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'Self-Management Intervention through Lifestyle Education for Kidney health' (the SMILE-K study): protocol for a single-blind longitudinal randomised control trial with nested pilot study

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Keywords

Chronic kidney disease, self-management, digital health, patient activation

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ABSTRACT

Introduction

Many people living with chronic kidney disease (CKD) are expected to self-manage their condition. Patient activation is the term given to describe the knowledge, skills, and confidence a person has in managing their own health and is closely related to the engagement in preventive health behaviors. Self-management interventions have the potential to improve remote disease management and health outcomes. We are testing an evidence- and theory-based digital self-management structured 10-week programme developed for CKD patients called 'My Kidneys & Me'. The primary aim of the study (SMILE-K) is to assess the effect on patient activation levels.

Methods and analysis

A single-blind randomised control trial (RCT) with a nested pilot study will assess the feasibility of the intervention and study design before continuation to a full RCT. Individuals aged 18 years or older, with established CKD stage 3-4 (eGFR of 15-59 ml/min/1.73m^2) will be recruited through both primary and secondary care pathways. Participants will be randomised into two groups: intervention group and control group. The primary outcome is the Patient Activation Measure (PAM-13). The full RCT will assess the effect of the programme on online self-reported outcomes which will be assessed at baseline, after 10-weeks, and then after 20-weeks in both groups. A total sample size of n=432 participants are required based on a 2:1 randomisation. A sub-study will measure physiological changes (e.g., muscle mass, physical function) and patient experience (qualitative semi-structured interviews).

Ethics and dissemination

This study was fully approved by the Research Ethics Committee-Leicester South on the 19/11/2020 (reference: 17/EM/0357). All participants are required to provide informed consent obtained online. The results are expected to be published in scientific journals and presented at clinical research conferences. This is protocol version 1.0 dated 27/01/2021.

Trial registration number

The study was prospectively registered as ISRCTN18314195 in December 2020.

Keywords

Chronic kidney disease, self-management, digital health, patient activation

INTRODUCTION

Chronic kidney disease (CKD) is a long-term condition associated with high morbidity and premature mortality[1], and has an estimated UK prevalence ~5–7%. In the UK, 70% of National Health Service (NHS) expenditure is spent on patients with long-term conditions such as CKD[2]. With less than 1% of time spent in contact with healthcare professionals, many patients are expected to self-manage their condition[2]. In CKD, the majority of people are managed in primary care rather than by kidney specialists[3]. Long-term CKD management requires a high level of patient engagement, both in decision-making and in the implementation of care[4]. For those with CKD, this encompasses a spectrum of behaviours ranging from adherence to medication and diet recommendations, maintaining physical activity, recognition and monitoring of risk factors (e.g., blood glucose and blood pressure), and self-adjustment of home-care routines[5]. Self-management interventions aim to facilitate an individual's ability to make appropriate lifestyle changes[6] and have shown beneficial impacts on various modifiable risk factors relevant to the progression of CKD (e.g. proteinuria, blood pressure, exercise capacity)[6 7]. The COVID-19 global pandemic has presented unique challenges for people living with CKD and has further highlighted the need for and importance of self-management.

In order to implement self-management behaviours and participate in healthcare decisions, patients must have knowledge of their condition, and patient education is a crucial pathway to ensuring that individuals can be taught to engage in self-management tasks[5]. Empirical studies have shown that patient education, including an understanding of CKD, is associated with better outcomes[5]. Patient activation is the term given to describe the knowledge, skills, and confidence a person has in managing their own health[8] and is closely related to the engagement of preventive health behaviors[4]. Studies have indicated that activated patients are more likely to attend screenings, check-ups and immunizations, as well as engage in healthy behaviors such as eating a balanced diet[9 10]. Increased patient activation is associated with improved health outcomes in many long term conditions[11 12]. In CKD lower patient activation is associated with worse cardiovascular disease risk profiles[13] and promoting patient activation in kidney disease care is increasingly being prioritized and has recently emerged as central to legislative policy in the United States[14] and UK[15]. In the UK, National Institute for Health and Care Excellence (NICE) clinical guidance recommends that

informational and educational programmes are offered to those with CKD, including information regarding what people can do to manage and influence their own condition. Interventions to increase patient activation are likely to improve self-management behaviour, and consequently this may be a suitable outcome for self-management-based interventions.

A range of barriers have prevented widespread implementation of comprehensive education for people with CKD and a recent systematic review of self-management interventions in CKD found many interventions lack patient engagement in their design, and the majority of interventions do not apply behavioural change theory to inform their development[7]. As such there remains a need for better and innovative self-management interventions for those with CKD[3 7]. Digital self-management interventions have the potential to improve remote disease management and health outcomes[16] and are increasingly becoming integrated into self-management to improve behaviour. The COVID-19 pandemic has also presented those with long-term conditions and their healthcare teams an opportunity to innovate and move towards an increasingly digitalised care, with particular emphasis on supporting patients from their own homes.

Developed in the UK, the structured DESMOND diabetes self-management group education programme has recently been shown to improve patient activation in individuals living with diabetes[17]. Based on the same principles, MyDESMOND is a global digital programme to provide ongoing support and guidance[18 19]. Using the MyDESMOND platform, we developed an evidence- and theory-based digital self-management programme for CKD patients called 'My Kidneys & Me'. The programme was developed in conjunction with patients and their families, key stakeholders, and a wide range of healthcare professionals including nephrologists, psychologists, physiotherapists, dieticians, exercise scientists, and pharmacists. The programme was developed using 'Intervention Mapping', a six-step framework used to guide behaviour change interventions and health education development[20]. A full and detailed description of the development of 'My Kidneys & Me' can be found in Lightfoot et al.[21].

Objectives and hypotheses

The primary aim of the proposed 'SMILE-K' research study is to assess the effect of a structured online self-management programme - 'My Kidneys & Me' - on patient activation levels and subsequent self-management behaviour. Further objectives include assessing the feasibility of using such an intervention in this population and exploring patient experience of the programme itself. We hypothesise that access to 'My Kidneys & Me' will increase patient activation, compared to usual care, in people living with CKD.

METHODS AND ANALYSIS

This protocol adheres to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) reporting recommendations[22] (Supplementary material S1).

Study design overview

A single-blind randomised control trial (RCT) with a nested pilot study will be used to assess the effect of the 'My Kidneys & Me' programme. An initial nested pilot study will assess the feasibility of the intervention and study design before continuation to a full RCT is considered. Continuation to the full RCT will be based on a pre-defined 'stop/go' criteria assessed after n=60 participants have been recruited. The study intervention period will last 20-weeks with outcome measures assessed at baseline (pre-intervention), week-10 (post-intervention), and week-20 (follow-up). A flow diagram showing the participant flow through the study can be found in **Figure 1**.

An optional sub-study will occur in parallel with the main study. This will consist of additional objective assessments of body composition, physical activity, and physical function to the main study outcome protocol, as well as qualitative interviews with participants to discuss their expectations and experiences of the intervention and study protocol.

Eligibility criteria

Individuals aged 18 years or older, with established CKD stage 3-4 (eGFR of 15-59 ml/min/1.73m^2) according to the NICE guidelines will be included. Those requiring any form of kidney replacement therapy (i.e., any modality of dialysis, or transplantation) or with insufficient command of English or any other precluding factors that prevent ability to give informed consent or comply with protocol will be excluded. For the sub-study, in addition, participants will be excluded if they are pregnant and/or if any element of protocol considered by own clinician or General Practitioner (GP) is contraindicated and/or the individual is deemed unfit due to physical impairment, significant co-morbidity, or other reason (e.g., unstable hypertension, arrhythmia, myocardial infarction <6 months, unstable angina, uncontrolled diabetes mellitus, advanced cerebral or vascular disease).

