex interventions are often insufficiently reported, making replication, synthesis and evaluation challenging (Möhler et al., 2015). As discussed in the previous chapter, it was hypothesised that complex interventions involving exercise, PA and dietary interventions, embedded with BCT's would be required to address post-transplant weight gain in new KTRs. The Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare (CReDECI 2) (Möhler et al., 2015) was utilised in this chapter to report the design, development, the testing and evaluation of the online intervention. Results from the testing and evaluation of the online intervention will be presented in subsequent chapters (chapters 4 and 6).

When considering the development of complex health interventions, it is important to clearly define terms. The term ‘development’ was used to describe the entire process of the intervention creation and development (O’Cathain, Croot, Sworn, et al., 2019) starting at the PhD commencement, to beyond the PhD fellowship. Whereas ‘design’ referred to a specific point within the overall development process where decisions were made regarding the content, structure and delivery of the intervention (O’Cathain, Croot, Sworn, et al., 2019). ‘Refinement’ referred to the small, iterative changes made to improve the online intervention (O’Cathain, Croot, Sworn, et al., 2019). Whereas feasibility studies are defined as:

> Studies designed to build the foundations for the planned intervention study (Tickle-Degnen, 2013, p. 171).

The term ‘evaluation’ was used to refer to the mixed methods design utilised to review the online intervention, its components, and the perspectives of the target population (Yardley, Morrison, Bradbury, & Muller, 2015).

3.4.3 Frameworks, theories, and approaches involved in intervention design, development and evaluation

The intervention developed for this thesis was titled ExeRTiOn (Exercise and weight in renal transplant online). It is important to note that the processes of online health intervention development, refinement and evaluation were iterative and non-liner, and multiple steps occurred simultaneously (Blandford, 2019; Bradbury, Watts, Arden-Close, Yardley, & Lewith, 2014; O’Cathain, Croot, Duncan, et al., 2019).

The design, development, and evaluation of the ExeRTiOn online intervention was informed by:

- The Medical Research Council (MRC) framework for complex interventions (Craig et al., 2008)

- The combined intervention design approach (O'Cathain, Croot, Sworn, et al., 2019), largely informed by the person-centred approach (Yardley, Ainsworth, Arden-Close, & Muller, 2015b) and the evidence and theory approach (O'Cathain, Croot, Sworn, et al., 2019)
- The guidance for digital healthcare development (Bradbury et al., 2014)
- The behaviour change wheel (BCW) (Michie, Van Stralen, & West, 2011)
- The behaviour change techniques taxonomy version 1 (BCTTv1) (Michie et al., 2013)
- A specific taxonomy of BCTs known to influence both PA and nutrition behaviours, The Coventry & London refined (CALO-RE taxonomy (Michie, Ashford, et al., 2011)
- The self-efficacy theory (Bandura, 1977)
- Motivational interviewing (Miller & Rollnick, 2013)
- Patient and public involvement (PPI)

The following section provides definitions of each of these key framework, theories and approaches, and demonstrates how they informed the ExeRTiOn online intervention.

3.4.3.1 Adoption of the MRC framework for complex interventions

The MRC principles were utilised to insure adequate reporting of the intervention components, outcomes and context (Moore et al., 2015). It is recommended by the MRC, that complex interventions are developed with strong theoretical background, and evidence combined from different sources (Craig et al., 2008). The key processes of the MRC framework for complex intervention development and evaluation including intervention development, feasibility and piloting, evaluation and implementation (Craig et al., 2008) were utilised. However, the development of the ExeRTIOn online

intervention, like other digital behaviour change interventions involved these steps occurring concurrently and iteratively (West & Michie, 2016). In this thesis, evaluation of the online intervention occurred both in the second, third, and fourth studies. Feasibility testing occurred within the mixed methods feasibility RCT (study 3), which included a nested qualitative evaluation (study 4). The thesis processes diagram, previously presented in this thesis, and represented below (figure 3.1), demonstrate how the four empirical studies of the thesis (studies 1 to 4) aligned with the MRC framework, the mixed methods design, and an iterative intervention development process. It will be revisited throughout this thesis as new information is presented.

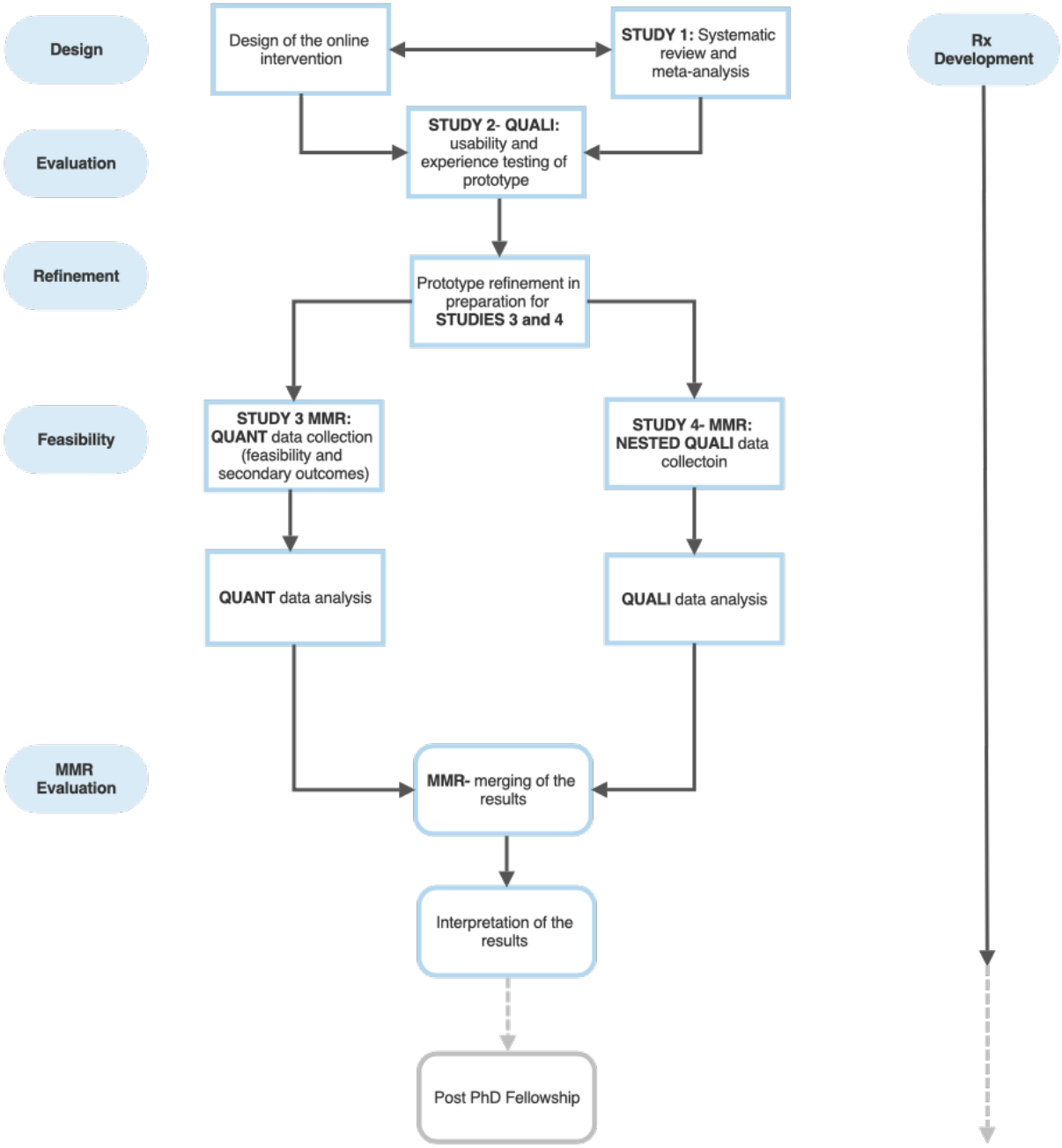


Figure 3-1 Thesis processes diagram in relation to the MRC framework

Note. This thesis processes diagram depicts how the thesis relates to the Medical Research Council (MRC) framework. The blue boxes on the far left indicate the components of the MRC framework (development, feasibility and piloting and evaluation). The central boxes show the four studies included in this PhD. As indicated by the box on the far right, intervention development is iterative, and will occur throughout the thesis and beyond.

This figure was designed based on a combination of the convergent mixes-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

QUALI= qualitative, QUANT=quantitative, MMR= mixed methods research and Rx=intervention

3.4.3.2 The combined and person-based approach to designing online intervention

The combined intervention design approach involves combining key approaches of intervention development to best suit the needs of the target group and context (O'Cathain, Croot, Sworn, et al., 2019). For the ExeRTiOn online intervention, a combined approach was used, largely involving existing theories and models such as the MRC framework, the BCW, alongside the person-based approach to ensure the product was fit for purpose. The person-based approach is defined as:

> Mixed methods research to systematically investigate the beliefs, attitudes, needs and situation of the people who will be using the intervention (Yardley, Ainsworth, Arden-Close, & Muller, 2015a, p. 1).

The person-based approach has been used alongside the BCW (Arden et al., 2021). Engagement with target-end users of the online intervention (KTRs) is central in achieving acceptability (Valdez & Ziefle, 2019). Therefore, the person-based approach largely informed the design, development and evaluation of the ExeRTiOn online intervention. It allowed for the focus of a target population (O'Cathain, Croot, Sworn, et al., 2019), the incorporation of theory, and the evidence base, which are recommended in digital online intervention development (Yardley, Morrison, et al., 2015). The person-based approach aligned with the MRC framework, the BCW, the pragmatic philosophical standpoint and mixed-methods study design employed by the research fellow. In addition, the person-based approach facilitated user-driven revisions of the ExeRTiOn online intervention to make it more feasible, and relevant to the target user group (new KTRs) and their specific context.

The person-based approach was facilitated through engagement of key stakeholders, including KTRs. The design team, led by the research fellow included the project supervisors (a consultant physiotherapist, a health psychologist and a nephrologist) and renal dietitians with experience from face-to-face renal weight management clinics

(Cook et al., 2008; MacLaughlin et al., 2010). The design team made the final decisions on content and held regular meetings with the TMG, and the software company (SPIKA Ltd) throughout the development and refinement process. This allowed for the implementation of changes based on user-feedback to ensure KTRs views and experiences were central to the intervention. The TMG included the design team, KTR expert patients, nephrologists and nurse specialists from a London-based kidney transplant clinic.

3.4.3.3 The Behaviour Change Wheel

The BCW (Michie, Atkins, & West, 2014b) is recommended for the development and evaluation of digital behaviour change interventions, and aligns both with the MRC framework and the person-based approach (West & Michie, 2016). The Capability Opportunity Motivation-Behaviour (COM-B) model is the central underlying theoretical model of the BCW, and involves the interactive components responsible for changing a target behaviour (Michie, Van Stralen, et al., 2011). In this model, behaviour is a result of the interactions of the individuals capability (physical and psychological), opportunity (physical and social) and motivation (automatic and reflective) (Michie, Van Stralen, et al., 2011) . Michie et al (2014b) defines physical capability as the 'physical skills, strength and or stamina' to perform the target behaviour. Whereas psychological capability refers to the mental capability to be able to engage with the thought processes, and the required psychological knowledge and skills (Michie, West, Campbell, Brown, & Gainforth, 2014). The physical opportunity involves physical barriers and facilitators from the surrounding environment (e.g. resources, time, cues and access) (Michie, Atkins, et al., 2014b; Michie, West, et al., 2014). Whereas social opportunity focuses on the opportunities that arise due to the surrounding cultural environment and social influences (Michie, West, et al., 2014).

Motivation includes the mental processes that direct behaviour change (Michie, West, et al., 2014). Reflective motivation refers to the conscious planning and decision making, whereas automatic motivation describes the emotional responses and the habitual processes (Michie, West, et al., 2014). The COM-B model has been used alongside the combined approach, and the person-based approach to develop complex interventions in a variety of healthcare settings including adherence in cystic fibrosis (Arden et al., 2021), and online interventions to address weight management in children living with excess weight (Curtis, Lahiri, & Brown, 2015).

In this thesis, the ExeRTiOn online intervention was designed to target both PA behaviour, engagement with the ExeRTiOn online resource, and healthy eating behaviours (including portion sizes and healthy eating choices). These behaviours were theorised to influence the outcome of maintaining body weight after kidney transplantation. Due to the context surrounding KTRs, an individualised online resource was selected as the mode of delivery. The ExeRTiOn online intervention was tailored around the complexity of the KTR patient group, and their clinical histories. This aligns with the MRC guidance as complex interventions are most effective if tailored to the local circumstances (Craig et al., 2008).

The BCW involves multiple levels. At its centre is the COM-B model for behaviour and intervention design (Michie, Van Stralen, et al., 2011). The second layer involves 9 intervention functions to address various aspects of the COM-B model (Michie, Van Stralen, et al., 2011). The final outer later involves 7 policy categories for delivering the intervention (Michie, Van Stralen, et al., 2011).

3.4.3.4 Behaviour change techniques

BCT's are defined as the 'active ingredients' that directly influence the targeted behaviour (Michie, Atkins, & West, 2014a). BCT's can be linked to the intervention functions of the BCW, and the COM-B model (Michie, Atkins, et al., 2014b). The selection of what BCT's to include in an intervention is based on which BCT's are thought to best influence the target behaviours (Michie, Atkins, et al., 2014b). Complexity is involved as BCT's can influence multiple intervention functions, and multiple BCT's can be applied simultaneously.

To ensure clear reporting, replication, and evidence synthesis, a taxonomy of known BCTs was developed (Michie et al., 2013). In addition, a specific taxonomy of BCTs known to influence both PA and nutrition behaviours, the CALO-RE taxonomy (Michie, Ashford, et al., 2011) has been developed. BCT's included in the CALO-RE taxonomy such as; action planning, goal setting and self-monitoring of behaviour(s) where found to positively influence both PA behaviour, and healthy eating behaviours (Michie, Ashford, et al., 2011). Guidelines for individual approaches to behaviour change (NICE, 2014a) recommend the use of recognised BCT's, and the consideration of the needs of intervention recipients when designing interventions. Therefore, BCT's from the CALO-RE taxonomy (Michie, Ashford, et al., 2011), and the BCTTv1 (Michie et al., 2013) were utilised in the design of the ExeRTIOn online intervention.

The ExeRTiOn online intervention was revised based on feedback from participants in study 2. After studies 1-4, the revised ExeRTiOn online intervention was retrospectively mapped to the BCW (Michie, Van Stralen, et al., 2011) and coded to the BCTTv1 (Michie, Atkins, et al., 2014a) . This retrospective mapping, and 'behavioural diagnosis' (West & Michie, 2016) of the required changes needed to influence target behaviours to

address weight gain prevention in new KTRs (PA, engaging with the online resource and healthy eating behaviour) will be presented in chapter 6 and Appendix F.

3.4.3.5 Self-efficacy

Self-efficacy can be defined as an individual's own belief in their capability to perform the targeted behaviour(s) (Bandura, 1977). This theory was originally designed for the exploration of fearful and avoidant behaviours (Michie, West, et al., 2014). Expected self-efficacy has a direct relationship with both behaviour initiation and maintenance (Michie, West, et al., 2014). The higher one's self-efficacy, the more likely they are to take part in the target behaviour (e.g. PA) , to reach the desired outcome (e.g., body weight maintenance in the first year of kidney transplantation). Moreover, self-efficacy theory is often utilised for the exploration of fearful and avoidant behaviours (Bandura, 1977; Michie, West, et al., 2014). In new KTRs, fear of injuring the new kidney has been associated with low self-efficacy (Zelle et al., 2016). Therefore, an intervention that promoted self-management and fosters self-efficacy is hypothesised to be beneficial for new KTRs (Jamieson et al., 2016).

Self-efficacy is influenced by 'mastery', which is the repeated practice of successful attempts of performing the behaviour, vicarious experiences which involves the opportunity to witness 'role models' successfully performing the behaviour, and verbal persuasion or encouragement that they will be able to succeed (Michie, West, et al., 2014). It was hypothesised that the ExeRTiOn online resource could increase the self-efficacy to perform the target behaviours (PA, engage with the ExeRTiOn online intervention, and follow a healthy diet). To increase self-efficacy, the ExeRTiOn online intervention included:

- Opportunities to successfully perform the target behaviours (being physically active after kidney transplant, following a healthy balanced diet, and engaging with the online intervention). This was enhanced through demonstration and practice of PA, healthy eating behaviours and support to use the ExeRTiOn online intervention
- Exposure to role model KTR's who provided examples of successfully performing target behaviours e.g., performing PA post-transplant. This was achieved through videos and quotes and tips from KTRs
- Encouragement and social support from the trial physiotherapist
- Goal setting and action planning
- And the use of visual analogue scales to rate both confidence and importance of individual goals, a recognised motivational interviewing technique (Hall, Gibbie, & Lubman, 2012), which re-affirmed participants confidence in their ability to achieve target behaviours

3.4.3.6 Motivational interviewing

Motivational interviewing informed the ExeRTiOn online intervention content, and the interactions between the trial physiotherapist/ research fellow and the research participants when using the online intervention. Motivational interviewing is an evidence-based behaviour change approach (Motivational Interviewing Network of Trainers (MINT), 2021), designed to change both motivation and behaviour. It can be defined as

> A collaborative, goal-orientated style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion (Miller & Rollnick, 2013, p. 29).

Open questions, affirmations, summaries are motivational interviewing techniques are used to strengthen an individual's motivation for changing behaviour (Miller & Moyers, 2017).

Whilst motivational interviewing was initially designed based on clinical observations to address problem drinking and later smoking behaviours (Miller & Rollnick, 2013; Rollnick & Miller, 1995), it has since been widely adopted into primary care (Barnes & Ivezaj, 2015) and the wider health and social care settings (Frost et al., 2018). Motivational interviewing has been used to promote PA behaviour (O'Halloran et al., 2014), weight loss (Barnes 2015), the reduction of body weight and the increase of PA to address CVD risk (Ismail et al., 2020), substance and gambling addiction (Frost et al., 2018), and to promote the self-management of PA in people living with type 2 diabetes (Soderlund, 2018). A renal specific weight management clinic, at the research fellow's institution has reported a significant reduction in body weight, and an increase in functional capacity outcomes using a multi-professional intervention using motivational interviewing (Cook et al., 2008; MacLaughlin et al., 2010; MacLaughlin et al., 2012).

Meta-analyses suggest motivational interviewing has the potential for weight loss in primary care settings (Barnes & Ivezaj, 2015), and there is moderate evidence of the effect of motivational interviewing on PA behaviour in people living with long term conditions and chronic disease (Frost et al., 2018; O'Halloran et al., 2014). However, trials often do not report the fidelity of motivational interviewing interventions or the level of staff training of those who are providing the interventions (Barnes & Ivezaj, 2015).

The research fellow who delivered the ExeRTiOn online intervention throughout the studies presented in this thesis, had completed prior training on motivational interviewing practises in both clinical and educational settings. This included working in both transplant clinics, and also the renal specific weight management clinic (Cook et al., 2008; MacLaughlin et al., 2010; MacLaughlin et al., 2012). Motivational interviewing was imbedded within the ExeRTiOn online intervention content, as well as interactions between the research fellow, and the research participants to address the target behaviours.

3.4.3.7 Patient and public involvement and the TMG

Patient and public involvement (PPI) involves engaging with both people who are living with the condition of interest, and wider stakeholders from the general public (Bagley et al., 2016). PPI is an essential part of the research process that ensures the research is of clinical need, ethically and morally sound, focuses on the needs and experiences of the people living with the condition, and the results are sufficiently disseminated to the people volunteering to take part in the research study (Bagley et al., 2016).

The work presented in this thesis had strong PPI presence, which was crucial to the person-based approach (Yardley, Ainsworth, et al., 2015b) utilised to design the ExeRTiOn online intervention. The use of PPI throughout studies 2, 3 and 4 ensured the research aligned with the first aim of the UK kidney research strategy which was to increase engagement of professionals, patients and the public with kidney research (Karet et al., 2016). The mixed-methods design utilised throughout the thesis ensured that participant experience was central to the design, development and feasibility evaluation of the ExeRTiOn online intervention.

The research fellow worked closely with a group of KTRs from the primary site transplant clinic contributed to the content for the prototype (n=4). KTRs contributed to the topics covered, top-tip quotes, examples of the worksheets such as problem-solving and activity planning, and they also featured in the educational videos alongside transplant. In addition, people who had received kidney transplants were invited to be members of the trial management group (TMG).

Table 3.1 demonstrates how the overall combined approach included all of these components; the person-based approach, the MRC framework, the BCW, the self-efficacy theory, motivational interviewing principles and PPI. This table is based on two publications on approaches to intervention development (O'Cathain, Croot, Sworn, et al., 2019; Yardley, Morrison, et al., 2015).

Table 3-1 The approaches and stages of intervention development of the ExeRTiOn online intervention

Intervention development stage	Intervention approach used	How this was achieved in this PhD project	Chapter in this thesis outlining the development
Planning	**Person-based approach (Yardley, Morrison, et al., 2015)** • Importance of qualitative work to understand the patient perspective, their context, and the context of the intervention • Often involves reviewing existing qualitive research or conducting original qualitative work	**PPI** • PPI prior to PhD studies to understand the context of the unit and how KTRs engage with online services such as renal patient view **Patient experts** • KTRs commenting on content, involved in videos, and patient 'top tips' quotes used throughout ExeRTiOn resource • Patient experts involved as members of the TMG **Qualitative work** • Study two to explore the qualitative experiences of KTRs and HCPs views on weight gain, PA after kidney transplant and thoughts on the protype of the ExeRTiOn intervention to aid refinement	• This chapter • Chapter 4 (study two publication) • Chapter 6 (qualitative results study 4)
	MRC framework approach (Theory and Evidence-based practice) (O'Cathain, Croot, Sworn, et al., 2019) • Assess the problem and the evidence existing on interventions to address the problem	**Review of the literature** • Systematic review completed on interventions to prevent weight gain in KTRs completed (study 1) • Review of the literature on similar products to promote PA and healthy eating **Revision of existing theories**	• Systematic review (chapter 2) • This chapter

		• Self-efficacy theory (Bandura, 1977) identified as an important theory • BCTs for increasing PA and healthy eating seen as important aspects to this project (Michie, Ashford, et al., 2011)	
Design	**Person-based Approach (Yardley, Morrison, et al., 2015)** • Clear treatment target and key features • Decisions on content and delivery • Creation of prototypes for testing • Engagement of the target population key	**Key features and decisions on content** • PPI throughout the project, including attendance at Trial management group (TMG) • Regular meetings with TMG and design team to discuss content and key features **Use of prototypes** • Qualitative evaluation of prototype in study two by the target-user group and experts in the transplant team • The results from study two were central to decisions made to refine the ExeRTiOn intervention to assist further acceptability and feasibility testing **Key features of ExeRTiOn online intervention** • The key features of the ExeRTiOn online intervention were informed by our qualitative work in study two (Castle, Greenwood, et al., 2020), alongside recognised BCTs such as goal setting and self-monitoring (Michie, Ashford, et al., 2011)	• This chapter • Chapter 4 (usability and experience testing, study 2)
	Theory based- approach (O'Cathain, Croot, Sworn, et al., 2019) • Relevant theories and evidence	• The design team decided the self-efficacy theory, and BCT's for food and activity behaviour change key features of this resource	• This chapter • Chapter 4

	Population-centred approach (O'Cathain, Croot, Sworn, et al., 2019) • Bringing together groups including key stakeholders for diverse opinions on treatment	**Engagement of stakeholders** • Engagement of stakeholders via the TMG • Engagement of target population KTRs and transplant health care professionals through study two and PPI	• Chapter 4 and 6
	Digital Intervention development (Bradbury et al., 2014) • Determine the key features of the intervention, and acceptability from the target group perspective	**Determine key behaviours to target** • Group discussions with both the design and TMG teams decided that physical activity and healthy eating behaviours were the target behaviours for this intervention to address weight gain • The key behaviour change techniques to incorporate from the evidence base included self-monitoring and goal setting **Target group perspective** • Qualitative input study two and PPI to explore the context	• Throughout this thesis
Development and Evaluation	**Person-based approach (O'Cathain, Croot, Sworn, et al., 2019; Yardley, Morrison, et al., 2015)** • Target user group perspective is key to information evaluation and optimisation of the intervention • Think-aloud interviews and mixed methods research are recommended **Digital Development guidance (Bradbury et al., 2014)** • Think-aloud interviews and mixed methods are also referred to in the digital development guidance	**Think-aloud interviews to gather user-group perspective** • Think-aloud interviews were used, alongside semi-structured interviews in Study two on the prototype of the ExeRTiOn intervention • This ensured refinement was person-base from the KTR perspective (target user group) **Treatment modifications and optimisation** • The results of study two assisted optimisation and refinement of the online intervention in preparation for study two	• This chapter (study 2) • Chapter 4 • Chapters 6 and 7

	• Mixed methods research design for studies 3 and 4 allows for further refinement of the intervention with longitudinal use and testing of intervention in a 'real life' setting • The results from studies 3 and 4 revealed further refinement suggestions that could be completed in future research projects post PhD completion	
MRC framework approach (Theory and EB practice) (O'Cathain, Croot, Sworn, et al., 2019) • Mixed methods research to assess feasibility and acceptability • Starting testing in smaller samples before progressing to 'real-life' settings • Aim to optimise intervention in preparation for a full scale RCT **Digital Development guidance (Bradbury et al., 2014)** • NB these steps are also referenced in digital development approaches (Bradbury et al., 2014)	**Mixed methods throughout thesis** • Study 2- qualitative research to inform revisions • Studies 3 and 4- mixed methods feasibility RCT to allow for further refinement, feasibility and acceptability testing	• This chapter • Throughout this thesis • Chapter 4 • Chapter 6
Digital intervention development (Bradbury et al., 2014) • Development and refinement are iterative processes • Is important to use methods for prioritising changes to digital interventions such as the MoSCoW method	**MoSCoW method for revisions to the ExeRTiOn resource** • The MoSCoW (must have, should have, could have, would like to have) method (Kuhn, 2009) is often used by digital development teams • This method was used for refining intervention after qualitative evaluation in study two	• This chapter • Chapter 4
Mapping to the BCW (O'Cathain, Croot, Sworn, et al., 2019) • The behaviour change wheel (BCW) (Michie, Van Stralen, et al., 2011) is a systematic process for	**Mapping final intervention**	• This chapter • Chapter 6

	behavioural change interventions that can be used for design or evaluation.	• This project utilised known BCTs to influence PA and healthy eating behaviours (Michie, Ashford, et al., 2011) • The refined online intervention was retrospectively mapped to the BCW framework for evaluation after collecting data from studies 3 and 4	• Appendix F
Implementation and future Trials	**Person-based Approach (Yardley, Morrison, et al., 2015)** • The evaluation of the intervention using 'real life' settings and contexts. • It is likely that further modifications will be required **MRC framework approach (Theory and Evidence based practice)(O'Cathain, Croot, Sworn, et al., 2019)** • Effectiveness studies after feasibility testing in wider samples	**Post PhD Fellowship** • The data from the four empirical studies in this will provide rich insight into the feasibility and acceptability of the ExeRTiOn online intervention • Further evaluation, in other studies such as an effectiveness RCT will occur post PhD fellowship	• **Research to be conducted Post PhD Fellowship** • Chapter 7 (discussion) will offer suggestions for future research

Note. PPI= patient and public involvement, KTR= kidney transplant recipients, HCP= health care professionals, PA= physical activity, MRC= medical research council, TMG= trial management group, BCTs= behaviour change techniques, MoSCoW= prioritisation matrix for digital revisions, BCW= behaviour change wheel, RCT=randomised controlled trial

3.4.4 The ExeRTiOn online intervention content

The research fellow led the design, development and evaluation of the ExeRTiOn online intervention throughout the thesis. A renal dietitian (GD) drafted the dietitian content for some of the healthy eating specific sessions. All content of the website, including resources, functions and videos were collated and created by the research fellow with input from the design team. The research fellow scripted, directed and filmed all the educational videos included in the online resource and project managed the design, development and conducted the research studies. The research fellow led meetings with the design team, TMG and software company to gather various perspectives and sought approval for the intervention.

The ExeRTiOn prototype, and final version consisted of one welcome session, followed by 12-weekly sessions. Twelve-weeks was selected as the intervention duration to align with the duration of an existing commissioned face-to-face renal rehabilitation program (Greenwood et al., 2018; Greenwood et al., 2012). In addition, as presented in chapter 2, evidence for weight gain prevention interventions for KTRs within the first year of transplantation is lacking, the design team drew on the mixed methods work from a 12-week online intervention that was developed for people living with excess weight and obesity in the primary healthcare setting (Bradbury et al., 2015). Detailed screen grabs and descriptions of the ExeRTiOn online intervention are displayed in chapter 4. The key aspects of the ExeRTiOn online intervention are summarised briefly below.

Key aspects of the ExeRTiOn prototype included:

- Graphical displays of self-reported body weight and PA through weekly data imputation

- Design of a goal setting planning template that included the confidence and importance motivational interviewing rulers (Hall et al., 2012)
- Motivational interviewing principles (Miller & Rollnick, 2013)
- Educational videos by expert transplant HCPs and patients
- A collection of online resources for self-directed reading called the 'my library' tab
- The Generalised Physical Activity Questionnaire (The Department of Health, 2009) was built into every 4th session to capture self-reported PA levels
- A kidney-specific home exercise diary and log was created
- A secure two-way messaging from the study physiotherapist to the patient, and from the patient to the study physiotherapist allowed for remote monitoring and support
- The front-end (participant facing) website where participants could log in and complete sessions and message the physiotherapist
- The back end (physiotherapist facing) website where the study physiotherapist could review log in data and message participants

3.5 Study 2- Usability and Experience testing of the ExeRTiOn protype

Qualitative methods of data collection were essential to gather feedback on our ExeRTiOn prototype from our target user group (new KTRs). This ensured a person-base approach was applied, and revisions were driven by participant experiences and usability issues.

3.5.1 Methods and design

The aim of study two was to evaluate the usability and experience of the ExeRTiOn online intervention, designed to prevent weight gain in new KTRs. Individual think-aloud and semi-structured interviews were used with a purposive sample of new KTRs and kidney transplant HCPs. Think-aloud interviews were used to assess usability, which is defined as how easily one can use and interact with an online system without any formal training (Benbunan-Fich, 2001). Semi-structured interviews captured experiential data regarding thoughts and experiences using the online intervention, and also experiences post transplantation with regard to weight gain and PA. The think-aloud and semi-structured interviews provided complementary data to identify problems and inform revisions to the online resource (Bradbury et al., 2014). Ethical approval and the trial protocol can be found in Appendix B. Study 2 has been published in a peer reviewed publication (Castle, Greenwood, et al., 2020) (chapter 4). Methodology for this study will be briefly summarised in this section and will be expanded upon in chapter 4.

3.5.2 Recruitment and eligibility

KTR participants were eligible for the study if they had received a live or deceased donor kidney transplant within the past three months, were able to sign a written

consent form in English and had a BMI of 18.5 kilograms per metre squared (kg/m^2) or above. Exclusion criteria included an active pregnancy, unstable medical conditions such as angina, or a documented medical history of cognitive impairment impairing them from taking part in website testing. Participants were recruited using patient information sheets, a document summarising data security and privacy, and written consent forms. Refer to Appendix B for copies of all study documents and ethical approval.

3.5.3 Sampling

KTRs were purposively sampled for a range of age, genders, and ethnicities. HCP participants were recruited from a London NHS kidney transplant team in a UK renal unit. HCPs were purposively sampled to include the following professions (two kidney transplant nurse specialists, one nephrologist from a transplant clinic, one renal physiotherapist with knowledge of kidney transplant recipients, and two renal dietitians).

Think-aloud interviews produce large amounts of rich data. A sample of 5 participants has been shown to uncover 80% of usability problems and issues (Benbunan-Fich, 2001). Therefore, a purposive sample of 10 KTRs and 5 HCPs should provide sufficient rich data on usability and experiential issues to inform intervention refinement.

3.5.4 Study Personnel

All interviews were conducted by the research fellow (EC) who had experience and training in qualitative research and identified with the pragmatic worldview.

3.5.5 Data collection

Data were collected in a single study visit for each participant. All study visits were completed in a private research room, on an NHS secure computer. All interviews were audio recorded for transcription, alongside interviewer fieldnotes. Each KTR participant completed two think-aloud interviews, then a semi-structured interview. A standardised protocol was used (see chapter 4). The first think-aloud interview task was the same for each KTR, and the welcome package and session one was tested. Next, they completed an additional session (session 2 to 12) that was randomly allocated to each KTR participant. Following this, the KTR participants underwent a semi-structured interview to capture their experience with weight gain, PA and the online intervention prototype. Chapter 4 presents the topic guides utilised for the think-aloud and semi-structured interviews.

HCP participants were given a demonstration of the online intervention, then completed the first task of the think-aloud interviews as per the KTR participants. The HCP participants were then given the option to further explore the ExeRTiOn online intervention if they chose to. Immediately following this they completed semi-structured interview questions exploring their experiences with the ExeRTiOn online intervention, but also working with KTRs and weight gain.

3.5.6 Statistical analysis

All interview data were transcribed verbatim and analysed using inductive reflexive thematic analysis (Braun & Clarke, 2006). NVIVO © Version 12 for mac was used. Inductive reflexive thematic analysis allowed for the identification of patterns of meaning across the interview dataset, and ensured the results were data-driven, from our KTRs. The benefits of reflexive thematic analysis is that it is accessible to multi-

professional researchers, and can be used with a multiple of world-views (Braun, Clarke, & Weate, 2016) including pragmatism. Thematic analysis facilitates the identification of patterns in meaning in relation to questions regarding experience, behaviours and views (Braun et al., 2016), and aligned with the aims of this qualitative study. The 6 phases of thematic analysis by Braun and Clarke (2006) were utilised to analyse the qualitative data as demonstrated by Table 3.2 below.

Table 3-2 Thematic Analysis Steps

Braun and Clarke (2006) six stages of thematic analysis.	**Activities that occurred during each stage of reflexive thematic analysis**
1. Familiarisation of the data across the whole dataset	• Transcription of all audio recordings • Reading and re-reading all transcriptions • memo and initial thoughts written down • Reviewing of all the field diary notes taken during the interviews
2. Generation of codes	• Inductive codes were created from the dataset included interesting data- driven features that could be then built into themes/ subthemes etc.
3. Searching for themes	All transcripts and initial inductive codes were reviewed to search for patterns of meaning
4. Revision of themes	• Themes were reviewed individually but also against other themes • Transcripts and audio recordings were re-visited to ensure the themes were data-driven • Discussions took place with external qualitative expert (JG) to refine and revise themes • Thematic maps were devised and reviewed to link each theme to its corresponding sub-theme

5. Defining and naming the themes	• Thematic maps were revised (4 versions during this analysis) • Each theme was defined clearly and named to summarise its meaning
6. Producing the report	• Key examples for each of the final theme were selected • Relevant literature was searched and related to the research study • The report was published in an open access journal (See chapter 4)

Note. This table summarises information from Braun and Clarke's (2006) user guide to thematic analysis.

Reflexivity and rigour were achieved through memo notes, reflective journaling and discussions with an external qualitative researcher (JG) to ensure codes were grounded in the dataset.

3.6 Refinement of the ExeRTiOn online intervention

The results of study two facilitated revisions to the ExeRTiOn prototype based on the person-centred approach (Yardley, Morrison, et al., 2015), and digital healthcare intervention guidance (Bradbury et al., 2014). The MoSCoW method prioritisation tool was utilised to revise the ExeRTiOn online resource based on study 2 results, in preparation for the mixed methods feasibility RCT (studies 3 and 4). The MoSCoW method (Kuhn, 2009) stands for:

- 'Must have' changes are deemed to be essential changes to the functionality of the website/online product
- 'Should have' changes are not essential but important features
- 'Could have' changes include useful to have features that are dependent upon budget constraints
- 'Would like' to have features include changes that are not currently needed, but perhaps could be considered in future projects

This prioritisation tool is often used by software developers to prioritise refinements and discussion of these changes within the design team (Bradbury et al., 2014). It was selected to implement revisions to the ExeRTiOn online resource as it is a recognised and recommended tool to revise a digital intervention (Bradbury et al., 2014), it allowed for transparent reporting and justification for all the changes that were made, and aligned with the researchers pragmatic worldview. The MoSCoW tool allowed for the clear communication of considered refinements (based on study 2 results), as well as practical and pragmatic considerations of budget constraints associated with the revisions made to the ExeRTiOn online intervention. The refinement process of the ExeRTiOn 2 prototype, based on the results from study 2 are summarised in figure 3.2.

Figure 3-2 Flow chart summarising how MoSCoW method facilitated prioritisation of revisions to the ExeRTiOn online intervention

Note. MoSCoW method stands for must have, should have, could have and would like to have changes to the online product (Kuhn, 2009), Rx= intervention, TMG= trial management group and RCT= randomised controlled trial

The key ‘must have’ refinements to the ExeRTiOn online intervention are summarised below. These are discussed in further detail both in Chapters 4, and Appendix C. Key ‘must have’ revisions included:

- The session list on the home screen dashboard needed to be simplified
- Navigation was improved by adding buttons, making buttons larger, and making headings more prominent
- A frequently asked questions (FAQs) tab with further ‘how to’ video tutorials was added
    - This was implemented with input from our KTR members of the TMG
- The content from some of the longer videos (session 2, 4 and 10) was reduced to less than 10 minutes
- The copy wording was updated throughout based on specific participant feedback
- Support from the physiotherapist/ research fellow was included in the design of the feasibility RCT

3.7 Studies 3 and 4- The feasibility RCT and a nested qualitative evaluation

3.7.1 Study overview

Studies 3 and 4 assessed the feasibility and experience of conducting a mixed methods RCT using the revised ExeRTiOn online intervention (IG) in comparison to usual care (UC). This 12-month study was designed as a QUANT+ QUALI study (Creswell, Clark, Gutmann, & Hanson, 2003), where both aspects of the data collection are given equal priority to inform the overall research question (Yardley & Bishop, 2012). QUANT data collection was crucial to gather data on feasibility outcomes to inform future research projects (Objective 5a, chapter 1, section 1.3.2). QUALI research was

crucial to provide rich experiential data to answer objective 5b of this thesis (see chapter 1, section 1.3.2). The QUALI inquiry of interest was to explore the experience taking part in the research study, the consenting procedures, the study visits, the experience using the ExeRTiOn online intervention (IG), and the interactions with the study team. Both the UC and IG perspectives were important to explore the acceptability and feasibility to inform future research.

3.7.2 Study design

The feasibility RCT was a bi-centre, mixed methods, randomised controlled feasibility trial (registered www.clinicaltrials.gov, reference NCT03996551). UC was compared to the revised ExeRTiOn online (IG). Ethical approval was sought, and obtained, from the London Dulwich Research Ethics Committee (REC) (reference 19/LO/1138) on the 6th of August 2019. See Appendix D for the ethical approval letter, study protocol, patient information sheets, data security documents, and consent forms. The study opened for recruitment on the 3rd of September 2019 at King's College Hospital NHS Foundation Trust (KCH), and at Guy's at St Thomas' Hospital (GSTT) on the 19th of February 2020. On the 6th of August 2020 a substantial amendment (reference; SA01.ExeRTiOn2 study) was approved to cease further recruitment due to the 2019 novel coronavirus disease (COVD-19) pandemic. Please refer to chapter 5, and Appendix E. Figure 3.3 below outlines the participant flow of this 12-month study.

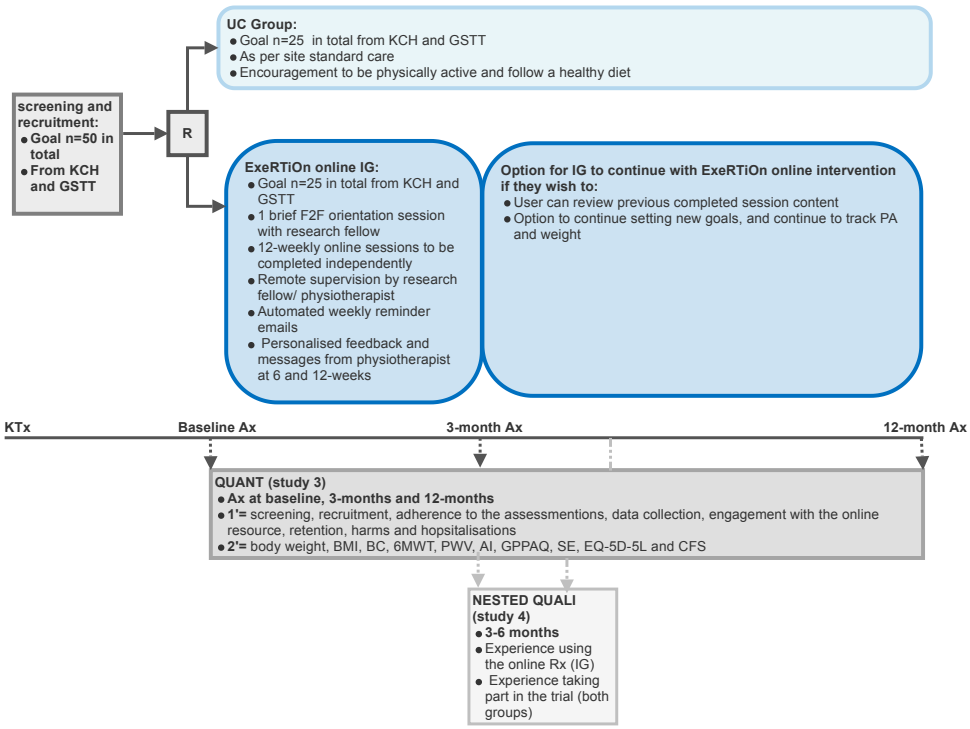


Figure 3-3 Study processes for the mixed methods feasibility RCT (studies 3 and 4)

Note. n=sample, KCH= King's College Hospital, GSTT= Guy's and St Thomas' Hospital, R= randomisation, UC= usual care, IG= intervention group, F2F= face-to-face, PA= physical activity, KTx=kidney transplantation, Ax= assessment, QUANT= quantitative outcomes,1'=primary outcomes, 2'=secondary outcomes, BMI= body mass index, BC= body composition, 6MWT= six-minute walk test, PWV= pulse wave velocity, AI=augmentation index, GPPAQ= General Practice Physical Activity Questionnaire, SE= self-efficacy questionnaire (healthy eating and exercise), EQ-5D-5L= EuroQol 5 Dimension 5 Level questionnaire, CFS=Chalder fatigue scale, QUALI= qualitative, Rx=intervention

3.7.3 Screening, recruitment, and participants

All potential participants were screened for eligibility criteria in the two London Renal units by the site principal investigators (EC and EA). Potential participants who met the eligibility criteria were given a patient information sheet, and a summary document of the data security and privacy policies in this study (see Appendix D). All study documents were reviewed and approved by the lead sponsor sites information governance officer, TMG, and ethical boards. If willing to take part in the study, written consent forms were completed. Participants were given a minimum of 24 hours (or at the participants convenience) to consider study participation. All potential participants were provided with the opportunity to ask questions. Detailed data on screening and consenting were taken as per the feasibility outcomes.

Participants were recruited using the following inclusion criteria:

- Over 18 years of age
- Able to provide written informed consent
- Participants had received a single organ kidney transplant from either a deceased or living donor within the past three months
- Access to a device with internet connection (either computer, laptop, smart phone or tablet)
- History of a BMI of greater than or equal to 18.5 kilograms per meter squared (kg/m^2). As highlighted in chapters 1 and 2, there is no recognised intervention to prevent weight gain in new KTRs, and KTRs living with and without obesity experience weight gain. Therefore, no upper limit to BMI was included in this study.

Participants were excluded if they were:

- Pregnant
- Had an unstable medical condition preventing them for participating in exercise (e.g., unstable angina)
- Had a significant cognitive impairment documented in medical records preventing them from engaging with the online intervention
- Or they were unable to complete the resource in English. This was due to limitations in financial costs of the software design. If feasibility and proof of concept, post-PhD studies to include different languages of the ExeRTiOn online resource

3.7.4 Feasibility outcomes

Primary outcomes considered trial feasibility. Feasibility outcome measures included: screening, recruitment, retention, engagement with the online intervention, adherence to study visits, safety and hospitalisations, the participants' experience of the intervention, and the participants' experience of taking part in the study. These feasibility outcomes are summarised in table 3.3.

Table 3-3 feasibility outcomes

Feasibility Outcomes	Data collected for outcome
Screening	• Number of participants screened per month • Proportion of screened potential participants that meet the inclusion criteria per month during the recruitment phase of the trial • Proportion of eligible people unwilling to participate with reasons given (e.g., work commitments, not interested)
Recruitment	• Number of participants recruited (of those who are assessed as eligible) per month • Time taken to recruit all participants for the study will be captured and reported • Recruitment rates will be compared between the two sites (KCH and GSTT)
Retention	• Number of participants retained in the trial per month • Reasons given for withdrawal • Retention rates will be compared between the two sites
Adherence to study visits	• Number and proportion of planned data collection visits that are completed in full will be compared across sites • Time taken to do each participant assessment • Acceptability of outcome measures (secondary outcomes)
Adherence levels to intervention	• Number of log-in attempts per participant for those in the intervention group • Average length of time spent on sessions (median or mean) for the intervention participants • Adherence rates to the intervention will be compared between the two sites
Adherence to study visits (all participants)	• Proportion of planned data collection visits that are completed in full length of time for the study visits • Time taken to do each participant assessment • Completion rates of study visits to allow assessment of the ability to collect measures for a definitive study (body weight, body mass index, body composition, quality of life, self-efficacy, fatigue, arterial stiffness and physical function). • Adherence to study visits will be compared between the two sites
Safety and hospitalisations	• Number of hospital admissions (non-elective, or elective who have had to stay in hospital > 24 hours), and reasons for admission • Expected and unexpected harms ○ Expected harms could include musculoskeletal injuries from performing exercises or slips and trips.
Qualitative experience of trial participation and intervention use	Semi-structured interviews to: • Evaluate experience and thoughts on the online intervention • The experiences participating in the trial

Note. KCH= King's College Hospital and GSTT= Guy's and St Thomas' Hospital.

3.7.5 Secondary outcomes (QUANT)

Secondary outcome data included anthropometric measures, BC, functional exercise capacity, self-reported PA, self-efficacy for physical exercise and healthy eating, quality of life, fatigue, and online intervention log in data.

3.7.5.1 Anthropometric measures

Anthropometric measures included body weight (measured in kilograms) waist circumference (measured in centimetres), hip circumference (measured in centimetres) and BMI (measured in kg/m^2). Change in body weight (kg) at each visit from baseline was also calculated and reported. Participants were asked to wear light, comfortable clothing to assessments, and body weight was assessed without shoes. Body weight was recorded at the start of each study visit, to the nearest 0.1 kilogram, using the Seca © (model 645) digital scales found in the renal unit at KCH (Seca, n.d.). Participant's height was measured in centimetres using a wall-mounted stadiometer. Waist circumference and hip circumferences were measured in standing, using tape measures and anatomical landmarks. The umbilicus was used as a reference point for the waist circumference, and the greater trochanter for the hip circumference.

3.7.5.2 Body Composition

Whilst body weight and BMI are readily reported in transplant recipients, it does not provide information on BC such as fat and muscle mass (Cupisti et al., 2018). BC is recommended as a good pre/post outcome in research settings (NICE, 2014b). Bio-electrical impediance analysis (BIA) was used to assess BC. BIA equipment calculates estimates of FM, LTM, hydration and BMI using whole-body electrical conduction. BC was estimated using the Fresenius BC Monitor (Fresenius BCM ©) (Gudivaka, Schoeller, Kushner, & Bolt, 1999; Macdonald et al., 2004), a CE marked device (NICE,

2017a). BIA has been found to provide accurate estimates of the gold standard dual-energy Xray-absorptiometry measurement of BC (Bellafronte et al., 2020). In addition, the BIA was selected to measure BC as it is small, non-invasive, has low participant burden, is portable, low cost and is readily available in clinical settings (Bellafronte et al., 2020; Cruz-Jentoft et al., 2019).

3.7.5.3 Functional Exercise Capacity

Functional exercise capacity was assessed using the six-minute walk test (6MWT). The 6MWT is a self-paced walking 'field test' where the participants is asked to walk for six minutes over a 30-meter measured shuttle. Participants are asked to continue to walk throughout the six minutes. It allows for stops to rest, however the six-minute count down timer continues. The 6MWT was initially created in 2002 by the American Thoracic Society as a sub-maximal measure of functional capacity for moderate to severe heart and lung disease conditions (American Thoracic Society, 2002). However, it has been used to measure functional status in other populations such as peripheral vascular disease, older patients, fibromyalgia and to assess functional status (American Thoracic Society, 2002). The 6MWT has also been used in ESKD participants (Kohl et al., 2012), and KTR participants (Anwar et al., 2014). A study in haemodialysis participants revealed that for every increase in 100 meters walked in the 6MWT, there was a 5% increase in survival (Kohl et al., 2012). For this feasibility RCT, standardised guidance and encouragement for the 6MWT were used (American Thoracic Society, 2002). The main outcome from the 6MWT is the six-meter walk distance (6MWD), which is the total distance recorded in meters achieved during six minutes.

3.7.5.4 Arterial Stiffness

As previously discussed in chapter 1, KTRs have an elevated CVR. Carotid-Femoral PWV is considered the gold standard measure of arterial stiffness (Van Bortel et al., 2012) and is a strong predictor of CVE, cardiovascular and all-cause mortality in KTRs (Dahle et al., 2015; Melilli et al., 2018). Research by the research fellow and research team prior to this thesis have shown favourable effects of aerobic and resistance exercise on PWV compared with usual care in KTRs (Greenwood et al., 2015; O'Connor et al., 2017). In the feasibility RCT (study 3) PWV and augmentation index (AI) were measured using the Vicorder system (Skidmore Industries, UK) using standardised procedures (Laurent et al., 2006) and calculations of arterial path length (Hickson et al., 2009). PWV and AI were measured 3 times per study visit, and then averaged for final scores of carotid-femoral PWV and AI.

3.7.5.5 Self-reported Physical Activity

Self-reported PA was measured by the General Practice Physical Activity Questionnaire (GPPAQ). The GPPAQ is a validated self-administered questionnaire (Physical Activity Policy Health Improvement Directorate, 2009; Physical Activity Policy Team Department of Health, 2012), which provided a short measure of PA levels (Wareham et al., 2003) with reasonable reliability (Ahmad et al., 2015). The GPPAQ has been validated in people living with CKD, with reported 96.6% sensitivity, 54.6% specificity, and 85.0% accuracy when compared to accelerometery (Wilkinson, Palmer, Gore, & Smith, 2020). In this study, the GPPAQ data were analysed as per the guidelines, and categorized using the physical activity index (PAI; active, moderately active, moderately inactive and inactive (The Department of Health, 2009).

3.7.5.6 Self-efficacy

Self-efficacy towards engaging with PA and healthy eating behaviours was assessed using the Nutrition Self-Efficacy Scale and the Physical Exercise Self-Efficacy Scales (Schwarzer & Renner, 2009). The higher someone's self-efficacy, the more likely they are to engage with the target behaviour(s) (Schwarzer & Renner, 2009). Both self-efficacy scales have been validated in a sample of 2549 participants (Renner, Knoll, & Schwarzer, 2000; Schwarzer & Renner, 2000). These scales have high internal consistency, the nutrition self-efficacy scale has a Cronbach's alpha of 0.87, and the exercise self-efficacy scale 0.88 (Schwarzer & Renner, 2009).

3.7.5.7 Health-related quality of life

Health-related quality of life was assessed by the European quality of life (EuroQol) 5 Dimension 5 Level (EQ-5D-5L) questionnaire (Devlin & Brooks, 2017). The questionnaire was initially developed in 1990 by the EuroQol Group as the EQ-5D-3L (EuroQol Research Foundation, 2019). It was revised to include five levels (EQ-5D-5L) to improve sensitivity (EuroQol Research Foundation, 2019). Permission was obtained to use this questionnaire. The EQ-5D-5L provides three data components: the EQ-5D-5L health state , a visual analogue scale (VAS) out of 100 (EQ-5D-5L VAS), and a specialised index value (EQ-5D-5L index value). The EQ-5D-5L health state includes five components (mobility, selfcare, usual activity, pain/discomfort, and anxiety and depression). Each component is self-rated from 1 to 5, with 1 being the lowest score, and 5 being the highest score (EuroQol Research Foundation, 2019). The EQ-5D-health state can then be converted into the single number EQ-5D-5L index value using region specific- values (EuroQol Research Foundation, 2021a). The EQ-5D-index value is highest at 1, and lowest at 0 with guidance stating it is

> Anchored at 1 (full health) and 0 (at a state as bad as being dead) (EuroQol Research Foundation, 2021c).

Reference values for the EQ-5D-5L-index have been published for England (Devlin, Shah, Feng, Mulhern, & van Hout, 2018). However, the NICE (2019) position statement presents concerns with the data quality and methodology of this UK study. Therefore, in study 3, the Van Hout et al (2012) method was used to calculate the EQ-5D-5L-index value as recommend by NICE (NICE, 2019). This calculation was completed using a downloadable calculator (EuroQol Research Foundation, 2021b). As per guidance, this study recorded and presented the EQ-5D-5L VAS, and index value for each participant at each timepoint (EuroQol Research Foundation, 2019). For the VAS component of the EQ-5D-5L, 100 indicates the best health imaginable, and 0 indicates the worse health imaginable (EuroQol Research Foundation, 2019). This questionnaire was used to measure self-reported quality of life as it is recommended by the NICE guidelines, is widely used in research internationally (Devlin & Brooks, 2017). It has been used in chronic disease groups and has been validated in KTRs as a measure of health status (Cleemput et al., 2004).

3.7.5.8 Self-reported fatigue

Fatigue was assessed by the Chalder Fatigue Scale (CFS) (Chalder et al., 1993). The scale contains eleven items, including two sub scales measuring the severity of physical (7 items) and mental fatigue (4 items). Each item is scored from 0 to 3, with 0 being better than usual and 3 being much worse than usual. The total score can range from 0 to 33, with higher scores representing greater levels of fatigue. This questionnaire has recently been used as a measure in people receiving renal dialysis therapy, with a Cronbach α of 0.91 demonstrating high internal reliability (Picariello, Moss-Morris, Macdougall, & Chilcot, 2016). Permission was sought to use this questionnaire.

3.7.5.9 Online intervention data

Additional online intervention data (IG only) were gathered throughout the study through the back-end physiotherapist website. These data included log in times, review of data entered into the online intervention such as goals, weight, PA and work sheets. The GPPAQ completed throughout the 12-week programme that was built into the online intervention to occur every forth session.

3.7.6 Clinical data collection

Clinical data collection included participant characteristics such as age, gender and ethnicity. Transplant data such as the donor type, number of previous transplants, episodes of acute rejection, immunosuppressant regime, hypertensive medication regime, diabetes history, diabetes management, CKD diagnosis and previous RRT (duration and type) were recorded from clinical records. Episodes of acute rejection were classified categorically (yes or no) from medical notes and biopsy reports occurring within the first three months of transplantation. The number of co-morbidities from clinical records was included. Comorbidities included a medical history of diabetes, hypertension, CVE, osteoarthritis, brain haemorrhage, CVR, cancer or respiratory disease. Resting heart rate measured in beats per minute (bpm) and resting blood pressure (mmHg) were recorded three times and averaged at each study visit (baseline, 3-months, and 12-month assessments).

eGFR was calculated using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation (measured in ml/ min/1.73m^2) (Levey et al., 2009). The CKD-EPI calculator (National Kidney Foundation, 2021) was used with serum creatinine blood results (μmol/L) from routine transplant clinic blood tests conducted on the same day as study visit. The CKD-EPI equation was used without the ethnicity correction factor as

this has been shown to lead to overestimation (Gama et al., 2020). The CKD-EPI equation was selected in preference to the Modification of Diet in Renal Disease (MDRD) method as it has been found to provide a more accurate and precise measure of eGFR (Levey et al., 2009).

3.7.7 QUALI interview data

Individual semi-structured interviews were chosen to collect qualitative data, as they would allow participants to freely report their experience for this individualised treatment. Semi-structured interviews allowed for flexibility and open questioning. Both topic guides were reviewed by the TMG, including PPI representation, refer to Appendix D.

Qualitative interviews were conducted between 3- and 6-months.The majority of the interviews were conducted by the research fellow (EC), with a proportion of the interviews were conducted by a master's research student (PD). Both interviewers had experience in conducting qualitative interviews. Training was conducted by EC with PD on the study protocol, topic guide and online intervention prior to conducting interviews. All interview data collected by PD (audio files and transcripts) were checked for accuracy and re-read by EC for data immersion in the early stages of reflective thematic analysis (Braun & Clarke, 2006). All analysis was performed by EC and refined with discussions with an external qualitative researcher (JG), and the supervisory team.

3.7.8 Study procedures

3.7.8.1 Randomisation

Participants were randomised with a computer generated list (Sealed Envelope Ltd, 2020), and allocated to either the 12-week ExeRTiOn online intervention or UC by a member of the research team. All participants were offered to complete study visits at baseline, 3-months, and 12-months. Due to the nature of the online intervention, participants and the research fellow were unable to be blinded to the provision of the intervention.

3.7.8.2 Usual care group

UC at both sites involved attendance at routine post kidney-transplant outpatient clinics. The minimum requirement of UC included the provision of the same leaflet on 'healthy eating after kidney transplantation' by a renal dietitian during the transplant inpatient stay, routine physiotherapy input during the surgical hospital admission on mobilisation post-surgery, and encouragement from the outpatient transplant clinic nephrologists and nurses to maintain a healthy diet and be physically active at routine post-transplant outpatient follow-up. In addition to the leaflet and routine education, UC at KCH (the primary site) also included up to two appointments with an outpatient renal physiotherapist. The first physiotherapy appointment was usually provided within the first two weeks of transplantation and involved education regarding post-operative precautions. Participants were instructed to avoid heavy lifting for six weeks, and to start with gradual progressive walking and functional mobility. The second appointment is at removal of ureteric stents (around five to eight weeks post-transplant), for exercise and PA counselling utilising motivational interviewing principles. UC at GSTT did not include any physiotherapy outpatient input. Both sites offer a renal rehabilitation face-to-face exercise service. Renal rehabilitation has been described in publications

(Greenwood et al., 2018; Greenwood et al., 2012). Briefly, renal rehabilitation consists of 12-weeks of physiotherapy-led exercise and education for 12 weeks, twice a week. However, this renal rehabilitation service is for all patients across the CKD trajectory and is not transplant specific. Renal rehabilitation is not routine clinical practice for new KTRs at either centre, therefore the renal rehabilitation programme is seen as an adjunct, not UC at both centres.

3.7.8.3 The ExeRTiOn intervention group

The ExeRTiOn online intervention design and development has been previously described. Further detail with screen grabs can be found in chapter 4. This trial involved the revised version of the ExeRTiOn online intervention. The retrospective mapping of the ExeRTiOn online resource to the BCW and the BCTTv1 is presented in chapter 6 and Appendix F. Participants who were randomised to the IG were able to independently log-on to any internet compatible device at any time of the day. At the start of this intervention, participants received a brief face-to-face session with the research fellow/physiotherapist to orientate participants to the online-resource content, features and functionality. The participants then completed the 12-weekly sessions independently, with remote monitoring by the research fellow. They also received two personalised messages of encouragement from the research fellow at 6- and 12-weeks. Messages were personalised from standardised templates dependant on the change in weight outcome (increase, decrease or maintenance of body weight) and the participant's individual PA data entered into the online intervention (refer to study protocol, Appendix D). If a participant had not logged in two weeks in a row, the research fellow would send a personalised secure message to the participant via the online intervention (see study protocol, Appendix D).

Each of the 12-weekly online sessions took approximately twenty minutes to complete. Sessions were locked until the previous session was completed, ensuring that sessions were completed in the set numerical order. Only one session could be completed over a seven-day period running from Monday to Sunday. Each session involved participants entering their weight (either measured at home or in transplant clinic) and PA (self-reported in minutes per week), watching a brief educational video by a specialist HCP and/or KTR, completing an activity, reviewing a summary page and then setting a goal. Once a session was completed, and the data entry fields for the individual interactive activities were locked, the participants could revisit the completed content at a later date if they wish to. After completion of the 12-week programme, participants were able to review any completed content, continue with tracking of PA and weight, and use the goal setting functions if they wished to do so (from week twelve to the end of the trial at the 12-month assessment).

The research fellow could download weekly reports from the back-end website. This included session log in times, goals, PA and weight tracking, GPPAQ scores, and free text entered from the session interactive activities. The back-end website also allowed the research fellow to use the two-way secure messaging system where the participant and research fellow/physiotherapist interacted within the website with encrypted messaging. The participants interactions with the intervention, and physiotherapist are summarised in the communications diagram (figure 3.4) on the following page.

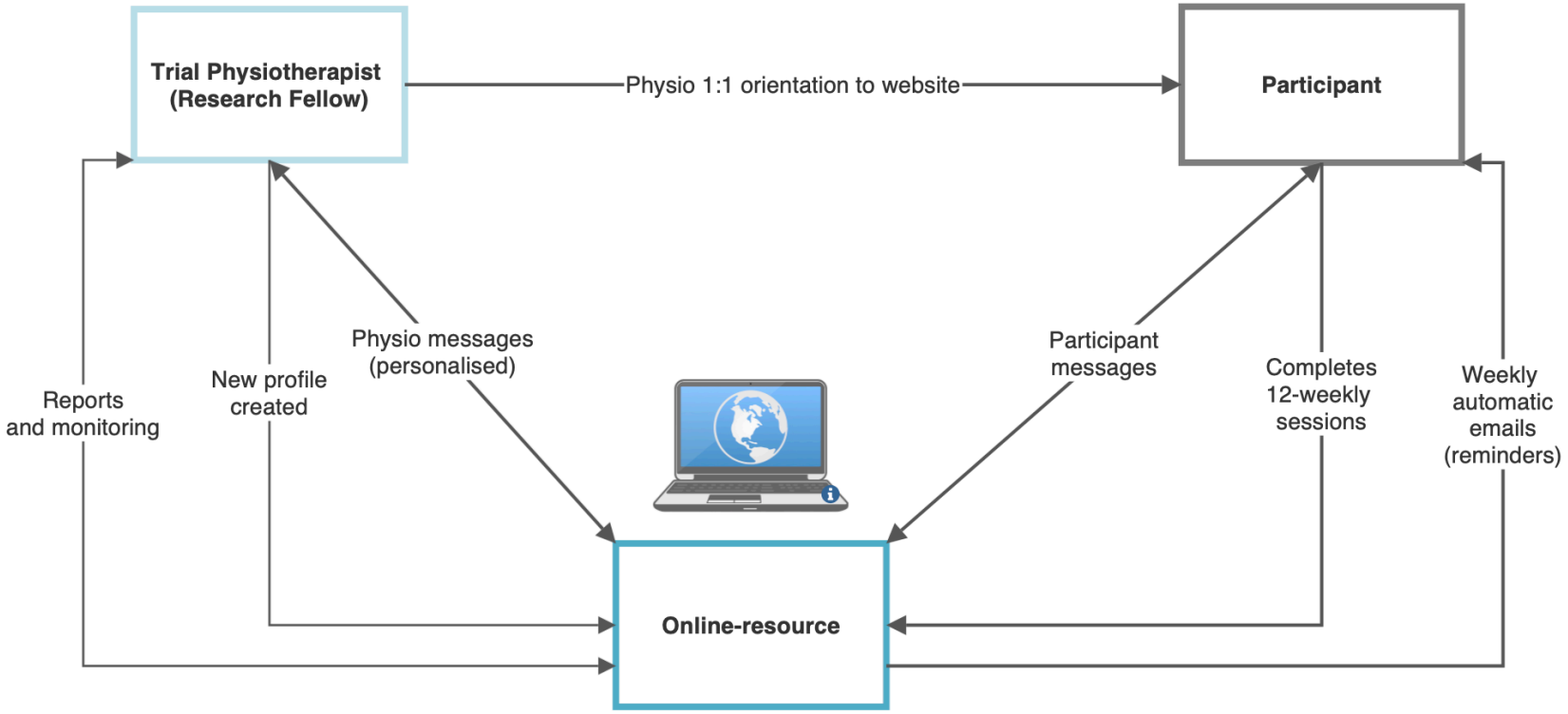


Figure 3-4 Interactions between the physiotherapist, participant and online intervention

Note. The physiotherapist created a new account for the participant and provided a brief 1:1 orientation session with the participant at the end of the baseline Assessment. All other intervention encounters are facilitated virtually throughout the online intervention. The participants completed the 12-weekly sessions independently on any internet compatible device. This includes a secure two-way message function between the participant and research fellow via the online intervention. The research fellow was able to monitor progress and download progress reports

3.7.8.4 Study visits

Secondary outcomes were assessed at three study visits (baseline, 3-months, and 12-months post randomisation). Baseline assessment occurred within the first three months of kidney transplantation, after the removal of the uretic stent. All outcomes were assessed on the same day in the same order. A window of flexibility of plus or minus seven days was allowed for the study visits. Any deviations in protocol were documented as file notes.

All assessments took place in the National Institute for Health Research (NIHR) Clinical Research Facility (CRF) laboratory at KCH. To minimise patient burden, where possible, study visits were booked for when participants were already attending the hospital site for routine clinical appointments. Participants were offered reimbursed travel fees (if required), and all participants were provided with a one-off inconvenience fee of £30 for taking part in the study. If participants withdrew from the study, reasons for doing so were recorded if participants were willing to disclose this information.

3.7.8.5 Study Personnel/ Professionals

The research fellow monitoring the online intervention, and providing feedback, was an experienced Renal Specialist Physiotherapist. To minimise allocation bias, randomisation was computer-generated by a separate member of the research team. EC had received training on motivational interviewing techniques (4 courses, which included a course to be a trainer in motivation interviewing completed prior to this PhD). In addition, the research fellow has over nine years' experience in exercise and PA prescription, and weight management in people living with CKD, including KTRs. The PhD Fellow completed training on QUALI and QUANT methods during a master's course (MRes). During this fellowship, the research fellow completed additional

training in QUALI data collection and analysis through the Social Research Association.

3.7.8.6 Data Management

Personal data was appropriately filed and stored securely as per the study site guidance, the study protocol, and the data security document (see Appendix D). All paper data were stored in locked filing cabinets and will be kept for five years. Electronic data and spreadsheets were stored on a private secured drive and password protected with limited access as per the hospital policy. All patient identifiable material was anonymised in place of trial ID numbers. Online intervention data from the intervention participants, was accessed on trust computers, was password protected, and had limited access (EC or SG only). The data from the ExeRTiOn online intervention was held in an encrypted state in line with NHS and GDPR policies. See data security document (Appendix D) for further details.

3.7.9 Sample size

3.7.9.1 Sample size for study 3 (feasibility RCT)

According to guidance feasibility studies should ask:

> Whether something can be done, should we proceed with it, and if so how (NIHR, 2021a).

As the primary aim of this study was to assess the feasibility of conducting the trial (screening, recruitment, adherence, capture adverse events, assess suitability of outcomes, capture experiences using the revised ExeRTiOn intervention and experiences taking part in the trial), the Consolidated Standards of Reporting Trials (CONSORT) guidelines for feasibility trials were followed (Eldridge, Chan, et al., 2016). Efficacy testing, formal hypothesis testing, primary outcome testing and power calculations are not recommended in feasibility trials (Eldridge, Chan, et al., 2016;

NIHR, 2019). Due to these guidelines, and consultation with an external statistician (RP), no formal power calculation or statistical significance testing was performed. Summary statistics were presented using either; means or medians, standard deviations (SDs) or interquartile ranges (IQRs) or proportions as appropriate were used with two-side 95% confidence intervals.

The initial target sample for this study was 50 participants across two sites. Refer to Appendix D for the study protocol. A sample size between 24 and 50 has been recommended to estimate SDs for use in a sample size calculation in a future study following the feasibility trial (Hooper, n.d.; Julious, 2005; Sim & Lewis, 2012). Achieving a target sample of 50 new KTRs would therefore facilitate a power calculation to be completed in preparation for a definitive trial. Changes in the final sample size due to COVID-19 will be presented in Chapter's 5 and 6.

3.7.9.2 Qualitative interview sampling (study 4)

All qualitative interview participants were purposively sampled (Patton, 2002) from the wider feasibility RCT sample. Participants from a range of ages, genders, treatment groups, adherence rates (IG), and were offered to take part in the additional individual qualitative interviews. Individual semi-structured interviews were used to capture experience of the online intervention, and the experience participating in the trial. A three to six months' time frame was chosen for the interviews to allow for adequate reporting of the study experience, and to minimise recall bias for those randomised to the ExeRTiOn online IG. These interviews were conducted con-currently to QUANT data collection.

Qualitative sample size and data saturation are contentious issues and often debated (Sim, Saunders, Waterfield, & Kingstone, 2018). Sim et al (2018) and Braun and Clarke (2019b) argue that the concept of data saturation does no align with inductive reflexive thematic analysis, as there is no fixed point of data saturation. The analysis is influenced by the researcher and the interpretative decisions made during the analysis process (Braun & Clarke, 2019b). The concept of 'information power', and that sample size will be influenced by the study aim, specificity of the sample, the existence of theory, the quality of communication between the researcher and participant, and the analysis strategy are acknowledged (Malterud, Siersma, & Guassora, 2016). For practicality, it is acknowledged that an upper limit of sample size is necessary for grant applications, but the exact sample size will be dependent on the qualitative analysis process itself (Sim et al., 2018). Francis et al. (2010) suggest a prior set sample of 10 interviews, with a further 3 interviews to assess no new themes are present could be an adequate sample size to indicate data saturation in theory-based interviews. The information power model (Malterud et al., 2016), and the importance of purposive sampling (Francis et al., 2010) were pragmatically applied to this study. The phenomenon of interest to investigate the experience using the ExeRTiOn online intervention and taking part in the study were very specific, participants were sampled purposively to review a breadth of experience in the trial and the interactions with the intervention, the main researcher has experience with qualitative techniques and communication techniques, and an inductive reflexive thematic analysis was used. Therefore, prior analysis estimated sample size of 5-10 rich interviews was set to uncover common patterns and themes from across the dataset. This estimated sample size was selected as it would allow for the exploration of experience regarding the online intervention, and participation in the trial. The final qualitative sample size was informed by the inductive reflexive analysis,

information power, and the meaning and themes derived from the analysis rather than a positivists approach describing the frequency of themes (Braun & Clarke, 2019b).

3.7.10 Statistical analysis

3.7.10.1 QUANT statistical analysis plan (study 3)

As this is a feasibility trial, no statistical significance testing was performed. Confidence intervals will be two sided at the 95% confidence level. Data from multiple sources (feasibility outcomes, assessment outcomes and qualitative interviews) were triangulated.

Participant characteristics such as age, gender, ethnicity, age of transplant, type of donor, past medical history, time on dialysis pre transplantation of those recruited to each group was described using summary statistics; means and SDs or proportions as appropriate.

Feasibility outcome analysis for the IG included:

- Screening, recruitment, retention and adherence rates were calculated and presented as proportions with 95% confidence intervals
- Reasons for declining to take part in the study were reported descriptively
- Reasons for withdrawal from the study were also reported descriptively
- Length of time to recruit the target sample was described using either by means and SDs, or median and IQRs
- Length of time taken to complete the assessments were described either by means and SDs, or median and IQRs
- Assessment outcomes such as body weight, BMI, BC, waist and hip circumference, 6MWT, PWV, AI, GPPAQ, EQ-5D-5L, Self-efficacy and CFS

were described either by means and SDs, or median and IQRs depending on data distribution

- Completion rates of all secondary outcomes were gathered
- Percentage of completed study visits, and proportion of assessment outcomes recorded for each study visit were calculated
- Mean time taken to complete the study visits, with confidence intervals were calculated
- Hospital admissions and reasons were explored descriptively
    - Proportions and confidence intervals will be calculated for hospitalisations, history of transplant biopsies, and diagnosis of PTDM during the trial
- Description of participants interaction with the online-resource (log-in times, interactions with the research fellow) were described either by means and SDs, or median and IQRs ranges
- Mean log-in time for the online intervention (IG) alongside confidence intervals were calculated
- Interactions with the research fellow through the trial online intervention were reported descriptively

Feasibility outcome analysis for the UC group included:

- Screening, recruitment, retention and adherence rates were calculated and presented as proportions with 95% confidence intervals
- Reasons for declining to take part in the study were reported descriptively
- Reason for withdrawal from the study were reported descriptively

- Length of time to recruit the participants were described either by means and SDs, or median and IQRs ranges
- Length of time taken to complete the assessments were described either by means and SDs, or median and IQRs ranges
- Assessment outcomes such as body weight, BMI, BC, waist and hip circumference, 6MWT, PWV, AI, GPPAQ, EQ-5D-5L, Self-efficacy and CFS were described by either by means and SDs, or median and IQRs ranges.
- Completion rates of all outcomes were gathered
- Percentage of completed study visits, and the proportion of assessment outcomes recorded for each study visit were calculated
- The mean time taken to complete the study visits, with confidence intervals was calculated
- Hospital admissions and reasons were explored descriptively
    - Proportions and confidence intervals were calculated for hospitalisations, history of transplant biopsies, and history of new onset of diabetes after transplant (PTDM).

Further quantitative analysis included calculation of changes scores, analysis of questionnaire data, change in medication use and associations. Change scores were calculated for body weight, BMI and BC. Data series line graphs for each group, including individual and summary (mean or median, with confidence intervals or IQRs ranges) were completed for body weight data across the 12-month study. Questionnaire data was calculated as per questionnaire guidance and summarised using either by means and SDs, or median and IQRs ranges.

Scatter plots were performed to explore correlations between the number of completed online sessions (IG) and body weight at 12-months, the number of completed online session (IG) and self-efficacy scales at 12-months, and body weight at 12-months with self-efficacy scales. For medical management, the total daily dose of immunosuppressant medications (tacrolimus, prednisolone and mycophenolate) was summarised using either means and SDs or median and IQRs ranges. Diagnoses of hypertension, type 1 diabetes, type 2 diabetes and PTDM were recorded and were summarised using descriptive statistics.

3.7.10.2 QUALI analysis plan

As little research has been conducted to date in online interventions to prevent weight gain in new KTRs (chapters 1 and 2), it was felt that an inductive, exploratory qualitative analysis, that accurately reflected the participants experiences was needed. All interviews were transcribed verbatim. Transcripts were imported in NVIVO for MAC © version 12 for data analysis. The analysis was conducted by the research fellow (EC) using a Reflexive Thematic Analysis (Braun & Clarke, 2006, 2019a), from a pragmatic philosophical standpoint (Yardley & Bishop, 2012). The six-stages of inductive reflexive thematic analysis (Braun & Clarke, 2006) as summarised previously in Table 3.2 were utilised in this study. Input into the analysis was provided by the supervision team (SG, JC and KB), and an experienced external qualitative researcher (JG) not directly involved in the intervention design. The principle of information power (Malterud et al., 2016) was used in this qualitative analysis. After initial coding the first three transcripts were checked for data richness. Use of reflective journaling, memos and discussions of themes and codes with an external research (JG) ensured the themes remained data driven.

3.7.10.3 Converging quantitative and qualitative data analysis

QUALI and QUANT data collection and analysis occurred separately and simultaneously. Convergence of QUALI and QUANT data allows for a richer understanding of the research question (Bazeley, 2009). Therefore, in this study, after individual analyses, QUALI and QUANT datasets were converged to enrich understanding of the feasibility and acceptability of the ExeRTiOn online intervention (studies 3 and 4 results will be presented in chapter 6). Equal weight was given to the QUANT and QUALI data in the integrated mixed methods analysis (Yardley & Bishop, 2012), and both data sets were from the same philosophical standpoint- pragmatism (Bazeley, 2009). Convergence of the QUANT and QUALI data sets was performed using triangulation, and tabulation to seek examples of convergence, complementary issues, or discrepancies (O'Cathain, Murphy, & Nicholl, 2010). This allowed for the identification of meta-themes (O'Cathain et al., 2010) to emerge across the whole mixed methods dataset. By combining the datasets, a rich and complete understanding of the experiences and feasibility of the study and the online intervention was achieved. The results of the QUANT, QUALI, and mixed methods integrated analysis including joint table displays will be presented in chapter 6.

3.7.11 Progression criteria

As studies 3 and 4 assess the feasibility, and experience of performing a RCT using the revised online intervention, progression criteria was set by the TMG prior to commencement of the feasibility RCT. The TMG included KTR representation and a statistician consultant. It is summarised in table 3.4 below.

Table 3-4 Progression criteria

Criteria	Pre-set cut offs
Screening of potential participants	• ≥ 50% deemed eligible approached to do the study consider progression to a definitive trial • If less than 50% and no significant valid reasons provided, consider not progressing to a further study
Recruitment rate	• ≥50% consider progression to a definitive trial • 40-49% TMG to discuss trial, and if valid modifiable reasons identified, the study may progress • ≤30% and there are no significant valid reasons provided, the study will not progress to a definitive trial
Retention rate at 12-months	• ≥ 60% progress research • 50-59% discuss with TMG. If valid reasons identified, the study may progress • ≤ 40% do not consider further research
Intervention adherence	• ≥ 60% of the intervention completed (≥ 7 out of the 12 sessions) • If less than 60% adherence, with no valid reasons from discussions with the TMG, the study may not progress
Safety and hospitalisations	• Capture and report any harms e.g., Slips/ trips • Capture and report unplanned hospitalisations • Capture and report any associated adverse events

Note. TMG= trial management group

3.8 Chapter summary

This thesis aimed to address an evidence gap by evaluating the usability, acceptability and feasibility of a bespoke online intervention for new KTRs. Mixed methods design was used, alongside a pragmatic philosophical standpoint. The results of the four empirical studies allowed for the design, development and evaluation of the ExeRTiOn online intervention. The updated thesis processes diagram below (figure 3.5) summarises the design of the online intervention, the refinement of the online intervention, the key data collection processes of studies 1,2, 3 and 4, the mixed methods approach, and the convergent design of the QUALI and QUANT datasets.

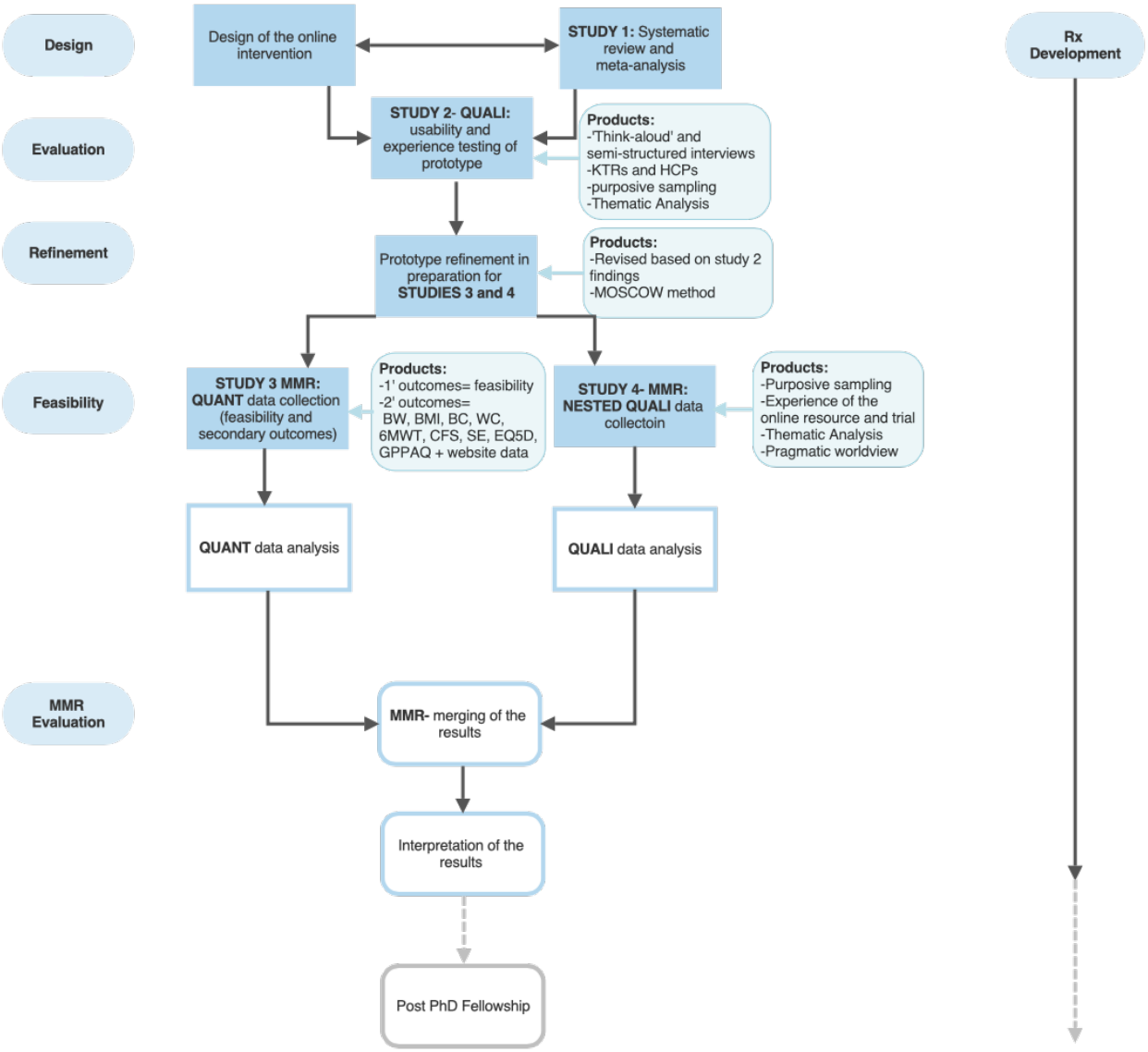


Figure 3-5 Updated thesis processes diagram to demonstrate methods

Note. The thesis process diagram has been updated the general methods the design of the ExeRTiOn online intervention, study 2, the refinement of the online intervention, study 3 and study 4. Products of each of these methodological stages are depicted by the additional rounded 'product' squares. This figure depicts how the 4 empirical studies in this Thesis align with the MRC framework, and are centred around views of the target end-user group (new KTRs).

This figure was designed based on a combination of the convergent mixed-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

QUALI= qualitative, QUANT=quantitative, MMR= mixed methods research, Rx=intervention, KTRs= kidney transplant recipients, HCPs= healthcare professionals, MoSCoW= must have, should have ,could have and would like to have changes, BW= body weight, BMI= body mass index, BC= body composition, WC= waist circumference, 6WMT= six-minute walk test, CFS= Chalder fatigue scale, SE= self-efficacy and EQ5D= EuroQol 5 domain.

Chapter 4 Study 2- assessment of the usability and experience of the ExeRTiOn online intervention prototype

4.1 Chapter overview

This chapter is dedicated to a peer-review open-access publication that summarised study 2 and focused on the first aim of the thesis (to create an online intervention to address weight gain), and objectives two to four. Engagement with the target-user group (new KTRs) was essential when using the person-centred approach (Yardley, Ainsworth, et al., 2015b). Qualitative research methodology has been previously described in the methods chapter. This chapter reports semi-structured and think-aloud interviews of KTRs and transplant HCPs to assess the usability, functionality and experience of the prototype online intervention.

4.2 Publication reference

This chapter is published in the following article:

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4.3 Published article

START OF PUBLISHED ARTICLE on next page

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Usability and experience testing to refine an online intervention to prevent weight gain in new kidney transplant recipients

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Objectives. Weight gain in the first year following kidney transplantation increases the risk of adverse health outcomes. Currently, there is no recognized intervention available to prevent weight gain after kidney transplantation. An online kidney transplant-specific resource, entitled Exercise in Renal Transplant Online (ExeRTiOn), has been co-created by a multi-professional team, including patients, to assist with weight prevention. This study aimed to evaluate patient and health care professional usability and experience of the ExeRTiOn online resource.

Design. Qualitative study utilizing 'Think-Aloud' and semi-structured interviews.

Methods. Participants (n = 17) were purposively sampled to include new kidney transplant recipients (n = 11) and transplant health care professionals (n = 6). Kidney transplant recipient participants were from a spread of physical activity levels based on scores from the General Practice Physical Activity Questionnaire (GPPAQ). 'Think-Aloud' interviews assessed the usability of ExeRTiOn. Semi-structured interviews explored participants' experience of ExeRTiOn, weight gain, and physical activity. The data set were analysed thematically. Participant characteristics, including login data and self-reported body weight, were collected.

Results. Data analyses identified valued intervention content and usability aspects which were summarized by two themes. The first theme 'You need to know how to manage yourself' included subthemes: (1) the resource filled a guidance gap, (2) expert patient content resonated, and (3) the importance of goal setting and monitoring progress. The second theme 'room for improvement' included subthemes: (2) web support and (2) content and operational change suggestions.

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Conclusions. Results have allowed for identification of potential areas for resource refinement. This has facilitated iterative enhancement of ExeRTiOn in preparation for a randomized controlled feasibility trial.

Statement of contribution

What is already known on this subject?

- Significant weight gain in the first year post-kidney transplantation increases the risk of adverse health outcomes, such as graft failure
- Weight gain remains an issue for kidney transplant recipients despite current advice on diet and exercise regimes
- Online interventions for weight loss in the overweight and obese populations have shown clinically important changes in body weight

What does this study add?

- Reports critical experiential and usability data for a novel online kidney transplant-specific weight gain prevention intervention
- Supports the use of goal setting and self-monitoring for promoting healthy physical activity and nutrition behaviour

Background

Post-kidney transplant weight gain

Despite the benefits of kidney transplantation for end-stage kidney disease (Ersoy, Ersoy, & Yildiz, 2012), Kidney Transplant Recipients (KTRs) are at risk of post-transplant diabetes (Baker, Mark, Patel, Stevens, & Palmer, 2017), coronary arterial disease (Baker *et al*., 2017), post-transplant hypertension (Ward, 2009), and significant weight gain (Friedman, Miskulin, Rosenburg, & Levey, 2003). Weight gain within the first year of receiving a kidney transplant is of clinical interest. One third of new KTRs experience post-transplant weight gain (Glicklich & Mustafa, 2019). Weight gain within the first year of greater than 5% is associated with a threefold increase in kidney graft loss (Ducloux, Kazory, Simula-Faivre, & Chalopin, 2005). Furthermore, weight gain of greater than 15% is associated with increased non-kidney related mortality within 10 years (Vega, Huidobro, De La Barra, & Haro, 2015). Therefore, interventions should target weight gain as a potentially modifiable risk factor for new KTRs (Henggeler *et al*., 2018).

Post-kidney transplant weight gain is multifactorial and may be influenced by increased appetite (Cashion *et al*., 2014), which can be further exacerbated by immunosuppressant medications (Aksoy, 2016), altered eating behaviours associated with the lifting of dialysis dietary restrictions (Stanfill, Bloodworth, & Cashion, 2012), reduced functional capacity due to preceding uremic myopathy (Koufaki, Greenwood, Macdougall, & Mercer, 2013), and muscle atrophy (Greenwood *et al*., 2015; Van Den Ham et al., 2005). In addition, KTRs do not reach the level of physical activity of age-matched healthy controls (Nielens *et al*., 2001). Qualitative reports have identified medication use, fear of injuring the new kidney, and the burden of other health problems as barriers to maintaining a healthy weight post-kidney transplantation (Stanfill *et al*., 2012). KTRs report early support services are desperately needed (Stanfill *et al*., 2012).

A systematic review and qualitative synthesis (n = 1,238 KTRs) evaluating the challenges and motivations towards self-management in KTRs concluded that enhancing self-efficacy, and providing an opportunity for social accountability, were motivators for self-management (Jamieson *et al*., 2016). Inconsistent and vague education from

clinicians, fear of graft rejection, medical side effects, and struggling to reverse behaviours established whilst on dialysis were identified as potential barriers (Jamieson *et al*., 2016). Fear of injuring the new kidney has also been associated with low self-efficacy (Zelle *et al*., 2016). These studies suggest that current KTR patient information needs are inadequately addressed. Early interventions to promote self-management and enhance self-efficacy for KTRs are warranted.

Access to physiotherapists and dieticians for overweight and obese people living with CKD is variable across the globe (Chan & Soucisse, 2016; Orazio, Murray, & Campbell, 2012; Stenvinkel, Ikizler, Mallamaci, & Zoccali, 2013). KTRs are not routinely offered weight management interventions in the UK. Attending multiple and frequent hospital appointments post-transplantation can be 'exhausting' (Jamieson *et al*., 2016). This can be exacerbated by return to work pressures and the aggregated travel burden to and from hospital, which makes attendance to additional face-to-face rehabilitation services challenging (Greenwood *et al*., 2015). Online interventions provide a possible solution to enhance care and reduce patient burden.

Weight gain prevention interventions

There is currently no universally accepted weight gain prevention intervention for new KTRs. Two randomized controlled trials (RCT's) have evaluated the effect of complex interventions on weight gain in KTRs (Henggeler *et al*., 2018; Tzvetanov *et al*., 2014). Henggeler *et al*. (2018) reported no significant difference in weight gain at 6 months, when comparing intensive nutrition support and exercise prescription to standard care. However, the overall study cohort gained less than 5% body weight in the first year, which is of clinical significance. This finding could be partially explained by the high standard of care offered in this study, which exceeds UK clinical practice for KTRs. Tzvetanov *et al*. (2014) showed no significant between-group difference in body mass index (BMI) when comparing 12 months of exercise and nutrition counselling to usual care in obese KTRs. A RCT compared the effects of 6 months of face-to-face nutrition counselling and physical activity by a renal dietician, to usual care on insulin sensitivity in new KTRs (Kuningas *et al*., 2019). Whilst there was no change in insulin sensitivity, the authors reported a significant mean between-group difference in body weight over the 6-month study (−2.47 kg [−4.01 to −0.92]; Kuningas *et al*., 2019).

Whilst no evidence exists for online interventions to prevent weight gain for KTRs, research from the obese and overweight literature suggests that online behavioural weight management interventions can help regulate food intake and modify activity, leading to clinically meaningful weight loss (Little *et al*., 2017; Neve, Morgan, Jones, & Collins, 2010). Online resources are likely to require personalized feedback and support to achieve statistically and clinically significant weight reduction (Sherrington *et al*., 2016). Research investigating online interventions to support KTRs is needed.

Design of the ExeRTiOn resource

A Patient and Public Involvement (PPI) exercise conducted at the authors Renal Unit, revealed that KTRs had difficulty accessing face-to-face weight management clinic services, and would value an online resource to help support them to adopt a healthy lifestyle after transplantation (Greenwood, 2015). This PPI exercise identified KTRs were connected with online services, and readily use 'PatientView' to track their blood results from home. PatientView is presently used by 90% of UK renal units (The Renal

Association, 2020). The authors felt that a reactive website would be more practical than a mobile application for this study. This would allow users to engage with the research from multiple Internet-compatible devices, and also reduce costs associated with mobile phone application updates. This PPI led to the inception of an online resource, and an appreciation of its existing context.

An online kidney transplant-specific resource, entitled Exercise in renal transplant online (ExeRTiOn) was designed by the research team, comprising of; four expert KTR patients, a psychologist, two renal physiotherapists, two renal dieticians, two renal specialist nurses, a nephrologist involved in kidney transplantation care, and input from a software company (SPIKA Ltd, London, UK). The KTR patient experts contributing to ExeRTiOn were volunteers from a UK renal unit from a range of different ages, genders, and ethnicities. They identified pertinent topics to be covered by ExeRTiOn and contributed to the content including patient quotes and tips. The physiotherapists and dieticians in the team were able to draw on experiences from an established face-to-face National Health Service (NHS) renal weight management clinic (Cook, MacLaughlin, & Macdougall, 2008; MacLaughlin *et al.*, 2012).

Design of the ExeRTiOn online resource, like the design and development of any other digital or complex intervention was non-linear, iterative and complex (Blandford, 2019; Bradbury, Watts, Arden-Close, Yardley, & Lewith, 2014; O'Cathain *et al.*, 2019). ExeRTiOn was designed pragmatically and utilized a combination approach intervention design (O'Cathain *et al.*, 2019). The initial design was informed by; input from our target population (KTRs), clinical experience from the renal weight management service, the self-efficacy theory (Bandura, 1977), recognized Behaviour Change Techniques (BCTs) to promote healthy eating and physical activity (Michie, Ashford, et al., 2011), and guidance for digital intervention development (Bradbury *et al.*, 2014; The LifeGuide Team, 2013; Yardley *et al.*, 2012).

Consensus meetings amongst the team identified relevant BCTs from the CALO-RE taxonomy to support healthy physical activity and diet (Michie, Ashford, et al., 2011) for the inclusion in the ExeRTiOn resource. These included the following: the setting and revision of goals, action planning, prompting of self-monitoring of physical activity and weight, motivational interviewing such as confidence and importance rulers (Hall, Gibbie, & Lubman, 2012), and education from clinical experts and patients (Michie, Ashford, et al., 2011). The online resource drew on Bandura's principle of self-efficacy, which can be defined as an individual's own belief in their capacity to perform a certain behaviour (Bandura & Adams, 1977). It was anticipated that the ExeRTiOn resource would enhance self-efficacy of healthy eating and physical activity behaviours.

The research team acknowledge that future feasibility testing and process evaluation are needed to further develop and evaluate the ExeRTiOn resource (Bradbury *et al.*, 2014; Moore *et al.*, 2015). Therefore, the results from this current study will inform a mixed-methods feasibility RCT where half the participants will receive the revised ExeRTiOn resource with monitoring from a study physiotherapist.

Study aims

Early involvement with key stakeholders and target users is crucial to uncover usability and experience, and to inform development and refinement of digital health care interventions (Blandford, 2019; Bradbury *et al.*, 2014). Therefore, this study aimed to evaluate the usability (functionality, navigation, and interactivity) of the patient-facing ExeRTiOn online resource, report participant experience using ExeRTiOn, and identify

emergent themes and valued content of ExeRTiOn in a sample of new KTRs and health care professionals (HCPs). This was achieved through think-aloud interviews and semi-structured interviews.

Methods

Summary of the ExeRTiOn resource content

For the purpose of this current study, participants were testing aspects of the patient-facing ExeRTiOn prototype in a supervised one-off research visit. They did not have access outside of the study visit. The ExeRTiOn prototype has 12 weekly sessions, including both a patient-facing website, and a physiotherapist-facing back-end website. Table 1 summarizes the content of the twelve sessions. Figures 1 and 2 demonstrate screen grabs.

The linked back-end website (see Figure 3), allows the study physiotherapist to monitor participant log in times, adherence to sessions, goals, weekly physical activity and weight graphs, and also answer any questions through the secure inbuilt messaging system.

After extensive testing of the ExeRTiOn prototype by the research team, content and functionality issues were rectified in preparation for qualitative evaluation. This included testing of both the patient-facing and back-end websites by the authors, the software company, and clinical colleagues who had not had direct involvement in the design.

Study design and procedure

This study employed 'think-aloud' and semi-structured interviews, in parallel with the Generalised Physical Activity Questionnaire (GPPAQ; Physical Activity Policy Health Improvement Directorate, 2009).

Ethical approval

A favourable ethical approval was provided (North West Greater Manchester Central Research Ethics Committee and the Health Research Authority) on the 23rd of March 2018. The study was registered online (clinicaltrials.gov). Consent was not given for the full publication of transcripts.

Participant recruitment

All participants were recruited from a London NHS Foundation Trust Renal Unit from the 31st of May 2018 to the 18th of February 2019 using approved patient information sheets, a document summarizing online data security and privacy specific to this study, and consent forms. Participants were purposively sampled (Patton, 2002) for a range of age, ethnicities and gender. KTR participants were included in the study if they had received a kidney transplant within the past 3 months, able to provide written consent, and had a BMI of 18.5 kg/m^2 or above. They were excluded from the study if they were pregnant, had an unstable medical condition (e.g., unstable angina), or had a significant cognitive impairment documented in medical records preventing them from testing ExeRTiOn. HCP participants were recruited from the kidney transplant multi-disciplinary team at a London NHS Trust. Recruitment ended when no new descriptive codes, categories, or

Table 1. Summary of the key components of the ExeRTiOn prototype

Session title	Sessions elements
Welcome Session*	Tick box agreement and expectations Introduction video by expert physiotherapist Virtual tour of website and main functions Baseline GPPAQ
Session 1: Goal setting	Video from expert physiotherapist and patient on SMART goal setting Summary of session including patient 'top tip' quotes User encouraged to set their first goal plan
Session 2: Managing Cravings	Video from expert renal dietician on cravings and hunger post-transplant Interactive activity: cravings versus hunger Summary of session including patient expert 'top tip' quotes User prompted to revisit goals/ set new goal
Session 3: Food planning and labels	Second GPPAQ Video from expert dietician on planning food and how to read food labels Reference resources in 'my library' such as food label card Summary of session
Session 4: Activity after transplant	Video from expert physiotherapist on activity after kidney transplantation Reference to resources in 'my library' Interactive activity: reviewing effort levels whilst exercising Summary of session
Session 5: Choosing your activity/exercise	Video from expert physiotherapist on exercise options, demonstration of a few key exercises from the home exercise diary tab Interactive activity: user selects the focus of their physical activity Reference to 'exercise diary' and 'my library' resources Summary of session
Session 6: Healthy eating- it's a balance	Videos from expert dietician on all the major food groups User able to select which video they choose to view Interactive activities on different food groups Signposting to resources in 'my library' Summary of session
Session 7: Quantity and Quality- they both matter	3rd GPPAQ Video from expert dietician on portion control tips and strategies Interactive activity on portion sizes Signposting to resources in 'my library' Summary of session
Session 8: Activity planning	Video from expert physiotherapist on how to plan activity Patient example of activity planning Interactive activity: activity plan template Summary of session
Session 9: Keeping on track whilst also having fun	Video from expert physiotherapist User able to select various topics such as eating out, on holiday, Christmas and celebrations to see top topics and further information

Continued

Table 1. (*Continued*)

Session title	Sessions elements
Session 10: Overcoming barriers	4th GPPAQ Video from expert physiotherapist with expert patient about common barriers to activity and food post-transplant Interactive worksheet on barriers Summary of session
Session 11: Problem solving	Video from expert physiotherapist on problem solving Interactive worksheet on problem solving Summary of session
Session 12: Preventing setbacks	Video on relapse prevention by expert physiotherapist Interactive worksheet summarizing key learning, barriers, and future plans Completion of 12-week programme content
Other components website	Secure message system to the study physiotherapist Home exercise diary tab including written and pictorial information of exercises that can be done at home or in a gym Short cut to goals page including SMART goal setting, action plan and using the confidence and important ruler My library tab which includes custom made resources and links to external websites Self-monitoring graphs of weight and physical activity

Note. Key: *Welcome session = this is completed by all users once at sign up to the online intervention SMART refers to Specific, Measurable, Achievable, Realistic, and Timed Goals, edu = education, GPPAQ = General Physical Activity Questionnaire which is built into the website to appear at the start of every 4th session to gather physical activity data.

themes emerged from the data. This was decided by consensus amongst the research team.

Data collection

All participants completed a single supervised study visit (taking approximately 50–90 min) between the 21st of November 2018 and the 1st of March 2019. Participant characteristics were recorded at study entry. All interviews were conducted in a private room within the NIHR Clinical research facility at a London NHS Foundation Trust Hospital. Qualitative data were collected via 'think-aloud' interviews (on the patient-facing ExeRTiOn website) and were immediately followed by a semi-structured interview using a topic guide. Refer to Supinfo S1 and Supinfo S2 for the topic guides.

Think-aloud interviews assess usability, which is defined as how easily one can use and interact with an online system without any formal training (Benbunan-Fich, 2001). In this study, 'think-aloud' interviews followed a standardized protocol including a 'warm-up activity' (Eccles & Arsal, 2017) to get participants accustomed to speaking out loud. Participants were set up with a testing account and password by the corresponding author. They were instructed to reset their password and use this account alongside their participant number ensuring no personal identifiable material were entered into the online testing platform. Participants then performed supervised tasks whilst vocalizing

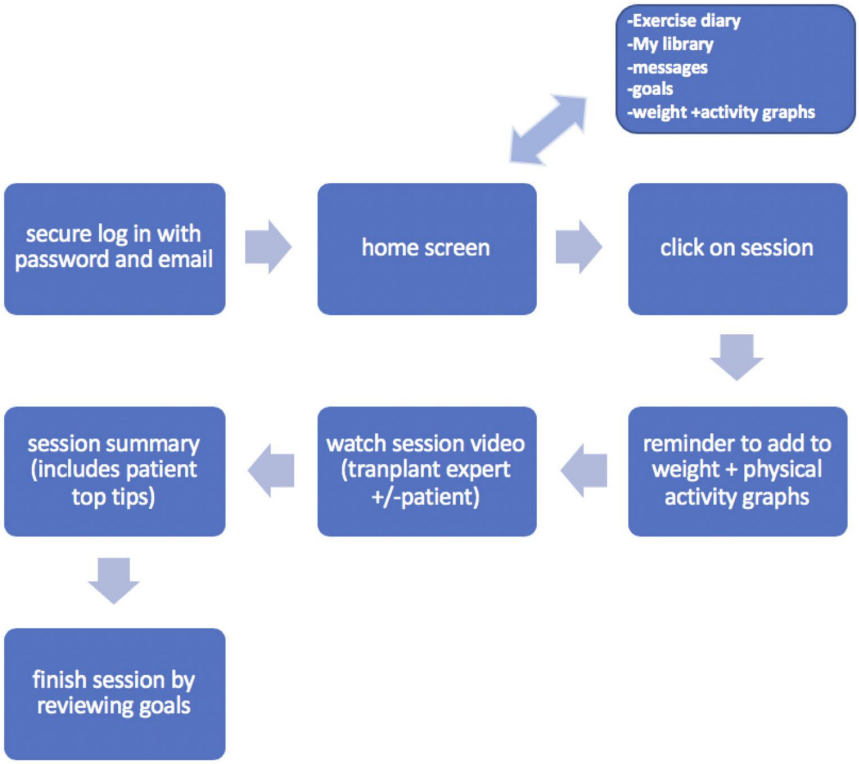

Figure 1. A typical flow for the user through the website. The user can either enter a session directly or engage with other functional tabs such as my library, message function, goal setting, and the weight and activity graphs.

out loud their actions and encounters with the online resource. Prompting from the researcher was standardized and kept to a minimum (Draper, 1998).

KTR participants completed 'Think-aloud' interviews on two different tasks on an NHS computer. Firstly, all the KTR participants reviewed the welcome session and goal setting session (session 1). These sessions were considered to be the key foundation sessions of ExeRTiOn and would therefore need to be reviewed by all participants. The second task involved reviewing an additional session (from session two to twelve), which was randomly allocated to each participant using a free online randomization website (List randomizer, n.d.). Sessions two to twelve were reviewed by a different KTR participant, based on this random allocation. For example, session two was randomly allocated to participant 01 to review, and session three was randomly allocated to participant 08 to review. Immediately following the two think-aloud tasks, KTR participants underwent an individual semi-structured interview to capture their experiences of ExeRTiOn, and their thoughts and experiences with weight gain and physical activity following kidney transplantation.

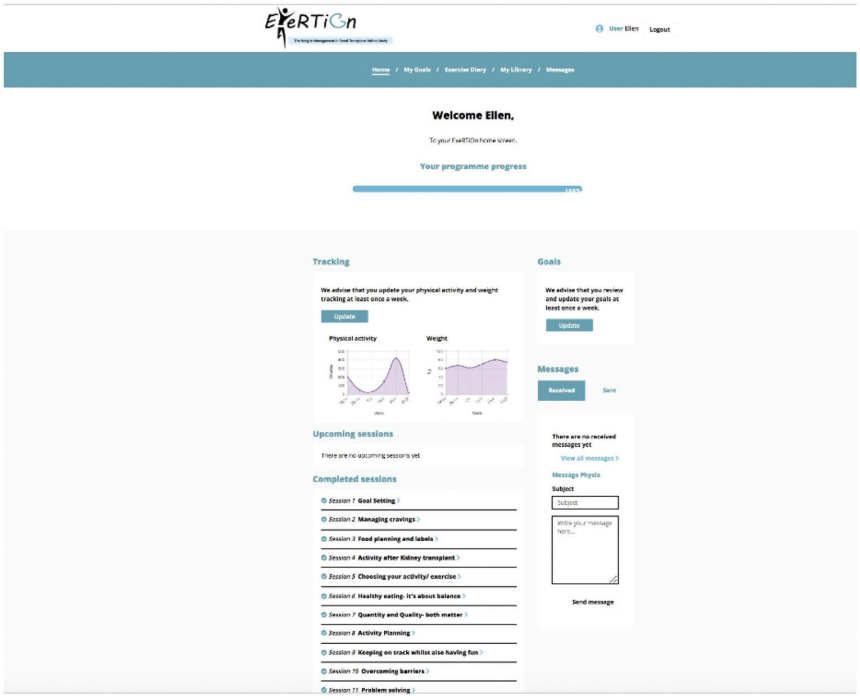

Figure 2. Home screen layout of patient-facing website. Home screen features include; progress bar, tracking, goals, sessions, and message function. Navigation panel at top of screen allows user to access goals page, exercise diary, my library, and messages.

HCP participants were provided with a tour of both the patient-facing website and the back-end websites, demonstrating the key features. They were then provided with a login and password to the patient-facing website and invited to complete 'think-aloud' interviews on both the welcome package and first session. They had the option to continue exploring sessions if they wished. This was followed immediately by a semi-structured interview to explore experiences of the ExeRTiOn prototype, and experiences working with KTRs in terms of weight gain and physical activity.

All interviews were audio-recorded, and field notes were completed. All transcripts were imported into NVivo © for mac (version 12) and coded as per the data analysis plan. The interviewer had extensive knowledge of the ExeRTiOn prototype. They were able to use field notes, alongside the transcripts, to decipher where in the website issues were occurring. Additional data collected included; GPPAQ data, website login data such as time taken to complete sessions, and self-reported physical activity (in minutes) and body weight (in kilograms) that was entered into the website. The GPPAQ data were analysed as per the guidelines (The Department of Health, 2009), and categorized using the physical activity index (PAI; active, moderately active, moderately inactive and inactive; The Department of Health, 2009).

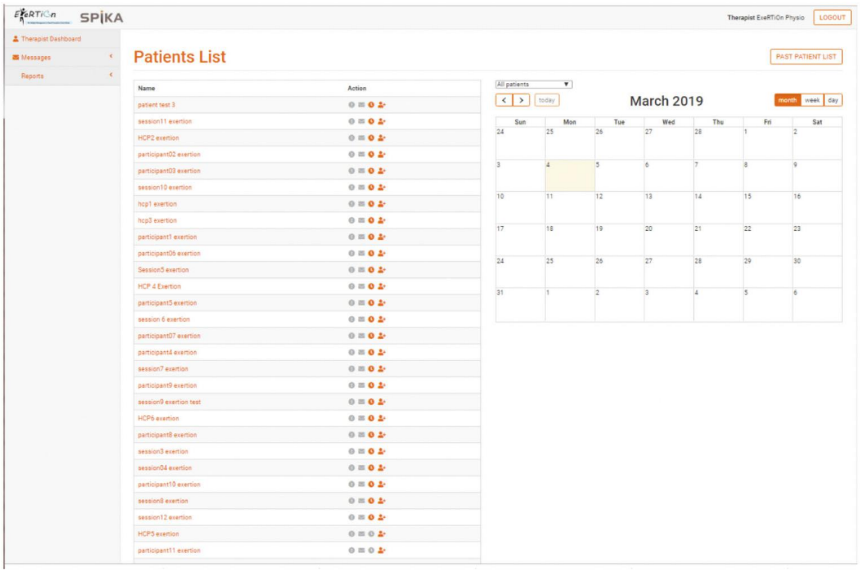

Figure 3. Physiotherapist home screen (back-end). The back-end website is linked to the patient-facing website. It requires a secure login and password. The back-end home screen allows the study physiotherapist to be able to view; messages to and from participants, view reports on weekly session compliance, session log in times, GPPAQ data, goals data, and weekly weight and physical activity data.

Data analyses

All interviews ('Think-aloud' and semi-structured) were transcribed verbatim. Transcripts were read and re-read, codes were created, and data were analysed inductively, using thematic analysis (Braun & Clarke, 2006, 2013). Memos were made to note where in the prototype usability issues, and positive and negative experiences were occurring. Deviate case codes were employed to ensure all perspectives that diverge from the dominant trends were not overlooked.

To ensure reflexivity, a reflective journal was used throughout the study to differentiate between participants experiences and the primary author's own thoughts and experiences. To ensure rigour, an external qualitative researcher (JG), with no involvement in creating ExeRTiOn, validated emergent codes and themes. These strategies aimed to insure that the themes were inductive, attributed to the content from the interviews conducted in this study, rather than the researchers' perceptions.

Results

A total of seventeen participants were recruited, including eleven KTRs and six HCPs. Figure 4 summarizes participant flow. Ten KTRs were recruited to test all the sessions. An additional KTR participant was recruited to achieve data saturation. This was deemed necessary as one participant required extensive prompting to use the computer (how to scroll, how to use a mouse etc). This participant took 55 min to complete task 1 compared

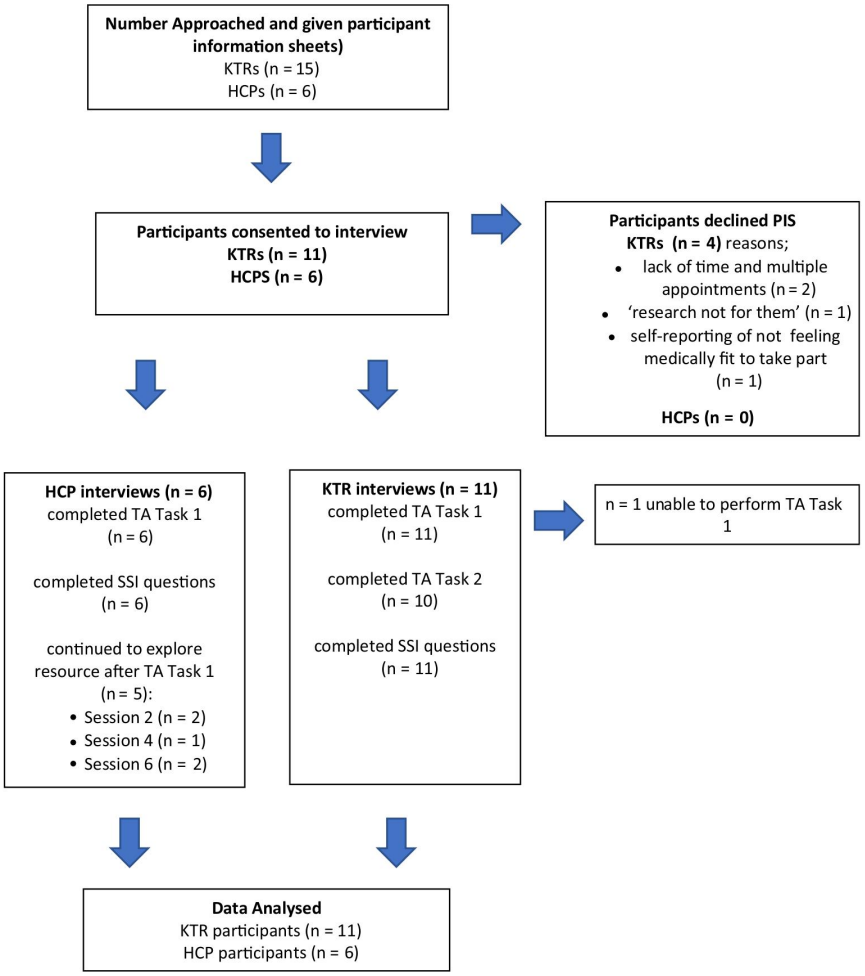

Figure 4. Participant flow diagram. KTR = Kidney Transplant Recipients, HCP = health care professionals, TA=' think aloud' interviews, SSI = semi-structured interviews. Interviews, SSI = semi-structured interviews.

to the mean time of 19.5 ± 12.9 min (range 6 to 55 min). This resulted in that participant just completing task 1 of the 'think-aloud' tasks, and the semi-structured interview questions. Participant 11 therefore completed the additional session (task 2). The mean time to complete task 2 was 13.6 ± 7.3 min (range 7 to 27 min). The mean time to complete task 1 for the HCP participants was 7.58 ± 6.97 min (range 3 to 21 min). All but one of the HCP participants continued to explore sessions after completing task 1 (Figure 4).

There were no dropouts from this study. All participants completed the one-off study visit. Due to the wealth of data generated from 'think-aloud' interviews, a sample of five

Table 2. KTR participant characteristics

Variable	KTR participants (n = 11)
Age participants (mean years)	50 ± 14
Males	45% (5)
Ethnicity	White Caucasian 54% (6) Black African and Caribbean 28% (3) Asian 9% (1) Other 9% (1)
Transplant vintage (mean days)	43 ± 19
Type transplant	91% (10) single Kidney transplant 9% (1) combined liver-kidney transplant
Donor Type	27% (3) Living related 73% (8) Deceased Donor
eGFR (mean) in ml/min/1.73 m^2	48 ± 19.2
Creatinine (mean) in mmol/l	136 ± 50
Number of comorbidities	1 46% (5) 2 36% (4) 3 9% (1) 4 9% (1)
Type of dialysis prior KTx	HD 36.5% (4) PD 36.5% (4) No dialysis 18% (2) HD and PD 9% (1)
Time on dialysis prior KTx (mean weeks)	26 ± 27
Smoking History	Non-smoker 73% (8) Ex-smoker 27% (3) Current smoker 0%
Diabetes diagnosis	T2 Diabetes 18% (2)
Hypertension diagnosis	82% (9)
Self-reported physical activity (mean in minutes with range)	82 ± 122 (10 to 410)
Self-reported weight (mean in kg with range	82.0 ± 18.5 (53.7 to 111)
BMI (mean in kg/m^2)	27.8 ± 3.8
Time taken to complete welcome and goals session (mean in minutes and range)	19.5 ± 12.9 (6 to 55 min)
Time taken to complete randomized session (mean in minutes and range)	13.6 ± 7.3 (7 to 27 min)
Type of goal set (proportions)	18% food goal (2) 73% activity goal (8) Set no goal 9% (1)

Note. Means and standard deviations are presented for continuous data. Frequency numbers and proportionate percentages are shown for categorical data. KTR = kidney transplant recipient, HD = haemodialysis, PD = peritoneal dialysis, kg = kilograms. Comorbidities included a medical history of; diabetes, hypertension, cerebrovascular event, osteoarthritis, brain haemorrhage, cardiovascular disease, cancer, or respiratory disease.

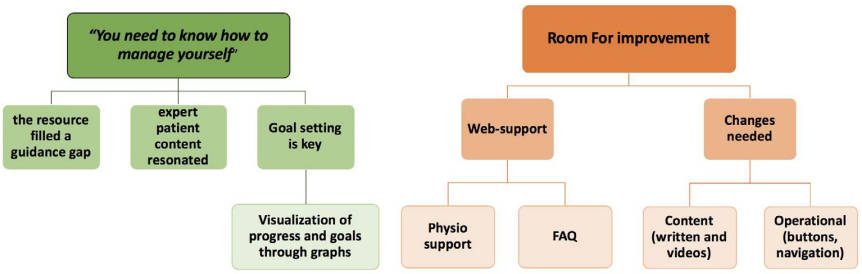

Figure 5. Summary of the emergent themes and subthemes from thematic analyses. The first theme was 'you need to know how to manage yourself'. Stemming from this included the following subthemes: (1) the resource filled a guidance gap, (2) expert patient content resonated, and (3) the importance of goal setting and monitoring progress. The second theme was room for improvement. Subthemes included (1) web support and (2) content and operational change suggestions.

participants is said to be able to uncover 80% of usability problems and issues (Benbunan-Fich, 2001). Therefore this sample was of sufficient size to detect any existing usability issues within the ExeRTiOn resource. Table 2 summarizes the KTR participant characteristics.

KTR participant GPPAQ PAI were; active (n = 4), moderately active (n = 1), inactive (n = 6). All KTRs were prescribed triple immunosuppressant therapy, including oral prednisolone (mean ± *SD* dosage 6.78 ± 3.2 mg, range 5–15 mg). HCP participants included a consultant nephrologist (n = 1), transplant nurses (n = 2), renal dieticians (n = 2), and a renal physiotherapist (n = 1), with a mean clinical experience of 12 ± 8 years.

Qualitative data were triangulated from transcripts, field notes, and reflective journal entries. Two themes emerged from the data set which are summarized in Figure 5.

Theme 1: You need to know how to manage yourself

This theme, which arose from reports across the whole data set, suggests that participants felt that the website was needed and could support new KTRs to follow a healthy lifestyle after transplantation.

> You know some of us, we just sit back, we don't care. After my transplant what else. You need to know how to manage yourself. You need to achieve your goal if you want to lose weight. (P04, female KTR)

> They need something like this. Definitely. Yeah Definitely without a shadow of a doubt. Because there was lot of things when I'd had the transplant that I was thinking I didn't know. And I've had to research or ask. This makes it a lot easier. (P07, female KTR)

There were three key subthemes that contributed to this theme including; (1.1) the importance of goal setting and monitoring progress, (1.2) the resource filled a guidance gap, and (1.3) Expert patient content resonated with participants.

1.1 The importance of goal setting and monitoring progress

Goal setting and planning was considered to be a key feature of ExeRTiOn by the majority of KTR and HCP participants. Goal setting was widely perceived as a tool to support users to shift their aspirations from general statements to precise dietetic and physical activity goals. It appeared to be important to participants that these goals were individualized to each user's ability to promote adherence.

> Setting the goals. Is it's a sort of-it's an achiever for you. Because when you set your goals you try and stick to them. You make sure it works out, like for health reason. When you set your goal, you have to make sure you go by them, because it's for your own good. For your own happiness and your confidence. (P01, male KTR)

In contrast, one participant varied from the rest of the data set and did not agree with the individualized goal setting approach. He reported he wanted a drop-down list of goals to select from.

> I'm lazy, I don't want to do that. That's if you had a list of goals, maybe 20 or 30, whatever it is. I can just go there and say, 'I want to lose weight'. (P11, male KTR)

Self-monitoring of weight and physical activity, through the tracking weight and physical activity graphs frequently aligned with accountability. Participants suggested these graphs could allow them to visually keep track of their progress.

> I think it's it will keep me on track. Especially doing the weight. (P05, female KTR)
>
> It's very simple, to just look at. I like this immediate-I can see exactly where I am going. Am I winning, or am I losing. (H05, female Nephrologist)

Setting goal plans, and tracking graphs of physical activity and weight, appeared to be valued by this sample and align with accountability.

1.2 The resource filled a guidance gap

Participants reported that ExeRTiOn was a helpful mode of delivery for providing new KTRs with much-needed specific physical activity and dietetic guidance after transplantation. Participants felt that ExeRTiOn answered their queries and could therefore bridge the guidance gap and assist their self-management after transplant.

> We have nowhere to turn to. I kept on saying 'is there a website? (P07, female KTR)
>
> It will be effective really. I mean when I had my transplant, I had to start asking 'what do I do? (P11, male KTR)

Some participants expressed feeling uncertain regarding the type and amount of activity they could initially perform post-transplant, which was exacerbated by fear of injuring the new kidney. Participants expressed the sentiment that ExeRTiOn could possibly address some of this unmet need.

> It's kind of hard to know how much you can do, how much you can't. Because at first, you don't want to do anything (laughter). Yeah. You can't even read a book. Erm its really nice to have guidelines and know where you're supposed to be. I think it's a really good idea. (P06, female KTR)

Figure 6 depicts a coding tree summarizing the subtheme 1.2.

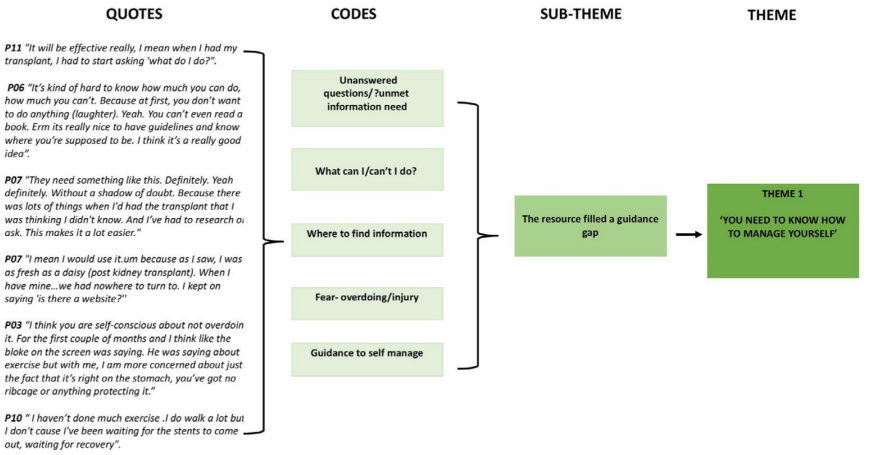

Figure 6. Detailed coding tree for subtheme 1.2. The coding tree depicts quotes and codes that form the subtheme: the resource filled a guidance gap.

1.3 Expert patient content resonated with participants

Having 'real' KTRs imbedded within the online resource, particularly featuring in the videos, and 'top tip' quotes on the summary pages, appeared to resonate and be meaningful to participants.

> Obviously the er doctor can only give what they've learn. They haven't necessarily experienced going through surgery so, yeah. You need a bit of a balance (P10, male KTR)
>
> It's nice hearing (patient expert name) talk. I just think it's—I guess for some patients it might seem daunting. Mightn't it? . . .If they want to start making changes to their lifestyle, and the way that he broke it down, and the way that he was explaining it, makes it seem nice and achievable (H03, female dietician)

This real world account was consistently valued by participants and appeared to normalize the variability of many participants post-operative experience.

> If you were doing that. You'd say 'well you know (patient expert name) been through that. You know and come out the other side'. Um which I thought was a big plus. (P05 a female KTR)

Whilst the majority of the sample valued the expert patient input, one participant did not agree with comments raised by the expert patient.

> I didn't necessarily agree with some of the things he said. You would be doing it by actually going and checking your weight. . . I didn't think you actually needed him. (P07, female KTR)

The majority of the participants felt it was important to have both the professionals and KTR experiences captured in the videos featured in the ExeRTiOn online resource. Honest and lived-in KTR experience was seen as a key feature.

Theme 2: Room for improvement

Whilst the website was well received by participants, there were aspects that could be improved to increase engagement with new KTRs. This theme encompassed the subthemes of the importance of web support from both the physiotherapist monitoring the website, and the website itself. This theme also encompassed content changes (text and video) and operational change suggestions (buttons and navigation).

2.1 Web support

There were various views on how the study physiotherapist, who would monitor the participants online profiles, should support participants to engage with ExeRTiOn. One suggestion to improve accessibility to the online content arose from a few participant interviews.

> Have you got a question and answer part of it? You could have like a drop down list of frequently asked questions and answers underneath. (P07, female KTR)
>
> I don't know if there is a help function on there. (P02, male KTR)

Participants welcomed the idea of weekly automated emails or messages through the website to remind them to complete the weekly sessions.

> If there's a 12-week programme, what would be useful would be a text reminder or an email reminder. (P02 a male KTR)

However if participants became unwell, or had issues engaging with ExeRTiOn, they felt they would want personalized and individualized feedback from the study physiotherapist, rather than an automated message.

> Probably something a bit more personal. . .because I think sometimes you think 'oh well that's just come out automatically'. (P09, female KTR)
>
> They have a chance to say 'well actually, I've got a bit of a problem because I was trying to do this and that didn't happen. (P07, female KTR)
>
> If something was going wrong, yes, rather than just getting an automatic message that was just saying 'keep going for your goals! and you're like 'well I haven't been on 3 weeks'. I would prefer something more personable. (H06, female dietician).

Some participants suggested an initial face-to-face induction session with the study physiotherapist would be needed.

> I think eer first steps you need it face to face to start with. . .then you can do it on your own at home. (P04, female KTR)

Others felt that if they weren't meeting their goals, they would like specific feedback from the physiotherapist.

> It may want some reminder if things are not progressing to say look um. 'You know your weight has increased' saying or not. Or 'your activity is not improved'. To give some feedback. (P08, male KTR)

Whilst the online intervention appears to promote self-management, participants express the need for some support from the website such as a frequently asked questions

tab and reminder emails. They also felt that personalized feedback from the study physiotherapist monitoring the website would improve participant experience and foster engagement.

2.2 Content and operational change suggestions

Usability testing revealed various examples of content and operational changes suggested by the participants. These included suggestions to simplify the session list layout on the home screen, the addition of extra navigation buttons, and increasing the size of headings and tick boxes.

> Have all the sessions there, you've still got ticks or what you have done and haven't done (P10, male KTR about simplifying home screen layout)
>
> I am assuming, I didn't go onto it, but assuming there is a button taking you back to the home screen? (P02, male KTR regarding an extra navigation button to assist returning to the home screen).

Whilst tracking of self-reported weight and physical activity was seen as a valued function of ExeRTiOn, participants suggested that the description of what type of activities that could be included needed clarification.

> So does physical activity include housework as well? Or not? (P02, male KTR)
>
> Does the physical activity include walking? Or is it just actual exercise? (P06, female KTR)
>
> I think I would like to know what activity I am allowed to include (H05, consultant nephrologist)

Written content changes, such as clearer definitions were suggested as strategies to enhance usability of ExeRTiOn.

There were a variety of responses from participants in regard to the ideal length of the educational videos within ExeRTiOn. The majority of the participants felt the videos were too long.

> I'd definitely say shorter than eleven minutes- I think. (P06, female KTR)
>
> It felt a bit too long. . . I was looking at how far we have got to go (P05, female KTR)
>
> About three (minutes). Because you need to get the attention. And them to not tune out and get bored. (H01, Kidney Transplant Nurse)

Some participants felt that the length of the video should depend on the subject matter and its importance.

> If it's 12 minutes and fills everything in, then it needs to be 12 minutes. (P03, male KTR)
>
> It depends on the subject, there's no point having a 3 minute video every time because one video might not fit enough in. (P10, male KTR)

The ideal length of video seemed to vary across the sample. To optimize engagement, the length of videos will be revised. Applying the constructive feedback from participant interviews to the planned revisions of the ExeRTiOn resource should improve experience and engagement.

Discussion

This study aimed to explore the usability and experience of the patient-facing ExeRTiOn prototype and identify valued content. The results from this study, have allowed the research team to better understand the target end-users (new KTRs), and involve them early in the intervention development process. Early involvement of target end-users in digital health intervention design and refinement can enhance acceptability (Valdez & Ziefle, 2019). To our knowledge, this is the first study to report the usability and experience of an online resource designed specifically to prevent weight gain for new KTRs.

The overall experience was deemed positive by both the KTR and HCP participants. The results, particularly Theme 1 'you need to know how to manage yourself', suggests that the experience of the online resource could perhaps assist with self-management. The recognized BCTs to support healthy eating and physical activity behaviour change; goal setting and prompting of self-monitoring behaviours (Michie, Ashford, et al., 2011) were valued by our sample of KTRs and HCPs (Theme 1.1). These valued functions could perhaps allow users to be accountable for their physical activity and weight.

The specific kidney transplant content was felt to be a crucial component to the success of the ExeRTiOn prototype. Participants identified that ExeRTiOn could fill an existing guidance gap within information that is currently provided post-kidney transplant (subtheme 1.2). A systematic review of qualitative studies reported that participants experienced 'frustrating ambiguities' when information provided by clinicians was unclear and conflicted previous recommendations, which influenced self-management behaviour (Jamieson *et al.*, 2016). Therefore, providing new KTRs with specific guidance on physical activity through the ExeRTiOn online resource could potentially address the identified inadequacies of education which may be encountered during routine post-operative kidney transplant care.

All but one of the KTR participants in this current study valued the patient expert content which helped to normalize the kidney transplant journey. Jamieson *et al.* (2016) also reported the positive benefit of peer-support and shared experience. Both KTR and HCP participants in this current study felt that an online resource was a worthwhile mode to deliver personalized education, self-monitoring and support, to promote and facilitate adoption of healthy eating and physical activity behaviours post-kidney transplantation.

Threats to user privacy is a challenge in digital health care (Blandford, 2019). Studies investigating user perceptions with digital health interventions suggest mental health data is perceived to be the most sensitive (Stawarz, Preist, Tallon, Wiles, & Coyle, 2018), in comparison to general and physical health data (Valdez & Ziefle, 2019). In this current study, there were no concerns raised about data security and privacy from participants. This is perhaps due to the detailed information provided during the recruitment process on data security and privacy. In addition, the ExeRTiOn prototype involved limited personal information, and focused on physical health data (weight, physical activity, and goals).

Participants in the current study felt that web support (subtheme 2.1) was an important issue to be addressed in revisions of the ExeRTiOn online resource. Optimizing support could improve resource usability and acceptability for new KTRs. Participants also felt that personalized feedback would perhaps foster better engagement. The need for human interaction and personalized feedback, is echoed in online weight loss studies in the overweight and obese populations (Bradbury, Dennison, Little, & Yardley, 2015; Sherrington *et al.*, 2016). The research team plan to review the support provided within

the ExeRTiOn online resource, and also the physiotherapist support that will accompany it, in the planned feasibility RCT.

Subtheme 2.2 (content and operational changes) demonstrates helpful suggestions from our participants on how the website might be optimized to enhance usability and experience. One of the suggested changes included reviewing the 'ideal' length of the educational videos. Whilst videos can be used as an effective education tool, considerations need to be made to ensure optimal learning and engagement (Brame, 2016). Research suggests that education videos need to be 6 min or less to achieve optimum median engagement of close to 100% (Guo, Kim, & Rubin, 2014). When the length of the video increased, the median engagement time reduced, with 9- to 12-min videos reporting only 50% median engagement (Guo *et al.*, 2014). In this current study, there was variance in participant reports as to the ideal length of the ExeRTiOn educational videos. The research team plan to reduce the length of videos to within 6 to 9 min.

Whilst there is some current evidence emerging, which evaluates the effects of face-to-face complex interventions that combine dietician input, exercise therapy and behaviour change on weight gain in KTRs (Henggeler *et al.*, 2018; Tzvetanov *et al.*, 2014), more research is warranted. Existing studies report variable intervention doses, standards of usual care, and outcomes, make it difficult to determine what the best intervention is to prevent weight gain in new KTRs. To our knowledge, ExeRTiOn is the first online resource to explore weight gain prevention in new KTRs.

The development and refinement of the ExeRTiOn online resource is a complex and iterative process. The results from this study will inform further refinements and research. Firstly the authors plan to utilize the MoSCoW method, a recognized prioritization tool, to inform the needed revisions to the prototype (Bradbury *et al.*, 2014). MoSCoW stands for; (1) 'Must have' changes the essential changes to enhance usability and experience, (2) 'Should have' changes which are important but no essential features, (3) 'Could have' changes include useful to have features (dependant on budget constraints), and, (4) 'Would like' features include changes that are not currently essential or important, but could be considered in future projects (Kuhn, 2009). The research team will prioritize the results from this current study, using the MoSCoW method, to inform the essential and important changes needed to enhance usability and experience of the ExeRTiOn resource. Refinements will be made with the software company in preparation for the planned follow-up feasibility RCT.

Secondly, the results from this current study will inform a *post-hoc* evaluation of the revised ExeRTiOn intervention using the Behaviour Change Wheel Methodology (Michie, Van Stralen, & West, 2011). This will allow the research team to evaluate the mechanisms of action, and also create a theoretical framework for this intervention (Michie, Atkins, & West, 2014).

Limitations

Limitations of this current study include its single-centre design, and the fact that the corresponding author who created ExeRTiOn also conducted the interviews. To address the potential interviewer bias, the following strategies were employed: (1) probing questions to address negative feedback of ExeRTiOn were utilized in the topic guide, (2) use of a reflective journal, and (3) the research team consulted an external qualitative researcher (JG) to validate codes and themes. Another limitation to this study is the fact that usability testing was conducted within a supervised one-off research study visit. This limitation will be addressed in the planned mixed-methods feasibility study. The study

team plan to interview a purposive sample of intervention participants who adhere to the 12-week ExeRTiOn resource, and those who do not adhere to the intervention. This will allow the research team to gather further data with the resource when it is used independently in participant's homes. A further limitation to note is that no human computer interaction researcher was involved in the study. However, one of the researchers and the software company had extensive experience working on previous health behaviour change online products, and this experience was critical. Despite the limitations, this study has allowed the research team to better understand their target audience of new KTRs and also ensure that the novel online resource will address their specific needs. Based on the results of this study, the research team plan to revise the ExeRTiOn resource, in preparation for a bi-centre mixed-methods feasibility RCT.

Conclusion

An online weight gain prevention resource, designed specifically for new KTRs, was created and evaluated by our research team. The ExeRTiOn online resource has the potential to provide new KTRs with much-needed information to foster self-management and mitigate the fear-avoidance behaviour that is often associated with returning to physical activity post-kidney transplantation. Both KTR and HCP participants identified that goal setting, self-monitoring graphs, patient expert content, and physiotherapy support were valued content in the ExeRTiOn prototype. This study has allowed the research team to further understand their target user population and make informed revisions to the online resource. Revisions will be implemented using the MoSCoW method prior to utilizing the ExeRTiOn resource in a planned RCT.

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Conflicts of interest

All authors declare no conflict of interest.

Author contribution

EC, SG, and JC conceived and designed the study. EC involved in data acquisition. EC, JG, SG, and JC analysed and interpreted the data. EC, JG, SG, and JC involved in statistical

analysis. SG, JC, and JG supervised and mentored the study. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. EC and SG take responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. Consent was not given for the full publication of transcripts.

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Supporting Information

The following supporting information may be found in the online edition of the article:

Supplementary Material S1 Topic Guide for KTR participants.
Supplementary Material S2 Topic Guide for HCP participants.

Supplementary Material ExeRTiOn study

S1. Topic Guide KTR Participants

S1.1 Introduction

- *Thank you for agreeing to take part today…*
- *Today we are going to complete some "Think-aloud' interviews to test the website. After this I will ask you some questions about your thoughts and experiences*
- *Happy for this to be recorded?*
- *This will be anonymised*

S1.2 Explain 'Think-aloud' Tasks

- *The "Think-Aloud" process allows us to test the online resource looking at how you find navigating different areas on the resource, how interactive it is and how you find the information.*
- *Remember we are testing the online resource, and how easy it is to use, not you as an individual*
- *We will ask you to complete 2 brief tests of the website today.*
    - *The first will look at the welcome package when patients start this online programme. The second will be testing one of the 12 sessions. We ask that whilst you do these tasks you continue to talk out loud as you do it.*
- *This verbal talking "out loud" as you use the online resource is really important for us to record and analyse so we can refine and redevelop this online resource.*
- *If you get stuck, please say out loud what you are having issues with. If you stop speaking out loud I will point to a sign asking you to "please keep talking".*
- *The researcher will tell you when to start and when to stop.*
- *Once you have completed this session, we will complete an informal interview where I will ask specific questions about how you found using the online resource.*

S1.3 Warm up 'Think-Aloud' task

- *Ok so let's try a practice task*
    - *What is 24 + 10? Talk out load as you figure it out. For example adding 10 to 12 I would do 10+10 is 20 ad 2 = 22….(1)*
    - *What is the 4th letter before F in the alphabet* **(answer B)** *(1, 2)*
    - *How did you find that?*
- *Any questions? Ok so now please get started with doing this looking at the website. and please remember to keep talking out loud."*

S1.4 Think-Aloud TASK#1

- *please log into the website with these details*

  [ellen to provide copy of test 1 log in details]
- ***We will not be using your name or any personal identifiable material for this study to test the website. Please follow through the screen to what you think you should do and remember to talk aloud as you do so….***

Possible prompts

- Take down notes when you intervene, if any expressions of emotion etc.
- Use keep talking sign
- If patients stuck (3)
    - *" what are you thinking now?"*
    - *"why did you do that?"*
- Completely stuck (3)
    - *"what do you think you would do If I wasn't here?"*
    - * write down prompts
    - *"was the problem solved"*

S1.5 Think-Aloud TASK#2

- *Please log out and now log in with these details…. [ellen provide login details)*
- *The second task is to complete session x which you have been randomly allocated*
- *Please work through as you see fit and remember to continue to talk aloud as you do so*

Possible prompts

- Take down notes when you intervene, if any expressions of emotion etc.
- Use keep talking sign
- If patients stuck (3)
    - *" what are you thinking now?"*
    - *"why did you do that?"*
- Completely stuck (3)
    - *"what do you think you would do If I wasn't here?"*
    - * write down prompts

"was the problem solved"

Think- Aloud References:

1. Ericsson KA, Simon HA. Protocol Analysis: Verbal Reports as Data 2nd ed. Cambridge, MA: The MIT Press; 1993. p. 375-9.
2. Eccles DW, Arsal G. The think aloud method: what is it and how do I use it? Qualitative Research in Sport, Exercise and Health. 2017;9(4):514-31.
3. Draper S. HCI Lecture 5- Think Aloud Protocols University of Glasgow1998 [Available from: http://www.psy.gla.ac.uk/~steve/HCI/cscln/trail1/Lecture5.html.

S1.6 Semi-structured Q's KTRs

	Possible probes
Experience	
• *How do you feel that your kidney transplant impacts on your day to day life?*	*How long have you had your transplant?*
• *What was your overall experience?*	*Positive experiences ex/PA KTx* *Any challenges ex/PA KTx*
• *What did you learn from using the online resource?*	
• *What is your experience with exercise or activity after KTx*	*Any challenges weight maintenance?*
• *What is your experience with maintaining your weight after KTx*	
Usability	
• *What did you find helpful about the online resource?*	*Please tell me more*
• *What did you find unhelpful about the online resource?*	*Examples?*
Navigation	
• *How do you find getting around the website?*	*Any positives* *Any negatives*
○ *Prompt: thoughts on homescreen layout?*	
• *What support do you think would be needed to use this website in the future?*	*How often support?* *What would that support look like (e.g. F2F/ phone/ msg)*
○ *Prompt: Frequency of support/ type (F2F/phone/msg)*	
Content	
• *These are the sessions we will provide to the patients…*	*Anything missed?* *Positives/ negatives*
• *Is there anything else you would like to see included?*	
• *What were your thoughts on the topics covered?*	
• *Videos?*	

    - Prompts: length/ HCP and patient
- Thoughts on enviro checklist

AOB:

- *Anything else you would like to say?*
- *Any other questions/ comments?*

S2. Topic Guide HCP participants

S2.1 Introduction

- *Thank you for agreeing to take part today…*
- *Consent again (V4)- TA and GPPAQ□*
- *Today we are going to complete some "Think-aloud' interviews to test the website. After this I will ask you some questions about your thoughts and experiences*
- *Happy for this to be recorded?*
- *This will be anonymised*

S2.2 Demonstration of the website

- Can I show you website?
- These are the main functions
    - Home screen tour
- These are the sessions
- Sessions roughly follow same format
    - Questionnaires, video from an expert, interactive activity, summary
    - Home screen and tracking
- Anything you want more info on? Sessions you would like to explore in detail
    - If so give log in (patient testing)
    - Think aloud an aspect they would like to look at in more detail.
- I am going to give you a log in then I want you to go through as you think you need to and talk out loud as you do so….

Think- Aloud References:

1. Ericsson KA, Simon HA. Protocol Analysis: Verbal Reports as Data 2nd ed. Cambridge, MA: The MIT Press; 1993. p. 375-9.
2. Eccles DW, Arsal G. The think aloud method: what is it and how do I use it? Qualitative Research in Sport, Exercise and Health. 2017;9(4):514-31.
3. Draper S. HCI Lecture 5- Think Aloud Protocols University of Glasgow1998 [Available from: http://www.psy.gla.ac.uk/~steve/HCI/cscln/trail1/Lecture5.html.

S2.3 Semi-structured Q's HCPs

Experience

Possible probes

Positive experiences
Challenges

- *What is your experience with weight gain and KTx patients*
- *What is your experience being PA or exercise after KTx*

Usability

Please tell me more
Examples?

- *What did you find helpful about the online resource?*
- *What did you find unhelpful about the online resource?*

Navigation

Any positives
Any negatives

How often support?
What would that support look like?
(e.g. F2F/ phone/ msg)

- *What support do you think a patient would need to use the website?*
    - *Patient friendly*
    - *How many patients of yours think could use this..*
    - *Prompts: feedback on homescreen layout*

Content

Anything missed?
Positives/ negatives

- *These are the sessions we will provide to the patients…*
- *What are your thoughts on the sessions covered?*
- *Is there anything else you would like to see included?*
- *Comment on the order of the sessions?*
    - *Prompt: explore video length/ HCP and patient*
    - *Prompt: explore enviro checklist thoughts*

AOB:

- *Anything else you would like to say?*
- *Any other questions/ comments*

END OF PUBLISHED ARTICLE

4.4 Chapter summary

This study, and manuscript, achieved the first aim of this thesis, to create an online intervention to address weight gain. It also addressed objectives 2, 3 and 4; a prototype of the online-intervention was constructed using a person-based approach, usability, functionality and experience of the protype was completed to aid refinement. Engaging with the target-user group (new KTRs) was essential when employing the person-centred approach (Yardley, Ainsworth, et al., 2015b) for intervention design. By combining think-aloud and semi-structured interviews, the research fellow was able to gather rich data in usability, and experience, using the prototype ExeRTiOn online-resource from both the new KTRs perspective and the transplant HCP perspective. This approach was important to facilitate revisions of the online intervention in preparation for the mixed methods feasibility RCT (studies 3 and 4). Figure 4.1 on the following page demonstrates an updated version of the thesis processes diagram.

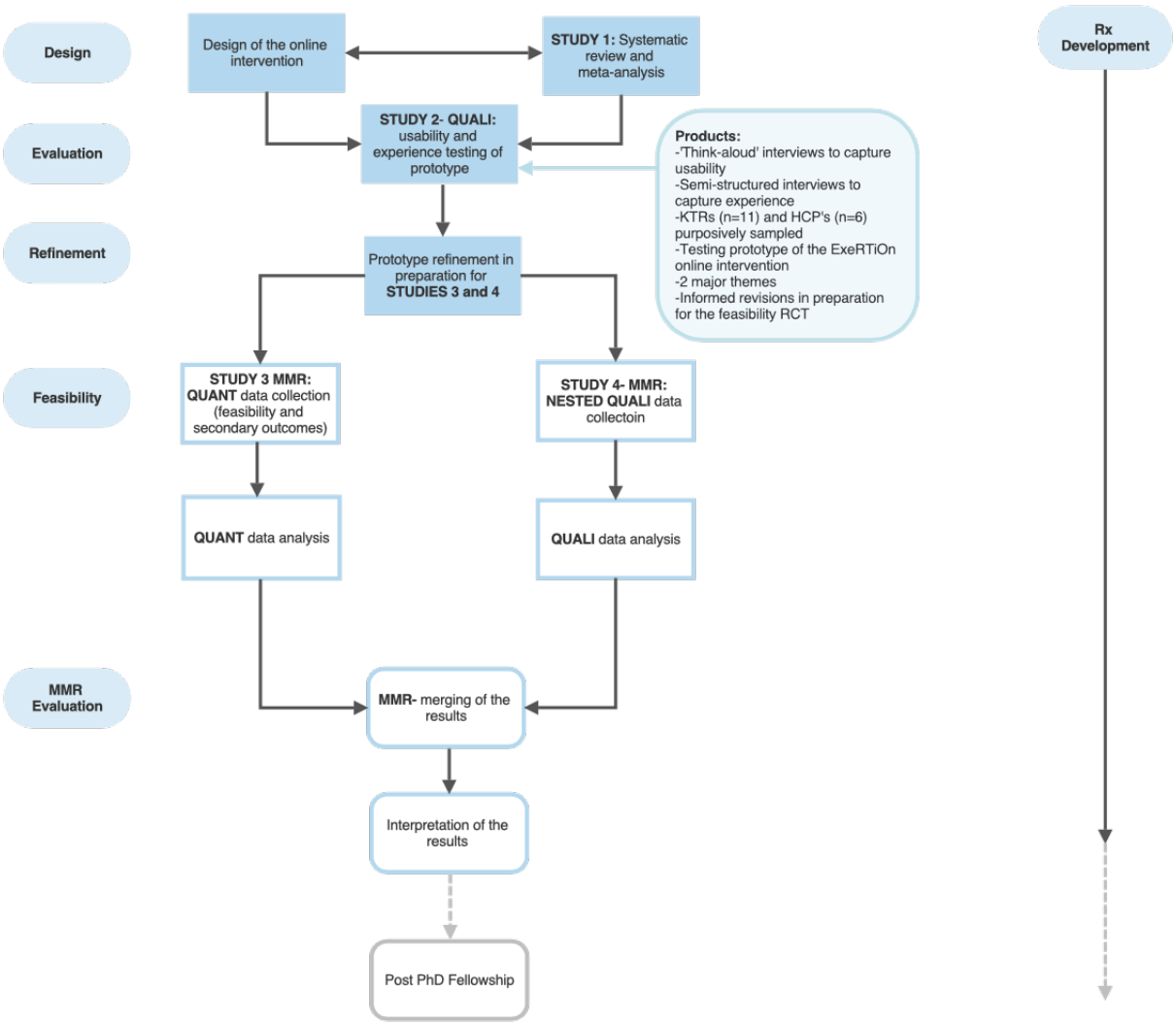


Figure 4-1 Updated Thesis Process Diagram to reflect completion of Study 2 (usability and experience)

Note. The thesis process diagram has been updated to reflect the completion of study 2 which are shown by the additional pale blue rounded square.

This figure was designed based on a combination of the convergent mixed-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

Rx= treatment development, KTRs= kidney transplant recipients, n= number of participants, HCPs= health care professionals ExeRTiOn= Exercise and weight management renal transplant online, RCT=randomised controlled trial, MMR= mixed methods research, QUANT=quantitative research, QUALI= qualitative research.

Chapter 5 Coping with the COVID-19 Global Pandemic

5.1 Chapter Overview

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (WHO, 2020) first hit the UK on the 31st of January 2020 (Sharma et al., 2020), and caused wide-spreading coronavirus disease (COVID-19) (WHO, 2020). This global pandemic has had a substantial impact on daily life. The first national UK lockdown was declared in March 2020. This unprecedented situation occurred during the PhD fellowship, and had a major impact on the population of interest (new KTRs). To contextualise the impact of the COVID-19 pandemic on this research fellowship, the onset of COVID-19 occurred after the creation and initial testing of the online intervention (study 2) and during the recruitment and assessment phase of the mixed methods feasibility study (studies 3 and 4). This chapter will therefore briefly summarise the impact of COVID-19 on KTRs, kidney transplant clinical services in the UK, and the resultant changes to the mixed methods feasibility RCT (studies 3 and 4) that were subsequently implemented with a pragmatic approach.

5.2 The impact of COVID-19 on Kidney Transplant Recipients in the UK

People living with CKD were found to have a greater risk of infection from COVID-19, which increased with age, later stages of CKD, immunosuppressant medications and haemodialysis (Kidney Care UK, 2020). The study target population (new KTRs) were categorised into the highest risk category the 'clinically extremely vulnerable group'. If KTRs were infected with COVID-19, they were anticipated to have a greater risk of adverse illness and mortality (Kidney Care UK, 2021). A renal-specific risk categorisation grid was developed by experts (BRS and RA de-shielding working group, 2020). Elevated risk was associated with two or more of the following risk

factors; male gender, history of either cardiovascular disease, hypertension, diabetes, Black, Asian and minority ethnicities, and a BMI of greater than 30kg/m^2. In addition, KTRs within the first three months of transplantation, or above sixty years of age, had an additional increase in risk (BRS and RA de-shielding working group, 2020).

On the 23rd of March 2020 people living with ESKD (including KTRs) were informed they must shield (The Renal Association, 2020b). Kidney Care UK, a patient charity completed an online survey (n=1211) in May 2020 and captured experiences on shielding from people living with CKD (including KTRs) (Kidney Care UK, 2020). This survey reported that two thirds of respondents had disruption in clinical care, four out of ten participants described an impact on their mental health, and confusion around shielding guidance was evident. Shielding in the UK from the first wave of COVID-19 was paused on the 1st of August 2020 (The Renal Association, 2020b). Further national UK lockdowns occurred from the 5th of November to the 2nd of December 2020, and from the 6th of January 2021, with restrictions starting to ease gradually from the 8th of March 2021 (Institute for Government, 2021). Both recruitment sites involved in the feasibility mixed methods RCT were located in South London which underwent local lockdowns and restrictions on the 19th of December 2020 due to a new rapid spreading variant of COVID-19 (Kirby, 2021).

During the second and third waves of COVID-19, shielding principles were slightly more lenient than during the first wave. Extremely clinically vulnerable people (including KTRs) were advised by the UK government to "stay at home as much as possible", to work from home, to accept the vaccine and to only leave their home for exercise and hospital visits with strict social distancing (Public Health England, 2021).

The UK Renal Registry COVID-19 report from the 1st of September 2020 to the 3rd of March 2021 the number of laboratory-confirmed cumulative cases of COVID-19 in England was 7078 cases for people living with CKD and 935 cumulative cases for people who had received a kidney transplant (UK Renal Registry, 2021). The cumulative deaths in England for people with CKD as a result of COVID-19 (reported 3rd March 2021) was 1641, and there were 135 cumulative deaths as a result of COVID-19 in people who had received a kidney-transplant (UK Renal Registry, 2021). It is important to acknowledge that not all units provided data for this report.

5.3 The impact of COVID-19 on Kidney Transplantation clinical services in the UK

The COVID-19 pandemic caused an immediate reduction in both transplantation procedures, and organ donation in the UK (Manara, Mumford, Callaghan, Ravanan, & Gardiner, 2020). On the 15th of March 2020 the NHS mandated that all non-urgent surgery should be suspended to free capacity for COVID-19 care. This had a direct effect on kidney transplantation activity in the UK, with only a few centres continuing to provide deceased donor kidney transplant surgeries (Sharma et al., 2020). Many of the transplant specialist staff were redeployed, and there were changes to the age of deceased donors to increase the capacity of intensive care unit beds for COVID-19 infected patients (Manara et al., 2020). Whilst in the UK there were reduction of all abdominal transplantations during lockdown, kidney transplantation numbers were substantially reduced by approximately 65 % when compared to 2019 data (Manara et al., 2020).

The BTS recommended that transplant units reduced face-to-face hospital attendance for all KTRs by utilising virtual clinics, rescheduling non-urgent appointments and

organising home delivery of immunosuppressant medications due to the elevated risk of KTRs to COVID-19 infection and complications (British Transplant Society, 2020). Rapid NICE guidance on renal transplants during COVID-19 was published in June 2020 (NICE, 2020). This guidance (NG178) recommended that all kidney transplantation sites should ensure that the appropriate infrastructures were in place to re-start or expand transplantation services. Guidance included rapid COVID-19 testing, patient and staff safety, COVID-19 secure areas, discussion of re-opening and expansion with NHS Blood and transplant and other transplantation and non-transplantation centres (NICE, 2020). The first wave of the pandemic lead to a shift in clinical practice for new KTR's to all face-to-face visits to a hybrid model of virtual clinics with only essential face-to-face visits to hospital sites.

5.4 The impact of COVID-19 on studies 3 and 4

In addition to study participants shielding from March 2020, there was further instruction from the research sponsor site (KCH) and the University (King's College London) that all non-essential research be paused from the 23rd of March 2020. Therefore, after discussion with supervisors, and transplant nephrologists at both sites (EA and SS), it was decided that all active recruitment and new baseline assessments for study 3 should be paused for four weeks to 'watch and wait'. It was agreed that participants already baselined and active in the mixed methods feasibility RCT (n=17) could be followed up remotely during shielding and national lockdown rather than with face-to-face appointments. All current trial participants (n=17), and patients who were awaiting entering the trial (n=3) were notified by telephone. The TMG, funders, and Research and Innovation teams (R&I) were notified that the study was "paused" for recruitment.

Four weeks later (17th April 2020), shielding was still ongoing, and the TMG agreed the study would remain 'paused to recruitment' and for face-to-face visits. Unfortunately, three participants from the second site (GSTT) who had been consented but had yet not completed baseline assessments and randomisation, no longer met the study criteria and were withdrawn. The CONSORT diagram, in the following chapter, chapter 6 will demonstrate this.

Due to the longevity of shielding for our target population (KTRs), the elevated risk of contracting COVID-19, and the risk of mortality, alongside the changes to transplant services, an extra-ordinary virtual TMG was called. The meeting was hosted by the research fellow (EC) on the 2nd of June 2020 via zoom. The meeting was attended by patient experts, PhD supervisors (SG, JC and KB), Consultant nephrologists from both sites (SS and EA), the university post graduate co-ordinator (RT), thesis committee external experts (MM and SS), the lead of renal research at the lead study site (SS), and a statistician consultant (RP). The research fellow presented data on feasibility outcomes such as recruitment and data collection prior to the pandemic. The group decided that there were sufficient data from the 17 participants recruited prior to COVID-19 to answer all feasibility questions and objectives. The impact on transplantation services as a result of COVID-19, meant that when kidney transplant services were to resume at research sites, only the very fit and low-risk patients would be considered, thus drastically changing the pragmatic and inclusive study sample. Due to the time remaining in the PhD fellowship (one year at the time of the meeting), and the impact this change would have on recruitment, the team decided that recruitment should cease completely for study 3, and active participants should be followed up through to the end of the study period. Refer to appendix E for minutes from the extra-

ordinary TMG meeting. The impact of COVID-19 on study processes (recruitment and assessment of participants) is summarised in figure 5.1 on the following page.

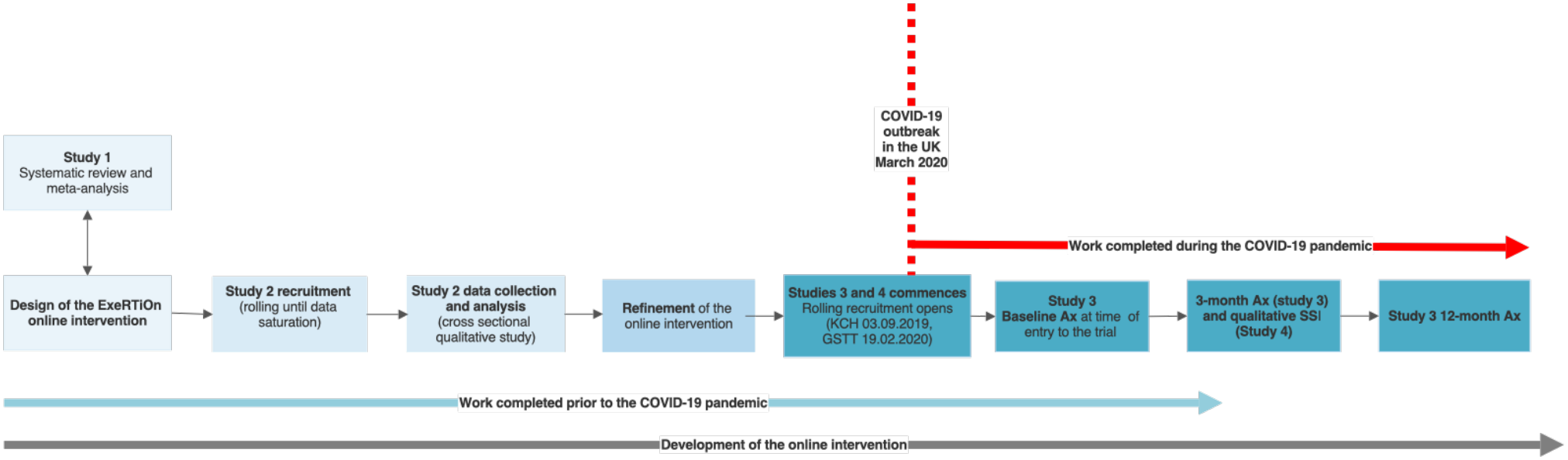


Figure 5-1The impact of COVID-19 on study processes

Note. Ax= refers to Assessment. Work completed prior to the COVID-19 outbreak in March 2020 is indicated by the blue horizonal arrow. It includes the initial design of the online intervention, the systematic review, study 2 from start to completion, some of the recruitment of studies 3 and 4, some baseline assessments of study 3- and one of the 3-month assessments (study 3) and qualitative interviews (study 4) . It is worth noting that due to the rolling recruitment of study 3, 20 participants were consented, 17 randomised and entered the trial prior to the outbreak of COVID-19 in the UK. The impact of COVID-19 is shown by the red dashed line and the red horizontal arrow. Development of the online intervention occurs throughout the thesis and will continue beyond the PhD Fellowship and is shown by the grey arrow

Immediately following this extra-ordinary TMG meeting, the research fellow notified all stakeholders, including research participants, the funder and R&I teams at each site. A non-substantial ethical amendment was completed and approved to allow remote follow-up of participants and the qualitative interviews. A substantial ethical amendment was submitted, and approved, to indicate changes in sample size for study 3, refer to Appendix E. Recruitment and research data was updated on all systems (EDGE, CPMS, and the research portfolio) to reflect no further recruitment would occur, and the final sample size for the feasibility RCT was 17 participants. During the first wave of COVID-19 (March to August 2020), all follow-ups were conducted remotely over the telephone. Unfortunately, not all QUANT outcomes were able to be collected remotely at the three-month data-collection during study 3. Missing data related to the pandemic are described in chapter 6. However, body weight, medications, renal blood test results and medical history were able to be collected from clinical records. Questionnaires and qualitative interviews were collected over the telephone. It was fortuitous that the studies intervention was designed to be delivered virtually, allowing the IG participants to have access to PA and healthy eating support during a challenging time where they would not have received this outside of the research study. Participants from both groups were signposted to kidney-specific advice on COVID-19 on charity websites (Kidney Care UK, 2021) during the remote telephone study follow up.

On the 24th of June 2020, after careful consideration with the sponsor site R&I team, the TMG and transplant consultants, it was agreed that face-to-face study visits, with the appropriate COVID-19 safety measures in place, could resume. The appropriate re-starting documentation was completed with the R&I team at the sponsor site. From the

24th of June 2020 to final data collection on the 22nd of March 2021, data collection was completed face-to-face with strict COVID-19 infection control measures. This included booking participants in for assessments only when they were coming in for face-to-face clinic visits to minimise hospital visits, personal protective equipment, private secure rooms in the CRF, vaccination of the research fellow, vaccination of participations, temperature scanning, and symptom screening prior to assessment. The result of booking study visits around existing face-to-face clinical visits had an impact on the assessment window (14 days), and this will be explored in the subsequent results and discussion chapters.

To reflect the impact of COVID-19 on our study sample, the topic-guide for the nested qualitative interviews (study 4) were revised (see Appendix D). During shielding, qualitative semi-structured interviews for the nested qualitative study (study 4) were conducted over the telephone rather than face-to-face. As per the study protocol (Appendix D), all qualitative interview participants were purposively sampled (Patton, 2002) from the wider feasibility RCT sample. Due to the reduction in the overall sample size (n=17) due to COVID-19, there was a reduction in the pool of participants to invite to take part in the nested qualitative interviews (study 4) . Due to these changes, the qualitative interviews was analysed using reflective thematic analysis as one data set, rather than analysing treatment groups separately.

5.5 Chapter Summary

Due to the extraordinary impact of COVID-19 on KTRs, transplant services, transplant clinical care, and the mixed methods feasibility RCT, this brief chapter has contextualised the results, which are presented in the following chapter. The research team were able to utilise a pragmatic approach to ensure that the research questions

were able to be answered whilst maintaining patient safety. Whilst COVID-19 has presented many challenges to global healthcare and research, there are many positive outcomes such as a shift to virtual treatments, and increased flexibility in treatment time for patients. In addition, virtual interventions, and their use, may be of enhanced value whilst the UK and other countries recover from the COVID-19 pandemic. The next chapter will outline the results of study 3 (the quantitative and feasibility data) and study 4 (the nested qualitative study). The feasibility study data presented in the next chapter also provides insight into conducting research of an online-resource during the COVID-19 pandemic.

Chapter 6 Studies 3 and 4 - A randomised controlled feasibility trial utilising the revised ExeRTiOn online intervention

6.1 Abstract

6.1.1 Background and purpose

Kidney transplantation is the gold standard intervention for end-stage-kidney disease but is not without risk. Adverse weight gain within the first year of receiving a kidney transplant is associated with adverse health outcomes. Previous chapters have highlighted that there is no recognised intervention to address weight gain in new KTRs, KTRs have asked for support with this issue, and usability and experience testing of the ExeRTiOn online intervention has been reported. Therfore, the aim of this feasibility study was to examine feasibility to screen, consent, recruit, collect data and retain participants randomised to either UC, or to the refined online IG to address weight gain prevention in new KTRs.

6.1.2 Study design

Mixed methods randomised controlled feasibility trial.

6.1.3 Setting and participants

This study included 17 new KTRs (median age 49 years, 10 males, median 62 days since transplant) randomised to the online IG (n=9) or UC (n=8). Participants were recruited from two south-London transplant sites, had a kidney transplant within 3-months, and had access to an internet compatible device. Exclusion criteria included history of an unstable medical condition (e.g., unstable angina), non-English speaking or age less than 18 years. At baseline assessment participants were randomised to either UC, or IG.

6.1.4 Intervention

The IG received access to the 12-week password-protected ExeRTiOn online intervention (see chapters 3 and 4). IG participants received weekly email reminders, remote monitoring by a research physiotherapist, and could contact the physiotherapist via a secure message function.The UC group received standard education to increase their PA and follow a healthy diet following transplantation.

6.1.5 Outcomes

Primary outcomes concerned feasibility. Feasibility outcomes included screening rates, consent rates, adherence to study visits, acceptability of outcomes, adherence to the online intervention, retention of participants, willingness to be randomised, adverse events, hospitalisations, experience using the online intervention and experience taking part in the feasibility trial. Semi-structured interviews gathered experience of participating in the trial and using the online intervention. Secondary outcomes were recorded at baseline, three months and twelve months. These included body weight, BMI, BIA, PWV, AI, 6MWT, the GPPAQ, Nutrition Self-Efficacy Scale and the Physical Exercise Self-Efficacy Scales, EQ-5D-5L and the CFS.

6.1.6 Results

Trial participation appeared feasible for both groups. Screening rate was 84.2% (95% CI 68.8 to 94.0), recruitment 62.5% (95%CI 43.7 to 79.0) and trial retention was 76.4% (95% CI 50.0 to 93.2) at 12-months. All pre-set progression criteria for screening, recruitment and retention were achieved. There were no associated adverse events. Qualitative analysis revealed four main themes; optimising participation and recruitment, the impact of COVID-19, engagement is a choice (technical and personal

factors) and mechanisms of action (assessment and intervention factors). The IG appeared to maintain median body weight across the study; 94.5kg, (IQR 63.0, 102.0) at baseline, 95.0kg, (IQR 66.7, 105.3) at 3-months and 94.7kg (IQR 77,2, 117.3) at 12-months. Whereas UC participants increased (81.3kg, (IQR 73.6,94.6), 86.2kg (75.4, 96.5) and 93.3kg (70.3, 101.9). IG increased 6MWD (450m, (IQR 450, 540), 525m (IQR 472.5, 615) and 495m (IQR 465, 615) and UC decreased 6MWD (517.5m (IQR 436, 570), 507.5m (IQR 442.5, 605) and 435m (IQR 435, 555)). All other outcomes were comparable across the sample.

6.1.7 Limitations

Not powered, small sample size, unblinded and recruitment ceased due to COVID-19.

6.1.8 Conclusions

Participant attitudes, experiences and engagement with the study and intervention provide insight for future trial design. Integrated mixed methods analysis demonstrate congruency of both datasets that a definitive RCT is feasible, warranted and welcomed by KTRs. A post-PhD multi-centre pilot RCT is required to inform a definitive RCT. Additional qualitative data should explore the experiences of those who decline participation and/or withdraw from the study.

6.2 Introduction to the feasibility mixed methods RCT (Studies 3 and 4)

Whilst kidney transplantation is the recognised gold standard treatment for ESKD (Dudley & Harden, 2011), it is not without risk (Devine et al., 2019). Compared to their age-matched counterparts, KTRs demonstrate a three to five times greater risk of CVD (Sarnak et al., 2003). This elevated CVR is thought to be due to a combination of traditional and transplant specific risk factors, which are exacerbated by immunosuppressant medications (Devine et al., 2019). Cardiac disease is the leading cause of death in all people receiving RRT. The latest UK Renal Registry report suggests 25.3% of deaths in people under 65 years living with CKD are attributed to cardiac disease (UK Renal Registry, 2019). In addition, cardiac disease contributes to 17.5% of all UK reported transplant deaths (UK Renal Registry, 2019). A retrospective analysis of over 20,000 KTRs in the UK revealed an increased BMI is an independent risk factor for delayed draft function, primary graft non-function and graft loss (Kostakis et al., 2020).

MS can be used to identify participants with high CVR, and includes the presence of hyperlipidaemia, hypertension, insulin resistance and obesity (Goldsmith & Pietrangeli, 2010). MS increases with post-transplant weight gain and has been associated with increased risk of graft loss, death by CVD, and the development of PTDM (Hricik, 2011; Pedrollo et al., 2017). In the dialysis population, there is evidence to suggest that the presence of obesity has been associated with survival benefits known as the 'obesity paradox' (Baker et al., 2021; Herselman et al., 2010). As discussed in chapter 1, this is not the case for KTRs. A systematic review demonstrated obesity is associated with mortality in KTRs (Ahmadi et al., 2014). In addition to this, an analysis of the UK Transplant Registry data revealed 78.3% of KTRs who had died during follow-up did so with a functioning kidney (Kostakis et al., 2020). Therefore, addressing modifiable

CVR factors, such as obesity, and weight gain are important to optimise clinical care for KTRs.

Weight gain within the first year of SOT has been associated with adverse clinical events, and poor transplant outcomes (Kugler et al., 2015; Saigi-Morgui et al., 2016). KTRs demonstrate rapid weight gain in the acute-post operative period (Beckmann et al., 2017). Weight gain within the first year of receiving a kidney is a critical health issue (Glicklich & Mustafa, 2019), and occurs in both KTRs living with and without obesity (Chan et al., 2014). Studies have reported over half of KTRs gain more than 5% of their body weight within the first year of transplant (Cashion et al., 2014; Forte et al., 2020). Post-transplant weight gain is usually accompanied with an increase FM, not LTM (Cashion et al., 2014). A recent study has shown a positive association with an increase in adipose tissue (visceral and sub-cutaneous) with insulin resistance in KTRs (Workeneh et al., 2019). Factors underlying post kidney transplant weight gain include; reduced physical function (Koufaki et al., 2013) and PA (Nielens et al., 2001), increased appetite, (Cashion et al., 2014) steroid medication use, (Aksoy, 2016) and the lifting of dietary restrictions (Stanfill et al., 2012). Therefore, interventions to address weight gain and address modifiable risk factors are warranted.

As presented in the systematic review of Chapter 2, there was no evidence that dietary, exercise, or combined interventions led to significant changes in body weight or BMI in the first-year post kidney transplantation. There were a small number of RCTs with significant methodological variation, and variable quality. This systematic review highlights the need for RCTs to investigate interventions designed specifically to address post-transplant weight gain in KTRs. Interventions were hypothesised to need

combined complex interventions such as dietary counselling, PA intervention and BCT'S to address the multifactorial problem of acute weight gain post KTx.

The qualitative study presented in chapter 4 assessed the usability and experience of an online intervention designed specifically to address post-transplant weight gain (Castle, Greenwood, et al., 2020). Study 2 led to iterative patient-led refinements to the ExeRTiOn online intervention to improve it's acceptability in preparation for this feasibility RCT. Therefore, the primary outcomes of interest for this study were to answer the key feasibility questions relating to screening, consenting, adherence, hospitalisations, data collection and experience. This facilitated the assessment of whether a future trial should be completed, and if so suggest aspects of trial design (Eldridge, Lancaster, et al., 2016a).

This chapter will address the second aim of this thesis, to explore the feasibility and acceptability of the online intervention for new KTRs. It will also address the fifth objective to conduct a feasibility mixed methods RCT to assess feasibility (5a), and capture and report experiences (5b) using the refined online intervention.

6.3 Methods

6.3.1 Study design

General Methods have been presented previously, see chapter 3 and Appendix D. Key methodological considerations for this feasibility RCT will be summarised below. This chapter includes two studies, study 3 includes the QUANT and feasibility outcomes, and study 4 includes the nested QUALI evaluation that form a mixed methods feasibility RCT.

Research ethical approval was sought and achieved (see Appendices D and E). Participants were invited for assessment at baseline, 3-months and 12-months (quantitative data, study 3). Randomisation occurred at baseline assessment with a member of the research team and the use of a computer generated list (Sealed Envelope Ltd, 2020). Due to the nature of the online intervention, participants and the research fellow were unable to be blinded to the provision of the online intervention. The CONSORT guidance for feasibility and pilot study were followed (Eldridge, Chan, et al., 2016).

6.3.2 Participants

Potential participants were identified from two South-London outpatient transplant clinic lists and approached during routine transplant clinic appointments. Participants were included if they were over the age of 18, had received either a living or deceased single organ kidney transplant within the past three months, had access to an internet compatible device and had a BMI of greater than or equal to 18.5 kg/m^2. Patients were excluded if they were pregnant or had an active medical condition preventing them from completing PA (such as unstable angina), a diagnosis of a significant cognitive impairment preventing them from engaging with an online intervention, or if they were unable to complete the online intervention in English. Principles of good clinical practise were utilised during the recruitment and consenting of participants.

6.3.3 Primary outcome

Primary outcomes centred around feasibility and included screening, recruitment, retention, engagement with the online intervention, adherence to study visits, safety and hospitalisations, the participants' experience of the intervention, and the participants'

experience of taking part in the study. Experiential data was collected through individual semi-structured qualitative interviews.

6.3.3.1 Progression criteria

Progression criteria was set prior to the commencement of the feasibility RCT by the TMG. Consideration into the disparate aspects of the feasibility evaluation will be decided by TMG consensus to discuss the next steps of research, including intervention refinement or efficacy evaluation. Progression criteria from chapter 3 is represented in Table 6.1 below.

Table 6-1 progression criteria for the feasibility RCT

Criteria	Pre-set cut offs
Screening of potential participants	• ≥ 50% deemed eligible approached to do the study consider progression to a definitive trial • If less than 50% and no significant valid reasons provided, consider not progressing to a further study
Recruitment rate	• ≥50% consider progression to a definitive trial • 40-49% TMG to discuss trial, and if valid modifiable reasons identified, the study may progress • ≤30% and there are no significant valid reasons provided, the study will not progress to a definitive trial
Retention rate at 12-months	• ≥ 60% progress research • 50-59% discuss with TMG. If valid reasons identified, the study may progress • ≤ 40% do not consider further research
Intervention adherence	• ≥ 60% of the intervention completed (≥ 7 out of the 12 sessions) • If less than 60% adherence, with no valid reasons from discussions with the TMG, the study may not progress
Safety and hospitalisations	• Capture and report any harms e.g., Slips/ trips • Capture and report unplanned hospitalisations • Capture and report any associated adverse events

Note. TMG= trial management group.

6.3.4 Secondary outcomes

6.3.4.1 Anthropometric measures

Anthropometric measures included body weight (measured in kilograms) waist circumference (measured in centimetres), hip circumference (measured in centimetres) and BMI (measured in kg/m^2). Change in body weight (kg) at each visit from baseline was also calculated and reported.

6.3.4.2 Body composition

BIA was used to assess BC. BC was estimated using the Fresenius BC Monitor (Fresenius BCM) (Gudivaka et al., 1999; Macdonald et al., 2004), a CE marked device (NICE, 2017a). FM, and LTM were recorded at each study visit.

6.3.4.3 Functional exercise capacity

Functional exercise capacity was assessed using the 6WMT. The 6MWT was completed once, at each study visit, using a standardised protocol (American Thoracic Society, 2002). Pre and post resting HR, total walk distance (6MWD) in meters was recorded.

6.3.4.4 Arterial stiffness

Arterial stiffness is a measure of CVR, and PWV is an independent predictor of cardiovascular events and mortality in KTRs (Melilli et al., 2018). Arterial stiffness was measured by PWV and the AI, using the Vicorder system (Skidmore Industries, UK). Standardised procedures (Laurent et al., 2006) and calculations of arterial path length (Hickson et al., 2009) were used. PWV and AI were measured three time per study visit, and then averaged for a final score of carotid femoral PWV and AI.

6.3.4.5 Questionnaires

Four questionnaires were completed by participants at each study visit. They include validated measures of self-reported PA, self-efficacy, quality of life, and fatigue. PA was measured by the GPPAQ, which has been validated in people living with CKD (Wilkinson et al., 2020). PA levels were classified into four categories; inactive, moderately inactive, moderately active and active (Physical Activity Policy Health Improvement Directorate, 2009).

Self-efficacy towards engaging in exercise, physical activity and food behaviours was assessed using the Nutrition Self-Efficacy Scale and the Physical Exercise Self-Efficacy Scales (Schwarzer & Renner, 2009). Higher self-efficacy questionnaire scores indicate an individual is more likely to change target behaviours such as physical exercise and healthy eating (Schwarzer & Renner, 2009).

Health-related quality of life was assessed by the EQ-5D-5L questionnaire (Devlin & Brooks, 2017). The EQ-5D-5L provides three data components (see Chapter 3): the EQ-5D-5L health state, the EQ-5D-5L VAS and the EQ-5D-5L index value. This questionnaire was selected to measure self-reported quality of life as it is recommended by the NICE (Devlin & Brooks, 2017; NICE, 2019) and it has been validated in KTRs as a measure of health status (Cleemput et al., 2004).

Fatigue was assessed by the CFS (Chalder et al., 1993). The scale contains eleven items, including two sub scales measuring the severity of physical (7 items) and mental fatigue (4 items). Each item is scored from 0 to 3, with 0 being better than usual and 3 being much worse than usual. The total score can range from 0 to 33, with higher scores representing greater levels of fatigue. Permission was sought to use this questionnaire.

6.3.5 Baseline demographics and clinical information

Participant's characteristics such as age, gender and ethnicity were collected. Transplant data such as the donor type, number of previous transplants, episodes of acute rejection, immunosuppressant mediation regimes, hypertensive medication regimes, diabetes history, diabetes management, CKD diagnosis and previous RRT were captured from clinical records. Resting BP and HR were recorded three times on the left arm at rest and averaged at each of the three study visits.

eGFR was calculated using the CKD-EPI creatinine equation (measured in ml/ min/1.73m^2) (Levey et al., 2009), and the CKD-EPI calculator (National Kidney Foundation, 2021). Serum creatinine blood results (μmol/L) from routine transplant clinic blood tests that were conducted on the same day as the study visits were used.

6.3.6 Study procedures

Ethical approval was sought, and obtained, from the London Dulwich REC (reference 19/LO/1138). Approvals were sought and obtained from both research sites (KCH and GSTT) (refer to appendices D and E). Potential participants were screened for eligibility by either the research fellow, or the transplant consultant. Patients were provided with patient information sheets and data security documents and given a minimum of 24 hours (or at the participants convivence) to consider study participation. Participants completed a written consent form, attended a baseline assessment, and were then randomised with a computer generated list (Sealed Envelope Ltd, 2020). They were allocated to either the 12-week ExeRTiOn online IG or UC by a member of the research team. The research fellow was not able to be blinded as they

were providing the intervention and completing study visits for their PhD Fellowship. Copies of the study protocol, patient information sheets, data security and privacy document and the consent form can be found in Appendix D.