Recruitment

Participants will be recruited through both primary and secondary care pathways across multiple sites in England. Primary care practices will identify eligible patients and provide them with an introduction flyer and study invitation letter, either during a consultation or via the post. If recruited from secondary care, the flyer will be provided during the patient's routine outpatient clinic visit by the nephrologist. Alternatively, patients may be recruited by postal means. Interested participants are requested to contact the research team by email who will then respond with further detailed information and an online consent form. When participants have consented, they are sent a link to complete the online outcome measures. In eligible patients, further information regarding the sub-study is provided. Once the baseline outcome measures have been completed, participants are randomised and provided access to the programme if appropriate. Access will be a secure link that ask participants to register and create a unique username and password. Once created, patients can then access 'My Kidneys & Me' (dashboard shown in **Figure 2**).

Randomisation

Participants will be randomised into two groups: intervention group and control group. Randomisation will be performed by the research team in a single-blind fashion. Participants will be stratified based on age (≤63, >63 years) to ensure comparatively equal representative age characteristics in both groups. These values are based on the median age attained from

preliminary unpublished data from two ongoing observational studies in non-dialysis CKD patients by our group. The control group will not be provided with the intervention during the study and will be asked to maintain their habitual lifestyle activities. The control group will be provided with the intervention upon study completion. The intervention group will be provided access to the online 'My Kidneys & Me' intervention.

Intervention

'My Kidneys & Me'

The 'My Kidneys & Me' programme forms part of the award-winning and quality assured MyDESMOND e-learning platform[21]. The educational sessions provide information about the kidneys, CKD, its treatment, and the different ways to self-manage and is written to accommodate for those with low patient activation levels. 'How to' booster sessions are interactive educational sessions, which provide instructions on how to perform the self-management behaviours and are released weekly. A summary of these sessions is found in **Table 1**.

The health trackers feature allows patients to self-monitor different aspects of their health that are involved in the self-management of the condition: body weight and measurements; fruit and vegetable intake; symptoms; smoking; cholesterol; and blood pressure. These allow patients to manually update their trackers and see their progress over time through graphs and charts. Similarly, the 'Activity' feature allows patients to track their physical activity, although this is broken down into different forms of activity. Patients can track how many steps they have walked and for how many minutes and can challenge others or invite up to five of their own friends and family to join these challenges. The patients can track this by either synchronizing the programme with their activity tracker (e.g., Fitbit) or they can enter their steps manually. They can also use a bespoke tracker created for 'My Kidneys & Me' to record their strength training progress and resources (e.g., instructional videos) will be available online. The Decision maker feature is a tool to help patients create and monitor their own health related goals, as this works through a series of questions to help patients identify which goals are most important to them and how they can achieve these by overcoming identified barriers.

Table 1. Summary of the 'How to' booster sessions

'How to' session	Summary of session
1. Get started	This is an introduction about the 'How to' sessions and explains what can be expected from them. This will be available from the start.
2. Set my own goals	The first 'How to' session introduces patients to what goals are, why they are important, how to create their own personalised goals and how to use an action plan. It is recommended that patients firstly read the 'Kidney disease and general health' and 'Reducing my health risks' educational sessions so that they can identify which areas they may want to set their own goals in.
3. Move more and be active	This session includes how to set an activity goal, how to break up sedentary time, how to do aerobic activity, and how to maintain activity levels. It is recommended that patients firstly read the 'Moving more and being active' educational session.
4. How to keep my muscles healthy through strength training	This 'How to' session provides instruction on how to safely take part in strength training exercises and how this could help them. It is recommended that patients firstly read the 'Keeping my muscles healthy' educational session.
5. Take control of my health	This session looks at taking medications and managing other conditions such as diabetes and hypertension. It is recommended that patients firstly read 'Kidney disease' 'Kidney disease and general health', and 'Reducing my health risks' educational sessions.
6. Get the most from my healthcare	This session covers information about why attending healthcare appointments is important, how to make the most out of appointments and how to decide which healthcare professional they may want to talk to for different areas so that they can share treatment decisions. It is recommended that patients firstly read 'Treatment options available'

	which includes information about their healthcare team and what appointments are for.
7. Eat well	This session covers how to make healthier food choices and adapt recipes. It is recommended that patients firstly read the 'Eating a healthy balanced diet' educational sessions.
8. Manage my symptoms	This session includes how to recognise and keep track of symptoms so that they can modify their lifestyle accordingly and speak to their healthcare professional if needed. It is recommended that patients firstly read 'Reducing my health risks and 'Managing my symptoms' educational sessions as this explains the common symptoms of CKD.
9. Improve my sleep quality	The penultimate session covers how to set sleep goals, improve sleep quality and monitor sleep. It is recommended that patients firstly read 'Improving my sleep quality' educational session.
10. Look after my well-being	The final session focuses on how to balance daily life with CKD and how to manage illness related stress. This also includes the importance of social support and how to talk to others. It is recommended that patients firstly read the 'Looking after my well-being' educational sessions.

Outcome measures

Nested feasibility outcomes

Before progression to the full RCT, we will assess feasibility outcomes on the first n=60 participants recruited. Based on these outcomes, a decision will be made to continue with the trial based on pre-specified progression criteria. These progression criteria will be developed with input from stakeholders in the study, researchers, and patients. The following feasibility outcomes will be assessed:

- *Recruitment rate:* The number of eligible patients and number consented will be recorded. Monthly recruitment rate and the time taken to recruit 25%, 50%, 75%, and 100% patients will be recorded.

- *Acceptability of randomisation and assessment procedure:* Acceptability of randomisation (and stratification variables) and procedures will be determined by comparison of randomized group characteristics, and by measuring loss to follow-up and by exploring patient' views about their participation in the research.
- *Programme usage and adherence to intervention:* Adherence will be assessed by the completion of sessions, and the use of the goal setting and health tracking features. We will also assess patterns and frequency of programme usage.
- *Attrition rate:* The number of dropouts (attrition rate) will be recorded.
- *Missing data:* Quantity of missing data (e.g., questionnaire return rate, outcome measures not completed)
- *Patient experience:* This will be attained through qualitative interviews in a sub-set of patients.

Primary study outcome

The primary outcome is the Patient Activation Measure (PAM-13), the most widely used instrument for measuring patient activation[8] which was piloted in the NHS through the UK Renal Registry (UKRR), and has been validated[23] and recommend for use in those with kidney disease[14 23]. The PAM-13 is a validated tool of 13 questions which assesses a patient's knowledge, skills, and confidence in managing their own health. The PAM-13 has demonstrated good internal consistency as well as adequate reliability and validity[8 24], including in those with kidney disease[23]. Answers are weighted and combined to provide a score on a scale from 0 to 100. The PAM allows respondents to be categorized into one of four levels with lower levels indicating low activation and higher levels indicating high activation. The PAM-13 will be assessed amongst a battery survey of other questionnaires that will be delivered online using Jisc Online Surveys (University of Leicester). As per SPIRIT recommendations, the timepoints for each outcome can be found in **Table 2.**

Table 2. Outcome measure timepoints

Item	Scale/test	Baseline	Week 10	Week 20
Main study†				
Demographics	-	X	-	-
Patient activation	PAM-13	X	X	X
Knowledge	CKD-SMKT	X	X	X
Health status	SF-12	X	X	X
Symptoms	KSQ	X	X	X
Sarcopenia	SARC-F	X	X	X
Illness perception	IPQ-R	X	X	X
Physical activity	GPPAQ	X	X	X
Diet	UKDDQ	X	X	X
Medication adherence	MARS-5	X	X	X
Healthcare use	EPQ	X	X	X
Physical function	STS-60	X	X	X
Clinical data	Full blood count, U&Es	X	X	X
Sub-study¥				
Anthropometry	Height, weight, BMI, waist and hip circumference	X	X	X
Muscle phenotyping	BIA, ultrasonography	X	X	X
Physical function	Gait speed, HGS, STS-60, TUAG	X	X	X
Physical activity	Accelerometery (7-day)	X	X	X
Qualitative component	Semi-structured interview	X	X	X