Participants attended the KCH NIHR CRF for assessments at baseline, 3-months and 12-months. For participant convivence, these were booked in around transplant clinical visits with an assessment window of fourteen days (plus or minus 7 days). Data collection at the study visits included transplant characteristics, medical history, body weight, waist circumference, BMI, BIA, PWV, AI, 6WMT, self-reported self-efficacy, CFS, GPPAQ and EQ-5D-5L. A purposive sample of participants from the study were invited to complete individual semi-structured interviews. Interviews were completed over the phone, or alongside study visits.

6.3.6.1 Online intervention group

Participants in the IG were provided with access to a secure online intervention to complete independently with any internet compatible device. The intervention included 12-weekly sessions. The online intervention included both a patient-facing website, and a back-facing physiotherapist website (monitored by the research fellow). The intervention development, components and the functionality of the ExeRTiOn online intervention have been previously reported in chapters 3, 4 and Castle et al (2020). All IG participants were provided with a brief one-to-one orientation session with the research fellow at the time of randomisation. IG Participants could contact the research fellow through a secure message function if they needed. Standardised automated reminder emails, and personalised messages were provided as per the research protocol (see Appendix D). After completion of the 12-week intervention, IG participants were

able to continue revisiting completed sessions until the end of the trial at the final 12-month study visit.

6.3.6.2 Usual care group

UC at both sites involved attendance at routine post kidney-transplant outpatient clinics. The minimum requirement of UC included:

- The provision of a leaflet on healthy eating after kidney transplantation by a renal dietitian during the transplant inpatient stay
- Routine physiotherapy input during the surgical hospital admission
- Encouragement from the outpatient transplant clinic nephrologists and nurses to follow a healthy diet, and be physically active during routine outpatient follow-up.

In addition to the above, the UC group at the primary site (KCH) included up to two appointments with an outpatient renal physiotherapist.

6.3.7 Sample size

6.3.7.1 Overall sample size

As stated in Chapter 3, as the primary aim of this study was to explore feasibility, formal power calculations were not completed. The CONSORT guidelines for feasibility trials was followed (Eldridge, Chan, et al., 2016). The initial target sample for the mixed methods feasibility RCT was 50 participants across both sites (see Appendix D for study protocol). A sample size between 24 and 50 has been recommended to estimate SDs for use in a sample size calculation in a future study following the feasibility trial (Hooper, n.d.; Julious, 2005; Sim & Lewis, 2012). Therefore, 50 participants was selected as it would allow for a power calculation to be completed to inform a future definitive trial.

6.3.7.2 Qualitative sampling

For the nested qualitative evaluation (study 4), a purposive sample (Patton, 2002) of participants were invited for individual semi-structured interviews. This would explore the experience of participating in the trial, and the experience using the online intervention. A range of age, gender, and adherence with the intervention were included in the qualitative sampling framework. The final qualitative nested sample size (study 4) was informed by the inductive reflexive analysis (Braun & Clarke, 2019a), information power (Malterud et al., 2016), and the meaning and themes derived from the analysis rather than a positivists approach describing the frequency of themes (Braun & Clarke, 2019b). A prior analysis estimated sample size of five to ten rich interviews would be sufficient to uncover common patterns and themes from across the dataset.

6.3.8 Statistical analysis

MMR design underpinned this feasibility RCT and was previously discussed in chapter 3. Quantitative (study 3) and qualitative data (study 4) data collection and analysis occurred separately and simultaneously in this feasibility study. As previously discussed in chapter 3, feasibility trial guidance was followed (Eldridge, Chan, et al., 2016), external statistician (RP) guidance was sought, and no statistical significance testing, power calculations or effect size estimates were performed. All continuous outcomes were analysed for normal distribution using histograms (Pallant, 2013). Two-sided confidence intervals were calculated at the 95% confidence level. Table 6.2 below summarises the statistical plans for each dataset (QUANT, QUALI and mixed methods analysis).

Table 6-2 Summary of the statistical plans

Outcomes	Statistical plan
Feasibility (QUANT)	• Screening, recruitment, retention and adherence (study visits and intervention) rates were calculated and presented as proportions with 95% confidence intervals • Reasons for declining to take part and or withdrawing from the study were reported descriptively • Length of time to recruit the target sample was described using either by means and SDs, or median and IQRs ranges • Length of time taken to complete the assessments were described either by means and SDs, or median and IQRs ranges • Percentage of completed study visits, and proportion of assessment outcomes recorded for each study visit were calculated • Mean time taken to complete the study visits, with confidence intervals were calculated • The reasons for hospital admissions and adverse events were explored by descriptively • Proportions of events such as transplant biopsies, transplant CMV, and adverse events with confidence intervals were calculated • Description of participants interaction with the online-resource (IG only) (log-in times, interactions with physiotherapists) were described either by means and SDs, or median and IQRs ranges • Mean log-in time for the online intervention (IG only) alongside confidence intervals were calculated • Interactions with the therapist through the trial online intervention will be reported descriptively
Secondary QUANT analysis	• Assessment outcomes body weight, BMI, BC, quality of life, self-efficacy, fatigue, arterial stiffness and physical function were described either by means and SDs, or median and IQRs ranges • Individual data series graphs were plotted for body weight over the three assessment points for both groups • Change scores for body weight, BMI and BC outcomes • Questionnaire data was calculated as per individual guidance for each outcome (see chapter 3), and summarised using either by means and SDs, or median and IQRs ranges • Correlations were performed between:

	○ The number of completed online sessions (IG) and body weight at 12-months ○ The number of completed online sessions (IG) and self-efficacy scales at 12-months ○ Body weight at 12-months and self-efficacy scales
QUALI analysis	• All interviews were recorded and transcribed • Transcribed verbatim were imported into NVIVO for MAC © version 12 for analysis • Data quality and richness was assessed using information power (Malterud et al., 2016) • Analysis was conducted by EC using: ○ A reflexive thematic analysis (Braun & Clarke, 2006, 2019a) ○ From a Pragmatic philosophical standpoint (Cherryholmes, 1992).
Coding the ExeRTiOn online intervention to the BCTTv1	• All interactions with physiotherapist via the online intervention were anonymised and imported into NVIVO • The ExeRTiOn online intervention and interactions with the physiotherapist through the trial online intervention were retrospectively mapped to the BCW and the BCTTv1 using NVIVO and a coding framework • See section 6.4.1.7 and Appendix F for further details
Integrated mixed Methods analysis	• QUALI and QUANT data collection and analysis occurred simultaneously and separately as per the thesis process diagram (see chapter 3) • A convergent mixed methods analysis was used for combining QUALI and QUANT data (Creswell & Plano Clark, 2018b) • Joint display tabulation was used to seek examples of convergence, complementary issues or discrepancies between the QUALI and QUANT databases (O'Cathain et al., 2010) • The progression criteria were reviewed to inform decisions regarding a definitive follow-up trial

Note. Refer to chapter 3 for further details.
CMV= cytomegalovirus, IG=intervention group, BMI= body mass index, BC= body composition, NVIVO=qualitative analysis software, EC= research fellow, BCTTv1= Behaviour Change Technique Taxonomy version 1, BCW= the behaviour change wheel, QUALI=qualitative and QUANT=quantitative

6.4 Results

6.4.1 Feasibility outcomes

6.4.1.1 Eligibility and recruitment

The study opened for recruitment on the 3rd of September 2019 at the primary sponsor site (KCH) and on the 19th of February 2020 at the secondary site (GSTT). The five-month delay to secure the green light at the secondary site were attributed to the changes in the Health Research Authority (HRA) processes, such as the model non-commercial agreement form (Health Research Authority, 2018) that was introduced during the trial set-up phase. This resulted in unanticipated contract delays at the secondary site regarding discussions of intellectual property between the site and hosting software company. The first participant was recruited at the sponsor site on the 20th of September 2019. Due to the COVID-19 pandemic, the study sample was adjusted. See chapter 5, and Appendix E.

Trial recruitment was halted on the 15th of March 2020 and subsequently ceased on the 2nd of June 2020 due to the COVID-19 pandemic and the shielding of KTRs. In total, 20 consented to the trial (16 from KCH and 4 from GSTT). Monthly screening and recruitment rates are tabulated in Table 6.3 below. Screening rates were defined as the number of potential participants that met the inclusion criteria per month during the recruitment phase of the trial. Non- eligible patients were classified as potential participants who did not meet the inclusion/ exclusion criteria for the study (see chapter 3).

Table 6-3 Monthly screening and recruitment figures

Month	Screened	Consented	Declined	Ineligible	Comments
SEP 2019	6	4	1	1	SEP-FEB 2019 recruitment at KCH only
OCT 2019	4	2	0	2	
NOV 2019	1	0	1	0	Reduced recruitment rates as Research Fellow on annual leave
DEC 2019	8	6	1	1	
JAN 2020	8	2	4	2	
FEB 2020	7	5	2	0	GSTT open for recruitment 4 patients recruited at GSTT 2 GSTT declined
MAR 2020	4	1	0	3	1 participant recruited prior to COVID-19 outbreak. KTRs categorised as EVC Recruitment and baseline assessment paused. Screening fail (n=3) given PIS but unable to consent.
15th MAR 2020	Recruitment and baseline Ax halted secondary to COVID-19 and shielding				
APR-MAY 2020	Recruitment and baseline Ax remain halted				
2nd JUN 2020	Recruitment ceased as per TMG Consent fail (n=3 GSTT participants) consented but were unable to complete Baseline Ax and randomisation These participants no longer met the study criteria and were therefore removed from the trial n=17 participants entered the trial and were randomised				

Note. Raw numbers of participants are provided in table. Reasons for ineligibility and declining to take part in the trial are provided in the subsequent CONSORT diagram. ESL refers to English as a second language, KCH= King's College Hospital (primary and sponsor site), GSTT= Guy's and St Thomas' Hospital, KTx= Kidney Transplant, Ax= assessment, PIS= participant information sheet, and EVC= extremely vulnerable category for the risk of COVID-19.

A detailed study consort diagram utilising the principles of the CONSORT 2010 extension for feasibility trials (Eldridge, Chan, et al., 2016) is shown on the following page (Figure 6.1). It demonstrates the screening, recruitment, adherence and participation throughout the 12-month feasibility RCT.

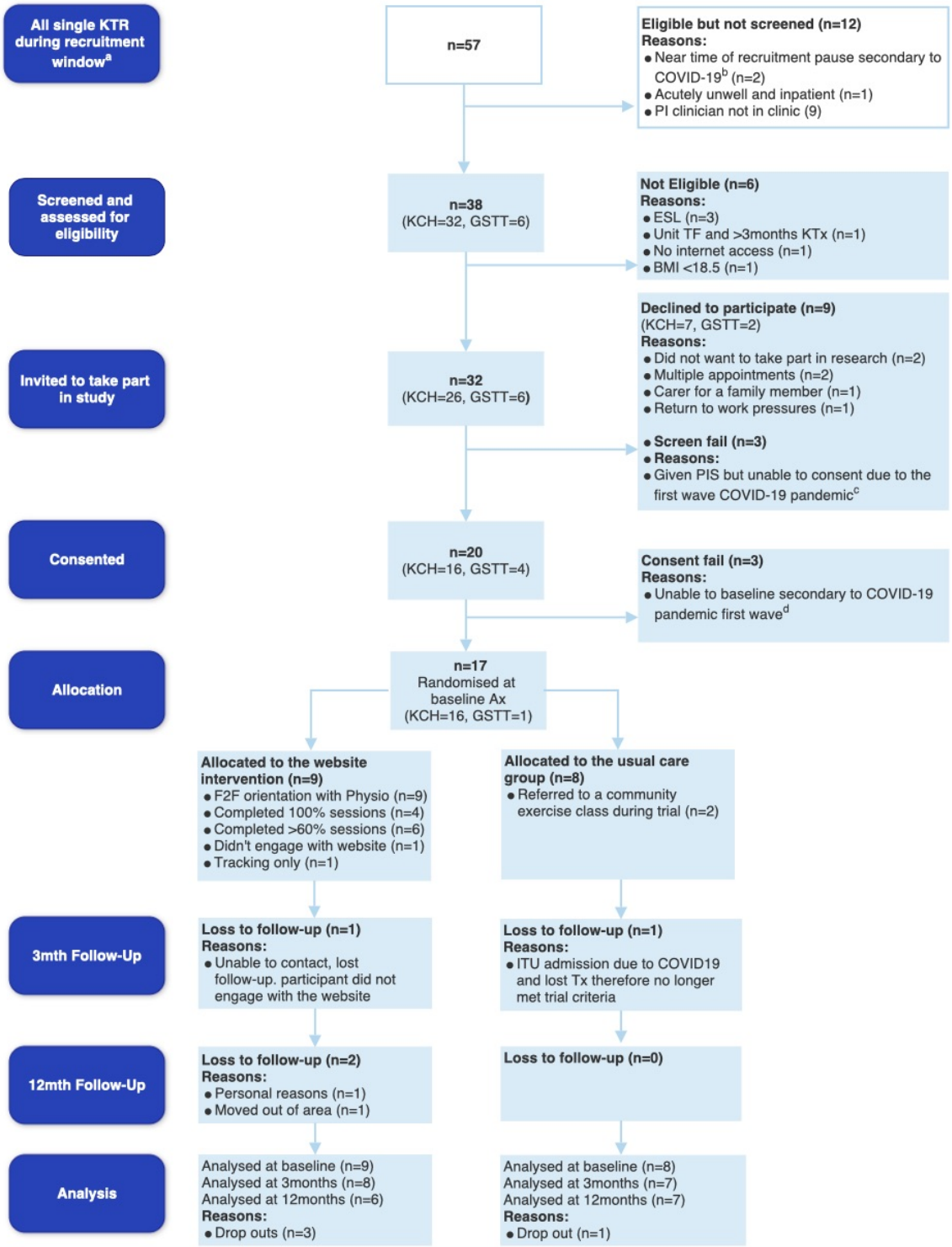


Figure 6-1 CONSORT flow diagram

Note. [a] indicates the recruitment window (3rd September 2019 -15th March 2020 for KCH and 19th February-15th March 2020 for GSTT), [b] indicates potential participants at KCH who were eligible days before recruitment was put on hold due to Coronavirus disease 2019 (COVID-19) on the 15th March 2020, [c] demonstrates the 3 potential participants at KCH who were given patient information sheets but unable to consent due to the first wave of COVID-19, and [d] indicates 3 participants who consented at GSTT but unfortunately due to pausing of recruitment, became ineligible and were therefore not baselined or randomised.

KTR= kidney transplant recipients, PI= Principal Investigator, KCH= King's College Hospital, GSTT= Guy's and St Thomas' Hospital, ESL= English as a second language, TF=transfer, BMI= body mass index and ITU= Intensive Care Unit.

6.4.1.2 Participant characteristics

Ten out of the seventeen participants recruited to study 3 were male (58.8%). The median age across the sample was 49.0 (IQR 39 to 59) years. Age was higher in the UC group (median 59.5 years) versus the IG (Median 39 years). All participants were consented within the first three months of receiving a kidney transplant. The median transplant vintage at baseline was 62 days (IQR 53.0, 68.0). Participants were representative of the south-London transplant population, with the main three ethnic groups represented (white Caucasian, black African and Caribbean and Asian) in this study sample. Participants in the UC group had a lower baseline body weight and BMI compared with the IG. Most of the participant population had not had a previous transplant, with only 23.5% of the participants having two or more kidney transplants. There were more deceased than living donor transplant recipients (76.5%). Only one participant did not receive any RRT prior to transplantation. Table 6.4 below depicts the baseline demographics of the total sample, and per group. Due to the small sample size (n=17) and the distribution, median and IQR were used to summarise continuous data. Due to the feasibility study design, and recommendations on feasibility study reporting, no statistical testing for difference between groups was performed (i.e. randomisation checks) (Eldridge, Chan, et al., 2016), which is also not advised in full RCTs (De Boer, Waterlander, Kuijper, Steenhuis, & Twisk, 2015).

Table 6-4 Participant demographics at baseline visit.

Variable		Total (n=17)	Intervention group (n=9)	Usual care (n=8)
Age	years	49.0 (39.0 to 59.0)	39.0 (33.0 to 44.0)	59.5 (53.5 to 65.0)
Sex	Males	10 (58.8%)	5 (55.6%)	5 (62.5%)
Ethnicity	White Caucasian	6 (35.3%)	3 (33.3%)	3 (37.5%)
	Black African and Caribbean	9 (52.9%)	5 (55.6%)	4 (50%)
	Asian	2 (11.8%)	1 (11.1%)	1 (12.5%)
Post-transplant time	days	62.0 (53.0 to 68.0)	62.0 (58.0 to 79.0)	59.0 (49.5 to 66.50)
Donor Type	Live Related	2 (11.8%)	1 (11.1%)	1 (12.5%)
	Live Unrelated	2 (11.8%)	1 (11.1%)	1 (12.5%)
	Deceased	13 (76.5%)	7 (77.8%)	6 (75.0%)
Two or more previous KTx		4 (23.5%)	3 (33.3%)	1 (12.5%)
Episodes of acute rejection		4 (23.5%)	2 (22.2%)	2 (25.0%)
CKD Diagnosis	GN	7 (41.2%)	5 (55.6%)	2 (25.0%)
	DN	2 (11.8%)	1 (11.1%)	1 (12.5%)
	HT	2 (11.8%)		2 (25.0%)
	Other and unknown	6 (35.3%)	3 (33.3%)	3 (37.5%)
RRT before KTx	Pre-emptive transplant	1 (5.9%)		1 (12.5%)
	HD	10 (58.8%)	6 (66.7%)	4 (50%)

	PD	3 (17.6%)	1 (11.1%)	2 (25%)
	HD and PD	3 (17.6%)	2 (22.2%)	1 (12.5%)
RRT duration pre KTx	months	34.0 (24.0 to 58.0)	37.0 (34.0 to 58.0)	30.0 (22.5 to 52.0)
Baseline body weight	kilograms	92.6 (72.0 to 96.1)	94.5 (63.0 to 102.0)	81.3 (73.6 to 94.6)
Baseline BMI	kg/m^2	27.9 (23.9 to 32.9)	30.0 (23.9 to 33.6)	26.8 (24.6 to 29.8)
Immunosuppression regime (total daily dose)	Tacrolimus	16.0 (8.0 to 20.0)	16.0 (10.0 to 20.0)	13.0 (6.0 to 24.0)
	Prednisolone	5.0 (5.0 to 7.5)	5.0 (5.0 to 5.0)	8.8 (5.0 to 10.0)
	Mycophenolate Mofetil	1000 (1000 to 1000)	1000 (500 to 1000)	1000 (1000 to 1000)
Baseline renal function ($mL/min/1.73m^2$)	CKD-EPI Creatinine eGFR	40 (32 to 60)	42.0 (29.0 to 64.0)	40.0 (33.0 to 44.0)
Smoking History	Current smoker	2 (11.8%)	1 (11.1%)	1 (12.5%)
	Ex-smoker	6 (35.3%)	3 (33.3%)	3 (37.5%)
Anti-hypertensive medications	Taking antihypertensives	11 (64.7%)	7 (77.8%)	4 (50.0%)
	Number of antihypertensive medications	1.0 (0.0 to 1.0)	1.0 (0.1 to 1.0)	0.5 (0.0 to 1.0)
Baseline BP (mmHg)	SBP	138.0 (121.0 to 149.0)	137.0 (121.0 to 148.0)	143.0 (117.5 to 150.0)
	DBP	83 (73.0 to 88.0)	83.0 (73.0 to 86.0)	85.5 (75.0 to 90.5)
Diabetes diagnosis	Type 1 diabetes	1 (5.9%)	1 (11.1%)	
	Type 2 diabetes	2 (11.8%)		2 (25%)
	PTDM	1 (5.9%)	1 (11.1%)	
Diabetic medication	Insulin only	3 (17.6%)	2 (22.2%)	1 (12.5%)

Number of comorbidities*	One	9 (52.9%)	6 (66.7%)	3 (37.5%)
	Two or more	8 (47.1%)	3 (33.3%)	5 (62.5%)

Note. Median and IQR ranges (IQR) are presented for continuous data. Proportion percentages and frequency numbers are shown for categorical data. * Indicates comorbidities included a medical history of diabetes, hypertension, cerebrovascular event, osteoarthritis, brain haemorrhage, cardiovascular disease, cancer or respiratory disease. Episodes of acute rejection were classified as yes or no within the first three months from medical notes and biopsy reports. CKD= chronic kidney disease, KTx=Kidney Transplant, CKD=chronic kidney disease, GN=glomerular nephritis, DN=Diabetic Nephropathy, HT=Hypertension cause, RRT= RRT, HD=haemodialysis, PD=peritoneal dialysis, PTDM=post-transplant diabetes mellitus, BMI=body mass index, eGFR=estimated glomerular filtration rate, BP= blood pressure SBP= systolic blood pressure and DBP= diastolic blood pressure

6.4.1.3 Retention of participants

Seventeen participants (16 from KCH and 1 from GSTT) out of the twenty participants that consented to take part completed baseline assessment and were randomised to either UC or the online IG. Thirteen out of seventeen participants (76.5%) remained in the study over the twelve-month follow-up period. Two participants dropped out of the study at the three-month assessment point, therefore only baseline data was available for them. Unfortunately, one participant (P13, UC group) contracted COVID-19, which resulted in a lengthy intensive care admission and the loss of their kidney transplant. They therefore no longer met the trial criteria and ceased participation in the trial. A second participant (P14, IG) was lost to follow-up despite emails, phone calls and a letter. The retention rate at the three-month assessment was 88% (95%CI 63.6 to 98.5%).

Two further participants (n=4 total) dropped out of the trial at the twelve-month assessment, therefore only baseline and three-month data was available. One participant (P05, IG) withdrew due to personal reasons. The final participant (P15, IG) was lost to follow-up as they moved out of London and subsequently transferred to another transplant unit. The retention rate at twelve-month assessment was therefore 76.4% (95%CI 50.0 to 93.2%).

Table 6.5 below summarised the key feasibility outcomes and progression criteria. This includes screening rates, consent rates, retention rates, adherence to study visits (baseline, three-months and twelve-months), adherence to the online intervention (IG only) and hospitalisations.

Table 6-5 Feasibility outcomes and progression criteria

Feasibility Measure	Definition	Rates with confidence intervals	Progression criteria	Notes
Screening rate	% Of screened participants that met the inclusion criteria during the study recruitment window	32/38 84.2% (95% CI 68.8 to 94.0)	≥50% deemed eligible approached to do the study	
Total consent rate	% Participants recruited from the total eligible potential participants in the units	20/32 62.5% (95%CI 43.7 to 79.0)	>50% of people approached consent to study who have been screened and deemed eligible to take part in the trial	Target sample of n=50 not met due to changes in recruitment criteria due to COVID-19 pandemic
Trial retention at 12 months	% Participants completed trial from total sample	13/17 76.4% (95% CI 50.0 to 93.2)	Retain ≥60% of the sample at 12 months follow up	Progression criteria for retention met despite COVID-19 pandemic
Adherence to data collection at baseline Ax	% Participants who attended the baseline study visit AND completed all secondary outcomes	17/17 100% (95% CI 80.5 to 100.0)		Full outcomes include Body weight, BMI, BIA, PWV, AI, 6MWT, EQ-5D-5L, CFS, GPPAQ and self-efficacy for physical exercise and nutrition
Adherence to 3-month Ax	% Of participants who attended a 3-month assessment	15/17 88.3%(95%CI 63.6% to 98.5%)		Two participants dropped out at 3-months (one in each group)

Adherence to data collection at 3-month Ax	% Participants completing full outcome data collection at 3-months assessment from total trial sample	9/17 52.9% (95% CI 27.8 to 77.0%)		Eight participants unable to complete full assessment due to shielding during the first wave of the COVID-19 pandemic BIA, PWV, AI, waist and hip circumference and 6MWT data were not captured
Adherence to 12-month Ax	% Of participants who attended a 12-month assessment	13/17 76.4% (95% CI 50.0 to 93.2)		Two further dropouts occurred at 12-months
Adherence to data collection at 12-month Ax	% Participants completing full outcome assessment at 12 months from total trial sample	13/17 76.4% (95% CI 50.0 to 93.2)		Participants were assessed around routine clinic visits due to COVID-19 pandemic
Adherence to the online intervention (IG only)	% Treatment group participants completing 60% (≥7/12) sessions	6/9 66.67% (95% CI 29.93 to 92.51)		6/9 participants adhered to 60% or more of the sessions Qualitative data further explored engagement
Safety and hospitalisation (adverse events)	% Of participants who had a NRAE. NRAE defined as a non-elective hospital admission, of >24 hours, not related to the study	5/17 29.4 (95% CI 7.8 to 51.1)	Capture and report	One participant had two NRAE's There were no related AE's (see section 6.4.1.5)

Expected and unexpected harms	Expected harms could include musculoskeletal injuries from performing exercises or slips and trips	No slips, trips or musculoskeletal injures reported	Capture and report

Note. Definitions, raw numbers, proportions, and 95% confidence intervals are shown for each of the feasibility outcomes above. Willingness to be randomised is reported in the qualitative results (section 7.3). Ax refers to assessment, BMI= body mass index, BIA= bioimpedance analysis, PWV= pulse wave velocity, AI= augmentation index, 6MWT= six-minute walk test, CFS=Chalder fatigue scale and NRAE= non-related adverse events

6.4.1.4 Transplant and medical management

The median eGFR, calculated with the epi-CKD equation, (IQR) was 40 (32 to 60), 43 (40 to 58.5) and 52 (33 to 66) over the twelve-month trial. Both groups increased eGFR over the twelve-month study. All but one participant was prescribed the standard triple immunosuppressant regime at baseline (Tacrolimus, Prednisolone and Mycophenolate Mofetil). At the three-month assessment, all participants were prescribed triple immunosuppressants (n=15). At the twelve-month assessment, all but one participant (n=12) was prescribed triple immunosuppressant. The median total daily dose of prednisolone was five milligrams throughout the twelve-month study.

One participant in the IG had a documented diagnosis of PTDM at baseline. In the UC group, there were initially no documented cases of PTDM. This increased only in the UC group to two and three participants respectively. Three out of the seventeen participants (n=2 IG, n=1 UC group) were prescribed insulin therapy for diabetes management, which remained consistent throughout the twelve-months. At baseline, no participants in the trial were prescribed a regime of oral, injectables and insulin therapy. However, at three- and twelve-month assessments this increased only in the UC group to two and three participants respectively. Hypertension management, BP recordings and HR appeared to be stable throughout the sample.

Over the twelve-month trial, seven out of the seventeen participants had an episode of transplant rejection. Participants were classified as having an episode of rejection from transplant biopsy reports in clinical records. Ten participants (five from each group) had one episode of CMV throughout the trial.

6.4.1.5 Hospitalisations

In total there were nine episodes of hospitalisations from six participants throughout the study period. One participant (UC group) had one planned admission for a transplant biopsy, and two unplanned hospital admissions. Reasons for planned hospital admissions included overnight stays associated with transplant biopsies (n=4). Non-related adverse events (NRAE) were defined as unplanned hospitalisations (greater than 24 hours admission), which were not related to the study. Five participants had a NRAE and accounted for six of the hospital admissions. One participant therefore had two NRAE's. Reasons for the six NRAE included:

- Admissions to intensive care unit (ITU) for COVID-19 (n=2)
- An urgent transplant renal artery angioplasty (n=1)
- Elevated blood glucose levels due to PTDM (n=1)
- An episode of CMV (n=1)
- An acute transplant rejection (n=1).

The NRAE's occurred in both treatment groups (n=3 IG, n=3 UC group). Out of the total sample, 47% had transplant biopsies during the study. Two participants received multiple biopsies.

Both recipients who contracted COVID-19 during the study, had subsequent ITU admissions (one in each group). One participant recovered completely and continued with the trial (IG participant). Unfortunately, the other participant who contracted COVID-19 (UC group), lost their transplant and was therefore unable to continue with the trial as they no longer met the study inclusion criteria at the three-month assessment time point. Table 6.6 below tabulates renal function, medication history, diabetes

diagnosis and management, episodes of rejection and CMV, resting BP and HR of participants throughout the sample over the twelve-month study period.

Table 6-6 Transplant and medical characteristics of sample (study 3)

Variable	Total sample			Online intervention group			Usual care		
	Baseline (n=17)	3-months (n=15)	12-months (n=13)	Baseline (n=9)	3-months (n=8)	12-months (n=6)	Baseline (n=8)	3-months (n=7)	12-months (n=7)
eGFR epi-CKD (mL/min/1.73m2	40 (32 to 60.0)	43 (40 to 58.0)	52 (33 to 66)	42 (29 to 64)	44 (41.5 to 62.5)	52.5 (50 to 66)	40 (33 to 44)	42 (33 to 50)	45 (27 to 66)
TDD Prednisolone (mg) (Median and IQR)	5 (5 to 7.5)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	5 (5 to 5)	8.8 (5 to 10)	5 (5 to 5)	5 (5 to 5)
TDD Tac (mcg/kg) (Median and IQR)	16 (8 to 20)	12 (5 to 14)	8 (5 to 10)	16 (10 to 20)	13.5 (5.5 to 14)	8.5 (6 to 10)	13 (6 to 24)	6 (4 to 14)	6 (4 to 14)
TDD MMF (mg) (Median and IQR)	1000 (1000 to 1000)	1000 (500 to 1000)	1000 (500 to 1000)	1000 (500 to 1000)	1000 (500 to 1000)	750 (500 to 1000)	1000 (1000 to 1000)	1000 (500 to 1000)	1000 (500 to 1000)
Diabetes medical management-insulin only	3 (17.6%)	3 (20%)	3 (23.1%)	2 (22.2%)	2 (25%)	2 (33.3%)	1 (12.5%)	1 (14.3%)	1 (14.3%)
Diabetes medical management-oral OR insulin		2 (13.3%)	3 (23.1%)					2 (28.6%)	3 (42.9%)

Diabetes Diagnosis-Type 1	1 (5.9%)	1 (6.7%)	1 (7.7%)	1 (11.1%)	1 (12.5%)	1 (16.7%)			
Diabetes Diagnosis-Type 2	2 (11.8%)	1 (6.7%)	1 (7.7%)				2 (25%)	1 (14.3%)	1 (14.3%)
Diabetes Diagnosis-(PTDM)	1 (5.4%)	3 (20%)	4 (30.8%)	1 (11.1%)	1 (12.5%)	1 (16.7%)		2 (28.6%)	3 (42.9%)
Prescribed antihypertensives	11 (64.7%)	11 (73.3%)	10 (76.9%)	7 (77.8%)	6 (75%)	4 (66.7%)	4 (50%)	5 (71.4%)	6 (85.7%)
Number of antihypertensives (Median, IQR)	1 (0 to 1)	1 (0 to 1)	1 (1 to 1)	1 (1 to 1)	1 (0.5 to 1)	1 (0 to 1)	0.5 (0 to 1)	1 (0 to 1)	1 (1 to 2)
SBP (mmHg)	138.0 (121.0 to 149.0)	128.0 (125.0 to 146.0)	130.0 (125.0 to 143.0)	137.0 (121.0 to 148.0)	127.5 (121.5 to 134.0)	133.5 (125.0 to 143.0)	143.0 (117.5 to 150.0)	132.0 (126.0 to 156.0)	130.0 (124.0 to 147.0)
DBP (mmHg)	83.0 (73.0 to 88.0)	83.0 (73.0 to 90.0)	83.0 (80.0 to 89.0)	83.0 (73.0 to 86.0)	80.5 (71.5 to 92.0)	84.5 (70.0 to 95.0)	85.5 (75.0 to 90.5)	84.0 (77.0 to 89.0)	83.0 (80.0 to 89.0)
RHR (bpm)	82.0 (74.0 to 88.0)	78.0 (71.0 to 84.0)	86.0 (78.0 to 90.0)	83.0 (74.0 to 88.0)	79.5 (71.5 to 93.5)	82.5 (72.0 to 94.0)	80.0 (71.0 to 90.0)	77.0 (71.0 to 80.0)	86.0 (81.0 to 90.0)
Episodes of rejection over 12-month trial			7 (41.2%)			3 (33.3%)			4 (50%)

Episodes of CMV over 12-month trial (n, %)	10 (58.5%)	5 (55.6%)	5 (62.5%)

Note. Continuous data presented as median with IQR ranges. Ordinal data is displayed using number of participants (n) and valid proportions (%).eGFR epi-CKD= estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation, TDD=total daily dose, Tac= tacrolimus, MMF= mycophenolate mofetil, mg=milligrams, mcg/kg= micrograms/kg, SBP= systolic blood pressure, DBP= diabetic blood pressure and RHR= resting heart rate
For diabetes management, medical notes were reviewed, and prescribed medications were categorised as insulin only, oral only, insulin and oral. Episodes of CMV were taken from documentation in participants medical notes. Episodes of rejection were categorised by confirmed acute rejection from transplant biopsy reports. PTDM refers to a documented diagnosis of post-transplant diabetes mellitus from medical records

6.4.1.6 Adherence with the online intervention

Nine, out of the seventeen participants, were randomised to the online intervention. Adherence with the 12-weekly sessions was varied. Six out of the nine IG participants (66%, 95% CI 29.9 to 92.5%) met the progression criteria of adhering to 60% or more of the 12 weekly sessions.

Four participants completed all the 12-weekly sessions and had an adherence rate of 100%. Three participants were partial completers with their individual adherence rates shown below:

- P06 completed 9 sessions (75% adherence rate)
- P07 completed 5 sessions (42% adherence rate)
- G03 completed 10 sessions (83% adherence rate)

One of the functionalities of the back-end website (refer to chapters 3 and 4) was the use of the session scheduling report function to track IG participants as they progressed through the twelve-weekly sessions. Table 6.7 below depicts the session schedule report. This was done to track IG participants progression and engagement with each of the twelve-weekly sessions. This report also facilitated purposive sampling of participants with varying levels of engagement, to allow the qualitative capture of experiences and any potential issues participants had with engaging with the online intervention. Qualitative results will be presented in section 6.4.3.

Table 6-7 Session completion for IG participants

Study ID	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7	Session 8	Session 9	Session 10	Session 11	Session 12
P05	21/10/19	25/10/19	30/10/19	06/11/19	15/11/19	28/11/19	29/11/19	10/12/19	18/12/19	19/12/19	27/12/19	01/01/20
P04	20/11/19	20/11/19	20/11/19	20/11/19	28/11/19	09/01/20	09/01/20	09/01/20	09/01/20	09/01/20	12/01/20	28/01/20
P06	26/12/19	26/12/19	26/12/19	30/12/19	25/02/20	25/02/20	25/02/20	25/02/20	25/02/20	29/02/20	17/02/20	24/02/20
P10	25/12/19	25/12/19	03/01/20	07/01/20	13/01/20	20/01/20	27/01/20	04/02/20	11/02/20	17/02/20	24/02/20	03/03/20
P07	04/01/20	30/01/20	30/01/20	30/01/20	30/01/20	03/02/20	10/02/20	17/02/20	24/02/20	02/03/20	09/03/20	16/03/20
P12	16/01/20	20/01/20	29/01/20	03/02/20	10/02/20	17/02/20	24/02/20	02/03/20	09/03/20	16/03/20	24/03/20	30/03/20
P14	26/02/20	02/03/20	09/03/20	16/03/20	23/03/20	30/03/20	06/04/20	13/04/20	20/04/20	27/04/20	04/05/20	11/05/20
G03	21/03/20	21/03/20	09/04/20	09/04/20	09/04/20	13/05/20	14/05/20	14/05/20	14/05/20	14/05/20	01/07/20	25/05/20
P15	11/03/20*	16/03/20	23/03/20	30/03/20	06/04/20	13/04/20	20/04/20	27/04/20	04/05/20	11/05/20	18/05/20	25/02/20

Note. The dates of completion of each session are shown in each box. The colours indicate session engagement, with green indicating the session was complete, orange indicating session started but not completed, and red indicating session not started. Two participants (P06 and G03) started a session but did not complete it.

* Indicates that whilst participant (P15) chose not to engage with the sessions, they logged into the online intervention seven times over the 12-weeks to track physical activity and weight

The ExeRTiOn online intervention was designed to release a new session weekly for twelve-weeks. However, some IG participants (e.g., P04, P06, P07, P10, P07, G03), chose to catch-up on missed sessions by completing multiple sessions in one sitting (see table 6.7). If IG participants did not engage with two sessions in a row, the research fellow would send a personalised 'trigger message' to the participant using the secure message function (see study protocol, Appendix D). If participants did not engage with this 'trigger message', the participant would receive a telephone call, or a brief contact, with the research fellow whilst they attended routine transplant clinic visits. The purpose of this was to encourage re-engagement with the online intervention. Seven out of the nine IG participants (P04, P05, P06, P07, G03, P15, P14) activated this 'trigger message'. Two out of the seven participants went on to re-engage with the online intervention after the trigger message, and to complete the twelve-week programme (P04 and P05).

Some participants logged on and completed sessions over the Christmas and New Year period (P05, P04, P06 and P10). As participants were enrolled to the trial and online intervention on a rolling basis, two participants were completing the online intervention during the first wave of the COVID-19 pandemic whilst participating in strict shielding practices (P12 and G03).

Whilst all IG participants were able to revisit the online intervention content after completing the twelve-week intervention, only three participants logged on and utilised the resource after the twelve-week intervention was complete (P04, P05, P15). Reasons for re-visiting the intervention after completing the twelve-week programme was explored in the qualitative interviews (refer to section 6.4.3). Table 6.8 below

demonstrates the log-in activity from the IG participants (n=9). It includes log-in data for each of the twelve-weekly sessions, completed GPPAQ scores within the online intervention and the use of the goal setting and tracking functions. Most participants engaged with the online intervention using a smart phone device (66.7%). The median number of sessions completed was ten (IQR 5 to 12). The median number of log ins within the twelve-week intervention was thirteen (IQR 7 to 22).

Table 6-8 Log-in data of online intervention participants (n=9)

Variable	Description	Online intervention group participants (n=9)
Log-in data	Device used	6 (66.7%) smartphones 1 (11.1%) tablet 1 (11.1%) laptop 1 (11.1%) PC
	No. of logins within the 12-week intervention Median and IQR	13 (7 to 22)
	No. of logins after the 12-week intervention	0 (0 to 1)
	Reason for logging in after the 12-week intervention	2 (22.2%) revisit completed content 1 (11.1%) continue with tracking function
Session data	Total No. sessions completed	10 (5 to 12)
	Session 1 median time in minutes (IQR)	5 (1 to 10)
	Session 1 completed within the 7 days of session release	3 (33.3%) ≤ 7days 4 (44.4%) ≥7 days
	Session 2 median time (IQR)	9 (6 to 16)
	Session 2 completed within the 7 days of session release	4 (44.4%) ≤ 7days 3 (33.3%) ≥7 days
	Session 3 median completion time (IQR)	6 (5 to 12)
	Session 3 completed within the 7 days of session release	4 (44.4%) ≤ 7days 3 (33.3%) ≥7 days
	Session 4 median completion time (IQR	7 (4 to 8)
	Session 4 completed within the 7 days of session release	6 (66.7%) ≤ 7days 1 (11.1%) ≥7 days

	S5 median completion time (IQR)	9 (8 to 10)
	Session 5 completed within the 7 days of session release	6 (66.7%) ≤ 7days 1 (11.1%) ≥7 days
	Session 6 median completion time (IQR)	4 (2 to 19)
	Session 6 completed within the 7 days of session release	2 (22.2%) ≤ 7days 4 (44.4%) ≥7 days
	Session 7 median completion time (IQR)	7 (6 to 7)
	Session 7 completed within the 7 days of session release	3 (33.3%) ≤ 7days 3 (33.3%) ≥7 days
	Session 8 median completion time (IQR)	4 (1 to 6)
	Session 8 completed within the 7 days of session release	2 (22.2%) ≤ 7days 4 (44.4%) ≥7 days
	Session 9 median completion time (IQR)	3 (1 to 5)
	Session 9 completed within the 7 days of session release	2 (22.2%) ≤ 7days 4 (44.4%) ≥7 days
	Session 10 median completion time (IQR)	9.5 (5 to 17)
	Session 10 completed within the 7 days of session release	4(44.4%) ≤ 7days 1 (11.1%) ≥7 days
	Session 11 median completion time (IQR)	18 (7 to 20)
	Session 11 completed within the 7 days of session release	3 (33.3%) ≥7 days 1 (11.1%) ≤ 7days
	Session 12 median completion time (IQR)	12 (8 to 19)
	Session 12 completed within the 7 days of session release	3 (33.3%) ≥7 days 1 (11.1%) ≤ 7days
Tracking function	Number of PA entries	5 (4 to 10)
	Total PA in minutes entered in the 12 weeks	650 (250 to 1736.0)
	1st entered PA	58.5 (10 to 138)
	Last entered PA	100 (60 to 360)
	Number of weight entries	4 (3 to 10)
	1st entered BW	94.2 (63.9 to 105.0)
	Last entered BW	93.3 (65.1 to 104.4)
GPPAQ PAI from every 4th session	PAI welcome session (n=9)	7 (77.8%) inactive 1 (11.1%) moderately inactive 1 (11.1%) moderately active
	PAI Session 3 (n=7)	6 (66.7%) inactive

		1 (11.1%) moderately inactive
	PAI session 7 (n=6)	5 (55.6%) inactive 1 (11.1%) active
	PAI session 10 (n=5)	3 (33.3%) inactive 2 (22.2%) moderately active
Goals	Number of goals set	3 (1 to 5)
	Type of goals set	2 (22.2%) PA only 1 (11.1%) diet only 4 (44.4%) both PA and diet 2 (22.2%) no goals set
	Confidence ruler for goal ≥ 5/10	6 (66.6%)
	Importance ruler for goal ≥ 5/10	7 (77.8%)

Note. Continuous data is summarised using median and IQR. Categorical data is shown using proportions. PA= physical activity, GPPAQ=General Practice Physical Activity Questionnaire, PAI= Physical activity index.

Table 6.9 below summarises the secure messages to and from the physiotherapist/ research fellow. This includes descriptive data on the number of messages, as well as the type of messages sent.

Table 6-9 Messages between the physiotherapist and online intervention participants

Message function variables	**Data IG participants (n=9)**
Physiotherapist to participant messages (Median and IQR)	5 (3 to 6)
Reasons for messages physio to participants	Trigger message (n=15) Encourage re-engagement (n=8) Progress report (n=13) Reply to participant update (n=5) Book re-assessment (n=2) Unable to contact (n=1)
Participant to physio messages (Median and IQR)	1 (0 to 2)
Reasons for messages from participant to physio	Re-assessment and trigger message (n=2) Reply progress report (n=2) Reply progress and book assessment (n=1)

Book assessment and discuss barrier (n=1)	

Note. Median and IQR presented for continuous data. Categorical data is presented as frequencies.

6.4.1.7 Fidelity of the online intervention

The ExeRTiOn online intervention was retrospectively mapped to the BCW, and coded to the BCTTv1 (Michie et al., 2013). To facilitate this process and link the ExeRTiOn intervention to the COM-B, the BCW intervention functions and the BCT's, a behavioural analysis was performed. The target audience was new KTRs. This allowed for the identification of the problem in behavioural terms, and the intervention target behaviours (Michie, Atkins, et al., 2014b), see table 6.10. The three target behaviours for the ExeRTiOn online intervention were:

1. Increase physical activity for new KTRs
2. Engagement with the ExeRTiOn online intervention
3. Follow a balanced diet (including healthy eating and portion sizes)

It was hypothesised that the outcome of these target behaviours would be the maintenance of body weight in the sample of new KTRs over the 12-month study.

Table 6-10 Exploring the behavioural problem and target behaviours of the ExeRTiOn online intervention

Behavioural problem	**Significant adverse unintentional weight gain within the first year of receiving a kidney transplant**		
Target behaviours	1. Increase physical activity	2. Engage with the ExeRTiOn online resource	3. Eat a balanced diet (portions, healthy eating)
Who needs to perform the behaviour	Person living with a kidney transplant	Person living with a kidney transplant	Person living with a kidney transplant
What do they need to do differently to achieve desired change	• Complete relevant sessions • Perform physical activity • Complete exercise programme within online resource	• Log on 1x week for 12-weeks to complete sessions • Track physical activity • Track body weight • Set goals	• Complete relevant sessions on food • Reduce portions • Balance meals
When do they need to do it?	• As much as possible • PA- daily if possible • Minimum of 5/7 days per week	• Weekly at a time/day that is convenient to them	• At each meal
Where do they need to do it	• Anywhere convenient with internet access to them as online intervention is accessible via website/tablet/PC/smartphone • Anywhere they are eating or performing PA		
With whom do they need to do it?	• Independent or with support from others if they prefer (e.g., friends, family, carers, trial physiotherapist		

Note. Table modified from (Michie, Atkins, & West, 2014c, p. 244). ExeRTiOn= exercise in renal transplant online, PA= physical activity and PC= personal computer

The online intervention content, physiotherapist message content and individual interactions with IG participants and the physiotherapist (research fellow), was coded for BCT's using the BCTTv1 (Michie et al., 2013). This allows for identification of any additional BCT's that were included in the delivery of the online intervention that were not pre-specified. All physiotherapist encounters were anonymised and imported to NVIVO for coding. Online intervention content was read and re-read and coded using the coding framework. The process is summarised in figure 6.2 below. Appendix F displays the coding framework that was used to identify each BCT, their location and frequency within the online intervention content, and from the physiotherapist messages and interactions.

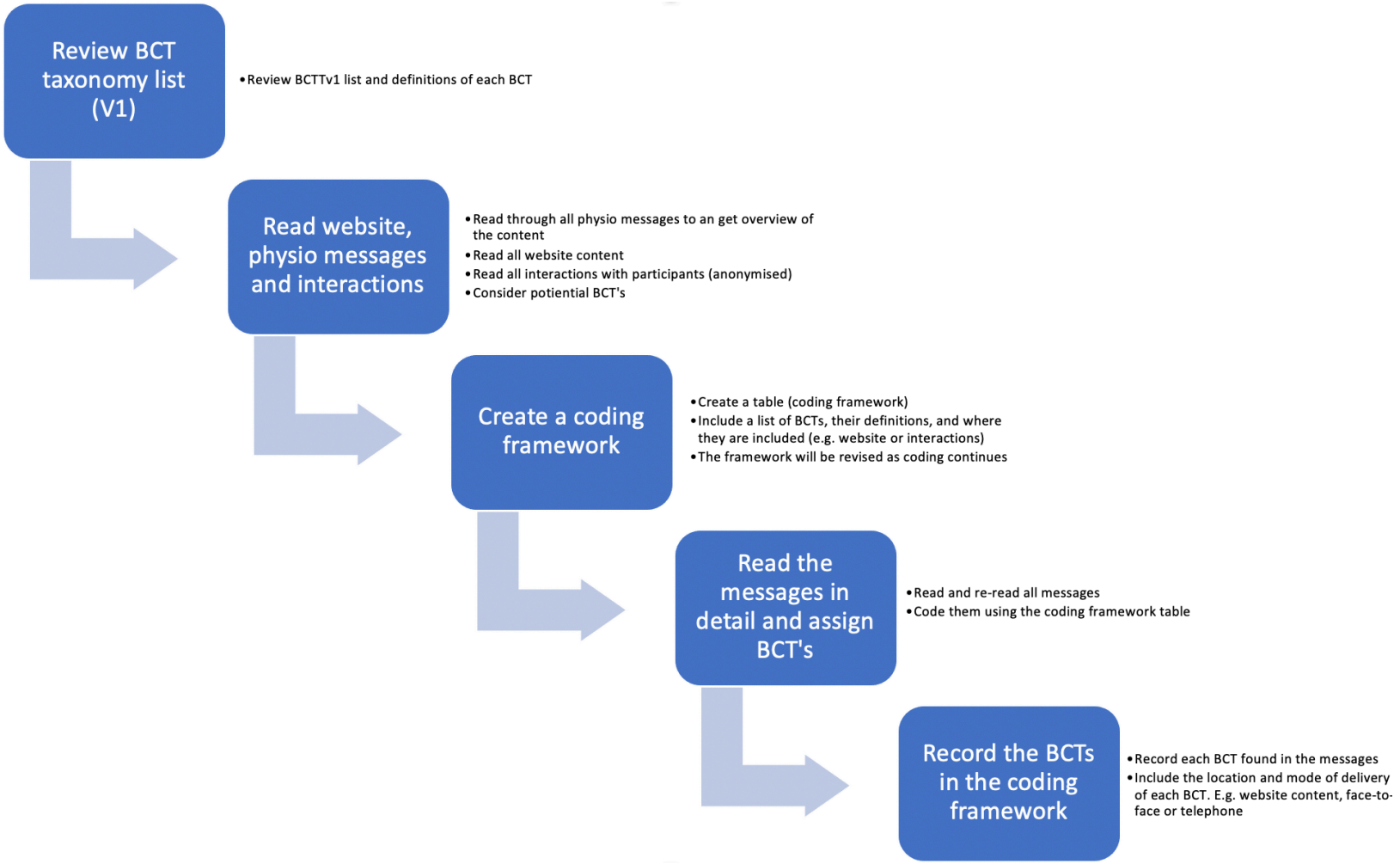


Figure 6-2 Process utilised to code physiotherapist messages to the BCT taxonomy V1 based on (S. Michie, Atkins, et al., 2014b).
A copy of the coding framework for the BCTs can be found in Appendix F.BCTs=behaviour change techniques

Whilst BCT's known to inform PA and healthy eating behaviours (Michie, Ashford, et al., 2011) were central to the design and development of the online intervention, post-hoc coding revealed additional BCT's within the intervention. Tables 6.11, 6.12 and 6.13 summarise how the ExeRTiOn online intervention facilitated each of the three target behaviours, using the COM-B model and BCW (Michie, Van Stralen, et al., 2011), and the BCTTv1 (Michie et al., 2013).

Table 6-11 Mapping ExeRTiOn to BCT's, intervention functions and the COM-B model for increasing physical activity (target behaviour 1)

COM-B Model Constructs	Intervention function	BCT (name and number)
Physical capability: Strength and flexibility to perform PA	**Training:** • Videos on how to perform PA and exercise • My library resources specific to exercise and PA • The home exercise diary	• Instruction on how to perform a behaviour (4.1) • Demonstration on how to perform a behaviour (6.1)
Psychological capability: Understanding why performing PA is beneficial to their KTx	**Education:** • Educational videos with selected HCP experts and a KTR expert	• Information on health consequences (5.1) • Self-monitoring of behaviour (PA tracking) (2.3) • Feedback on behaviour (Physio messages) (2.2)
Reflective motivation: Belief that PA is helpful AND **Automatic Motivation:** • Performing PA becomes a habit	**Persuasion:** • Demonstrate video to induce positive feelings to complete sessions • Top tip quotes from people living with a KTx	• Credible source (KTR) (9.1) • Credible source (HCPs) • Verbal persuasion about capacity (15.1)

• Tracking PA becomes a habit		
Reflective motivation: Belief that PA is helpful, Skills to regularly perform PA	**Education and Training:** • Increase knowledge and understanding relating to PA, and to increase skills required to be physically active post KTx	• Goal setting (behaviour) (1.1) • Problem solving (1.2) • Action planning (1.4) • Self-monitoring of behaviour (2.3) • Review of behaviour goal (1.5) • Social support unspecified (3.1)
Automatic Motivation: • Performing PA becomes a habit • Tracking PA becomes a habit	**Modelling:** • Video's with KTR experts and Transplant HCPs	• Demonstration of behaviour (6.1) • Credible source (9.1) • Behaviour practice/rehearsal (8.1)
Social opportunity: ExeRTiOn PA content culturally and socially appropriate to the individual	**Enablement:** • Support from trial physiotherapist/ friends/ family	• Social support (unspecified) (3.1) included the message interactions from physiotherapist to participants

Note. COM-B stands for capability (psychological and physical ability, opportunity (physical and social), motivation (reflective and automatic) and behaviour (Michie, Van Stralen, et al., 2011). PA= physical activity, BCT= behaviour change technique, KTx= kidney transplant, KTR= kidney transplant recipient and HCP= healthcare professional.

Table 6-12 Mapping ExeRTiOn to BCT's, intervention functions and the COM-B model for engagement with the ExeRTiOn online resource (target behaviour 2)

COM-B Model Constructs	Intervention function(s)	BCT (name and number)
Psychological capability: Skills to engage with the website	**Training and education:** • Videos on how to complete the online resource (FAQ tab) • Orientation session with physiotherapist after randomisation	• Instruction on how to perform a behaviour (4.1) • Demonstration on how to perform a behaviour (6.1) • Behaviour practice/rehearsal (8.1)
Automatic motivation: Logging onto the website becomes a habit	**Modelling:** • Video's with trial physiotherapist demonstrating how to use the online resource (FAQ's tab)	• Demonstration of behaviour (6.1) • Credible source (9.1) • Habit formation (8.3)
	Environmental restructuring: • Providing on-screen prompts and cues • Providing email prompts and cues to engage with the website	• Prompts and cues (7.1)
Reflective motivation: Believe that completing a session is preferable to not completing a session	**Enablement:** Reduce barriers to engage with website	• Social support unspecified (3.1)

Note. COM-B stands for capability (psychological and physical ability, opportunity (physical and social), motivation (reflective and automatic) and behaviour (Michie, Van Stralen, et al., 2011). FAQ=frequently asked questions tab.

Table 6-13 Mapping ExeRTiOn to BCT's, intervention functions and the COM-B model for following a healthy diet (target behaviour 3)

COM-B Model Constructs	Intervention function	BCT (name and number)
Psychological capability: Understanding why eating a balanced meal is beneficial for them and their KTx	**Training:** • Videos on how to perform healthy and balanced eating • My library resources and home exercise and PA diary	• Instruction on how to perform a behaviour (4.1) • Demonstration on how to perform a behaviour (6.1)
	Education: • Educational videos with selected HCP experts and KTR expert	• Information on health consequences (5.1) • Self-monitoring of behaviour (BW tracking) (2.3) • Feedback on outcome of behaviour (Physio messages) (2.2)
Reflective motivation: Belief that eating a healthy balanced meal is good for their health	**Persuasion:** • Demonstrate video to induce positive feelings to complete sessions	• Credible source (KTR) (9.1) • Credible source (HCPs) (9.1)
Automatic motivation: Eating balanced meal becomes a habit Completing weight tracking becomes a habit	**Modelling:** • Video's with KTR experts and Transplant HCPs	• Demonstration of behaviour (6.1) • Credible source (9.1) • Conserve mental resource (11.3)
Social opportunity: Dietetic session content socially and culturally appropriate to the individual	**Enablement:** • Support from trial physiotherapist/carers/family	• Social support unspecified (3.1)

Note. COM-B stands for capability (psychological and physical ability, opportunity (physical and social), motivation (reflective and automatic) and behaviour (Michie, Van Stralen, et al., 2011). KTR= kidney transplant recipient, KTx= kidney transplant and HCP= healthcare professional.

Eleven additional BCT's were discovered through the retrospective mapping of the ExeRTiOn online intervention to the BCW. These BCT's included aspects of the intervention that were considered by the design team; however, they were not initially coded directly to the BCT taxonomy. An example of this was the food label card that was within session four and the 'my library' tab of the intervention. This was retrospectively coded as BCT conserve mental resource (11.3) as it satisfies the BCT's definition to provide advice on ways to reduce the demand of mental resources to facilitate the target behaviour of following a healthy diet (Michie, Atkins, et al., 2014b). In addition to this, many BCT's were delivered simultaneously. For example, as per the BCTTv1 guidance BCT's 4.1 (instruction on how to perform a behaviour) and 6.1 (demonstration of the behaviour) are often performed simultaneously (Michie et al., 2013), and thus should be coded to reflect this.

Out of the eleven additional BCT's, six were found in the online intervention package, and four were found within the physiotherapist contacts (either via message, telephone or face-to-face). Appendix F depicts a full list of all the BCT's and where they were located, and additional BCT's found from retrospective mapping to the BCW.

The most frequently represented BCT in the online intervention was BCT 7.1 ‘prompt and cues’ (Michie et al., 2013) that was used 25 times in the twelve-week programme. These prompts inbuilt into the online intervention were consistently throughout each of the 12-weekly sessions, and facilitated the participants with engaging with the online intervention. The most frequent BCT in the physiotherapist interactions was BCT 3.1 ‘social support unspecified’(Michie, Atkins, et al., 2014b) which was used 83 times in total. This included advice, praise and encouragement throughout the personalised messages, signposting to support and encouragement during the ‘trigger messages’ to participants. Social support unspecified was thought to influence each of the three target behaviours of the ExeRTiOn onine intervention.

The least frequent BCT in the online intervention was BCT 15.1 ‘verbal persuasion’ (Michie, Atkins, et al., 2014b) that was used only once in the 12-week programme per participant. This was used in session four when the physiotherapist informed participants in the video that they could safely exercise post-transplant to target increasing physical activity behaviour. The least frequent BCT in the physio messages and interactions was BCT 6.1 ‘demonstration of behaviour’ which was used 6 times and was always used with BCT 4.1 ‘instruction on how to perform a behaviour’(Michie, Atkins, et al., 2014b). Demonstration of behaviour included assisting participants with password resets, and online intervention troubleshooting. This facilitated the target behaviour of engaging with the ExeRTiOn online intervention.

6.4.1.8 Outcome Acceptability

Data collection for the feasibility RCT was completed on the 22nd of March 2021. Median time to complete the full assessment, with IQR for each assessment visit, was 70 (60 to 88) minutes for baseline assessments (n=17), 48 (30 to 60) minutes for three-

month follow-up (n=15) and 50 minutes (48 to 53) minutes for twelve-months assessment (n=13). Complete baseline data were collected from all seventeen participants.

Whilst missing data did occur at the three- and twelve-month visits for some outcomes, there appeared to be no objections to any of the secondary outcome assessments by participants. The 6MWT was particularly valued by participants and is discussed further in the qualitative data. Missing data three- and twelve-month follow-up appeared to be due mainly to study dropouts (n=4), and challenges associated with conducting research in an extremely clinically vulnerable population during the COVID-19 pandemic. In all active trial participants, there was complete data for all questionnaire outcomes (GPPAQ, self-efficacy, CFS and EQ-5D-5L) at each time point. The only missing questionnaires were due to dropouts (n=3) and the participant who had to be withdrawn from the study due to losing their transplant (n=1).

At three months, eight participants were unable to complete full assessment outcomes due to shielding during the first wave of the COVID-19 pandemic. Six of the fifteen participants completed their three-month assessments virtually over the telephone. Therefore BIA, PWV, AI, waist and hip circumference and 6MWT data were not captured for these participants. Clinical data such as body weight, BP, and transplant outcomes were collected virtually from transplant clinic visit data. Questionnaire data (GPPAQ, self-efficacy scales, EQ-5D-5L and CFS) were all recorded over the telephone during remote follow-up. In addition to the six participants who had virtual three-month follow-up, one participant (P09) was unable to perform the 6MWT or the AI assessment at the three-month time point. This was due to the three-month assessment occurring at the cusp of the COVID-19 outbreak in the UK, prior to the

introduction of shielding principles. The assessment was conducted in a clinical space to minimise travelling throughout the hospital, and therefore there was no safe space to perform the 6MWT. Unfortunately, there was also equipment failure during that visit with the Vicorder device, and subsequently we were unable to capture the AI.

At the twelve-month assessment, twelve out of the thirteen remaining participants completed all the required data collection. Whilst the research and clinical teams did advise that face-to-face assessments could be re-introduced in June 2020, one participant in the UC group still requested virtual follow-up rather than a face-to-face assessment. Therefore, only questionnaires and clinical data were collected from this participant at the final twelve-month assessment.

6.4.2 Secondary outcomes

All continuous outcomes were analysed for normal distribution using histograms (Pallant, 2013). Median and IQR were used to summarise continuous data due to the small sample size. The median body weight with IQR for the study sample was 92.6 (72.0 to 96.1) kilograms (kgs) at baseline, 91.7 (69.0 to 103.3kg) at three-months, and 93.3 (77.2 to 101.9kg) at twelve-months. Although just observational, the IG appeared to maintain a stable bodyweight throughout the twelve-month study displaying median (IQR) body weight of 94.5 (63.0 to 102.0) kilograms at baseline, 95.0 (66.7 to 105.3) kilograms at three-months and 94.7 (77.2 to 117.3) kilograms twelve-months. In contrast, the UC group appeared to increase their weight over the twelve-month study period, with median (IQR) body weight of 81.3 (73.6 to 94.6) kilograms at baseline, 86.2 (75.4 to 96.5) kilograms at three-months and 93.3 (70.3 to 101.9) kilograms at twelve-months. Figures 6.3 and 6.4 below display the body weight recordings across the twelve-month trial for the IG participants and the UC group participants.

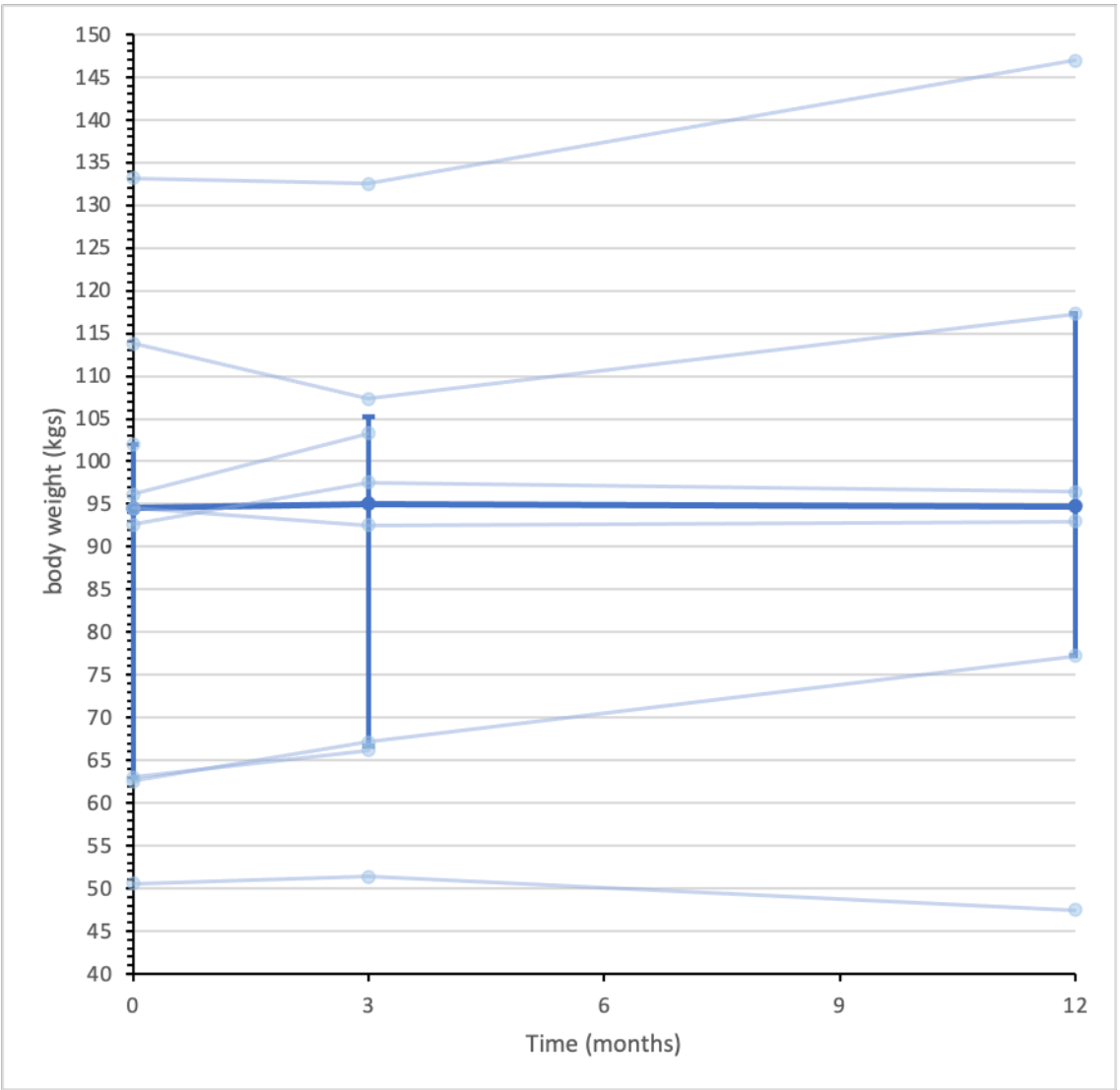


Figure 6-3 Data series graph demonstrating individual and median body weight values across the feasibility RCT in the IG participants (n=9)

Note. Individual data series for participants in the intervention group depicted by the pale blue lines. Median depicted by darker blue line, with IQR error bars. Median was calculated from all recorded data at each assessment point. n=9 at baseline, n=8 at 3-months and n=6 at 12-months

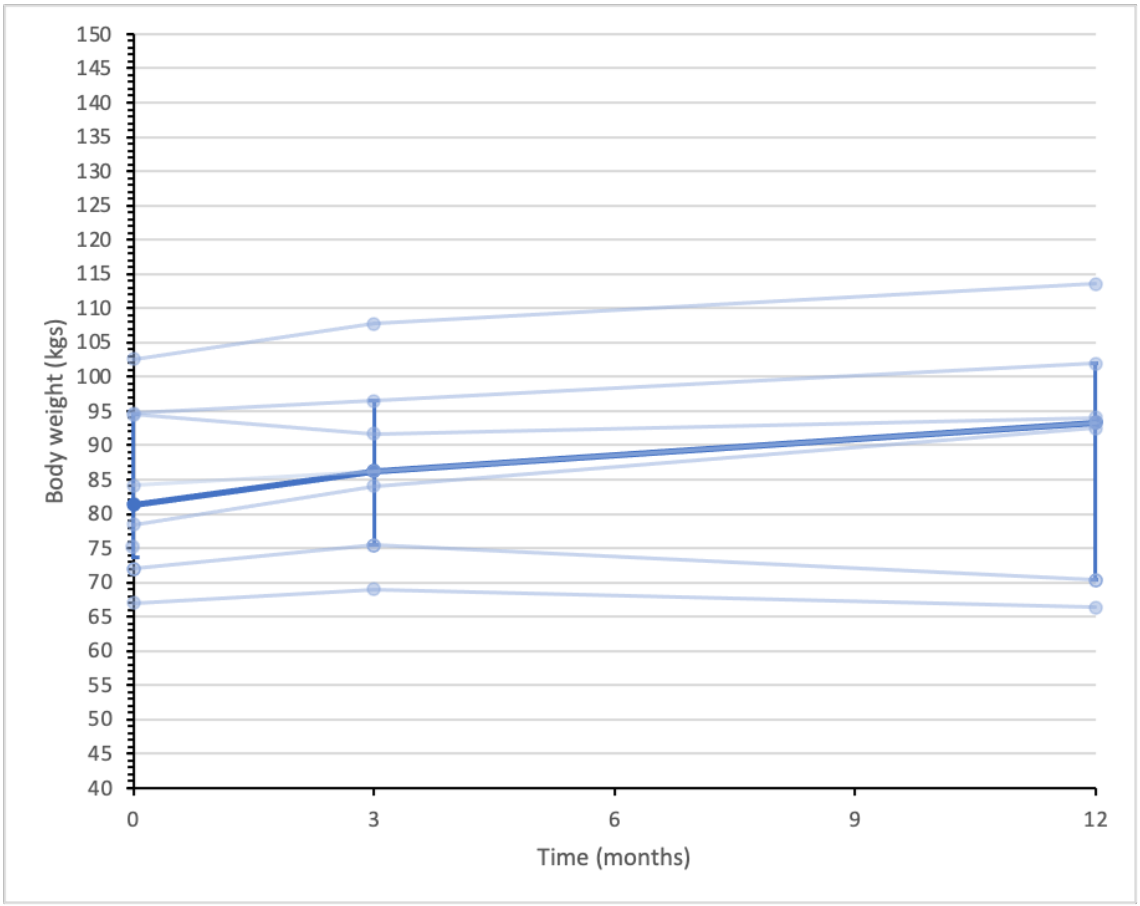


Figure 6-4 Data series graph demonstrating individual and median body weight values across feasibility RCT in the usual care group (n=8)

Note. Individual data series for participants in the usual care group are depicted by the pale blue lines. Median depicted by darker blue line, with IQR error bars. Median was calculated from all recorded data at each assessment point. n=8 at baseline, n=7 at 3-months and n=7 at 12-months

Twelve-month follow-up visits were scheduled around existing face-to-face clinic appointments due to COVID-19, and practises to minimise hospital visits for participants. As a result of this, six participants (three from each group) had their twelve-month follow-up visit outside of the fourteen-day assessment window (±7 days). For the six participants, the median (IQR) days outside of the assessment window was 47 days with an IQR of 12 to 66 days. Consultation with the trial advisory statistician resulted in a decision to perform a sensitivity analysis (see Appendix D). Body weight line graphs were completed for each group, with and without participants who had their final assessment outside the assessment window. In the treatment group, it appears that body weight may have been influenced by the participants exceeding this treatment

window. One participant in the IG had her transplant clinic rescheduled multiple times, which resulted in her final assessment taking place 106 days beyond the assessment window. In the UC group, there appeared to be less variance and delays with final assessments. However, due to the small sample size, all participants data available at each time point was included in data summaries for comparison and transparency. No additional statistical tests were conducted, due to the feasibility study design and feasibility reporting guidance (Eldridge, Chan, et al., 2016).

Change scores were calculated for all body weight related outcomes (body weight, BMI and BC) and are summarised in Table 6.12 below. As previously reported, COVID-19 influenced the data-collection at the three-month assessment for outcomes collected face-to-face such as BC. Therefore, change scores for FM and LTM included fewer participants at the three-month timepoint. There appeared to be a higher increase in median (IQR) body weight from baseline to 12-months in the UC group +7.2 (-0.7 to 10.9 kgs) compared with the IG +3.7 (-1.5 to 13.8 kgs). All participants appeared to decrease LTM and increase in FM.

Table 6-14 Change scores body weight, BMI and body composition

Change variable	Time period	Total sample	Online intervention	Usual care
ΔBW (kg)	baseline to 3-months	2.10 (-0.7 to 4.9)	2.0 (-1.4 to 4.7)	2.1 (1.8 to 5.1)
	3 to 12-months	5.4 (-1.1 to 8.4)	5.3 (-1.1 to 10.1)	5.4 (-2.7 to 7.1)
	Baseline to 12-months	3.8 (-0.7 to 10.9)	3.7 (-1.5 to 13.8)	7.2 (-0.7 to 10.9)
ΔBMI (kg/m^2)	baseline to 3-months	0.6 (0.1 to 2.1)	0.7 (-0.5 to 2.0)	0.6 (0.1 to 2.1)
	3 to 12-months	2.2 (-0.4 to 2.9)	1.8 (-0.8 to 3.8)	2.2 (-0.4 to 2.3)
	Baseline to 12-months	1.4 (-0.3 to 4.4)	1.3 (-0.6 to 5.4)	2.8 (-0.3 to 4.4)
ΔLTM (%)	baseline to 3-months	-1.0 (-4.8 to 1.8)	-4.6 (-8.5 to 4.3)	0.9 (1.2 to 1.8)
	3 to 12-months	-3.0 (-3.3 to 2.3)	0 (-3.3 to 3.3)	-3.0 (-10.5 to 2.3)
	Baseline to 12-months	-3.3 (-8.3 to 0.4)	-3 (-5.5 to 1.1)	-5.4 (-8.6 to -0.3)
ΔFM(%)	baseline to 3-months	1.1 (-1.1 to 3.6)	3.2 (-4.7 to 6.1)	0.3 (-1.1 to 1.4)
	3 to 12-months	2.3 (-1.5 to 4.3)	1.0 (-2.4 to 4.3)	2.3 (-1.5 to 7.9)
	Baseline to 12-months	3.3 (0.3 to 7.4)	3.1 (-1.1 to 6.9)	5 (0.5 to 7.6)

Note. Δ indicates change, BW=body weight, BMI= body mass index, LTM= lean tissue mass and FM= fat mass. As LTM and FM involved face-to-face data collection, there was limited data for this outcome at 3-months which could impact on change scores (n=8 from baseline to 3-months, n=5 from 3 to 12 months, and n=12 from baseline to 12-months)

All secondary outcomes for the overall sample, and each group, are tabulated in table 6.13 on the following page. Due to the small sample size and distribution of data, median and IQR were used to summarise continuous data. Median BMI, waist circumference, hip circumference and PWV, and AI appeared comparable across the sample.

In the IG, 6MWD median (IQR) measurements were 450m (450 to 540) at baseline, 525m (472.5 to 615m) at three-months, and 495m (465 to 615m) at 12-months. In contrast, in the UC group, the median 6MWD (IQR) were 517.5 (436 to 570) meters at baseline, 507.5 (442.5 to 605m) at three-months, and 435 (435 to 555m) at 12-months.

Table 6-15 Secondary QUANT outcome data

Variable	Total sample			Online intervention group			Usual care		
	Baseline (n=17)	3-months (n=15)[a]	12-months (n=13)[b]	Baseline (n=9)	3-months (n=8)[a]	12-months (n=6)	Baseline (n=8)	3-months (n=7)[a]	12-months (n=7)[b]
Body Weight (kg)	92.6 (72.0 to 96.1)	91.7 (69.0 to 103.3)	93.3 (77.2 to 101.9)	94.5 (63.0 to 102.0)	95.0 (66.7 to 105.3)	94.7 (77.2 to 117.3)	81.3 (73.6 to 94.6)	86.2 (75.4 to 96.5)	93.3 (70.3 to 101.9)
BMI (kg/m^2)	27.9 (23.9 to 32.9)	28.9 (25.2 to 33.1)	29.4 (27.8 to 35.0)	30.0 (23.9 to 33.6)	30.6 (23.2 to 34.5)	32.2 (29.4 to 36.2)	26.8 (24.6 to 29.8)	27.1 (25.2 to 32.2)	28.2 (23.5 to 34.4)
Waist circumference (cm)	108.0 (91.5 to 119.0)	111.0 (94.5 to 114.0)	112.0 (99.0 to 120.5)	108.0 (86.0 to 119.0)	97.3 (91.3 to 107.0)	110.5 (95.0 to 120.0)	105.5 (96.8 to 115.5)	111.5 (111.0 to 124.0)	112.0 (111.0 to 129.0)
Hip circumference (cm)	107.2 (98.0 to 110.0)	109.0 (100.0 to 115.0)	111.5 (104.5 to 117.5)	107.5 (107.0 to 110.0)	105.0 (98.3 to 112.5)	114.5 (105.0 to 115.0)	102.3 (95.8 to 113.6)	109.0 (106.0 to 117.0)	107.0 (104.0 to 120.0)
FTI (kg/m^2)	12.9 (10.9 to 20.1)	15.5 (11.3 to 16.1)	18.8 (15.7 to 24.5)	15.5 (12.1 to 20.1)	15.6 (10.2 to 15.9)	21.1 (14.8 to 26.4)	12.1 (10.7 to 18.7)	12.6 (11.3 to 21.7)	17.4 (16.6 to 22.5)
FM (kg)	30.1 (22.8 to 44.9)	33.6 (28.0 to 42.8)	41.7 (36.2 to 53.6)	36.2 (24.9 to 47.9)	33.3 (20.6 to 37.2)	45.7 (34.4 to 53.7)	28.3 (22.2 to 44.1)	39.2 (28.3 to 51.7)	41.7 (37.9 to 48.8)

FM (%)	38.1 (29.7 to 45.7)	38.5 (36.1 to 47.1)	45.6 (39.0 to 51.6)	38.1 (29.9 to 42.1)	38.1 (26.8 to 42.1)	47.3 (37.0 to 55.4)	37.6 (28.9 to 46.6)	43.5 (36.6 to 50.6)	44.6 (41.0 to 47.9)
LTI (kg/m^2)	12.7 (10.9 to 15.0)	13.5 (10.9 to 15.8)	11.8 (10.6 to 13.0)	12.7 (11.5 to 15.1)	15.4 (12.2 to 18.9)	11.8 (9.4 to 13.5)	12.3 (10.7 to 14.7)	12.5 (10.9 to 13.5)	11.8 (11.6 to 12.2)
LTM (kg)	40.5 (30.2 to 44.6)	39.3 (30.6 to 48.4)	34.5 (29.3 to 40.4)	40.7 (29.3 to 46.7)	48.2 (36.1 to 53.1)	30.3 (25.8 to 43.8)	37.2 (32.3 to 42.8)	32.5 (30.6 to 39.5)	35.6 (34.3 to 38.8)
LTM (%)	48.2 (35.9 to 57.2)	48.8 (36.3 to 52.4)	37.5 (30.2 to 48.4)	48.2 (39.2 to 57.8)	50.4 (44.7 to 64.0)	37.5 (26.7 to 51.4)	49.0 (35.0 to 55.6)	40.4 (30.1 to 50.8)	39.3 (33.7 to 45.3)
6MWD (meters)	510.0 (450.0 to 540.0)	515.0 (465.0 to 615.0)	472.5 (425.0 to 577.5)	450.0 (450.0 to 540.0)	525.0 (472.5 to 615.0)	495.0 (465.0 to 615.0)	517.5 (435.0 to 570.0)	507.5 (442.5 to 605.0)	435.0 (435.0 to 555.0)
PWV (m/sec)	7.4 (6.8 to 9.6)	7.4 (7.2 to 7.8)	7.8 (7.1 to 9.9)	6.9 (6.6 to 7.4)	6.9 (6.4 to 7.4)	7.1 (6.2 to 7.9)	8.6 (7.4 to 9.8)	7.8 (7.4 to 8.0)	9.9 (7.6 to 10.8)
AI (%)	23.0 (19.6 to 29.0)	27.0 (15.8 to 29.5)	20.3 (18.0 to 26.0)	22.0 (19.6 to 27.0)	21.5 (15.8 to 27.0)	18.7 (18.0 to 19.6)	28.7 (20.0 to 33.0)	29.5 (20.5 to 35.5)	26.0 (21.0 to 27.6)

Note. Median and Interquartile ranges (IQR) are presented for continuous data. Proportion percentages and frequency numbers are shown for categorical data.
BMI= body mass index, FTI= fat tissue index, FM= fat mass, LTI= lean tissue index, LTM= lean tissue mass, 6MWD= six-minute walk distance, PWV= pulse wave velocity and AI= Augmentation index. [a] indicates for 3-month assessments 7 out of 15 participants completed their assessment virtually due to COVID-19. Therefore, BIA outcomes, waist and hip circumference, six-minute walk test, PWV and AI are reported in a reduced sample (4 in online intervention group and 3 in the usual care group). [b] indicates at 12-month assessment one participant (UC) declined a face-to-face assessment therefore for face-to-face outcomes the sample will be reduced to 12 out of the 13 remaining participants at 12-month follow-up

Questionnaire data for PA (GPPAQ), fatigue (CFS), self-efficacy (SE for nutrition and physical exercise behaviours), and quality of life (EQ-5D-5L) appeared comparable across the sample and is summarised in table 6.14 below. There was an overall reduction in the number of participants classified as ‘inactive’ with the GPPAQ questionnaire. Fourteen participants were classified as ‘inactive’ at baseline, and five participants were ‘inactive’ at 12-months. There was also a slight reduction in both groups of the number of participants classified as “active”.

Table 6-16 Questionnaire data

Variable	Total sample			Online intervention group			Usual care group		
	Baseline (n=17)	3-months (n=15)	12-months (n=13)	Baseline (n=9)	3-months (n=8)	12-months (n=6)	Baseline (n=8)	3-months (n=7)	12-months (n=7)
GPPAQ PAI -inactive	14 (82.4%)	4 (26.7%)	5 (38.5%)	7 (77.8%)	3 (37.5%)	2 (33.3%)	7 (87.5%)	1 (14.3%)	3 (42.9%)
GPPAQ PAI -mod. inactive		4 (26.7%)	3 (23.1%)		1 (12.5%)	1 (16.7%)		3 (42.9%)	2 (28.6%)
GPPAQ PAI -mod. active	2 (11.8%)	4 (26.7%)	4 (30.8%)	1 (11.1%)	3 (37.5%)	3 (50%)	1 (12.5%)	1 (14.3%)	1 (14.1%)
GPPAQ PAI -active	1 (5.9%)	3 (20%)	1 (7.7%)	1 (11.1%)	1 (12.5%)			2 (28.6%)	1 (14.3%)
SE-Nutrition	16 (15 to 20)	17 (14 to 20)	19 (14 to 20)	16 (15 to 20)	16.5 (14.5 to 19.5)	16 (12 to 20)	17.5 (15.0 to 20.0)	17.0 (14.0 to 20.0)	20.0 (15.0 to 20.0)
SE-Physical Exercise	15 (13 to 17)	13 (12 to 18)	14 (11 to 15)	13 (11 to 13)	12 (11 to 15.5)	13.5 (10 to 15)	17.5 (15.0 to 19.5)	17.0 (13.0 to 19.0)	14.0 (11.0 to 19.0)
CFS-Total	13 (10 to 13)	10 (7 to 13)	12 (11 to 16)	13 (13 to 15)	12.5 (7.5 to 15.5)	12 (9 to 16)	11.5 (8.5 to 13.0)	9.0 (7.0 to 11.0)	13.0 (11.0 to 17.0)
CFS mental	4 (3 to 4)	4 (2 to 4)	4 (4 to 6)	4 (3 to 4)	4 (3 to 6.5)	5 (4 to 6)	4.0 (3.0 to 4.0)	4.0 (1.0 to 4.0)	4.0 (3.0 to 5.0)

CFS Physical	9 (7 to 11)	6 (5 to 8)	8 (6 to 10)	9 (9 to 11)	7 (4.5 to 10)	7 (5 to 10)	8.0 (5.0 to 9.0)	6.0 (5.0 to 7.0)	9.0 (7.0 to 13.0)
EQ-5D-index	0.7 (0.6 to 1.0)	0.8 (0.7 to 0.9)	0.8 (0.7 to 0.9)	0.7 (0.6 to 0.8)	0.8 (0.7 to 0.9)	0.7 (0.7 to 0.9)	0.9 (0.7 to 1.0)	0.8 (0.7 to 1.0)	0.8 (0.8 to 1.0)
EQ-5D-VAS	75 (50 to 85)	80 (65 to 90)	75 (65 to 85)	75 (5o to 90)	85 (70 to 90)	75 (60 to 85)	80 (6o to 85)	80 (65 to 90)	75 (65 to 92.5)

Note. GPPAQ PAI= General Practice Physical Activity Questionnaire, PAI=physical activity index, SE=self-efficacy, CFS=chalder fatigue scale, EQ-5D-5L-index and EQ-5D-VAS refers to index values, and visual analogue self-reporting's on quality of life. Continuous data are summarised using Median (interquartile ranges). Categorical data are summarised using number and proportions. Proportions are for within group sample sizes at each study data collection point

There was a large positive correlation between the number of completed online intervention sessions and the self-efficacy for nutrition scores at 12-months in the IG participants (rho=0.832 p=0.04, n=13). There was no association between the number of completed online intervention sessions and body weight at twelve-months in the IG participants (rho=-0.2, p=0.8, n=6). There was no significant correlations between body weight at 12-months and the self-efficacy physical exercise scale (rho=0.003, p=0.9, n=13) or the self-efficacy nutrition scale (rho=-0.4, p=0.8, n=13) in the overall study sample.

6.4.3 Qualitative results

Thirteen participants from the feasibility sample were invited to, and completed, individual semi-structured interviews between 31st January 2020 to the 20th of August 2020. Most of the interviews were conducted by the research fellow, with some interviews being conducted by a master's research student (PD), following training and supervision. One interview was conducted face-to-face prior to the COVID-19 pandemic. The remaining twelve interviews were conducted over the phone due to shielding principles during the first wave of the COVID-19 pandemic. Topic guides were amended to include two questions regarding the impact of COVID-19 as it was an important contextual event. Refer to appendix D for a copy of the topic guide.

To address the research question: to capture and report; a) the experience using the online intervention, and b) the experience and feasibility in taking part in the trial, the thirteen qualitative participants were purposively sampled. The sampling framework used (see chapter 3) included participants from both groups, a range of gender, age and ethnicity and a range of engagement level participants (IG). The characteristics of the qualitative interview participants (n=13) can be seen in table 6.17 and 6.18.

Table 6-17 Characteristics of QUALI interview participants (study 4)

		Total qualitative interviews (n=13	**Online intervention Group (n=8)**	**Usual care Group n=5)**
Age in years	Median (IQR)	43.0 (33.0 to 59.0)	36.0 (32.5 to 43.5)	60 (59 to 60)
Males	Number (%)	7(53.8%)	8 (50%)	3(60%)
Ethnicity	White Caucasian	5 (38.5 %)	3 (37.5%)	2 (40%)
	Black African and Caribbean	6 (46.2%)	4 (50%)	2 (40%)
	Asian	2 (15.4%)	1 (12.5%)	1 (20%)
Time post-transplant (days)	Median (IQR)	62.0 (56.0 to 68.0)	61.0 (57.0 to 69.5)	65.0 (53.0 to 68.0)
RRT before transplant	Number (%)	19 (76.9%)	7 (87.5%)	3 (60%)
Number of co-morbidities	One	7 (53.8%)	6 (75%)	1 (20%)
	Two	5 (38.5%)	2 (24%)	3 (60%)
	Three	1 (7.7%)		1 (20%)
Engagement with online intervention (IG only)	Completed all 12 sessions		4 (50%)	
	Completed tracking only		1 (12.5%)	
	Completed between 5-10 sessions		3 (37.5%)	

Note. Due to purposive sampling, medians and interquartile ranges (IQR) are presented for continuous data. Proportion percentages and frequency numbers are shown for categorical data.
Comorbidities included a medical history of diabetes, hypertension, cerebrovascular event, osteoarthritis, brain haemorrhage, cardiovascular disease, cancer or respiratory disease and RRT=renal replacement therapy

Table 6-18 Individual interview participant characteristics (study 4)

Participant study identifier	Group (UC or IG)	Age	Gender (M/F)	Time post-transplant (days)	Ethnicity
P01	UC	71	F	90	White Caucasian
P02	UC	59	M	53	White Caucasian
P03	UC	43	M	47	Asian
P04	IG	33	M	119	Asian
P05	IG	44	M	72	Black African and Caribbean
P06	IG	59	F	48	Black African and Caribbean
P07	IG	31	F	58	Black African and Caribbean
P08	UC	60	M	65	Black African and Caribbean
P09	UC	60	F	68	Black African and Caribbean
P10	IG	43	F	56	White Caucasian
P12	IG	39	M	60	White Caucasian
P15	IG	32	M	62	White Caucasian
G03	IG	33	F	67	Black African and Caribbean

Note. P indicates primary site (King's College Hospital), G= secondary site (Guy's and St Thomas' Trust), M= male, F=female, UC= usual care group, IG= online intervention group

6.4.3.1 Interview participant's context

When considering MMR under a pragmatic worldview, it is important to appreciate the context in which the research is conducted. The broader context, and time of data collection are an important component of qualitative research (Braun & Clarke, 2021). The complexity around evaluating behaviour change interventions is not just about the BCT's used, and their interactions, but about the context in which the intervention is set (Michie, West, Sheals, & Godinho, 2018). Separation of qualitative data from the temporal context can be viewed as a threat to validity (Braun & Clarke, 2021). Therefore, the qualitative interview participants were asked about their experience and context of receiving their kidney transplants. Whilst not related to the research qualitative questions directly, they provide insight into the context of the experiences of the participants' post-kidney transplantation, and the context in which the ExeRTiOn online intervention was tested. These findings are important to contextualise the overall findings of the mixed methods feasibility RCT.

Generally, the participants from the two south London transplant units felt much better after having a transplant when compared with RRT. Participants describe the reversal of fatigue symptoms and feeling 'free from the machine'.

> I feel very well. Unlike when I was on dialysis... I feel very well and I [pause] can do things that I wasn't able to do during the dialysis, umm I drink well, I eat well. (P05, male, IG)

> When you come back from dialysis. Argh [pause] you don't feel yourself. You just feel sleepy sleepy. You don't even have an appetite to eat. Just sleepy sleepy. Weak. Tired. But now, since I have had my kidney, I feel I am alive [laughs] (P09, female, UC group)

Whilst it was common for participants to experience reversal of some of the symptoms and complications associated with haemodialysis, participants expressed

concern when they were navigating the initial acute post-transplant period. Concern appeared to be linked with uncertainty.

> I went through quite a lot of different treatments, uhm doctors not knowing, I think that kind of put me uneased as well (G03, female, IG)

> I had terrible problems with Tacrolimus. I couldn't see, they were sensitive to the light... The nurses themselves didn't even know about it (P08, male, UC group)

When asked what advice they would like to offer new KTRs, research participants expressed the importance of self-management, perseverance and a positive mind-set when accommodating to the ups and downs of acute post-transplant care.

> Look after it. Mind your bloods, good blood levels, good blood pressure levels and good diet. And not do anything excessively (P08, male, UC group)

> Take it day by day. Find the resources, and you know- move your body in ways that make you happy, and that feel good. And you know focus on things that are working as well (P10, female, IG)

In summary, participants in the acute post-transplant period find the reversal of dialysis symptoms to be positive. However, there are ups and downs in the acute post-transplant period, and self-management, and a positive mindset can assist with this. Appreciation of the context of the interview participants, particularly the acute post-transplant period, provides rich context to the results that follow.

6.4.3.2 Reflexive thematic analysis

Thematic analysis revealed four main themes relating to the experience of using the online intervention, and the experience and feasibility of taking part in the trial. The first theme revolved around optimising participation and recruitment. This included three subthemes; that research participation was important and altruistic, clear communication and rapport were essential, and recruiting participants acutely after a kidney transplant appeared to be acceptable. The second theme captured the impact of COVID-19 on the participants. This included the subthemes, the impact of shielding on mental and physical wellbeing, and the importance of social support. The third theme explored the

concept that engagement with the online intervention is a choice. This included both technical and personal factors that could influence the choice to engage, or not engage with the online intervention. The fourth theme involved; proposed mechanisms of actions, with intervention and assessment that facilitated a positive study experience. Figure 6.5 below summarises the final thematic map. Refer to the appendix G for further evidence of the qualitative analytical process including earlier iterations of the thematic map.

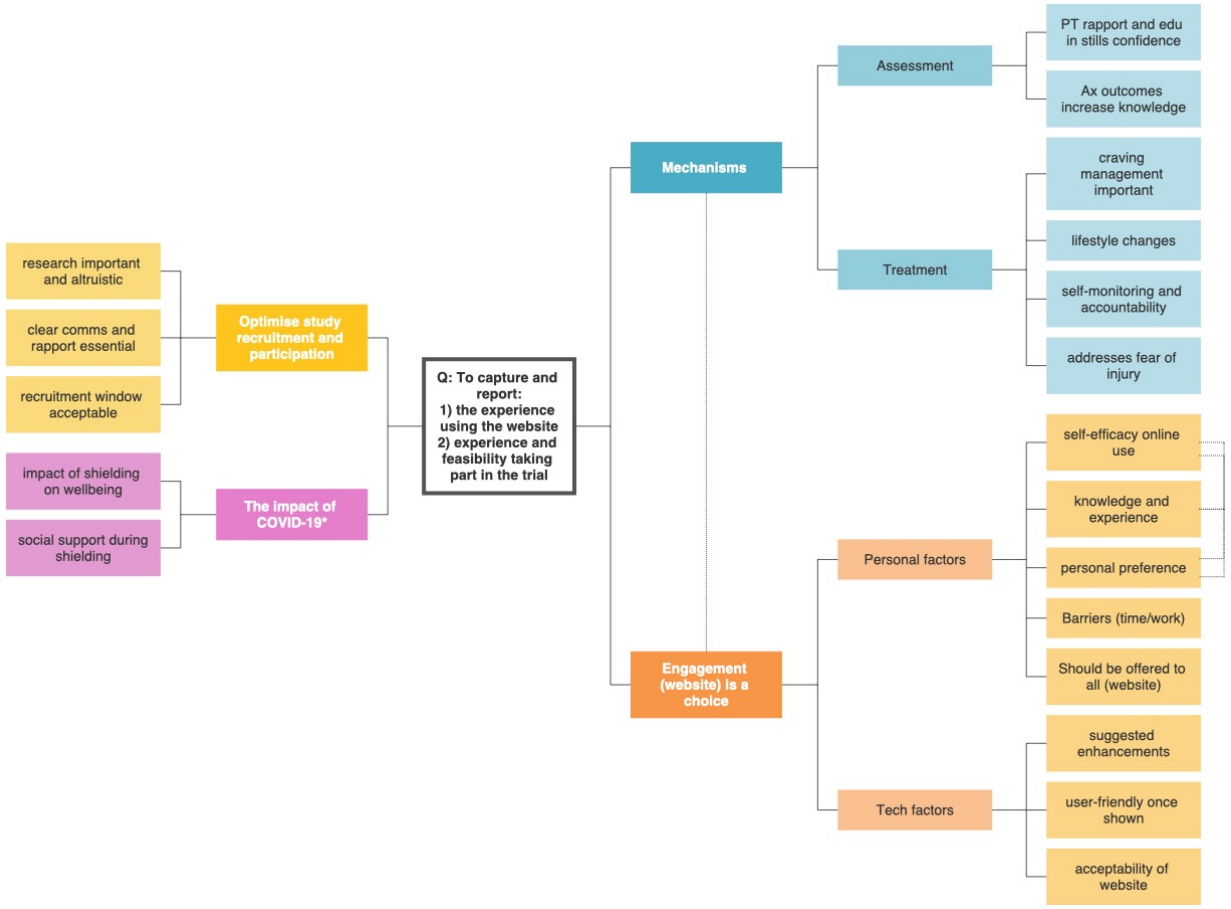


Figure 6-5 Thematic map from the thematic reflexive analysis

Key themes are represented in different colours. Hierarchy within each theme are shown by depth of colour. Dotted lines show potential interactions. * Depicts the first wave of COVID-19 and the shielding enforced to Kidney Transplant Recipients (23rd March 2020 to the 1st of August 2020). Q= research question, PT=physiotherapist, edu=education, Ax=assessment, tech=technical and comms=communication

6.4.3.3 Theme 1: Optimising participation and recruitment

Research participation was seen as an important act to 'give back' to the community after receiving the 'gift' of a kidney transplant.

> I am happy to do research, and you know, if it helps the next person down the line. because somebody in front has helped me. (P01, female, UC group)

> When I had one taken out, kidney taken out, I've given it straight to, I've donated it to the cancer research… because if I can help in anyway, by helping someone else, you know- all be it. (P02, male, UC group)

Participants reported that research was an important process. This altruistic view contributed to participation in the study and was valued by our participants.

Participants across the dataset identified clear written and verbal communication, with the ability to ask questions, had contributed to a positive experience when signing up to the study.

> Yeah, it was good there was no pressure, I felt like I could ask questions. Uhm, you know the paperwork I filled out was pretty self-explanatory, uhm it was very detailed you know it was very good. (P03, male, UC group)

> Explained very well thank you. And I am- I would be asking the questions if I need to. (P01, female, UC group)

Participants valued the opportunity to ask questions when signing up to the trial. Rapport with the research staff further strengthened the study experience.

> I think initially having that talk with physio did help me um because all you hear is hearsay quite a lot, especially when you're in the kidney clinic and talking to other participants, you're not sure who, who is being honest and who's not [laughter] but it just creates more paranoia and curiosity. (G03, IG)

Being able to discuss the study and ask questions to a specialist renal physiotherapist was seen as an important way to get accurate information.

A widespread view was that recruitment within the first three months after receiving a kidney transplant was acceptable.

> It's not an unreasonable time. And I think especially where your your target people are [acute post KTx]. Their likely to have the time. Um. at that you know- it's not as if they're you know. they're not, especially in the first 3-months, they're not leaping around, um. Worrying about you know a busy schedule. (P10, female, IG)

> When I was recruited, I just wanted to kind of get going and basically see what the website was all about (P07, female, IG)

Participants felt three months was also a feasible recruitment window as there was ample free time within the first three-months. Participants were eager to get started if randomised to the IG.

In contrast, one participant felt that the three-month recruitment window post-transplant surgery was too short. They felt that kidney transplant surgery took a significant time to recover from.

> I thought it was too soon. Because after the operation, I didn't even feel myself for the past- the last three- six months. (P09, female, UC group)

> With this kind of operation from this end of your stomach to the other side [laugh] I think I think at least 1 year (P09)

The three-month post kidney transplant window appeared overall to be acceptable to new KTRs. Overall, participants felt they had free time which they could use to engage with the research study. In contrast, one UC participant felt that perhaps a longer recruitment window was needed due to her longer recovery time.

6.4.3.4 Theme 2: The impact of COVID-19

The impact of COVID-19 was a consistent theme across the whole datasets and affected both groups. A commonly held view from the participants was that shielding measures had a direct impact on physical and mental wellbeing.

> It has made exercise a bit more difficult because I look after my son full-time now at home and it's hard to carve out time to exercise and I can't run in the park, I can't go to classes. So were were doing Joe Wickes every day, but that's not the same as being outside in the fresh air exercising… you just have to kind of adapt, I'm probably not doing as much as I would've done if I wasn't shielding. (P03, male, UC group)

> I was told not to go out and since then I have not been out, because I can't go and exercise. I can't do what I used to do so I need to stay indoors. (P05, male, IG)

A commonly held view was that the rigid shielding restrictions appeared to have a negative impact on mental wellbeing and mood as demonstrated by the quote below.

> Um. But I just feel like I don't want to do nothing, I can't be bothered, I just want to be left alone. So-And because I'm having other personal issues as well. (P06, female, IG)

Unique barriers were experienced by participants from being at home during shielding, which influenced PA. This had the potential to adversely affect motivation to perform PA behaviours. Participants suggested that support, and mental resilience were needed to navigate the challenges arising from shielding and the COVID-19 pandemic.

> We've stayed indoors because of looking after our boy [grandson], you know everyone's been helpful. you know shopping gets delivered, medicines get delivered, we don't have to go out…But that's just me. I've I've never let things worry me. I don't worry about things I can't change. (P01, female, UC group)

> And them, um. you know, I am lucky, I have a partner, so it's not like I am not talking to people every day, you know somebody face-to-face every day. I think there is a lot of value in that…I can't imagine being single during this period, that must be really difficult. Or you are living alone, even if you do have a partner, coz- [pause] I-I just can't even imagine that. Um. So, I feel quite lucky. So that's probably why it's been relatively easy to to kind of adapt. (P15, male, IG)

Mental resilience, having a positive mindset, and support from partners, family and the community were identified in this dataset.

Remote support from the research fellow (physiotherapist) was valued by IG participants in this challenging time.

> I think, um it will help because I spoke to my physio quite a bit, she used to call me and um, she, she would, I'd tell her sometimes and shed be like you know what you know keep busy, do this and do that and stuff like that she would give me advice. (G03, female, IG)

> Especially during the coronavirus um period um, the pandemic period um, you know it was just helpful to have that tool… Because you know sometimes you just need some to re-assure you that you someone to tell you OK this is what you need to do and this is what you should do and stuff like that, I think it was very useful for me to have that in my hand. (G03, female, IG)

One participant revealed that the ability to access the online intervention on her smart phone meant that she didn't feel an impact of 'lockdown' on her participation in the trial.

> Interviewer: Has there been anything else COVID-19 has made it harder for you to do, in regard to the trial?
>
> P07: uhm no, because like I said I can access it on my phone that I have with me, so no. (female, IG)

The secure-message function within the online intervention provided a mode to support participants during this period. Whilst the impact of COVID-19, and the strict shielding practises of the first wave of COVID-19 in the UK, presented challenges for our new KTR participants. The support from family, friends, and potentially the online intervention were identified as support strategies.

6.4.3.5 Theme 3: Engagement with the online intervention is a choice

A dominant theme across the dataset was that engagement with the online intervention was an individual choice. This choice could be influenced by personal and technical factors, which form the sub-themes.

6.4.3.5.1 Personal factors

Personal factors identified from the participants that could influence the choice to engage, or not engage, with the online intervention included barriers, previous knowledge and experience, personal preference for intervention delivery, and self-efficacy. Despite these personal factors, participants felt that the online intervention should be offered to all new KTRs.

Barriers such as time, work and childcare could impact on the choice to engage, or not engage, with the online intervention. For example, one participant discussed the

impact of working from home on his mental fatigue, and therefore his ability to engage with the online intervention.

> We are both [partner] definitely working slightly longer for working from home. And therefore, you feel tired from a different way … the knock-on effect of that is is I look- you know I log in to do my weight, and physical, [completes tracking] and then I kind of think -argh [sighs] I am not really in the right place right now to do um. A physical course [a website session]. (P15, male, IG)

'Trigger messages' (refer to 6.4.1.6 online intervention adherence) from the research fellow/physiotherapist were identified as a method to navigate personal barriers and re-engage with the online intervention.

> She [research fellow] helped me go to the website, and in the beginning, I actually forgot about going to the website because I uh wasn't used to, so she actually reminded me sometimes to go and do my exercise. (P05, male IG).

Personal barriers, such as work fatigue, could impact on engagement with the online intervention. Contact with the physiotherapist via the online intervention could be a potential strategy to assist with re-engagement.

Participants with previous knowledge and experience of PA appeared to be motivated, and demonstrate self-efficacy for being physically active, and following a healthy diet after transplant.

> It was just [pause] just following the programme through [completing sessions]…Um but that was just my personal thing. Just because I have- you know I have the knowledge and the confidence to be doing my own thing. (P10, female, IG)

> When I used to exercise on my own even prior to my transplant, I used to- you know, kind of look at myself and see what have I done in the last week, you know have I exercised enough, have I eaten well, you know have I been naughty with my eating. (P04, male, IG)

One participant expressed that a structured group exercise class, like renal rehabilitation, was not needed.

> I didn't think I needed them [renal rehabilitation class] um . so much intensive care really. Um being you know forced into exercise. Because I am quite happy with it [exercise] before that [transplant]. And um. Yeah. It's worked out okay. I need to do little bit more exercise now. Um to get back. To lose a few kilograms. (P08, male, UC group)

Participants with previous exercise experience of PA appeared to have confidence in managing healthy behaviours such as PA post-transplant.

Personal preference regarding the type and delivery of an intervention to prevent weight gain for new KTRs varied across the dataset. This personal preference appeared to closely relate with self-efficacy for online use and, previous knowledge and experience with PA practices. Group interventions, particularly for the exercise component of the intervention, appeared to be preferable to some participants.

> I think if it was something more like [pause] let me see [pause] in a group or more personal thing, think like not on the phone you get into a group to do the exercises it would be more motivating to do it. (P06, female, IG)

A rare view was the desire for one-to-one, face-to-face, interventions with a physiotherapist.

> As I say it's just you know you're getting the information as I think of it in first-hand, and if I got any questions, I can actually ask them and get the answer the way I want the answer… I think being face-to-face you know uhm you have got that 1-1 sort of thing. (P02, male, UC)

Group exercise interventions were identified as a potential strategy to foster peer-motivation when engaging with interventions to prompt PA post kidney transplant. However, some participants may prefer a one-to-one individualised intervention.

A more exceptional experience was reported by a UC participant who had experience with a face-to-face group renal rehabilitation class prior to having a kidney transplant. They reported difficulties accessing the face-to-face renal exercise class.

> Interviewer: So how did you feel about that- being in that group?
> P09: In that group [UC], at that particular time, I needed that. being on the website. Because going to the gym. It was a bit of stress. It would be a bit of stress for me. Because waiting for ambulance- coming, it's not coming. and then get there, and [laughs] I do that exercise for one hour and waiting for transport for two hours… with the condition I was, at that time, after the operation, I don't think, [laughs] that kind of thing, I don't think I would have strength for that. (P09, female, UC group)

The participant identified that the online intervention could have provided a preferable mode to deliver exercise intervention around her post-transplant recovery.

> If I had a website that I could begin looking for as. You know-doing exercise. you know. That won't- not rushing [laughs]. Maybe when I wake up in the morning, then I put it on. And do it maybe in the afternoon or evening. I put it on then. Yeah, that would be fine. (P09, female, UC group)

Access to the online intervention was seen to offer flexibility in providing exercise interventions in the post-operative phase of kidney transplant recovery.

There appeared to be a direct relationship between personal preference and self-efficacy for online use. Those who had self-efficacy and confidence for online use, may prefer online interventions.

> I think it depends on the person, personally I-I because I am tech savvy you know I use and I-I use lots of apps anyway I think I would be fine, but I think some people who weren't so digitally savvy would prefer face to face. I think it's more either or, but I think the combination of the two would probably be ideal. (P03, male, UC)

> You know I am very happy doing online programmes. Um. and I do do a lot of online programmes actually, it's a good medium. And you can access people you might not otherwise been able to. (P10, female, IG)

In contrast those with poor self-efficacy for online use perhaps would tend to prefer face-to-face behaviour interventions.

> Personally, I am glad I actually got to go rather than doing it on the computer… because I am-I am useless on a computer for a start, um, I don't feel confident at all on a computer. I'd rather be face to face with uhm [pause] with the person that is sorting it out for me you know (P02, male, UC group)

Self-efficacy and personal preference for the mode of delivery of a behavioural intervention post kidney-transplant appeared to be linked.

A dominant view from both groups in the dataset was that the online intervention should be offered to all new KTRs.

> **Interviewer:** is there anything else you would like to see included in this?
> **P05:** actually um-um-um the piloting, so it is not everyone who has access to the site so if-if it can be made possible for everyone. (P05, male, IG)

> I almost think it would be really good as a compulsory thing to just put out there… just you can turn it down, but it's nice that it's presented there [in transplant clinic]. It would be cool to know this is the kind of thing that is presented to people once they have had a transplant. because there are going to be people who are in worse positions then me, maybe who are

> less mobile, maybe they are older, they are whatever, and I think, it would be good to give them the option. Because it's always nice to have the option to do this. (P15, male, IG)

Despite personal factors such as barriers, previous knowledge and experience, personal preference for intervention delivery, and self-efficacy, a dominant view was that the online intervention should be offered to all new KTRs post-surgery. One participant suggested that a method for offering the online intervention to new KTRs could be an 'opt-in' referral process to facilitate individual choice.

6.4.3.5.2 Technical factors

Stakeholder input was crucial in development, refinement and evaluation of the digital healthcare intervention. Technical factors were seen to influence the choice to engage, or not engage, with the online intervention. Interview participants provided suggestions to enhance future iterations of the online intervention. A suggestion was to reduce the length of some of the sessions, particularly sessions 10 (barriers) and 11 (problem solving).

> The problem-solving thing, um [pause] um there was steps where it said identify the problems as soon as possible, and then you write things like oh you're out of breath, and then it would then ask you how then like using different words like, like you know to describe becoming short breath when walking up the stairs, when walking to work or anything like that. I mean like, it was a bit too much, there was a lot of things that you had to write down. (G03, female, IG)

Another suggested technical enhancement was to have different ability levels for the exercise diary component of the online intervention.

> Maybe under different tabs for example-different link or tab. This is for older people, with less strength. As then. then for I don't know younger participants because I have seen some there was some transplant participants I have seen at Guy's, they are younger. They can lift more whilst they recover from the wound and stuff. (P12, male, IG)

A recurrent enhancement suggestion was for the online intervention to offer live virtual group exercise classes, instead of pre-recorded exercise instruction videos and

the written exercise diary, this was seen as a potential way to increase motivation and engagement.

> I would say um instead of pictures, maybe get videos, uhm but I think there is a video where there is instructing, what sort of exercises would look like. (G03, female, IG)

Some participants felt that no further revisions were required to the online intervention, and it was straight forward.

> If I'm honest I don't think there is much of a change in my opinion. I found there was far much more on that site erm that I even needed yes so in my opinion- it's you know rather than going on the internet, rather than going on you know other websites and stuff I found that this particular website that there was a lot on there to help. (P04, male, IG)

> I don't really want to say this could be improved when it's totally fine…so far for me everything is fine, there are no improvements that need to be done. (P07, female, IG)

Participant feedback and experience with the online intervention was crucial to inform further research in online intervention delivery. Reducing the length of some of the sessions, providing levels of exercise prescription, and potentially providing group virtual classes may enhance acceptability of future iterations of this online intervention.

Overall, the online intervention was shown to be user-friendly. Participants reported that the layout and spread of the online intervention was easy to use and follow. They valued having the brief 1:1 orientation session with the physio to show them how to use the resource.

> It was very-very easy because the first day she actually uh she actually bookmarked the site for me so any-any-anytime I went on there it was easy to enter. (P05, male, IG)

> She showed me on her own app how to do everything uhm on the website and once she demonstrated it to me, I was able to do it myself. (G03, female, IG)

> To be honest it was easy, to for me to you know, absorb the information there. It was nice, nicely spread out and you know all the videos and stuff were well explained. umm. I had no problems with you know, getting used to it whatsoever. So, it was pretty nice. You know, the font, everything. (P12, male, IG)

The orientation to the online intervention, and particularly the research fellow downloading the online intervention onto the home screen of their smart phones, was valued and assisted engagement.

In contrast, one participant expressed difficulty getting used to the online intervention despite the 1:1 orientation session.

> To navigate around it, I found, I found it a bit difficult at first, I didn't really get it, I had to keep trying and trying and trying. (P06, female, IG)

However, with repeated use, this did get easier.

> The more you use it, the more you get used to it, so then it is not so bad... I realised that if I just give it go, then I would be able to do it. (P06, female, IG)

A brief face to face orientation session with the physiotherapist, including assistance on downloading the reactive online intervention onto personal smart phone devices, was one of the technical factors that could promote engagement with the online intervention. Some participants may require varying levels of on-going support and encouragement.

Generally, the online intervention was seen as an acceptable resource for new KTRs. The videos were seen as a good mode of education delivery, almost like face-to-face.

> Obviously, the videos, because it's like argh. Almost face to face…it was good. The videos was were the length , it wasn't too long it wasn't too short you know. (P12, male, IG)

> The videos are good the videos are not like long videos. It's very short, 2 minutes, so you know- it is easy to listen to, it's not like jumping jumping or it's just, uh whenever I saw the time, the times on the video I was encouraged to watch it because long videos its actually long videos, with the shorter videos I was enjoying them. (P05, male, IG)

> Like the website was straight forward and the videos explained anything that if I'd had queries to, the videos would answer it. (P07, female, IG)

Videos could be an acceptable mode of delivery for new KTRs to receive education regarding physical activity and maintaining a balanced diet post-transplant, and warrant further exploration in future studies.

The 12-week programme length was also deemed acceptable to IG participants. It was seen as an opportunity to set weekly physical activity and healthy eating goals.

> You see for me I almost looked at it like it was a twelve-week session, so it was like a twelve-week target right, so I kind of said to myself -oh ok so I've got time to catch up, catch up when I fall back. they were like set out as like weekly plans, so that's what was helpful to me. (P04, male, IG)

The language used within the online intervention was viewed as a supportive space for new KTRs.

> You know there is emphasis in your programme on goals, and you know, letting people have that space, to you know 'how do you feel goals? do you feel confident that you will achieve it?' [ref to the confidence and importance ruler in goal setter function]. Um so the language around it was very very good. (P10, female, IG)

Engaging the target user group (KTRs) remained crucial throughout this research project to ensure that the online intervention is fit for purpose. Participants in the IG who were interviewed felt that the online intervention was acceptable and was a supportive space to support physical activity and healthy eating after receiving a kidney transplant. Orientation to the online intervention, downloading the online intervention to devices, and making enhancements could further facilitate engagement.

6.4.3.6 Theme 4: Mechanisms of action

A common experience from participants was that the intervention, and the study processes, helped participants feel supported with their PA and, in some cases, healthy eating behaviours. There appeared to be assessment factors and online intervention factors that therefore contributed to the mechanisms of action.

6.4.3.6.1 Assessment factors

Participants in both groups found the assessment process to be a reassuring additional 'check-up'.

> Yeah. I think that one was good. Because [pause] we need these things to check if everything is working well in our life. So yeah. I think it helped. It put my mind- it give me piece of mind. (P09, female, UC group)

The research assessment process provided participants with 'piece of mind'. The six-minute walk test and the bioimpedance tests appeared to be the most valued outcomes from the participant perspective.

> **Interviewer**: what your overall experience of this research trial has been like for you?
> **P01** excellent. excellent. It has shown me that I can walk. If I put my mind to it [laughs]... really walk. (P01, female, UC group)

> I think it was good to get a benchmark of where I was, so every test I did every assessment I did, I was told so that's good maybe this is not so good, you may want to improve it uhm I thought that was really helpful. (P03, male, UC group)

> I was more muscles than my fat because I was very worried about the fat. but when she-she measured the muscles within me and the fat she told me that I was more muscles than the fat I was thinking of. She-she even went ahead to tell me about the percentage of muscles that I had so I was very very uh-u-h I actually felt very good. (P05, male, IG).

Completing the six-minute walk test after post-transplant surgery (after stent removal) at the baseline visit with the specialist renal physiotherapist (research fellow) appeared to provide participants with confidence in their walking ability, irrespective of group allocation. Being provided with information on their fat and muscle mass during outcome assessment was also seen to be valuable. Assessment visits provided an opportunity for 'benchmarking' and were seen as a key mechanism contributing to the overall positive study experience.

Confidence in PA after transplant surgery was also enhanced by the interactions with the physiotherapist during the study visits by participants in both groups.

> Because it was like straight after my transplant, so I wasn't like 100% perfect physically. But she made it quite easy, it didn't take much out of me to do the things she asked… :it was excellent She's excellent. She made me feel comfortable and uh [pause] she's welcoming so that's it really. (P06, female, IG participant)

> Excellent, they made you so- there so friendly yeah and made you feel so confident, that I was well [pause] well pleased…uhm yeah uhm yeah it was just the conversation you're having whilst you're doing the trial uhm, I think makes you a lot more at ease anyway. Like [physio name] [pause] you know talking to her like she was my sister sort of thing not as like a doctor. You know yeah it made you feel very comfortable. (P02, male, UC group)

Having the assessment completed by a specialist physiotherapist, with clear communication and rapport, appeared to be of value to participants in both groups. The advice and interaction from an 'expert' appeared to reassure participants.

6.4.3.6.2 Treatment factors

Exposure to the online intervention appeared to foster healthy behaviour change for PA and healthy eating behaviours. This was achieved by education, addressing fear of injuring the new kidney, monitoring and promoting accountability, and providing knowledge and skills to manage cravings.

> It was motivating for losing weight, I would say, and making changes in different ways such as eating habits, erm exercising habits, or structuring your exercising (P04, male, IG)

> Yes yes, to learn about the-the-the exercise, yes about the exercise, so I go there to remind myself about the exercise and-and-and the cravings. And-and sometimes I-I show the uh food the proportion to my wife and telling her that and I need to eat more vegetables and fruits than the carbohydrate. (P05, male, IG)

> **PD**: Ok excellent, excellent. And did that result in any changes in your everyday life?
> **P07:** well, it made me do exercise, for someone who doesn't like exercise at all, uhm [laughter] it made me at least do 10 minutes a day, because obviously I have the kids and now that they are not in school so at least taking 10 minutes out of my day, to do that. I've actually started to do that, and it's been a thing I have been doing since so that's helped.

In contrast, participants from the UC group reported little to no difference in their PA and healthy eating behaviours

> Um yeah, unfortunately. [laughs] um I'm eating a bit more than I was (P02, male, UC group)

Providing specific education on PA, cravings, and healthy eating post kidney transplantation appeared to act as a vehicle for behaviour change. Some participants engaged their family members with the educational content.

Fear of injuring the new kidney, particularly acutely post-transplant surgery was widespread in this dataset.

> If I do exercise, what if I damage my new kidney, that's the only thing that comes to your mind...: but when I saw the exercises on there, it was very much um, you know puts you at ease and you know, you knowing that it's not anything that is going to hurt you physically. (G03, female, IG)

> When I started, I had pains in my abdomen, but gradually it went away, as I began to exercise (P05, male, IG)

> More confident, you know… Because sometimes I didn't know what can I do, you know at home. I didn't want to get like you know- not damage the kidney but, you know, because of my haematoma I couldn't do certain exercises before. But after, you know- I gained more confidence to you know exercise myself at home. (P12, male, treatment group)

The online intervention was seen to provide 'baby steps' or 'steppingstones' to build up PA after surgery.

> What the exercise on the website does is, is quite um almost like a baby step kind of thing, like it is all up to your pace, it's all up to um what pace you can do, and I think the more active you have become, the more you can go faster, the more you can do extra steps or anything like that, so without it I don't think I would have like you know recovered as fast as I did. (G03, female, IG)

> If you are somebody who is maybe not that physical, and maybe you're spurred on by having a transplant and you want to um. Become fitter, or healthier or, maybe you were really fit before you want on dialysis for a few years you became you know less fit and unwell etc. And you want to get back into it, this is-this seems like a good steppingstone to do that. Because it's sort of prompting you. (P15, male, IG)

Gradually building up PA, through the online intervention was seen as a mechanism for the online intervention to improve PA and confidence.

In contrast, participants in the UC group reported that they didn't want to push their PA after kidney transplantation.

> I don't want to sort of overwork it and end back up at stage 1 again. (P02, male, UC group)

> It was a big wound. It was really, paining. and it maybe could affect your kidney. Because I don't know how the kidney. I don't to shake the kidney, I don't want anything to go wrong, so I take it easy. So that that was why you know taking it easy. Not to do stress

> there. Serious exercise, or shaking myself, or doing something worse, just taking it easy. (P09, female, UC group)

The online intervention could perhaps address fear of injury for new KTRs by facilitating gradual return to PA, and to instil confidence.

Managing cravings (session 2) was seen as an essential topic of education for new KTRs.

> I think a lot of people who have just had a transplant are not aware of how much cravings you will go through. And I think people put a lot of weight on at the beginning because they, they just think they are hungry but actually they are not hungry, they actually are cravings you know. [laughs]… So, I think having this tool, if they had this tool at the beginning, I think it would help them quite a lot. (G03, female, IG)

> **Interviewer**: has there been any changes to your everyday life?
> **P06**: Well like- the choice I make when it comes to food. [pause] yeah, um that was helpful… It's helped me to make better choices when I eat, or I was having problems with craving at first. But when I watched that video on how to manage cravings that was helpful. So, I'd say that one, that one stood out, I forgot about that one, that one stood out, that video

The cravings session was valued as it provided information and strategies to manage cravings that was not provided by clinical services. The online intervention, particularly session 2 and session 4, empowered participants to address eating and PA behaviours to counteract cravings.

> After watching the video, [pause] and because I realised, I was putting on weight as well. And then watching the videos. And the video on physical activity, I can't remember now but that um it just made want to go out and get some fresh air and walk a bit. Because that is one of the things, I use to help me stop craving. [pause] like a bit, I find sitting down watching TV I would crave more. But if I am not in the house even if I'm not feeling cravings there is no fridge to go to. But when I am outside, I go for walks with my daughter or just on my own, then I wouldn't have anything even I am feeling it to eat. (P06, female, IG)

Education on cravings, distraction techniques, and increasing PA appeared to support participants manage cravings.

Self-monitoring, monitoring remotely by the research fellow appeared to facilitate accountability and motivate participants to be physically active and monitor their weight after transplantation.

> With the tracking your weight and you're exercising, or you know your activities through your day or your week. I found by keeping a track of it kind of motivates you to want to add more to the activity part, and then to the part where you've got the weight, your-I mean for myself as well I look at it and I'm like you know I want to try and bring that weight down down down. (P04, male, IG)

> So, my point there is in terms of being accountable to something. Even though it's not a- a human being, you are being accountable to a system, and you know-you know for these 12 weeks, you need to you know, every week you need to be putting the inputs in [weight and activity tracker]. And then you are seeing for yourself, it's like 'oh no'. It kind of made me probably go for more walks, in all honesty. Because it's like, 'oh no. I don't want to do worse, than I did last week'. (P10, female, IG)

Being able to self-monitor PA, and visually see progress, allowed participants to feel accountable for their PA and healthy eating behaviours.

Remote monitoring by the research fellow appeared to influence motivation and engagement.

> **P04**: I definitely found that motivating as well because as crazy as it sounds it's like you don't want to disappoint the person, you know that is trying to help you, and I feel like it's a good thing for yourself, because then it keeps you motivated as well.

> **Interviewer:** And what was your main motivation do you think for using the online resource?
> **P10** [laughs]. Probably could I could I could see you! [laughs] [physio name] is going to be in touch if I haven't done it'. I didn't want to let you down!..That's the personal connection there, everything boils down to a relationship at the end of the day. So, I know you, I have had that initial session, with you, and you know I know that you know this is your research and you care about it. So, I -you know. I was like ' no I must I must do this'. It's not the sole reason, but it's a strong motivating factor. Um. to know that this is- you know this is this is going into something that is important. (Female, IG).

Access to the physiotherapist through the secure message function enhanced the positive experience of using the online intervention.

> I'd say it has been a good experience, because if I've had any problems then I'd just um send a message through the [pause] uhm the website messaging uhm part of it... And I normally get a reply back the same day or very next day (P07, female, IG)

> She helped me go to the website, and in the beginning, I actually forgot about going to the website because I uh wasn't used to, so she actually reminded me sometimes to go and do my exercise. (P05, male IG).

The message function allowed for trouble shooting, but also reminded participants to re-engage.

In contrast, a rarely held view, by one participant was they did not want to bother the physiotherapist.

> I just didn't want to bother her, so I tried to figure it out myself, which probably wasn't the greatest thing… I just didn't want to bother her; I liked to figure things out myself first. (P06, female, IG participant).

An overreaching view was that the online intervention self-monitoring, monitoring by physiotherapist, and access to physiotherapist via the secure message function contributed to the online intervention being a helpful intervention for acute KTRs. Self-monitoring and monitoring appeared to be valued by participants, and to contribute to motivation and engagement.

Consistently across the whole dataset, based on these observed positive mechanisms of action, participants reported they would recommend the online intervention to other new KTRs.

> They can learn how to manage their weight and how to erm [pause] yeah how to erm [pause] and how to look after the kidney, because that is a part of it as well. And also, how to just live a healthier lifestyle really. (P06, female, IG)

> **Interviewer**: do you have any advice for people in similar situation to you.
> **P05**: um you know maybe this exercise, is um voluntary exercise and um-um it depends on the individual maybe some don't want the information to known by anybody. But I-I-I-I would say it is very helpful and uh-uh-uh it actually gives you more knowledge about the uh your cravings, your diet so uh yes it very good to everyone else coming from a transplant.

The online intervention was well received by the IG participants and would be recommended to other new KTRs to facilitate self-management and support PA and healthy eating behaviours post kidney transplant surgery.

6.4.4 Integration of qualitative and quantitative findings

To present the mixed methods findings, the convergence of QUANT and QUALI data is presented. Key concepts from both data sets, and the research aims and objectives were

tabulated side-by-side using a joint summary display (Creswell & Plano Clark, 2018b). This process facilitated direct comparison of data sets and reveal meta-themes. Convergence was defined as when qualitative and quantitative results agreed, divergence was used when results showed disagreement, and expand referred to when one set of results is enhanced by the other (Creswell & Plano Clark, 2018b). The joint summary below (table 6.16) facilitates integration of the QUANT and QUALI data sets to provide a rich understanding of the experiences of taking part in the study, using the intervention and overall feasibility. The joint summary was loosely based on an example table from Creswell et al (2018c). The progression criteria is shown within the joint display to facilitate interpretations of the mixed methods results.

Table 6-19 Joint display table of quantitative, qualitative and mixed methods meta-inferences

Common Concepts	Progression criteria	QUANT results	QUALI results	Mixed meta-inferences (confirm, discordance or expand) with rationale
Screening of potential participants	≥ 50% deemed eligible approached to do the study	*Screening rate:* 84.2% (95% CI 68.8 to 94.0)	*No data available*	• Screening rates exceeded progression criteria • KTRs who did not consent to the trial were not interviewed • Future qualitative data could expand this
Recruitment of participants	≥ 50% of people approached consent to study who have been screened and deemed eligible to take part in the trial	*Recruitment rate:* 62.5% (95%CI 43.7 to 79.0)	*Theme 1: Optimising participation and recruitment:* • *Research altruistic process:* I am happy to do research, and you know, if it helps the next person down the line. because somebody in front has helped me. (P01, female, UC group) • Clear communication essential: Yeah, it was good there was no pressure, I felt like I could ask questions. Uhm, you know the paperwork I filled out was pretty self-explanatory, uhm it was very detailed you know it was very good. (P03, male, UC group)	• *Confirm* • *Rationale:* Recruitment rate exceeded progression criteria • Overall qualitative data suggested research was an important process and participation was assisted through clear communication and rapport with the physiotherapist • All but one participant expressed the recruitment

			• Recruitment window acceptable: It's not an unreasonable time. And I think especially where your target people are. Their likely to have the time (P10, female IG) • One divergent example recruitment window acceptable: I thought it was too soon. Because after the operation, I didn't even feel myself for the past- the last three- six months. (P09, female, UC group)	window (first 3-months after transplant surgery) was feasible and acceptable
Study retention	Retain ≥60% of the sample at 12 months follow up	76.4% (95% CI 50.0 to 93.2)	Participants were not formally interviewed when they withdrew from the study. However, reasons for drop out were collected. Reasons for withdrawal included: • Personal issues (n=1) • Moving out of area (n=1) • Loss to follow up (n=1) • Medically withdrawn (lost kidney transplant) (n=1)	• *Partially confirm, further research warranted* • *Rationale:* Despite COVID-19, good retention rates were evident in this study sample • Variable reasons for dropouts • Further qualitative data collection could further explore this

Study visits adherence and experience	No set progression criteria. Capture and report.	*Adherence to study visits* • Baseline: 85% (95% CI 62.11 to 96.79) • 3months: 88.3%(95%CI 63.6% to 98.5%) • 12months: 76.4% (95% CI 50.0 to 93.2)	*Theme 4: Mechanisms of action (assessment factors):* Yeah. I think that one was good. Because [pause] we need these things to check if everything is working well in our life. So yeah. I think it helped. It put my mind-it give me piece of mind. (P09, female, UC group) • *Rapport and education:* Because it was like straight after my transplant, so I wasn't like 100% perfect physically. But she made it quite easy, it didn't take much out of me to do the things she asked… :it was excellent She's excellent. She made me feel comfortable and uh [pause] she's welcoming so that's it really. (P06, female, IG participant) They're so friendly yeah and made you feel so confident, that I was well [pause] well pleased… the conversation you're having whilst you're doing the trial uhm, I think makes you a lot more at ease anyway. Like [physio name] [pause] you know talking to her like she was my sister sort of thing not as like a doctor. You know yeah it made you feel very comfortable. (P02, male, UC group)	• *Confirm* • *Rationale:* Overall, the study visits were seen as a positive experience and reasons for this were presented in the qualitative analysis • There was satisfactory adherence rates of participants completing study visits (despite COVID-19) • Particularly Theme 1 from the qualitative analysis demonstrated that the assessment process was seen as a positive experience, providing participants with a 'check-up', facilitated by physiotherapists rapport, the education and assessment outcomes

			• *Increasing knowledge:* I think it was good to get a benchmark of where I was, so every test I did every assessment I did, I was told so that's good maybe this is not so good, you may want to improve it uhm I thought that was really helpful. (P03, male, UC group)	
Acceptability of secondary Outcomes	No set progression criteria. Capture and report.	*Adherence to data collection (all outcomes assessed)* Baseline: 17/17 100% (95% CI 80.5 to 100.0) 3months: 9/17 52.9% (95% CI 27.8 to 77.0%) 12months: 13/17 76.4% (95% CI 50.0 to 93.2)	*Body weight, BMI, anthropometric measures, arterial stiffness and questionnaires- no qualitative data available* • *Six-minute walk test valued:* **Interviewer**: what your overall experience of this research trial has been like for you? **P01** excellent. excellent. It has shown me that I can walk. If I put my mind to it [laughs]... really walk. (P01, female, UC group) • *BIA assessment valued:* I was more muscles than my fat because I was very worried about the fat. but when she-she measured the muscles within me and the fat she told me that I was more muscles than the fat I was thinking of. She-she even went ahead to tell me about the	• *Confirm* • *Rationale:* Incomplete full data collection of all outcomes at 3 and 12-months were due to COVID-19, not due to participants declining to take part in these assessment outcomes • Qualitative data (Mechanisms of Action-Assessment theme) suggests the assessment experience was positive for both groups

			percentage of muscles that I had so I was very very uh-u-h I actually felt very good. (P05, male, IG). • Assessment experience (all outcomes) provided an opportunity for benchmarking: I think it was good to get a benchmark of where I was, so every test I did every assessment I did, I was told so that's good maybe this is not so good, you may want to improve it uhm I thought that was really helpful.(P03, UC)	• The six-minute walk test and BIA were particularly valued interventions
Intervention adherence	% Treatment group participants completing 60% (≥7/12) sessions	*Adherence to online intervention sessions* 6/9 66.67% IG completed 60% sessions (95% CI 29.93 to 92.51) *Individual adherence rates/sessions completed:* • 12 sessions (n=4)	*Theme 3: Engagement is a choice:* You know I am very happy doing online programmes. Um. and I do do a lot of online programmes actually, it's a good medium. And you can access people you might not otherwise been able to. (P10, female, IG) I think if it was something more like [pause] let me see [pause] in a group … it would be more motivating to do it. (P06, female, IG) • *Barriers:* We are both [partner] definitely working slightly longer for	• *Confirm and QUALI further Expands reasons for difficulties adhering with online intervention* • *Rationale:* progression criteria satisfied for adherence to the intervention, with six of the nine IG participants completing 60% or more of the sessions • Qualitative results expand and give depth to adherence data

	• 10 sessions (n=1) • 9 sessions (n=1) • 5 sessions (n=1) • 0 sessions (n=1) • Tracking only (n=1)	working from home. And therefore, you feel tired from a different way … the knock-on effect of that is is I look- you know I log in to do my weight, and physical, [completes tracking] and then I kind of think -argh [sighs] I am not really in the right place right now to do um. A physical course [an online intervention session]. (P15, male, IG) • *Reminders helped re-engage:* She [research fellow] helped me go to the website, and in the beginning, I actually forgot about going to the website because I uh wasn't used to, so she actually reminded me sometimes to go and do my exercise. (P05, male IG). • *Enhancements:* The problem-solving thing, um [pause] um there was steps where it said identify the problems as soon as possible, and then you write things like oh you're out of breath, and then it would then ask you how then like using different words like, like you know to describe becoming short breath when walking up the stairs, when walking to work or anything like that. I mean like, it was a bit too	• Purposive sampling of variable engagement levels with the online intervention provided insight into reasons and factors influencing adherence with the online intervention. • Personal preference and choice should drive the mode of delivery of interventions to support new KTRs control their weight post-acute transplantation • The choice to engage or not engage is influenced by technical and personal factors and should be offered to all new KTRs • Individual adherence rates can be matched to the qualitative data.

		much, there was a lot of things that you had to write down. (G03, female, IG) Maybe under different tabs for example-different link or tab. This is for older people, with less strength. As then. then for I don't know younger patients because I have seen some there was some transplant patients I have seen at Guy's, they are younger. They can lift more whilst they recover from the wound and stuff. (P12, male, IG) I don't really want to say this could be improved when it's totally fine…so far for me everything is fine, there are no improvements that need to be done. (P07, female, IG)	• G03 started the 11th session (problem solving) but only completed 10 sessions. Her qualitative data suggests session 10 was too long, could impact adherence, and perhaps needs revisions in future iterations • One participant who completed tracking only (P15), did not receive the trigger messages as didn't complete the welcome session. He also attributes work changes due to COVID-19 as a barrier to adherence • Another participant who re-engaged with the programme after receiving trigger message (P05) completed the 12 sessions and would recommend all KTRs get access to the resource
	• *Should be offered to all:*	**Interviewer:** is there anything else you would like to see included in this? **P05:** actually um-um-um the piloting, so it is not everyone who has access to the site so if-if it can be made possible for everyone. (P05, male, IG) I almost think it would be really good as a compulsory thing to just put out there… just you can	

			turn it down, but it's nice that it's presented there [in transplant clinic]. (P15, male, IG)	
Intervention experience	No set progression criteria. Capture and report.	*Online intervention log in rates* *Median (IQR):* • Number sessions completed 10 (5 to 12) • Logins within 12-week online intervention 13 (7 to 22) • Full log in data is available in table 7.6 *BCT's most frequently used:* • BCT 7.1 'prompt and cues' was used 25 times the	*Theme 3: Engagement is a choice* • *User friendly:* She showed me on her own app how to do everything uhm on the website and once she demonstrated it to me, I was able to do it myself. (G03, female, IG) To be honest it was easy, to for me to you know, absorb the information there. It was nice, nicely spread out and you know all the videos and stuff were well explained. umm. I had no problems with you know, getting used to it whatsoever. So, it was pretty nice. You know, the font, everything. (P12, male, IG) • Contrasting quote user friendly: To navigate around it, I found, I found it a bit difficult at first, I didn't really get it, I had to keep trying and trying and trying. (P06, female, IG) • Improved with repeated use: The more you use it, the more you get used to it, so then it is not so bad... I realised that if I just give it go, then I would be able to do it. (P06, female, IG)	• *Expand* • *Rationale:* Qualitative results were crucial in exploring participants experience with the online intervention • Most participants found the online intervention easy to use, which was assisted by an induction with the research fellow. However, one participant found it initially challenging • Participants particularly valued the craving management (session 2), the gradual build-up of physical activity to support fear avoidance, the self-monitoring and monitoring by the physiotherapist. These were

	12-week online intervention • BCT 3.1 ‘social support unspecified’(Michie, Atkins, et al., 2014b) was used 83 times in the physiotherapist interactions	*Theme 4: Mechanisms of action (treatment factors):* It was motivating for losing weight, I would say, and making changes in different ways such as eating habits, erm exercising habits, or structuring your exercising (P04, male, IG) • *Cravings management valued:* I think a lot of people who have just had a transplant are not aware of how much cravings you will go through. And I think people put a lot of weight on at the beginning because they, they just think they are hungry but actually they are not hungry, they actually are cravings you know. [laughs]… So, I think having this tool, if they had this tool at the beginning, I think it would help them quite a lot. (G03, female, IG) It’s helped me to make better choices when I eat, or I was having problems with craving at first. But when I watched that video on how to manage cravings that was helpful. So, I’d say that one, that one stood out, I forgot about that one, that one stood out, that video	suggested as mechanisms of action for the online intervention • Prompting and social support could have contributed to the experience of using the online intervention and marry with the subtheme of monitoring under theme 4

- *Self-monitoring:*

  With the tracking your weight and you're exercising, or you know your activities through your day or your week. I found by keeping a track of it kind of motivates you to want to add more to the activity part, and then to the part where you've got the weight, your-I mean for myself as well I look at it and I'm like you know I want to try and bring that weight down down down. (P04, male, IG)

- *Physio monitoring:*

  I'd say it has been a good experience, because if I've had any problems then I'd just um send a message through the [pause] uhm the website messaging uhm part of it... And I normally get a reply back the same day or very next day (P07, female, IG)

- *Gradual build-up of exercise provided confidence:*

  What the exercise on the website does is, is quite um almost like a baby step kind of thing, like it is all up to your pace, it's all up to um what pace you can do, and I think the more active you have become, the more you can go faster, the more you can do extra

			steps or anything like that, so without it I don't think I would have like you know recovered as fast as I did. (G03, female, IG) • *Would recommend to others:* They can learn how to manage their weight and how to erm [pause] yeah how to erm [pause] and how to look after the kidney, because that is a part of it as well. And also, how to just live a healthier lifestyle really. (P06, female, IG)	
Willingness to be randomised	No set progression criteria. Capture and report.	*No quantitative data*	*Theme 3: Engagement is a choice (personal factors)* • *Would have liked the online intervention/ choice:* I think it depends on the person, personally I-I because I am tech savvy, you know I use and I I use lots of apps. Anyway, I think I would be fine, but I think some people who aren't so digitally savvy would prefer face to face, I think it's more either or, but I think the combination of the two would probably be ideal. (P03, male, UC group) In that group [UC], at that particular time, I needed that. being on the website. Because going to the gym. It was a bit of	• *Partially confirm, further research warranted* • Whilst there is no quantitative data relating to willingness for randomisation, qualitative data provides insight into personal choice, preference, and the overall feeling that the online intervention should be offered to all KTRs

stress… If I had a website that I could begin looking for as. You know-doing exercise. you know. That won't- not rushing [laughs]. Maybe when I wake up in the morning, then I put it on. And do it maybe in the afternoon or evening. I put it on then. Yeah, that would be fine. (P09, female, UC group)

- *Should be offered to all:*

  Interviewer: is there anything else you would like to see included in this?
  P05: actually um-um-um the piloting, so it is not everyone who has access to the site so if-if it can be made possible for everyone. (P05, male, IG)

  I almost think it would be really good as a compulsory thing to just put out there… just you can turn it down, but it's nice that it's presented there [in transplant clinic]. It would be cool to know this is the kind of thing that is presented to people once they have had a transplant. because there are going to be people who are in worse positions then me, maybe who are less mobile, maybe they are older, they are whatever, and I think, it would be

			good to give them the option. Because it's always nice to have the option to do this. (P15, male, IG) *Theme 4: Mechanisms of action (treatment factors* • *Would recommend to others:* I would say it is very helpful and uh-uh-uh it actually gives you more knowledge about the uh your cravings, your diet so uh yes it very good to everyone else coming from a transplant (P05 male IG).	
Safety and hospitalisations	No set progression criteria. Capture and report.	5 participants had NAEs 5/17 29.4 (95% CI 7.8 to 51.1) Tx biopsies	Whilst there was no specific quotes on adverse events, the background quotes demonstrate the ups and downs in the post-transplant journey: I went through quite a lot of different treatments, uhm doctors not knowing, I think that kind of put me uneased as well (G03, female, IG) I had terrible problems with Tacrolimus. I couldn't see, they were sensitive to the light... The nurses themselves didn't even know about it (P08, male, UC group)	• *Suggest confirming* • *Rationale:* There were no related adverse events. There were five nonrelated adverse events, and no slips, trips or musculoskeletal injures reported • Whilst there was no qualitative data specific to AE's or transplant biopsies, qualitative data highlighted the ups- and-

			downs experienced by participants acutely after receiving a kidney transplant

Note. This table is loosely based on figure 7.3 , an example joint display table for a convergent MMR study from Creswell (2018c, pp. 229-230). QUANT indicates quantitative data, an QUALI indicates qualitative data from studies 3 and 4. NA refers to data not being available.

6.5 Discussion

The main aim of this chapter was to explore the feasibility and acceptability of the online intervention for new KTRs. This was achieved through the objectives 5a) to assess the feasibility to screen and recruit participants, measure adherence to study visits and the intervention, and capture safety outcomes (quantitative outcomes, study 3) and b) to capture and report the experience of using the online intervention over 12 weeks, and the experience of taking part in the feasibility study (qualitative outcomes, study 4). The mixed methods integrated analysis and joint display table allowed for meta-themes to encompass both datasets to provide a richer understanding of the acceptability, feasibility and experience of the ExeRTiOn online intervention for new KTRs.

6.5.1 Discussion of meta-themes

6.5.1.1 Screening, recruitment and retention

Clear reporting of screening rates (the proportion of participants that were screened that met eligibility criteria) and recruitment rates (the proportion of participants recruited from the total number of eligible participants) can facilitate the assessment of external validity and generalisability. The screening rate for this study were 84.2%, which exceeded the pre-set progression criteria screening rate (50%). Previous RCT's utilising combined face-to-face combined dietary and PA interventions for KTRs report variable screening rates of 32% (Schmid-Mohler et al., 2019), 54% (Henggeler et al., 2018) and 71.5% (Kuningas et al., 2019). Serper et al (2020) achieved a screening rate of approximately 41.8% in their sample of kidney and liver transplant recipients. However, inclusion and exclusion criteria varied widely (refer to the systematic review presented in chapter 2). The results from this mixed methods feasibility RCT suggest that the pragmatic inclusion and exclusion criteria could be replicated in future studies. Further

research would benefit from clear reporting of screening rates to facilitate assessment of the external validity.

Study 3 achieved a recruitment rate of approximately 62.5%, which exceeded the progression criteria of 50%. Qualitative analysis in study 4 (particularly theme 1), identified rapport, and clear communication with the research fellow who was known to the transplant clinic were key factors contributing to optimising participation and recruitment. All but one participant found the recruitment window of three months post-transplant achievable. The recruitment rate data in our datasets were comparable to the existing literature. Previous RCT's utilising combined interventions in new KTRs demonstrate good recruitment rates of 57.5% (Kuningas et al., 2019), 58% (Schmid-Mohler et al., 2019), 61.7% (Henggeler et al., 2018) and 71.4% (Serper et al., 2020). Further studies would benefit from qualitative interviews of those who decline consenting to digital healthcare interventions.

Retention of participants in both groups this feasibility RCT was partially confirmed by the integrated mixed methods analysis. Despite COVID-19, retention rates were good at twelve-months (76.4%) and exceeded the progression criteria (>60%). The retention rate was comparable to previous face-to-face exercise interventions in people living with CKD (Heiwe & Jacobson, 2011). In addition, the adherence rates show promise, given that dropout rates tend to be higher with digital health interventions when compared with face-to-face delivered interventions (Eysenbach, 2011). Our feasibility RCT presented various reasons for dropouts including loss to follow up (n=1), personal reasons (n=1), moving out of area (n=1) and losing the kidney transplant due to an admission with COVID-19 (n=1). However, participants who withdrew from the trial

were not interviewed in study 4. Further studies would benefit from qualitative data to explore factors contributing to retention and withdrawal.

6.5.1.2 Adherence to outcome assessment

Whilst there were no set progression criteria for study adherence, integrated analysis showed congruency between the QUALI and QUANT datasets. Adherence rates at each of the three study visits (85%, 88% and 76%) were satisfactory despite the COVID-19 pandemic occurring during data collection (see chapter 5). Previous studies using exit surveys and semi-structured interviews have reported participation with online interventions are positive and improve accountability in KTRs (Gibson et al., 2020; Serper et al., 2020). The nested qualitative analysis in this study (study 4) builds on these findings. Our interview participants suggest specific mechanisms of action (theme 4) to postulate reasons for the positive study experience. Particularly the subtheme 'assessment factors' suggests that the study visit assessments were positive and provided participants with an additional 'check-up'. The rapport with the research fellow, the education provided, and the assessment outcomes themselves provided increased knowledge, confidence and experience for the KTRs.

There were incomplete data collection due to COVID-19 at three and twelve-month assessments. Despite this, data sets confirm the acceptability of secondary outcomes. Nonparticipation in assessments was not due to issues with the outcomes themselves, it was more due to the shielding that occurred during the COVID-19 pandemic (see chapter 5).

6.5.1.3 Adherence with the online intervention

One of the main challenges and characteristics of the evaluation of online health interventions is the phenomenon known as 'law of attrition' (Eysenbach, 2005a):

> The phenomenon of participants stopping usage and/or being lost to follow-up (Eysenbach, 2005b, p. 2).

The CONSORT eHealth checklist recommends clear reporting of log-in rates, engagement rates, session times, and attrition rates (Eysenbach, 2011). Our study clearly reports log-in rates, adherence and session times of all intervention participants (refer to previous section 6.4.1.6 regarding IG adherence). The progression criteria for adhering to the online intervention was satisfied, with six of the nine participants (66.7%) completing 60% or more of the online intervention sessions. Previously published research (see systematic review, chapter 2) has reported intervention adherence good rates. Gibson et al (2020) reported 78% of their intervention group participants completed the twelve live video calls with a dietitian and PA specialist. Schmid Mohler et al (2019) reported 88.5% of their intervention group completed seven or more face-to-face sessions, 86.9% completed four or more sessions, and over 57.4% completed more than three sessions out of the total nine sessions. However, these studies included supervised interventions delivered either via supervised video-calls with a dietitian and or PA expert (Gibson et al., 2020), or face-to-face visits with a nurse (Schmid-Mohler et al., 2019). In comparison, our feasibility RCT, whilst demonstrating lower adherence rates, the intervention was completed independently by our IG participants with minimal remote monitoring by the research fellow/physiotherapist. Further studies would benefit from cost-effectiveness evaluations of more independent online interventions.

Integrative mixed methods analysis allowed participants who did not complete all of the twelve-weekly sessions to be matched across the QUANT and QUALI data sets (see

table 6.16). QUALI analysis (theme 3) suggested that engagement was a personal choice, and there were different factors (technical and personal) that contributed to the decision to engage (or not) with the online intervention. QUALI data was able to enrich the online intervention adherence data, suggesting that perhaps some sessions were too long (e.g., session 11) and could deter participants from continuing with the ExeRTiOn online intervention. Participants suggested that the personalised 'trigger messages' facilitated re-engagement with the online intervention. Other participants suggested working from home during the COVID-19 pandemic, and the associated fatigue, presented as barriers to engaging with the online intervention. Further qualitative investigation of non-completers of digital interventions requires further exploration.

6.5.1.4 Experience of the online intervention

Online weight management interventions that include brief human interaction and personalised feedback have been shown to be clinically and statistically effective in the general population, and people living with excess weight (Bradbury et al., 2015; Little et al., 2016; Sherrington et al., 2016). In this feasibility study, qualitative data revealed the importance and value of self-monitoring, monitoring by the research fellow, and a brief one-to-one orientation on how to use the online intervention were crucial to its success. The need for support to engage with online interventions is echoed in the few studies that explore PA and dietary combined interventions in new KTRs. Exist survey data from Serper et al (2020) reported participants would have valued technical support and contacts with the research team. Study 2 (chapter 4), identified personal feedback and a brief orientation session could enhance engagement (Castle, Greenwood, et al., 2020).

The coding of the ExeRTiOn online intervention to the BCTTv1 (see fidelity of intervention 6.4.1.7 and appendix F) revealed that prompt and cues (BCT 7.1) and social support unspecified (BCT 3.1) were the most frequently used BCTs. From the QUALI data both the social support (unspecified) (3.1), goal setting behaviour (BCT 1.1), self-monitoring of behaviour (BCT 2.3) and outcome of behaviour (BCT 2.4) were valued by participants. Self-monitoring and goal setting are suggested BCTs to promote PA and healthy eating behaviours (Michie, Ashford, et al., 2011), and were included in the intervention by Kuningas et al (2019) discussed in chapter 2. The optimum level of support required to facilitate engagement with online interventions in KTRs remains to be discovered. As this is a feasibility study, it was not designed to evaluate effectiveness, or the mechanisms responsible for the treatment effect. Future study design would benefit from the evaluation of what the most effective 'active ingredients' and unpicking which BCT's potentially mediate the treatment effect of the online intervention. The following chapter (chapter 7, general thesis discussion) will further explore recommendations for both revisions to the ExeRTiOn online intervention, and areas for future research. The efficacy, and cost-effectiveness for different doses and interventions warrant exploration in the KTR population.

QUALI data can provide understanding of participants experiences with new interventions and is a benefit of MMR. The qualitative data in this feasibility RCT (study 4) reported that most participants found the ExeRTiOn online intervention easy to use. The brief face-to-face induction with the research and setting up the IG participants with the online intervention was valued by our participants. However, one participant found it initially challenging to use. Serper et al (2020) reported all participants felt the study improved their diet. However, participants would have liked to set goals beyond purely step goals (Serper et al., 2020). Gibson et al (2020) reported

their video call intervention improved awareness of PA and dietary behaviours, and participants would recommend it to others (see systematic review, chapter 2). The support needed during engagement with the online intervention may need to be individualised and warrants exploration in future research.

Craving management (session 2), the gradual build-up of PA to reduce fear avoidance, self-monitoring and remote monitoring by the physiotherapist were identified as valued content of the ExeRTiOn online intervention by participants. These were suggested as mechanisms of action for the online intervention. Increasing exercise videos, and the potential for group video exercise classes was suggestions to improve the online intervention (Theme 3 engagement is a choice). Similarly, Gibson et al (2020) reported participants would prefer the option to play-back the videos to increase flexibility. Further studies would benefit from exploring delivery of educational videos to include both live and on-demand content.

6.5.1.5 Experience taking part in the feasibility RCT

QUALI analysis (study 4) revealed the 6WMT was valued by our participants to provide confidence in their functional ability, particularly acutely post kidney transplantation. Booth et al (2001) reported similar findings in a sample of advanced cancer participants completing the incremental shuttle walk test. Participants post walk test demonstrated increased confidence in their functional abilities, as did their family members (Booth & Adams, 2001). The 6MWT is self-paced, and requires only a straight corridor of 30 meters (American Thoracic Society, 2002). The 6MWT has been shown to predict mortality in other SOT recipients (Anwar et al., 2014), and be reproducible and low cost to use in children and adolescent KTRs (Watanabe, Koch, Juliani, & Cunha, 2016). There is no suggested minimally clinically important

difference for the 6MWT in KTRs. However, a study in haemodialysis participants revealed that for every increase in 100 meters walked in the 6MWT, there was a 5% increase in survival (Kohl et al., 2012). In study 3, the IG appeared to increase their 6MWD (median with IQR); 450 (450 to 540) meters at baseline, 525 (472.5 to 615m) at three-months, and 495 (465 to 615m) at 12-months. In comparison, the UC groups 6MWD were 517.5 (436 to 570) meters at baseline, 507.5 (442.5 to 605m) at three-months, and 435 (435 to 555m) at twelve-months. These results suggest that the 6MWT is an outcome that warrants further exploration and could provide meaningful information to KTRs and clinicians to build confidence post transplantation.

An increase in FM is often reported in KTRs participants despite combined, exercise and dietetic interventions (Henggeler et al., 2018; Karelis et al., 2016; Leasure et al., 1995; Painter et al., 2002). As presented in the systematic review (Chapter 2), Kuningas et al (2019) was the only RCT to reveal a significant between-group difference in FM comparing their 6-month intervention to UC. BC measurements such as FM and LTM appeared comparable across groups in our feasibility RCT. However, these measures of BC included missing data due to COVID-19 and not being able to collect these face-to-face outcomes at 3-month assessment. Qualitative data revealed participants valued the BIA assessment. Future studies would benefit from including these measures in larger sample trials.

6.5.1.6 Willingness to be randomised

Issues with randomisation, contamination bias, and willingness to be randomised are not always reported but provide crucial information when determining feasibility of a study and intervention. In study 4, QUALI data provided insight into personal choice and preference regarding the engagement with the online intervention. A recent trial

reported potential contamination bias was reported in control group participants who were unhappy with not receiving a step recording device (Serper et al., 2020). No other combined RCT's from the systematic review (see chapter 2), reported issues with randomisation.

6.5.1.7 Hospitalisations and adverse events

The systematic review presented in chapter 2 highlighted adverse events were not always reported in RCT's. Only three out of the six combined intervention RCT's identified in our systematic review (see chapter 2), reported no associated adverse events or safety concerns (Henggeler et al., 2018; Kuningas et al., 2019; Serper et al., 2020) . Whilst there were five adverse events in study 3, they were not related to trial participation. In addition, there were no slips, trips or injuries associated with completing the online intervention independently. Other studies have raised concerns for recruiting participants within the first six months of transplantation (Gibson et al., 2020). However, this feasibility study reveals it is possible to complete assessments and reported no related adverse events in a sample of new KTRs recruited within the first three months of transplantation. One participant in the nested qualitative interviews (study 4) suggested that perhaps three-to-six-month recruitment window may be more preferable for KTRs.

6.5.2 Limitations

As this was a feasibility trial, it was not powered to detect change in body weight or any of the secondary outcomes. Guidelines for development and evaluation of digital healthcare interventions suggest that the use of descriptive quantitative statistics are adequate (West & Michie, 2016). To estimate SDs for a sample size calculation for a definitive study, a sample of 24 to 50 participants are recommended (Hooper, n.d.;

Julious, 2005; Sim & Lewis, 2012). Whilst this study was initially set to recruit 50 participants, the implications of COVID-19 meant that the sample was reduced to 17 (see chapter 5). This was based on pragmatic and transparent decisions by the TMG to cease recruitment in June 2020 (see Appendix E). Despite this, the remaining participants were able to continue with the trial with appropriate safety measures in situ. The CONSORT extension for feasibility state that formal hypothesis testing for efficacy is not recommended (Eldridge, Chan, et al., 2016). In addition, the NIHR suggest feasibility trials investigate what research can be done in a future study, and do not need to include a primary outcome or power calculation as this is left to the main (definitive) trial (NIHR, 2019). Therefore, it is beyond the scope of this feasibility RCT, and against guidance to estimate effect size and provide power calculations for definitive trials. Despite this limitation, the study provides insight into feasibility, and offers recommendations for a future multi-centre pilot RCT. Further implications for research will be explored in the following discussion chapter.

The reduced sample of participants in study 3 subsequently impacted the number of participants that were available for the nested semi-structured interviews in study 4. Therefore, there was a risk of convenience sampling. Attempts were made to reduce this risk by using a sampling framework that included a range of participants from both groups (UC and IG), a range of engagement rates (IG participants), ages, gender and ethnicities. Reflexivity was enhanced through reflective journals, a small portion of the interviews being conducted by an additional researcher (MSc student PD), and validation of qualitative analysis and themes by an external qualitative researcher (JG). Malterud et al (2016) state that it may not be realistic for exploratory studies to provide an exhaustive description of a new phenomenon, but rather provide new and rich insights. Through studies 3 and 4, we were able to provide rich insight into the

experience and feasibility of the online intervention and participating in the trial through an integrated mixed methods analysis.

Another limitation of the feasibility RCT include the single-centre design. Whilst it was initially designed to be bi-centre, delays in research contracts and the COVID-19 pandemic resulted in only one participant being recruited from the secondary site. This will be explored in the following chapter. However, this feasibility study did achieve its progression criteria, and future studies would benefit from multi-centre design.

The COVID-19 pandemic, and the strict shielding practises particularly in the first and second wave in the UK could have influenced the interventions target behaviours (PA and healthy eating) and questionnaire data. UC participants could have experienced reduced PA and exaggerated the effects of the intervention on secondary outcomes. However, data for PA (GPPAQ), fatigue (CFS), self-efficacy (SE for nutrition and physical exercise behaviours), and quality of life (EQ-5D-5L) appeared comparable across the sample. Qualitative data suggested support from family members and the community assisted participants manage the unique challenges presented by the COVID-19 pandemic (theme 2). Fortuitously, the intervention could be delivered online, and most of the outcomes could be collected remotely, allowing the research fellow to continue with the study, and support the participants during this challenging time. One participant reported the calls and support from the research fellow and the online intervention supported her wellbeing during the pandemic.

Lack of blinding could have influenced the results from study 3. Due to the nature of the study design, exercise and behavioural studies are often unable to achieve double blinding. As this study was completed by the research fellow as part of the PhD thesis,

data collection, intervention delivery and analysis were all completed by the research fellow (EC). However, supervision was provided by the TMG which included participants experts. QUALI data (study 4) was validated by an external qualitative researcher (JG), and guidance was sought from an external statistician for QUANT analysis (RP). Future follow-up studies should include different research personnel conducting the intervention and assessments, including blinding of the outcome assessors to improve validity.

6.5.3 Suggestions for a future definitive trial

The results from studies 3 and 4 suggest it is feasible to conduct a RCT using the ExeRTiOn online intervention in a sample of new KTRs. To increase external and internal validity, a multi-centre pilot RCT is warranted to inform a definitive RCT. Research questions regarding the effectiveness of the ExeRTiOn online intervention on weight gain prevention, it's scope across multiple sites, and its cost-effectiveness warrant exploration in future studies. It is also important to consider mechanism of action by conducting process analyses and understanding moderators and mediators of treatment effects. Future qualitative research to evaluate the experiences of those who decline or withdrawal from the intervention is also required to further assess acceptability and reach.

Future studies would benefit from including participant-centred outcomes, such as 'life participation' that has been listed as a core outcome measure by a group of international KTRs and HCPs from the Standardized Outcomes in Nephrology (SONG) Transplantation group (Ju et al., 2019). Participants reported experience and outcome measures such as the participants activation measure (PAM) (Hibbard, Mahoney, Stockard, & Tusler, 2005), which has become popular in renal research (Hamilton,

Caskey, Casula, Inward, & Ben-Shlomo, 2018; Nair & Cavanaugh, 2020; Wilkinson, Memory, Lightfoot, Palmer, & Smith, 2021)would be worth pursuing.

The ExeRTiOn online intervention was designed to prevent weight gain within the first year of kidney transplantation (Castle, Greenwood, et al., 2020). Whilst this study is a feasibility RCT so causation and statistical testing is not encouraged, feasibility data can inform future trial design and its components (Eldridge, Chan, et al., 2016). The secondary outcome data in study 3 suggest the IG appeared to maintain body weight throughout the 12-month trial (94.5 kgs at baseline, 95.0 kgs at three-months and 94.7kgs at 12-months). In contrast, the UC group appeared to increase body weight (81.3 kgs at baseline, 86.2kgs at three-months, and 93.3 at twelve-months). A reduction in five percent of body weight from baseline measures is widely considered to be clinically meaningful to reduce glycaemia and CVD risk factors (American College of Cardiology/American Heart Asssociation Tast Force on Practise Guidelines & Obesity Expert Panel, 2014; Ryan & Yockey, 2017; Williamson, Bray, & Ryan, 2015). A RCT by Henggeler et al (2018) powered their study to detect a clinical difference of five kilograms in KTRs. Kuningas et al (2019) reported their 6-month dietitian-led combined intervention was associated with a significant difference of -2.47 kg (95% CI -0.4 to -0.9, p=0.002) in body weight change over the 6-month follow up when compared with usual care. The median body weight in the ExeRTiOn online IG group from baseline to 12-months is less than 5kg and less than 5% of the baseline median weight, suggesting the potential for clinical benefit. Therefore, future studies should include measures of body weight, alongside participants valued measures such as the 6MWT and the BIA.

In this study the median BMI, waist circumference, hip circumference and PWV and AI appeared comparable across groups. The meta-analysis presented in chapter 2 revealed no RCT had an impact on BMI. NICE guidelines for the assessment and management of obesity recommend that whilst BMI can assess adiposity, interpretation requires caution (NICE, 2014b). Clinicians need to consider the addition of waist circumference assessment in people with a BMI of less than 35kg/m^2 and the impact of highly muscular individuals on BMI recordings (NICE, 2014b). In addition to body weight, BMI and waist circumference, BIA may provide an additional useful tool pre and post intervention to assess fat and fat free mass (NICE, 2017b). Whilst BMI is often used clinically in KTR care, it should never be used in isolation. Future studies would benefit from inducing body weight, waist and hip circumference, and BMI alongside BIA data to provide a complete picture of body weight, adiposity and fat and fat free mass in new KTRs.

PWV is a measure of arterial stiffness is an independent predictor of cardiovascular events and mortality for KTRs (Melilli et al., 2018). Previous work by the research fellow and research team has shown aerobic training and resistance training compared with no exercise training can positively influence PWV in KTRs (Greenwood et al., 2015; O'Connor et al., 2017). The PWV values appeared comparable across both groups in study 3. This could be explained by the fact that the ExeRTiOn online intervention was designed to promote participants-led PA, rather than the completion of structured exercise interventions.

6.6 Chapter Summary

This chapter summarises the results of the mixed methods feasibility trial (studies 3 and 4), which was designed to assess the feasibility and capture and report the experience of

using the online intervention. It achieved the second aim of the thesis and the fifth thesis objective. Both data sets were congruent in suggesting further research into this field is warranted and welcomed by new KTRs. Online intervention delivery may have the potential to provide education and support remotely and further research is required. Despite the limitations, all pre-set feasibility criteria were met. A follow-up pilot RCT to inform a definitive RCT is warranted to further evaluate the effectiveness and cost-effectiveness of the ExeRTiOn online intervention. Outcomes such as body weight, BMI, BIA, 6MWT and the PAM ® could be of interest. Future studies would benefit from qualitative data to capture the experiences of KTRs who decline to take part and drop out of online intervention studies to provide insights into acceptability. Figure 6.6 below summarises the products of the concurrent qualitative and quantitative analysis, and the integrated mixed methods analysis which will be further explored in the following chapter.

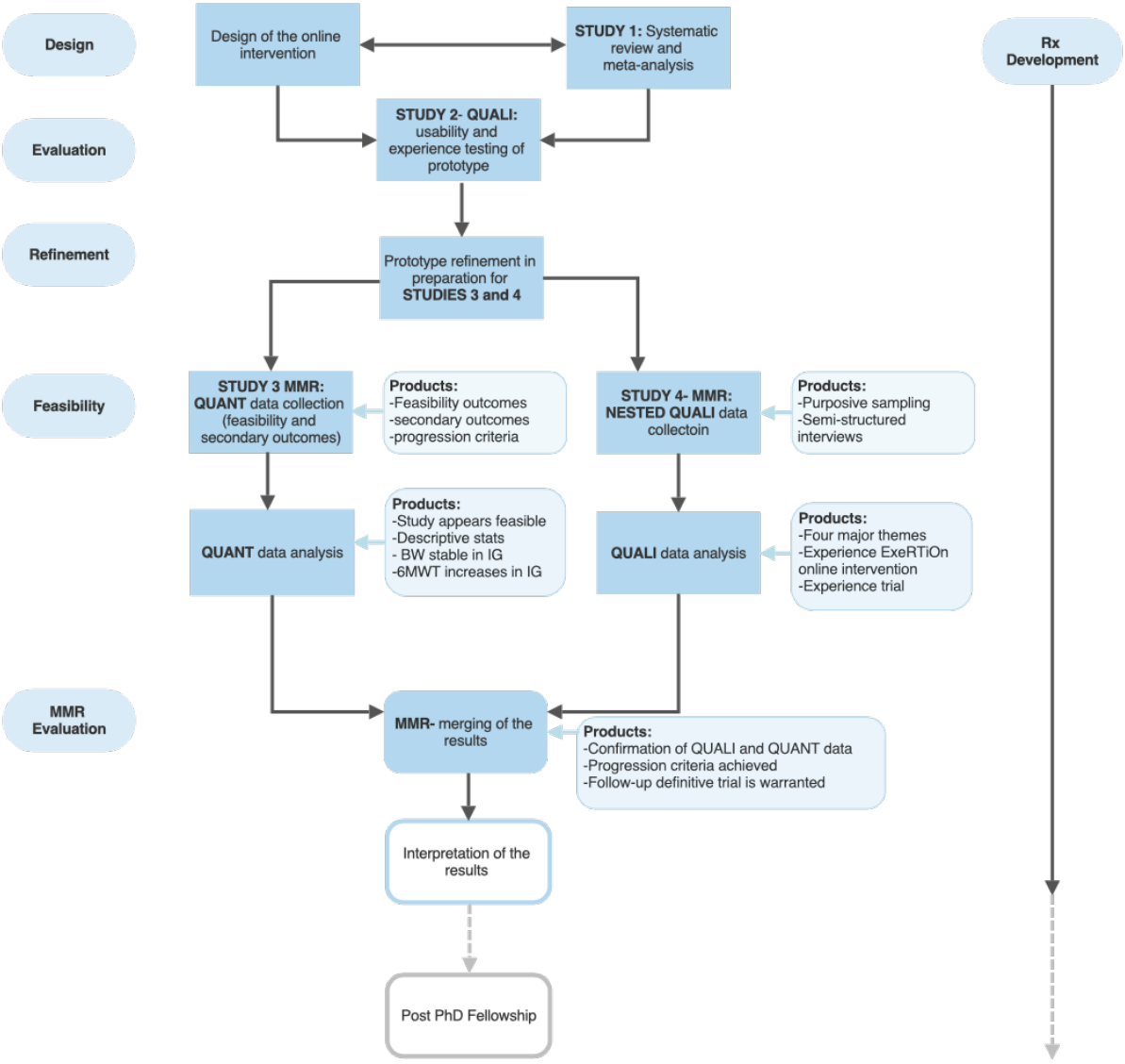


Figure 6-6 Updated thesis process diagram demonstrating the results of the mixed methods feasibility RCT (studies 3 and 4)

Note. Study processes completed to this stage of the thesis are shaded in blue and demonstrates the key learnings in this chapter.

QUALI= qualitative, QUANT=quantitative, MMR= mixed methods research.

Data collection, results (QUANT and QUALI) and the products of the merged mixed methods results are depicted by the additional blue boxes.

This figure was designed based on a combination of the convergent mixes-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

Chapter 7 General thesis discussion

7.1 Chapter overview

This chapter provides an integrated discussion of the work conducted during the PhD fellowship. Firstly, the main findings of the four empirical studies will be summarised. Next, the aims and objectives as stated in chapter 1 will be revisited and discussed in relation to the existing evidence base where the theses novel contribution will be discussed. Finally, the strengths, limitations, recommendations for practice, future research and policy will be explored.

7.2 Summary of the thesis main findings

Table 7.1 on the following page summarises the main findings from the four empirical studies included in the thesis:

1. The systematic review (study 1, chapter 1)
2. The usability and experience testing of the ExeRTiOn prototype (study 2, chapter 4)
3. The feasibility RCT (chapter 6), including the feasibility and quantitative data (study 3) and the nested qualitative evaluation (study 4)

Table 7-1 Summary of main findings from the thesis

Study	Main findings

Study 1, chapter 1: Do exercise, physical activity, dietetic or combined interventions improve body weight in new kidney transplant recipients: a narrative systematic review and meta-analysis	• 7 databases searched from January 1985 to April 2021 using a registered protocol
	• PICO search criteria:
	  ○ Population: new single organ adult KTRs within one year of transplantation
	  ○ Intervention: Post-transplant interventions consisted of either exercise, PA, dietary interventions, or a combination thereof
	  ○ Comparator: UC, standard care or no intervention
	  ○ Outcomes: primary outcomes included repeated measures of body weight (kg) and BMI (kg/m2)
	  ○ Secondary outcomes included BC, physical function, PA levels, self-efficacy towards PA and mood
	  ○ Study type: RCT's or quasi-experimental controlled trials
	  ○ Limitations: English language, after 1985
	• Of the 1198 articles screened, 16 met the search criteria (10 RCTs, and 6 non-RCTs)
	• Small number of trials with small samples (range from 8 to 452 KTRs) and variable quality (5 RCT's were classified as 'high-risk',1 as 'some-concerns' and 3 as 'low-risk' for bias)
	• Only one RCT by Kuningas et al (2019) demonstrated a favourable effect on body weight and FM for its 6-months combined dietitian led face-to-face intervention compared with UC
	• Random-effect meta-analysis revealed no significant differences in post-intervention body weight (-2.5 kg, 95% CI -5.22 to 0.22) or BMI (-0.4 kg/m^2, 95% CI -1.33 to 0.54)
	• Methodological heterogeneity including variation in intervention dose, type and duration
	• Statistical heterogeneity was not significant
	• Sensitivity analysis suggested combined interventions warrant further investigation

	• Higher quality RCT's are needed to evaluate the immediate and longer-term effects of combined interventions on body weight in new KTRs • Hypothesis that combined interventions, including PA, dietary advice and recognised BCTs are needed to address weight gain after kidney transplantation
Study 2, chapter 4: Usability and experience testing to refine an online intervention to prevent weight gain in new KTRs	• Ethical approval received, and trial registered clinicaltrials.gov (NCT03699059) • 17 participants purposively sampled and agreed to take part in a one-off qualitative interview ○ 11 KTRs within the first 3months of transplantation, and 6 transplant HCPs • All participants completed one study visit (taking approximately 50 to 90 minutes) including think-aloud interviews immediately followed by a semi-structured interview to gather usability and experiential data • KTR participants mean time (± SD) to complete the welcome session and session 1 (goals) (Think-aloud task one) was 19.5±12.9 minutes (range 6 to 55 mins) • KTR participants mean time (± SD) to complete task two (randomised session 2 to 12) was 13.6 ± 7.3 minutes (range 7 to 27 minutes) • One KTR participant took 55 minutes to complete task one, and therefore did not complete Task 2 and an additional KTR was sampled to test the session • HCP participants mean time (± SD) to complete task one was 7.6±7.0 minutes (range 3 to 21 minutes) • There were no dropouts • Mean age of KTR (± SD) was 50± 14 years, transplant vintage was 43±19 days, 45% were male, eGFR was 48± 19.2 ml/min/1.73m^2, 54% where white Caucasian, 28% were black African and Caribbean, 9% were Asian, and 9% where other ethnicity

	• 18% of participants choose to set a food goal, 73% chose to set a physical activity goal, and one participant (9%) set no goal
	• Reflective thematic analysis revealed two themes
	  o 'Theme 1: you need to know how to manage yourself' included the sub-themes the resource filled a guidance gap, expert participants content resonated, goal setting is key, and visualisation of progress was valued
	  o Theme 2: Room for improvement included web support (physio support and FAQ), and changes needed (content and operational).
	• All participants (KTR and HCP) found the protype online intervention acceptable and felt it warranted further exploration
	• Results allowed the research fellow and research team to better understand target end users (new KTRs), and involve them with testing and refinement
	• Limitations: single centre design, one-off use of the prototype per participant
	• Strengths: there were no concerns raised regarding data security and privacy from participants, the intervention was acceptable
	• Results informed revisions of the resource using the MoSCoW prioritisation method in preparation for the feasibility RCT ensuring the intervention is person-based

Studies 3 and 4, chapter 6: The weight gain prevention in Renal Transplant Online study- A randomised controlled feasibility trial	• Ethical approval sought and obtained, registered on clinicaltrials.gov NCT03996551
	• 17 participants randomised to either UC or online IG
	• Intended sample was initially 50 participants but was reduced due to COVID-19 (see chapters 5 and 6)
	• QUANT feasibility findings:
	  o Screening rate=84.2% (95% CI 68.8 to 94.0
	  o Consent rate=62.5% (95%CI 43.7 to 79.0)
	  o Retention at 12 months=76.4% (95% CI 50.0 to 93.2)
	  o Adherence to baseline Ax=85% (95% CI 62.1 to 96.8)

- Adherence to 3month Ax=88.3%(95%CI 63.6% to 98.5%)
- Adherence to 12month Ax=76.4% (95% CI 50.0 to 93.2)
- Adherence to the IG=66.7% (95% CI 29.9 to 92.5) completed 60% sessions
- Safety and hospitalisations=29.4 (95% CI 7.8 to 51.1) had a non-related adverse event
- Expected and unexpected harms= nil

- Fidelity of the intervention:
  - Retrospective coding of the online intervention content and interactions with the research fellow coded to the BCTTv1
  - Revealed 21 BCTs, 11 additional BCTs
  - Most frequent BCT in the online intervention was BCT7.1 (prompt and cues) facilitated the engagement with the online intervention
  - Most frequent BCT in the interactions was BCT3.1 (social support unspecified) which facilitated all three target behaviours (increase physical activity, engage with the ExeRTiOn intervention, and follow a balanced diet)
- Adherence to the intervention:
  - 6/9 participants achieved progression criteria of achieving >60% of the 12-weekly sessions
  - Individual completion rates included 100% (n=4), 83% (n=1), 75% (n=1), 42% (n=1), tracking only (n=1), no completion (n=1)
  - Mixed methods integrated analysis allowed for exploration of non-completion of sessions such as barriers to working from home during the COVID-19 first wave, and the need to reduce session 11 content
- QUANT secondary outcome findings:
  - The IG appeared to maintain a stable bodyweight throughout the 12-month study compared with UC:

        - Body weight (kg, median and IQR) for IG; 94.5 (63.0 to 102.0) at baseline, 95.0 (66.7 to 105.3) at 3-months and 94.7 (77.2 to 117.3) at 12-months
        - Body weight (kg, median and IQR) for UC group; 81.3 (73.6 to 94.6) at baseline, 86.2 (75.4 to 96.5) at 3-months and 93.3 (70.3 to 101.9) at 12-months
    - The IG appeared to increase their 6WMD in comparison to the UC group:
        - IG 6MWD (meters, median and IQR); 450 (450 to 540) at baseline, 525 (472.5 to 615m) at 3-months, and 495 (465 to 615m) at 12-months
        - UC group 6MWD; 517.5 (436 to 570) at baseline, 507.5 (442.5 to 605m) at 3-months, and 435 (435 to 555m) at 12-months
    - Median BMI, waist circumference, hip circumference and PWV, and AI appeared comparable across the sample
- QUALI feasibility findings:
    - Reflexive thematic analysis from a pragmatic world view revealed four main themes
    - Theme 1: optimising recruitment and participation could be explained by the importance of research, clear communication and rapport, and the acceptability of the recruitment window
    - Theme 2: COVID-19 pandemic influenced well-being, and social support could be helpful
    - Theme 3: Engagement with the website was a choice, influenced by personal and technical factors
    - Theme 4: There were assessment and treatment mechanisms contributing to positive study experience
    - Overall, the study and website were acceptable, and participants felt the website ‘should be offered to all’ new KTRs
- Mixed methods findings:
    - Progression criteria exceeded for all outcomes and a future study is warranted
    - QUANT and QUALI datasets converged

	• Limitations: single centre design, not powered, small sample • Strengths: progression criteria were achieved; mixed methods analysis reveals further studies are warranted in this field • Recommend future studies to consider a multi-centre pilot-RCT to inform a definitive RCT to evaluate effectiveness and cost-effectiveness

Note. PICO= stands for population, intervention, outcome, comparator. KTRs= kidney transplant recipients, PA= physical activity, RCTs=randomised controlled trials, non-RCTs=non-randomised controlled trials such as quasi-experimental trials with a control group, BMI=body mass index, FM= fat mass, UC=usual care, IG= intervention group, HCPs=healthcare professionals, SD=standard deviation, MoSCoW= prioritisation tool standing for must have, should have, could have and would like to have changes, Ax= assessment, BCTTv1= behaviour change taxonomy version 1, BCT= behaviour change technique, COVID-19= Coronavirus disease 2019, IQR= interquartile range, BC= body composition, 6WMD= six-minute walk distance resulting from a six-minute walk test, QUANT=quantitative and QUALI= qualitative

7.3 Revision of the thesis aims and objectives

This thesis set out to achieve two aims:

1. To create an online intervention to address weight gain in new KTRs
2. To explore the feasibility and acceptability of the online intervention for new KTRS.

To demonstrate how these aims were achieved, the five objectives will be presented in reference to the thesis results, and the contributions to the wider published literature.

7.3.1 Objective 1: To review and synthesise the current evidence regarding weight gain prevention interventions for new KTRs

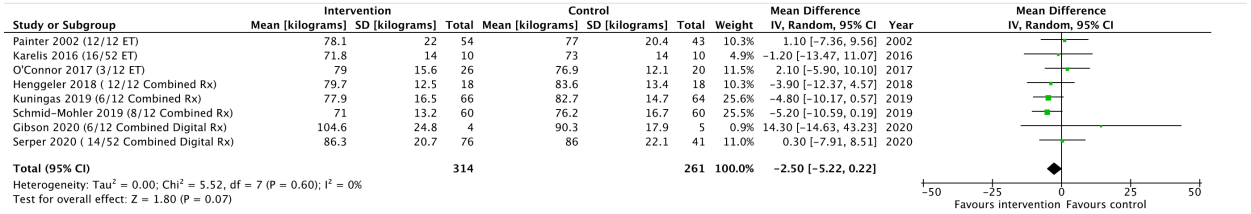
Through the four empirical studies included in this PhD thesis, there has been novel contribution to the evidence base for weight gain prevention interventions for new KTRs. The systematic review and meta-analysis (study 1) presented in chapter 2 achieved the first objective of the thesis. Results from the systematic review and meta-analysis suggest the current evidence evaluating interventions to address body weight and BMI in the first year after a kidney transplant are limited. Only ten RCT's, consisting of mainly small samples, limited power, lack of long-term follow-up, variable sample characteristics, and variable intervention types and duration met the inclusion criteria (see chapter 2, tables 2.2, 2.3 and Appendix A). This limited the ability to perform pooled estimates. Whilst meta-analyses of post-intervention body weight and BMI values revealed no significant effect, a post-hoc exploratory sensitivity analysis reported combined interventions could have the potential to influence body weight, but not BMI in new KTRs (Appendix A).