Note.
PAM-13 = Patient Activation Measure; CKD-SMKT = Chronic Kidney Disease Self-Management Knowledge Tool; SF-12 = 12-Item Short Form Health Survey; KSQ = Kidney Symptom Questionnaire; IPQ-R = Illness Representations Questionnaire (Brief); GPPAQ = General Practice Physical Activity Questionnaire; UKDDQ = UK Diabetes and Diet Questionnaire; MARS-5 = Medication Adherence Report Scale; EPQ = Modified Economic Patient Questionnaire; STS-60 = Sit-to-stand-60; U&Es = Urea and electrolytes; HGS = Handgrip strength; TUAG = Timed-up-and-go' test

†Main study outcomes delivered online to all patient

¥Sub-study outcomes assessed in a sub-set of patients. Qualitative interviews may be performed at any of the timepoints

Secondary outcomes

Alongside a bespoke self-reported demographic questionnaire, other validated questionnaires in the online survey, which capture different aspects of self-management and lifestyle behaviours that are addressed in 'My Kidneys & Me', include:

- *Chronic Kidney Disease Self-Management Knowledge Tool (CKD-SMKT):* The CKD-SMKT is a validated 11-item questionnaire, which assesses kidney disease patients' knowledge of various key self-management behaviours and kidney health[25].

- *12-Item Short Form Health Survey (SF-12):* The SF-12 is a multipurpose short form survey with 12 questions. The SF-12 assesses patients mental and physical functioning and overall health-related-quality of life (QoL)[26].

- *Kidney Symptom Questionnaire (KSQ):* The KSQ assesses the frequency, intrusiveness, and total impact of a range of 13 common kidney disease-related symptoms. This questionnaire has been validated by our group[27] and used widely in the literature[28].

- *SARC-F questionnaire:* The SARC-F questionnaire includes five components: strength, assistance walking, rise from a chair, climb stairs, and falls. SARC-F scores range from 0 to 10 and a score ≥4 is predictive of sarcopenia[29].

- *Illness Representations Questionnaire (Brief) (IPQ-R):* The IPQ-R is a widely accepted measure of illness representations. These components are identity, cause, timeline, consequence, and controllability/cure. The questionnaire consists of three parts: an identity scale, a structure scale, and a causal scale[30].

- *General Practice Physical Activity Questionnaire (GPPAQ):* The GPPAQ was developed by the World Health Organization and Department of Health detailing a 4-level Physical

Activity Index (PAI) reflecting an individual's current physical activity. The GPPAQ is a validated measure of physical activity behaviour in CKD[31].

- *UK Diabetes and Diet Questionnaire (UKDDQ):* The UKDDQ is a 25-item questionnaire designed to assess diet and dietary behaviours. Respondents are asked to identify how often they consumed certain foods (vegetables, fruits, sugary drinks, processed meat) over that last month[32]. Responses will be scored as per previous research[33]. This questionnaire is sensitive to changes following an intervention[34].

- *Medication Adherence Report Scale (MARS-5):* The MARS-5 is a non-disease specific questionnaire used to measure adherence to medications and has been previously used in CKD. This comprises of five questions regarding changing medication dosage, forgetting to take medication, consciously stopping taking medication, skipping medication, and using less than prescribed[35].

- *Modified Economic Patient Questionnaire (EPQ):* We will use a modified version of the 'Economic Patient Questionnaire (EPQ)' to assess participants' use of inpatient and outpatient services and data on non-hospital-based health and social care use at all assessment points[36].

When the participant consents to the study, the researcher will access their clinical records and extract information such as blood and urine results to gather information of kidney function, proteinuria, iron status, and lipid profiles. We will record prescribed medication. Self-reported co-morbidities will be checked against those recorded in the medical notes.

Sub-study

In an optional sub-study, the following additional physical assessments will be performed during a visit to a hospital site:

- *Anthropometry:* Height, weight, body mass index (BMI), and waist and hip circumference will be measured in line with established procedures. Resting heart rate and blood pressure will be assessed using a standard sphygmomanometer device.

- *Muscle phenotyping:* Muscle and fat mass/size/thickness, and body fat % will be measured using a free-standing bioelectrical impendence analysis (BIA) monitor and B-mode ultrasonography of the rectus femoris muscle. These are painless, non-invasive methods for measuring body composition. Our group has recently validated our BIA device against dual-energy X-ray absorptiometry (DXA)[37] whilst ultrasonography can be used to assess sarcopenia in CKD[38 39].

- *Gait speed:* The participant is asked to walk a 4m course at their 'usual' walking speed, with a walking aid if normally used[40].

- *Handgrip strength (HGS):* Handgrip strength will be assessed using a handheld dynamometer (Jamar Plus+ Digital). Participants will be asked to hold the dynamometer with their shoulder at 0 degrees flexion and elbow at 90-degree flexion. Participants will be asked to squeeze the dynamometer handle maximally for 3 seconds. The peak force output (kg) from the three attempts from both the dominant and non-dominant hand will be recorded[41].

- *Sit-to-stand-60 test:* Sit-to-stand (STS) tests are a good measure of functional ability and have been used extensively in CKD patients. Our group has extensive use and knowledge of this test, and published reliability and validation data for it[42]. The patient starts from a seated position on a hard, upright chair, with the feet flat on the floor and the knees bent at 90°. For the test, the patient simply stands up fully and then sits down again to the starting position, without using the hands (one repetition). The STS-60 test involves completing as many STS cycles as possible in 60 seconds. Participants will also be asked to record a STS-60 score as part of the online survey.

- *Timed-up-and-go' test (TUAG):* The TUAG assesses mobility and requires dynamic balance. The participant will be asked to rise from a chair, walk 3 metres, turn around a cone, and sit back down[40].

- *Accelerometery:* To accurately measure objective physical activity, patients will wear a wrist accelerometer (GENEActiv) for a 7-day period before the intervention and post-intervention[31 43].

Familiarisation of objective physical performance measures will be performed before baseline assessments. In order to assess any potential differences in administering the questionnaires online, participants in the sub-study will also be asked to complete the same questionnaires via paper format.

In the sub-study, semi-structured interviews will be held with a researcher trained in qualitative methodology. Individual interviews will last between ~30 to 60 minutes. Interviews will take place in private area. For those unable to attend a face-to-face interview, interviews may also be performed via telephone using a secure recording device as used currently in other studies by our group. Patients recruited may be interviewed on at least one occasion (e.g., before and/or after the intervention). Topics in this interview will include current self-management knowledge, skills, confidence and behaviours, and attitudes towards lifestyle self-management. Topics of the subsequent interviews will include experiences of the intervention, the quality of the content, the quality of the delivery method, reasons for non-adherence with the intervention, and healthcare usage.

Patient and public involvement

A full description of how patients and their families were involved in the development of the programme can be found in Lightfoot et al.[21]. In summary, a study patient steering group was formed consisting of ten individuals living with kidney disease and two family members. An initial priority setting workshop determined key topics of interest to this group, including lack of educational support from healthcare professionals. Following this, we developed an educational booklet which was co-designed using our patient steering group. This booklet was disseminated to local primary care practices where individuals provided feedback on the

content. The information in this booklet was then adapted for digital use and was termed 'My Kidneys & Me' by the patient group. We also performed semi-structured interviews with patients around self-management and the use of educational resources. Key examples of feedback from patients included the following: 1) to provide a symptom tracker to enable self-monitoring of symptoms; 2) include a separate session on sleep; 3) include a separate session on well-being, emphasising the importance of looking after mental health; 4) use of myth and fact quizzes as a way to test knowledge; 5) state how long sessions should take in the introduction. Once 'My Kidneys & Me' was developed, members of the steering group were provided with access to the programme to provide initial comment. The patient steering group assisted with the selection of questionnaires for the study, and reviewed the final questionnaire survey to ensure that it was acceptable. Throughout the study, the steering group will be used to develop a suitable and relevant topic guide exploring exploration of their attitudes towards self-management and the impact these have on their lives. The group will also be used to interpret initial and final findings. In addition, the patient steering group will support the development of the lay summary outputs to be disseminated to patients and the public.

Data analysis

Sample size calculation

With PAM-13 as the primary outcome in the full RCT, a total sample size of n=432 participants are required based on a 2:1 randomisation (n=288 in the intervention group and n=144 in the control group). This was based on previously published PAM-13 data by our group [13] and on the required power to detect a minimal clinically significant difference of 4 points in the PAM-13[44-46]. For the initial nested pilot study, a pragmatic sample size of n=60 participants (n=40 in the intervention group and n=20 in the control group, based on 2:1 randomisation) will be used. We aim to recruit at least 10 patients into the optional sub-study.

Statistical analysis

Participant demographics and clinical characteristics will be analysed using descriptive statistics. The primary outcome is the PAM-13 where answers are weighted provide a score on a scale from 0 to 100. As recommended by Twisk et al.[47], estimates of treatment effect will be assessed by longitudinal analysis of covariance. In this method the outcome variable measured at the different follow-up measurements (post-intervention at week 10, follow-up at week 20) is adjusted for the baseline value of the outcome. Analysis will be performed using 'intention-to-treat' (ITT) analysis. In an ITT approach, patients are analyzed by how they were randomised regardless of their actual compliance with treatment. For patient-reported outcomes missing data items will be handled according to established protocols for the validated surveys. Additional post-hoc analysis will be performed to determine if differences exist in PAM score changes between those with low and high PAM scores.

In the sub-study, interview recordings will be professionally transcribed verbatim. The precise analytical methodology used may change based on the nature of the data collected, however thematic analysis will be used as an initial foundation for data analysis as it provides a systematic model for managing and mapping the data. Analysis will follow recognised steps (e.g., familiarisation, initial and confirmation of coding (using NVivo), defining themes). In an integrative strategy, any available quantitative data will be used to inform the qualitative analysis.

ETHICS AND DISSEMINATION

To carry out this study, we will consider the Good Clinical Practice (GCP) guidelines of the local governance organisations (University of Leicester and University Hospitals of Leicester NHS Trust) thus guaranteeing the protection of the rights, the safety, and the well-being of the participants of the trial in compliance with the principles of the Declaration of Helsinki, as well as the credibility of the data obtained in the clinical trial. All participant data entered into the 'My Kidneys & Me' will be managed through the MyDESMOND platform. Data entered as part of the online outcomes is managed by Jisc Online Surveys under a University of Leicester license. A full informative sheet explaining the study in detail, the voluntary nature of the research, and the procedure for the protection of their personal data will be provided along

with the online consent form. Patients will be given the opportunity to contact the researchers with any questions prior to the informed consent. The informed consent obtained from study participants will be online.

This study was fully approved by the Research Ethics Committee (REC)-Leicester South and Health Research Authority (HRA) on the 19/11/2020 (reference: 17/EM/0357). The results are expected to be published in scientific journals and presented at clinical research conferences in 2024. Findings will be disseminated to patients and the wider kidney and healthcare community via social media platforms, interest groups, recruiting sites, and institutions associated with the research team. Any subsequent changes to the study protocol will reviewed by the REC and HRA through appropriate amendments. Any significant protocol changes will be stated on the ISRCTN Registry. The study was prospectively registered as ISRCTN18314195.

SUMMARY

'My Kidneys & Me', an online self-management and lifestyle education programme, aims to increase patient activation and promote self-management behaviours. If this is achieved, it is anticipated that the intervention will achieve its distal aims of improving patient QoL, physical function, and symptom burden whilst experiencing fewer hospital admissions and saving costs to the NHS.

DECLARATIONS

Ethics approval and consent to participate

This study was fully approved by the Research Ethics Committee-Leicester South on the 19/11/2020 (reference: 17/EM/0357). All participants will provide consent either online or face-to-face (sub-study). All participants will be given the opportunity to ask questions before completing the consent process. The trial is sponsored by the University of Leicester (rgo@le.ac.uk).

Consent for publication

N/A

Availability of data and materials

N/A

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the design of the SMILE-K trial protocol. CLJ and TJW drafted the manuscript contributing equally. All authors read and approved the final manuscript.

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LIST OF ABBREVIATIONS

BIA	Bioelectrical Impendence Analysis
BMI	Body Mass Index
CKD	Chronic Kidney Disease
CKD-SMKT	Chronic Kidney Disease Self-Management Knowledge Tool
COVID-19	Coronavirus Disease-2019
DXA	Dual-Energy X-Ray Absorptiometry
eGFR	Estimated Glomerular Filtration Rate
EPQ	Modified Economic Patient Questionnaire
EWGSOP	European Working Group on Sarcopenia in Older People
GCP	Good Clinical Practice
GP	General Practitioner
GPPAQ	General Practice Physical Activity Questionnaire
HGS	Handgrip Strength
HRA	Health Research Authority
IPQ-R	Illness Representations Questionnaire
ITT	Intention-To-Treat
KSQ	Kidney Symptom Questionnaire
MARS-5	Medication Adherence Report Scale
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PAI	Physical Activity Index
PAM-13	Patient Activation Measure
QoL	Quality of Life
RCT	Randomised Control Trial
REC	Research Ethics Committee
SF-12	12-Item Short Form Health Survey
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
STS	Sit-To-Stand
TUAG	Timed-Up-And-Go