Weight gain is most common within the first year of kidney transplantation (O'Brien & Hathaway, 2016). Therefore, the systematic review included in the thesis (chapter 2) focuses specifically on KTRs within the first year of transplantation. A recent Cochrane review by Conley et al (2021) included combined behavioural weight loss interventions for people with CKD. However, only KTRs who were living with excess weight or obesity were included, making it difficult to determine weight gain prevention. Due to the limited research in the field, further adequately powered RCT's with clear and effective interventions, utilising combined interventions with BCT's and longer-term follow-up are needed to answer this important clinical question of weight gain within the first year of transplantation.

To our knowledge the systematic review presented in the thesis was novel, since it is the first systematic review and meta-analysis to examine the effects of either exercise, nutrition or combined intervention on body weight specifically within the first year of kidney transplantation. Previously published systematic reviews with either exercise and PA interventions (Calella et al., 2019; Chen et al., 2019; O'Brien & Hathaway, 2016; Oguchi et al., 2019), or dietary interventions (Palmer et al., 2017a) often excluded combined interventions. In addition, the participants included in these previous systematic reviews included KTRs that were greater than one year post transplant or did not specify the transplant vintage of included participants (Calella et al., 2019; Chen et al., 2019; O'Brien & Hathaway, 2016; Oguchi et al., 2019; Palmer et al., 2017a). Therefore, it was difficult to determine the intervention effects on weight gain prevention within the first year of receiving a new kidney transplant from the previously published systematic reviews.

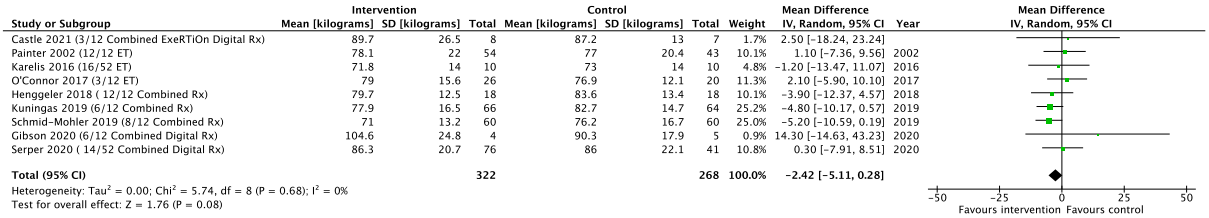
To explore how the findings from the feasibility mixed methods RCT presented in chapter 6 contributes to the existing evidence base, the meta-analyses presented in chapter 2 was re-run to include the post-intervention body weight and BMI values from the feasibility RCT (study 3, chapter 6). In the previous meta-analysis, the first follow-up value post intervention was used, so for consistency, values were taken from the 3-month study visit from study 3 (chapter 6). Tables 7.2 to 7.5 on the following page demonstrate the original and updated meta-analysis for body weight and BMI post-intervention values.

Table 7-2 Original meta-analysis body weight (post-intervention values) from chapter 2



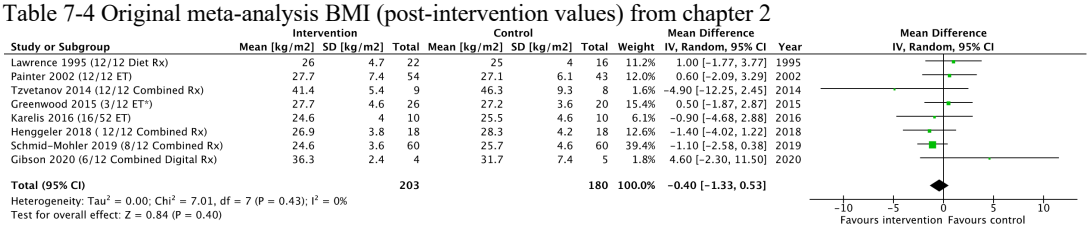
Note. Post-intervention values used for meta-analysis. Standard deviation calculated from SEM for Lawrence et al (1995) and Henggeler et al (2018). Schmid-Mohler et al (2019) provided BW and BMI data for KTR alone (n=120) on request. Studies with multiple intervention arms (O'Connor et al., 2017; Serper et al., 2020) were combined. Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx= intervention

Table 7-3 Updated meta-analysis body weight (post-intervention values) including chapter 6 data



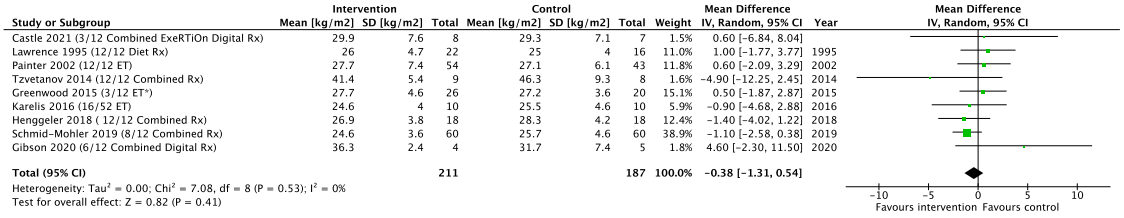
Note. Post-intervention values for Castle et al 2021 (chapter 6) were added to the original meta-analysis.

Table 7-4 Original meta-analysis BMI (post-intervention values) from chapter 2



Note. Post-intervention values used for meta-analysis. BMI was not reported in O'Connor et al (2017). Therefore, * indicates BMI from primary study manuscript (Greenwood et al., 2015). BMI values from Tzvetanov et al (2014) were calculated from mean change and baseline values. Standard deviations were calculated from SEM in Henggeler et al (2018). Fractions in the study column depict the length of interventions in months (/12) or weeks (/52), ET refers to exercise intervention and Rx= intervention

Table 7-5 Updated meta-analysis BMI (post-intervention values) including chapter 6 data

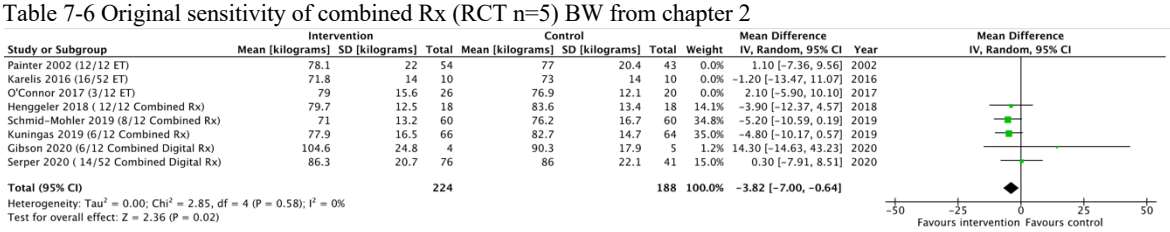


Note. Post-intervention values for Castle et al 2021 (chapter 6) were added to the original meta-analysis.

The inclusion of the chapter 6 body weight and BMI data to the meta-analyses (see tables 7.2 to 7.5 on the previous page), revealed that the effect remains non-significant on body weight (-2.4kg, 95% CI -5.11 to 0.28) and BMI (-0.38kg/m^2, 95% CI -1.3 to 0.54). The wide confidence intervals and small sample in Chapter 6, and the use of post-intervention values could have potentially contributed to this non-effect. In study 3 presented in chapter 6, the UC group started with a lower baseline weight then increased in body weight over the 12-month study. Whereas the IG appeared to maintain over the 12-months. Inadequate reporting of data precluded the ability to conduct a meta-analysis using change scores for the other RCT's (refer to systematic review in chapter 2). Whilst post-intervention values have been shown to provide a more conservative estimate of effect than change scores (Fu & Holmer, 2016), they do not account for differences at baseline at baseline, or changes from baseline.

Tables 7.6 to 7.9 on the following page demonstrate the original and updated post-hoc sensitivity analysis comparing combined interventions, and single interventions on body weight and BMI.

Table 7-6 Original sensitivity of combined Rx (RCT n=5) BW from chapter 2

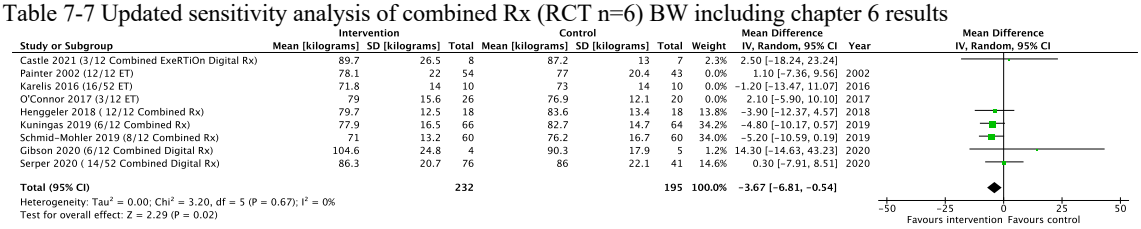


Study or Subgroup	Intervention Mean [kilograms]	Intervention SD [kilograms]	Intervention Total	Control Mean [kilograms]	Control SD [kilograms]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Painter 2002 (12/12 ET)	78.1	22	54	77	20.4	43	0.0%	1.10 [−7.36, 9.56]	2002
Karelis 2016 (16/52 ET)	71.8	14	10	73	14	10	0.0%	−1.20 [−13.47, 11.07]	2016
O'Connor 2017 (3/12 ET)	79	15.6	26	76.9	12.1	20	0.0%	2.10 [−5.90, 10.10]	2017
Henggeler 2018 (12/12 Combined Rx)	79.7	12.5	18	83.6	13.4	18	14.1%	−3.90 [−12.37, 4.57]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	71	13.2	60	76.2	16.7	60	34.8%	−5.20 [−10.59, 0.19]	2019
Kuningas 2019 (6/12 Combined Rx)	77.9	16.5	66	82.7	14.7	64	35.0%	−4.80 [−10.17, 0.57]	2019
Gibson 2020 (6/12 Combined Digital Rx)	104.6	24.8	4	90.3	17.9	5	1.2%	14.30 [−14.63, 43.23]	2020
Serper 2020 (14/52 Combined Digital Rx)	86.3	20.7	76	86	22.1	41	15.0%	0.30 [−7.91, 8.51]	2020
Total (95% CI)			**224**			**188**	**100.0%**	**−3.82 [−7.00, −0.64]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.85$, df = 4 (P = 0.58); $I^2 = 0\%$
Test for overall effect: Z = 2.36 (P = 0.02)

Note. Combined interventions referred to interventions including PA, exercise, dietary and behaviour change components. ET refers to exercise training, Rx= intervention.

Table 7-7 Updated sensitivity analysis of combined Rx (RCT n=6) BW including chapter 6 results

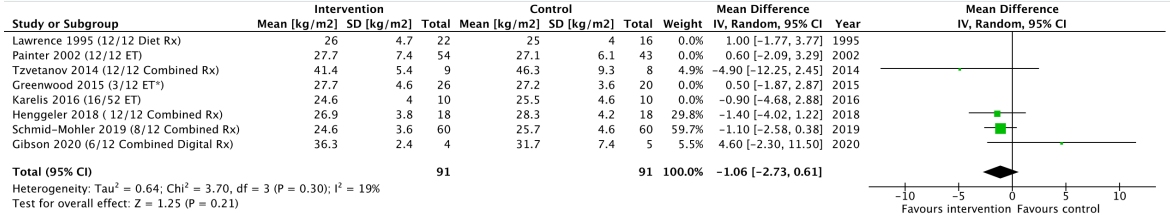


Study or Subgroup	Intervention Mean [kilograms]	Intervention SD [kilograms]	Intervention Total	Control Mean [kilograms]	Control SD [kilograms]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Castle 2021 (3/12 Combined ExeRTiOn Digital Rx)	89.7	26.5	8	87.2	13	7	2.3%	2.50 [−18.24, 23.24]	
Painter 2002 (12/12 ET)	78.1	22	54	77	20.4	43	0.0%	1.10 [−7.36, 9.56]	2002
Karelis 2016 (16/52 ET)	71.8	14	10	73	14	10	0.0%	−1.20 [−13.47, 11.07]	2016
O'Connor 2017 (3/12 ET)	79	15.6	26	76.9	12.1	20	0.0%	2.10 [−5.90, 10.10]	2017
Henggeler 2018 (12/12 Combined Rx)	79.7	12.5	18	83.6	13.4	18	13.8%	−3.90 [−12.37, 4.57]	2018
Kuningas 2019 (6/12 Combined Rx)	77.9	16.5	66	82.7	14.7	64	34.2%	−4.80 [−10.17, 0.57]	2019
Schmid-Mohler 2019 (8/12 Combined Rx)	71	13.2	60	76.2	16.7	60	34.0%	−5.20 [−10.59, 0.19]	2019
Gibson 2020 (6/12 Combined Digital Rx)	104.6	24.8	4	90.3	17.9	5	1.2%	14.30 [−14.63, 43.23]	2020
Serper 2020 (14/52 Combined Digital Rx)	86.3	20.7	76	86	22.1	41	14.6%	0.30 [−7.91, 8.51]	2020
Total (95% CI)			**232**			**195**	**100.0%**	**−3.67 [−6.81, −0.54]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.20$, df = 5 (P = 0.67); $I^2 = 0\%$
Test for overall effect: Z = 2.29 (P = 0.02)

Note. Combined interventions referred to interventions including PA, exercise, dietary and behaviour change components. ET refers to exercise training, Rx= intervention. The original sensitivity analysis has been updated to include chapter 6 data (Castle et al 2021) as shown in the table above.

Table 7-8 Original sensitivity of combined Rx (RCT n=4) on BMI from chapter 2

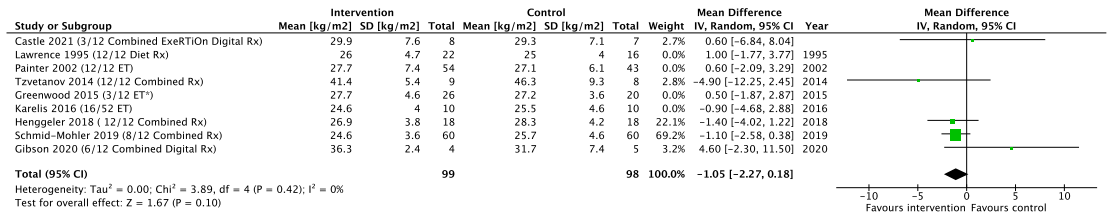


Study or Subgroup	Intervention Mean [kg/m2]	Intervention SD [kg/m2]	Intervention Total	Control Mean [kg/m2]	Control SD [kg/m2]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Lawrence 1995 (12/12 Diet Rx)	26	4.7	22	25	4	16	0.0%	1.00 [−1.77, 3.77]	1995
Painter 2002 (12/12 ET)	27.7	7.4	54	27.1	6.1	43	0.0%	0.60 [−2.09, 3.29]	2002
Tzvetanov 2014 (12/12 Combined Rx)	41.4	5.4	9	46.3	9.3	8	4.9%	−4.90 [−12.25, 2.45]	2014
Greenwood 2015 (3/12 ET*)	27.7	4.6	26	27.2	3.6	20	0.0%	0.50 [−1.87, 2.87]	2015
Karelis 2016 (16/52 ET)	24.6	4	10	25.5	4.6	10	0.0%	−0.90 [−4.68, 2.88]	2016
Henggeler 2018 (12/12 Combined Rx)	26.9	3.8	18	28.3	4.2	18	29.8%	−1.40 [−4.02, 1.22]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	24.6	3.6	60	25.7	4.6	60	59.7%	−1.10 [−2.58, 0.38]	2019
Gibson 2020 (6/12 Combined Digital Rx)	36.3	2.4	4	31.7	7.4	5	5.5%	4.60 [−2.30, 11.50]	2020
Total (95% CI)			**91**			**91**	**100.0%**	**−1.06 [−2.73, 0.61]**	

Heterogeneity: $Tau^2 = 0.64$; $Chi^2 = 3.70$, df = 3 (P = 0.30); $I^2 = 19\%$
Test for overall effect: Z = 1.25 (P = 0.21)

Note. Original sensitivity analysis with combined interventions from chapter 2.
Rx=intervention, BMI=body mass index, ET=exercise training

Table 7-9 Updated sensitivity analysis of combined RCT (r=5) BMI including chapter 6 results



Study or Subgroup	Intervention Mean [kg/m2]	Intervention SD [kg/m2]	Intervention Total	Control Mean [kg/m2]	Control SD [kg/m2]	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Castle 2021 (3/12 Combined ExeRTiOn Digital Rx)	29.9	7.6	8	29.3	7.1	7	2.7%	0.60 [−6.84, 8.04]	
Lawrence 1995 (12/12 Diet Rx)	26	4.7	22	25	4	16	0.0%	1.00 [−1.77, 3.77]	1995
Painter 2002 (12/12 ET)	27.7	7.4	54	27.1	6.1	43	0.0%	0.60 [−2.09, 3.29]	2002
Tzvetanov 2014 (12/12 Combined Rx)	41.4	5.4	9	46.3	9.3	8	2.8%	−4.90 [−12.25, 2.45]	2014
Greenwood 2015 (3/12 ET*)	27.7	4.6	26	27.2	3.6	20	0.0%	0.50 [−1.87, 2.87]	2015
Karelis 2016 (16/52 ET)	24.6	4	10	25.5	4.6	10	0.0%	−0.90 [−4.68, 2.88]	2016
Henggeler 2018 (12/12 Combined Rx)	26.9	3.8	18	28.3	4.2	18	22.1%	−1.40 [−4.02, 1.22]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	24.6	3.6	60	25.7	4.6	60	69.2%	−1.10 [−2.58, 0.38]	2019
Gibson 2020 (6/12 Combined Digital Rx)	36.3	2.4	4	31.7	7.4	5	3.2%	4.60 [−2.30, 11.50]	2020
Total (95% CI)			**99**			**98**	**100.0%**	**−1.05 [−2.27, 0.18]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.89$, df = 4 (P = 0.42); $I^2 = 0\%$
Test for overall effect: Z = 1.67 (P = 0.10)

Note. Sensitivity analysis updated to include chapter 6 results

The addition of chapter 6 findings to the exploratory sensitivity analysis (see tables 7.6 to 7.9 on previous page), suggest that combined interventions could have the potential to influence body weight (-3.67 kg, 95% CI 6.8 to -0.54) but not BMI (-1.05 (-2.27 to 0.18). The systematic review (study 1), and the addition of chapter 6 data to the meta-analyses adds to the evidence base regarding the effects of combined interventions on body weight and BMI in new KTRs. However, samples for the feasibility RCT (study 3) presented in chapter 6 were small, with variation shown by wide confidence intervals. Therefore, caution is required as these were post-hoc exploratory sensitivity analyses.

7.3.2 Objective 2: To construct a prototype of a bespoke online intervention to assist with weight gain prevention in new KTRs using a person-based approach

Whilst there is an established clinical need to address weight gain for KTRs, particularly within the first year, there are no interventions available to address this. Despite national guidance recommending KTRs receive support with weight gain (Baker et al., 2021; The British Renal Society, 2020), clinical pathways and access to specialist allied health personnel such as dietitians are lacking across the UK (Kostakis et al., 2020). At commencement of this PhD, there was only one published RCT that included a combined intervention to address weight gain in new KTRs (Henggeler et al., 2018). Whilst the combined intervention provided in Henggeler et al (2018) referenced goal setting, it did not provide detailed reporting of interventions. In contrast, the work presented in this thesis demonstrated the coding of the ExeRTiOn online intervention to the BCW and the BCTTv1, contributing to the existing evidence base by clearly reporting the design, development, and evaluation of a theory-driven complex intervention.

Evidence regarding the use of online interventions to support people living with CKD are growing. A recent Cochrane review by Stevenson et al (2019) evaluated the risks and benefits of online e-health interventions for people living with kidney disease (including KTRs). The authors concluded that there is low quality evidence for e-health interventions, and further research with interventions that utilise theoretical frameworks, self-monitoring and personalised education are warranted (Stevenson et al., 2019). Whilst evidence was emerging for online interventions to support people living with CKD, only 15 studies (35%) of those included in this Cochrane review utilised KTRs, and none addressed weight gain prevention (Stevenson et al., 2019) . Whilst there was no weight gain prevention online interventions published at commencement of this PhD, there was literature suggesting acceptability, feasibility and clinical and statistical effect of online behaviour change interventions to address weight management in people living with excess weight and obesity (Bradbury et al., 2015; Little et al., 2016; Yardley et al., 2014; Yardley et al., 2012).

When establishing a need for any online product, it is important to consider access to the internet. The latest Office of National statistics report (2019) demonstrates that access to the internet is increasing, with 93% of households in Great Britain had access to the internet. In addition, people living with CKD in the UK engage with clinical platforms to monitor their health with 90% of UK renal units using 'Participants View' (The Renal Association, 2020a). In addition, access to renal specific exercise professionals (Greenwood et al., 2014) and dietitians (Kostakis et al., 2020) are lacking across the UK. An online intervention appeared to warrant exploration to provide support on a wider scale to allied-health professionals to address weight gain. Due to the gap in the literature identified by the systematic review (chapter 2), the research fellow

felt the design, and testing of the acceptability and feasibility of an online intervention specifically designed to address weight gain prevention in KTRs was a warranted and novel contribution to the research literature and could address this clinical need.

Alongside the review of the existing literature, the research fellow led a multi professional design team, within the wider study team to create the prototype of the online intervention. This design process has been previously discussed in both the published study one manuscript (Castle, Greenwood, et al., 2020) and previous chapters (chapters 3 and 4). The online ExeRTiOn intervention was designed using the combined approach (O'Cathain, Croot, Sworn, et al., 2019), largely informed by the person-centred approach (Yardley, Ainsworth, et al., 2015b), the BCW (Michie, Van Stralen, et al., 2011) and MRC framework for complex interventions (Craig et al., 2008). Refer to section 3.4.3 for a discussion of the theories and frameworks that influenced the ExeRTiOn online intervention.

7.3.3 Objective 3: To test the usability, functionality and experience using the prototype online intervention to aid refinement and acceptability

Study 2 of this thesis, and the published manuscript by Castle et al (2020) presented in chapter 3 and 4 addresses this objective. West & Michie et al (2016) argue that acceptability research is a crucial component in the evaluation of digital healthcare interventions. Research has shown that by engaging with the target end-users and stakeholders early in the design process, acceptability of digital healthcare interventions can be enhanced (Valdez & Ziefle, 2019). Therefore, study 2 was designed to follow the guidelines for digital healthcare interventions design and evaluation (Bradbury et al., 2014) by utilising a combination of think-aloud and semi-structured interviews to gather usability and experience data. Purposive sampling of acute KTRs (n=11) and transplant

HCPs (n=6) facilitated the assessment of the usability, functionality, and experience of a range of characteristics of our target end users (new KTRs). Purposive sampling can address limitations with generalisability that may occur during inductive qualitative investigations with small samples that can occur during development of digital healthcare interventions (Bradbury et al., 2014). A similar inductive qualitative approach was used to assess a 12-week online weight management programme in participants living with excess weight and obesity (Yardley et al., 2012).

The issue of addressing concerns relating to data security and privacy can be reported in digital healthcare interventions (Blandford, 2019). This was not reported by our participants in either of studies 2, 3 or 4 included in this thesis. Perhaps this was due to the detailed information provided to participants during the recruiting process (see protocol in the Appendices B and D), and the availability of this information on the ExeRTiOn online intervention homepage.

Study 2 contributes to the existing evidence base by transparently reporting the design, and early testing of the ExeRTiOn prototype online intervention. It adds to the existing evidence base of interventions designed utilising the 'person-based approach' (Yardley, Morrison, et al., 2015). Study 2 demonstrates transparent reporting of inductive qualitative approaches to assess usability and experience during intervention development. Whilst three studies have emerged during the PhD thesis to influence PA and or food intake in KTRs, usability testing and the role of participants in intervention design is not described (Gibson et al., 2020; O'Brien et al., 2020; Serper et al., 2020).

Study 2 suggests that the ExeRTiOn online intervention was acceptable to our purposive sample new KTRs and HCPs (study 1 chapter 4) by reporting critical

experiential and usability data. The qualitative research embedded throughout this thesis ensured experiential data, and suggestions for enhancing the ExeRTiOn online intervention were captured. Throughout this thesis, as well as the engaging KTRs in the design, refinement and evaluation process, this study included a strong multi-professional research team partnered with a software company. The pragmatic approach allowed the research fellow to incorporate research data, evidence, and participant driven changes to the ExeRTiOn online intervention.

7.3.4 Objective 5: To conduct a feasibility mixed methods RCT to a) assess the feasibility to screen and recruit participants, measure adherence to study visits and the intervention, and capture safety outcomes (QUANT), and b) capture and report the experience of using the online intervention over 12-weeks, and the experience of taking part in the feasibility study (QUALI)

A feasibility study asks whether something can be done, should we proceed with it, and if so, how (Eldridge, Lancaster, et al., 2016b, p. 1).

By conducting the mixed methods feasibility RCT (studies 3 and 4) presented in chapter 6, this final objective was achieved. All pre-set progression criteria for feasibility outcomes were met (see chapter 6). The ExeRTiOn online intervention was feasible, and acceptable from our integrated mixed methods results. In addition, studies 3 and 4 has allowed the research fellow to better understand the context of new KTRs within a London transplant unit. Understanding the context of complex interventions is crucial in complex intervention development (O'Cathain, Croot, Duncan, et al., 2019). By purposively sampling participants from both study groups, and of a range of age, gender, and adherence (IG), we were able to capture and report the experience of using the online intervention and the experience taking part in the trial (study 4, chapter 6).

The results and discussion sections of the previous chapter suggest that despite its limitations, a pilot multi-centre RCT is warranted to further explore the ExeRTiOn online intervention in KTRs. The mixed methods feasibility RCT contributes to the evidence base as it provides transparent reporting of feasibility outcomes, mixed methods data, and adds to the small amount of research of online interventions for KTRs. In addition conducting research trials can be expensive, therefore the success of a feasibility trial can suggest chances of success in future research (NIHR, 2019). Table 7.10 (on the following page) demonstrates a comparison of the thesis findings to the combined RCT's identified in our systematic review (chapter 2) to contextualise the results. Further sub-sections of this chapter will explore the implications of studies 3 and 4 for clinical practice, and suggest future trial designs, and the implications on policy.

Table 7-10 Summary of thesis findings and published literature: feasibility outcomes compared to combined intervention RCT's from the systematic review (chapter 2)

Studies	Total sample size	Rx	Screening rate (% and 95% CI)	Consent rate (% and 95% CI)	Retention rate (% and 95% CI)	Rx adherence (% and 95% CI)	Experience (QUALI data)	Safety/ hospitalisations	Other
Castle et al (2020) (study 2, chapter 4)	17 11KTRs 6 HCPs	NA	NA purposive sampling	73.3% (95% CI 44.9 to 92.2%)	No dropouts	NA	2 Themes: you need to know how to manage yourself and room for improvement Both groups felt resource warranted further research	NA	Usability and experience testing of ExeRTiOn prototype to aid refinements
Castle et al 2021 (studies 3 and 4, chapter 6)	17	Combined intervention Online BCTs 12-weeks Independent with remote monitoring	84.2% (95% CI 68.8 to 94.0) Pragmatic eligibility criteria	62.5% (95%CI 43.7 to 79.0)	76.4% (95% CI 50.0 to 93.2) at 12-months	66.67% (95% CI 29.93 to 92.51) achieved 60% or	4 Themes: optimising recruitment, the impact of COVID-19, engagement is a choice, and mechanisms	29.4 (95% CI 7.8 to 51.1) % participants who had a NRAE No expected or unexpected harm	Study during COVID-19 pandemic

						more of sessions			
Gibson et al (2020)	10	Combined intervention Teleconference 6-months	NR	100% (95% CI 69.2 to 100%)	90% (95% CI 55.5 to 99.8%) at 12-months	78% for 12-sessions	4 themes: strengths of intervention components, challenges in study, adherence to study components and improvements to the study components	NR	Report of first 10 eligible participants suggests preliminary results
Serper et al (2020)	66 KTRs 66 LTRS	Combined online intervention with incentives and step tracker, versus step tracker versus controls 14-weeks	41.9% (95% CI 37.2 to 46.7%)	71.4% (95% CI 64.1 to 77.9%)	82.1% (95% CI 86.0 to 96.2%) at 4-months	Mean adherence to step goals was 74%	Exit survey revealed participants enjoyed the study. To improve the study participants would like tech assistance, track different activities and non-step goals	NR	Rates only provided for combined sample (KTRs and LTRs) Unable to calculate 95% CI for adherence from report

Schmid-Mohler et al (2019)	123 combined transplants (120 KTRs)	Combined intervention Face-to-face 8-months	32.2 % (95% CI 27.5 to 37.1%)	58.0% (95% CI 51.2 to 64.7%)	97.6% (93.0 to 99.5%) at 8-months	88.5% completed ≥ 7 Rx sessions 86.9% completed ≥ 4 Rx sessions	NA	NR	Rates reported for combined sample (Kidney and kidney-pancreas Tx) Report re-hospitalisation of Rx group but no further details Unable to calculate 95% CI for adherence rates from trial report
Kuningas et al (2019)	130 KTRs without diabetes	Combined intervention Face-to-face 6-months	71.5% (95% CI 66.2 to 76.4%)	57.5% (95% CI 50.8 to 64.1%)	79.2% (95% CI 71.2 to 85.8%) at 6-months	NR	NA	'No safety concerns'	KTRs without diabetes with a mean of 8-months post Tx
Henggeler et al (2018)	37	Combined intervention Face-to-face	54.1% (95% CI 44.3 to 63.6%)	61.7% (95% CI	70.3% (95% CI 53.9 to	NR	NA	No adverse events linked to trial	High levels of standard care (4 dietitian sessions

		12-months		48.2 to 73.9%)	84.1%) at 12-months			38 admissions	in one year) compared with clinical practice in the UK
Tzvetanov et al (2014)	17	Combined intervention Face-to-face 12-months	NR	NR	64.7% (95% CI 38.3 to 85.8%) at 12-months	100%	NA	NR	KTRs living with obesity Limited trial reporting

Note. The combined-intervention RCT's from the systematic review (see chapter 2) were compared with the work generated from this thesis for feasibility outcomes (studies 2 and 3). When information was available in published manuscripts, screening, consenting, retention and adherence rates were calculated with 95% confidence intervals using an online statistical calculator (Kohn & Senyak, 2021). Rx refers intervention, CI= confidence interval, QUALI= qualitative research, KTRs= kidney transplant recipients, HCPs= health care professionals, NA= not applicable, BCT's = behaviour change techniques, COVID-19- Coronavirus disease 2019, NRAE =non-related adverse event and was defined as a non-elective hospital admission, of >24 hours, not related to the study. NR= not reported, LTRs= liver transplant recipients and Tx= transplant

7.4 Strengths and limitations

7.4.1 Systematic review and meta-analysis (study 1, chapter 2)

To our knowledge, the systematic review presented in chapter 2 was the first systematic review and meta-analysis that included exercise, PA, dietary or combined interventions, and their effect on body weight in new KTRs. The systematic review focused on body weight and BMI as primary outcomes. Therefore, it is possible that further studies reporting secondary outcomes, but not body weight or BMI were excluded in this search.

This systematic review, and project focused on KTRs rather than all SOTs. However, KTRs have requested specific education and support (Castle, Greenwood, et al., 2020; Stanfill et al., 2012). KTRs also experience a unique fear avoidance pattern associated with PA, (Zelle et al., 2016) and experience rapid weight gain in the acute post-operative period (Beckmann et al., 2017). Focusing the systematic review on KTRs within the first year of kidney transplantation could have precluded studies with additional insights into this research field. However, as weight gain within the first year is associated with adverse clinical outcomes (Ducloux et al., 2005; Vega et al., 2015), the research fellow felt it was crucial to investigate the first-year post kidney transplantation.

The research fellow acknowledges the impact that the methodological variation (sample characteristics, intervention type, dose, and duration) of the ten RCT's may have had on the validity of the pooled effects of interventions on body weight or BMI. However, statistical heterogeneity was not significant. In addition, by performing the meta-

analyses on body weight and BMI, and exploring this with sensitivity analysis, this systematic review provides novel implications for future research studies in this field.

7.4.2 Design and refinement of the ExeRTiOn online intervention

One of the main strengths of this PhD thesis is the involvement of our target population, new KTRs throughout this research fellowship to design, refine and evaluate the feasibility of the ExeRTiOn online intervention. The pragmatic standpoint, the creation of the resource using recognised intervention designs such as the person-centred approach (Yardley, Morrison, et al., 2015), and evidence based theory (see section 3.4, chapter 3), the research fellow was able to pragmatically address usability, feasibility and acceptability questions. Through early engagement with stakeholders, such as KTRs, HCPs and researchers, the research team were able to ensure the resource was fit-for-purpose for our target end users. Engaging KTRs and HCP in studies 2, 3 and 4, and throughout this thesis allowed the resource to be person-based and refined based on study results and our target end-user group.

Another strength was the use of a range of multi-professional experts who were included in the design team of the ExeRTiOn online intervention (Castle, Greenwood, et al., 2020). This included collaboration with researchers, HCPs, KTRs and a software company. The intervention drew on relevant behaviour change theories (Michie, Atkins, et al., 2014b; Michie et al., 2013), theories of self-efficacy (Bandura, 1977), the evidence base and development of digital healthcare guidance (Bradbury et al., 2014; West & Michie, 2016). In addition, the ExeRTiOn online intervention was retrospectively mapped to the BCTTv1 (Michie et al., 2013), and the BCW (Michie, Van Stralen, et al., 2011), facilitating clear reporting of the active ingredients of the ExeRTiOn intervention. Whilst similar combined intervention RCT's identified in the

systematic review (Chapter 2, table 2.3) by Henggeler et al (2018) and Kunginas et al (2019) report the use of goal setting and BCT's, the work in this thesis contributes to the evidence base by retrospectively mapping all BCT's and the interactions with the research fellow / physiotherapist to the BCTTv1 (see section 6.4.1.7 chapter 6, and Appendix F).

Resources, and timescales are reported restraints to address in the development of digital behaviour change interventions (West & Michie, 2016). Unfortunately, budget and time pressures could have influenced the number of changes made when revising the prototype online intervention that occurred between the usability and experience study (study 2) and the feasibility RCT (studies 3 and 4) included in this PhD Thesis. However, the process was pragmatic and transparent, with negotiations with the software company, and prioritisation of changes based on the results and participant feedback from study 2. In addition, there is a need for online interventions to be conducted using digital development frameworks and in a timely fashion. Otherwise, there is a risk of the online intervention being outdated when development and research is published, due to the fast changing technology landscape (Murray et al., 2016). The research team addressed this by using a pragmatic approach, using the participants-centred intervention design, referencing digital intervention development processes, conducting multiple studies, and using mixed methods design to capture experience, feasibility, acceptability and usability. The MoSCoW method allowed the research fellow to address revisions in a pragmatic, transparent, and prioritised manner (Kuhn, 2009). It allowed the research fellow to balance limitations with cost, and time restraints of the PhD fellowship with the thesis aims and objectives.

7.4.3 Study 2 (usability and experience)

Limitations from the second study have been outlined in a peer review publication (Castle, Greenwood, et al., 2020) and in chapter 4. The main limitations include the single-centre design, and the research fellow who led the project also completed the individual interviews (think-aloud and semi-structured interviews). However, this was addressed by; asking probing questions for negative feedback, use of a reflective journal, and the consultation of an external researcher to validate codes and themes. The use of a combination of think-aloud and semi-structured interviews are suggested methods in digital healthcare intervention guidelines (Bradbury et al., 2014). Whilst usability testing was conducted in the one-off study visit, studies 3 and 4 involved the participants using the complete 12-week resource independently, with multiple assessments, collecting mixed methods outcomes to further gather experiences using the online resource and any additional usability issues.

7.4.4 Studies 3 and 4 (mixed methods feasibility RCT)

Unfortunately, due to COVID-19 (see chapter 5), the sample size was reduced from 50 to 17 KTRs. The impact of the reduced sample impacted the ability to estimate SDs for a future sample size (see chapter 6 discussion). Therefore, based on guidance for feasibility study reporting, testing for efficacy was not performed (Eldridge, Chan, et al., 2016). A recent publication has suggested guidance for study reporting of trials occurring during the COVID-19 pandemic (Cesari et al., 2021). The authors recommend transparent reporting's of any changes to the study protocol that occurred due to COVID-19. The research fellow has transparently reported the changes and documented the decisions throughout the thesis process to facilitate transparent reporting and contextualise the research findings (see Chapters 5 and 6, and Appendix E). Despite the reduction in overall participants, the sample were able to continue with

the trial with appropriate COVID-19 safety procedures and demonstrated a good retention rate of approximately 76% at 12-months. Despite this limitation of a reduced sample, studies 3 and 4 provide insight into feasibility, and offers recommendations for a future definitive trial design.

In addition to the reduced sample, the studies 3 and 4 were initially designed to be bi-centre. However, due to limitations described in the previous chapter, only one participant from the second site was included in the final study sample. The research fellow who provided the ExeRTiOn online intervention had previous experience in both transplant care and motivational interviewing. This made it difficult to separate the effect of the research fellow versus the ExeRTiOn online intervention. A follow-up study, with multiple centres, without physiotherapists in the transplant centres is warranted to explore this further.

The online IG appeared to have a lower median age of 39 years (IQR 33 to 44), with participants ages ranging from 31 to 59 years of age. The UC group had a median age of 59.5 years (IQR 53.5 to 65), with participants ranging from 43 to 71 years of age. Whilst the age in the IG may have been lower than the UC group for study 3, purposive sampling in study 2 allowed the prototype of the ExeRTiOn to be tested by a KTR sample ranging from 31 to 74 years (Median 51 years). It is possible that differences in years of age between the groups would have been rectified if further participants were able to be recruited.

The limitation of the lack of blinding of the assessor and intervention provider (research fellow) has been addressed in the previous chapter's discussion. Due to the nature of the study design, exercise and behavioural studies are often unable to achieve double

blinding. As this research was conducted as part of a PhD Fellowship, all analysis was conducted by the research fellow. However, as this was a feasibility study, not an efficacy study, this is less of an issue. Support was sought from an external statistician and supervisors. Future studies would benefit from the blinding of the outcome assessor.

At the time of conceptualisation of studies 3 and 4, given the knowledge, skills of the research fellow, and the free availability of the questionnaire, the self-efficacy questionnaires by Schwarzer and Renner (2009) were selected to assess self-efficacy for PA and healthy eating behaviours. In hindsight, the research fellow perhaps would now consider an alternative validated and licenced measure; the participants activation measure (PAM®) (NHS England, 2018). The PAM® measures an individual's knowledge, skills and confidence to manage their own health and has good reliability and validity in other long term conditions such as cancer and rheumatoid arthritis (Nair & Cavanaugh, 2020). The PAM® facilitates the aim of the NHS five year forward plan (NHS England, 2017) to support people to manage their own care and wellbeing (NHS England, 2018). It allows researchers to classify activation into four levels from disengaged and overwhelmed to maintain behaviours and pushing forward (NHS England, 2018). These four levels outline key behaviour characteristics to facilitate person centred self-care (NHS England, 2018). The use of PAM ® in the renal population is growing in recent years as evident by recent publications (Hamilton et al., 2018; Nair & Cavanaugh, 2020; Wilkinson et al., 2021). The Renal Association publishing the findings of its feasibility study across 14 renal units in the UK (The Renal Association, 2019). In addition, the PAM ® was shown to increase following a well-known diabetic self-management programme (DESMOND) (Miller et al., 2020). As the use and evidence for the PAM® measure continues, future studies could consider

its use as a secondary outcome to assess the effectiveness of the online intervention to facilitate self-management in KTRs.

The lack of assessment of dietary intake in the feasibility RCT (study 3) to assess positive changes to dietary habits could have limited the ability to detect change in healthy eating behaviours. However, this feasibility study was designed to inform future research, and the previous chapter describes suggestions for outcomes in future studies such as a combination of weight, BMI, BC, the PAM ® and the 6MWT. As mentioned in the previous chapter, outcomes for future studies should be meaningful to participants, and reflect our mixed methods results (see discussion section, chapter 6). Qualitative results suggest that the BIA and the 6MWT were valued outcomes and meaningful to our participants. Future studies should continue with PPI to ensure the balance is maintained between the number of outcome measures, and outcomes that are clinically relevant, and most importantly meaningful outcomes to our service users.

The COVID-19 pandemic, and the strict shielding practises particularly in the first and second wave in the UK could have influenced the interventions target behaviours of PA and healthy eating. UK participants surveys in people living with CKD reported disruptions with clinical care, confusion around shielding practises, and an impact on mental wellbeing (Kidney Care UK, 2020) (see chapter 5). However, the qualitative analysis, particularly theme 2 provided rich insight into the impact of physical and mental being, and social support on our participants. Having support from family, friends, and HCPs assisted participants with these unique challenges.

One participant in the online IG (G03) reported the calls and support from the research fellow during COVID-19, and the online intervention supported her wellbeing during

this period. Fortuitously, the intervention could be delivered online, and most of the outcomes could be collected remotely, allowing the research fellow to continue with the study, and support the participants during this challenging time. Despite the impact of COVID-19 on this study visit, there were only two admissions of trial participants with COVID-19. Additional insights into online interventions, and research during a pandemic were discovered during this PhD thesis that would not have occurred without COVID-19.

Whilst this research team did not include a health technologist, the team did include a health psychologist with experience working in other online intervention studies, as well as health care professionals, and participants experts. In addition, there were good relationships and contracts with the software company, and research fellow to design and refine the online intervention using a pragmatic approach. The strong participant input by the target user group throughout this PhD ensured that it was person-centred and would be fit-for-purpose for our target population.

Some of the complex analytical processes (see chapter 6) such as coding the online intervention to the BCTTv1 and the BCW, and the mixed methods integration were completed by the research fellow. However, they were validated by the supervisors. By mapping the intervention to the behaviour change taxonomy, and completing three studies, including mixed methods analysis, the research fellow was able to explore inferences across the data sets, consolidate research skills, and transparently report methodology and findings.

7.5 Implications

7.5.1 Potential implications for clinical practice

Research has shown new KTRs report fear of harming the new kidney (Zelle et al., 2016). Furthermore, a recent UK survey has shown despite the recognised clinical need to support new KTRs with their weight, there is variation in access to renal dietitians across UK transplant centres (Kostakis et al., 2020). The British Renal Society recent workforce planning document, published by experts in the field recommends the inclusion of renal dietitians and physiotherapists within the transplant multi professional team (The British Renal Society, 2020). Recent clinical practice guidelines regarding exercise for people living with CKD recommend all KTRs should have access to weight management support (Baker et al., 2021). There is a need to increase access to physiotherapists and dietitians to support KTRs post transplantation. During this PhD fellowship, the research fellow contributed to both guidance documents. Overall, there is a need for data, and future research that examines the effectiveness of treatments to prevent weight gain in new KTRs to inform clinical practice.

7.5.2 Implications for future research

The four empirical studies presented here have demonstrated the following novel findings:

- There is a gap in the existing literature regarding interventions to address weight gain prevention for new KTRs (study 1, chapter 2)
- The ExeRTiOn online intervention is acceptable to new KTRs and HCPs (study 2, chapter 4)
- The ExeRTiOn online intervention, and an RCT utilising it is feasible (studies 3 and 4, chapter 6)

- Future research into the effectiveness and cost-effectiveness is required post PhD fellowship (discussion, chapter 6).

Whilst assessment of intervention effectiveness was beyond the scope of this PhD thesis, suggestions for the implications of this work is possible. As demonstrated in the previous section, the thesis was able to achieve the aims and objectives. However, there remains to be unanswered research questions regarding online interventions to address post-transplant weight gain in new KTRs. Murray et al (2016) offer suggestions for research questions to evaluate digital healthcare interventions. It is recommended that a definitive study should only be considered when there is minor revisions to the product, and it is likely to show benefit, and be cost effective (Murray et al., 2016). Whilst these unanswered questions are beyond the scope of this PhD thesis, a follow-up definitive trial, post PhD could address the following questions:

- Is the ExeRTiOn online intervention effective in the prevention of weight gain after kidney transplantation?
    - What is the ideal level of support needed to deliver the online intervention?
    - What is the ideal length of the intervention?
    - What are the most effective active ingredients in the online intervention?
    - Was BCTs and other psychosocial variables change overtime and mediate treatment effects (addressing the questions “why does the intervention work”)
    - Is the delivery of the online intervention achievable at other transplant centres? And is it scalable?
    - Who does the intervention work best for (moderation effect)
    - Is the provision of the online intervention cost effective? And sustainable?

Michie et al (2014a) and West et al (2016) argue that evaluation of complex interventions including BCTs should extend beyond measurement of effectiveness. These authors suggest interventions are evaluated within the context, but also interventions are evaluated for acceptability, practicability, effectiveness, affordability, safety and equity (APEASE) (Michie, Atkins, et al., 2014a; West & Michie, 2016). The data presented in this thesis suggests that the ExeRTiOn online intervention is acceptable, feasible to our samples of south-London new KTRs, with no associated adverse safety concerns. Future research should therefore evaluate the practicability to provide the intervention in other settings and sites, the effectiveness and cost effectiveness of the online intervention, and issues relating to equity of care. Qualitative data is needed to explore those who decline or withdraw from the intervention to assess the reach. MMR designs could be utilised to further evaluate the ongoing research questions.

7.5.2.1 Future trial design

The ideal study design for a future definitive trial evaluating the effectiveness of the ExeRTiOn online intervention warrants careful consideration. Our results suggest a post-PhD multi-centre pilot RCT to inform a definitive RCT are required. A limitation of the RCT study design is the ethical dilemma of potentially withholding an intervention to participants who are randomised to the UC or control group (Jewell, 2011). However, as there is no established intervention for weight gain prevention for new KTRs, effectiveness must first be evaluated. Therefore, the research fellow plans to conduct a multi-centre pilot RCT post PhD to inform the power of a multicentre definitive RCT to evaluate clinical effectiveness and cost effectiveness of the ExeRTiOn online intervention.

Recent guidelines to extend the CONSORT statement to address pilot and feasibility studies have been published (Eldridge, Chan, et al., 2016). Feasibility trials evaluate whether research can and should be done (Eldridge, Lancaster, et al., 2016a; NIHR, 2019). Whereas a pilot study, in addition to looking at these questions, is a smaller scale version of the main RCT study to evaluate whether the components of the main trail will work together (Eldridge, Lancaster, et al., 2016a; NIHR, 2019). A pilot RCT to investigate the effect of the ExeRTiOn online intervention across multiple transplant sites would align with the MRC framework for the design and evaluation of complex interventions as it would allow for any anticipated uncertainties of the main trial to be addressed before progressing to the evaluation of effectiveness (Craig et al., 2008).

Whilst the work in this thesis has addressed acceptability and feasibility, it remains yet to be answered if the ExeRTiOn online intervention can be rolled out across multiple sites. With complex interventions, particularly behavioural interventions, it is hard to examine which component such as the rapport, and/or the intervention itself are causing effect (O'Cathain, Croot, Duncan, et al., 2019). It would therefore be important to evaluate a variety of sites including primary and secondary transplant sites, sites inside and outside of London, and sites with and without renal physiotherapists in the post-PhD multi-centre pilot RCT. Qualitative work from studies 2 and 4 suggest the element of support, rapport and supervision from the research fellow, a renal specialist physiotherapist, with training in both motivational interviewing and transplant care, could have contributed to the participant experiences. The role of the research fellow could have contributed to the study participation by:

- Enhancing the usability of the ExeRTiOn online intervention (Theme 1, study 2)
- The optimisation of participant recruitment (theme 1, study 4)
- The technical factors influencing the engagement (subtheme, theme 3, study 4)

- Education within the assessment process (theme 4, study 4)
- Assistance and support to address fear of injury (theme 4, study 4).

A mutli-centre pilot RCT is planned to further the evaluation of the ExeRTiOn online intervention across multiple sites. This will allow for the exploration of the effect of the research fellow on the ExeRTiOn intervention, data collection, further evaluation of the intervention, and inform a power calculation for a definitive RCT.

As outlined in study 1, chapter 2, there is no recognised intervention to prevent weight gain for people acutely post kidney transplantation. Clinical factors such as pre-transplant renal replacement history, age, and baseline body weight and BMI can influence body weight measurements. Baseline body weight, and muscle mass may vary across KTR participants. Participants who received longer periods of haemodialysis demonstrated higher muscle depletion, reduced muscle mass and sarcopenia compared with KTRs (Bellafronte et al., 2020). As weight gain effects both KTRs living with and without obesity (Chan et al., 2014; Dimény, 2002), stratification of these clinical variables influencing baseline body weight would be an important aspect to include in the planned multi-centre pilot RCT design. In addition, the use of sub-groups warrants exploration in the follow-up multi-centre pilot RCT. The exploration of sub-groups into categories such as KTRs who are underweight, normal weight, overweight or obese would provide useful data in the potential effects of the ExeRTiOn online intervention in new KTRs.

To address the impact of shielding during the first wave of the COVID-19 pandemic on access to exercise classes for people living with kidney disease Kidney Beam was created. Kidney Beam (Kidney Beam, 2021) provides online specialist group exercises, and educational videos for people living with CKD. The research fellow has contributed

to the Kidney Beam working group, and content. A study is currently underway to evaluate the clinical use and cost effectiveness of the Kidney Beam online platform across multiple UK sites (IRASID291403, NCT04872933)(NIH U.S National Library of Medicine, 2021). The post-PhD pilot could utilise the Kidney Beam infrastructure, by hosting the ExeRTiOn online intervention in future research projects. This could address the qualitative feedback from our participants regarding the provision of group exercise class videos.

Another uncertainty that could be addressed by the future pilot study would be detailed process evaluation as per the MRC guidance (Craig et al., 2008) to further evaluate the intervention. The multi-centre pilot study post PhD would allow the research fellow to explore uncertainties relating to multi-centre delivery of the intervention, non-physiotherapist sites, further explore research outcomes, long term follow-up, process evaluation (casual mechanisms), and cost implications. Following the results of this future pilot study, a definitive RCT could be conducted to evaluate the effectiveness of the ExeRTiOn online intervention.

As previously presented in the systematic review (chapter 2) and previous discussion sections, it is crucial for future studies to include adequate long-term follow-up. Only two RCT's (O'Connor et al., 2017; Schmid-Mohler et al., 2019) included in the systematic review presented in chapter 2 included long-term follow up at twelve-months after a period of intervention cessation. In study 3, participants were followed up approximately 12-months after entering the trial, and nine months after the completion of the twelve-week intervention. Future studies would be encouraged to include longer-term follow up to allow for the assessment of the longer-term effect of weight gain prevention interventions.

Whilst this thesis has involved MRC complex intervention design and evaluation processes such as design, evaluation, refinement and feasibility (Craig et al., 2008), these processes are not linear and often can occur concurrently (O'Cathain, Croot, Duncan, et al., 2019). Therefore, the research fellow suggests further refinement of the online intervention, and evaluation using a multi-centre pilot RCT to inform a definitive trial for the assessment of effectiveness.

7.5.2.2 Suggested outcome measures

The previous chapter (see chapter 6) has suggested outcomes for future research in this field, including participants and clinically meaningful outcomes. The future planned multi-centre pilot RCT will investigate primarily the change in body weight and other outcomes. Suggested measures for future studies to evaluate the ExeRTiOn online intervention include body weight, BMI, BIA, the 6MWT and the PAM ®. The BIA is a particularly important outcome, as weight gain after kidney transplantation has been shown to be associated with an increase in adipose tissue in the truncal region (Workeneh et al., 2019), and a reduction in lean tissue mass (Wołoszyk, Małgorzewicz, Chamienia, & Dębska-Ślizień, 2020). The inclusion of participants advocates throughout future study design and evaluation, as utilised in this thesis will ensure the person-based approach of intervention design is at the forefront.

7.5.2.3 Suggested enhancements for the ExeRTiOn online intervention

At the end of this PhD fellowship there were two published studies that included online interventions in new KTRs to address either healthy eating behaviours and or PA (Gibson et al., 2020; Serper et al., 2020). However, Gibson et al (2020) recruited participants within the first six to twelve months of transplantation and Serper et al

(2020) reported a median transplant vintage of 9.5 months, making it difficult to determine the effects of the intervention on acute kidney transplant recipients' weight gain. Intervention duration ranged from four (Serper et al., 2020) to six months (Gibson et al., 2020). Whilst the ExeRTiOn online intervention was only three-months in duration, it aligned with the duration of existing commissioned face-to-face renal rehabilitation services provided in the NHS (Greenwood et al., 2012). Parallel chronic disease groups demonstrate similar lengths of disease-specific rehabilitation programmes, of six to eight weeks for pulmonary rehabilitation, and ten to twelve weeks for cardiac rehabilitation (The British Heart Foundation, n.d.; The British Lung Foundation, 2020). Therefore, a three-month intervention appears reasonable for new KTRs.

Our renal population in the UK engage with other clinical online platforms such as renal patient view (The Renal Association, 2020a). The ExeRTiOn resource was created as a website, compatible with either a computer, tablet or smart phone to facilitate wider acceptability of content. The ExeRTiOn online intervention was revised based on participants feedback after study 2 and before studies 3 and 4. However, the qualitative data from study 4 suggests further enhancements could be made to the online intervention in preparation for the post-PhD pilot and definitive effectiveness trial. A summary of participant suggestions to further enhance the ExeRTiOn online intervention to enhance are presented in table 7.11 on the following page.

Table 7-11 Suggested enhancements of ExeRTiOn resource from qualitative data

Suggested revision	Location of revision	Supporting quote
Reduce the length of session videos	Session 10 overcoming barriers, Session 11 problem solving	The problem-solving thing, um [pause] um there was steps where it said identify the problems as soon as possible, and then you write things like oh you're out of breath, and then it would then ask you how then like using different words like, like you know to describe becoming short breath when walking up the stairs, when walking to work or anything like that. I mean like, it was a bit too much, there was a lot of things that you had to write down..there was quite a lot of steps (G03, female, IG)
Add additional exercise workout videos	Home exercise tab and session, Session 5 choosing your physical activity/exercise	I would say um instead of pictures, maybe get videos, uhm but I think there is a video where there is instructing, what sort of exercises would look like (G03, female, IG)
Group exercise classes	New addition to website functionality	I think if it was something more like [pause] let me see [pause] in a group… to do the exercises it would be more motivating to do it (P06, female, IG)
Insure different levels of difficulty for exercise content	Exercise diary tab/ exercise resources	Maybe under different tabs for example- different link or tab. This is for older people, with less strength. As then. then for I don't know younger patients because I have seen somewhere was some transplant patients I have seen at Guy's, they are younger. They can lift more whilst they recover from the wound and stuff. They can do more than that. They would want to do more. So, um (P12, male, IG)
Some participants may require additional support to engage with the resource	Support to engage with website	Yeah, because to navigate around it, I found, I found it a bit difficult at first, I didn't really get it, I had to keep trying and trying and trying (P06, female, IG) Did get easier with time and frequent use: Yeah, the more you use it, the more you get used to it, so then it is not so bad.. but then I realised that if I just give it go, then I would be able to do it. (P06, female, IG)
Accessibility		I can access it on my phone that I have with me (P07, female, IG)

Participants valued being able to use the website on multiple platforms such as smartphones	It was very-very easy because the first day she actually uh she actually bookmarked the site for me so any-any-anytime I went on there it was easy to enter (P05, male, IG)

Note. The table above summarises future intervention revisions from the participant interviews in study 4 (nested qualitative study) presented in the previous chapter

Based on learning during the PhD process, the research fellow would also recommend the following revisions to the ExeRTiOn online intervention package:

- Update the styling if the website (with PPI input) to ensure the resource does not appear outdated
- Ensure standardisation of education post kidney transplantation for both groups and consider a passive education booklet for both groups on PA and dietary advice post-transplant
- Continue with a strong multi-professional research team and include further health psychology input, and input from technology scientists to ensure active ingredients can be examined
- Continue with the physiotherapy support alongside the ExeRTiOn online intervention as per the feasibility study protocol (orientation session, messages)
- Future studies would benefit from recording physiotherapists hours reviewing the website to inform cost analysis
- Include sites with and without physiotherapy support

Whilst evidence with complex interventions are becoming more popular, particularly in behaviour change interventions, there is a need for consisting reporting of the key intervention components to ensure research is transparent, able to replicated and included in future evidence synthesis (Craig et al., 2008). Our systematic review, presented in chapter 2, show the gap in the literature regarding interventions designed to specifically address weight gain prevention in new KTRs. This thesis contributes to the existing evidence base by clearly reporting the active ingredients of the ExeRTiOn online intervention (studies 2, 3 and 4) and by coding it to the BCW (Michie, Van

Stralen, et al., 2011) and the BCTTv1 (Michie et al., 2013) (see section 6.4.1.7 in chapter 6 and appendix F).

From the small feasibility RCT (study 3), it is not possible to examine causation, or the effect of individual BCT's that were components of the ExeRTiOn online intervention, as this was not one of the primary research objectives. The research fellow is aware of the limitations in reporting beyond the feasibility findings. In addition, intervention fidelity and adherence, as well as the context in which it is used can influence results (Michie et al., 2018). Our studies included in the thesis suggest our participants valued goal setting and self-monitoring that have been shown to facilitate PA and healthy eating behaviour change (Michie, Ashford, et al., 2011). Table 7.12 below summarises all the BCT's included in the ExeRTiOn online intervention, their location, and any available supporting qualitative evidence. Future studies would benefit from clear reporting of the active ingredients, evaluation and modelling to investigate the effective active ingredients of the ExeRTiOn intervention. The limited existing evidence summarised in our systematic review suggests further studies should consider combined interventions, with recognised BCT's to address PA and healthy eating behaviours after kidney transplantation.

Table 7-12 BCTs in ExeRTiOn intervention and QUALI evidence

BCT	BCT definition from BCTTv1 (Michie, Atkins, et al., 2014a)	Location (Website, interactions with physio or both)	Frequency of BCT's	Qualitative evidence (if available)
1.1 Goal setting (behaviour)	Set a goal defined in terms of targeted behaviours (PA ± healthy eating)	Website	11 per-participants during 12-weeks	I liked the fact that you can[pause] record [pause] uhm like, uhm like the exercise you do and how long you do it for…uhm, [pause/sigh] it is a bit like savings, like if you want to save in your bank and then obviously you, you save, I mean you know you have set yourself a goal and that is it there and you need to do it, basically it's like that. Like so you set yourself a goal, whatever it is like, you know I am going to do a 10-minute walk around the block, or I am going to, like whatever it is, you can set that goal and then you like a specific time, like to give yourself to do that. And I just found that very helpful, because like I said to me it's like relating to savings (P07, female, IG)
				you know there is emphasis in your programme on goals, and you know, letting people have that space, to you know 'how do you feel goals? do you feel confident that you will achieve it?' [ref to the confidence and importance ruler in goal setter function]. Um so the language around it was very very good (P10, female, IG)
1.2 Problem solving	Prompt ± Analyse the factors influencing behaviour Generate potential options to address barriers	Website	4 per-participants during 12-weeks	I think one of the most helpful ones were erm, sort of breaking barriers with foods eating and habits and the type of foods, you know that would be better to eat and avoid, Erm as I tend to just find my own routines but sometimes when you've got something to go by its quite more motivating erm so I found that motivating, and I also thought erm by doing things all of a sudden it could be a lot harder to go by, By doing things gradual it's definitely a lot more easier, [pause] a lot more doable as a target so yeah. For myself and you know my opinion to others will be start gradual and just to start at a really slow pace, it's no point try to jump it is, it just doesn't work (P04, male, IG)

	Includes relapse prevention Cannot just be barrier identification, must have solution			The problem-solving thing, um [pause] um there was steps where it said identify the problems as soon as possible, and then you write things like oh you're out of breath, and then it would then ask you how then like using different words like, like you know to describe becoming short breath when walking up the stairs, when walking to work or anything like that. I mean like, it was a bit too much, there was a lot of things that you had to write down..there was quite a lot of steps (G03, female, IG)
1.4 Action planning	Detailed planning of behaviour and must include prescription and detail	Website	12 per-participant during 12-weeks	*See quotes for 1.1 as 1.4 applied with 1.1 in the goal setting template on the website
1.5 Review of behaviour goal	Review of goal with patient	Interactions with physio (message function)	15 contacts for 7 participants	Not available
1.9 Commitment	Ak to affirm/ re affirm statements to show commitment to target behaviour change	Website	12 per-participant during 12-weeks	You know there is emphasis in your programme on goals, and you know, letting people have that space, to you know 'how do you feel goals? do you feel confident that you will achieve it?' [ref to the confidence and importance ruler in goal setter function]. Um so the language around it was very very good (P10, female, IG)
2.1 Monitoring of behaviour by others	Record/observe behaviour, person aware but receives no feedback	Website	4 per-participant during 12-weeks	Not available

without feedback				
2.2 Feedback on behaviour	Monitor and provide info/feedback on behaviour	Both	2 per-participant during 12-weeks 41 contacts for 9 participants	The thing is from me, you might not receive messages, so often, because of being lazy, but from er, from yourself, if I receive a messages, I know for me that's like you know a little kick saying you know go on get on what you need to do (P04, male, IG)
				Interviewer: And what was your main motivation do you think for using the online resource? **P10** [laughs]. Probably could I could I could see you! [interviewer physio in website]. [laughs] 'Ellen's going to be in touch if I haven't done it' [both laugh]. I didn't want to let you down!..That's the personal connection there, everything boils down to a relationship at the end of the day.
2.3 Self-monitoring of behaviour	Having a method to monitor and record behaviour as part of a strategy	Website	13 per-participant during 12-weeks	I found by keeping a track of it kind of motivates you to want to add more to the activity part, and then to the part where you've got the weight, your-I mean for myself as well I look at it and I'm like you know I want to try and bring that weight down down down [pause] (P04, male, IG)
				Its lovely to have the imagery of the the charts. So- with the activity levels and the weight. To kind of just see for yourself, over the weeks um. and to make connections with that. So, for example there was a big dip when argh- I did at the time. I am just going back a few weeks. Have quite a bad cough. And I was just taking it- I was taking it right down. So just to- yeah. To see the visual of that, that was great. Um. [pause] (P10, female, IG)
2.4 Self-monitoring of outcome of behaviour	Devise method for recording and monitoring the outcome of the behaviour	Website	13 per-participant during 12-weeks	*See quotes for 2.3 above as tracking function of website included self-monitoring of behaviour (PA) and outcome (weight) which are highlighted in quotes above

2.7 Feedback on outcomes of behaviour	Monitor and provide feedback on outcome of target behaviour	Interactions (message function)	20 contacts for 8 participants	*See quotes for 2.2 as feedback for behaviour (PA) was provided alongside feedback on outcome (weight) in physio messages
3.1 Social support (unspecified)	Advise or provide social support includes praise and encouragement when directed at behaviour	Interactions (majority through message function)	83 contacts for 8 participants	I think, um it will help because I spoke to my physio quite a bit… I'd tell her sometimes and shed be like you know what you know keep busy, do this and do that and stuff like that she would give me advice (G03, female, IG on physio call during lockdown)
4.1 Instruction on how to perform a behaviour	Advise on how to perform behaviour *Code with 6.1	Both	4 per-participant during 12-weeks 15 contacts for 7 participants	I would say um instead of pictures, maybe get videos, uhm but I think there is a video where there is instructing, what sort of exercises would look like (G03, female, IG) It was nice, nicely spread out and you know all the videos and stuff were well explained. umm. I had no problems with you know, getting used to it whatsoever. So, it was pretty nice. You know, the font, everything (P12, male, IG)
6.1 demonstration of the behaviour	Observable example of performing the behaviour (can be film, pictures) *Code with 4.1	Both	4 per-participant during 12-weeks 6 contacts for 4 participants	*See quotes for 4.1 above, as 4.1 and 6.1 provided together
6.2 Social comparison	Compare performance of one with another to draw attention	Interactions (message function)	8 contacts per 6 participants	Not available

7.1 Prompts cues	Prompts to cue behaviour	Both	25 per-participant during 12-weeks 24 contacts for 6 participants	um she helped me go to the website, and in the beginning, I actually forgot about going to the website because I uh wasn't used to, so she actually reminded me sometimes to go and do my exercise. But it was better I actually came comfortable with the site, so I was-was always there weekly (P05, male, IG)
8.1 Behavioural practice/rehearsal	Prompt practise/rehearsal of behaviour one or more times to increase skills and habit	Website	13 per-participant during 12-weeks	It was motivating for losing weight, I would say, and making changes in different ways such as eating habits, erm exercising habits, or structuring your exercising erm…(silence) the type of foods that we eat [pause] (P04, male, IG) I was getting used to it. you know, to keep you know. Logging in. To not forget. But then after that, after some time it was just click on Monday and do it…It just happens. I didn't argh I didn't do alarms and stuff; I didn't do any reminders for this. Argh after a while it was just Monday Monday Monday. It's session time. You know (P12, male, IG)
8.3 Habit formation	Prompt rehearsal and repetition of behaviour repeatedly *Code with 8.1	Website	13 per-participant during 12-weeks	*See quotes for 8.1 above, as 8.1 and 8.3 coded together as per BCCTv1
9.1 Credible source	Verbal or visual comms from a credible source for or against targeted behaviour	Both	19 per-participant during 12-weeks	that talk with physio did help me um because all you hear is hear say quite a lot, especially when you're in the kidney clinic and talking to other patients, you're not sure who, who is being honest and who's not [laughter] but it just creates more paranoia and curiosity (G03, female, IG)

			8 contacts for 4 participants	when she-she measured the muscles within me and the fat she told me that I was more muscles than the fat I was thinking of. She-she even went ahead to tell me about the % of muscles that I had so I was very very uh-u-h I actually felt very good…I actually wanted to know how I was doing so if-if-if the muscle in me and the fat in me could be measured always for me that is ok for me to know how I am doing (P05, male, IG)
11.3 Conserving mental resources	Advise on methods for reducing demands on mental resources to facilitate behaviour change	Website	3 per-participant during 12-weeks	you know I-I-I actually learnt never knew certain things. I-I-I never knew those things until I actually went to the website, and I was lectured on how to eat and how to exercise… um, um as I was doing the uh-uh muscles, the cravings the exercises, the proportions. Let's say the food label card is something I never knew about, I was supposed to buy food that was less fatty, and are certain things I actually learnt (P05, male, IG)
12.4 Distraction	Advise/arrange alternate focus to avoid triggers of unwanted behaviours	Website	2 per-participant during 12-weeks	so really- after I saw that video then I kind of changed my attitude. I realised that if you are feeling cravings, it is not because you are hungry, and I can take my mind off it by occupying my time doing something else, rather than just sitting there and giving into the cravings that I was dealing with (P06, female, IG)
15.1 Verbal persuasion about capability	Inform patient they can successfully do the wanted behaviour and they will succeed	Website	1 per-participant during 12-weeks	Because it was like straight after my transplant, so I wasn't like 100% perfect physically. But she made it quite easy, it didn't take much out of me to do the things she asked… :it was excellent She's excellent. She made me feel comfortable (P06. Female, IG, during assessment)

Note. BCT= behaviour change techniques, BCTTv1= behaviour change taxonomy version 1 as per Michie et al (2014a)

* Indicates where quotes may cover multiple BCTs as per the BCTTv1guidance

Contacts for the website intervention were presented as the potential number per participant if completing the 12-week intervention. Whereas frequencies of BCT's for the interactions with the research fellow are presented as the number of contacts that were provided (total) and the number of participants

Qualitative data was added were available. BCT= behaviour change technique and PA= physical activity

7.5.3 Potential implications for policy

The digital landscape is forever changing (Murray 2016). There is a need for research to be disseminated, and competed within a timely, robust fashion (Murray et al., 2016). There are ethical considerations regarding funding allocation, funding constraints, and avoiding duplication of digital healthcare intervention research (West & Michie, 2016). During this PhD thesis, particularly during the feasibility RCT, the research fellow encountered contract delays as it was one of the first digital behaviour intervention studies requiring contracts with a software company in the sponsoring site. As digital healthcare is an immerging research speciality, the research community would benefit from establishing a stronger infrastructure to support clinical academics, HCP and researchers wishing to engage with software companies to research digital healthcare interventions.

The NIHR are currently working on developing a national digital strategy (NIHR, 2021b) and are engaging with stakeholders (Nother, 2021). To addressed the increased demand for digital-research infrastructure our trust have since included digital research as one of the key outcomes for the research priorities (King's College Hospital, 2019). Subsequently, a digital research officer has been appointed to the R&I office to facilitate digital research, contracts, and discussions around intellectual property.

The COVID-19 pandemic has accelerated the interest and delivery of virtual service delivery and tele-health in the renal community (Stauss, Floyd, Becker, Ponnusamy, & Woywodt, 2021). However, in the UK to date no national tariff for virtual clinics exists (Stauss et al., 2021), which warrants further exploration by commissioners and stakeholders. The UK Kidney Research Consortium (UKKRC) is a collaborative group

formed by the leading UK renal organisations and a kidney charity. The UKKRC's aim is to:

> Facilitate the best collaborative clinical research for health in kidney disease (Kidney Research UK, 2021a)

To address the expanding research into digital healthcare, and the need for evaluation, the UKKRC have recently set up a new workstream focusing on the UK Renal MedTech Research (Kidney Research UK, 2021b). The research fellow has been appointed the deputy co-lead for the UKKRC digital workstream. These new workstreams (NIHR and UKKRC) should contribute to facilitating infrastructure to support researchers creating and evaluating digital healthcare interventions in the future.

The Cochrane review by Stevenson et al (2019), recommended given the low quality evidence for e-health interventions for people living with CKD, further research with interventions that utilise theoretical frameworks, self-monitoring and personalised education are warranted. As highlighted by our systematic review, and subsequent chapters in this thesis, research exploring the use of online delivery of interventions to support KTRs requires further investigation. Further infrastructure is required to support research to conduct research into the effectiveness of digital healthcare interventions. Engagement with end-users, stakeholders, clinicians and commissioners is requires so clinicians and commissioners have tariffs to address digital healthcare interventions to allow for evaluation of cost effectiveness.

7.6 Chapter summary

This chapter has provided evidence of how this thesis has addressed each of the five objectives, contributing to the two aims:

1. To create on online intervention to address weight gain in new kidney transplant recipients

2. To explore the feasibility and acceptability of the online intervention for new kidney transplant recipients

Strengths and limitations and implications for both clinical practice, future research, and policy have been suggested. Figure 7.1 on the following page presents an updated version of the thesis processes and depicts the suggestions for a post-PhD multi-centre pilot RCT (in grey).

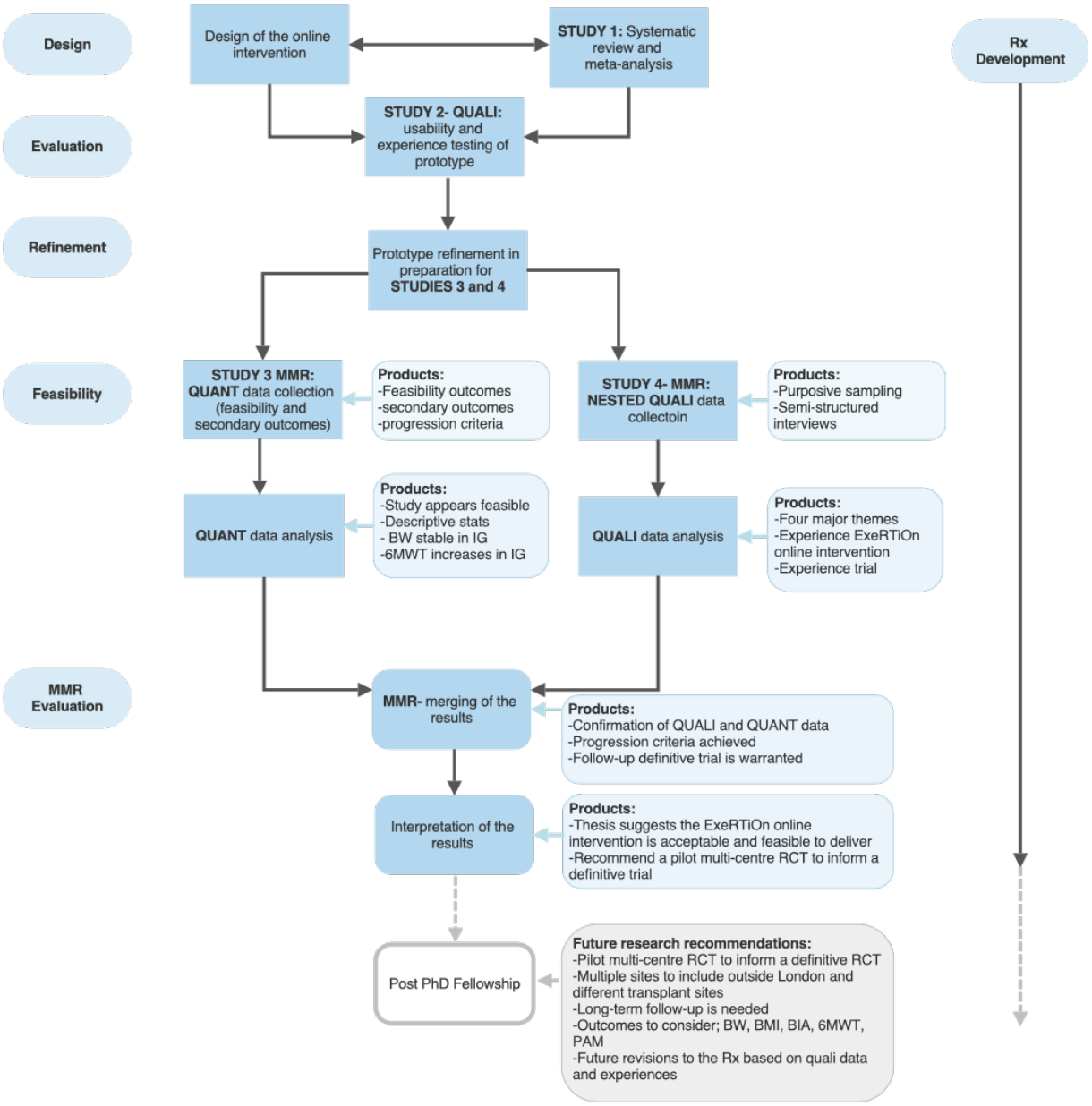


Figure 7-1 Updated thesis process diagram to depict the thesis findings (blue) and suggestions for future research (grey)

Note. The thesis process diagram has been updated to reflect the interpretations of the results (shown in blue) and the suggestions for post PhD research (shown in grey).

Rx= intervention, QUANT= qualitative, QUALI= qualitative, MMR= mixed methods research.

This figure was designed based on a combination of the convergent mixes-methods flow diagram (Creswell & Plano Clark, 2018a, p. 76) and concepts from the MRC framework for design and evaluation of complex interventions (Craig et al., 2008).

Chapter 8 Thesis conclusions

Weight gain is a clinical issue for KTRs, particularly during the first year of receiving a new kidney transplant. Despite clinical guidance to recommend access to support from specialist HCPs (such as renal dietitians and physiotherapists), no treatment is available to support new KTRs with weight gain prevention. Most importantly, new KTRs have asked for interventions to support them with this issue.

The systematic review presented in chapter 2 highlighted the lack of evidence that dietary, exercise, or combined interventions led to significant changes in body weight or BMI post kidney transplantation. The number and quality of intervention studies were low, with variable intervention design. Further RCT's were suggested to evaluate the immediate and longer-term effects of combined interventions on body weight in new KTRs.

This thesis sought to address aims and objectives regarding the design, acceptability, and feasibility of an online intervention, specifically designed to address weight gain prevention for new KTRs. Therefore, the ExeRTiOn online intervention was designed by a multi-professional group (including patient input), led by the research fellow, informed by the combined intervention design, focusing on the person-based approach. Transparent reporting of the design, development, and intervention components of the ExeRTiOn online intervention should facilitate future evidence synthesis, replication and contribute to the evidence base. Findings from studies 2, 3 and 4 presented in this thesis suggest the ExeRTion online intervention is acceptable to our KTRs, and it is feasible to conduct a RCT using the ExeRTiOn online intervention.

Potential implications from the thesis findings have been presented. A multi-centre pilot RCT is required post-PhD to evaluate uncertainties regarding multi-centre delivery of the online intervention, and to inform a power calculation for a definitive RCT trial. The COVID-19 pandemic has seen an acceleration of digital and virtual healthcare provision. Evaluation of effectiveness and cost-effectiveness of digital interventions to support weight gain prevention is required. The current work underway in the UK creating specific workstreams to support digital research from the NIHR, and the UKKRC should facilitate infrastructure to support further research in this field.

Chapter 9 References

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Appendix A. Systematic Review documents (Study 1)

- Completed PRISMA checklist
- Search strategy example (Medline database)
- Screening form
- Table summarising the detailed sample characteristics
- Table summarising the study characteristics of the non-RCT studies (n=6)
- Table summarising interventions in non-RCT studies
- Risk-of-bias plots for non-RCT's
- Post-hoc sensitivity analysis

A completed PRISMA checklist for the systematic review and meta-analysis presented in study 1(chapter 2).

SOURCE: *From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	53
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	51,52
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	52,53
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	52,53
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Pg 53, Appendix A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	53-56
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	56
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix A (medline search)

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	56-57, Appendix A study screening form
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	57-58
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	57-58
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	57, 79, Appendix A ROB non-RCT's
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	57-58
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	57-58, meta-analysis found on page 80-82

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	79, Appendix A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	83, Appendix A sensitivity analysis (post hoc)
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	86-89

			PRISMA flow diagram page 60
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 2.2 and 2.3 page 63-72
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	79, Appendix A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Meta-analysis 80-82
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	80-82
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	79, Appendix A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	83, Appendix A sensitivity analysis (post hoc)
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	86-89

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	91-92
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	92
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Declaration page 16

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Search strategy example using Medline database (systematic review, chapter 2)

Platform: OvidSP

Database coverage: 1946 to present

Limits: 1985, English

Date of search: 26th June 2020. The search was re-run on the 6th of April 2021 in all databases and the PRISMA diagram and systematic review chapter was updated.

Search Terms: see below, Mesh terms adapted to fit database

Search line number	Searches	Result
1	exp Kidney Transplantation/	92244
2	(kidney adj3 transplan*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	102708
3	(renal adj3 transplan*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	48156
4	exp Diet Therapy/	51883
5	diet* therap*.mp.	60692
6	diet* modification*.mp.	3285
7	diet* intervention*.mp.	7883
8	diet* treatment*.mp.	9923
9	nutrition treatment*.mp.	191
10	nutrition intervention*.mp.	2346
11	exp Exercise Therapy/	46650
12	exercise* therap*.mp.	39158
13	exercise* rehab*.mp.	698
14	exercis* interventio*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	5364
15	exp Exercise/	180448

16	exercis*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	358637
17	activit* physical.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	915
18	physical activit*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	102929
19	training exercis*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1606
20	exp Behavior Therapy/	70594
21	behavio?r therap*.mp.	32036
22	behavio?r modification*.mp.	2896
23	conditioning therap*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	502
24	(behavio?r adj2 change).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	16862
25	(behavio?r adj2 technique*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1746
26	behavio?r change technique*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol	791

	supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	
27	weight gain prevention.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	264
28	weight gain treatment*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	39
29	exp Obesity/	198824
30	obesity.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	299884
31	exp Weight Gain/	30126
32	(weight adj1 gain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	72620
33	(weight gain or loss).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	967411
34	weight change*.mp.	10682
35	(body weight adj2 (gain or loss or change)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	21027
36	((bmi or body mass index) adj2 (gain or loss or change)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	4261
37	exp Body Weight/	441621

38	(body adj2 weight*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	344949
39	1 or 2 or 3	110856
40	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	637509
41	29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38	1508242
42	39 and 40 and 41	217
43	limit 42 to (english language and yr="1985 -Current")	188

Screening form (Systematic review, chapter 2)

Review Question: Weight gain prevention interventions in Kidney transplant recipients, a systematic review				
Inclusion criteria:	• **Population-** This will be defined as new Kidney Transplant recipients within the first year following surgery • **Intervention**- treatments to prevent weight gain (either singular or combined of physical activity or exercise advice, nutritional/dietician advice and or behavioural change techniques) • **Comparator**-usual care/ standard care • **Outcome**- weight gained post-transplant (baseline to six months or baseline to 12 months). • **Study type**- randomised controlled trials, systematic reviews, non-randomised controlled trials or quasi-randomised controlled trials.			
Author name and year				
Title and journal				
Full text papers include or exclude paper		**Include**	**Exclude**	**Notes**
Population	New Kidney Transplant Recipient	□ kidney transplant recipient (within first year)	□ Kidney transplant recipient > 1 year □sample includes other CKD participants	
Outcome	Primary outcome: Weight gain	□baseline weight provided □follow up weight provided	□ no reporting of body weight at baseline □no reporting of weight at follow up (either 3, 6 or 12 months)	
Outcome	Secondary outcomes	□body weight as secondary outcome □reports BMI □Bioimpedance □ physical function □mood □ self-efficacy □physical activity	□no recording of body weight □no recording of secondary outcomes listed	

Study design	Study type	□ randomised controlled trials □ non randomised controlled trials	□ studies with no control group
Intervention	Weight gain prevention intervention	□ includes an intervention aimed to prevent weight gain (either singular or combined of physical activity or exercise advice, nutritional/dietician advice and or behavioural change techniques) □ include interventions measuring body weight and BMI (combined, physical activity or nutritional)	□studies that include a drug in the intervention group
Other factors	Publication year and language	□English □studies > 1985	□ exclude papers not in English □ exclude papers published before 1985
Overall decision	**□ Included**		**□ Excluded**

Table summarising the detailed sample characteristics (systematic review, chapter 2)

RCT's are presented first (n=10) followed by the non-RCTs (n=6)

Study primary author, year and country or origin	Specifics of sample	Group (Usual care= RCTs, comparators= non-RCTs)	Sample at start of the study (n)	Dropouts (n and %)	% Males	Age M ± SD	KTx vintage (mean in months)
		RCT's (n=10)					
Lawrence 1995 (UK)**(Lawrence et al., 1995)**	• Hyperlipidaemic KTRs • Diabetics excluded	Total sample	38	NI	NI	NI	NI Mean. Randomised after KTx
		Intervention	22	NI	59%	50 (range 20-70*)	
		Usual care	16	NI	22%	56 (range 31-71*)	
Painter † 2002 and 2003(Painter et al., 2003) (USA)	• Excluded if physical limits to exercise or psych issues	Total sample	167	70 (42%) ‡	NI	NI	NI mean. Recruited one month after KTx
		Intervention	54	29	55.5%	39.7±12.6	
		Usual care	43	41	69.1%	43.7±10.7	
Tzvetanov 2014(Tzvetanov et al., 2014) (USA)	• KTRs with BMI > 30 • Excluded if unable to participate in exercise	Total sample	17	6 (35.3%) ‡	NI	NI	NI mean. Rehab started 8.6±6.2 months after KTx
		Intervention	9	0	50%	46.6±6.9	
		Usual care	8	6	37.5%	45±19	
O'Connor †		Total sample	46	4 (8.7%)	58.7%	51.8±12.5	6.58±4.51

2017 and Greenwood 2015 (UK)	• Long-term follow up ExeRT trial cohort (Greenwood et al., 2015) • 42/60 cohort followed up at 12 months (9 months after cessation Rx. • 3 groups: AT, RT and UC • Pragmatic inclusion criteria	Intervention 1 (AT)	13	1	77%	53.9±10.7	6.09±4.86
		Intervention 2 (RT)	13	3	54%	54.6±10.6	7.39±5.13
		Usual care	20	0	50%	49.5±10.6	6.37±4.0
Henggeler 2018 (NZ)	Excluded if BMI > 40 or < 18.5.	Total sample	37	11 (29.7%)‡	69.4%	NI	NI mean. Recruited within the first month of KTx
		Treatment	19	6	67%	49.2±14.6	
		Usual care	18	5	72%	48.3±13.9	
Kuningas 2019(UK)	KTRs without diabetes	Total sample	130	27 (20.8%)	54.6%	NI	NI mean total sample
		Treatment	66	10	43.7%	47.7±13.1	≈ 8±6 months
		Usual care	64	17	56.5%	47.4±13.7	≈8±5 months
Karelis 2016(Canada)	• KTRs without diabetes • Non smokers • Low ETOH Sedentary (< 2hrs exercise/week)	Total sample	24	4 (16.66%)	50%	NI	NI mean. KTx 6-8 weeks earlier
		Treatment	12	2	50%	45.3±14	
		Usual care	12	2	50%	39.4±8	
Schmid-Mohler 2019 (Switzerland)	• combined KTR and kidney-pancreas transplants (n=123) • n=120 KTR	Total	123§ (120 KTR)	3 (2.5%)§	61.8%§	50.2±13.1§ (50.5±13.1) KTR)	NI mean. Recruited < 6 weeks post Tx
		Usual care	62§ (60 KTR)	1 (1.6%)§	62.9%§	49.8±12.6§	

		Treatment	61[§] (60 KTR)	2 (3.3%)[§]	60.7%[§]	50.5±13.8[§]	
Serper 2020 (USA)	• combined sample of KTR and liver transplant recipients (n=127 • n= 65 KTRs	Total	127[§] (65 KTR)	10 (7.8%)[§]	64%[§]	52±13[§]	9.5 (3-17)[§¶]
		Usual care (Arm1)	42[§] (20 KTR)	1 (2.4%)[§]	64%[§]	50±15[§]	8.4 (3.7-16)[§¶]
		Device only (Arm 2)	44§ (22 KTR)	4 (9%) [§]	68%[§]	53±12[§]	6.5 (3-13) [§¶]
		Treatment and device (Arm 3)	41§ (23 KTR)	5 (12.2%)[§]	58%[§]	54±13[§]	13 (4-19) [§¶]
Gibson 2020(USA)	• KTRs recruited between 6-12 months post-transplant (n=10) • included if BMI ≥ 22kg/m^2, able to participate in study visits over the trial length, English speakers, able to report data weekly (either by phone, email or fax) and access to the internet. • Exclusion criteria includes unwillingness to be	Total	10	1	5 (50%)	44.6±10.0	NI on mean. However recruitment of participants within 6 to 12 months post kidney transplant
		Usual care	5	0	2 (40%)	44.0±11.0	
		Treatment	5	1	3 (60%)	45.2±10.2	

		randomized, participation in weight management or physical activity programme.