UKDDQ	UK Diabetes and Diet Questionnaire
UKRR	UK Renal Registry

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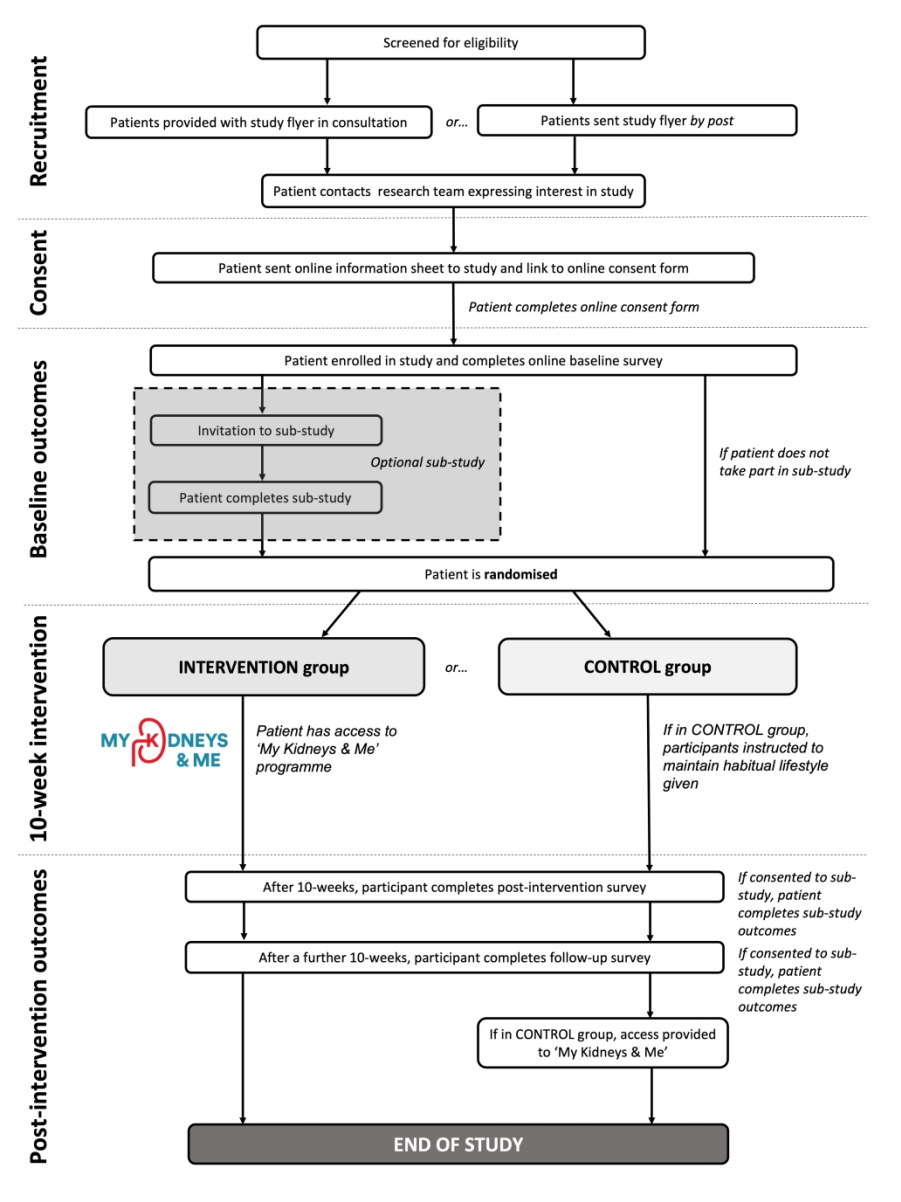
FIGURES

Figure 1. Study flow diagram

Figure 2. 'My Kidneys & Me' dashboard page



SMILE-K study flow diagram

300x398mm (300 x 300 DPI)

My Kidneys & Me dashboard

181x87mm (300 x 300 DPI)

Supplementary material S1. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents

Section/item	Item No.	Description	Page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	24
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	24
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	24
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 2 and Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	24
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	24
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A – online form
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

'Self-Management Intervention through Lifestyle Education for Kidney health' (the SMILE-K study): protocol for a single-blind longitudinal randomised control trial with nested pilot study

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'Self-Management Intervention through Lifestyle Education for Kidney health' (the SMILE-K study): protocol for a single-blind longitudinal randomised control trial with nested pilot study

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Keywords

Chronic kidney disease, self-management, digital health, patient activation

Word count = 4000 words

ABSTRACT

Introduction

Many people living with chronic kidney disease (CKD) are expected to self-manage their condition. Patient activation is the term given to describe the knowledge, skills, and confidence a person has in managing their own health and is closely related to the engagement in preventive health behaviours. Self-management interventions have the potential to improve remote disease management and health outcomes. We are testing an evidence- and theory-based digital self-management structured 10-week programme developed for CKD patients called 'My Kidneys & Me'. The primary aim of the study (SMILE-K) is to assess the effect on patient activation levels.

Methods and analysis

A single-blind randomised control trial (RCT) with a nested pilot study will assess the feasibility of the intervention and study design before continuation to a full RCT. Individuals aged 18 years or older, with established CKD stage 3-4 (eGFR of 15-59 ml/min/1.73m^2) will be recruited through both primary and secondary care pathways. Participants will be randomised into two groups: intervention group (receive My Kidneys & Me in addition to usual care) and control group (usual care). The primary outcome of the nested pilot study is feasibility and the primary outcome of the full RCT is the Patient Activation Measure (PAM-13). The full RCT will assess the effect of the programme on online self-reported outcomes which will be assessed at baseline, after 10-weeks, and then after 20-weeks in both groups. A total sample size of n=432 participants are required based on a 2:1 randomisation. A sub-study will measure physiological changes (e.g., muscle mass, physical function) and patient experience (qualitative semi-structured interviews).

Ethics and dissemination

This study was fully approved by the Research Ethics Committee-Leicester South on the 19/11/2020 (reference: 17/EM/0357). All participants are required to provide informed consent obtained online. The results are expected to be published in scientific journals and presented at clinical research conferences. This is protocol version 1.0 dated 27/01/2021.

Trial registration number

The study was prospectively registered as ISRCTN18314195 in December 2020.

Keywords

Chronic kidney disease, self-management, digital health, patient activation

Strengths and limitations of this study

- This study will be conducted as a large randomised controlled trial and will assess the effect of an online self-management and lifestyle education programme ('My Kidneys & Me') on patient activation levels and subsequent self-management behaviours in people with kidney disease.
- The secondary outcomes of the study will assess the feasibility of using such an intervention in this population and explore patient experience of the programme itself.
- The nested pilot study will assess the feasibility of the intervention and study design before continuation to a full RCT; progression criteria will be developed with specified targets for progression based on feasibility outcomes.
- The use of Patient and Public Involvement in the intervention development and study design will ensure that they are acceptable, suitable, and relevant to the target population.

The primary limitation of this study is lack of acceptability of randomisation and assessment

INTRODUCTION

Chronic kidney disease (CKD) is a long-term condition associated with high morbidity and premature mortality[1], and has an estimated UK prevalence ~5–7%. In the UK, 70% of National Health Service (NHS) expenditure is spent on patients with long-term conditions such as CKD[2]. With less than 1% of time spent in contact with healthcare professionals, many patients are expected to self-manage their condition[2]. In CKD, the majority of people are managed in primary care rather than by kidney specialists[3]. Long-term CKD management requires a high level of patient engagement, both in decision-making and in the implementation of care[4]. For those with CKD, this encompasses a spectrum of behaviours ranging from adherence to medication and diet recommendations, maintaining physical activity, recognition and monitoring of risk factors (e.g., blood glucose and blood pressure), and self-adjustment of home-care routines[5]. Self-management interventions aim to facilitate an individual's ability to make appropriate lifestyle changes[6] and have shown beneficial impacts on various modifiable risk factors relevant to the progression of CKD (e.g. proteinuria, blood pressure, exercise capacity)[6 7]. The COVID-19 global pandemic has presented unique challenges for people living with CKD and has further highlighted the need for and importance of self-management.

In order to implement self-management behaviours and participate in healthcare decisions, patients must have knowledge of their condition, and patient education is a crucial pathway to ensuring that individuals can be taught to engage in self-management tasks[5]. Empirical studies have shown that patient education, including an understanding of CKD, is associated with better outcomes[5]. Patient activation is the term given to describe the knowledge, skills, and confidence a person has in managing their own health[8] and is closely related to the engagement of preventive health behaviours[4]. Studies have indicated that activated patients are more likely to attend screenings, check-ups and immunizations, as well as engage in healthy behaviours such as eating a balanced diet[9 10]. Increased patient activation is associated with improved health outcomes in many long term conditions[11 12]. In CKD lower patient activation is associated with worse cardiovascular disease risk profiles[13] and promoting patient activation in kidney disease care is increasingly being prioritized and has recently emerged as central to legislative policy in the United States[14] and UK[15]. In the UK, National Institute for Health and Care Excellence (NICE) clinical guidance recommends that

informational and educational programmes are offered to those with CKD, including information regarding what people can do to manage and influence their own condition. Interventions to increase patient activation are likely to improve self-management behaviour, and consequently this may be a suitable outcome for self-management-based interventions.

A range of barriers have prevented widespread implementation of comprehensive education for people with CKD and a recent systematic review of self-management interventions in CKD found many interventions lack patient engagement in their design, and the majority of interventions do not apply behavioural change theory to inform their development[7]. As such there remains a need for better and innovative self-management interventions for those with CKD[3 7]. Digital self-management interventions have the potential to improve remote disease management and health outcomes[16] and are increasingly becoming integrated into self-management to improve behaviour. The COVID-19 pandemic has also presented those with long-term conditions and their healthcare teams an opportunity to innovate and move towards an increasingly digitalised care, with particular emphasis on supporting patients from their own homes.

Developed in the UK, the structured DESMOND diabetes self-management group education programme has recently been shown to improve patient activation in individuals living with diabetes[17]. Based on the same principles, MyDESMOND is a global digital programme to provide ongoing support and guidance[18 19]. Using the MyDESMOND platform, we developed an evidence- and theory-based digital self-management programme for CKD patients called 'My Kidneys & Me'. The programme was developed in conjunction with patients and their families, key stakeholders, and a wide range of healthcare professionals including nephrologists, psychologists, physiotherapists, dieticians, exercise scientists, and pharmacists. The programme was developed using 'Intervention Mapping', a six-step framework used to guide behaviour change interventions and health education development[20]. A full and detailed description of the development of 'My Kidneys & Me' can be found in Lightfoot et al.[21].

Objectives and hypotheses

The primary aim of the proposed 'SMILE-K' research study is to assess the effect of a structured online self-management programme - 'My Kidneys & Me' - on patient activation levels and subsequent self-management behaviour. Further objectives include assessing the feasibility of using such an intervention in this population and exploring patient experience of the programme itself. We hypothesise that access to 'My Kidneys & Me' will increase patient activation, compared to usual care, in people living with CKD.

METHODS AND ANALYSIS

This protocol adheres to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) reporting recommendations[22] (Supplementary material S1).

Study design overview

A single-blind randomised control trial (RCT) with a nested pilot study will be used to assess the effect of the 'My Kidneys & Me' programme. An initial nested pilot study will assess the feasibility of the intervention and study design before continuation to a full RCT is considered. Continuation to the full RCT will be based on a pre-defined 'stop/go' criteria assessed after n=60 participants have been recruited. The study intervention period will last 20-weeks with outcome measures assessed at baseline (pre-intervention), week-10 (post-intervention), and week-20 (follow-up). A flow diagram showing the participant flow through the study can be found in **Figure 1**.

An optional sub-study will occur in parallel with the main study. This will consist of additional objective assessments of body composition, physical activity, and physical function to the main study outcome protocol, as well as qualitative interviews with participants to discuss their expectations and experiences of the intervention and study protocol.

Eligibility criteria

Individuals aged 18 years or older, with established CKD stage 3-4 (eGFR of 15-59 ml/min/1.73m^2) according to the NICE guidelines will be included. Those requiring any form of kidney replacement therapy (i.e., any modality of dialysis, or transplantation) or with insufficient command of English or any other precluding factors that prevent ability to give informed consent or comply with protocol will be excluded. For the sub-study, in addition, participants will be excluded if they are pregnant and/or if any element of protocol considered by own clinician or General Practitioner (GP) is contraindicated and/or the individual is deemed unfit due to physical impairment, significant co-morbidity, or other reason (e.g., unstable hypertension, arrhythmia, myocardial infarction <6 months, unstable angina, uncontrolled diabetes mellitus, advanced cerebral or vascular disease).

Recruitment

Participants will be recruited through both primary and secondary care pathways across multiple sites in England. Primary care practices will identify eligible patients and provide them with an introduction flyer and study invitation letter, either during a consultation or via the post. If recruited from secondary care, the flyer will be provided during the patient's routine outpatient clinic visit by the nephrologist. Alternatively, patients may be recruited by postal means. Interested participants are requested to contact the research team by email who will then respond with further detailed information and an online consent form. When participants have consented, they are sent a link to complete the online outcome measures. In eligible patients, further information regarding the sub-study is provided. Once the baseline outcome measures have been completed, participants are randomised and provided access to the programme if appropriate. Access will be a secure link that ask participants to register and create a unique username and password. Once created, patients can then access 'My Kidneys & Me' (dashboard shown in **Figure 2**).

Randomisation

Participants will be randomised into two groups: intervention group and control group. Randomisation will be performed by the research team in a single-blind fashion. Study investigators, clinicians, and research staff from external recruiting sites are blinded to the group allocation of their participants. Participants will be stratified based on age (≤63, >63

years) to ensure comparatively equal representative age characteristics in both groups. These values are based on the median age attained from preliminary unpublished data from two ongoing observational studies in non-dialysis CKD patients by our group. The control group will not be provided with the intervention during the study and will be asked to maintain their habitual lifestyle activities. The control group will be provided with the intervention upon study completion. The intervention group will be provided access to the online 'My Kidneys & Me' intervention.

Intervention

'My Kidneys & Me'

The 'My Kidneys & Me' programme forms part of the award-winning and quality assured MyDESMOND e-learning platform[21]. The educational sessions provide information about the kidneys, CKD, its treatment, and the different ways to self-manage and is written to accommodate for those with low patient activation levels. A summary of the education sessions can be in the My Kidneys & Me development paper[23]. 'How to' booster sessions are interactive educational sessions, which provide instructions on how to perform the self-management behaviours and are released weekly. A summary of these sessions is found in **Table 1**.

The health trackers feature allows patients to self-monitor different aspects of their health that are involved in the self-management of the condition: body weight and measurements; fruit and vegetable intake; symptoms; smoking; cholesterol; and blood pressure. These allow patients to manually update their trackers and see their progress over time through graphs and charts. Similarly, the 'Activity' feature allows patients to track their physical activity, although this is broken down into different forms of activity. Patients can track how many steps they have walked and for how many minutes and can challenge others or invite up to five of their own friends and family to join these challenges. The patients can track this by either synchronizing the programme with their activity tracker (e.g., Fitbit) or they can enter their steps manually. They can also use a bespoke tracker created for 'My Kidneys & Me' to record their strength training progress and resources (e.g., instructional videos) will be available online. The Decision maker feature is a tool to help patients create and monitor their own health related goals, as this works through a series of questions to help patients identify

which goals are most important to them and how they can achieve these by overcoming identified barriers.

Table 1. Summary of the 'How to' booster sessions

'How to' session	Summary of session	Duration of session (minutes)
1. Get started	This is an introduction about the 'How to' sessions and explains what can be expected from them. This will be available from the start.	5
2. Set my own goals	The first 'How to' session introduces patients to what goals are, why they are important, how to create their own personalised goals and how to use an action plan. It is recommended that patients firstly read the 'Kidney disease and general health' and 'Reducing my health risks' educational sessions so that they can identify which areas they may want to set their own goals in.	25-30
3. Move more and be active	This session includes how to set an activity goal, how to break up sedentary time, how to do aerobic activity, and how to maintain activity levels. It is recommended that patients firstly read the 'Moving more and being active' educational session.	15-20
4. How to keep my muscles healthy through strength training	This 'How to' session provides instruction on how to safely take part in strength training exercises and how this could help them. It is recommended that patients firstly read the 'Keeping my muscles healthy' educational session.	15-20
5. Take control of my health	This session looks at taking medications and managing other conditions such as diabetes and hypertension. It is recommended that patients firstly read 'Kidney disease'	15-20