Note. RCT indicates randomised controlled trial, M= mean, SD=standard deviation, KTR= kidney transplant recipient, numbers indicate references (see list below), KTx= kidney transplantation, NI- no information, BMI=body mass index, Rx= treatment, AT= aerobic training, RT= resistance training, UC= usual care

*= standard deviation not provided and unable to be calculated

†= study with two publications from the same research study

‡ = significant dropouts, data only given for those who completed follow up

§= data from transplant combined sample

¶= median and IQR provided by authors, only in publication

**= standard deviations manually calculated

Study primary author, year and country or origin	Specifics of sample	Group (Usual care= RCTs, comparators= non-RCTs)	Sample at start of the study (n)	Dropouts (n and %)	% Males	Age M ± SD	KTx vintage (mean in months)
		Non RCT's (n=6)					
Leasure 1995(Leasure et al., 1995) (USA)	• 18-64 years • Willing to attend 3x week exercise for 12 weeks • Quasi-experimental two group repeated measure design	Total sample	8	3 (37.5%)‡	Not reported	NI	NI mean. Started trial 8 weeks post KTx
		Treatment	2	Not reported	Not reported	NI	
		Comparator	3	Not reported	Not reported	NI	
Patel 1998 (UK)	• Stable KTR • Comparison group received no treatment	Total sample	33	NI	69.7%	NI	NI mean. KTx 2months
		Treatment	11	NI	81.8%	39±17	
		Comparator	22	NI	63.6%	40±11	
Jezior 2007(Poland)	• Treatment group= KTR Recruited from weight reduction programme (mean BMI 33.35kg/m^2). i.e. KTRs living with excess weight or obesity	Total sample	452	NI	NI	NI	NI
		Treatment	34	NI	NI	NI	NI
		Comparator	418	NI	NI	NI	NI

	• Comparator group monitored weight records for 56 months (mean BMI 25.9 kg/m^2)						
Sharif 2008 (UK)	• KTR, grouped depending on their glucose tolerance. N=36 glucose intolerance did intensive Rx, n=79 control (leaflet) • No diagnosis of Diabetes	Total sample	115	4(3.5%)	76.3%	NI	NI Mean. Recruited 6months and later after KTx
		Treatment	36	4	79%	55 ±12** (SEM2)	
		Comparator	79	0	75%	50±17.78** (SEM2)	
Teplan 2014(Teplan et al., 2014) (Czech Republic)	• 1st KTx (cadaveric) • Excluded if recent cardiac event, cannot have smoked within the past 3 years	Total sample	238	16 (6.7%)	53.8%	NI	NI Mean. Recruited within first 6months KTx
		Treatment	116	8	49.2%	58±7	
		Comparator	122	8	53.8%	55±8	
Lorenz 2015(USA)	• Single KTR only (no combined Tx) • Comparator group from 2 years earlier (post-hoc analysis)	Total sample	307	NI	57%	51±13	NI mean. First visit within 3 weeks of KTx
		Treatment	145	NI Note adherence Rx 36.5%	57.2%	51±14	
		Comparator	162	NI	56.8%	52±13	

Note. RCT indicates randomised controlled trial, M= mean, SD=standard deviation, KTR= kidney transplant recipient, numbers indicate references (see list below), KTx= kidney transplantation, NI- no information, BMI=body mass index, Rx= treatment, AT= aerobic training, RT= resistance training, UC= usual care

*= standard deviation not provided and unable to be calculated

†= study with two publications from the same research study

‡ = significant dropouts, data only given for those who completed follow up

§= data from transplant combined sample

¶= median and IQR provided by authors, only in publication

**= standard deviations manually calculated

Table summarising the characteristics of the included non-RCT studies (n=6) (systematic review, chapter 2)

First author, year (country of origin)	Study duration (months)	Sample	Groups	Outcomes (primary and secondary)	Results (for primary and secondary outcomes)	Comments
Leasure et al (1995) **(USA)**	6	n=8 KTRs	**IG:** Exercise only for 12 weeks **IG2:** Initial 12 weeks no exercise, then exercise 12 weeks	**Primary:** Not stated **Secondary:** BC (hydrostatic weight and bioimpedance), strength (Cybex dynamometer), mean arm muscle area (skinfolds), endurance exercise tolerance test, nutritional assessment (4-day food diary), BW, BMI, and symptoms frequency distress scale for medication side effects	**Primary/secondary:** • Increased fat weight (4%) initial post-transplant phase • No between-group difference BW or BC • Both groups gained fat weight and reduced lean weight. • No consistent between-group difference in strength at 20 weeks • No participants reached VO^2max • No between-group difference in distress scale for medication • All participants reported elevated appetite and difficulty following a low calorie/fat/salt diet	• Small sample size with dropouts (3 dropouts) • Convenience sampling • AEs not reported • Limited reporting • No longer-term follow-up • Descriptive statistics due to limited sample size
Patel et al (1998) **(UK)**	12	n=33	**IG:** Dietitian-led intensive dietary education for 4 months **CG**: Post-hoc controls receiving no dietary advice. From 4 years earlier	**Primary:** weight gain and BMI at 4 months and 1-year post KTx **Secondary:** BW, height, BMI, diet histories (subjective assessment by dietitian), PA	**Primary:** • Significant between-group difference in BW and BMI at 4- and 12-months favouring IG • 5.5kg weight gain in IG vs 11.8kg in CG **Secondary:** • Increased self-reported PA IG	• AEs not reported • Confounding variables not controlled for • Limited reporting • Control group was from KTRs 4 years earlier who had not

					• IG decreased high fat and sugar food and increased fruit and veg (diet histories)	received dietary intervention • Limited trial reporting contributing to 'no-information' score for risk-of-bias
Jezior et al (2007) **(Poland)**	6	n= 452, n=34 IG	**IG:** Ax with education on the harms of weight gain, and then dietary advice 2nd visit **CG**: Retrospective controls 4.5 years after KTx . no specific information given.	**Primary:** Not stated **Secondary:** BW, waist/hip/thigh circumference, bioimpedance skinfold tests and 3-day dietary history	**Primary/secondary:** • 27% IG increased BW during 6-months vs 80% CG during 4.5years • IG demonstrated a mean weight loss of 2kg in 6-months with an associated reduction in BMI • CG demonstrated a weight gain of approx. 0.62kg per six months	• AEs not reported • Preliminary results of a weight reduction programme • IG were included OW and OB KTR enrolled from a weight loss programme • No further publications • Limited reporting • No between-group testing of BW • Difficult to compare groups as significant difference in time since transplant (6 months IG vs 4.5 years CG)
Sharif et al (2008) **(UK)**	Mean follow-up 8.2	n=115 KTR, grouped dependin g on GT	**IG:** IGT patients. Given Diet and exercise for 6 months **CG**: Normal GT. Given	**Primary:** change in GT **Secondary:** BW, height, self-reported PA	**Primary:** • Significant within group difference in the IG with a significant reduction in 2-hr postprandial glucose levels (*P*=0.012)	• Only KTRs with no diagnosis of PTDM were eligible • Participants allocated to groups based on GT

			education about the risks of IGT and received leaflets on healthy lifestyle and exercise		• Significant within group increase in glucose levels (P=0.001) in CG **Secondary:** • Good adherence IG throughout the study with 100% adherence to the dietitian visits, 94% completed food diary, and 88% maintained exercise diary • No significant changes in BW in either group • Significant within-group difference in self-reported PA in both groups, IG appeared to have a higher gain in PA	• AEs not reported • Unclear number of Rx visits • Preliminary work for the CAVIAR trial by Kuningas 2019 (Kuningas et al., 2019)
Teplan et al (2014) **(Czech Republic)**	6	n=238	**IG:** 6-months ET (AT) **CG**: Matched controls, no ET	**Primary:** ADMA (blood marker for risk of cardiovascular disease) **Secondary:** blood lipids, HbA1C. Insulin, BP, Height, BW	**Primary:** • Significant between-group difference favouring IG vs UC for reduced ADMA levels **Secondary:** • No significant difference in HbA1c, insulin, BP or blood lipids between groups • Significant between-group difference in BMI and waist circumference with an increase in the CG compared with IG (P<0.02)	• AE not reported • BW not reported • Reasons for dropouts (n=12) at 6-months not reported
Lorenz et al (2015) **(USA)**	12	n=307	**IG:** 90 days pedometer and PA **CG:** Post-hoc controls, no PA Rx	**Primary:** Adherence to Rx **Secondary:**	**Primary:** • IG adherence to PA prescription was 36.5% • 44.8% of IG returned PA diaries	• AEs not reported • Low adherence to Rx prescription 36.5%

	Metabolic parameters (HTN, hyperlipidaemia, PTDM), renal bloods	**Secondary:** • No significant between-group difference between groups for 4-month weight gain, PTDM, lipids, or kidney function • Lower BP at four-months post KTx IG vs CG • Less impaired fasting glucose IG vs CG (between-group analysis, *P*=0.04) • Adherent IG participants were less likely to gain weight (*P*=0.01)	• Additional data (SD) provided by authors on request • BMI not reported

Note. KTRs= kidney transplant recipient, IG= intervention Group, CG= control group, BW= body weight (kg), BMI= body mass index (kg/m2),AE=adverse event, Ax= assessment, GT= glucose tolerance, IGT= impaired glucose tolerance, PA= physical activity, AT= aerobic training, ADMA=asymmetric dimethylarginine, HbA1c=haemoglobin A1c, BP= blood pressure, HTN= hypertension, PTDM= post-transplant diabetes mellitus and SD-= standard deviation, vs=versus

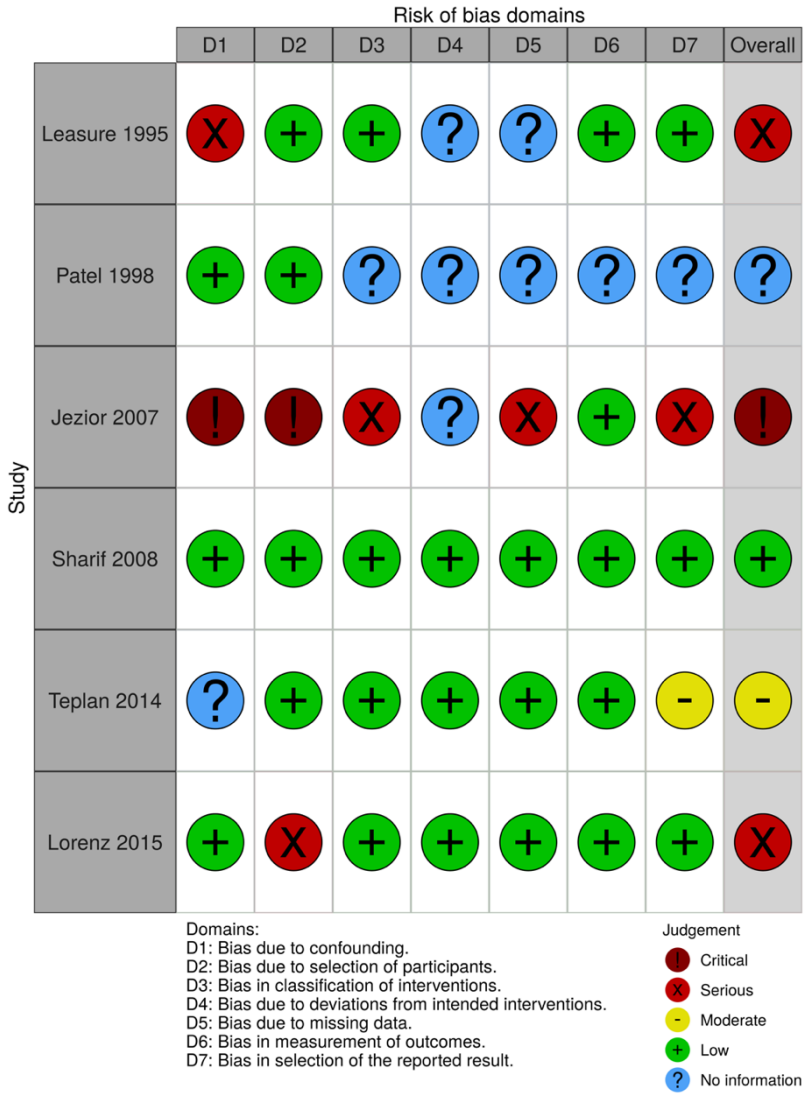
Table summarising interventions in non-RCT studies

Study	Rx type	Rx Description	Rx Behaviour components	Provider	Duration	Frequency	Intensity	Type of ET	Time (in mins)
Leasure 1995	Exercise	• ET started 8 weeks after KTx • Progressed from 30 to 60 minutes • Mode: F2F	• NI	PT	12 weeks	36 sessions/ 12 weeks, 3x week, 1x week supervised	AT based on HR; RT based on Ax	AT + RT	30-60
Patel 1998	Diet	• Verbal and written edu on exercise and healthy lifestyle • edu on snacks, shopping, convenience foods, stress, weight management, alcohol and smoking • Mode: NI, assume F2F	• Goal setting (BCT) for diet or weight loss	RD	4 months	NI	NA	NI	NI
Jezior 2007	Other (measures and edu)	2 x F2F visits: • Visit 1=measures taken (weight, height, waist, bioimpedance, skinfolds, dietary questionnaires) and edu on negative effects of obesity • Visit 2= dietary guidance (limited information reported)	• Information about health consequences of obesity on mortality after transplant	Phys	NI	2x visits over 6 months	NA	NA	NA

Sharif 2008	Combined	• Lifestyle edu • Multiple components • Healthy eating edu based on Diabetes UK guidelines • Graded ET • Food and exercise diaries • Mode: NI, assume F2F	• Self-monitoring (diaries)	RD	6 months	RD= NI sessions ET=2hrs per week	NI	AT=walking, jogging, swimming	AT 120 minutes/ week
Teplan 2014	Exercise	• Cycling on stationary bikes • Mode: F2F	• NI	Phys	6 months	2-3x week (1x week independent)	60-70% difference in HR	AT	60
Lorenz 2015	PA	• Prior to discharge participants in Rx group given a pedometer and recording sheet for 90 days • Mode: F2F to give pedometer, steps taken independent	• Self-monitoring behaviour (PA)	Self-directed	90 days (≈2.96 months)	Daily	Advised to walk as many steps as possible in 20 mins	AT= walking	20

Note. Rx indicates treatment, ET= exercise training, edu=education, F2F=face-to-face, NI= no information, RD= renal dietitian, NA= not applicable, KTx= Kidney transplant, PT= Physiotherapist, Ax=assessment, AT= aerobic training, HR= hear rate, RT= resistance training, BCT= behaviour change techniques, HRM= heart rate max, Phys.= Physician, 1:1= one on one (individual treatment), CBT= cognitive behavioural therapy, P.Tr= Personal trainer, PA= physical activity, 1RM= one repetition maximum, UC= usual care, HRR- heart rate reserve, reps= repetitions, SMART goals= specific measurable achievable realistic and timed goals, Ex. Phys= Exercise Physiologist, PTDM= post-transplant diabetes mellitus, and APN= advanced practice nurse

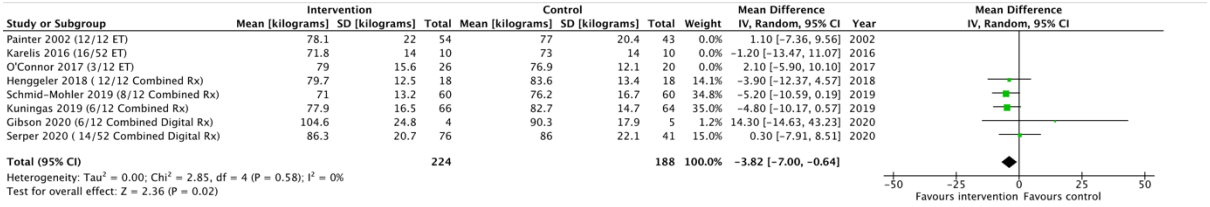
Risk-of-bias plots for non-RCT's (systematic review, chapter 2)



Post-hoc sensitivity Analysis

To explore the relationship between the type of intervention (exercise, diet or combined) and BW and BMI, the following sensitivity analyses were performed.

1. Combined interventions and post-intervention BW (5 RCT's)

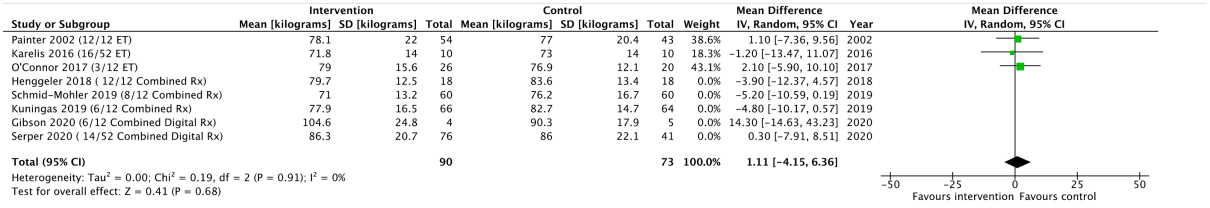


Study or Subgroup	Intervention Mean [kilograms]	SD [kilograms]	Total	Control Mean [kilograms]	SD [kilograms]	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Painter 2002 (12/12 ET)	78.1	22	54	77	20.4	43	0.0%	1.10 [-7.36, 9.56]	2002
Karelis 2016 (16/52 ET)	71.8	14	10	73	14	10	0.0%	-1.20 [-13.47, 11.07]	2016
O'Connor 2017 (3/12 ET)	79	15.6	26	76.9	12.1	20	0.0%	2.10 [-5.90, 10.10]	2017
Henggeler 2018 (12/12 Combined Rx)	79.7	12.5	18	83.6	13.4	18	14.1%	-3.90 [-12.37, 4.57]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	71	13.2	60	76.2	16.7	60	34.8%	-5.20 [-10.59, 0.19]	2019
Kuningas 2019 (6/12 Combined Rx)	77.9	16.5	66	82.7	14.7	64	35.0%	-4.80 [-10.17, 0.57]	2019
Gibson 2020 (6/12 Combined Digital Rx)	104.6	24.8	4	90.3	17.9	5	1.2%	14.30 [-14.63, 43.23]	2020
Serper 2020 (14/52 Combined Digital Rx)	86.3	20.7	76	86	22.1	41	15.0%	0.30 [-7.91, 8.51]	2020
Total (95% CI)			**224**			**188**	**100.0%**	**-3.82 [-7.00, -0.64]**	

Heterogeneity: Tau² = 0.00; Chi² = 2.85, df = 4 (P = 0.58); I² = 0%
Test for overall effect: Z = 2.36 (P = 0.02)

Mean Difference IV, Random, 95% CI
-50 -25 0 25 50
Favours intervention Favours control

2. Single interventions (ET only) and post-intervention BW (3 RCT's)

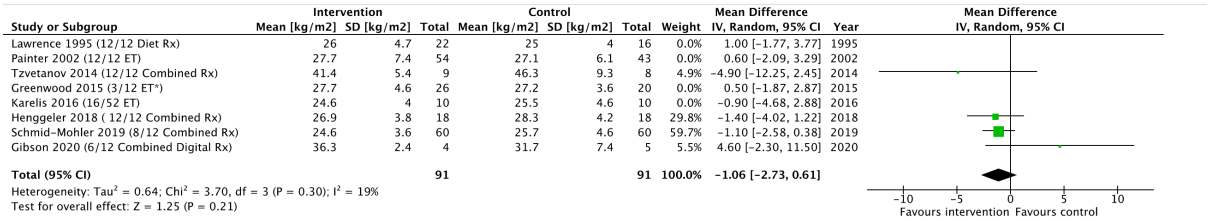


Study or Subgroup	Intervention Mean [kilograms]	SD [kilograms]	Total	Control Mean [kilograms]	SD [kilograms]	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Painter 2002 (12/12 ET)	78.1	22	54	77	20.4	43	38.6%	1.10 [-7.36, 9.56]	2002
Karelis 2016 (16/52 ET)	71.8	14	10	73	14	10	18.3%	-1.20 [-13.47, 11.07]	2016
O'Connor 2017 (3/12 ET)	79	15.6	26	76.9	12.1	20	43.1%	2.10 [-5.90, 10.10]	2017
Henggeler 2018 (12/12 Combined Rx)	79.7	12.5	18	83.6	13.4	18	0.0%	-3.90 [-12.37, 4.57]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	71	13.2	60	76.2	16.7	60	0.0%	-5.20 [-10.59, 0.19]	2019
Kuningas 2019 (6/12 Combined Rx)	77.9	16.5	66	82.7	14.7	64	0.0%	-4.80 [-10.17, 0.57]	2019
Gibson 2020 (6/12 Combined Digital Rx)	104.6	24.8	4	90.3	17.9	5	0.0%	14.30 [-14.63, 43.23]	2020
Serper 2020 (14/52 Combined Digital Rx)	86.3	20.7	76	86	22.1	41	0.0%	0.30 [-7.91, 8.51]	2020
Total (95% CI)			**90**			**73**	**100.0%**	**1.11 [-4.15, 6.36]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.41 (P = 0.68)

Mean Difference IV, Random, 95% CI
-50 -25 0 25 50
Favours intervention Favours control

3.Combined interventions and post-intervention BMI (4 RCT's)

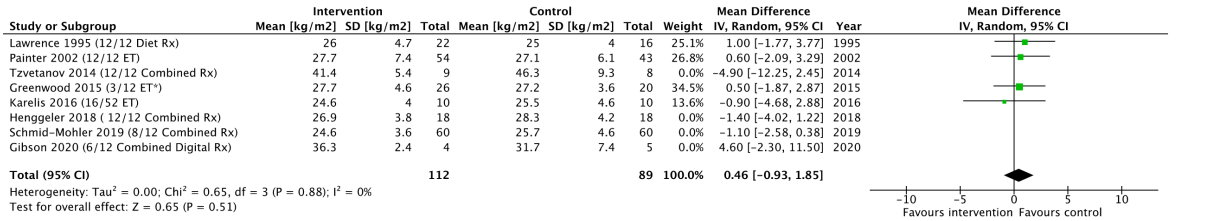


Study or Subgroup	Intervention Mean [kg/m2]	SD [kg/m2]	Total	Control Mean [kg/m2]	SD [kg/m2]	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Lawrence 1995 (12/12 Diet Rx)	26	4.7	22	25	4	16	0.0%	1.00 [-1.77, 3.77]	1995
Painter 2002 (12/12 ET)	27.7	7.4	54	27.1	6.1	43	0.0%	0.60 [-2.09, 3.29]	2002
Tzvetanov 2014 (12/12 Combined Rx)	41.4	5.4	9	46.3	9.3	8	4.9%	-4.90 [-12.25, 2.45]	2014
Greenwood 2015 (3/12 ET*)	27.7	4.6	26	27.2	3.6	20	0.0%	0.50 [-1.87, 2.87]	2015
Karelis 2016 (16/52 ET)	24.6	4	10	25.5	4.6	10	0.0%	-0.90 [-4.68, 2.88]	2016
Henggeler 2018 (12/12 Combined Rx)	26.9	3.8	18	28.3	4.2	18	29.8%	-1.40 [-4.02, 1.22]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	24.6	3.6	60	25.7	4.6	60	59.7%	-1.10 [-2.58, 0.38]	2019
Gibson 2020 (6/12 Combined Digital Rx)	36.3	2.4	4	31.7	7.4	5	5.5%	4.60 [-2.30, 11.50]	2020
Total (95% CI)			**91**			**91**	**100.0%**	**-1.06 [-2.73, 0.61]**	

Heterogeneity: Tau² = 0.64; Chi² = 3.70, df = 3 (P = 0.30); I² = 19%
Test for overall effect: Z = 1.25 (P = 0.21)

Mean Difference IV, Random, 95% CI
-10 -5 0 5 10
Favours intervention Favours control

4. Single modality interventions and post-intervention BMI (4 RCT's)



Study or Subgroup	Intervention Mean [kg/m2]	SD [kg/m2]	Total	Control Mean [kg/m2]	SD [kg/m2]	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Lawrence 1995 (12/12 Diet Rx)	26	4.7	22	25	4	16	25.1%	1.00 [-1.77, 3.77]	1995
Painter 2002 (12/12 ET)	27.7	7.4	54	27.1	6.1	43	26.8%	0.60 [-2.09, 3.29]	2002
Tzvetanov 2014 (12/12 Combined Rx)	41.4	5.4	9	46.3	9.3	8	0.0%	-4.90 [-12.25, 2.45]	2014
Greenwood 2015 (3/12 ET*)	27.7	4.6	26	27.2	3.6	20	34.5%	0.50 [-1.87, 2.87]	2015
Karelis 2016 (16/52 ET)	24.6	4	10	25.5	4.6	10	13.6%	-0.90 [-4.68, 2.88]	2016
Henggeler 2018 (12/12 Combined Rx)	26.9	3.8	18	28.3	4.2	18	0.0%	-1.40 [-4.02, 1.22]	2018
Schmid-Mohler 2019 (8/12 Combined Rx)	24.6	3.6	60	25.7	4.6	60	0.0%	-1.10 [-2.58, 0.38]	2019
Gibson 2020 (6/12 Combined Digital Rx)	36.3	2.4	4	31.7	7.4	5	0.0%	4.60 [-2.30, 11.50]	2020
Total (95% CI)			**112**			**89**	**100.0%**	**0.46 [-0.93, 1.85]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 3 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.65 (P = 0.51)

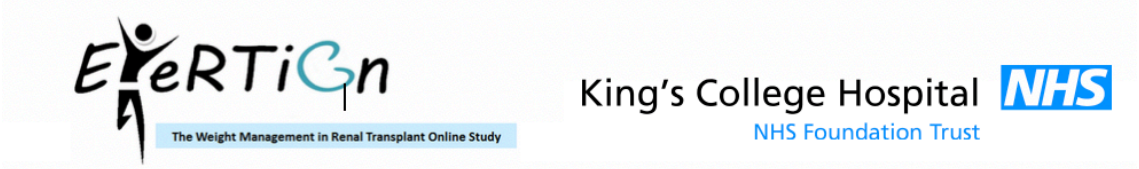
Mean Difference IV, Random, 95% CI
-10 -5 0 5 10
Favours intervention Favours control

Appendix B. Study 2 documents

- Protocol study 2
- Ethical approval
- Patient information sheets (kidney transplant recipients and healthcare professional participants)
- Data security and privacy document
- Consent forms (kidney transplant recipients and healthcare professional participants)

* Topic guides are included in chapter 4 as supplementary material to the publication

Protocol for study 2 (usability and experience testing of the online intervention prototype)



PROTOCOL

FULL TITLE: A study to assess the acceptability of an online weight prevention programme for new kidney transplant recipients - The wEight in Renal Transplant Online Study (ExeRTiOn).

Short Title: The wEight management in Renal Transplant Online Study- ExeRTiOn

Chief Investigator:
Dr Sharlene Greenwood- Consultant Physiotherapist, King's College Hospital.

Student and Principal Investigator:
Ellen Castle - Senior Renal Physiotherapist, King's College Hospital

Supervisors:

1. Dr Sharlene Greenwood- Consultant Renal Physiotherapist, King's College Hospital.
2. Dr Joseph Chilcot- Health Psychology unit, Institute of Psychiatry, Psychology & Neuroscience (IoPPN)
3. Professor Iain Macdougall, Consultant Nephrologist King's College Hospital.

Co-investigators:

1. Dr Helen MacLaughlin- Consultant Renal Dietitian, King's College Hospital.
2. Fiona Sharples- Transplant Matron, King's College Hospital.
3. Emmanuel Mangahis- Senior Research Nurse, King's College Hospital.
4. Jennifer Barsana- Senior Research Nurse, King's College Hospital.

This trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirements.

Appendix C.

Sponsor Representative: Liba Stones, R&D Manager, King's College Hospital

Funder: King's College Hospital

Study Site: King's College Hospital, London, SE5 9RS

Table of Contents

1 INTRODUCTION

The primary aim of this project is to create an online weight management tool (Physical activity, weight management and cognitive behavioural therapy) to prevent significant weight gain following kidney transplantation. Designing the online interactive weight management resource for kidney transplant patients will involve patient and health care professional input through Qualitative methodology such as 'Think-Aloud' interviews and one-to-one semi-structured interviews. This online resource will be called "exertion" and will be created by the research team, with technical support from the SPIKA Software Company.

Results from this study will refine the resource, and lead to a study application for a randomised controlled feasibility trial where we plan to test the "exertion" online application. Therefore this project has potential to influence clinical practice for kidney transplant recipients. It will allow patients, who may not have routine access to physio or dietetic input to address weight gain with support. A study flow chart summarising the project can be found below.

1.1 STUDY FLOW DIAGRAM ExeRTiOn

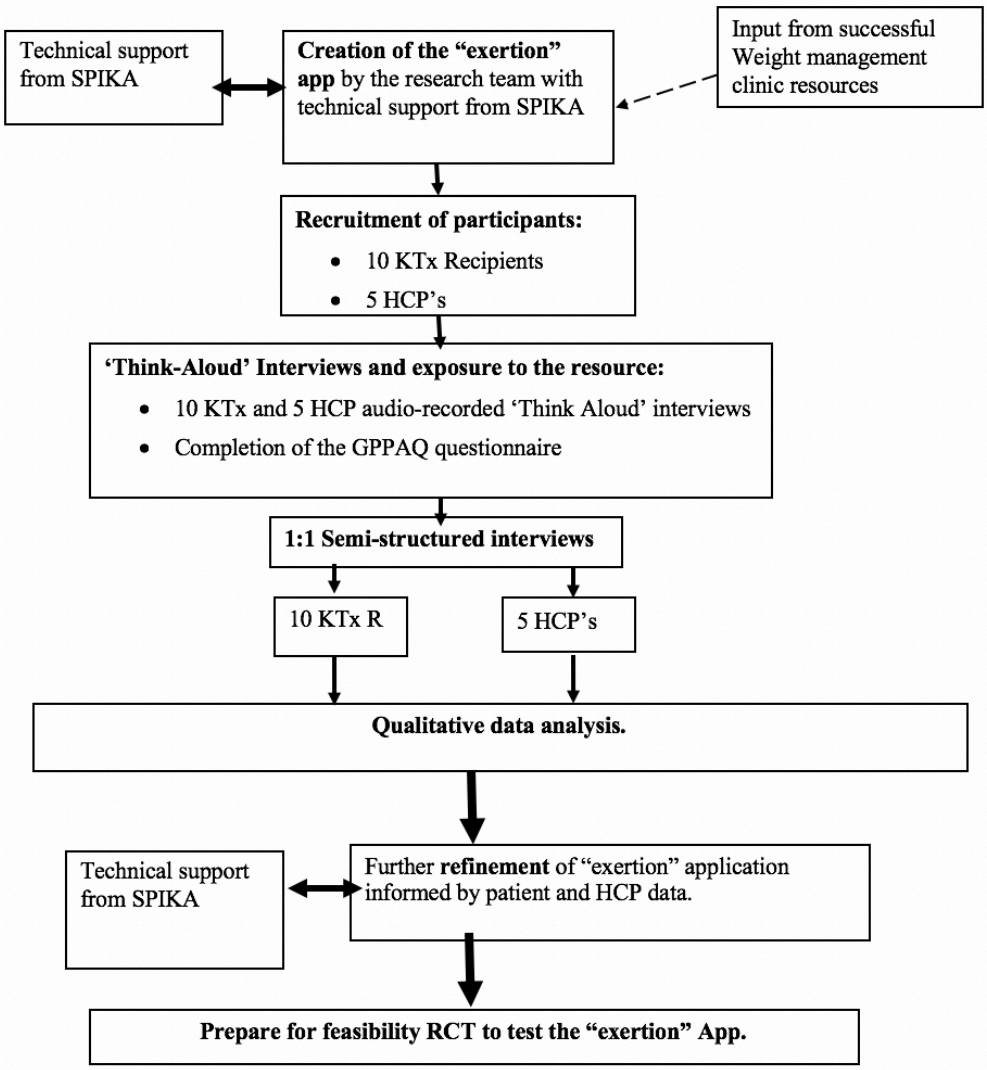


Figure 1. Study flow diagram.

2 BACKGROUND AND RATIONALE

Physical activity and exercise play a beneficial role in maintaining the health of those with chronic illnesses however poor physical functioning among patients with chronic kidney disease (CKD) is well recognised (1, 2). Kidney Transplantation (KTx) is an effective treatment option for life threatening end-stage kidney disease and becomes cost-effective over the average lifespan of the transplant, although it is not without associated risk. The use of modern immunosuppression therapies have improved the life-expectancy of the kidney graft; however, there is a high prevalence of diabetes, cardiovascular disease and obesity (3, 4). It has been established that recipients of KTx increase their physical activity level in the subsequent years after transplantation due to improved quality of life; however, within that time they do not reach the level of physical activity of those of age-matched healthy controls (5). A reason for this is that despite the reversal of many of the prevailing uraemic symptoms following KTx, functional capacity remains compromised due to a combination of prior deconditioning, uraemic myopathy, muscle atrophy and muscle pathology as a result of immunosuppression therapy (6, 7).

Weight gain is a significant and real issue for kidney transplant recipients (8, 9). Obesity remains a widespread issue for KTx recipients with an estimated two thirds of the population being overweight or obese (8). Research suggests that patients who gain more than 15% of their initial weight during the first year after receiving a kidney transplant, they have a higher chance of dying from conditions not related to their kidney function within ten years (9). Although weight gain and maintaining a programme of activity are real concerns for KTx recipients, they are not routinely offered specialist physical activity or weight management programmes in the UK. There are some community schemes for exercise and weight management available. However kidney transplant patients report they are not always understanding of the specific issues surrounding kidney transplantation. Extra appointments, travel time, and return to work where highlighted as barriers to participate in our supervised kidney transplant study (10). Robust research reviews suggest that online behavioural weight management interventions can help people regulate food intake and activity, and on average can lead to clinically meaningful weight loss (11, 12). Therefore there is a need to create an online weight management and physical activity tool, specific to KTx recipients, imbedded with cognitive behavioural therapy and motivational interviewing methods to address post-transplant weight gain. I would like to create this app with input from the research team, kidney transplant patients, and health care professionals (HCP's) working in the transplant team at a South London Teaching Hospital.

2.1 Primary Objective

To create a patient focused online weight management and physical activity tool for new transplant recipients called "exertion".

2.2 Secondary Objectives

a) To explore the current themes through qualitative data collection:

- Components of the "exertion" resource that are helpful/ unhelpful
- Any difficulties/ barriers to using the "exertion" application

- Any difficulties/ barriers to participating in the study
- Strengths of the "exertion" resource
- Weaknesses of the resource
- Patient experience and learning using the online resource
- Transplant health care professional experience and knowledge reviewing the online resource

b) to explore self-reported physical activity levels through the General Physical Activity (GPPAQ) questionnaire(13-16). The GPPAQ questionnaire is a short, self-administered, validated questionnaire allowing classification into physical activity index categories. It has low patient burden as it can be completed in twenty to thirty seconds (14).

3 STUDY DESIGN

This study is a qualitative study and intervention planning study to create and refine an online resource for weight management in new kidney transplant recipients, which will be named "exertion".

3.1 Objectives and hypothesis:

The aim of this qualitative study is to use qualitative methods to create and refine a weight management, exercise/ physical activity online resource for patients with kidney transplant recipients.

This study involves data collection via:

- Think-aloud interviews- Participants (10 KTx recipients and the 5 HCP's) will start the one off study visit by completing a 'think-aloud' interview using the exertion online resource. This will be audio-recorded as well as observational notes collected by the researcher
- After the 'Think-aloud' interviews, participants will then complete a semi-structured interview.
- Demographic data including age, gender, occupation, smoking history, medical history, medication lists and baseline body weight (kg).
- Website/ resource log in data
- Self-reported physical activity levels using a brief, self-administered questionnaire (GPPAQ) will be captured through the exertion website
- Field notes and observations from Think Aloud interviews and semi-structured interviews

We aim to recruit 10 new kidney transplant (KTx) recipients and 5 transplant health care professionals (HCP) to explore the following themes through 'Think-Aloud' interviews:

- The functionality of the "exertion" online resource for KTx recipients
- The functionality of the "exertion" online resource from a HCP perspective

- KTx participants interpretation of the "exertion" modules and resource as a whole
- HCP participants interpretation of the "exertion" modules and resource as a whole
- Thought processes involved to use the "exertion" application
- Recommendations from participants
    - Likes/dislikes
    - Barriers/ easier to use sections
- Highlight individual differences in the use of the "exertion" resource

We aim to explore the following themes through semi-structured individual interviews and focus groups:

- What components of the online resource (exertion) are helpful/ unhelpful from a kidney transplant perspective
- What components of the online resource are helpful/unhelpful from a kidney transplant HCP perspective
- Are there any difficulties/ barriers participating in the study?
    - And are they what were expected or different?
- Patients experiences and learning using the online application, and when the changes were noticed
- Anything missing/ they would recommend adding to the application.

Trial duration per participant: One study visit.

Estimated total trial duration: 13 months in total to create resource and have it reviewed by patients and health professionals (7 months to create, 3 months to test and 3 months to refine).

3.2 The "exertion" Online Resource

The "exertion" (exercise in renal transplant online) resource will be created by the research team, including physiotherapists and dietitians working in renal specific weight management, with technical software support from SPIKA Company. This is a single centre study at King's College Hospital recruiting 10 kidney transplant recipients and 5 health care professionals from the transplant clinical team. As this study will involve patient interviews and qualitative data, ethical approval will be sought.

The resource will include individually tailored physical activity (PA) (e.g.: walking and cycling), recorded using a pedometer or smart phone apps. PA will be based on current guidelines recommending a minimal amount of 1000 kcal/week expended for health benefits, with optimal benefits associated with 1500-2000kcal/ week. Dietary information from the existing weight management programme at King's College Hospital (KCH) will be accessible to the patients online, including resources like "managing cravings", "goal setting" and "problem solving". The intervention will involve monthly web-based sessions that will

start at 6 weeks post transplantation and continue until 12 months post-transplant surgery. For the purpose of this current study, participants will only have access to the online application in a one of session to review and refine the resource. It is clinical practice at our centre for KTx recipients to be cleared to resume structured physical activity post ureteric stent removal which occurs approximately 6 weeks post-surgery.

The packages will focus on modelling prescribed PA and healthy eating advice, and will involve cognitive behavioural techniques to support behavioural change. Recognised behavioural change techniques will be used which will include goal setting, evaluating outcome expectancies and values, self-regulation action planning), and behaviour monitoring will form the core principles. The sessions will also aim to increase treatment self-efficacy (physical activity) and reduce fear avoidance (using basic acceptance and commitment therapy principles). Tailored feedback will include encouragement and virtual rewards if maintaining weight. Weight gain will trigger initial referral to an automated recovery package. This package will be built into the interventional platform and automatically activate given an increase in weight. The nature of this package is to ensure that following weight gain, the patient remains engaged with this interventional programme and will provide additional behavioural support. The online tool will be accessible either online, or via a smart phone or tablet as a health application (app).

We plan for the resource to allow participants to select modules to work through on a monthly basis over a 12 month period. Behavioural change tools and resources will be embedded within the "exertion" resource. For this current study, participants will access the online exertion resource at a one off supervised research visit. Participants will not have exposure or access to this online resource outside this study visit. The main modules will include information and interactive text on the following areas:

1. Managing cravings and prednisolone
2. Goal setting for activity and food planning
3. Portion sizes and the NHS healthy plate
4. Patient examples of strategies to plan activity (physical activity planning)
5. Patient examples of strategies to eating out/ holidays with low fat diets (food planning)
6. Reading food labels and making healthy food choices
7. Identifying barriers
8. Problem solving
9. Relapse prevention
10. Planning for the future

To ensure the modules are interactive, participants will be asked questions relating to:

- Number of steps and self-reported physical activity levels
- Weight, height, BMI
- Portion sizes
- Individual SMART goals regarding food and activity. The participants will be asked if they have achieved these set goals.
- Problem solving questions for activity and food

- Rating the importance and confidence in ability to make changes to food an activity using a VAS (visual analogue scale)
- -Reported physical activity levels through the GPPAQ questionnaire. The GPPAQ questionnaire has been built into the online resource.

4 STUDY SCHEDULE

Assessments:

After written consent is received, participant's demographic baseline information at entrance to the trial will be recorded. Study participants (10 KTx recipients and 5 HCP) will undergo 'Think-aloud' interviews to assess the usability of the exertion resource. Usability is defined as how easily someone can use and interact with the online system without any formal training (17). The research team plan to conduct 'Think-aloud' interviews and semi-structured interviews in the 15 participants or until data saturation is achieved. 'Think-aloud' interviews provide a valid source of data concerning participant thinking as the participant is asked to vocalise as they perform a task, supervised by the researcher (18). Therefore in this study, the main researcher will record verbatim from participants as they talk out loud whist accessing and using the exertion resource. The researcher will also record field observation notes during the think aloud interviews. Verbal speech and site log in data will be recorded from these sessions. We estimate these interviews will take 60-90 minutes. During exposure to the website during the 'Think-Aloud' interviews, participants will be asked to complete a short self-reported physical activity questionnaire (GPPAQ) via the website. This questionnaire involves 3 brief questions on self-reported validated physical activity and it has been shown to be simple to use, time friendly and reliable (14-16).

After the 'Think-aloud' participants will complete a one-on-one semi-structured interview to review their thoughts and experiences on using the exertion resource. Please refer to summary of study flow diagram on page 5 and schedule of assessment (Table 1) below. Having the semi-structured interviews on the same day as the 'Think-aloud' interviews or the reviewing of the resource will minimise patient burden and recall bias. Topic guides have been devised for the 'Think-aloud' and semi-structured interviews. These may evolve as the study progresses.

Table 1- Schedule of Assessment

Procedure	Recruitment	Visit 1
Screening and informed written consent	X	
Medical history and demographics		X
'Think-Aloud' interviews: - 10KTx - 5 HCP		X

- Estimate 60-90 minutes total		
GPPAQ questionnaire (self-reported physical activity)		X
Semi structured individual interviews (n=10 KTx, n=5 HCP)		X

4.1 Distress protocol

As participants will be discussing exercise and food intake whilst using the online resource and during the semi-structured interviews the team have devised a distress protocol (modified from Distress Protocol for qualitative data collection, C.Haigh and G. Witham, Department of Nursing Manchester Metropolitan University).

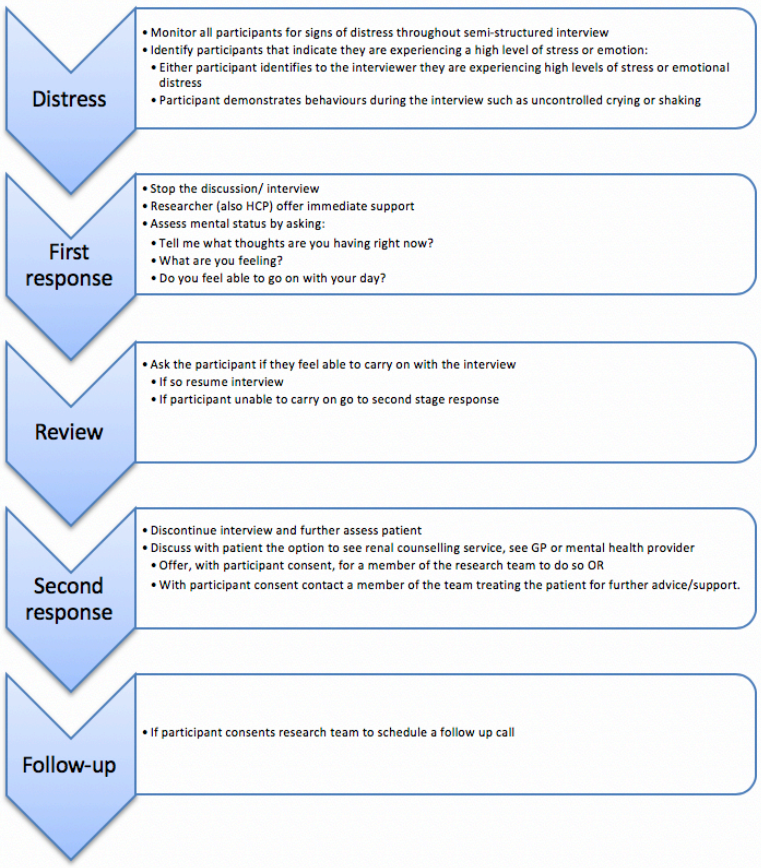


Figure 2. Distress Protocol

5 CONSENT

Patients will be screened and identified by clinicians working in the transplant team, and also the main researcher (EC). Potential participants will initially be provided with patient information sheet (the current Research Ethics Committee (REC) and Health Research Authority (HRA) approved version) and a covering letter explaining the trial to them and inviting them to participate in the trial. The research team will meet the potential participants face to face during their clinical visit to offer the patient information letter and cover letter. They will have time to consider the trial and decide whether or not they wish to take part, and to discuss the trial with their family and friends if they would like to. If they are non-English speakers, they will be offered the opportunity to discuss the study in detail and ask any questions via the language line phone translation service. Transplant staff members will also be approached and provided with the information sheet, cover letter and ample time to consider consenting to the trial (a minimum of 24 hours).

At their next clinic appointment, potential KTx participants will have plenty of time to discuss the trial further and to have any questions that they may have about the trial answered from a member of the research team. The nature and requirements of the trial will be carefully explained. The investigator will explain that there is no obligation for a potential participant to enter the trial, that trial entry is entirely voluntary, and that it is up to the potential participant to decide whether or not they would like to join. It will also be explained that they can withdraw at any time during the trial, without having to give a reason and that their decision will not affect the standard of care they receive. Any reasons for non-participation will be recorded if the information is volunteered.

Participants if willing to participate will be consented as per the GCP guidelines. Only adults above the age of 18, with capacity to consent will be accepted into the study. Non-English speakers will be consented via language-line phone translation service. The participant and responsible clinician will sign the informed consent form and the responsible clinician will perform a final confirmation of eligibility. Informed consent will be obtained before any trial-related procedures are undertaken. A copy of the signed informed consent form will be given to the participant. The original signed form will be retained at the study site in the Investigator Site File and a copy placed in the medical notes. A copy will also be sent to the Chief Investigator of the study. With KTx participant's prior consent, their General Practitioner (GP) will also be informed of their participation of the study.

6 ELIGIBILITY CRITERIA

Participants will be included based on the following inclusion and exclusion criteria. Those who are ineligible, or decline to participate will be captured on the secure and encrypted recruitment and screening log.

6.1 Eligibility criteria for the KTx recipient participants (n=10)

6.1.1 Inclusion criteria:

- Adult patient (18 years+)
- male or female
- Able to provide written informed consent

- < 3 months post-transplant. NB. Our team has decided to recruit patients within the first three months post transplants as most patients at our centre are not cleared to start a formal physical activity or exercise plan until they have ureteric stents removed which usually occurs at 6 weeks post-transplant surgery.
- Access to Internet connected computer, smart-phone or tablet. NB. Our team has completed a waiting room survey and our patients often use internet to view their clinical blood results through "renal patient view", therefore do not perceive internet access as a barrier to this study.
- A Body Mass Index (BMI) greater than or equal to 18.5 (healthy range).

6.1.2 Exclusion criteria:

- Age < 18 years of age
- Pregnancy
- Unstable medical conditions such as angina, uncontrolled hypertension or diabetes, congestive cardiac failure, active myocarditis, cardiac arrhythmia, co-morbid catabolic condition, psychiatric illness.
- Participated in a structured exercise or physical activity intervention in the last three months
- BMI of less than 18.5 (classified as underweight)
- Significant cognitive impairment preventing them from engaging with online interactive material

6.2 Eligibility criteria for the Transplant Health Care Professionals (n=5)

6.2.1 Inclusion criteria:

- A nephrologist, kidney doctor, nurse or member of the multi-disciplinary team who actively work with kidney transplant patients at King's College Hospital
- Adult above 18 years of age
- Able to provide written consent
- Access to Internet connected computer, smart-phone or tablet.

6.2.2 Exclusion criteria:

- Pregnancy
- Unstable medical conditions such as angina, uncontrolled hypertension or diabetes, congestive cardiac failure, active myocarditis, cardiac arrhythmia, co-morbid catabolic condition, psychiatric illness.

7 RECRUITMENT

7.1 Selection of Participants

All participants will be recruited from King's College Hospital renal outpatients. Potential participants will be identified when presenting for their routine post-transplant hospital clinic visits by the transplant clinical team. Patients who fulfil the inclusion criteria will have their eligibility confirmed by the research team. Each patient must meet all of the inclusion criteria, and none of the exclusion criteria at entry to the trial. After confirming eligibility, eligible patients will be approached by an appropriately trained member of the research team who routinely work in the transplant clinic, to ascertain interest in entering the study. This individual (likely to be either the PI or CI of the study) 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. Screening logs will be kept on the secure "renal physio" drive and will be encrypted for confidentiality. All eligible and ineligible patients, plus those declining to participate will be logged on the secure screening log.

Throughout the trial duration, participants will be encouraged to ask questions and will be reminded that they can withdraw at any time without their clinical care being affected. No payment is to be offered to the participants taking part in the trial.

8 STATISTICAL METHODS

8.1 Sample Size

We will interview a purposive sample of KTx patients to include a range of gender and age. We will aim to also recruit a purposive sample of kidney transplant HCP. 'Think-aloud' interviews produce large amounts of rich data and usability problems. Therefore this research team aims to do think aloud interviews on 10 KTx recipients and 5 HCPs.

Individual semi-structured interviews will utilise appropriate topic guides that will be developed and discussed with the patient advisory group, and the steering group. We will continue with individual interviews until we reach data saturation, there is no new data, no new themes, no new coding and we are able to replicate the study (19, 20).

8.2 Statistical Analysis

Baseline demographics of the patients will be described using summary statistics. Continuous variables will be summarised using the mean and standard deviation (SD) if approximately normally distributed. Continuous variables that are not normally distributed will be summarised using the median and IQR.

Qualitative analysis: Data will be collected through in-depth feedback about our online intervention materials; field notes, individual interviews and 'Think-aloud' interviews. 'Think-aloud' interviews will be used to elicit participants' reactions to sessions of the online intervention; participants will be observed and asked to comment aloud on reactions to every aspect of the different sessions. Semi-structured interviews will explore participants' overall impressions of the online intervention. These qualitative techniques will allow for themes and sub-themes to emerge. The website will be designed to record user entries, and observational field notes about participants' use of the intervention will also be collected. Individual interviews will be transcribed verbatim and analysed using an inductive thematic analysis approach (21), informed by techniques of grounded theory (19), including line-by-line open coding grounded in data and constant comparison of all instances of codes. Deviant case codes will be employed to ensure that perspectives that diverge from dominant trends are not overlooked.

8.3 Randomisation procedures

There is no randomisation in this study.

9 PATIENT AND PUBLIC INVOLVEMENT (PPI)

Patient and public involvement is crucial for developing and evaluating this resource. Our renal care group is fortunate to have a group of patients from across the Chronic Kidney Disease trajectory in our research group. They have reviewed all associated study documentations to ensure it is appropriate for patients. This group of patient experts will also assist in reviewing lay summaries for dissemination of research.

PPI is crucial to this project to create and refine a resource for the patients by transplant patients and members of the transplant HCP team.

10 FUNDING

The research team has been awarded £25,000 to create the "exertion" resource through the King's College Hospital charity fund. The team are in the process of applying to the Allied Health Professional Kidney Research UK (KRUK) Fellowship. If successful, this fellowship would cover the student's salary, study fees. If the team are unsuccessful in securing the KRUK grant, this study will be absorbed by the renal rehab team with adjusted time-lines.

11 DATA HANDLING AND MANAGEMENT

All paper data recording sheets will be stored in lockable filing cabinets at the renal rehab team office for 5 years. Documents will also be archived using the secure iron mountain software. Electronic data spreadsheets will be kept on the private renal rehab team drive and will be password protected. All patient indefinable details (name, address, hospital number) will be removed in place of trial ID numbers.

All staff involved in this research project will ensure data is handled with strict confidentiality in line with local trust policies. Data will be reviewed regularly by the student, and monitored by the supervisors. The lead researcher (EC) will transcribe all interviews.

Information gathered from the online resource will be anonymised and protected by a secure log in feature.

12 PEER AND REGULATORY REVIEW

This study has been peer reviewed within KCH, by an independent and relevant peer reviewer/committee, the renal research governance board on the 11th of October 2017. The Sponsor has accepted these reviews as adequate evidence of peer review.

The study was deemed to require regulatory approval from the following bodies (list). Each approval will be obtained before the study commences.

- HRA
- REC

13 MONITORING AND AUDITING

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

14 INDEMNITY ARRANGEMENTS

KCH will provide NHS indemnity cover for negligent harm, as appropriate and is not in the position to indemnify for non-negligent harm. NHS indemnity arrangements do not extend to non-negligent harm and NHS bodies cannot purchase commercial insurance for this purpose; it cannot give advance undertaking to pay compensation when there is no negligence attributable to their vicarious liability. The Trust will only extend NHS indemnity cover for negligent harm to its employees; substantive and honorary, conducting research studies that have been approved by the R&I Department. The Trust cannot accept liability for any activity that has not been properly registered and Trust approved. Potential claims should be reported immediately to the R&I Office.

15 ARCHIVING

During the study, all data will be kept securely and confidentially at the Renal Physio office. After the study has ended, paper data recording sheets, the Trial Master file and patient consent forms will be kept locked and secure for 5 years. All documents will be archived at a long term storage facility (Iron Mountain) for 5 years. Data spreadsheets will be encrypted, name and contact details removed, and stored on a private renal physio team folder with limited access.

16 PUBLICATION AND DISSEMINATION POLICY

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

- Conference presentation of study process and resource design of "exertion" at either the American Society of Nephrology conference and the British Renal Society Conference
- Conference presentation of study results at either the American Society of Nephrology conference or the British Renal Society Conference
- Publication of the resource design of "exertion" resource
- Publication of the study findings

17 REFERENCES

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Appendix 1: PROTOCOL VERSIONS

Version No	Version Date	Detail the reason(s) for the protocol update
1.0	31.10.2017	Original protocol involved two phases: 1) designing resource and 2) Feasibility Randomised Controlled Trial to further test online resource. As per guidelines by the South-London REC committee, the research team has separated this study into separate applications.
2.0	11.01.18	NA this is the current version of the protocol of the qualitative study to design the exertion resource
3.0	06.03.18	Changes as per suggestions from the REC and HRA
4.1	29.10.18	Revision of method of assessment to increase rigour of the study. All participants will now complete the 'Think-aloud' interview and the brief GPPAQ questionnaire. The team are also requesting an extension on recruitment timeframe from 1st February 2019 to 1st June 2019 due to contract and software build delays. This has no financial implications to the study.

Ethical Approval documents for study 2

Health Research Authority

Dr Sharlene Greenwood
King's College Hospital
Physiotherapy Department
Denmark Hill, London
SE5 9RS

Email: hra.approval@nhs.net

23 March 2018

Dear Dr. Greenwood,

Letter of HRA Approval

Study title:	**The Weight management and Exercise in Renal Transplant Online Study- ExeRTiOn Study**
IRAS project ID:	**241928**
REC reference:	**18/NW/0124**
Sponsor	**King's College Hospital NHS Foundation Trust**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further from the HRA.

How should I continue to work with participating NHS organisations in England?
You should now provide a copy of this letter to all participating NHS organisations in England, as well as any documentation that has been updated as a result of the assessment.

This is a single site study sponsored by the site. The sponsor R&D office will confirm to you when the study can start following issue of HRA Approval.

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland, Scotland and Wales?
HRA Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland, Scotland and Wales.

If you indicated in your IRAS form that you do have participating organisations in one or more devolved administration, the HRA has sent the final document set and the study wide governance report (including this letter) to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with Northern Ireland, Scotland and Wales.

How should I work with participating non-NHS organisations?
HRA Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Mrs Liba Stones
Tel: 02032991980
Email: kch-tr.research@nhs.net

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **241928**. Please quote this on all correspondence.

Yours sincerely

Kelly Rowe
Assessor

Email: hra.approval@nhs.net

Copy to: *Mrs Liba Stones, Kings College Hospital, Sponsor contact*
Mrs Ellen Castle, Kings College Hospital, Student

IRAS project ID	241928

List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
GP/consultant information sheets or letters [GP letter kidney transplant participants]	V2	31 January 2018
Interview schedules or topic guides for participants [topic guide semi-structured interviews]	V2	31 January 2018
Interview schedules or topic guides for participants [Think-aloud interviews]	V1	09 February 2018
Interview schedules or topic guides for participants [sign for think-aloud interviews]	V1	09 February 2018
IRAS Application Form [IRAS_Form_19032018]		19 March 2018
Letters of invitation to participant [letter invite V2]	V2	06 March 2018
Other [CV research team member]		
Other [Letter from South London REC meeting]		
Other [Response research team REC letter]		
Other [addressing REC and HRA comments 16.3.18]	V1	16 March 2018
Other [data recording sheet]	V3	06 March 2018
Participant consent form [HCP consent form V3]	V3	06 March 2018
Participant consent form [patient consent form V3]	V3	06 March 2018
Participant information sheet (PIS) [PIS HCP V3]	V3	06 March 2018
Participant information sheet (PIS) [PIS patients V3.]	V3	06 March 2018
Research protocol or project proposal [Protocol exertion study]	V3	06 March 2018
Summary CV for Chief Investigator (CI) [CI CV (SG)]	V1	31 January 2018
Summary CV for student [CV main researcher EC]		
Summary CV for supervisor (student research) [CV JC]		

Summary of HRA assessment

The following information provides assurance to you, the sponsor and the NHS in England that the study, as assessed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing, arranging and confirming capacity and capability.

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	Single site NHS sponsored study, no additional agreements expected. Applicant has confirmed that the IP arrangements are currently being organised between King's College Hospital and SPIKA software company.
4.2	Insurance/indemnity arrangements assessed	Yes	No comments
4.3	Financial arrangements assessed	Yes	Funding has been secured from Kings College Hospital. A funding application is pending to Kidney Research UK for the PhD Fellowship. The applicant confirms the study will continue if the application is unsuccessful.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments

Section	HRA Assessment Criteria	Compliant with Standards	Comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
There is one participating NHS site, study activities will be conducted as per protocol. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website. If Chief Investigators, sponsors or Principal Investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the Chief Investigator, sponsor or Principal Investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).
The student will act as PI at site. GCP training is not a generic training expectation, in line with the HRA/MHRA statement on training expectations.

IRAS project ID	241928

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
As site is also sponsor, it is anticipated that existing contractual arrangements are in place.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

North West - Greater Manchester Central Research Ethics Committee

3rd Floor
Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 0207 104 8019

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

12 November 2018

Mrs Ellen Castle
Senior Renal Physiotherapist
King's College Hospital
Physiotherapy Department
Se5 9RS

Dear Mrs Castle

Study title:	**The Weight management and Exercise in Renal Transplant Online Study- ExeRTiOn Study**
REC reference:	**18/NW/0124**
Amendment number:	**SA01**
Amendment date:	**29 October 2018**
IRAS project ID:	**241928**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

The Sub-Committee found no ethical issues with this amendment.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Notice of Substantial Amendment (non-CTIMP)	SA01	29 October 2018
Other [GPPAQ]		
Other [CRF form]	3	29 October 2018

Participant consent form [HCP consent form V4. 29.10.18 draft track changes]	4.0	29 October 2018
Participant consent form [patient consent V4 29.10.18draft track changes]	4.0	29 October 2018
Participant information sheet (PIS) [PIS HCP V4.29.10.18.draft track changes]	4	29 October 2018
Participant information sheet (PIS) [PIS patient V4.29.10.18 draft track changes]	4	29 October 2018
Research protocol or project proposal [exertion protocol V4.0 29.10.18draft trackchangesGPPAQ]	4.0	29 October 2018

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our Research Ethics Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

18/NW/0124:	**Please quote this number on all correspondence**

Yours sincerely

PP: Chair

E-mail: nrescommittee.northwest-gmcentral@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *The R&D Office*
Mrs Ellen Castle, King's College Hospital

North West - Greater Manchester Central Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 08 November 2018

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mr J Addison	Retired Librarian	Yes	Vice Chair
Miss Isabelle Butcher	PhD Researcher	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Katherine Ashley	REC Manager
Ms Zainab Tauqeer	REC Assistant

Patient information sheet (kidney transplant recipient participants followed by healthcare professional participants)

King's College Hospital NHS
NHS Foundation Trust

Ellen Castle
Senior Renal Physiotherapist

Dr Sharlene Greenwood
Consultant Renal Physiotherapist

The Renal Unit
Unit 6 KCH Business Park
London, SE5 9RS

Direct Tel: 0203 299 6725
Direct Fax: 0203 299 6940

Patient Information Sheet V4. 29th October 2018

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1. Study title

The wEight management in Renal Transplant Online Study – ExeRTiOn

2. An invitation

You are being invited to take part in a research study. Joining the study is entirely up to you. Before you decide, it is important for you to understand why the research is being done and what it will involve. One of our team will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

3. What is the purpose of the study?

Weight gain is common after kidney transplantation. This is thought to be due to a combination of medications increasing your appetite, lifting of

dietary restrictions, and feeling better than before transplantation as you have a working kidney. Significant weight gain has been associated with poor health outcomes. There is currently no universally accepted treatment for kidney transplant patients. We aim to create an online health resource to help transplant patients manage their weight. With this study, we aim to get kidney transplant patients and health-care professionals in the transplant team to review and help us refine this online resource.

4. Why have I been invited?

You have been invited to take part in the study because you have received a kidney transplant recently, within the last 3 months.

5. Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. You will be able to keep this information sheet and think about taking part. You are free to discuss the information with anyone you wish including your family and friends. If you agree, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

Taking part in this research is entirely voluntary. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

6. What will happen to me if I take part?

If you agree to take part, the doctor or physiotherapist will explain the proposed study and the various things that this will involve for you. He/she will give you this information sheet and will ask you to sign the accompanying consent form so that you can be enrolled into the study. As this study involves you trialling the app and being interviewed by a member of the research team to discuss your thoughts, there are minimal associated risks. You will also be asked to complete a short questionnaire looking at your activity levels.

A typical course of events for you might be as follows:

After signing the consent form in the Clinic, you will be invited to take part in the study. The researcher will review your demographic information such as your age, gender, and occupational and job title. You will then be invited to complete a one of study visit involving reviewing the online resource with the researcher or to complete a 'Think-Aloud' interview. Think-Aloud' interview involves you trialling the resource, with a researcher observing and making notes. As you review the resource you are asked to talk out loud as you use it and comment on what you think is useful or not useful when you interact with the online resource. After this 'Think-aloud' interview, you will be asked to complete a semi-structured interview where you will have the opportunity to share your thoughts and experiences on using the app. The researcher will record your thoughts and experiences through a Dictaphone and take notes during the assessment. We estimate this one off study visit will take from 60-90 minutes.

7. What do I have to do?

If you agree to take part in this study, you will be reviewing and commenting on the online resource. You will attend a one off study visit which we will book to be on the same day as one of your kidney transplant appointments. During this study visit all participants will be asked to to complete a 'Think aloud' interview followed by a one-one interview. We estimate the total appointment will take 60-90 minutes. The study visit will take place at the clinical research facility, first floor, Cheyne Wing at King's College Hospital.

You will start the research visit with either a) the 'Think-Aloud' interview and finish with a b) interview to discuss your thoughts and experiences using the online resource.

a) The 'think-Aloud' interview: 10 Kidney transplant participants will complete the 'Think Aloud' interviews. Here the researcher will take you to a research room with a computer and provide you with a log in. You will be asked to log onto the health application to trial the app. 'Think- Aloud' interviews involve you saying out loud what you are doing whilst you do it. You will be asked to log in, and work your way through the options on the screen whilst saying what you are doing out loud. The researcher will be taking notes and audio recording the session so we can assess the usability of the online resource and see what needs to be changed. For example you might say "I am logging on and selecting my first goal…." Throughout the 'Think-Aloud interview' it is important that you keep talking out loud as you use the online resource. This helps the researcher evaluate the resource and record your experience. The researcher will

place a sign in the room to remind you to keep talking out loud as you use the online resource. Whilst you are reviewing the online resource you will be asked to complete a quick questionnaire looking at your physical activity levels.

b) The one-on-one interview: After completing the 'Think Aloud' Interview all participants will then complete an informal face to face interview with the researcher. This is your opportunity to provide your feedback and experience of using the online resource whilst it is fresh in your mind. This interview will also be audio-recorded so the researcher can evaluate the online resource. Please note all audio-recordings will be anonymised and stored securely by the research team. We will arrange this one off study visit around existing hospital appointments to minimise your travel to the hospital. Once this is completed the study visit and your involvement in the study is finished.

8. What are the possible benefits of taking part?

The main benefit is to help improve care for future patients. You will also have input into creating a patient tool "exertion" and to learn about your motivating factors for exercise. This app may have potential benefits including reducing weight gain and improving physical activity and fitness.

9. What are the possible disadvantages and risks of taking part?

If you do agree to take part in this study, there will be additional time involved to complete the one off study visit. This will involve interviews reviewing the "exertion" online resource. To minimize your inconvenience, the one off study visit will be scheduled around your routine transplant clinic appointments.

10. What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time; and if you would like to do so; please speak to your study physiotherapist or doctor.

Your decision to withdraw from the study will not affect the care you receive.

If you were to become unwell and lose the capacity to make your own decision, you will be withdrawn from the study. This means any information gathered for this study before this point will be anonymised and used for the study. You would not be asked to perform any further assessments.

If you withdraw your consent;

- Information collected about you may be used if you are happy with this.
- You can withdraw consent for all information collected to be destroyed where this is possible
- We would like to keep in contact with you through your doctor or GP so that we can know about your progress.

11. What if new information becomes available?

As we are creating a new health application, if new information becomes available, we will keep you informed throughout the duration of the study.

12. What happens when the research study stops?

When the study is over, we will send you a summary of the results and will be happy to discuss this with you further if you wish.

13. What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to your study physiotherapist who will do their best to answer your questions: Ellen Castle, 0203 299 6725.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office are below:
King's College Hospital Patient Advisory and Liaison Service (PALS) on 0203 299 9000.

Every care will be taken in the course of this study. However in the unlikely event that you are injured by taking part, compensation may be available.

In the event that something does go wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital NHS Trust but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study physiotherapist or doctor if you would like more information on this.

14. Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the study will be kept strictly confidential and secure. Data will be anonymised and may be shared with other researchers and collaborators within the research team. All paper data recording sheets will be stored securely in lockable filing cabinets at the renal rehab office for 5 years. Documents will also be archived using iron mountain software. Electronic data spreadsheets will be kept on the private renal rehab team drive and will be password protected. All patient indefinable details (name, address, hospital number) will be removed in place of trial ID numbers.
All staff involved in this research project will ensure data is handled with strict confidentiality in line with local trust policies. Data will be reviewed regularly by the student and monitored by the supervisors. Interviews will be transcribed by the main researcher, Ellen Castle. Any information collected by the online resource will be anonymised and protected by secure log in function.

15. Involvement of the General Practitioner/Family Doctor (GP)

With your consent, your GP will be informed of your involvement in the trial. Any other medical practitioners who treat you, e.g. should you be admitted to hospital for any reason, will also be informed.

16. Will you have access to my medical notes?

Relevant sections of your medical notes and data collected during the trial will be looked at, in confidence, by authorised individuals from the study team.

17. What will happen to the results of the research study?

The results will be presented at scientific meetings and also published in the scientific literature.

18. Who is organising and funding the research?

This research trial is being sponsored by King's College Hospital. One of the study team (Ellen Castle) will be working on this trial for her PhD application. Ellen is currently in the process of applying for funding to complete this project as her PhD.

19. Who has reviewed the study?

The study has been reviewed internally within the Renal Unit at King's College Hospital and has been reviewed by the Sponsor
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the North West-Greater Manchester Central Research Ethics Committee. It has also been approved by the Health Research Authority and each local hospital will also give confirmation that the study can go ahead.

20. Information on study sponsor and personal data

King's College Hospital is the sponsor for this study based in London in the United Kingdom. We will be using information from you and your renal medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. King's College Hospital will keep identifiable information on you for 5 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting the study leads Ellen or Sharlene on 0203 299 6725. Or via email:

kch-tr.exertion@nhs.net . Please also refer to the data security and privacy document for this study.

King's College Hospital will collect information from you and your medical records for this research study in accordance with our instructions.

King's College Hospital will use your name, King's college hospital number, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from King's College Hospital and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people in King's College Hospital who will have access to information that identifies you will be people who need to contact you to book your assessment or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number, hospital number or contact details.

King's College Hospital will keep identifiable information about you from this study for 5 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to research to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country and abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research (**https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/**)

This information will not identify you and will not be combined with other information in a way that could identify you or to affect your care. It will not be used to make decisions about further services available to you, such as insurance.

21. Contacts for further information

Ellen Castle
Senior Renal Physiotherapist
King's College Hospital, London SE5 9RS
0203 299 6725
Ellen.castle@nhs.net

Sharlene Greenwood
Consultant Renal Physiotherapist and Chief Investigator of this study
King's College Hospital, London, SE5 9RS
0203 299 6725
Sharlene.greenwood@nhs.net

22. Thank you

Thank you for considering taking part and taking the time to read this information sheet.
If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.

Version 4. 29th October 2018
IRAS project ID: 241928

Ellen Castle
Senior Renal Physiotherapist

Dr Sharlene Greenwood
Consultant Renal Physiotherapist

The Renal Unit
Unit 6 KCH Business Park
London, SE5 9RS

Direct Tel: 0203 299 6725
Direct Fax: 0203 299 6940

Health Care Professional (HCP) Information Sheet V4. 29th October 2018.

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1. Study title

The wEight management in Renal Transplant Online Study – ExeRTiOn).

2. An invitation

You are being invited to take part in a research study. Joining the study is entirely up to you. Before you decide, it is important for you to understand why the research is being done and what it will involve. One of our team will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

3. What is the purpose of the study?

Weight gain is common after kidney transplantation. This is thought to be due to a combination of medications increasing appetite, lifting of dietary restrictions, and feeling better than before transplantation due to having a working kidney. Significant weight gain has been associated with poor health outcomes. There is currently no universally accepted treatment for kidney transplant patients. We aim to create an online health resource to help transplant patients manage their weight. With this study, we aim to get kidney transplant patients and health-care professionals in the transplant team to review and help us refine this online resource.

4. Why have I been invited?

You have been invited to take part in the study because you are a health care professional working in the renal transplant outpatient team at King's College Hospital. The research team is also evaluating experiences of this online resource in a cohort of kidney transplant recipients.

5. Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. You will be able to keep this information sheet and think about taking part. You are free to discuss the information with anyone you wish including your family and friends. If you agree, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason.

Taking part in this research is entirely voluntary. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form.

6. What will happen to me if I take part?

If you agree to take part, the researcher will explain the proposed study and the various things that this will involve for you. He/She will give you this information sheet and will ask you to sign a consent form so that you can be enrolled into the study. As this study involves you trialling the app and being interviewed by a member of the research team to discuss your thoughts, there are minimal associated risks. You will also be asked to complete a short questionnaire looking at your activity levels.

A typical course of events for you might be as follows:

After signing the consent form in the clinic, you will be invited to take part in the study. The researcher will review your demographic information such as your age, gender, and occupation and job title. You will then be invited to review the online resource with the researcher starting with completing a 'Think-Aloud' interview. The 'Think-Aloud' interview involves you trialling the online resource, with a researcher observing and making notes. As you review the resource you are asked to talk out loud as you use it and comment on what you think is useful or not useful when you interact with the online resource. Whilst reviewing the resource, you will be asked to complete a quick questionnaire looking at your physical activity levels. Straight after the 'Think-Aloud' interview, you will be asked to complete a semi-structured interview where you will have the opportunity to share your thoughts and experiences on using the online resource. The researcher will record your thoughts and experiences through a Dictaphone and take notes during the assessment. We estimate this one off study visit will take from 60-90 minutes.

7. What do I have to do?

If you agree to take part in this study, you will be reviewing and commenting on the online resource. You will attend one study visit.
In the study visit all participants will be asked to complete a 'Think-aloud' interview followed by a one-one interview. We estimate the total appointment will take 60-90 minutes. The study visit will take place at the clinical research facility, first floor, Cheyne Wing at King's College Hospital.

You will start the research visit with a)the 'Think-Aloud' Then you will complete b) the interview to discuss your thoughts and experiences using the online resource.

a) The 'Think-Aloud' interview: All participants (10 Kidney Transplant recipients and 5 health care professionals) will complete the 'Think Aloud' interviews. Here the researcher will take you to a research room with a computer and provide you with a log in. You will be asked to log onto the health application to trial the online resource. 'Think- Aloud' interviews involve you saying out loud what you are doing whilst you do it. You will be asked to log in and work your way through the options on the screen whilst saying what you are doing out loud. The researcher will be taking notes and audio recording the session, so we can assess the usability of the online resource and see what needs to be changed. For example you might say "I am logging on and selecting my first goal…." Throughout the 'Think-Aloud interview' it is important that you keep talking out loud as you use the online resource. This helps the researcher evaluate the resource

and record your experience. The researcher will place a sign in the room to remind you to keep talking out loud as you use the online resource.

b) The one-on-one interview: After completing the 'Think Aloud' Interview, all participants will then complete an informal face to face interview with the researcher. This is your opportunity to provide your feedback and experience of using the online resource whilst it is fresh in your mind. This interview will also be audio-recorded so the researcher can evaluate the online resource. Please note all audio-recordings will be anonymised and stored securely by the research team. We will complete these assessments all together in a one off study visit at a time that is convenient for you. Once this is completed the study visit and your involvement in the study is finished.

8. What are the possible benefits of taking part?

The main benefit is to help improve care for future transplant patients. You will also have input into creating a patient tool "exertion" and to learn about your motivating factors for exercise. This app may have potential benefits including increasing knowledge of strategies to improve physical activity and adopt a healthy diet.

9. What are the possible disadvantages and risks of taking part?

If you do agree to take part in this study, there will be additional time involved to complete the one off study visit. This will be interviews reviewing the "exertion" online resource.

10. What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time; and if you would like to do so; please speak to your study physiotherapist.

If you withdraw your consent;

- Information collected about you may be used if you are happy with this.
- You can withdraw consent for all information collected to be destroyed where this is possible

11. What happens when the research study stops?

When the study is over, we will send you a summary of the results and will be happy to discuss this with you further if you wish.

12. What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to your study physiotherapist who will do their best to answer your questions: Ellen Castle, 0203 299 6725.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office are below:
King's College Hospital Patient Advisory and Liaison Service (PALS) on 0203 299 9000.

Every care will be taken in the course of this study. However in the unlikely event that you are injured by taking part, compensation may be available.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital NHS Trust but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study physiotherapist if you would like more information on this.

13. Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the study will be kept strictly confidential and secure. Data will be anonymised and may be shared with other researchers and collaborators within the research team. All paper data recording sheets will be stored securely in lockable filing cabinets at the renal rehab office for 5 years. Documents will also be archived using iron mountain software. Electronic data spreadsheets will be kept on the private renal rehab team drive and will be password protected. All patient indefinable details (name, address, hospital number) will be removed in place of trial ID numbers.

All staff involved in this research project will ensure data is handled with strict confidentiality in line with local trust policies. Data will be reviewed regularly by the student and monitored by the supervisors. Interviews will be transcribed by the main researcher, Ellen Castle. Any information collected by the online resource will be anonymised and protected by secure log in function.

14. What will happen to the results of the research study?

The results will be presented at scientific meetings and also published in the scientific literature.

15. Who is organising and funding the research?

This research trial is being sponsored by King's College Hospital. One of the study team (Ellen Castle) will be working on this trial for her PhD application. Ellen is currently in the process of applying for funding to complete this project as her PhD.

16. Who has reviewed the study?

The study has been reviewed internally within the Renal Unit at King's College Hospital and has been reviewed by the Sponsor
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by North West-Greater Manchester Central Research Ethics Committee. It has also been approved by the Health Research Authority and each local hospital will also give confirmation that the study can go ahead.

17. Information on study sponsor and personal data

King's College Hospital is the sponsor for this study based in London in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. King's College Hospital will keep identifiable information on you for 5 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting the study leads Ellen or Sharlene on 0203 299 6725. Or via email: kch-tr.exertion@nhs.net . Please also refer to the data security and privacy document for this study.

King's College Hospital will collect information from you for this research study in accordance with our instructions.

King's College Hospital will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded, and to oversee the quality of the study. Individuals from King's College Hospital and regulatory organisations may look at your research records to check the accuracy of the research study. The only people in King's College Hospital who will have access to information that identifies you will be people who need to contact you to book your assessment or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, or contact details.

King's College Hospital will keep identifiable information about you from this study for 5 years after the study has finished.

When you agree to take part in a research study, the information about your research may be provided to research to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country and abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care

Research (**https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/**)

This information will not identify you and will not be combined with other information in a way that could identify you.

18. Contacts for further information

Ellen Castle
Senior Renal Physiotherapist
King's College Hospital, London SE5 9RS
0203 299 6725
Ellen.castle@nhs.net

Sharlene Greenwood
Consultant Renal Physiotherapist and Chief Investigator of this study
King's College Hospital, London, SE5 9RS
0203 299 6725
Sharlene.greenwood@nhs.net

19. Thank you

Thank you for considering taking part and taking the time to read this information sheet. If you decide to take part in the study, we will give you a copy of the information sheet and a signed consent form to keep.

Data security and privacy document (provided with patient information sheet at time of consent)

Ellen Castle
Senior Renal Physiotherapist

Dr Sharlene Greenwood
Consultant Renal Physiotherapist

The Renal Unit
Unit 6 KCH Business Park
London, SE5 9RS

Direct Tel: 0203 299 6725
Direct Fax: 0203 299 6940

Data Security and Privacy document for The ExeRTiOn study V1 3rd August 2018

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1. Study title

The wEight management in Renal Transplant Online Study –ExeRTiOn

2. Overview

In this section we outline the data processes that happen as part of ExeRTiOn and explain what data will be collected and what happens to that data.

Handling your information securely and confidentially is extremely important to us.

As well as the data security processes we outline below, ExeRTiOn will log you out automatically after 20 minutes of inactivity.

We also recommend:

- Logging out whenever you have finished working on ExeRTiOn
- Keeping your ExeRTiOn username and password in a secure place
- Not sharing any unnecessary personal information or contact details with your guide via your online messages (this is explained in more detail below).

3. Device security

Your security and privacy on ExeRTiOn depends on the device you use to access the website. You are able to use ExeRTiOn on a computer, tablet or smartphone, as long as you are connected to the Internet.

Data Security and Privacy Document for the ExeRTiOn study
Version 1.0 3rd August 2018
IRAS project ID: 241928

To ensure maximum security, we recommend you keep your software up-to-date, choose strong passwords which are not easy to guess, use security protection software and avoid unsecured public internet connections.

4. Cookies

Most websites these days use 'cookies' to help the website run smoothly. Cookies are tiny text files that are made by the website. They provide a way for the website to remember you and the preferences you select. They are temporarily stored on your computer or device. When you come to the home screen of the ExeRTiOn website you can choose to accept all the cookies with one click or click on the 'cookie settings' for more information. When you click on the 'cookie settings' you will be able to opt-in and opt-out depending on the type of cookies you select. The software company helping King's College Hospital build this website and host this website (SPIKA) meets NHS Digital standards for privacy, confidentiality, security and General Data Protection Regulation (2018) GDPR.

5. Who developed ExeRTiOn?

A team of researchers at King's College Hospital developed ExerRTiOn. ExeRTiOn at King's College Hospital works in partnership with:

1. The NHS – a healthcare professional from the Renal Outpatients Department will have referred you to ExeRTiOn.
2. SPIKA – a software development company who programmed ExeRTiOn. SPIKA host and maintain the website. SPIKA meets NHS Digital standards for privacy, confidentiality, security and General Data Protection Regulation (2018) GDPR.

6. My personal data- what personal data/information will Exertion ask me for?

ExerRTiOn is a website. So that you can use ExeRTiOn, we need you to register with an email address. ExeRTiOn will need to ask you the following information to set up your account:

1. Your name.

2. Your email address

3. So that we can keep track of your health – we will also ask you to complete self-report questions about your goals, activity and weight.

7. My personal data- Why does ExeRTiOn need to collect this personal information?

Because ExeRTiOn provides a service for the NHS your healthcare team needs accurate and up-to-date information. Collecting this information means that your healthcare team can monitor your progress. They are able to contact you to provide you with extra support either by email, the ExeRTiOn in-site messaging service, over the telephone or by arranging an appointment to meet face-to-face.

8. Where is my data kept?

The ExeRTiOn website is hosted by SPIKA. This means that the data collected by ExeRTiOn is held on a secure database managed by SPIKA. This database is located in Ireland in a securely protected and approved provider cloud solution. SPIKA are a registered software company and are compliant with GDPR (General Data Protection Regulation 2018).

When you register for ExeRTiOn you are assigned an anonymous Exertion ID, which is stored with your data. Additionally, because your data is confidential, the data that ExeRTiOn collects is held in an encrypted state. Data is securely managed in line with NHS and GDPR policies.

9. Who can access my personal information?

So that ExeRTiOn can be used in the NHS we have to follow strict privacy, confidentiality online security procedures and including the new GDPR guidelines.

The research team, based at the Renal Unit at King's College Hospital, will only ever access your personal information. Ellen Castle, the PhD student and senior renal physiotherapist will review the data and reply to any questions you have. ExeRTiOn will never share your information with other parties without your written consent. For example, if access is needed to your ExeRTiOn account due to a technical error we will ask for your consent for a member of the technical team to do this. The main researcher (Ellen Castle) will act as gatekeeper of the data. If there are any technical issues with the website, once she asks for your consent, she can grant temporary access for SPIKA software technicians to resolve the issue.

10. Does ExeRTiOn collect other information about me?

To help the team at King's College Hospital improve the website, ExeRTiOn collects information about:

1. Length of time users spend logged in to ExeRTiOn
2. Number of sessions completed
3. Type of sessions completed
4. Number of messages sent between you and your guide (Please note the content of these messages will NEVER be seen by King's College Hospital unless you consent to this as part of a research study)
5. Completion of sessions
6. Goal setting results
7. Weight and Physical activity recordings
8. During your face to face visits with the main researcher (Ellen Castle), you will be asked to provide your date of birth, medical history, medication list, address and contact phone number. This information will not be loaded on to the ExeRTiOn website. All research records will be kept secure and confidential as per the King's College Hospital confidentiality guidelines.

This information is ALWAYS anonymous and will never include data that can identify you as an individual.

11. Does ExeRTiOn share my information with anyone else?

The study team will mark on your renalware records that you are taking part in the study.

If you have a technical problem or question, the main researcher Ellen Castle will receive the following information if you submit a question/concern via the "Contact Us" form on the ExeRTion website:

1. Your email address
2. Information you type in your message

In order to solve a technical problem, support from the SPIKA software team who programmed ExeRTiOn may be needed. We will never share your information with SPIKA or ask them to look into the problem without gaining your informed consent first.

The ExeRTiOn website will never share your personal information with anyone without your consent.

12. Links

Some sessions may contain links to other websites, which are owned, operated or maintained by third parties. If you click on a third party link, you will be directed to that website in a new tab. We provide these links as helpful sources of further information, not as an endorsement, authorisation or representation of our affiliation with that third party, nor as an endorsement of their privacy or information security policies or practices. We do not have control over third party websites and we do not have control over their privacy policies and terms of use.

13. Who can see what I write in ExeRTiOn?

When you join ExeRTiOn you will be linked to the main researcher (Ellen Castle). Your Ellen is a qualified healthcare professional who will provide you with support during your time on the programme, either by phone, online messaging or both. Ellen is part of your renal healthcare team so will be able to see your personal details, including name, date of birth, phone number and email address.

In order to ensure that her support is relevant and specific to you, and to ensure your wellbeing, Ellen will be able to see your progress on the website, i.e. which sessions you have completed and your weight and physical activity scores. She will also be able to see your goals and tasks. Additionally, she is able to see the notes you make during the sessions, as this can help structure their support.

14. The Exertion Team at King's College Hospital

Data Protection Officer for the ExeRTiOn study: Ellen Castle- Senior Renal Physiotherapist at King's College Hospital and PhD Student.

Supervisors: Dr Sharlene Greenwood and Dr Joseph Chilcot.

Data Protection Officer at King's College Hospital is: Nick Murphy-Okane

Information Governance Advisor at King's College Hospital: Jon Curtiss Green

15. The legal bits

Information collected by Exertion will in line with General Data Protection Regulation (2018). Our lawful basis for collecting this information includes:

Consent to participate in this study.

16. Your rights

Your personal data will be processed in accordance with your rights under data protection legislation.

Your rights are:

a. Right to be informed
b. Right to gain access to your data
c. Right of rectification (e.g. change inaccurate information)
d. Right to erasure (e.g. to delete records held about you on the ExeRTiOn platform)
e. Right to restriction (e.g. to stop processing information about you)
f. Right to portability (e.g. to move or transfer your data)
g. Right to object (e.g. to change your mind)
h. Right not to be subject to automatic profiling or decision making (e.g. to know if a decision was made by a computer rather than a person)

17. Summary

Your personal information will be managed and shared in line with the General Data Protection Regulations (2018), Data Protection Act 2018 and common law duty of confidentiality.

1. The ExeRTiOn website will ask for personal information. This information will be stored in line with NHS Digital data privacy and security standards.
2. ExeRTiOn is developed and owned by King's College Hospital and is a provider for the NHS and follows NHS Digital data privacy and security standards.
3. The ExeRTiOn website will collect anonymous information about the length of time spent logged in to ExeRTiOn, number of online sessions completed, and number of online messages sent. This information will be used by research team at King's College Hospital to improve the ExeRTiOn website.
4. Filling in the ExeRTiOn contact us form, means your email address and typed message will be seen by the main researcher (Ellen Castle).
5. If you experience a technical problem, Ellen Castle at King's College Hospital will respond to your concern and gain your consent for the web-developers of ExeRTiOn to access my information.

If you have any concerns or further questions, please contact the ExeRTiOn team using the form, which you can find in 'Contact Us.' Or you can send an email to:

kch-tr.exertion@nhs.net

You can find more tips for staying safe online at www.cyberaware.gov.uk.

Consent forms (kidney transplant recipient participants followed by healthcare professional participants)

Ellen Castle, Senior Renal Physiotherapist
Dr Sharlene Greenwood, Consultant Renal Physiotherapist
The Renal Unit, King's College Hospital
London, SE5 9RS
Direct Tel: 0203 299 6725 / Direct Fax: 0203 299 6094

A study to assess the acceptability of an online weight prevention programme for new kidney transplant recipients- The wEight management in Renal Transplant Online Study (ExeRTiOn).

ExeRTiOn Study

Patient ID……

Please Initial below

1.	I confirm that I have read and understand the Participant Information Sheet (Version 4.0 Dated 29th October 2018) I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw from study treatment at any time, without necessarily giving any reason, and without my medical care or legal rights being affected.	
3.	I understand that sections of any of my relevant medical notes and data collected during the trial will be looked at, in confidence, by authorised individuals from the study team at King's College Hospital NHS Foundation Trust, my NHS Trust, King's Clinical Research Facility, as well as by regulatory authorities, to check that the study is being carried out correctly. I give permission for these individuals to have access to my records.	
4.	I confirm that I have read and understand the data security and privacy document (Version 1.0 Dated 3rd August 2018) and understand how my data will be used and stored. .	
5.	I understand that if I withdraw from the study, no further data will be collected for the study. With your consent, data collected from when you participated in the study will be used and kept anonymised.	
6.	I agree to my GP being informed of my participation in the study.	
7.	I agree to the interviews being audio-taped and used anonymously for research purposes. I understand that the recording will be treated as confidential, stored securely and destroyed once the results of the study have been published.	
8.	I understand the researchers may use direct quotations from the interviews in publications, but that these will be anonymous, and it will not be possible to identify me from any quotations used.	
9.	I agree to take part in the study	

Signature of patient		
& **PRINTED** name		Today's date: dd/mmm/yyyy
Signature of person taking consent: & **Printed** name		Today's date: dd/mmm/yyyy

Ellen Castle, Senior Renal Physiotherapist
Dr Sharlene Greenwood, Consultant Renal Physiotherapist
The Renal Unit, King's College Hospital
London, SE5 9RS
Direct Tel: 0203 299 6725 / Direct Fax: 0203 299 6094

A study to assess the acceptability of an online weight prevention programme for new kidney transplant recipients- The wEight management in Renal Transplant Online Study (ExeRTiOn).

ExeRTiOn Study

HCP ID……

Please Initial below

1.	I confirm that I have read and understand the HCP Participant Information Sheet (Version 4.0 Dated 29th October 2018) I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw from study treatment at any time, without necessarily giving any reason, and without my medical care or legal rights being affected.	
3.	I understand that demographic information such as my job title, age, gender, will be collected during the trial and will be looked at, in confidence, by authorised individuals from the study team at King's College Hospital NHS Foundation Trust, my NHS Trust, King's Clinical Research Facility, as well as by regulatory authorities, to check that the study is being carried out correctly. I give permission for these individuals to have access to my records.	
4.	I confirm that I have read and understand the data security and privacy document (Version 1.0 Dated 3rd August 2018) and understand how my data will be used and stored.	
5.	I understand that if I withdraw from the study, no further data will be collected for the study. With you consent, data collected from when you participated in the study will be used and kept anonymised.	
6.	I agree to the interviews being audio-taped and used anonymously for research purposes. I understand that the recording will be treated as confidential, stored securely and destroyed once the results of the study have been published	
7.	I understand the researchers may use direct quotations from the interviews in publications, but that these will be anonymous, and it will not be possible to identify me from any quotations used.	
8.	I agree to take part in the study	

Signature of patient		
& **PRINTED** name		Today's date: _____ dd/mmm/yyyy
Signature of person taking consent:		Today's date: _____
& PRINTED name		dd/mmm/yyyy

Appendix D. A copy of MoSCoW change list (ExeRTiOn revisions)

- Example of MoSCoW report (8th April 2019) with a list of changes from study 2, and example quotes
- An Example of the excel shared spreadsheet between research fellow and software company to show revision progress

MoSCoW Report ExeRTiOn study 8th April 2019

The table below shows key changes from the results of study 2 and evidence from quotes using the MoSCoW framework for prioritisation

MUST HAVES (Key requirements to change)

	To change	**Supporting quotes**
1.	Change home screen so list of session is fixed, prominent for user to see (minimise L and R scrolling) and use ticks to indicate completed session, not session available	**H04** *"maybe actually it would be good to have the sessions at the top because it's linking in with education isn't it?"* ***H06*** *"and maybe that's just sessions [session list] and they are greyed out? In order 1, 2, 3... Just tick them. So tick means it's done."* ***P10*** *"so don't maybe don't even take, like session 6 out and have it at the top. Just have all the sessions there, you've still got ticks or what you have done and haven't done".* ***P08*** *"this one? Now where? Upcoming session. Oh. Upcoming session. So that is the one. Activity after transplant?" [Going to select session 4 not 3!].*
2.	Add a button from goal setting page to home screen as many users not using navi pane after setting goal "finish"	P07 "*Right so where do I go now" [after setting goal].* P07 says *'Yeah. Or next."*P07 *"I am computer literate. That's a shortcut the process when you're doing it. Your automatic thought is 'Hang on. I'm doing next all along. Now what have I got?!"* *P02. "I mean, I am assuming, I didn't go on it, but assuming there is a button taking you back to the home screen?"* *P08 "and how do we get rid of this?" [Leave goal setting page].* *P08 "either next either next or end session". p09 "Or previous. Cause obviously all the other ones you've got Next or previous".* *P10 "maybe once you've completed your goal, click home or something."*
3.	Tick box button bigger/ more prominent welcome page agreement	*P01 "it says please tick the box to show you have read the agreement and understands the terms of using exertion. So [pause].Now I am going to ask my Physio how I can get through to the box, to start ticking" [prompt]. P01 "agree with?" Int responds "You may have to scroll down if you can't see it"* *P08 "The only thing I can think at this point. That you've got questions about emergency...I think that should be separate and in bold rather than there [agreement copy suggestion]."* *P11. "Please tick the box. This box again needs to be a bit [pause]. Bigger "*
4.	Clear buttons and headings video screens. Users missing heading above videos, also	*P03 "What I was going to say was might be an idea to, coz I was gunna just skip it. I was thinking of skipping it [video]. For most people they are going to see 12 hours 51 and think to themselves I have seen this video before. Do I need to see it again? You might need to make it obvious this video has not been seen before".*

	To change	Supporting quotes
	needing prompting how to play, how long the video is etc. Therefore need clear headings, clear play/pause buttons and clear time tracking	*P05. "We haven't got a start, have we? Hmmm. is this start? What about if we were to click on that?"* *13. P07 "I don't know. What else? Do they want me to start it? [Pause]. No that's paused it. Welcome video. [Clicking noise]."* *H06 "I know this kind of sounds um particular, but I might make these a little bit bigger. The only reason I say this [clicking], is before the actual thing came on" In*
5.	Create FAQ And how-to tab. User had good example of ways to make website easier for a range of users.	*P06. "And then the bits- I just feel like maybe, it's all a bit mashed together. erm... 'How to use the website'". P06 "Maybe a like, you know, yes like a big you know 'Help Me' button." P06. 'So people like 'I have no idea what's going on here." and then each video could have a heading...You know, whenever you need help with this bit." [Meaning screen grab videos under help screen].* *P11. "On the message function, you should show that one there." [Suggest demo msg function].* *P07 "have you got a question and answer part of it?"* *IDEAS VIDEOS: HOW TO SET GOALS (emphasise if looking at reducing weight ex and food goals), HOW TO REVISE GOALS, HOW TO TRACK ACTIVITY ,HOW TO TRACK WEIGHT, HOW TO FILL IN GPPAQ, MY LIBRARY FEATURES, EXERCISE DIARY TAB, HOW TO SEND A MESSAGE, TOUR OF WEBSITE HOMEPAGE, HOW TO LOG OUT*
	Tracking PA: Clear copy as to what PA means and when week starts (e.g. Monday to Sunday)	*H05 "Yeah. No. I think I would I would like to know what activity I am allowed to include, tin the physical activity, coz it can be-er you know. People have completely different views of what is" [copy added on activity definition tracking].* *P02 "Um this week from what day? Will it be from Monday? Saturday? Or how far do I go back." P02 "So does physical activity inclulde housework as well? or not? "P06 "Does the physical activity include walking? Or is it just like actual exercise?". P08 "Does the activity include. Um-what you do during normal daily activity for example walking to the shop". P08 "so that may need to be said as a combination of all activities... whether thats planned activities as suppose as well as you know. walking to the bus stop". P10 "Erm from when should I go by? "*
6.	Make GPPAQ clearer by adding 2 a-> d like paper copy so user knows to answer all	*H01 "so what do I do?"* *P02 "The questionnaire. Um. I s'pose for me there was half one option and half another. So for me I guess there are people that are mobile in their roles and do a certain amount in the office and a certain amount. .."*

	To change	Supporting quotes
	questions to move to next screen	*P09 "Oh I have to answer each one?". P09 "So I just saw one, two, three so I answered one of each. Obviously I answered one in one but it's just the two- you get the variety [Q2 has sub-questions]". P09 "yeah. Unless you put A, B, C, D for these ones [Q2]."*
7.	Enviro checklist- have it for the first session, then after that just one question "are you in the right environment to complete a session? Yes or No. patients could click on an "I" button or icon to get tips suggestions (phone on silent, close other browsers etc.)	*P06 "I mean, this is the kind of things that I would probably do by myself anyway- I mean probably I'll play music and stuff like that. But that is something that I have always in the background". P06 "Shall I do I have to click all these again?"* *P08 "I think it's probably going to be unnecessary". P08 "that would be useful at least initially".* *P11 "why all these questions. Why are you asking all these questions?" P11 "I don't know that they are useful".* P09 "*you'll probably find someone be sat on the train one day doing it. And thinking sod it.*"
8	Therapist website: Need full goal info to provide assistance (goal, conf and importance scale in report). Would also be good to capture session time (current report) they log in after completing session	*H05 "so it would be interesting to see how many actually do that"* *H05 being able to review completed/achieved goals "are you looking at the achievement of goals? As well? Whether they actually achieve the goals that they set?"*
	Therapist website will need full access to log in data after finishing sessions	Will need visibility of log in and revisit sessions (even if just time log on for) and also any further goals, weight, activity added.
9	Remove interactive activity session 1	*P07 "mmm yeah. You don't need both [don't need interactive activity and setting own goal].*

	To change	Supporting quotes
		P03. "Have a go at picking which of these statements these statements are a SMART goal...right I want to lose a little bit of weight. Next." [User does not notice copy feedback]. *P10 "I don't wanna necessarily lose weight, I wanna lose fat". [Interactive activity].*
10	Edit video session 1 to reduce length and Ellen to edit the volume (point where it goes up and then down swiftly)	*P05 "was this longer than your bit? What you said? It has gone right across the screen hasn't it?" P05 "perhaps it could be cropped slightly?"* *P05 "Definitely have him talk about is important for me. I don't know if it could be slightly shorter?"* *P07 "far too long. Because What you'd said had got the point across. I think."* *.P03. "Okay. Goal setting experience. Oh! It's still going?" [User reading out title during video].*
11	Edit session 2 video-splice audio and add static picture of hunger scale so not Robbie holding it	*P11 edit video "[showing hunger scale]. I cannot see that." [Splice audio and keep hunger scale image there rather than Rob holding it up].*
12	Edit session 2 interactive activity	*Q1 P11: "the wording is not right". P11. "Over the last few hours I'm feeling. Like .I'm feeling weak or... I want to eat something. That's much better. "Q5 P11 unclear copy "' I can't shake this feeling. I think my body is trying to tell me something' [pause]. This is a gain some abstract question [re-reads to self-]." P11. "It could be hunger or it could be cravings... It's not really adding nothing".*
13	Update video session 4- reduce length, slice audio for RPE scale bit	*P06: well you can't actually." P07. "Yeah It's just too long to sit there and listen to it all."[To add BORG and trim audio to picture)*
14	Edit content session 4 interactive activity	*P07. "And then what does it ask me to do? If you're working at a moderate medium level. What number would you select for the options below? 12 to 15. mmmhmm. I don't wanna go too hard do I. Umm. Probably 13. SO what I don't understand what I'm supposed to be doing here sorry [interactive activity session 4]." P07 'having talked about the scale in the video, you are working at a medium moderate medium level. What number would you select from the option? Oh moderate medium. mmm [pause]. Probably set 13. That one". Int to P07 "what was making you unsure?" P07 responds "The way it's written." P07 'Instead of 'if you are working' put 'if you are exercising'... at the correct level. And then you can put in brackets 'moderate stroke medium'...'which range would you select. From the option from the options below... Because that isn't just one number. And it say's number." MAKE A FOCUS ON QUOTES P07 ""*

	To change	Supporting quotes
		Yeah I like to do it actually as highlighted in colour". "Make a thing of it". P07 "speech bubbles".
15	Edit/ reduce content session 10 video	*P03: ' I mean that's quite a lot of video watching. And people could be like, I just come home from work, do I want to see another 12 minutes of this? And some bloke talking about his life. Which gives an example of how things are, but the chances are they might think do you know what I might just skip it.' P03: "I mean do you need the fella talking for so much? Coz that's quite a long session. .. What you said beforehand is more; I know that's an example but maybe just give the examples with you're talking. I Think that's an example, but maybe just give the examples with your talking. I think it's probably food to do that bloke on the first session [goals]. But that was a bit long the second session- the barriers."*
16	Session content session 10. Make it clear you can click more than one	*P03' Oh. Let's just read that 'it can be difficult to maintain a healthy lifestyle with a kidney transplant. Food and activity goals. Is it hunger, cravings, fatigue, time, work, pressure, family, other commitments, fear of injuring new kidney, cost motivation. Wow is it one? Do you click on one? Or is it a few" [seeking feedback interactive activity].*
17.	Session 11- clear that you need to put something in each box before progressing to next session	*P02 "ok. [Clicking]. So clicking next. Have I filled everything in? [Patient scrolling]. Umm ticked the first one. Other. It looks like its waiting for something there but? Umm I will put NA in the final box" [user had to put something in every box for it to progress through]. P02. "So the only thing on there is it wasn't clear I had to put something in the box to close it."*
18	Disclaimer on home screen	*EC to add copy on home screen disclaimer "this website is now live. It was updated in this date and no further updates will be made until the study closes"*
19	Reminders	*Auto email reminders to log on weekly (nil other emails)* *Therapist input (private and personalised via msg) if drop off, at six weeks and 12 weeks.*

SHOULD HAVE CHANGES= IMPORTANT FEATURES

	To change	Supporting quotes
1.	Goal setting page: clear copy how to edit goal, increase word count on goal setting template	*P01 "you know, the setting, the thing the way that because when I put something, it didn't take it. The space."[User unable to type full goal into template word count restriction].* *P05 "what's happening there? Argh it must have hit a word limit?"* *P10 "yeah. Don't need much more, but maybe a little bit more in case you need an explanation"*

		P09 "And obviously I hovered over edit, thinking it would edit. I didn't realise that I have to click on that one."
2.	User having option to download a report at the end of the 12 week programme	*H02 "If they want to [pause]. To download their information at the end. Can, will this download like a graph of my weight loss of my progress or something like that?"* *P06 responds "Hundred percent. That would be really really good 'cause anyway, like seeing you progress, you know in a very kind of graph like that-being able to really track it and see it all together".*
3.	Minimise scrolling Hard to implement throughout removed	*1. Int to P04 "you're on the summary page of the first session. You're looking for a button are you?" P04 responds "Yeah." [Field notes- minimise scrolling so user can find next buttons].* *P06. "People who are less you know, used to scrolling down or maybe can the box be a little bit smaller, so they can see the screen without having to scroll down maybe?"[screen smaller for video less space so can view buttons]*
4.	Feature speech bubbles/ bold/ colour to emphasise patient quotes (S2, S4, S7 and S12)	*P07. "Make a thing of it. [Patient quotes].P07 "Because that's quite important. Coz you want to know what other people do and what other people think… because that is so relevant". P07 "like speech bubbles".*
5.	My library- option to print and download all resources (not just some)	*H02 "You know the tools the [pause] the eating tools and the cravings things? Can they print that?"* *H02. "If would I be using this as a patient, I would download the tools into my phone without necessarily logging into the thing every day".* *H03. "Is the 'my library' where the resources are?.. Can these things be printed?'.*
6.	Add copy to highlight expandable links (Session 2 cravings, session 6, etc.) **Remove there is already copy on this session 6 and session 2 has already been highlighted**	*1.Int to H06 "… click there or something, for activity 2? H06" or unless they automatically all open up and then you get the option to shut them?" Interviewer to H06 "maybe I need to put um-just a bit of copy saying 'click headings below to reveal'. H06 responds "yeah. or anything like that. Yeah.".* *2.Int to H04 "and again, some patients, have talked about those clear buttons, like maybe we have something that says 'expand here.' Ho4 responds "yeah I think that's great".*

COULD HAVE- useful to have (not central)

	To change	**Supporting quotes**
1.	Estimate time takes to do session on session list on home screen	*H05. "I just don't know how long it is. Um and When you are doing these sessions, do you say roughly how much time."* *"Yeah at the beginning. So someone knows whether or not they are about. Whether or not they can commit to that".*

	To change	Supporting quotes
2.	"Complete session" button on summary page confusing some patients. Change to "Next" button.	*.P10 "Do I click complete, yeah?" [Click complete at summary page]. P11 "[reading screen summary page]. Now set your own SMART goal. Revise goals. Complete session [clicking noise. Pause]. That's it?". P08 "It says complete session. I am worried if I click complete session it will get me out. So previous". .."Interviewer-rather than complete session.*
3.	Clearer copy and process to reset password. Also need brighter log in bar	*"Should I put testing and then put the password? Or just put the password here? Because on the other one, I did it just said testing" [seeking clarification]." P04 "It's saying new password. And it must be 8 characters [int: okay] so do I need to do it to myself?" P07 "Oh password must have eight characters. I didn't read that bit. Should have [laughter]." P11. "So this is not coming in" [trying to type log in]. Int to P11 "Yes. Argh. Did that need to be brighter for you [log in bar]. P11: Yes it needs to be"*
5.	Reduce content on the HEP- click and expand links	H04. *"Yeah. I think maybe you do need it. Even in terms of this, in terms of exercise diary, it is lots of information that's on the paper ones. Isn't it. But even having some of it where maybe you click and expand it... benefits of exercise, you can click and expand it." H04. How to exercise safely. Maybe that's at the top, just as a non-expandable thing?" [Click expands some parts of HEP to minimise scrolling]. H04 "you don't want to necessarily get too overwhelming".*
6.	Updating resources my library	H06. FOOD DIARY ADD PICS "I would probably put pictures here by the way." FOOD LABEL CARD H06 "one of the things I find um. That people sometimes get confused with this, and I notice the um more recent ones include mils...which can help for things like fluid and the like. I think it gets generous on sugar fluids. Because obviously then its five grams per 100mls. If that makes sense? So it's just kind of this part as well [pointing food label card]."

WOULD LIKE- Not needed now, may be useful in the future

	To change	Supporting quotes
1.	Clear buttons home screen	*P03 "We advise that you. I wonder if you could have. This goal setting I know it doesn't seem it might not seem too obvious but maybe it should say something 'click here'. Just to make sure that you are definitely know that the click on that bit first? I don't know". Interviewer askes P03 "oh so for that session "click here". P03 resp "Yes. Click here on each of those". P03 "It said session 1. It's not really completely obvious to say to actually say to actually click on it. It just looks like things to do". [NB. Only one patient expressed this issue].*

2.	Change order confidence and importance ruler	*"H01 "swap it around. Yeah. Needs to be positive first". NB. Only one person suggested this.* *[NB only expressed by one HCP]*
3.	Calendar function	*P02 "so the only other thing, I am thinking in terms of a, is there, would there be again I am thinking ahead, is there a calendar on here you can go onto and see that actually Yes, that's, so where you put these goals in, there's a calendar function that says and you can go and look for December the 5th only thing that's in my head".* *[NB. Only one patient expressed this issue].*
4.	Notes function	*Section to add notes- P10 "it's somewhere you can put your notes in? When people are at home in their comfort zone, they might not put everything down they need to. If they've got it on a different sort of system. They've got to go out of their way to log on, they have to log on. They're not just sitting at home, they've got somewhere to put it, and obviously they can easily keep track of previous progress from when they first started it"* *[NB. Only one patient expressed this issue].*
5.	Drop down function goals	*P11 (only patient) who wanted drop down boxes "why don't you make it pick and click button" "I'm lazy; I don't want to do that".* *[NB. Only one patient expressed this issue].*
6.	Therapist Interaction: changes meds/ Transplant	**THERAPIST INTERACTION: WHAT HAPPENS IF ANY CHANGES TX/MED: P02** *"If for example my creatine went the wrong way, or my what what then? How does the website or how could we manage that?".* ***P02.*** *"again I am thinking ahead, would this link in. So I don't know if this is relevant to a physio but would this link into, would you need to know our change in medication? Things like that?"* ***P03*** *"Something about medication maybe?"*
7.	Include stress/ MH Links in my library *memo- here or higher up?	*H03 and P07 P07 and hub: "There's also some things that they can do themselves, there's a number of apps available… such as calm and all these other ones." P07 "talk about counselling..'And if you can't get one locally or you can't get one with any space (counselling) in at the hospital then here are some options'". H03 "Maybe like a future thing or something even things on erm sleep?" H03 "Erm stress. I don't know how they impact on managing those. 'Cause I guess it can impact on weight, exercise and that kind of thing. ". Int to H03 "Would it be a featured session or a resource?" H03: "Maybe a session?"*
8.	Change white background in videos	*CHANGE WHITE BACKGROUND (VIDEO S2, 4 and S7): H03 "the white background is fine, I dunno, a little bit clinical? Not sure. I don't know…not that you should have to redo the videos for the sake of the background or anything". H01 "Mr white on white".*

4	Feedback on GPPAQ **This can be done via the physio personal msgs therefore remove**	*H04 "I am wondering if people whether patients will be interested to know what their outcome is... I guess it's a bit of a double edged sword isn't it? Because you don't want to, if patients are classified as inactive you don't necessarily want to give them that feedback. That red bold 'you're inactive'. H05 "I mean um and then I do a questionnaire like this, like the patients do, and what feedback do I get from that?"*

An Example of the excel shared spreadsheet between research fellow and software company to show revision progress

ExeRTiOn - Study 2 Enhancements List

#	Page	Feature	Enhancement	Priority	Screenshot link	comments queries for sab		Sab comments	Dependency	STATUS
"MUST" haves= key/essential requirements to change										
1	homescreen page	display of sessions	have one list of sessions in order rather than upcoming and previously completed. Use ticks to indicate that the session has been completed, not that it is available [current].	MUST HAVE	https://snag.gy/SNlF8E.jpg	Users getting confused by sessions being ticked when available rather than completed sessions. Can we use a bold when they are available, greyed out when they are not ready and tick when completed? Also have one list of sessions rather than 2 (upcoming and completed). Also users reading left to right (tracking to goals) rather than entering session. Might be easier for me to explain over the phone to get your ideas on how to improve this		don't show the tick until it is completed		COMPLETED
2	goal setting screen	no button back to home	please add a back to home button or a finish button to this page.	MUST HAVE	https://snag.gy/2vNKOE.jpg	users not looking for the button on the navi pane at top. Therefore needing a "Finish" "Next" or "click home" button				COMPLETED
3	welcome agreement page	enlarge tick box for welcome agreement	please make this tick box bigger and more contrasting so visible to user. Also make associated text with box more prominent. This will allow user to more easily progress to the next stage of welcome package.	MUST HAVE	https://snag.gy/KONyWd.jpg	testing showed users needed prompting to find box to click on to progress		Perhaps a different colour and/or text bigger? Check with designer.		IN PROGRESS
4	Video page (all sessions)	heading and video play/pause/ track buttons	Please make heading text above videos more prominent. (bold heading text). Also please make a prominent video play/ pause button and make the timing of video display more promient	MUST HAVE	https://snag.gy/kcPiv5.jpg	From screen shot link you can see when the video starts playing, the play/ pause button and tracking pane are hidden. Also users needed prompting on how to press play on video. Also headings above video are in normal text (not heading text)		up to 2 headings in a session. How can we make the 'play' feature easier to understand? Add copy? Is it possible to keep the play functions always visible while video is playing?		WITHDRAWN
5	homescreen page	FAQ/ help function	Users would like a FAQ/Help button that can be visible from the home screen and navi pane at the top	MUST HAVE	https://snag.gy/njD9Cz.jpg	Sab- I will need to draft some "How to" screen share videos for this and draft the FAQ copy. I assume I will need to use the reformated new website to do my how to videos? So it matches what the user will see.	Videos for Ellen to draft: How to set goals (moved from session 1 as per line below), how to revise goals, how to track activity and weight, how to fill in GPPAQ, my library features, exercise diary tab, how to send a message, tour of website, reset password.	Ellen has already drafted the FAQ for review. Possible to add videos to this page? (~9 video's). Relared to #6		IN PROGRESS
6	goal setting session 1 video	remove second video	remove "how to set goals" video and add this to the FAQ/help page	MUST HAVE	https://snag.gy/kcPiv5.jpg	see comment above		related to #5		INPROGRESS
7	tracking pop up box	copy physical activity	please update copy on physical activity tracking to read *"Enter your physical activity in MINUTES here. It can either be a total amount of minutes for the week (starting monday), or you can add your activity daily (in minutes) each day you are active, and it will tally up your weekly total.Physical activity minutes includes any planned exercise, walking or activities around the house".* **Please add a box for the**	MUST HAVE	https://snag.gy/RZbGpu.jpg	update copy		Make the input box smaller and add the copy "minutes" on the right hand side		COMPLETED

8	tracking pop up box	enhance navigation	add a "finish tracking" or a "next" button so that user can click on this at the bottom of the tracking pane rather than scrolling up for the X	MUST HAVE	https://snag.gy/XPtM1d.jpg	users needing prompting to scroll up, find X. Users suggested "Next" button as this is used throughout resource	Add a button at the bottom of the page that will close the pop up. "Next/continue"	**COMPLETED**
9	GPPAQ questionnaire page (every 4th session starting welcome page)	update copy/headings so user completes GPPAQ	add 2a, 2b, 2c, 2d to sub quesitons under Q2 so user knows they have to select an answer for each of these subquestions, not just one for 1 one for 2 and one for 3	MUST HAVE	https://snag.gy/jvBu5f.jpg		Update the questions in #2 with a, b, c etc.	**COMPLETED**
10	Enviro checklist	before each session	please only have this checklist at the welcome session. After this please just have the following text : *"to get the most out of this study, we recommend that you work in the right kind of environment. For example minimise distractions. Please click Yes to confirm you are ready to complete a session"* . Yes or no radio buttons to progress to next page	MUST HAVE	https://snag.gy/evBKL0.jpg	users finding that after the first time of seeing this checklist they get desensitised and just click yes yes yes. Some users finding this annoying. Therefore have full checklist on welcome sessoin and then in subsequent sessions just have the updated copy and one Yes or No radio button	Ellen will provide the full copy needed to add - remove the radio button selections and just have a 'yes/no' option to continue.	**IN PROGRESS**
11	Therapist/ back end website	session time report	Needs to be updated so that once user completes session, but re-visits or logs in to do anything on website, this is captured	MUST HAVE	https://snag.gy/ZIP3Gm.jpg	need to capture raw log in data for example once someone has completed the sessions, do they log on and revisit? Even if it is just the time they are on for, and if they add any physical activity/ weight or goals this is added to the respective reports	need to check time/date last login (i.e. want to make sure the last login report (currently exists) continues to capture login post completion of 12 sessions).	**CONFIRMED: data continues to capture after user completed sessions**
12	Therapist/ back end website	goals report	need higher visibility on goals- can this be a report excel which has full goal, and then the rated confidence and importance	MUST HAVE	https://snag.gy/nGJ6ro.jpg	physio needs to see full goal (at present just brief goal) to be able to provide advice and input tailored to that individual	report for ALL goals for each user. On individual person screen would like to should the FULL goal (currently shows partial). Also to have all the goals for the patient (preference is to have is as a downloaded file in excel and not on the partient page)	**IN PROGRESS**
13	log in screen	disclosure statement added	please add the following copy: *"This site has been updated on the XX/XX/XX, no further updates will occur until the study closes"*	MUST HAVE	https://snag.gy/aBlQyR.jpg		Copy update - need to check where is the best to place it.	
14	Session 1 video page	Session 1, video 1 (SMART GOALS)	Ellen to reduce the content of this video and fix sound and send to Sabeya so it will be replaced	mUST HAVE	**EC to edit video and resend**	Feedback from users- too long therefore Ellen to edit and resend for Sabeya to upload.	Replace video 1. Ellen will provide	**IN PROGRESS**
15	Session 1 interactive activity	interactive activity where user selects options	Please remove this interactive activity. Therefore session 1 will go as follows: video-> summary-> goal setting page	MUST HAVE	https://snag.gy/y250Dd.jpg		remove interactive activity page ONLY for this session - user goes from video page directly to summary page	**COMPLETED**
16	Session 2 video	Video to be edited	Ellen to edit video to splice audio and focus on hunger scale	MUST HAVE	**EC to edit video and resend**		Replace video - Ellen to provide	**IN PROGRESS**
17	Session 2 interactive activity	Interactive activity session 2 (Cravings)	Edit the copy on the first statement so it reads *"my appetite is building gradually over the past few hours"*	MUST HAVE	https://snag.gy/64AUNX.jpg		copy change - change the first bold statement with copy provided.	**IN PROGRESS**
18	Session 2 interactive activity	interactive activity session 2 (Cravings)	Remove completely the fifth statement reading *""I can't shake this feeling. I think my body is trying to tell me something!"*	MUST HAVE	https://snag.gy/64AUNX.jpg		Remove question and answers	**IN PROGRESS**

ExeRTiOn - Study 2 Enhancements List

#	Page	Feature	Enhancement	Priority	Screenshot link	comments queries for sab	Sab comments	Dependency	STATUS
	activity	(Cravings)	*feeling. I think my body is trying to tell me something!"*						
19	Session 2 interactive activity	expandable links at bottom of page	Please add copy above the expandable links at the bottom of the page *"click on the words in blue below to reveal more information about managing cravings"*	MUST HAVE	https://snag.gy/64AUNX.jpg		Add copy, only add once on top of the first one		IN PROGRESS
20	Session 4	video session 4	Ellen to edit video (splice audio over RPE scale) and reduce length of video and send back	MUST HAVE	**EC to edit video and resend**		Replace video		IN PROGRESS
21	Session 4	Interactive activity	Update copy of interactive activity to read *"Having talked about the RPE scale in the video, if you are exercising at the correct level (moderate/medium), which range of numbers on the scale would you select from the options below"*	MuSt HAVE	https://snag.gy/dbua7o.jpg		Copy update		COMPLETED
22	Session 5	Video Session 5	EC to edit session 5 video- remove how to at the end and move it to the "how to tab"	MUST HAVE	https://snag.gy/k6iHKg.jpg		Replace video		IN PROGRESS
23	Session 10	Session 10 video	EC to edit video session 10 and reduce the length and send to sab	MUST HAVE	**EC to edit video and resend**		Replace video		IN PROGRESS
24	Session 10	Session 10 interactive activity	Please update the copy at the top of the screen so it reads *"It can be difficult to maintain a healthy lifestyle after kidney transplant surgery. Think about your main barrier that makes it difficult to continue with your food and/or activity goals. Select which of the options below best explain your current barriers. You can select multiple barriers".*	MUST HAVE	https://snag.gy/kEwI3y.jpg		Copy update (replaceing existing copy)		COMPLETED
25	Session 11	Session 11 interactive activity	update copy above final box on interactive activity so it reads *"Step 6 - List the steps required to carry out your chosen solution then do it.* *To overcome my barrier and achieve my solution I need to: please note if you only have one or two solutions, type NA in the remaining box to progress to the next page"*	MUST HAVE	https://snag.gy/9IoWcF.jpg				COMPLETED
26	Data security doc	replace data security doc	replace current data security doc with updated document EC will send as attachment to sabeya.	Must have	data security doc is avaible from initial screen (log-in screen and needs to be updated and replaced)		Copy updates - Ellen to send a tracked change doc		IN PROGRESS
37	Reminder emails	auto emails sent to users	Please only have weekly reminder email on Sunday / Monday to do session. Please remove email if user has not logged on. Feedback from our testing revealed that users would prefer a persoanlised msg from physio if they are having issues	MUST HAVE	Auto emails just to be reminder, not if not logging on. This will need to be done manually by the physio. Sab- can we discuss this?		Keep Mon to remind ALL users to start their session. Remove Fri email for users if not logged in. And remove any other reminder email if haven't logged in.		IN PROGRESS
28	goal setting page	increase word restrictions for setting goal	please increase the word limit slightly for goal setting template	MUST HAVE	https://snag.gy/utCKDI.jpg	some users could not fit their goal into the word restrictions	Change limit for EACH box - find out what current limit is and then agree with Ellen what to change it to.		COMPLETED
SHO									
29	goal setting page	edit button	please make clearer user can edit goal. Maybe text next to edit button "click here to edit your goal"	SHould have	https://snag.gy/a7JHDS.jpg	Sab- one of our 'must' options is to have the goals as a report on therapist end. If this was the case each time the goal was edited, it would be re-entered into the	Check with UX designer - how can we make the 'edit' button more easily understood? E.g. change label?		

Sheet1 Lookup +

ExeRTiOn - Study 2 Enhancements List

#	Page	Feature	Enhancement	Priority	Screenshot link	comments queries for sab	Sab comments	Dependency	STATUS
30	Session 12	option for user download report	user idea to have the option to download a report with their goals/ weight and activity graphs	Should have	https://snag.gy/bmDqA4.jpg	Sab- can we discuss this? Thanks	An option to provide the user a summary report of their goals, activity and weight graphs.		
31	Summary pages Session 2, Session 4, Session 7 and Session 12	patient	make "top tips from fellow kidney transplant recipients" more of a feature on the summary pages (session2, 4, 7 and 12). One user has suggested blue text and speech bubbles	should have	https://snag.gy/ohP27U.jpg	key finding from my study is patients really valued the patient expert quotes. Can we make this more of a feature.	How can we style the top tips in mentined sessions to be more stand out, e.g. blue text or blue box. Check with UX designer		
32	my library tab	option for all resources to be printed and downloaded	Make it possible for all resources (1 to 5) to be printed and downloadable. Currently only an option on 4 (activity planner)	should have	https://snag.gy/rptsxa.jpg		1,2,3,5 - add links to download. Ellen would PDF versions of each.		
33	updating resources	updating healthy plate and food label card	EC to uopdate food label card to include drinks, update my library healthy plate to have pics of food groups	Nice to have	**EC to update food label and healthly plate and send back to Sab**		Image update - what is the best format to provide? And what quality?		
34	goal	option for goal to be printed and downloaded by user	option to download and print goal	should have	https://snag.gy/zKWpAb.jpg		Similar to #30 - have a link/button to download goals.		
"coul									
35	home screen page	estimate time takes to do sesion on session list on homescreen	add session estimates from ellens data for average time it takes to complete each session next to session list	nice to have	sabeya- had issues snaggy after should haves. Can try again in future if we get to the could/ nice to haves		Editing labels - agree with Ellen the copy		
36	session summary (all sessions)	update button	button currently reads "finish session". Please change to "next" and add copy- please click next to progress to goal setting page to finish your session"	Nice to have			Copy update for all sessions		
37	log in page	increase contrast/ visibility of log in and email bars	please make bars to type email into more contrasting for user	Nice to have			Add a border to the login boxes - check with designer		
38	home exercise diary tab	reduce content	have the safety info as full text and the rest as expandable links on the web page version	Nice to have			All main titles as expandable links apart from How to Exercise Safely		
39	tracking physical activty	tracking physical activity	user could select different types of activity to record. E.g activites around the home, walking, gym, running and add the minutes in	nice to have			Adding radio button/checkbox of activities - above the graph. Record data each week (ideally not override) and have a report in the admin site to download. Also potentially adding the activity on the patient page		
40	bolder buttons on home screen	buttons	make buttons more visible/ contrasting home screen			NB expressed by 1 user only			
41	goal setting template	change order confidence and importance scale	reverse order 10 to 0 for confidence and importance			NB expressed by 1 user only			
42	calander fucntion	link goals to calander function	calander function so user can add notes on goal etc.			NB expressed by 1 user only			
43	notes function	add a notes tab	adding notes tab so user can make comments (Diary)			NB expressed by 1 user only			
44	drop down function goals					NB expressed by 1 user only			
45	Med changes and		one user highlighted how chronic would be informed if meds/ bloods						

ExeRTiOn - Study 2 Enhancements List

#	Page	Feature	Enhancement	Priority	Screenshot link	comments queries for sab	Sab comments	Dependency	STATUS
40	bolder buttons on home screen	buttons	make buttons more visible/ contrasting home screen			NB expressed by 1 user only			
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42	calander fucntion	link goals to calander function	calander function so user can add notes on goal etc.			NB expressed by 1 user only			
43	notes function	add a notes tab	adding notes tab so user can make comments (Diary)			NB expressed by 1 user only			
44	drop down function goals					NB expressed by 1 user only			
45	Med changes and transplant changes		one user highlighted how physio would be informed if meds/ bloods changed						
46	stress/ MH links		one HCP and one patient identified stress and links could be added to my library						
47	white background videos		future projects could change video screen. Only expressed by 2 HCPS not patients						

Appendix E. Feasibility RCT (studies 3 and 4) documents

- Protocol feasibility RCT
- Initial ethical approval
- Patient information sheet
- Data security and privacy document
- Consent form
- Topic guides used during nested qualitative interviews (study 4)
- Sensitivity analysis for assessment window (feasibility RCT)

ExeRTiOn 2- A Randomised Controlled Feasibility Trial

Full title: ExeRTiOn 2- The Weight gain prevention Renal Transplant Online study. A Randomised Controlled Feasibility Trial

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Funder:	Kidney Research UK AHP PhD Fellowship Grant (awarded to Ellen Castle) 2nd July 2018 to the 1st of July 2021 Ref: AHPF_001_20171122
IRAS Reference	262007
KCH R&I number	KCH19-109
REC number	REC 19/LO/1138
Previous linked study:	This study is a follow on study from the ExeRTiOn study (KCH18-085, IRAS 241928)

Protocol Version and Date V3.1 22nd June 2020

CONTENTS

KEY WORDS

Exercise

Weight Management

Online treatment

Kidney Transplantation

Weight gain

LIST OF ABBREVIATIONS

6MWT	Six minute walk test. This is a measure of exercise capacity
A	Adverse Event
BCM	Body composition monitor
BMI	Body mass index
CI	Chief Investigator
CRF	Case Report Form
EQ5D	A standardized measure developed by the EuroQol Group to measure health related quality of life over five dimensions
ExeRTiOn	Exercise and weight management in Renal Transplant Online
GPPAQ	General Practice Physical Activity Questionnaire
GSTT	Guy's and St Thomas' Hospital
HCP	Health Care Professional
HRA	Health Research Authority
KCH	King's College Hospital
KTx	Kidney transplant
KTR	Kidney transplant recipient(s)
PI	Principal Investigator
PIS	Participant Information Sheet
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event

STUDY SUMMARY

STUDY OVERVIEW	
Full title	**ExeRTiOn 2- The Weight gain prevention Renal Transplant Online study. A Randomised Controlled Feasibility Trial**
Short title	ExeRTiOn 2- a Randomised Controlled Feasibility Trial
Objectives	**Trial objective:** To conduct a bi-centre randomised controlled feasibility trial that will evaluate the feasibility of a novel online resource for new kidney transplant recipients.
Type of trial	A bi-centre mixed-methods feasibility RCT in new Kidney Transplant Recipients at King's College Hospital (KCH) and Guy's and St Thomas' Hospital (GSTT).
Primary outcome	**Feasibility:** • Including recruitment, retention, collection of measures, adherence to the website (treatment group only) and participants perceptions of the online resource and participation in the trial • Ability to collect measures for a definitive study (body weight, body mass index, body composition, quality of life, self-efficacy, fatigue, arterial stiffness and physical function) • Safety: hospital admissions
Trial design and methods	• This is a mixed methods study. Patients will be randomised into either usual care, or exposure to the online 'ExeRTion' resource. • Quantitative data will be collected at baseline visits, 12 weeks, and 12 months (3 study visits). All study visits will be performed at the King's CRF Unit. • **Nested qualitative study**: Semi-structured interviews will be conducted in a purposive sample of intervention group participants at 3 months, and both groups at 6 months.
Health condition(s) or problem(s) studied	This study will specifically recruit new kidney transplant recipients. They will be recruited within the first three months of receiving their kidney transplant from either the post-transplant outpatient clinics at King's College Hospital or Guy's and St Thomas' Hospital.
Target sample size	**Total Sample:** We aim to recruit 50 participants, 25 participants to each arm, Usual care or exposure to the online resource across these two sites. June 2020- update to sample due to COVID19. Refer to section 10.2 **Nested Qualitative Sample:** We aim to purposively sample5 to 10 participants from the intervention group at 3 months, and approximately 16 participants across both groups at 6 months and conduct individual semi-structured interviews.
Trial design and methods	Study visits will occur at three time points:

	• baseline (pre-intervention for the intervention group, at time of randomisation) • 12 weeks (post online intervention for the intervention group) • 12 months
Trial duration per participant:	The participants will individually be in the study for 12 months. Those in the intervention group will receive a 3 month online intervention, with the option to continue using it for the remaining 9 months of the study.
Main inclusion/exclusion criteria:	Participants will be recruited to the study based on the following inclusion and exclusion criteria: **Inclusion criteria:** • Adult patient (18 years+) • male or female • Able to provide written informed consent • < 3 months post-transplant. NB. Our team has decided to recruit patients within the first three months post transplants as most patients at our centre are not cleared to start a formal physical activity or exercise plan until they have ureteric stents removed which usually occurs at 6 weeks post-transplant surgery. • Access to Internet connected computer, smart-phone or tablet. NB. Our team has completed a waiting room survey and our patients often use internet to view their clinical blood results through "renal patient view", therefore do not perceive internet access as a barrier to this study. • A Body Mass Index (BMI) greater than or equal to 18.5 (healthy range). **Exclusion criteria:** • Age < 18 years of age • Pregnancy • Unstable medical conditions such as angina, uncontrolled hypertension or diabetes, congestive cardiac failure, active myocarditis, cardiac arrhythmia, co-morbid catabolic condition, psychiatric illness • Participated in a structured exercise or physical activity intervention in the last three months • BMI of less than 18.5 (classified as underweight) • Significant cognitive impairment preventing them from engaging with online interactive material • Unable to complete the online resource in English

Statistical methodology and analysis:	• Feasibility outcomes will be described as either; proportions with 95% confidence intervals, means and standard deviations or medians with interquartile ranges • Qualitative data will be analysed using thematic analysis, and elements of grounded theory such as line by line coding
STUDY TIMELINES	
Study Duration/length	24 months
Expected Start Date	16th June 2019
End of Study definition and anticipated date	30th July 2021
Key Study milestones	• Ethics submission by start of May 2019 • First patient recruited by 31st June 2019 • Last patient recruited by 1st December 2019 • Study finishing by 31st June 2021
STORAGE of SAMPLES (if applicable)	
Human tissue samples	N/A to this study
Data collected / Storage	Data will be kept on site in secure, lockable files at the team's office.

1 SUMMARY

The primary aim of this trial is to assess the feasibility of a novel online weight gain prevention resource (Physical activity, weight management and behavioural change techniques) for new kidney transplant recipients. A previous study, conducted by the research team 'ExeRTiOn' (KCH:18-85, IRAS:241928), provided usability feedback to refine this online resource in a purposive sample of new kidney transplant recipients and members of the transplant multi-disciplinary team.(unpublished data)[1].

This current study will recruit a sample of new kidney transplant patients, from two transplant clinics (King's College Hospital and Guy's and St Thomas' Hospital). Participants will be randomised equally to either the 12 week online intervention (n=25), or usual care (n=25). Intervention group participants will have the option to continue using the website once the 12 week programme has been completed up until the end of the trial (12 months).This includes revisiting previously completed content (videos and links) and continuing to set new goals and track physical activity and weight if they wish to do so.

Quantitative data will be collected at three study visits (baseline, 12 weeks and 12 months). Qualitative data will be collected from a purposive sample of intervention group (5-10) participants at 3 months, to explore the experience of using the online resource via semi-structured interviews. Further semi-structured interviews will occur at 6 months from a purposive sample of approximately 16 participants from both groups to explore overall experiences of the trial until data saturation is reached.

If this study is successful, we hope that the results of this study will form an application for a multi-centre, powered efficacy Randomised Controlled Trial. This project has potential to influence clinical practice for new kidney transplant recipients. It will allow patients, who may not have routine access to physiotherapy or dietetic input to address exercise and nutrition behaviours. A study flow chart summarising the project can be found below.

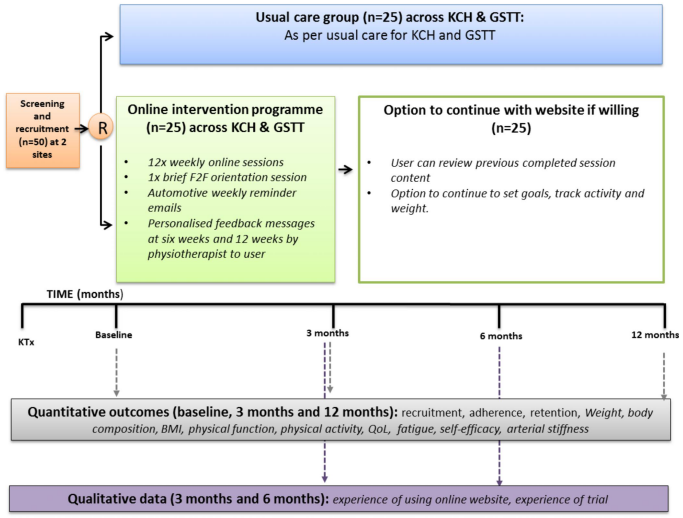

Figure 1. Study flow diagram. KTx= kidney transplant, R=randomisation, F2F= face to face session with physiotherapist, QoL= quality of life, BMI= Body Mass Index, KCH= King's College Hospital, GSTT=Guy's and St Thomas' Hospital.

2 BACKGROUND AND RATIONALE

2.1 Weight gain in kidney transplantation

The benefits of exercise and physical activity for people with Chronic Kidney Disease is well established and recommended [2-5]. Whilst Kidney transplantation can be a cost-effective treatment option for end-stage kidney disease, it is not without risk. There is a high prevalence of diabetes, cardiovascular disease and obesity in kidney transplant recipients [6, 7]. Weight gain is a real issue for new kidney transplant recipients, with up to 2 thirds of the population classified as overweight or obese [8, 9]. Kidney transplant recipients (KTR) who gain more than 15% of their initial weight in the first year following transplantation have a higher chance of dying of non-kidney related causes within 10 years [9]. In addition to this weight gain, KTR do not reach the level of physical activity of those of age-matched healthy controls [10]. Weight gain in new KTR appears to be influenced by multiple factors including; lifestyle changes associated with transplantation, appetite stimulation by immunosuppressant medications, changing of eating behaviour by the lifting of dialysis dietary restrictions, reduced functional capacity due to prevailing uremic myopathy and muscle atrophy which are exacerbated by immunosuppressant medications [11-13].

Although preventing weight gain and maintaining a physical active lifestyle are real issues for kidney transplant recipients, access to specialised renal physiotherapists and dietitians is not routine practice in the United Kingdom (UK). In addition to this, patients are often attending multiple clinic appointments, returning to work and they may also have significant distances to travel to hospital appointments. These present as barriers to participating in additional face-to-face rehabilitation services [14]. A qualitative study (n=7) in patients who gained more than 12 percent body weight in the first year after receiving a kidney transplant, reported medications use, the removal of dietary restrictions that were imposed whilst on haemodialysis, fear of injuring the new kidney, and burden of other health problems to be the main barriers to maintaining a healthy weight and physically active lifestyle after kidney transplantation [15]. They requested early support services to address lifestyle changes for diet and activity [15]. The results from this study, in addition to the research teams' small qualitative study in our local population (unpublished data), suggested that an online intervention to provide patients with the information and skills to address physical activity and nutrition behaviours post transplantation, is warranted.

A recent review of the literature revealed only two completed Randomised Controlled Trials with published results that evaluate specific weight gain prevention interventions for new kidney transplant recipients [16, 17]. Both studies involved face-to-face complex interventions (behaviour change, exercise counselling with dietitian input) and report maintenance in body weight in their intervention groups. Henggeler et al [16] randomised 37 new KTR to either usual care or a specialist face-to-face nutritional intervention (dietitian input, behaviour change and exercise counselling). They revealed no significant difference between groups in weight gain at six months. It is however of note that the overall mean weight gain in the study sample was below 5%, which is significantly lower than previously reported weight gain in new kidney transplant recipients of up to 10-15%, and is of clinical benefit and significance [9]. Another point of consideration is that the standard care

group in this trial received four individualised renal dietitian consultations, which is significantly more than UK practice and could have diminished the effects of the intervention.

The second Randomised Controlled Trial by Tzvetanov et al, randomised 17 obese new KTR to either usual care or a complex intervention of exercise, behavioural change and nutrition for 12 months. Whilst they reported a stable BMI and weight in the treatment group, they do not report baseline body weight measures, making it difficult to evaluate the results in their entirety on percentage of weight gained post transplantation [17].

There are a further two Randomised Controlled Trial Protocols that have been published comparing complex weight gain prevention interventions (face-to-face) to usual care, however results are yet to become available[18, 19]. There is a need for theoretically and evidence based interventions, with sufficient exercise dose to be explored and researched in this population. Online healthcare could provide an avenue of interest to provide new KTR with the skills and information needed to address physical activity, exercise and nutrition behaviours to prevent weight gain post kidney transplantation.

2.2 Purpose

The purpose of this current study is to use the refined version of the ExeRTiOn online resource, in a randomized controlled trial design, to see if it is a feasible intervention for new kidney transplant patients. As the primary centre (KCH) has a well-established physiotherapy renal team, we have included a second site that does not have existing physiotherapy services within kidney transplant clinics (GSTT).

3 OBJECTIVES

3.1 Trial objective

To conduct a bi-centre randomised controlled feasibility trial that will evaluate the feasibility of a novel online resource for new kidney transplant recipients.

3.2 Feasibility outcomes

Primary (feasibility) outcome measures include:

- Screening:
  - Number of participants screened per month
  - Proportion of eligible people unwilling to participate with reasons given (e.g. work commitments, not interested etc.)
- Recruitment:
  - Number of participants recruited per month
  - Recruitment rate (>50% of people approached consent to study who have been screened and deemed eligible to take part in the trial)

- Randomisation:
  - Willingness to be randomised to either the usual care group or the online intervention group will be captured

  Retention:
  - Number of participants retained in the trial per month
  - We aim to retain >65% of the sample at 12 months follow-up
  - Reasons given for withdrawal
- Adherence levels to intervention:
  - website log in data for those randomized to the intervention group
  - We will aim for the intervention group to adhere to 60% of the sessions on the online resource
- Adherence to study visits all participants:
  - proportion of planned data collection visits that are completed in full length of time for the study visits
  - We will also assess the time taken to do each participant assessment
  - The research team also wish to assess the ability to collect measures for a definitive study (body weight, body mass index, body composition, quality of life, self-efficacy, fatigue, arterial stiffness and physical function). These outcomes are listed section 5.2
- Safety
  - number of hospital admissions (non-elective, or elective who have had to stay in hospital > 24 hours), and reasons for admission
  - Expected and unexpected harms
  - All participants will be asked about admissions at each study visit and clinical records will be monitored for admissions throughout the trial
- Similarities and differences in recruitment, retention and adherence between the research sites (KCH and GSTT) will be investigated
- Experience and thoughts on using the online resource captured via semi-structured interviews in a sub-sample of the intervention group participants at 3 months
- Experience and thoughts on participating in the trial, and if users continue to revisit the resource. This will be captured via semi-structured interviews in a sub sample of participants across the study at 6 months

3.3 Nested Qualitative Study

Qualitative data is essential to capture participant experience during this feasibility RCT. It will be collected at two time points within the trial. Topic guides will be formulated and developed in consultation with PPI partners who form part of this trials study group. The research team will conduct these individual semi-structured interviews until data saturation is reached, i.e. no new themes, codes are revealed and we are able to replicate the study [20, 21].

3.3.1 3 month individual semi-structured interviews

At 3 months a purposive sample of approximately 6 to 10 intervention group participants will complete semi-structured interviews until data saturation is reached. Participants will be purposively sampled to reflect a range of ages and levels of engagement with the online intervention. This objective of these interviews is to explore experiences of using the online resource.

3.3.2 6 month individual semi-structured interviews

At 6 months a purposive sample of approximately 16 participants from both groups will complete semi-structured interviews. Participants will be purposively sampled to ensure a range of participants from both the trial sites and groups and a range of ages. These interviews will explore participants' experiences in the trial, and in those who completed the intervention, their experiences if they chose to or not to continue with the online resource after 12 weeks. We hope to explore experience, facilitators and barriers whilst using the online ExeRTiOn resource and the overall experience of taking part in the ExeRTion 2 trial.

4 STUDY DESIGN

4.1 Study type

A bi-centre Randomised Controlled Feasibility Trial in new kidney transplant recipients

4.2 Estimated enrolment and duration

We estimate that each participant will be in the trial for twelve months. We will allow for 6 months to recruit our sample and anticipate the overall trial will run for 24 months.

4.3 Sample size

We plan to consent 50 patients across two sites with 30 being recruited from KCH and 20 being recruited from GSTT. 25 participants will be randomised to usual care, and 25 will be randomised to the treatment group. A sample size between 24 and 50 has been recommended for feasibility trials [22-24].

The research team plan to achieve a 50% consent rate for this trial. Therefore if 100 eligible participants are identified, the study team will be able to estimate a consent rate of 50% with a 95% confidence interval of +/- 10% (40 to 60% consent rate) [22].

Calculation of confidence interval widths (in %): $1.96x \sqrt{(px\ (1-p)/n)}$. Where p=0.5 (50% consent rate).

NB. June 2020- update to target sample. Please refer to section 10.2

4.4 Randomisation

Patients will be randomised by a separate member of the research team using a computer generated list (sealedenvelope.com) to either the usual care group or intervention group. 25 patients will be randomised to the intervention group, and 25 patients will be randomised to the usual care group, irrespective of their site.

4.4.1 Blinding and bias

Unfortunately, due to the nature of the intervention, participants are unable to be blinded. As the specialist physiotherapist (EC) is also a PhD student, the assessments and interventions will be carried out by her. To allow for honest feedback on the resource and trial and to eliminate bias, qualitative interviews will be completed by a separate member of the research team, who has not had input into designing the intervention.

4.5 Statistical plan

As this is a feasibility trial, no statistical significance testing will be performed. Confidence intervals will be two sided at the 95% confidence level. Data from multiple sources (feasibility outcomes, assessment outcomes and qualitative interviews) will be triangulated.

4.5.1 Baseline characteristics:

Participant characteristics of those recruited to each group will be described using summary statistics; means and standard deviations or proportions as appropriate.

4.5.2 Feasibility outcomes

- Screening, recruitment, retention and adherence rates will be calculated and presented as proportions with 95% confidence intervals
- Length of time to recruit the 50 patients will be described either by means and standard deviations, or median and interquartile ranges
- Length of time taken to complete the assessments will be described either by means and standard deviations, or median and interquartile ranges
- Description of participants response to the treatment (log-in times, interactions with physiotherapists) will be described either by means and standard deviations, or median and interquartile ranges
- Assessment outcomes such as; Body weight, body mass index, body composition, quality of life, self-efficacy, fatigue, arterial stiffness and physical function will be described. Either by means and standard deviations, or median and interquartile ranges
- Reasons for withdrawal will be collated
- Qualitative interviews will be transcribed and translated verbatim and analysed using thematic analysis approach [25], informed by techniques of grounded theory such as line-by-line coding and constant comparison [20] Data triangulation (from multiple sources) will enhance the reliability of the results [26] and attainment of data saturation in this study

4.5.3 Progression to definitive trial criteria:

The team will progress to a definitive trial if this trial appears feasible based on the following criteria:

- Revision of the feasibility outcomes by the trial management group

- Revision of participant feedback from qualitative interviews indicate meaningful benefit to participants
- Difference in weight (prevention of weight gain) is at a clinically meaningful level based on consultation of clinical experts in the field
- The feasibility to establish which outcomes to include in a definitive study will be assessed
- Willingness to be randomised by participants will also be reviewed

5 STUDY SCHEDULE

5.1 Assessments

After written consent is received, participant's baseline demographic information will be recorded at entrance to the trial. Patients from both study sites and groups will be assessed at baseline, 3 months (post intervention) and 12 months as per Table 1 on the following page . Qualitative interviews will be conducted as per the previous description in section 3.3.

Table 1: Schedule of Assessments at both sites (KCH and GSTT)

	Screening and recruitment	**Baseline**	**3 months**	**12 months**
Visit No	**1**	**2**	**4**	**5**
Window of flexibility for timing of visits:		+/- 7 days	+/- 7 days	+/- 7days
Informed Consent	X			
Medical History and medication list review	X	X	x	X
Eligibility confirmation	X			
Blood pressure and heart rate		X	X	X
Weight (kg)		X	X	X
Waist circumference (cm)		X	X	X
Body mass index (kg/m2)	X Screened from notes	X	X	X
Bioelectrical impedance		X	X	X
Generalised Physical Activity Questionnaire (GPPAQ)		X	X	X
Chalder Fatigue Scale		X	X	X
Self-efficacy questionnaires for exercise and nutrition		X	X	X

Quality of life (EQ5D) questionnaire		X	X	X
Randomisation		After baseline visit	X	X
Adverse Events Review		x	x	X
Additional website data (intervention group only gathered throughout the study) • Log in data • Review of data entered into the website such as goals, weight, physical activity, work sheets • Review to see if patient achieved the goals they set with the programme. GPPAQ completed throughout the 12 week programme 3 times built into the website				
Qualitative sub-study (n≈ 5 to 10 participants at 3 months and approximately 16 participants at 6 months) • Individual interviews on ExeRTiOn users (intervention group) at 3 months • Individual interviews of purposive sample of trial participants at 6 months				

Assessments will be conducted either over the phone, or when clinically suitable, given the COVID19 pandemic, in the Clinical Research Facility at King's College Hospital. All attempts will be made to book study visits around existing clinic appointments to minimise burden on participants. Assessments will be completed in the same standardised order as reported below.

5.2 Outcomes assessed at study visits

Outcomes assessed include measures of anthropometric measures, patient reported outcomes, measures of physical function and cardiovascular risk.

5.2.1 Patient reported outcomes:

Self-reported Physical activity: measured by the general practice physical activity questionnaire (GPPAQ). The GPPAQ is a validated self-administered [27, 28] which provides a short measure of physical activity levels [29] which reasonable reliability [30].

Self-reported self-efficacy for physical exercise and nutrition: Self-efficacy can shed insight into an individual's beliefs in their capability to achieve a goal or a targeted behaviour to change [31]. The higher someone's self-efficacy, the more likely they will change their behaviour and adopt a healthier lifestyle [32]. This study will assess self-efficacy towards changing exercise, activity and food behaviours through The Nutrition Self-Efficacy Scale and the Physical Exercise Self-Efficacy Scales [32] Both these scales have been validated in a sample of 2549 participants [33, 34]. These scales have high internal consistency, the nutrition self-efficacy scale has a Cronbach's alpha of 0.87, and the exercise self-efficacy scale 0.88 [32].

Quality of Life: The EQ5D is a quality of life questionnaire designed by the EuroQual group [35] and has been validated in kidney transplant patients [36].

Fatigue: The Chalder Fatigue Scale [37] contains 11 items, including two sub scales measuring the severity of physical (7 items) and mental fatigue (4 items). Each item is scored from 0 to 3, with 0 being better than usual and 3 being much worse than usual. The total score can range from 0 to 33,

with higher scores representing greater levels of fatigue. This questionnaire has recently been used as a measure in renal dialysis patients, with a Cronbach α of 0.91 demonstrating high internal reliability [38].

5.2.2 Anthropometric measures and resting blood pressure:

- Body weight (measured in kilograms)
- Waist circumference (measured in cm)
- Body mass index (BMI) (measured in kg/m^2)
- Resting heart rate (beats per minute) and Blood Pressure (measured mmHg)
- Bio impedance will be measured by the Fresenius Body Composition Monitor (Fresenius BCM) [39, 40], the best validated device in the renal population against the gold-standard methods of body composition [41, 42], and has been used in dialysis patients [43-45]. This device is CE marked [46].

5.2.3 Physical Function and Cardiovascular risk measures:

Arterial Stiffness: Carotid-Femoral pulse wave velocity (PWV) is considered the gold standard measure of arterial stiffness [47] and is a strong predictor of cardiovascular and all-cause mortality in kidney transplant recipients [48]. PWV will be measured using the Vicorder system (Skidmore Industries, UK) at carotid and femoral points using standardised procedures [49] and calculations of arterial path length [50]. Transition times and PWV will be measured 3 times per assessment and then averaged for a final score of carotid-femoral PWV.

Physical Functional Capacity: The six minute walk test (6MWT) will be conducted using the standardised guidelines [51] and will physical function capacity. It is self-paced and requires patients walking for six minutes and allows for stops during the test.

5.3 Distress protocol

As participants will be discussing exercise and food intake whilst using the online resource and during the semi-structured interviews the team have devised a distress protocol (modified from Distress Protocol from Haigh and G. Witham 2015 [52]. In the previous qualitative study (IRAS 241928), this distress protocol did not have to be utilised when discussing weight and exercise experiences with new kidney transplant patients (unpublished data). The distress protocol can be found in Figure 2 on the following page.

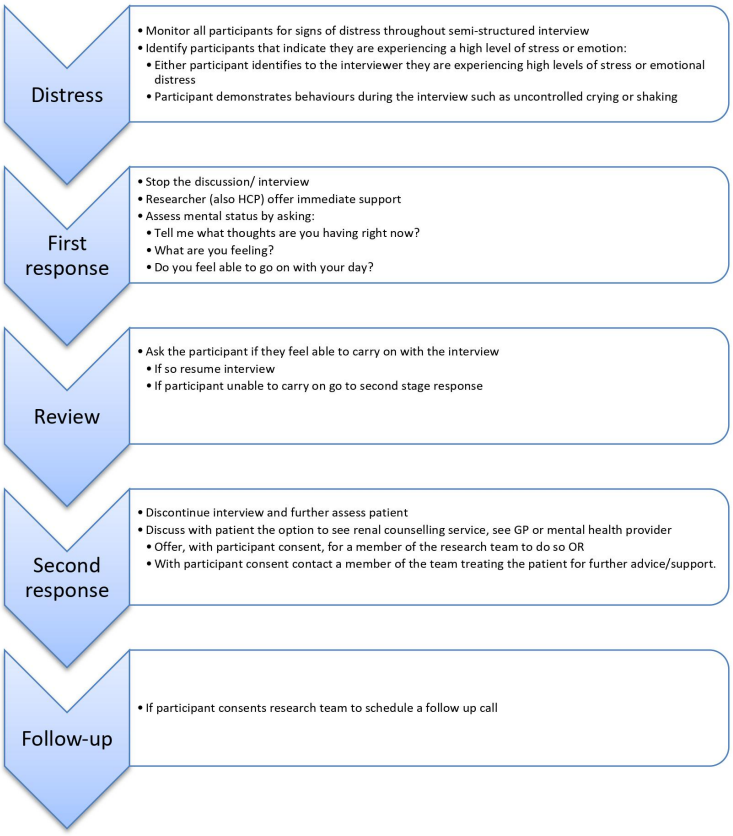

Figure 2. Distress Protocol for qualitative interviews.

5.4 Usual Care

Usual care will be defined as routine- clinical post-operative care including routine visits with nurses and nephrologists at their post-transplant clinic visits. The minimum requirement of usual care will include provision of a leaflet on eating after transplant, routine physiotherapy input during their transplant surgery hospital admission, and encouragement from the transplant clinic nephrologists and nurse to maintain a healthy lifestyle.

5.4.1 Usual Care at King's College Hospital

In addition to standard clinical care previously described, patients at the primary site will have up to 2 appointments with an outpatient physiotherapist. Once within the first 2 weeks on education regarding post-operative precautions and functional mobility, and the second appointment around

5-8 weeks post op where they will discuss exercise and physical activity advice post removal of uretic stents.

5.4.2 Usual Care at Guy's and St Thomas'

There is currently no routine physiotherapy provided during outpatient transplant clinics at this secondary centre. Therefore participants will receive the minimum level of usual care as defined by 5.4 above.

5.5 The online intervention

Participants randomised to the intervention group, will receive access to the online resource (ExeRTiOn). This includes 12 weekly sessions, and the option to revisit session content, continue with tracking and goal setting over the remaining 9 months of the study. The website will be monitored a specialist physiotherapist who provides structured, personalised input.

5.5.1 Components of the online intervention

The key components of the online resource are behavioural change techniques, specialised dietitian advice and exercise and physical activity advice post kidney transplantation.

All sessions follow the same format:

1. User logs in
2. User can either start session and is then prompted to track activity and weight or they can enter the activity and weight first
3. The user watches a short educational video on the topic by an expert from the renal team
4. Some activities then have an interactive activity
5. There is a summary page
6. The user is taken to the goals page to either set a goal or revisit a previously set goal. The user also uses a confidence and important ruler to assess their goals [53]. Here the user is asked to rate on a scale from 0 to 10 how confident they are in achieving the goal, and how important it is to them

The key sessions and specific elements to each session are summarised in Table 2 on the following page.

Table 2- Key components of the ExeRTiOn online resource

Session number	Session name	Behavioural Change Taxonomy used	Sessions elements
Welcome Session	Welcome to ExeRTiOn	• Self-monitoring • Education by specialist	• Introduction video • Agreement between participant and physio • Virtual tour of website • Introduction to tracking feature • Baseline intervention GPPAQ
Session 1	Goal setting	• Self-monitoring weight and activity • Edu by specialist • SMART Goal setting • Action planning	• Video from expert on how to set a SMART goal with patient input • User sets their first goal action plan
Session 2	Managing Cravings	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert renal dietitian on cravings and hunger post-transplant • Promotion of the hunger scale • Interactive activity • User prompted to revisit goals/ set new goal
Session 3	Food planning and labels	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert dietitian on planning food and how to read food labels • Reference resources in 'my library' • Second GPPAQ
Session 4	Activity after transplant	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert physio on activity after kidney transplantation • Reference to resources in 'my library' • Interactive activity
Session 5	Choosing your activity/exercise	• Self-monitoring weight and activity • Edu by specialist • Demonstration of behaviour (exercise)	• Video from expert physio on exercise options, demonstration of a few key exercises • Interactive activity

Session number	Session name	Behavioural Change Taxonomy used	Sessions elements
		• SMART goal setting +/- revision of goals	• Reference to 'exercise diary' and 'my library' resources
Session 6	Healthy eating- it's a balance	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert dietitian • User able to select which food group they would like more information on, and each has a separate video by specialist renal dietitian +/- interactive activity • Signposting to resources in 'my library'
Session 7	Quantity and Quality-they both matter	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• 3rd GPPAQ • Video from expert dietitian on portion control tips and strategies • There is an interactive activity • Signposting to resources
Session 8	Activity planning	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert physio on how to plan activity post-transplant highlighting a patient example • Option to activity plan
Session 9	Keeping on track whilst also having fun	• Self-monitoring weight and activity • Edu by specialist • SMART goal setting +/- revision of goals	• Video from expert physio • User able to select various topics such as eating out, on holiday, Christmas and celebrations to see top topics and further information
Session 10	Overcoming barriers	• Self-monitoring weight and activity • Edu by specialist • Problem solving • SMART goal setting +/- revision of goals	• 4th GPPAQ • Video from expert physio with expert patient about common barriers to activity and food post-transplant • Interactive worksheet on barriers
Session 11	Problem solving	• Self-monitoring weight and activity • Edu by specialist • Problem solving • SMART goal setting +/- revision of goals	• Video from expert physio on how to problem solve • Interactive worksheet on problem solving technique
Session 12	Preventing setbacks	• Self-monitoring weight and activity • Relapse prevention • Problem solving • Focus on past successes	• Video on relapse prevention by expert physio • Interactive worksheet • If willing patient able to revisit completed sessions, and continue tracking or goal setting during the length of the trial (optional)

5.5.2 Physiotherapist Support during the online intervention

A Specialist Physiotherapist will have access to the therapist (back-end) website, which will allow monitoring of the session completion, log-in times and review of goals, and self-reported weight and physical activity. Participants will be made aware of this. Support during the 12-week online intervention will be standardised to include; weekly automatic reminder emails (generated by the website), alerting them to the unlocked session each Monday, and 3 interactions with the specialist physiotherapist. These interactions will occur at the start of the intervention (face-to-face), half way through the online resource (personalised message) and at the end of the .online resource programme.

5.5.2.1 Face-to-Face induction with Specialist Physiotherapist

At the start of the online intervention, intervention group participants will have one brief face-to-face appointment (approximately 20 minutes) with the specialist physiotherapist. The patient will be set up with an account to an email of their choice and provided with a tour on the main functions of the website.

5.5.2.2 Personalised Feedback at six and 12 weeks

To ensure engagement and promotion of changes to food and activity behaviours, participants in the intervention group will receive a personalised message of encouragement half way through the sessions (week six), and at completion of the sessions (week 12). These individual messages will be sent through the website from the physiotherapist directly and will be based on the individual participant. Examples of messages for the three scenarios at six and twelve weeks (1. maintained weight, 2. reduced weight and 3. gained weight) are shown below. Please note these are just examples and will be individualised based on each participants' online resource profile.

1. If the participant has maintained their baseline weight they will be encouraged to continue with their goals and physical activity and diet plans.
    - An example message could be: *"Well done. You have successfully managed to maintain your weight. Remember to keep setting yourself goals and track your weight and activity"*

2. If the participants have reduced their weight they will be congratulated and encouraged to continue with their goals and physical activity/ diet plans.
    - An example copy could be: *" Congratulations! Your hard work seems to be paying off and you have reduced your weight. You might find it helpful to review your goals and continue to track your activity and weight each week"*

3. If the participants have gained weight, the difficulty of this process will be highlighted to normalise the experience and promote engagement. Support will be offered via the message system with words of encouragement specific to the individual participant's profile.
    - An example message could read: *"Our clients tell us that reducing weight after a kidney transplant can be really hard. Well done on continuing to work through your ExeRTiOn sessions. If you would like some tips on how to tweak your goals to meet your targets please send the physio a message through your message button".*

5.5.2.3 Personalised Feedback if participant is not engaging

, A standard protocol for engaging with participants if they have not logged two sessions in a row will include a personalised message from the physiotherapist. An Example can be found below.

> *"Dear (name),*
>
> *I hope everything is ok? Please let me know if you would like to arrange a chat or visit with me. You can do this by either sending me a message through the ExeRTion home screen, or via sending me an email to kch-tr.exertion@nhs.net.*
>
> *Kind regards,*
>
> *Ellen (your ExeRTiOn Physiotherapist)"*

After sending this message, if the participant then fails to engage, the physiotherapist will make contact over the telephone to ascertain reasons for non-engagement. This will be reported as part of the feasibility evaluation of this trial. All interactions will the physiotherapists will be logged.

6 CONSENT AND RECRUITMENT

Patients will be screened and identified by clinicians working in the transplant team, and also by the site PI's. Potential participants will initially be provided with their specific site patient information sheet (the current Research Ethics Committee (REC) and Health Research Authority (HRA) approved version) and a covering letter explaining the trial to them and inviting them to participate in the trial during their clinical visits. They will have time to consider the trial (a minimum of 24 hours) and decide whether or not they wish to take part, and to discuss the trial with their family and friends if they would like to.

Potential participants will be followed up and have the opportunity to discuss the trial further and to have any questions that they may have about the trial answered from a member of the research team. The Principal Investigator at each site will explain that there is no obligation for a potential participant to enter the trial, that trial entry is entirely voluntary, and that it is up to the potential participant to decide whether or not they would like to join. It will also be explained that they can withdraw at any time during the trial, without having to give a reason and that their decision will not affect the standard of care they receive. Any reasons for non-participation will be recorded if the information is volunteered.

If willing to participate, participants will complete a written consent form based on the GCP guidelines and the eligibility criteria below. A copy of the signed informed consent form will be given to the participant. The original signed form will be retained at the study site in the Investigator Site File and a copy placed in the medical notes. A copy will also be sent to the Chief Investigator of the study. With KTx participant's prior consent, their General Practitioner (GP) will also be informed of their participation of the study.

Throughout the trial duration, participants will be encouraged to ask questions and will be reminded that they can withdraw at any time without their clinical care being affected.

7 ELIGIBILITY CRITERIA

Participants will be recruited to the study based on the following inclusion and exclusion criteria:

7.1 Inclusion Criteria

- Adult patient (18 years+)
- male or female
- Able to provide written informed consent
- < 3 months post-transplant. NB. Our team has decided to recruit patients within the first three months post transplants as most patients at our centre are not cleared to start a formal physical activity or exercise plan until they have ureteric stents removed which usually occurs at 6 weeks post-transplant surgery.
- Access to Internet connected computer, smart-phone or tablet. NB. Our team has completed a waiting room survey and our patients often use internet to view their clinical blood results through "renal patient view", therefore do not perceive internet access as a barrier to this study.
- A Body Mass Index (BMI) greater than or equal to 18.5 (healthy range).

7.2 Exclusion Criteria

- Age < 18 years of age
- Pregnancy
- Unstable medical conditions such as angina, uncontrolled hypertension or diabetes, congestive cardiac failure, active myocarditis, cardiac arrhythmia, co-morbid catabolic condition, psychiatric illness.
- Participated in a structured exercise or physical activity intervention in the last three months
- BMI of less than 18.5 (classified as underweight)
- Significant cognitive impairment preventing them from engaging with online interactive material
- Unable to complete the online resource in English. For this small feasibility study, we do not have the budget to translate the resource into multiple languages. However if this study is successful, we will revisit this in a multi-centre randomized controlled trial application.

8 PATIENT AND PUBLIC INVOLVEMENT (PPI)

Extensive PPI has been conducted for this study as patient and public involvement is crucial that this website is acceptable and feasible for the target audience, kidney transplant recipients. We have three expert patients from the study group who have reviewed this protocol to assess its patient burden level and acceptability.

Our renal care group is fortunate to have a group of patients across the Chronic Kidney Disease trajectory in our research group. They have reviewed all associated study documents and ensured they are appropriate for patients. This group will also assist in reviewing lay summarised for the dissemination of research.

In addition to this, the research team have recently completed a small qualitative study assessing the acceptability of this online resource in a cohort of new kidney transplant recipients (n=11) and kidney transplant healthcare professionals (n=6). Both health care professionals and more importantly KTR participants positively reviewed the online resource and positively valued the videos, goal setting and self-tracking functions. Suggestions on revisions for the online resource were based on the results of this small study. The results of this small study (unpublished) suggest that the online resource is acceptable, and worth exploring in this current feasibility randomised controlled trial.

9 FUNDING

The research team was previously awarded £25,000 to complete the original draft of the ExeRTIOn website through the King's College Hospital charity fund. Research costs for this study are supported by Ellen Castle's PhD Grant through Kidney research UK. This grant includes from the 2st of July 2018 to the 1st of July 2021 (AHPF_001_20171122 £203, 437.44).

All attempts will be made for study visits to occur when participants are already attending routine post-transplant clinic appointments. Where this is not possible, there is a travel reimbursement available for up to £20 per participant. For their participation in the trial, each participant will be provided with an inconvenience fee of £30 per participant.

10 DATA HANDLING AND MANAGEMENT

10.1 Trial data

The storage of personal data on manual files will be appropriately filed and stored securely in the renal rehab team office as per the Trust confidentiality policy. All paper data recording sheets will be stored in lockable filing cabinets at the Renal Rehab Team office for 5 years . Electronic data spreadsheets will be kept on the private renal rehab team drive and password protected. This drive has limited access. All patient identifiable material will be removed in place of trial ID numbers.

Storage of personal information on NHS computers will have appropriate access controls in place to ensure that access to confidential research information is restricted to those who need the access. Website data (only intervention group participants n=25) will be accessed on KCH Trust computers and will be limited to the CI and PhD student and will be password protected. Participants have their own selected password to log into their profile. The data the online resource collects is held in an encrypted state in line with NHS and GDPR policies.

Date of birth, address, phone number etc will not be recorded on the website. The participants will be allocated a trial ID, and asked to enter their preferred name and email address.

10.2 Trial management group

A trial management group consisting of the CI, PI's, external statistician, patient experts will meet either face to face or on a telephone call to review recruitment, adherence and retention at least 3 times per year.

June 2020- update to study design due to COVID 19. On the 2nd of June 2020 the study team conducted a virtual 'extra-ordinary' TMG meeting. Attendance included the lead for the trial and PhD student (EC), all supervisors (SG, JC,KB), CI of the study (SG), PI for primary site (EC), PI for secondary site (GSTT), statistician consultant (RP), PostGraduate chair of the university (RT), Consultant Nephrologist and lead of renal research at primary site (SS), external expert (MM) and patient expert (MW). The team reviewed all data to date against the feasibility ouctomes, and the clinical situation with our target group. The group decided that the study would not recruit any further participipants, and the data on the 17 paritcipants recruited prior to COVID19 would sufficiently answer the fesability outcomes and study questions. Both R and I sites were informed. Study funder was informed. Changes to the study include submission for an ethical ammeddment to reflect no further recruitment. The team will also plan to conduct questionnaires and qualitative interviews over the telephone on the 17 participants, until it is clinically indicative to collect the outcomes face to face.

10.3 Website data (intervention group)

Website data will be managed as per the data security document titled "Data security and privacy document for the ExeRTiOn study 2 V1. 4th March 2019 ". Information Governance such as Data capture, use and sharing have been assessed and approved by the lead of Information Governance for the trust Nick Okane-Murphy and approved on the 21st of May 2019.

10.4 Protocol deviations and violations

A deviation is usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and R&I Office should be notified immediately of any case where the above definition applies during the study conduct phase

10.5 Trust incidents and near misses

An incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.
b. It is contrary to specified or expected standard of patient care or service.
c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d. It puts the Trust in an adverse position with potential loss of reputation.
e. It puts Trust property or assets in an adverse position or at risk.

Incidents and near misses must be reported to the Trust through DATIX as soon as the individual becomes aware of them.
A reportable incident is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a) It is an accident or other incident which results in injury or ill health.
b) It is contrary to specified or expected standard of patient care or service.
c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d) It puts the Trust in an adverse position with potential loss of reputation.
e) It puts Trust property or assets in an adverse position or at risk of loss or damage.

11 PEER AND REGULATORY REVIEW

The study has been peer reviewed in accordance with the requirements outlined by King's College Hospital (KCH) R&I and Guy's and St Thomas' Hospital. This study has been reviewed as part of an educational programme. The Sponsor (KCH) has verified that the supervisor of the project has undertaken sufficient review of the protocol in line with the requirements of his/her department.

The study was deemed to require regulatory approval from the following bodies (list). Each approval will be obtained before the study commences.

- HRA
- REC

12 MONITORING AND AUDITING

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

13 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files.

14 INTELLECTUAL PROPERTY

Agreements and Statement of works specific to this project have been drawn up between KCH R &I department and the software company SPIKA.

15 INDEMNITY ARRANGEMENTS

KCH will provide NHS indemnity cover for negligent harm, as appropriate and is not in the position to indemnify for non-negligent harm. NHS indemnity arrangements do not extend to non-negligent harm and NHS bodies cannot purchase commercial insurance for this purpose; it cannot give advance undertaking to pay compensation when there is no negligence attributable to their vicarious liability. The Trust will only extend NHS indemnity cover for negligent harm to its employees; both substantive and honorary, conducting research studies that have been approved by the R&D Department. The Trust cannot accept liability for any activity that has not been properly registered, and Trust approved. Potential claims should be reported immediately to the R&I Office

16 ARCHIVING

During the study, all data will be kept securely and confidentially at the Renal Physio office at KCH after the study has ended paper data recording sheets, the trial master file, and patient consent forms will be kept locked and secure for 5 years. Data spreadsheets will be encrypted, name and contact details removed, and stored on a private team specific folder with audited and restricted access.

17 PUBLICATION AND DISSEMINATION POLICY

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

1. Conference presentation of study findings at either the American Society of Nephrology conference and/or the British Renal Society conference
2. Publication of study findings and results
    - The student will act as primary author (EC), with senior authorship by the supervisors (JC and SG)

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19 APPENDICES

19.1 Appendix 1: Protocol versions

Versions No	Version Date	Status
V1.1	24th May. 2019	Previous version of the protocol (prior REC/HRA review)
V2	16th July 2019	Addressing feedback and comments from REC/HRA review.
V2.1	16th August 2019	Additional comments from REC/HRA. This is the current version.
V3.1	22nd June 2020	Changes to the study delivery as a result of COVID19 and ethical amendment submitted. Changes to: - No further recruitment of participants - Phone follow up

Initial ethical approval feasibility RCT (studies 3 and 4)

Health Research Authority

London - Dulwich Research Ethics Committee
Health Research Authority
Skipton House
80 London Road
London
SE1 6LH

Telephone: 0207 104 8241

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

06 August 2019

Dr Sharlene Greenwood
King's College Hospital
Physiotherapy Department
Denmark HIll, London
SE5 9RS

Dear Dr Greenwood

Study title:	**ExeRTiOn 2- The Weight Gain prevention in Renal Transplant Online study. A Randomised Controlled Feasibility Trial**
REC reference:	**19/LO/1138**
Protocol number:	**1**
IRAS project ID:	**262007**

Thank you for your letter of 19 July 2019, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair and Committee Member, Dr Jiafeng Feng.

Confirmation of Ethical Opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Number	Condition
1	Please make sure there are no incidences of the misspelling of “Guy’s” and “Principal” throughout the study as there are incidence of “Guys’” in the Protocol and GP Letter and “Principle” in the Participant Information Sheet.
2	Please make sure “comples” is correctly spelt in the Protocol as what is assumed as “complex”.

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

It is a condition of the REC favourable opinion that all clinical trials are registered on a publicly accessible database. For this purpose, clinical trials are defined as the first four project categories in IRAS project filter question 2. For clinical trials of investigational medicinal products (CTIMPs), other than adult phase I trials, registration is a legal requirement.

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral:
https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We will audit these as part of the annual progress reporting process.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical Review of Research Sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites listed in the application subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS/HSC sites

I am pleased to confirm that the favourable opinion applies to any non-NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved Documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
GP/consultant information sheets or letters [GP Letter V2.]	V2	16 July 2019
Interview schedules or topic guides for participants [Topic guide 3	V1	04 March 2019

months]		
Interview schedules or topic guides for participants [topic guide 6 months]	V1	04 March 2019
IRAS Application Form [IRAS_Form_10062019]		10 June 2019
IRAS Application Form XML file [IRAS_Form_10062019]		10 June 2019
IRAS Checklist XML [Checklist_19072019]		19 July 2019
Letter from funder [PhD grant award letter]		
Non-validated questionnaire [Self-efficacy questionnaire]	V1	04 March 2019
Other [data security document]	V1	04 March 2019
Other [CRF for patient visits]	V1	04 March 2019
Other [CRf for quali visits]	V1	04 March 2019
Other [Response to REC and HRA]	V1	17 July 2019
Participant consent form [GSTT consent form V2.]	V2	16 July 2019
Participant consent form [KCH consent form V2]	V2	16 July 2019
Participant information sheet (PIS) [KCH.PIS. V2.16thJuly.2019]	V2	16 July 2019
Participant information sheet (PIS) [GSTT.PIS.V2.16thJuly 2019]	V2	16 July 2019
Research protocol or project proposal [V2. ExeRTiOn2 Protocol]	V2	16 July 2019
Summary CV for Chief Investigator (CI) [CV for SG (CI)]		02 May 2019
Summary CV for student [CV student]		
Summary CV for supervisor (student research) [Supervisor 2 CV]		
Validated questionnaire [chalder fatigue scale]	V1	19 February 2019
Validated questionnaire [GPPAQ]	V1	04 March 2019
Validated questionnaire [EQ5D]	V1	04 March 2019

Statement of Compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:
https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/LO/1138	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely

PP
Mr Colin Stansfield
Vice Chair

Copy to: Anne-Marie Murtagh

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Sharlene Greenwood
King's College Hospital
Physiotherapy Department
Denmark Hill
London SE5 9RS

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

27 August 2019

Dear Dr Greenwood,

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**ExeRTiOn 2- The Weight Gain prevention in Renal Transplant Online study. A Randomised Controlled Feasibility Trial**
IRAS project ID:	**262007**
Protocol number:	**1**
REC reference:	**19/LO/1138**
Sponsor:	**King's College Hospital NHS Foundation Trust**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **262007**. Please quote this on all correspondence.

Yours sincerely,

Emma Stoica
Approvals Manager

Email: hra.approval@nhs.net

Copy to: *Anne-Marie Murtagh kch-tr.research@nhs.net*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Contract/Study Agreement template [MNCA]		
GP/consultant information sheets or letters [GP letter V2.1]	V2.1	16 August 2019
Interview schedules or topic guides for participants [Topic guide 3 months]	V1	04 March 2019
Interview schedules or topic guides for participants [topic guide 6 months]	V1	04 March 2019
IRAS Application Form [IRAS_Form_10062019]		10 June 2019
Letter from funder [PhD grant award letter]		
Non-validated questionnaire [Self-efficacy questionnaire]	V1	04 March 2019
Organisation Information Document	HRA v1	
Other [Response to REC and HRA]	V1	17 July 2019
Other [Response HRA.REC 16.Aug]		16 August 2019
Other [data security document]	V1	04 March 2019
Other [CRF for patient visits]	V1	04 March 2019
Other [CRf for quali visits]	V1	04 March 2019
Participant consent form [GSTT consent V2.1]	V2.1	16 August 2019
Participant consent form [KCH Consent V2.1]	V2.1	16 August 2019
Participant information sheet (PIS) [KCH.PIS V2.1]	V2.1	16 August 2019
Participant information sheet (PIS) [GSTT PIS. V2.1]	V2.1	16 August 2019
Research protocol or project proposal [Protocol V2.1]	V2.1	16 August 2019
Schedule of Events or SoECAT	HRA v1	
Summary CV for Chief Investigator (CI) [CV for SG (CI)]		02 May 2019
Summary CV for student [CV student]		
Summary CV for supervisor (student research) [Supervisor 2 CV]		
Validated questionnaire [chalder fatigue scale]	V1	19 February 2019
Validated questionnaire [GPPAQ]	V1	04 March 2019
Validated questionnaire [EQ5D]	V1	04 March 2019

IRAS project ID	262007

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
There are two site-types in the study: KCH (the sponsor) - recruitment of participants and all study assessments and intervention GSTT - recruitment of participants	You should work with your sponsor R&D office to make arrangements to set up the study at the sponsor trust (KCH). The R&I office will confirm to you when the study can start following issue of HRA and HCRW Approval. Research activities should not commence at the other participating NHS organisation (GSTT) prior to their formal confirmation of capacity and capability to deliver the study.	An Organisation Information Document has been submitted and the sponsor is intending to use a separate site agreement, which is an unmodified mNCA.	The sponsor secured funding for the study. The sponsor is not providing funding to the NHS trust recruiting participants (GSTT). Please note that the SoECAT submitted for this study has not been authorised by an AcoRD Expert. HRA or HCRW sign off is for versioning only. This sign off does not constitute authorisation of the content of the SoECAT or confirmation that the cost attribution is appropriate.	Local Principal Investigators should be in place at the NHS organisations.	Where no prior arrangements are in place, network staff (or similar) undertaking any of the research activities at the NHS trusts, would be expected to obtain an honorary research contract from one NHS organisation (if University employed), followed by Letters of Access for subsequent organisations. This would be on the basis of a Research Passport (if University employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm enhanced DBS checks, including appropriate barred list checks, and occupational health clearance.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.

Ellen Castle
Study Physiotherapist (Senior Renal Physiotherapist)
Tel: 020 3299 6725

Dr Sharlene Greenwood
Consultant Renal Physiotherapist

The Renal Unit
Unit 6 KCH Business Park
London, SE5 9RS

King's College Hospital Patient Information Sheet V2.1 16th August 2019

Study title

ExeRTion 2-The Weight gain prevention Renal Transplant Online study. A Randomised Controlled Feasibility Trial.

PART 1

1. An invitation

We'd like to invite you to take part in our research study. Joining the study is entirely up to you, but before you make a decision, we would like you to understand why the research is being done and what it would involve for you. One of our team will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have. We suggest this should take about 10 minutes. Please feel free to talk to others about the study if you wish.

The first part of this Participant Information Sheet tells you the purpose of the study and what will happen to you if you choose to take part.

The second part will give you more detailed information about the conduct of the study. Please ask if anything is unclear.

2. What is the purpose of the study?

The purpose of this study is to see if a new online resource is a feasible treatment option for new kidney transplant recipients. The online resource provides participants with information to improve physical activity and achieve a healthy weight to prevent weight gain after kidney transplant surgery. Weight gain can affect some people after receiving a kidney transplant. This is thought to be due to a variety of reasons such as medications that increase your appetite, the lifting of food restrictions that may have been in place whilst you received dialysis and having a healthy appetite with a functioning kidney. Significant amounts of weight gain can affect health outcomes, and there is no current universally accepted treatment to prevent weight gain after transplant. Therefore our team have recreated this online resource, alongside feedback from kidney transplant patients to improve physical activity and to achieve a healthy weight.

The study is asking a group of patients who have received a kidney transplant if they are willing to take part in this study. It will involve 3 assessments over 12 months. If you are randomly allocated to the treatment group, you will receive access to the online website. The website has 12 weekly sessions (lasting approximately 20 to 30 minutes).

The overall aim of the study is to see if this online resource is a helpful and feasible option for new kidney transplant recipients to prevent weight gain after transplant surgery.

3. Why have I been invited?

You have been invited to take part in the study because you have recently received a kidney transplant. We expect approximately 50 patients will take

part in this study across two hospital sites (King's College Hospital and Guy's and St Thomas' Hospital).

4. Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. You will be able to keep this information sheet and think about taking part. You are free to discuss the information with anyone you wish including your family and friends. If you agree, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

Taking part in this research is entirely voluntary. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

5. What will happen to me if I take part?

a) Signing up to the study
A member of the research team (a doctor or physiotherapist) will approach you during your transplant clinic and if you wish, provide you with information on this study. Members of this research team are also clinicians working in the transplant team. Therefore they have access to medical records. If you agree to take part in this study, the doctor of physiotherapist will explain the study in detail, and the various things it will involve. They will give you this information sheet and ask you to sign a consent form so that you can be enrolled in the study. They will also give you a data security document which further describes the website.

b) A typical course of events for you might be as follows:
After signing the consent form in the Clinic, you will be invited to take part in the study. The researcher will review your demographic information such as your age, gender, and medical history. You will then be invited to complete an initial study visit at the clinical research facility at King's, where you will complete some questionnaires looking at your physical activity levels, fatigue, quality of life and how confident you are to change your activity and food routines. The researcher will then measure your weight, your body composition (fat levels, muscle levels and fluid levels),

how stiff your blood vessels are and how far you can walk in six minutes. This is at your own pace and you can have rests if you need to. All of these tests are non-invasive. We estimate this study visit will take approximately 45 to 60 minutes.