	'Kidney disease and general health', and 'Reducing my health risks' educational sessions.	
6. Get the most from my healthcare	This session covers information about why attending healthcare appointments is important, how to make the most out of appointments and how to decide which healthcare professional they may want to talk to for different areas so that they can share treatment decisions. It is recommended that patients firstly read 'Treatment options available' which includes information about their healthcare team and what appointments are for.	15-20
7. Eat well	This session covers how to make healthier food choices and adapt recipes. It is recommended that patients firstly read the 'Eating a healthy balanced diet' educational sessions.	20-25
8. Manage my symptoms	This session includes how to recognise and keep track of symptoms so that they can modify their lifestyle accordingly and speak to their healthcare professional if needed. It is recommended that patients firstly read 'Reducing my health risks and 'Managing my symptoms' educational sessions as this explains the common symptoms of CKD.	10-15
9. Improve my sleep quality	The penultimate session covers how to set sleep goals, improve sleep quality and monitor sleep. It is recommended that patients firstly read 'Improving my sleep quality' educational session.	10-15
10. Look after my well-being	The final session focuses on how to balance daily life with CKD and how to manage illness related stress. This also includes the importance of social support and how to talk to others. It is recommended that patients firstly read the 'Looking after my well-being' educational sessions.	15-20

Outcome measures

The primary outcome of the nested pilot study is feasibility, and the primary outcome of the full RCT is the Patient Activation Measure (PAM-13).

Nested feasibility outcomes

Before progression to the full RCT, we will assess feasibility outcomes on the first n=60 participants recruited. Based on these outcomes, a decision will be made to continue with the trial based on pre-specified progression criteria. These progression criteria will be developed with input from stakeholders in the study, researchers, and patients. The following feasibility outcomes will be assessed:

- *Recruitment rate:* The number of eligible patients and number consented will be recorded. Monthly recruitment rate and the time taken to recruit 25%, 50%, 75%, and 100% patients will be recorded.
- *Acceptability of randomisation and assessment procedure:* Acceptability of randomisation (and stratification variables) and procedures will be determined by comparison of randomized group characteristics, and by measuring loss to follow-up and by exploring patient' views about their participation in the research.
- *Programme usage and adherence to intervention:* Adherence will be assessed by the completion of sessions, and the use of the goal setting and health tracking features. We will also assess patterns and frequency of programme usage.
- *Attrition rate:* The number of dropouts (attrition rate) will be recorded.
- *Missing data:* Quantity of missing data (e.g., questionnaire return rate, outcome measures not completed)
- *Patient experience:* This will be attained through qualitative interviews in a sub-set of patients.

Primary study outcome

The primary outcome of the full RCT is the Patient Activation Measure (PAM-13), the most widely used instrument for measuring patient activation[8] which was piloted in the NHS through the UK Renal Registry (UKRR), and has been validated[24] and recommend for use in those with kidney disease[14 24]. The PAM-13 is a validated tool of 13 questions which assesses

a patient's knowledge, skills, and confidence in managing their own health. The PAM-13 has demonstrated good internal consistency as well as adequate reliability and validity[8 25], including in those with kidney disease[24]. Answers are weighted and combined to provide a score on a scale from 0 to 100. The PAM allows respondents to be categorized into one of four levels with lower levels indicating low activation and higher levels indicating high activation. The PAM-13 will be assessed amongst a battery survey of other questionnaires that will be delivered online using Jisc Online Surveys (University of Leicester). As per SPIRIT recommendations, the timepoints for each outcome can be found in **Table 2.**

Table 2. Outcome measure timepoints

Item	Scale/test	Baseline	Week 10	Week 20
Main study†				
Demographics	-	X	-	-
Patient activation	PAM-13	X	X	X
Knowledge	CKD-SMKT	X	X	X
Health status	SF-12	X	X	X
Symptoms	KSQ	X	X	X
Sarcopenia	SARC-F	X	X	X
Illness perception	IPQ-R	X	X	X
Physical activity	GPPAQ	X	X	X
Diet	UKDDQ	X	X	X
Medication adherence	MARS-5	X	X	X
Healthcare use	EPQ	X	X	X
Physical function	STS-60	X	X	X
Clinical data	Full blood count, U&Es	X	X	X
Sub-study¥				
Anthropometry	Height, weight, BMI, waist and hip circumference	X	X	X
Muscle phenotyping	BIA, ultrasonography	X	X	X

Physical function	Gait speed, HGS, STS-60, TUAG	X	X	X
Physical activity	Accelerometery (7-day)	X	X	X
Qualitative component	Semi-structured interview	X	X	X

Note.
PAM-13 = Patient Activation Measure; CKD-SMKT = Chronic Kidney Disease Self-Management Knowledge Tool; SF-12 = 12-Item Short Form Health Survey; KSQ = Kidney Symptom Questionnaire; IPQ-R = Illness Representations Questionnaire (Brief); GPPAQ = General Practice Physical Activity Questionnaire; UKDDQ = UK Diabetes and Diet Questionnaire; MARS-5 = Medication Adherence Report Scale; EPQ = Modified Economic Patient Questionnaire; STS-60 = Sit-to-stand-60; U&Es = Urea and electrolytes; HGS = Handgrip strength; TUAG = Timed-up-and-go' test

†Main study outcomes delivered online to all patient
¥Sub-study outcomes assessed in a sub-set of patients. Qualitative interviews may be performed at any of the timepoints depending on participants' voluntary participation and/or their status in the study

Secondary outcomes

Alongside a bespoke self-reported demographic questionnaire, other validated questionnaires in the online survey, which capture different aspects of self-management and lifestyle behaviours that are addressed in 'My Kidneys & Me', include:

- *Chronic Kidney Disease Self-Management Knowledge Tool (CKD-SMKT):* The CKD-SMKT is a validated 11-item questionnaire, which assesses kidney disease patients' knowledge of various key self-management behaviours and kidney health[26].

- *12-Item Short Form Health Survey (SF-12):* The SF-12 is a multipurpose short form survey with 12 questions. The SF-12 assesses patients mental and physical functioning and overall health-related-quality of life (QoL)[27].

- *Kidney Symptom Questionnaire (KSQ):* The KSQ assesses the frequency, intrusiveness, and total impact of a range of 13 common kidney disease-related symptoms. This questionnaire has been validated by our group[28] and used widely in the literature[29].

- *SARC-F questionnaire:* The SARC-F questionnaire includes five components: strength, assistance walking, rise from a chair, climb stairs, and falls. SARC-F scores range from 0 to 10 and a score ≥4 is predictive of sarcopenia[30].

- *Illness Representations Questionnaire (Brief) (IPQ-R):* The IPQ-R is a widely accepted measure of illness representations. These components are identity, cause, timeline, consequence, and controllability/cure. The questionnaire consists of three parts: an identity scale, a structure scale, and a causal scale[31].

- *General Practice Physical Activity Questionnaire (GPPAQ):* The GPPAQ was developed by the World Health Organization and Department of Health detailing a 4-level Physical Activity Index (PAI) reflecting an individual's current physical activity. The GPPAQ is a validated measure of physical activity behaviour in CKD[32].

- *UK Diabetes and Diet Questionnaire (UKDDQ):* The UKDDQ is a 25-item questionnaire designed to assess diet and dietary behaviours. Respondents are asked to identify how often they consumed certain foods (vegetables, fruits, sugary drinks, processed meat) over that last month[33]. Responses will be scored as per previous research[34]. This questionnaire is sensitive to changes following an intervention[35].

- *Medication Adherence Report Scale (MARS-5):* The MARS-5 is a non-disease specific questionnaire used to measure adherence to medications and has been previously used in CKD. This comprises of five questions regarding changing medication dosage, forgetting to take medication, consciously stopping taking medication, skipping medication, and using less than prescribed[36].