After this initial assessment, you will be allocated randomly (like flipping a coin) to receive either access to this online website for 12 weeks, or normal care. As there is currently no recognised universal treatment for weight gain prevention for new kidney transplant patients, the research team need to test in a scientific way if this new website is a feasible treatment option. To do this we need to randomly allocate half of the participants to the online website group and half to the usual care group. To ensure this study is performed in a scientific manner, we cannot select which group you are allocated to and you will be randomised by a separate member of the research team. You will be asked not to tell the person conducting the assessments which group you have been allocated into.

If you are randomised to the usual care group, you will continue with your routine clinic appointments and attend 2 more study visits (one at 3 months and one at 12 months

If you are randomly allocated to the online resource group, you will be provided with a log in to the website and will attend a 1:1 visit with your Physio Ellen who will give you a brief tutorial on how to use this website. She will do this when you are already attending clinic to see the transplant team to minimise additional journeys. You will then be asked to log onto this website by yourself once a week, to complete the 12 week programme. Your progress will be monitored by your physio Ellen, who will give you feedback at six weeks and 12 weeks via the online website secure messaging. If you have any questions throughout the website you can send your Physio a secure message. You will also receive weekly reminder emails to log on and complete your session. If you do not log in 2 weeks in a row, your physio will send you a private message to touch base with you and offer support. After you have completed the online resource, you will have the option to continue using the tracking facilities (weight and activity) and being able to view the content until the end of the study (six months in total).

At 3 months' time and six months' time both groups will be attend another study visit were the same tests from the start of the study will be repeated

(questionnaires, weight, body composition, stiffness of blood vessels and six minute walk test). More detail of what will happen at each assessment will, be summarised in a table.

Table 1- Assessments completed over the study

	Baseline	**3 months**	**12 months**
Visit No	**1**	**2**	**3**
Blood pressure and heart rate	X	X	X
Weight (kg)	X	X	X
Waist circumference (cm)	X	X	X
Body mass index (kg/m2)	X	X	X
Bioelectrical impedance (body composition)	X	X	X
Generalised Physical Activity Questionnaire (GPPAQ)	X	X	X
Chalder Fatigue Scale	X	X	X
Self-efficacy questionnaires for exercise and nutrition	X	X	X
Quality of life (EQ5D) questionnaire	X	X	X
Arterial stiffness	X	X	X
Six minute walk test (physical function)	X	X	X
Additional website data (intervention group only gathered throughout the study) • Log in data • Review of data entered into the website such as goals, weight, physical activity, work			

sheets • Review to see if patient achieved the goals they set with the programme. GPPAQ completed throughout the 12 week programme 3 times built into the website
Qualitative sub-study • Individual interviews on ExeRTiOn users (treatment group) at 3 months • Individual interviews of purposive sample of participants at 6 months

During the study, a selected number of participants will be asked to attend an initial 45 to 60 minute visit to discuss their experiences using the online resource and being part of the trial. 5 to 10 patients will be invited from the online website group to take part in these interviews discussing their experiences using the website. Roughly 16 participants from both groups will be invited to have an individual interview to discuss their experiences during the trial at six months into the trial. These will be audio recorded and completed by a member of the research team. Your recording will be anonymised.

6. What are the alternatives for treatment?

This study is testing a new online treatment to help prevent weight gain in the first year post kidney transplant. There are currently no other treatments for this at both King's College Hospital or Guy's and St Thomas' Hospital. If you decide not to take part in the trial, you will continue with your usual clinic visits at your post-transplant clinic.

7. What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get from this study will help improve the future treatment of people with kidney transplant recipients. We hope by taking part in this study you will be able to have some non-invasive tests to show your weight and fitness that you may not get access to outside of the trial. The main benefit is to help improve the care for future patients. Your comments and feedback will also improve the online website for future use. The website has potential benefits including improving physical fitness and diet.

8. What are the possible disadvantages and risks of taking part?

If you do agree to take part in this study, there will be additional time involved to complete the study visits. This will involve the 3 study visits over the 12 month study. To minimize your inconvenience, the one off study visit will be scheduled around your routine transplant clinic appointments. There are no known risks with taking part in this study.

9. Who is organising and funding this study?

The lead researcher overlooking this study is Dr Sharlene Greenwood. She has conducted lots of studies in the past investigating exercise and also healthy eating for patients with chronic kidney disease. The research will be performed by a specialist Renal Physiotherapist (Ellen Castle) who is also completing her PhD and will be supervised by Dr Greenwood. Ellen Castle has received funding to complete this study and her PhD through Kidney Research UK. The study is sponsored by King's College Hospital. The access that you receive for the online resource and physiotherapist will be covered by the study.

10. How have patients and the public been involved in this study?

People who have received kidney transplants, and also members of the transplant team have been heavily involved in this project. This is crucial to ensure this online resource contains what people who have had a kidney transplant feel they need.

The research team have recently completed a study at King's College Hospital in a group of new kidney transplant recipients, and also members of the kidney transplant team testing the online resource. These comments have allowed us to further edit and refine this online resource for this study.

Expert kidney transplant patients have also reviewed this study design to take into account patients opinions, the frequency of visits and also the tests carried out in this study.

11. Who has reviewed this study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by _____ Research Ethics Committee. It has also been approved by the Health Research Authority and each local hospital will also give confirmation that the study can go ahead.

12. Expenses and payments

Every attempt will be made to arrange your study visits to occur when you are already attending your clinic visits, to minimise additional visits up to the hospital. When this is not possible, there is a travel reimbursement available for up to £20 per person. For your participation in the trial, each participant will be provided with an inconvenience fee of £30 per person.

13. What happens when the research study stops?

When the study is over, we will send you a report explaining the results of the study. We will be happy to discuss these further with you if you wish.

PART 2

14. What if new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your study doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study, he/she may ask you to sign a second consent form, to re-consent to this study with this updated information.

This new information that becomes available might specifically affect you and your health. If this happens, your study doctor might consider that you should withdraw from the study. He/she will explain the reasons for withdrawing from the study and arrange for your care to continue.
If the study is stopped for any other reason, we will tell you and arrange for your continuing care.

As we are creating a new online resource, if new information becomes available, we will keep you informed throughout the duration of the study.

15. What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time; and if you would like to do so; please speak to your study physiotherapist or doctor.

Your decision to withdraw from the study will not affect the care you receive.

If you were to become unwell and lose the capacity to make your own decision, you will be withdrawn from the study. This means any information gathered for this study before this point will be anonymised and used for the study. You would not be asked to perform any further assessments.

If you decide to withdraw from the study;

- Information collected about you may be used if you are happy with this.
- This information will be anonymised and will be stored appropriately
- No further information will be collected from you once you withdraw from the study.

16. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to your study physiotherapist who will do their best to answer your questions: Ellen Castle, 020 3299 6725.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office are below:
King's College Hospital Patient Advisory and Liaison Service (PALS) on 020 3299 9000.

Every care will be taken in the course of this study. However in the unlikely event that you are injured by taking part, compensation may be available.

In the event that something does go wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against King's College Hospital NHS Trust, but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study physiotherapist or doctor if you would like more information on this.

17. Will my taking part be kept confidential?

All information which is collected about you during the course of the study will be kept strictly confidential and secure. Data will be anonymised and may be shared with other researchers and collaborators within the research team. All paper data recording sheets will be stored securely in lockable filing cabinets at the renal rehab office for 5 years. Documents will also be archived using a secure archiving system. Electronic data spreadsheets will be kept on the private renal rehab team drive and will be password protected. All patient identifiable details (name, address, hospital number) will be removed and replaced by trial ID numbers.

All staff involved in this research project will ensure data is handled with strict confidentiality in line with local trust policies. Data will be reviewed regularly by the student and monitored by the supervisors. Interviews will be transcribed by the study physiotherapist, Ellen Castle. Any information collected by the online resource will be anonymised and protected by a secure log in function.

Relevant sections of your medical notes and data collected during the trial will be looked at, in confidence, by authorised individuals from the study team.

18. Information on study sponsor and personal data

King's College Hospital is the sponsor for this study based in London in the United Kingdom. We will be using information from you and your renal medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. King's College Hospital will keep identifiable information about you for 5 years after the study has finished.

Your rights to access, change or remove your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we

will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information
https://www.kch.nhs.uk/about/corporate/data-protection

King's College Hospital will collect information from you and your medical records for this research study. The study research team King's College Hospital will keep your name, hospital number, and contact details confidential. The research team at King's College Hospital will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from King's College Hospital and regulatory organisations may look at your medical and research records to check the accuracy of the research study. King's College Hospital will only receive information without any identifying information.

19. Involvement of the General Practitioner/Family Doctor (GP)

With your consent, your GP will be informed of your involvement in the trial. Any other medical practitioners who treat you, e.g. should you be admitted to hospital for any reason, will also be informed.

20. What will happen to the results of the research study?

The results will be presented at scientific meetings and also published in the scientific literature.

21. Thank you

Thank you for considering taking part and taking the time to read this information sheet. If you decide to take part in this study, we will give you a copy of the information sheet and a signed consent form to keep.

22. Further information and contact details

Sharlene Greenwood
Consultant Renal Physiotherapist and Chief Investigator of this study
King's College Hospital, London, SE5 9RS
020 3299 6725
Sharlene.greenwood@nhs.net

Ellen Castle
Senior Renal Physiotherapist
Study Physiotherapist and Principal investigator at King's College Hospital
King's College Hospital, London SE5 9RS
020 3299 6725
Ellen.castle@nhs.net

Data security document feasibility RCT

King's College Hospital NHS
NHS Foundation Trust

Ellen Castle
Senior Renal Physiotherapist

Dr Sharlene Greenwood
Consultant Renal Physiotherapist

The Renal Unit
Unit 6 KCH Business Park
London, SE5 9RS

Direct Tel: 0203 299 6725
Direct Fax: 0203 299 6940

Data Security and Privacy document for The ExeRTiOn 2 study V1 4th March 2019

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1. Study title

ExeRTiOn2- The Weight gain prevention in Renal Transplant Online Study. A Randomised Controlled Feasibility Trial.

2. Overview

In this section we outline the data processes that happen as part of ExeRTiOn 2 study and explain what data will be collected and what happens to that data.

Handling your information securely and confidentially is extremely important to us.

We will refer to the online resource you will use as part of the study, if you are randomised to the treatment group as "ExeRTiOn".

As well as the data security processes we outline below, ExeRTiOn will log you out automatically after 20 minutes of inactivity.

We also recommend:

- Logging out whenever you have finished working on ExeRTiOn
- Keeping your ExeRTiOn username and password in a secure place
- Not sharing any unnecessary personal information or contact details with your Physio via your online messages (this is explained in more detail below).

Data Security and Privacy Document for the ExeRTiOn2 study
Version 1.0 4th March 2019**IRAS project ID**: 262007.
ExeRTiOn2 study

3. Device security

Your security and privacy on ExeRTiOn depends on the device you use to access the website. You are able to use ExeRTiOn on a computer, tablet or smartphone, as long as you are connected to the Internet.

To ensure maximum security, we recommend you keep your software up-to-date, choose strong passwords which are not easy to guess, use security protection software and avoid unsecured public internet connections.

4. Cookies

Most websites these days use 'cookies' to help the website run smoothly. Cookies are tiny text files that are made by the website. They provide a way for the website to remember you and the preferences you select. They are temporarily stored on your computer or device. When you come to the home screen of the ExeRTiOn website you can choose to accept all the cookies with one click or click on the 'cookie settings' for more information. When you click on the 'cookie settings' you will be able to opt-in and opt-out depending on the type of cookies you select. The software company helping King's College Hospital build this website and host this website (SPIKA) meets NHS Digital standards for privacy, confidentiality, security and General Data Protection Regulation (2018) GDPR.

5. Who developed the online website called 'ExeRTiOn'?

A team of researchers at King's College Hospital developed ExerRTiOn. ExeRTiOn at King's College Hospital works in partnership with:

1. The NHS – a healthcare professional from the Renal Outpatients Department will have referred you to ExeRTiOn.
2. SPIKA – a software development company who programmed ExeRTiOn. SPIKA host and maintain the website. SPIKA meets NHS Digital standards for privacy, confidentiality, security and General Data Protection Regulation (2018) GDPR.
3. A group of kidney transplant patients and members of the transplant team (doctors, nurses, physiotherapists and dietitians) have reviewed this website and provided the team with valuable feedback, which has been incorporated into the design of this website.

6. My personal data- what personal data/information will Exertion ask me for?

ExerRTiOn is a website. So that you can use ExeRTiOn, we need you to register with an email address. ExeRTiOn will need to ask you the following information to set up your account:

1. Your name.

2. Your email address

3. So that we can keep track of your health – we will also ask you to complete self-report questions about your goals, activity and weight.

7. My personal data- Why does ExeRTiOn need to collect this personal information?

Because ExeRTiOn is a research study conducted within the NHS, the research team needs accurate and up-to-date information. Collecting this information means that your research team can monitor your progress whilst using the online resource. They are able to contact you to provide you with extra support either by email, the ExeRTiOn in-site messaging service, over the telephone or by arranging an appointment to meet face-to-face.

8. Where is my data kept?

The ExeRTiOn website is hosted by SPIKA, a software company. This means that the data collected by ExeRTiOn is held on a secure database managed by SPIKA. This database is located in Ireland in a securely protected and approved provider cloud solution. SPIKA are a registered software company and are compliant with GDPR (General Data Protection Regulation 2018).

When you register for ExeRTiOn you are assigned an anonymous Exertion ID, which is stored with your data. Additionally, because your data is confidential, the data that ExeRTiOn collects is held in an encrypted state. Data is securely managed in line with NHS and GDPR policies.

9. Who can access my personal information?

So that ExeRTiOn can be used in the NHS we have to follow strict privacy, confidentiality online security procedures and including the new GDPR guidelines.

The research team, based at the Renal Unit at King's College Hospital, will only ever access your personal information. Ellen Castle, the PhD student and senior renal physiotherapist will review the data and reply to any questions you have. ExeRTiOn will never share your information with other parties without your written consent. For example, if access is needed to your ExeRTiOn account due to a technical error with the online resource, we will ask for your consent for a member of the technical team to do this. The main researcher (Ellen Castle) will act as gatekeeper of the data. If there are any technical issues with the website, once she asks for your consent, she can grant temporary access for SPIKA software technicians to resolve the issue.

10. Does ExeRTiOn collect other information about me?

To help the team at King's College Hospital improve the website, ExeRTiOn collects information about:

1. Length of time users spend logged in to ExeRTiOn
2. Number of sessions completed
3. Type of sessions completed

4. Number of messages sent between you and your guide (Please note the content of these messages will NEVER be seen by King's College Hospital unless you consent to this as part of a research study)
5. Completion of sessions
6. Goal setting results
7. Weight and Physical activity recordings
8. During your face to face visits with the main researcher (Ellen Castle), you will be asked to provide your date of birth, medical history, medication list, address and contact phone number. This information will not be loaded on to the ExeRTiOn website. All research records will be kept secure and confidential as per the King's College Hospital confidentiality guidelines.

This information is ALWAYS anonymous and will never include data that can identify you as an individual.

11. Does ExeRTiOn share my information with anyone else?

The study team will mark on your renalware records that you are taking part in the study.

If you have a technical problem or question, the main researcher Ellen Castle will receive the following information if you submit a question/concern via the "Contact Us" form on the ExeRTion website:

1. Your email address
2. Information you type in your message

In order to solve a technical problem, support from the SPIKA software team who programmed ExeRTiOn may be needed. We will never share your information with SPIKA or ask them to look into the problem without gaining your informed consent first.

The ExeRTiOn website will never share your personal information with anyone without your consent.

12. Links

Some sessions may contain links to other websites, which are owned, operated or maintained by third parties. If you click on a third party link, you will be directed to that website in a new tab. We provide these links as helpful sources of further information, not as an endorsement, authorisation or representation of our affiliation with that third party, nor as an endorsement of their privacy or information security policies or practices. We do not have control over third party websites and we do not have control over their privacy policies and terms of use.

13. Who can see what I write in ExeRTiOn?

When you join ExeRTiOn you will be linked to the main researcher (Ellen Castle). Your Ellen is a qualified renal physiotherapist who will provide you with support during your time on the programme, either by phone, online messaging or both. Ellen is part of your

renal healthcare team so will be able to see your personal details, including name, date of birth, phone number and email address.

In order to ensure that her support is relevant and specific to you, and to ensure your wellbeing, Ellen will be able to see your progress on the website, i.e. which sessions you have completed and your weight and physical activity scores. She will also be able to see your goals and tasks. Additionally, she is able to see the notes you make during the sessions, as this can help structure their support.

14. The Exertion Team at King's College Hospital

Data Protection Officer for the ExeRTiOn2 study: Ellen Castle- Senior Renal Physiotherapist at King's College Hospital and PhD Student.

Supervisors: Dr Sharlene Greenwood and Dr Joseph Chilcot.

Data Protection Officer at King's College Hospital is: Nick Murphy-Okane

Information Governance Advisor at King's College Hospital: Jon Curtiss Green

15. The legal bits

Information collected by Exertion will in line with Data Protection Act (2018). Our lawful basiss for collecting this information includes;

Consent to participate in this study.

16. Your rights

Your personal data will be processed in accordance with your rights under data protection legislation.

Your rights are:

a. Right to be informed
b. Right to gain access to your data
c. Right of rectification (e.g. change inaccurate information)
d. Right to erasure (e.g. to delete records held about you on the ExeRTiOn platform)
e. Right to restriction (e.g. to stop processing information about you)
f. Right to portability (e.g. to move or transfer your data)
g. Right to object (e.g. to change your mind)
h. Right not to be subject to automatic profiling or decision making (e.g. to know if a decision was made by a computer rather than a person)

17. Summary

Your personal information will be managed and shared in line with the General Data Protection Regulations (2018), Data Protection Act 2018 and common law duty of confidentiality.

1. The ExeRTiOn website will ask for personal information. This information will be stored in line with NHS Digital data privacy and security standards.
2. ExeRTiOn is developed and owned by King's College Hospital and is a provider for the NHS and follows NHS Digital data privacy and security standards.
3. The ExeRTiOn website will collect anonymous information about the length of time spent logged in to ExeRTiOn, number of online sessions completed, and number of online messages sent. This information will be used by research team at King's College Hospital to improve the ExeRTiOn website.
4. Filling in the ExeRTiOn contact us form, means your email address and typed message will be seen by the main researcher (Ellen Castle).
5. If you experience a technical problem, Ellen Castle at King's College Hospital will respond to your concern and gain your consent for the web-developers of ExeRTiOn to access my information.

If you have any concerns or further questions, please contact the ExeRTiOn team using the form, which you can find in 'Contact Us.' Or you can send an email to:

kch-tr.exertion@nhs.net

You can find more tips for staying safe online at www.cyberaware.gov.uk.

Consent form feasibility RCT (studies 3 and 4)

Ellen Castle, Study Physiotherapist & Principle Investigator
Dr Sharlene Greenwood, Consultant Renal Physiotherapist & Chief Investigator
The Renal Unit, King's College Hospital
London, SE5 9RS
Direct Tel: 020 3299 6725

ExeRTion 2-The Weight gain prevention Renal Transplant Online study. A Randomised Controlled Feasibility Trial.

Patient ID……

Please Initial below

1.	I understand that my participation is voluntary and that I am free to withdraw from study treatment at any time, without necessarily giving any reason, and without my medical care or legal rights being affected.	
2.	I understand that if I withdraw from the study at any time, no further data will be collected for the study. However data already collected from when you participated in the study will be retained and kept anonymised for the duration of the study, and after the study finishes.	
3.	I understand that sections of any of my relevant medical notes and data collected during the trial will be looked at, in confidence, by authorised individuals from the study team at King's College Hospital NHS Foundation Trust as well as by regulatory authorities, to check that the study is being carried out correctly. I give permission for these individuals to have access to my records.	
4.	I agree to my GP being informed of my participation in the study.	
5.	I understand that I may be contacted to take part in an individual interview to discuss my experiences in the trial. I agree to the interview being audio-taped and used anonymously for this study. I understand that the recording will be treated as confidential, stored securely and securely destroyed once the study has been published in line with the NHS Code of Practice for record retention.	
6.	I understand the researchers working in this study may extract and use direct quotations from the interviews in publications, but that these will be anonymous, and it will not be possible to identify me from any quotations used.	
7.	I confirm that I have read and understand the Participant Information Sheet (Version 2.1 Dated 16th August 2019). I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
8.	I confirm that I have read and understand the data security and privacy document (Version 1.0 Dated 4th March 2019) and understand how my data will be used and stored.	
9.	I agree to take part in the study	

Signature of patient		
& **PRINTED** name		Today's date: _____ dd/mmm/yyyy
Signature of person taking consent:		
& **Printed** name		Today's date: _____ dd/mmm/yyyy

Topic guides used during nested qualitative interviews (study 4)

King's College Hospital NHS
NHS Foundation Trust

ExeRTiOn 2– EXPERIENCE ONLINE RESOURCE

INTRO

- *Thank you for agreeing to take part today…*
- *There are no right or wrong answers- we are interested in your experience using the online resource.*
- *I am going to ask you some questions about your thoughts and experiences with using the online resource. This will help us further improve the website.*
- *If you are happy I will now start to record.*
- *This will be anonymised*
- **Interviewer: State participant number, interviewer initials and date of interview**

SECTION 1

Demographics

- *Before we begin to discuss your experiences with the online resources, can I please check the study information I have is correct?*
    - *Prompts: Age, born in the UK, lived in the UK/ elsewhere etc, employment*

Story of transplant and trial

- *Could we start by first telling me about your transplant journey so far?*
    - *Prompts* How have things been going since your transplant..*: positive/ negative experiences*
    - *Transplant centre- GSTT vs KCH*
- *Can you tell me about your involvement in the study so far?*
    - *Prompts: group, participation to date*

SECTION 2

Resource

- *Could you tell me about your initial thoughts and feelings towards the online resource?*
    - *Prompts: thoughts and feelings*

Usability

- *"Did you find it(online resource) helpful?*
    - Prompts: If so, why? / If not, why? (depending on the answer given)

- *"Was there anything you found to be unhelpful?*
  - *Prompts:* If so, what?/if not why? (depending on the answer given)

- *What device did you mainly use to access the website?*
  - *Prompts: smart phone, PC, laptop, tablet, combination*

Navigation

- *"How did you find getting around the website?"*
  - Prompt: *Home screen layout*
  - *Easy? Enjoyable? Time taken- good/bad?*

Motivation for use/ willingness to use (depending on engagement levels)

- *What was your main motivation for using the resource?*

  OR

- *Why did you not use the resource?*
  - *Prompts: can you tell me more about this? Examples?*

- *Will you continue to use it after the 12 weeks*
  - *Prompts:- If so why, if not why (dependant on answer)*

- *AND THEN-"If it was an option, would you continue to use the website after the trial finishes?"*
  - Prompt – *Why would they use in different contexts? (dependant on their answers)*

Content

- *"What were your thoughts on the topics covered?"*
  Prompts:
  - *did you use the physio messaging?*
  - *How did you feel about it?*
  - *What were your motivators for using it?*
  - *What prevented you?*
  - *What were your thoughts when using the resource?*

Behaviour

Did it change the way you went about your daily life?"

- ***Prompt:*** *This might include any differences to routines, activity, socialising, eating etc?*

SECTION 3:

Final thoughts

- *Is there anything else you would like to see included?*
- *Would you recommend this to other people in your situation?*
- *Do you have any advice for people in a similar situation to you?*

Have your thoughts/perceptions/experiences changed significantly since the introduction to shielding in the response to the COVID19?

I've come to the end of my questions – anything to add?

- Any questions for me

Thank you for your time!

End of recording

ExeRTiOn 2-EXPERIENCE OF TRIAL

INTRO

- *Thank you for agreeing to take part today…*
- *Today we are going to discuss your experiences taking part in this research study. There are no right or wrong answers- we are interested in a range of experiences.*
- *If you are happy I will now start to record*
- ***Prompt for interviewer: state date, participant number, group, site and interviewer initials***
- *This will be anonymised*

SECTION 1:

Demographics

- *Before we begin to discuss your experiences with the online resources, can I please check the study information I have is correct?*
    - *Prompts: Age, born in the UK, lived in the UK/ elsewhere etc, employment*

Story of transplant and trial

- *Can you tell me about your transplant journey so far?*
    - *Prompts* How have things been going since your transplant…: *positive/ negative/ neutral experiences*
    - *Where are you being managed for your transplant care? - GSTT vs KCH*
- *Can you tell me about your involvement in the study so far?*
    - *Prompts: group, participation to date*

SECTION 2:

Now looking at your experience in the trial;

- *What was your overall experience in the trial like?*
    - *Prompts:*
    - *Experience on recruitment within first three months of Transplant*
    - *experience- communication with team, recruitment to trial, assessments*

- *What aspects do you think went well- If so why?*
- *What aspects of the trail do you think could be improved?- If so Why?*

- ***As you know, half the people were randomised to the online website, half to usual care***

[select which question a) or b) based on randomisation]

a) What was your experience being in the online website group

- *Prompts:*
  - *any changes to your everyday life?*
  - *Would you/ have you continued to use the website after the 12 weeks*
    - *If so why, If not why not?*

b) What was your experience being in the usual care/ non website group?

SECTION 3:

- *What where your experiences of the trial tasks?*
  - *Prompt: study visits/ randomisation/ recruitment/ interaction with team*
- Did your participation in the study change anything about your day to day life?
  - Prompt: *This might include any differences to routines, activity, socialising, eating etc?*
- *Would you participate in a trial again?*
  - *Prompts: If so why? If not why?*
- *Would you recommend the trial to others?*
  - *Prompts: If so why? If not why not?*

FINAL THOUGHTS

- *Is there anything else you would like to see included?*
- *Would you recommend this to other people in your situation?*
- *Do you have any advice for people in a similar situation to you?*

Have your thoughts/perceptions/experiences changed significantly since the introduction to shielding in the response to the COVID19?

I've come to the end of my questions – anything to add?

- Any questions for me

Thank you for your time!

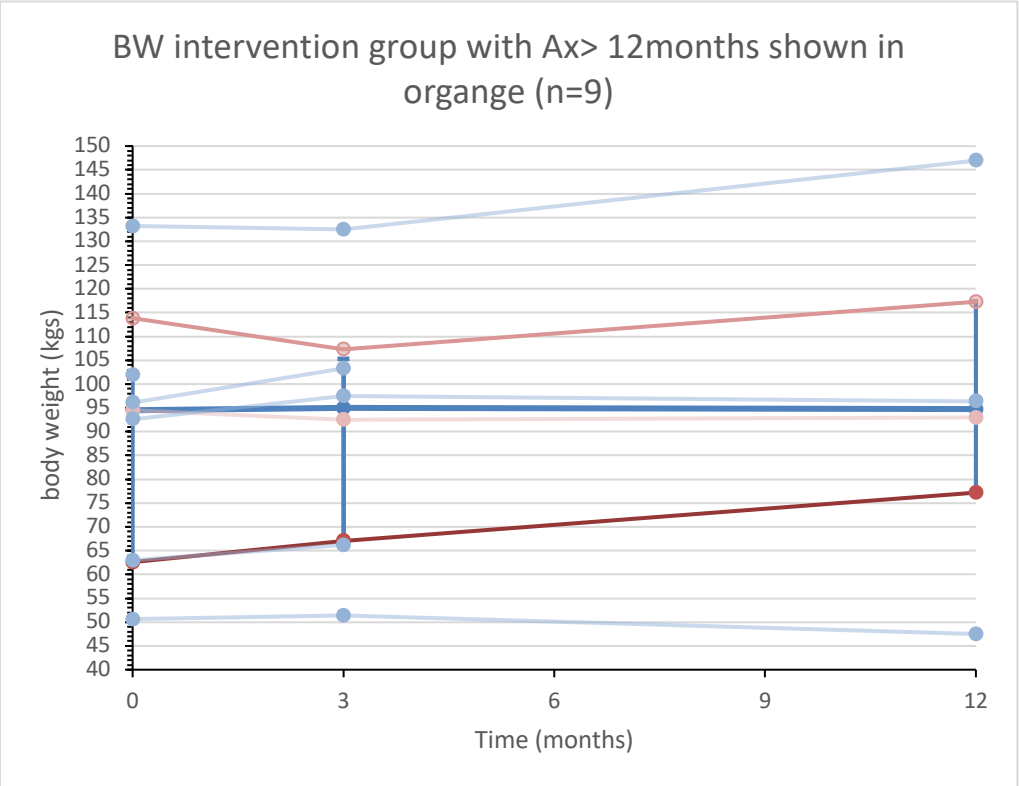
Sensitivity analysis for assessment window (feasibility RCT)

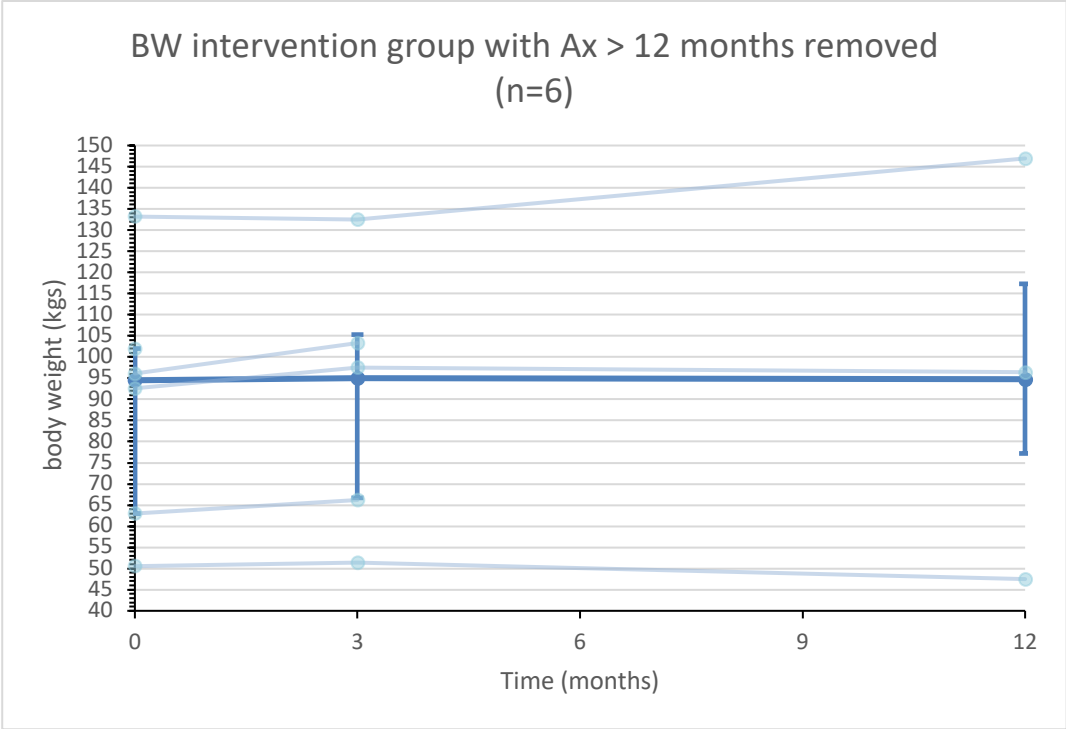
Description:

Sensitivity analysis graphing body weight performed on the 26th of March 2021. Due to the impact of COVID-19 on studies 3 and 4 (refer to chapters 5 and 6), some of the final 12-month assessments exceeded the 14 day (+/- 7 days) assessment window stated in the protocol. To assess the impact of these assessments that occurred >12months on BW, graphs were performed. Graph 1 below demonstrates the BW in the website group with all participants with complete data (n=6).

Intervention group:

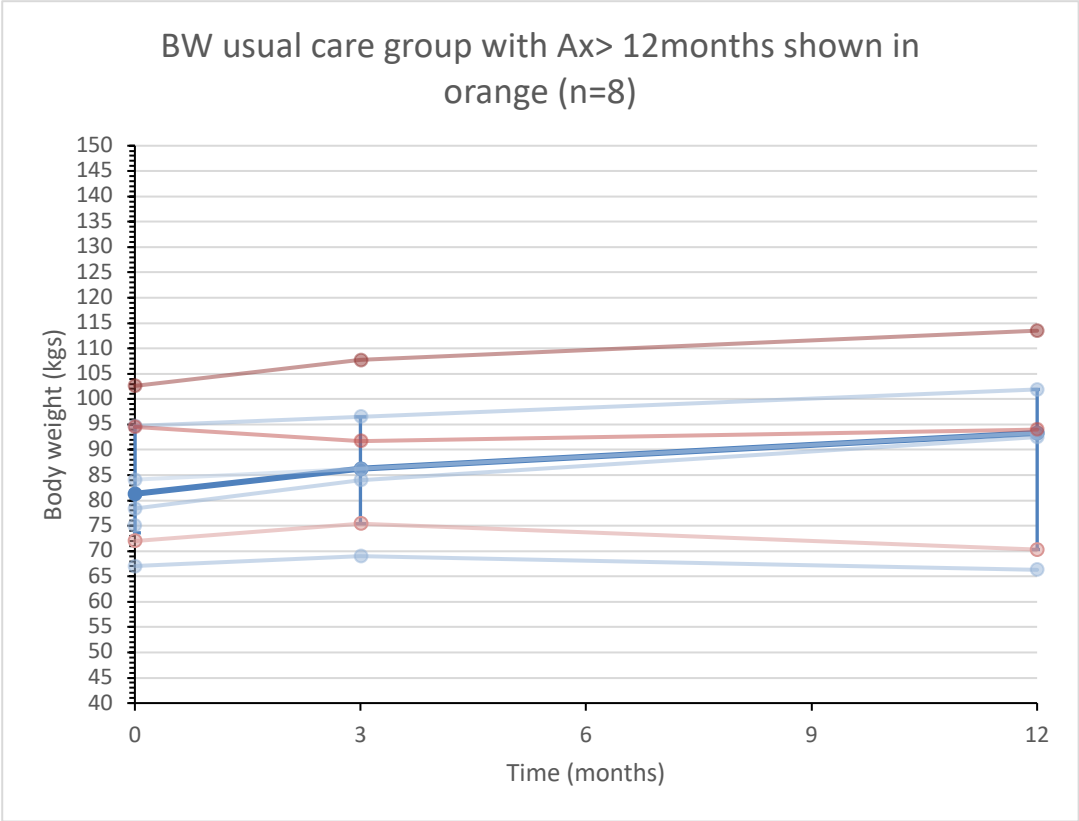
- median line and IQR shown in blue in both graphs
- graph on the left shows participants outside the assessment window (P04 12 days, P06 106 days P12 66 days) shown in orange. Stronger the shade, the longer the delay of assessment
- Graph on the right shows the removal of these participants

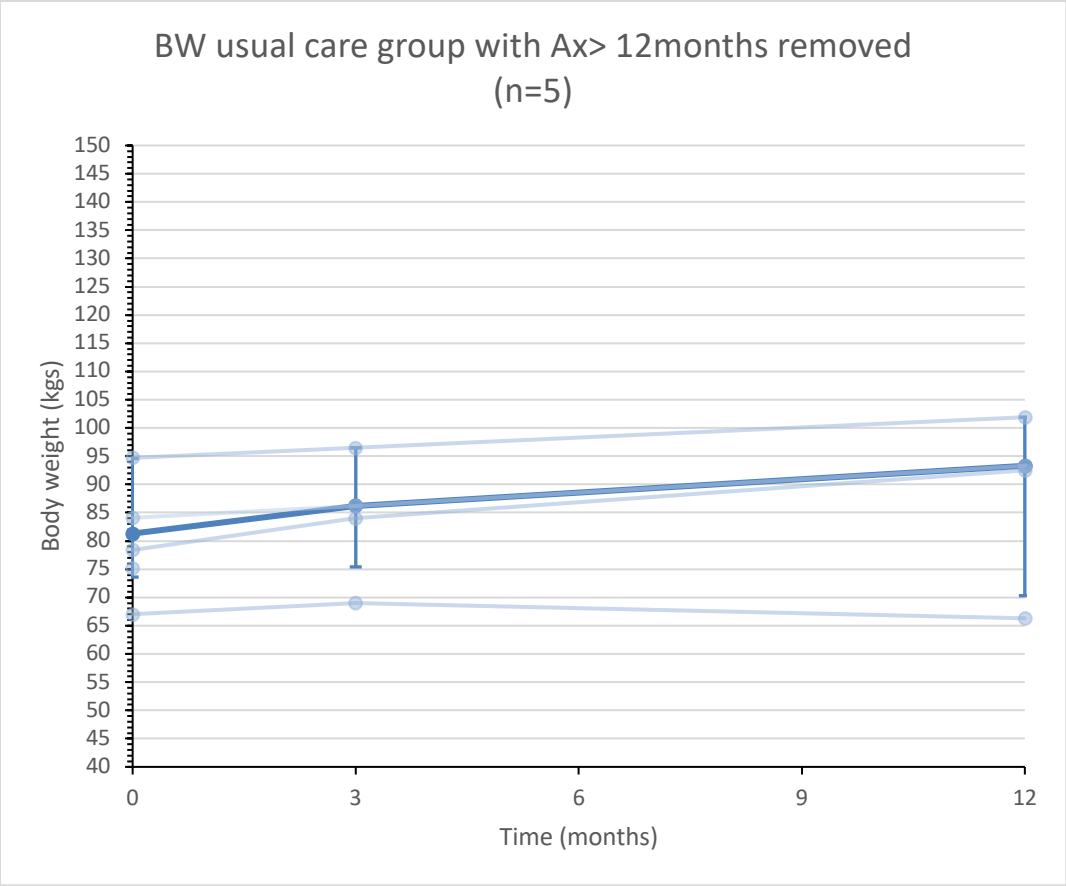




Usual care group:

- median line and IQR shown in blue in both graphs
- graph on the left shows participants outside the assessment window (P09 66 days, P16 28 days, P11 10 days) shown in orange. Stronger the shade, the longer the delay of assessment
- Graph on the right shows the removal of these participants





Means with and without 12-month assessment outliers

	BW Baseline	BW 3-months	BW 12-months
IG (all data at each time point	N=9 94.5 (63.0 to 102.0)	N=8 95.0 (66.7 to 105.3)	N=6 94.7 (77.2 to 117.3)
IG (with outliers removed)			N=3 96.4 (47.5 to 147.0)
UC group (all data at each timepoint	N=8 81.3 (73.6 to 94.6)	N=7 86.2 (75.4 to 96.5)	N=7 93.3 (70.3 to 101.9)

UC group (with outliers removed)			N=5 92.9 (79.4 to 97.6)

Findings from sensitivity analysis:

- INTERVENTION GROUP: Two participants out of the 3 participants with final assessments > 12 months showed weight gain. However so did one of the participants who was assessed at the correct window. Small sample size.
- USUAL CARE GROUP: Two of the participants who fell outside the assessment window gained weight, one decreased. They seem to fit with the overall pattern of the graph.
- OVERALL: small sample, therefore all participants with full data displayed in main text.

Appendix F. Changes due to COVID-19 (chapter 5)

- Approved non-substantial amendment due to COVID-19 (March 2020)
- Substantive amendment approval due to COVID-19 (August 2020)
- Extra-ordinary TMG minutes (2nd June 2020)

Approved non-substantial amendment due to COVID-19 (March 2020)

Partner Organisations:
Health Research Authority, England NIHR Clinical Research Network, England
NHS Research Scotland NISCHR Permissions Co-ordinating Unit, Wales
HSC Research & Development, Public Health Agency, Northern Ireland

Notification of Non-Substantial/Minor Amendments(s) for NHS Studies

This template **must only** be used to notify NHS/HSC R&D office(s) of amendments, which are **NOT** categorised as Substantial Amendments.
If you need to notify a Substantial Amendment to your study then you MUST use the appropriate Substantial Amendment form in IRAS.

Instructions for using this template

- For guidance on amendments refer to http://www.hra.nhs.uk/research-community/during-your-research-project/amendments/
- This template should be completed by the CI and optionally authorised by Sponsor, if required by sponsor guidelines.
- This form should be submitted according to the instructions provided for NHS/HSC R&D at http://www.hra.nhs.uk/research-community/during-your-research-project/amendments/which-review-bodies-need-to-approve-or-be-notified-of-which-types-of-amendments/ . If you do not submit your notification in accordance with these instructions then processing of your submission may be significantly delayed.

1. Study Information

Full title of study:	ExeRTiOn 2- The Weight gain prevention Renal Transplant Online study. A Randomised Controlled Feasibility Trial
IRAS Project ID:	262007
Sponsor Amendment Notification number:	NSA 1
Sponsor Amendment Notification date:	13 March 2020
Details of Chief Investigator:	
Name [first name and surname]	Dr Sharlene Greenwood
Address:	Physiotherapy Department King's College Hospital Denmark Hill
Postcode:	SE5 9RS
Contact telephone number:	07966 150024
Email address:	Sharlene.greenwood@nhs.net
Details of Lead Sponsor:	
Name:	King's College Hospital NHS Foundation Trust The R&I Office| 161 Denmark Hill | London SE5 8EF
Contact email address:	kch-tr.research@nhs.net
Details of Lead Nation:	
Name of lead nation *delete as appropriate*	**England**
If England led is the study going through CSP? *delete as appropriate*	**No**
Name of lead R&D office:	King's College Hospital NHS Foundation Trust The R&I Office| 161 Denmark Hill | London SE5 8EF

Partner Organisations:
Health Research Authority, England NIHR Clinical Research Network, England
NHS Research Scotland NISCHR Permissions Co-ordinating Unit, Wales
HSC Research & Development, Public Health Agency, Northern Ireland

Partner Organisations:
Health Research Authority, England NIHR Clinical Research Network, England
NHS Research Scotland NISCHR Permissions Co-ordinating Unit, Wales
HSC Research & Development, Public Health Agency, Northern Ireland

2. Summary of amendment(s)

This template **must only** be used to notify NHS/HSC R&D office(s) of amendments, which are **NOT** categorised as Substantial Amendments.
If you need to notify a Substantial Amendment to your study then you MUST use the appropriate Substantial Amendment form in IRAS.

No.	Brief description of amendment *(please enter each separate amendment in a new row)*	Amendment applies to *(delete/ list as appropriate)*		List relevant supporting document(s), including version numbers *(please ensure all referenced supporting documents are submitted with this form)*		R&D category of amendment *(category A, B, C) For office use only*
		Nation	**Sites**	**Document**	**Version**	
1	Given the current medical situation with COVID-19, to decrease patient burden, we would like to be able to offer participants to have the nested qualitative interviews (purposive samples at 3 and 6 months) the option to have their interview conducted over the telephone to minimise additional attendance to the hospital. The participants will have the option to either have the interview face-to-face when they are attending already for a hospital appointment or via telephone. The telephone interviews will be conducted confidentially on NHS phones, audio recorded, and transcription will remain the same as the original protocol. The topic guides will remain the same.	England	All sites or list affected sites	PIS KCH PIS GSTT Consent form KCH Consent form GSTT Protocol	V2.2 V2.2 V2.2 V2.2 V2.2	
2	Also given COVID-19, we would like to extend our recruitment by 3 months (to September 2020 rather than June) in case this situation impacts recruitment. The clinical team has agreed to absorb this extension.	England- All sites affected		Protocol	V2.2	
3						
4						
5						

[Add further rows as required]

3. Declaration(s)

Declaration by Chief Investigator

- I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
- I consider that it would be reasonable for the proposed amendment(s) to be implemented.

Signature of Chief Investigator: …….  ……

Print name: …Dr Sharlene Greenwood…

Date: 13th March 2020

Optional Declaration by the Sponsor's Representative (as per Sponsor Guidelines)

The sponsor of an approved study is responsible for all amendments made during its conduct.

The person authorising the declaration should be authorised to do so. There is no requirement for a particular level of seniority; the sponsor's rules on delegated authority should be adhered to.

- I confirm the sponsor's support for the amendment(s) in this notification.

Signature of sponsor's representative: RAHMAN AHMED

Print name RAHMAN AHMED

Post: RESEARCH & INNOVATION GOVERNANCE MANAGER

Organisation King's College Hospital NHS Foundation Trust

Date 17/03/20

Substantive Amendment approval due to COVID-19 (August 2020)

London - Dulwich Research Ethics Committee
Health Research Authority
Skipton House
80 London Road
London
SE1 6LH

Tel: 0207 104 8089

06 August 2020

Mrs Ellen Castle
PhD Student
King's College Hospital
Renal Rehab Team
Dulwich Hospital
London
SE22 8PT

Dear Mrs Castle

Study title:	**ExeRTiOn 2- The Weight Gain prevention in Renal Transplant Online study. A Randomised Controlled Feasibility Trial**
REC reference:	**19/LO/1138**
Protocol number:	**1**
Amendment number:	**SA01.ExeRTiOn2 study**
Amendment date:	**22/06/2020**
IRAS project ID:	**262007**

The above amendment was reviewed at the meeting of the Sub-Committee held via correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [262007_SA01.ExeRTiOn2study_22Jun2020_Locked24Jul20_130725]	V1	22 June 2020
Research protocol or project proposal [protocol ExeRTion2. V3.1.22ndJune2020]	V3.1	22 June 2020

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 262007:	**Please quote this number on all correspondence**

Yours sincerely
PP

Dr Thomas Kabir
Chair

E-mail: dulwich.rec@hra.nhs.uk

London - Dulwich Research Ethics Committee

Attendance at Sub-Committee of the REC meeting via Correpsondence

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Thomas Kabir	Public Involvement in Research Manager	Yes	
Mr Colin Standfield	Charity Worker	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Charlotte Ferris	Approvals Officer
Ms Jade Robinson	Approvals Administrator

Extra-ordinary TMG minutes (2nd June 2020)

NB. Patient experts 1 and 2 anonymised for this appendix document

Present	Apologies
Chair- Ellen Castle (EC) PhD Fellow Dr Sharlene Greenwood (SG) 1st supervisor Dr Joseph Chilcot (JC) 2nd supervisor Dr Kate Bramham (KB) 3rd supervisor Dr Sapna Shah (SS) Transplant consultant and lead of renal research at KCH and Thesis Committee advisor Dr Ellie Asgari (EA) Transplant consultant and PI at GSTT xxx patient expert 1 Dr Matthew Maddocks (MM)- Thesis Committee advisor Prof Richard Thompson- PGC Thesis Committee KCL Rachel Philips- stats advisor	Xxxx - patient expert 2 Matthew Maddocks- left discussion early

1. Update on study figures via slides- EC

EC	• Refer to slides attached.
	  o EC updated on PHD so far, feasibility outcomes and information for each outcome, funding situation (funding ceases 1st July 2021 with no scope for extension)
	• **NB. amendment to slide 7 and 8** (screening and recruitment) 27 patients approached for the study not 17. This will slightly affect confidence intervals.
	  o 20 patients consented
	  o 3 patients from GSTT consented but not baselined and randomised (due to COVID and are no longer meeting recruitment criteria)
	  o 17 in the trial (baselined and randomised)
	  o 7 patients declined taking part in the study- we have reasons for this

2. discussion next steps for project and PhD

EC	**Proposed two options (refer to slides attached)** **A)** write up what we have on the n=17. This includes; creation of the resource, study 1 qualitative work, systematic review, study 3 (17 new patients) including 2x qualitative sub studies **B)** extend recruitment and sample however we would need to consider funding (runs out for EC on the 1st of June), ethics, safety of patient group (who are high risk), EC working remotely due to medical history
RT	**Update from KCL perspective:** - There will be a possibility of a KCL hardship fund. Information will come out from the university soon on this - Agree to look at the project from a PhD point of view but also a project point of view - Advised group that whilst the expected deadline for a PHD is 3 years, the absolute deadline is 4 years - So no hard stop and chucked out at 3 years

	- End absolute thesis deadline (4 years)= 1st October 2022. Not suggesting this is the best option, but highlighting do not have to submit by 1st of October 2021 unless you want to. Don't worry about the time, accept money is a far bigger issue. And we all know that going back to full time work without writing up is a major issue. Not encouraging this. Not encouraging to run on into 2022 before thesis is written up for sure. - Over now to the thoughts of the committee on technicalities of running the study
SS	**Update on the clinical situation of KCH Transplant Clinic:** - At present, drastic reduction in the number of kidney transplant patients coming through clinics in light of COVID19 - On average approximately 25% of the usual visits (Face to face) that we have in transplant clinic and that will continue for the foreseeable future. other patients seen virtually - The issue is also this study recruits the newly transplanted patients (within first 3-months) for this study (ExeRTiOn2) - The deceased and living donor programme are currently on hold - They are likely to restart transplantations within the next few weeks, but they will be only for a selected number of patients who are considered fit enough to undergo transplantation in the current era, who want to undergo transplantation now, and are willing to accept the risks. And we (the clinical team) think the risk: benefit is within their interest. - So it will be a markedly reduced number of patients coming through the service over the next year. - To wait to recruit a few more patients, on that basis, would be difficult. - The likelihood is the people that we do see who are in the first year, we will be doing face to face visits. At least up until 3-months fairly regularly. And then, alternate visits. Suspect this will be virtual or face to face depending on the clinical situation. - The current cohort of patients within their first year, are also still having some face to face appointments, the 17 patients, EC may not know who is coming into clinic face to face from this study cohort. - Suggestion for SS, EC and SG to link in to see if any of the current n=17 are coming in face to face and whether we could get some of the other data outcomes - There may be some capacity to see them, whilst they are coming up for their transplant appointment. Highlighted this would be difficult to do within renal outpatients because of the clinical flow and the minimal footfall we want in the area. - But it may be worth speaking with Elka, the CTF, to work out if a room could be utilised there, so the patient could then leave renal outpatients, and go there and have the face to face assessment just to bulk out the excellent data we already have. - To get as full a data set as I can. -
EA	**Update on GSTT clinical picture:** - Same as KCH - Depends on timelines, early next year they may be more regular transplants. However the next few months are on hold. There is talk about considering transplanting a few donors, but they are in the 'super fit' category
EC	**EC working remotely due to medical history and risk of COVID19** - Not shielding but high risk and working from home at the moment. Happy to be guided by what is safe for the patients but also for the study and for myself as well.
RT	**Option to interrupt PhD** - Given this, the other thing we haven't thought about would be interruption of the PhD.

	- Obviously there are patients currently in the study- how much ongoing work there is would need to be considered and we wouldn't want to lose the ones we have in the study now. - in terms of the funder, is there any score for pausing this funding and PhD?
EC	**Re: interrupt PhD** - EC haven't considered this route so far because the current cohort (17 participants) follow ups are until April next year. - Those in the website group albeit, only 9, are finding it helpful. - Wouldn't want to take this away from them during shielding. - That would be my main concern with stopping and restarting. - Happy to see other people's thoughts.
SG	**Update from primary supervisor** - SG advised as she is Ellen's line manager and also supervisor, she is aware of Ellen's background. - Highlighted it has been difficult for Ellen at home in this situation and she has been working hard keeping on top of all the patients in the study remotely. - Realistically, if people feel there is a sufficient amount of people already in the second study, we (the team) can help to get those face to face outcomes for follow ups within our clinical team. - Suggests we look to support Ellen to finish next year this will be the best for her. - Ellen has been concerned if there is enough information there to write up the PhD - Welcomed Rachel's thoughts on going forward, from a stats point of view, will there be enough data to look at the confidence intervals etc. around the feasibility outcomes.
JC	**RE: Is there enough data/ information already** - Agrees with Sharlene - Alerted in the zoom chat Matt has posted point about the confidence intervals for recruitment - Looking at that there is enough to say about the potential true consent rate
MM	**Contributed to discussion via messaging function** - Rich data currently with 17 participants that can be enhanced by qualitative work (also question around COVID and shielding) - Unsure what disruption of study would add - Apologies leaving the meeting early - Is going to put Ellen in touch with one of his PHD students in a similar situation for shared learning
RP	**RE: enough data/ information already** Clarifying 17/23 or 17/24? For screening and recruitment?
EC	**Apologies and clarifies screening and recruitment data:** - 20 consented in total, but 17 of these baselined and randomised, 3 consented from GSTT around time of COVID lockdown so no baseline and are no longer suitable for the study as > 3-months post-transplant. 7 declined in total. **Therefore 27 approached- from these 27:** - **20 consented – 3 of these not baselined, 17 in trial** - **7 declined (reasons recorded)** EC- to update the slides-> this has been done and attached to these minutes
JC and RP	**RE; updated data** - This creeps up Confidence intervals a bit - but still okay - May be slightly below 50%
JC	**Input from second supervisor- Recommends continue with data on 17 participants and not to recruit further:**

	- Ordinarily would want more than 17 participants, but given everything said in this meeting, there is such a rich amount of data, in terms of tracking the logins, the qualitative aspects, you can make some reasonable estimate of what you think the consent rate is going to be. - You will have enough questionnaire data with big confidence intervals to make some estimates for a power calc for a future study. **The danger to trying to continue to recruitment:** - There is a tremendous amount of uncertainty for everybody - If you do try to recruit in these more restricted services now, we don't know if the consent rate is somehow related to COVID and other issues - So if we approach 4 more people, and they all say no, is that because of something related to COVID anxiety, or not wanting to do something extra. Which is understandable. - That would significantly accept the data and say it is less feasible, when actually it's nothing to do with feasibility it's to do with COVID-19. - Also difference in the sample- only super fit will be transplanted in the next year. - Therefore vote not to extend recruitment, as we will not get data that is generalisable. - We have enough data to answer our questions.
EC	- Thanks all for comments - Suggest call with Rachel re stats plan - Suggest we have a lot of website data to explore - Agree it would be base case scenario to have at least 20 in the study, but realistically, there is such a change with this group of people with COVID we have answered the research questions as best as we can, hopefully, we would have enough to look at power calcs for a further study post PhD looking at efficacy. But I hope we should have enough data, including qualitative work to suggest further refinements of the intervention itself.
RT	- Agrees, enough detailed data - Bottom line- happy to write it up. - Amount of data is not an issue, is EC happy to write it up and put together a story
KB	**Input from third supervisor:** - Agreed with discussions so far - The PhD learning process is not going to change if we get 3 more patients in - Its disappointing but the content of the data is going to be so different due to COVID and you can't do anything about that. It's out of your hands. Similar to having all your cells die. It's unavoidable. These things happen
EC	- Apologies- error with adding KB to the call. - Update KB on discussions so far, group in agreeance we have enough for feasibility, and the PhD work. - Grateful for the team and support that we were ahead of things before lockdown hit. Acknowledge other students with no data - Thanks for support and help. - EC welcomes further comments from supervisors
SG	- Acknowledges EC doing a great job. - Agrees with the discussions today- these are exceptional times, and we would all like to see this study progress further. - It was really important to EC to get everyone's views to say there is enough here. And to put the mind at rest that there is enough to write up the PhD. But also that there is some really important data that I have already have to progress this onto another study. And we think that we should progress this on to another study and happy to support through that. - Grateful for everyone's time and guidance on this call

RT	It's about compromises; - It's not how we wanted to run the study originally - We are not going to analyse the data in the exactly the same way, but don't apologise for that. - This is how it is - And EC has done what she can - Agree with Joe's comments about recruitment in the world of COVID-19 is completely different. - You just have to come out with that and say- NO we decided we weren't going to recruit in a completely different environment because that wouldn't have been representative. - Agree with Kates comment- the PhD is about an educational process, it's not about getting data. The more data you have the easier you can write up but that's.
xxxx	**Kidney transplant recipient perspective:** Advised from a patient point of view, he hope the project succeeds. He thinks it's fantastic, and it would have helped him in the early phase post-transplant to have something like this. People don't know, until you experience it, before you could go to a gym and physically do that and get on with rebuilding yourself. Its slow baby steps. This is great. From his point of view, and he is sure most patients he would hope this project succeeds.
RT	Apart from recruitment, the other thing that has struck since COVID is there will likely be two extremes- one group who may get fitter in lockdown, and another who may go the other way.
EC	Suggests this would be interesting to look at around the 12 month data how physical activity has been affected by lock down in the 17 participants and their body weight may be influenced by lock down. Invited any final comments from the group.
ALL	**In agreement will plan A- no further recruitment and enhance data of 17 participants with qualitative work. To aim for a most full data set as possible for the 17 participants** - All in agreement to cease further recruitment. To complete study with n=17 participants. - EC to speak with SS and SG re: when clinically suitable to get further outcomes face to face and have the team support this if EC remains working from home - EC- added there has been a question added to qualitative interviews to ask around COVID and shielding
EA	Wished to have recruited more at GSTT but looking forward to the results and would love to collaborate for future projects in this area.
EC	thanked EA for her help at GSTT site. Unfortunate that we had just started getting patients on board at GSTT in Feb 2020 before lockdown. Would greatly appreciate EA to continue in the TMG.
RT	- Advised thesis committees to happen every 6 months - Advised can make these more frequently if EC feels this is helpful
EC	Thanks all for time and guidance
SG	Thanks everyone for their time
ACTIONS	- EC to send minutes to all- done - EC and RP to meet to discuss stats presentation- booked

	- EC to organise a supervisor meeting to discuss logistics and plans
	  o EC to update R and D both sites, and funders with plan
	  o Data collection plans for support by team and when this would be appropriate for transplant patients
	
	- EC to speak with SS and SG re: when it is suitable to collect data face to face and support from the team whilst EC is working remotely
	
	- EC to organise a thesis committee meeting for the next few months with SS, MM, RT, SG, JC and KB

Appendix G. BCTT (version 1) coding framework (studies 3 and 4)

This appendix demonstrates the detailed BCT coding presented in chapter 6. All messages and contact notes were anonymised, then coded to the BCTTv1 using the framework in NVIVO for mac ©.

- Table 1 Appendix F- BCT's in the ExeRTiOn online intervention package based on the BCTTv1 (Michie, Atkins, et al., 2014a) and their location and frequencies
- Table 2 Appendix F- demonstrates the BCT's in the messages and interactions with the research fellow/ physiotherapist, their location, the number of patients and the frequencies
- Table 3 Appendix F- Additional BCT's found in the ExeRTiOn online intervention package
- Table 4 Appendix F- Additional BCT's found in the Physiotherapist interactions
- Green highlighter= newfound techniques not in protocol for website or assessment
- Blue highlighter= unexpected BCTs from messages/ physiotherapist interactions
- Yellow highlighter= other findings/ research fellow memos

Table 1. Appendix F- BCT's in the ExeRTiOn online intervention package

BCT code	BCT label	BCT definition from BCTTv1 (Michie, Atkins, et al., 2014a)	Target behaviour(s)	Location	Frequency per patient during 12 weeks	Total frequency possible per patient during the 12-weeks
1.1	Goal setting (behaviour)	• Set a goal defined in terms of targeted behaviours (PA ± healthy eating)	INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	• Session 1 goal setting • Each session prompted to use goal-setting template	I I I I I I I I I I I	11
1.2	Problem solving	• Prompt ± Analyse the factors influencing behaviour • Generate potential options to address barriers • Includes relapse prevention • Cannot just be barrier identification, must have solution	INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	• S2 interactive activities, select options to target cravings barrier • S10 barriers worksheet- identify barriers and then suggest strategies to overcome them	I I I I	4

				• S11 problem solving worksheet to brain storm all potential barriers, then select most useful, and re-evaluate • S12 reflection worksheet for relapse prevention in final session		
1.4	Action planning	• Detailed planning of behaviour and must include prescription and detail	INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	• each session in goal setting template patient asked for specifics of goal- what, why, where, with who	I I I I I I I I I I I	12
1.9	Commitment	• ask to affirm/ re affirm statements to show commitment to target behaviour change	INCREASE PHYSICAL ACTIVITY	• confidence and importance	I I I I I I I I I I	12

			EAT A BALANCED DIET	scales for each goal setting template (prompted in each session) automatically generates “this goal is important to me” and “I am confident I can achieve it”	I I	
2.1	Monitoring of behaviour by others without feedback	• record/observe behaviour • person aware • no feedback	INCREASE PHYSICAL ACTIVITY	• GPPAQ build into the website to capture physical activity index at welcome session, S3, S7 and S10 without feedback	I I I I	4
2.2	Feedback on behaviour	• monitor and provide info/feedback on behaviour	INCREASE PHYSICAL ACTIVITY	• the personalised physio messages at six weeks and 12 weeks include	I I	2

				the physio reporting on weight, activity and goals		
2.3	Self-monitoring of behaviour	• having a method to monitor and record behaviour as part of a strategy	INCREASE PHYSICAL ACTIVITY	• prompt to record Physical activity each session and in welcome session	I I I I I I I I I I I I	13
2.4	Self-monitoring of outcome of behaviour	• devise method for recording and monitoring the outcome of the behaviour	EAT A BALANCED DIET	• patient to track their weight each clinic, and enter in the website weekly (recommend weekly) • prompt at start of each session and welcome session to add recorded weight	I I I I I I I I I I I I	13

4.1	Instruction on how to perform a behaviour	• advise on how to perform behaviour	INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	• S1 how to set goal • S2 craving management skills • S3 how to read food labels • S4 how to exercise post-transplant • S5 exercise options and safety (how to warm up cool down) • S7 how to have portion control/ healthy plate • S8 how to plan activity • S10 how to identify barriers	I I I I

				• S11 how to problem solve		
6.1	demonstration of the behaviour	• Observable example of performing the behaviour (can be film, pictures)	INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	• S1 written goal setting example • S3 dietitian in video shows how to read food label with card • S5 exercise options demonstrated by physio in video • Written home exercise programme as a resource within the website	I I I I	4
7.1	Prompts cues	• Prompts to cue behaviour	ENGAGE WITH EXERTION ONLINE INTERVENTION	• Prompts built into the website to track physical activity and weight at the start of each	I I I I I I I I I I I I I I I I I I I I I I I I I	25

				session and the welcome session • Prompt build into each session at the end to review goal or set new goal		
8.1	Behavioural practice/rehearsal	• Prompt practise/rehearsal of behaviour one or more times to increase skills and habit	ENGAGE WITH THE EXERTION ONLINE INTERVENTION INCREASE PHYSICAL ACTIVITY	• As above prompts to perform tracking activity/weight	I I I I I I I I I I I I I	13
8.3	Habit formation	• Prompt rehearsal and rep of behaviour repeatedly • Code with 8.1	ENGAGE WITH THE EXERTION ONLINE INTERVENTION	• repetitive repetition of PA and weight as above	I I I I I I I I I I I I I	13
9.1	Credible source	• verbal or visual comms from a credible source for or against targeted behaviour	ENGAGE WITH THE EXERTION ONLINE INTERVENTION	• Videoʼs with expert patient, physio and dietitian in welcome session	I I I I I I I I I I I I I I I I	19

			INCREASE PHYSICAL ACTIVITY EAT A BALANCED DIET	and sessions 1 to 12 • Top tip patient quotes in sessions 2, 4, 7, 9, 11 and 12 •		
11.3	Conserving mental resources	• Advise on methods for reducing demands on mental resources to facilitate behaviour change	EAT A BALANCED DIET	• Recommend use food label card to prompt healthy eating choices S3 • Recommend to use hunger scale to categorise cravings versus hunger S2 • Recommend the use of the healthy plate to prompt portion control S7	I I I	3
12.4	Distraction	• Advise/arrange alternate focus to avoid trigger's of unwanted behaviours	EAT A BALANCED DIET	• Recommended distraction	I I	2

				examples in cravings session video and activities		
15.1	Verbal persuasion about capability	• Inform patient they can successfully do the wanted behaviour and they will succeed	INCREASE PHYSICAL ACTIVITY	• Education in S4 by physio that they can safely exercise post-transplant • ? this occurring with 6MWT/ Ax	I	1

Table 2. Appendix F- BCT's found in the messages and contacts with physiotherapist/ research fellow

BCT	Lable	Definition from BCTTv1 (Michie, Atkins, et al., 2014a)	Target behaviour	Location and example	Number of patients	Total frequency of all messages/contacts
1.5	Review of behaviour goal	• Review of goal with patient	INCREASE PHYSICAL ACTIVITY	• Review of goal in messages • 2x TC goal review with G03 over lockdown • The remaining were via message function	7	15
2.2	Feedback on behaviour	• monitor and provide info/feedback on behaviour	INCREASE PHYSICAL ACTIVITY	• feedback on log in rates (and if not logged in) via physio message • feedback on PA behaviour and steps • Majority of this was done via message function with 5 of the total frequency conducted via F2F or telephone call for those who were not engaging	9	41

2.7	Feedback on outcomes of behaviour	• monitor and provide feedback on outcome of target behaviour	FOLLOW A BALANCED DIET	• at progress report at six and 12 weeks, if patient had reduced or maintained weight they were informed of this • all total frequency for this BCT provided via message function	8	20
3.1	Social support (unspecified)	• advise or provide social support • includes praise and encouragement when directed at behaviour	INCREASE PHYSICAL ACTIVITY FOLLOW A BALANCED DIET ENGAGE WITH THE EXERTION ONLINE RESOURCE	• encouragement or praise on progress through message function • signposting to support via message function for support if needed • The majority of this BCT was delivered via messages • However, 5 patients received 7 contacts via F2F or via TC. This was to encourage re-engagement after trigger message was initiated and patients hadn't re-engaged as per protocol	8	83

4.1	Instruction on how to perform a behaviour	• advise on how to perform behaviour	INCREASE PHYSICAL ACTIVITY FOLLOW A BALANCED DIET ENGAGE WITH THE EXERTION ONLINE RESOURCE	• how to log into website, how to reset password, how to send message or use home exercise function • Only 3/15 contacts provided by message • Remaining 12 contacts over 6 patients were provided F2F (6) or TC (6) • 12 contacts included trouble shooting to reset password, enable cookies, signpost to HEP on website	7	15
6.1	demonstration of the behaviour	• Observable example of performing the behaviour • This is always provided with 4.1 above	INCREASE PHYSICAL ACTIVITY FOLLOW A BALANCED DIET ENGAGE WITH THE EXERTION ONLINE RESOURCE	• All contacts of the 6 total were provided with 4.1 • They were all face to face or via telephone with 4 patients • They involved password resets, troubleshooting, how to enable cookies etc.	4	6

6.2	Social comparison	• Compare performance of one with another to draw attention	INCREASE PHYSICAL ACTIVITY	• Compare to other KTRs • All completed via messages.	6	8
7.1	Prompts cues	• Prompts to cue behaviour	ENGAGE WITH EXERTION ONLINE INTERVENTION	• Prompts to log into the website • E.g. trigger message initiated • 4 contacts were provided F2F, 2 via telephone, with the majority and remaining contacts completed via trigger messages (message function)	6	24
9.1	Credible source	• verbal or visual comms from a credible source for or against targeted behaviour	INCREASE PHYSICAL ACTIVITY FOLLOW A BALANCED DIET ENGAGE WITH THE EXERTION ONLINE RESOURCE	• physiotherapy provided verbal comms on exercise or healthy lifestyle • three were provided over the telephone during consultants when discussing changes to the study with COVID in Rx group participants • The remaining and majority of the contacts were	4	8

			provided in the messages to particpants from the physio

Table 3. Appendix F- additional BCT's found in the ExeRTiOn online package

BCT name and number as per BCTTv1	Definition of BCT	Mode of delivery (online intervention)	Notes
1.9 commitment	Ask to affirm/ re-affirm statements to showcase commitment to target behaviour to change	Online intervention goal setting function	• Participants asked to rate confidence and importance scales for each goal setting template (prompted in each session) automatically generates *"this goal is important to me"* and *"I am confident I can achieve it"* • This was not initially coded as a BCT when Rx designed
2.1 monitoring of behaviour without feedback	Record or observe a behaviour with the person being aware but not providing feedback	Online intervention- GPPAQ questionnaire	• GPPAQ build into the online intervention to capture physical activity index at welcome session, S3, S7 and S10 without feedback • This was not initially coded as a BCT when Rx designed
2.4 self-monitoring outcome of behaviour	devise method for recording and monitoring the outcome of the behaviour	Online intervention tracking function	• Participant tracked their weight each clinic, and enter on the online intervention weekly (recommend weekly) • Prompt at start of each session and welcome session to add recorded weight • Whilst self-monitoring of behaviour (BCT 2.3) was included in treatment design, self-monitoring of the outcome of behaviour change (body weight) was not coded as a BCT

2.6 biofeedback	Record outcome assessment using a device and provide results	Assessment with physio at baseline, 3-months and 12-months	• This incidentally occurred with participants in both group at all outcome assessments (baseline, 3-months and 12-months) for BIA, 6MWT, Blood pressure and was revealed during qualitative analysis (see section 6.4.3)
15.1 verbal persuasion about capacity	Inform participant they can successfully do the wanted behaviour and they will succeed	Online intervention content (Session 4)	• Education in session 4 by physio that they can safely exercise post-transplant • This was not initially coded as a BCT when Rx designed
11.3 Conserve mental resources	Advise on methods for reducing demands on mental resources to facilitate behaviour change	Online intervention content	• Education in S4 by physio that they can safely exercise post-transplant • This was not initially coded as a BCT when Rx designed
12.3 distraction	Advise/arrange alternate focus to avoid triggers of unwanted behaviours	Online intervention content	• Recommended distraction examples in cravings session video and activities • This was not initially coded as a BCT when Rx designed

Note. BCT refers to behaviour change technique, BCTTv1 refers to behaviour change technique taxonomy (version 1), online intervention refers to BCT imbedded within session content and online intervention functions, F2F refers to face-to-face contacts where the participant would have a brief contact with physio in transplant clinic, TC refers to telephone contacts

Table 4. Appendix F- Additional BCT's found in the interactions between the trial Physiotherapist and participant

BCT name and number as per BCTTv1	Definition of BCT	Mode of delivery (message, TC or F2F)	Notes
1.5 Review behaviour (goal)	Review of goal with participant	• TC n=2 • Message function n=13	• 7 participants had 15 uses of this BCT • Majority through messages and progress messages from physio to participant • One participant (G03) had 2 telephone contacts over the lockdown period as a response to not replying to trigger message • This was not initially coded as a BCT when Rx designed
2.2-feedback of behaviour	Monitor and provide info/feedback on behaviour	• Majority provided by message function • F2F and TC's (n=5 contacts)	• Feedback on log in rates (and if not logged in) via physio message • Feedback on PA behaviour and steps • F2F or telephone call for those who were not engaging • This was not initially coded as a BCT when Rx designed

3.3 social support (emotional)	Advice/ provide emotional social support by friends/family or staff This includes principles of Motivational interviewing	• Messages • 1 contact provided via TC during lockdown	• Motivational interviewing techniques mainly delivered by message function • Examples include affirmations, reflections, and open questions in messages to participants • 1 of these contacts provided by TC (G03) to affirm efforts during a TC follow-up during lockdown • This was not initially coded as a BCT when Rx designed
6.2 social comparison	Compare performance of one with another to draw attention	• Message function	• Compare to other KTRs • This was not initially coded as a BCT when Rx designed

Note. BCT refers to behaviour change technique, BCTTv1 refers to behaviour change technique taxonomy (version 1), message refers to the message function within the online intervention allowing the physiotherapist to send secure messages to the online intervention participants, F2F refers to face-to-face contacts where the participant would have a brief contact with physio in transplant clinic, TC refers to telephone contacts and Rx refers to intervention

Appendix H. Examples from reflexive thematic qualitative analysis (study 4)

- Evolution of qualitative themes and reflexive analysis

Evolution of qualitative themes and reflexive analysis (study 4)

Appendix J.

The six steps of Braun and Clarke (2006) reflective thematic analysis was used:

- Data was transcribed and memo notes taken (stage 1)
- Initial line by line codes completed all transcripts (stage 2)
- Codes grouped into draft themes (stage 3)
- Themes reviewed (stage 4)
- Themes defined and named (stage 5)
- Report completed and results written up (stage 6)

Initial codes (from stage 2 of the analysis) were ordered in NVIVO into groups for patterns in the dataset. This was then summarised physically on a wall 'mind-map' to visually display key concepts during the analysis. Each stage of qualitative analysis was document in NVivo, reflexive journaling of the research fellow, the physical wall mind-map, and by downloading codebook (Microsoft word) files with corresponding quotes. Each time a change was completed on the refinement of codes, each of these systems were updated. Photos were taken at each stage of the refinement.

The images and figures below demonstrate just some of the changes made during the reflexive inductive thematic analysis that was conducted using Braun and Clarke (Braun & Clarke, 2006, 2019a) to demonstrate examples of the research process. The photograph below depicts some of the earlier codes and concepts on the wall mind-map that occurred during stages 3 of thematic analysis where codes are being grouped into potential themes.

Note. Early photograph (21st Jan 2021) of key concepts in post-its. Draft themes are shown in the bigger post-it's with associated codes in the smaller post-its. All refinements were checked against individual transcripts and the data set as per the analysis plan discussed in the methods chapter.

Note. Photograph (taken later 29th Jan 2021) above shows the codes starting to be refined into key clusters of concepts. Yellow small post its separate out the new themes. Down from six to 5 with background context still needing exploration. At each stage of

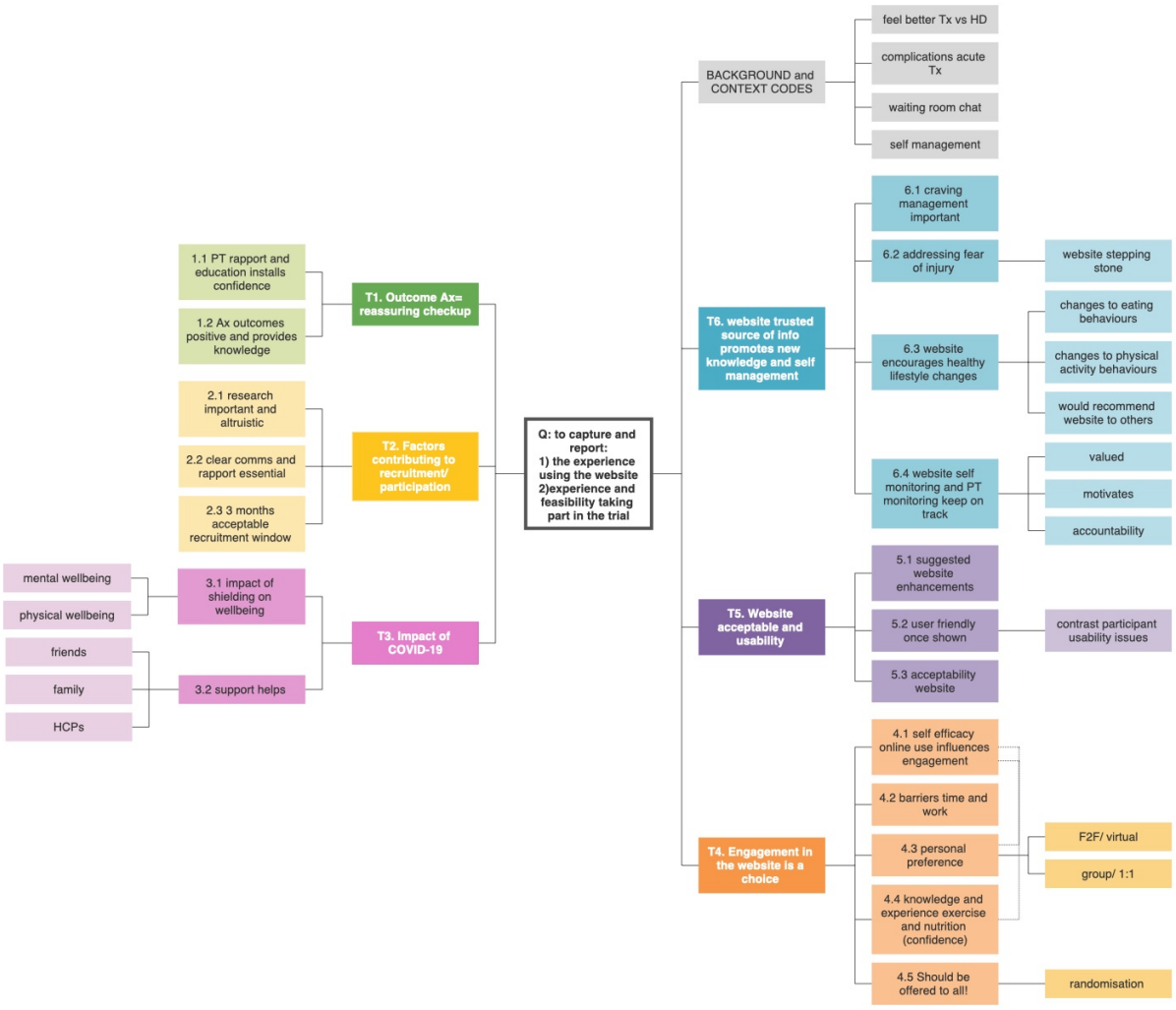
refinement, the wall was re-photographed, NVIVO updated, and a new codebook (word document) downloaded to summarise and justify each refinement. Each change was validated with codes and quotes one by one.

Note. Photo above (29th Jan 2021) depicts further re-organisation of concepts as analysis was progressed; codes were moved around within the codes. Concepts that needed to be reviewed further such as those shown on the right-hand side of the photo with yellow text on the small post-its warranted further exploration of the dataset. Themes are starting to be further refined in **stage 4** of the analysis by using transcripts and the whole dataset.

Photograph above (2nd Feb 2021) shows the key concepts/ themes forming around the central research qualitative question exploring the feasibility and acceptability of the website and taking part in Study 3. Draft themes are represented by the bigger post its, with codes and subthemes shown as smaller posits with arrows. Draft themes are linked directly to the research question. Concepts that need to be re explored in the dataset are not linked directly to the research question, demonstrating further review was required. Yellow thought bubbles were added to demonstrate queries that would need to be reviewed in the data set and in future analytical steps such as the write up stage (stage 6).

Note. Photograph above shows further refinement and is dated on the 9th of February 2021. It shows that themes and sub-themes hierarchy is being refined as concepts are checked against individual quotes and the data set as a whole. (stage 4 progressing into stage 5 of analysis).

The figure below shows a refined mind-map of the same stage in the analysis progress, stage 4 progressing into stage 5 of the thematic reflexive analysis.

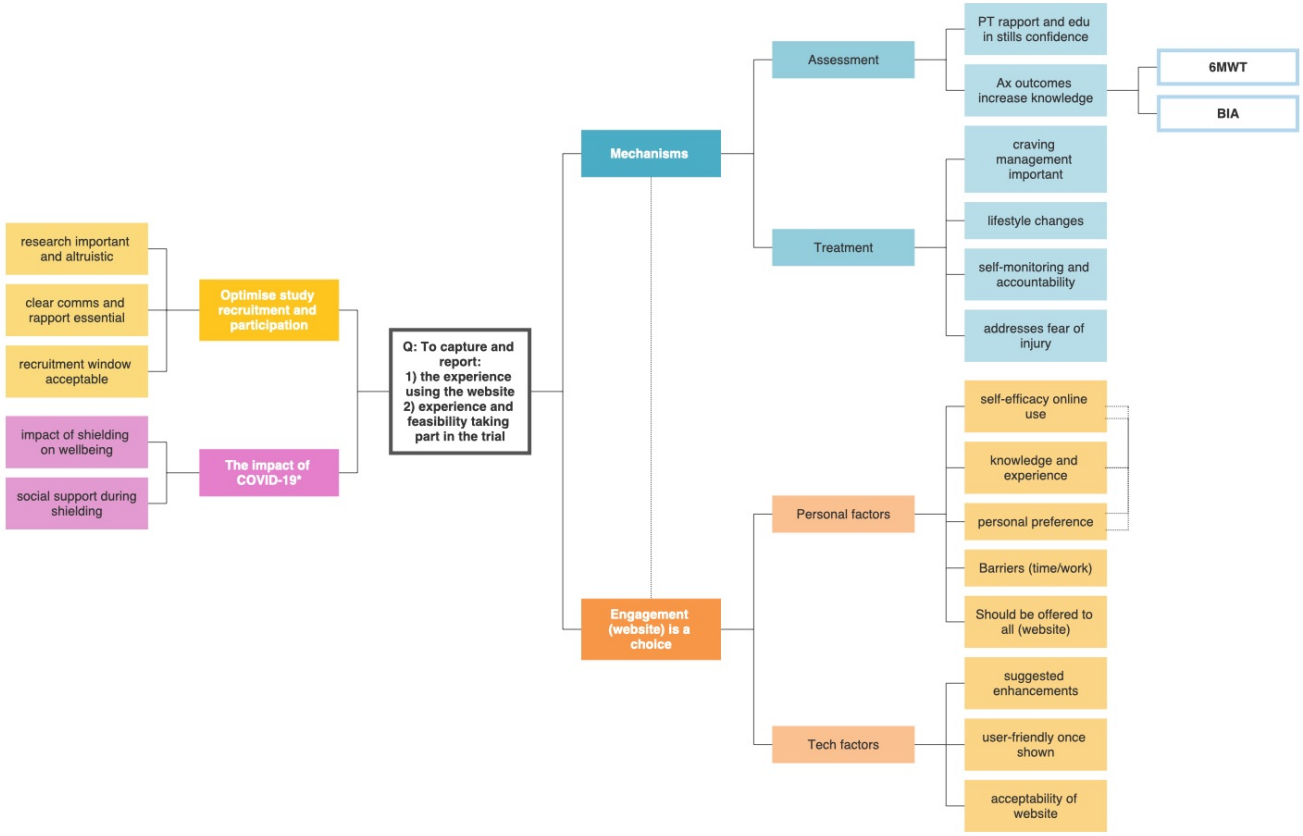


Note. The figure above shows draft themes that were reviewed and discussed with EC and JC on the 18th of February 2021. Different draft themes are represented by different colours. Related concepts are shown in the same colour with different shades to demonstrate the hierarchy within each concept.

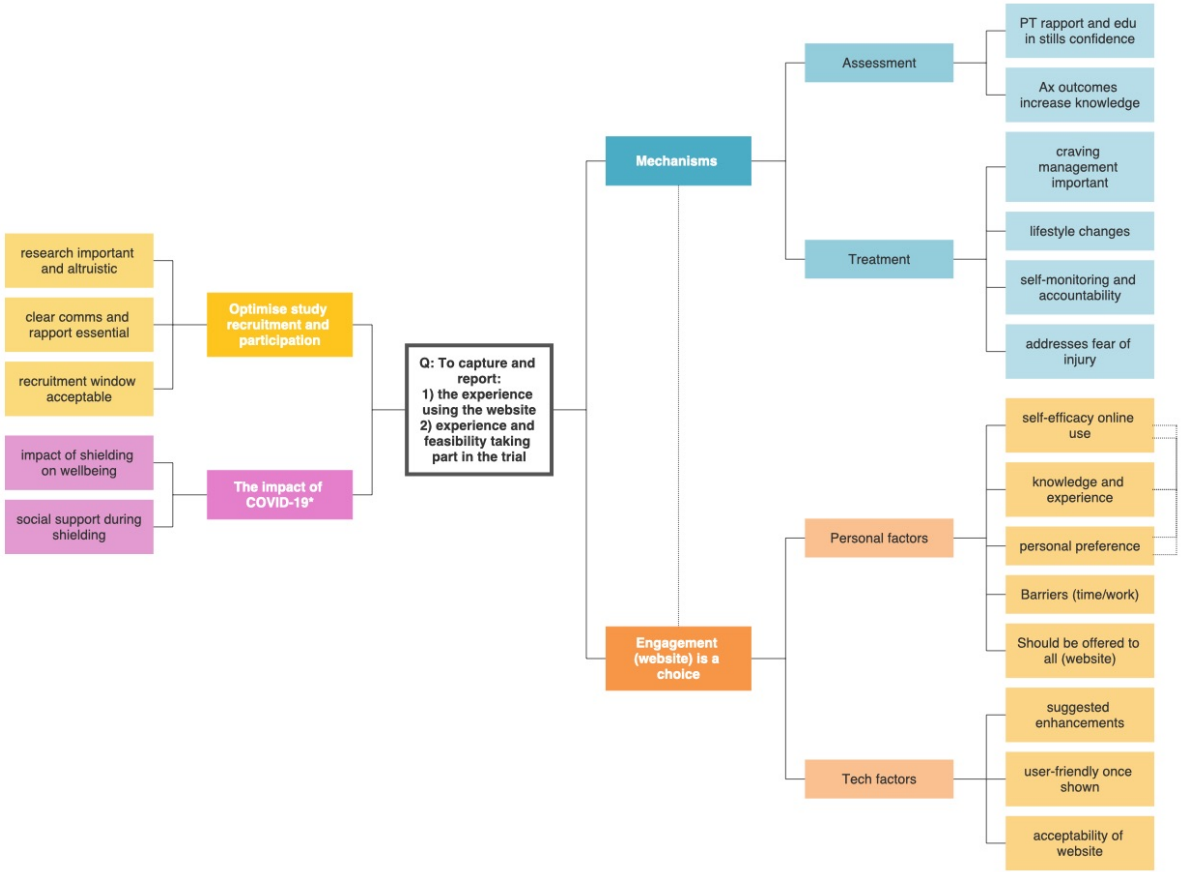
These were refined into the final themes (stage 5) by re-reading and reading the data, and looking for common patterns across the dataset as per reflexive thematic analysis methodology described by Braun and Clarke (Braun & Clarke, 2006, 2019a). This is showing **stage 5** of the analysis where themes are defined clearly.

Note. Photograph from the 18th of Feb 2021 shows largely the mind-map structure after meeting with external expert JC to agree final themes and subthemes. Final refinement of themes involved discussion with an external qualitative expert (JC). The final themes mind map was then checked and validated against the whole data set of qualitative interviews. Discussion points and points of reflection are shown by the yellow and green thought bubbles. Key themes are shown in larger post-it's with subthemes depicted by arrows and smaller post-its.

The two figures that follow show refinement that occurred during and after this meeting to form the final themes presented in the results section of this thesis.



Note. This figure shows how the codes and themes are starting to get developed and refined. You can see the removal of the 'background context' quotes from the mind map. These quotes described the context of the participants transplant journey, but do not relate to the main themes or research question. The research felt it was important to describe the context of the participants. Therefore, the key context quotes are summarised in section 7.3.1 (participants context) and were removed from the main themes. T4 (engagement with the website is a choice) and T5 (website acceptability and usability) have been combined to form personal and technical factors to engage or not engage with website. T2 (factors contributing to recruitment) has been refined into the yellow theme above (optimise study recruitment and participation). The impact of COVID remains a standalone theme and the sub-codes have been refined to two. T1 (outcome assessment reassuring check-up) has been combined with T6 (website trusted source info) as they both are discussing the core concept of mechanisms in both the assessment and intervention process.



Note. The final figure above shows the final thematic map which is displayed in the results chapter. Here the themes have been refined. This is effectively the **end of stage 5** where all themes have a clear definition and **stage 6 (write up)** is ready to commence. **Stage 6 of the analysis (producing the report) was completed from the 25th of February to the 29th of April 2021.**

Examples of reflexivity, rigor and validation from research fellows field diary

To demonstrate these important qualitative concepts, two examples have been selected below.

1. as previously discussed themes defined and refined (end of stage 5) in preparation for write up (stage 6) between EC and JG on the 18th of February 2021.

2. On the 29th of April 2021 another meeting took place between JG and EC to discuss the potential of a new theme emerging in the write up phase. EC felt that perhaps two of the subthemes 'should be offered to all' from theme engagement is a choice, and subtheme 'would recommend to others' from theme mechanisms of action could be pulled out into their own theme. After discussions with JG, and revision of the dataset and transcripts, it became evident that there was not enough depth for this to be its own theme. It was agreed this remained best placed as subthemes as per the final figure thematic map. These concepts could be revisited in chapter conclusions. It was an important learning to be aware of the temptation of researcher's bias. By discussing this with an external expert, and going back to transcripts and the dataset, this could be validated.