- *Modified Economic Patient Questionnaire (EPQ):* We will use a modified version of the 'Economic Patient Questionnaire (EPQ)' to assess participants' use of inpatient and outpatient services and data on non-hospital-based health and social care use at all assessment points[37].

When the participant consents to the study, the researcher will access their clinical records and extract information such as blood and urine results to gather information of kidney function, proteinuria, iron status, and lipid profiles. We will record prescribed medication. Self-reported co-morbidities will be checked against those recorded in the medical notes.

Sub-study

In an optional sub-study, the following additional physical assessments will be performed during a visit to a hospital site:

- *Anthropometry:* Height, weight, body mass index (BMI), and waist and hip circumference will be measured in line with established procedures. Resting heart rate and blood pressure will be assessed using a standard sphygmomanometer device.

- *Muscle phenotyping:* Muscle and fat mass/size/thickness, and body fat % will be measured using a free-standing bioelectrical impendence analysis (BIA) monitor and B-mode ultrasonography of the rectus femoris muscle. These are painless, non-invasive methods for measuring body composition. Our group has recently validated our BIA device against dual-energy X-ray absorptiometry (DXA)[38] whilst ultrasonography can be used to assess sarcopenia in CKD[39 40].

- *Gait speed:* The participant is asked to walk a 4m course at their 'usual' walking speed, with a walking aid if normally used[41].

- *Handgrip strength (HGS):* Handgrip strength will be assessed using a handheld dynamometer (Jamar Plus+ Digital). Participants will be asked to hold the dynamometer with their shoulder at 0 degrees flexion and elbow at 90-degree flexion. Participants will be asked to squeeze the dynamometer handle maximally for 3 seconds. The peak force output (kg) from the three attempts from both the dominant and non-dominant hand will be recorded[42].

- *Sit-to-stand-60 test:* Sit-to-stand (STS) tests are a good measure of functional ability and have been used extensively in CKD patients. Our group has extensive use and knowledge of this test, and published reliability and validation data for it[43]. The patient starts from a seated position on a hard, upright chair, with the feet flat on the floor and the knees bent at 90°. For the test, the patient simply stands up fully and then sits down again to the starting position, without using the hands (one repetition). The STS-60 test involves completing as many STS cycles as possible in 60 seconds. Participants will also be asked to record a STS-60 score as part of the online survey. Minimal guidance via an instruction sheet will be provided for participants, but no other instructions (i.e. monitoring via a video call) will be utilised.

- *Timed-up-and-go' test (TUAG):* The TUAG assesses mobility and requires dynamic balance. The participant will be asked to rise from a chair, walk 3 metres, turn around a cone, and sit back down[41].

- *Accelerometery:* To accurately measure objective physical activity, patients will wear a wrist accelerometer (GENEActiv) for a 7-day period before the intervention and post-intervention[32 44].

Familiarisation of objective physical performance measures will be performed before baseline assessments. In order to assess any potential differences in administering the questionnaires online, participants in the sub-study will also be asked to complete the same questionnaires via paper format.

In the sub-study, semi-structured interviews will be held with a researcher trained in qualitative methodology. Individual interviews will last between ~30 to 60 minutes. Interviews will take place in private area. For those unable to attend a face-to-face interview, interviews may also be performed via telephone using a secure recording device as used currently in other studies by our group. Patients recruited may be interviewed on at least one occasion (e.g., before and/or after the intervention). Up to three interviews will be conducted with participants depending on their voluntary participation and/or their status in the study: 1) pre- and/or 2) post-intervention (at 10-weeks), and/or 3) after the follow up phase (at 20-

weeks). Topics in this interview will include current self-management knowledge, skills, confidence and behaviours, and attitudes towards lifestyle self-management. Topics of the subsequent interviews will include experiences of the intervention, the quality of the content, the quality of the delivery method, reasons for non-adherence with the intervention, and healthcare usage.

Patient and public involvement

A full description of how patients and their families were involved in the development of the programme can be found in Lightfoot et al.[21]. In summary, a study patient steering group was formed consisting of ten individuals living with kidney disease and two family members. An initial priority setting workshop determined key topics of interest to this group, including lack of educational support from healthcare professionals. Following this, we developed an educational booklet which was co-designed using our patient steering group. This booklet was disseminated to local primary care practices where individuals provided feedback on the content. The information in this booklet was then adapted for digital use and was termed 'My Kidneys & Me' by the patient group. We also performed semi-structured interviews with patients around self-management and the use of educational resources. Key examples of feedback from patients included the following: 1) to provide a symptom tracker to enable self-monitoring of symptoms; 2) include a separate session on sleep; 3) include a separate session on well-being, emphasising the importance of looking after mental health; 4) use of myth and fact quizzes as a way to test knowledge; 5) state how long sessions should take in the introduction. Once 'My Kidneys & Me' was developed, members of the steering group were provided with access to the programme to provide initial comment. The patient steering group assisted with the selection of questionnaires for the study, and reviewed the final questionnaire survey to ensure that it was acceptable. Throughout the study, the steering group will be used to develop a suitable and relevant topic guide to explore participants attitudes towards self-management and the impact these have on their lives. The group will also be used to interpret initial and final findings. In addition, the patient steering group will support the development of the lay summary outputs to be disseminated to patients and the public.

Data analysis

Sample size calculation

With PAM-13 as the primary outcome in the full RCT, a total sample size of n=432 participants are required based on a 2:1 randomisation (n=288 in the intervention group and n=144 in the control group). This was based on previously published PAM-13 data by our group[13] and on the required power (β=0.8; α=0.05) to detect a minimal clinically significant difference of 4 points in the PAM-13[45-47], and an expect attrition rate of 25%. For the initial nested pilot study, a pragmatic sample size of n=60 participants (n=40 in the intervention group and n=20 in the control group, based on 2:1 randomisation) will be used. We aim to recruit at least 10 patients into the optional sub-study.

Statistical analysis

Participant demographics and clinical characteristics will be analysed using descriptive statistics. The primary outcome is the PAM-13 where answers are weighted provide a score on a scale from 0 to 100. As recommended by Twisk et al.[48], estimates of treatment effect will be assessed by longitudinal analysis of covariance. In this method the outcome variable measured at the different follow-up measurements (post-intervention at week 10, follow-up at week 20) is adjusted for the baseline value of the outcome. Analysis will be performed using 'intention-to-treat' (ITT) analysis. In an ITT approach, patients are analyzed by how they were randomised regardless of their actual compliance with treatment or intervention. For patient-reported outcomes missing data items will be handled according to established protocols for the validated surveys. Additional post-hoc analysis will be performed to determine if differences exist in PAM score changes between those with low and high PAM scores.

In the sub-study, interview recordings will be professionally transcribed verbatim. The precise analytical methodology used may change based on the nature of the data collected, however thematic analysis will be used as an initial foundation for data analysis as it provides a systematic model for managing and mapping the data. Analysis will follow recognised steps (e.g., familiarisation, initial and confirmation of coding (using NVivo), defining themes). In an integrative strategy, any available quantitative data will be used to inform the qualitative analysis.

Considerations

This study aims to evaluate the effect of an evidence- and theory-based digital self-management structured 10-week programme developed for CKD patients called 'My Kidneys & Me' on patient activation (PAM-13). The use of a nested pilot study to assess the feasibility of the intervention and study design before continuation to a full RCT is a strength of the study. This will enable us to make necessary adjustment and changes if the feasibility data suggests that participants do not engage with the intervention or that outcome measures are not being completed. Despite including the patient steering group in the selection of questionnaires and review of the final questionnaire survey, there is potential that the questionnaire survey may risk overburdening the participants and affect missing data and evaluation accuracy. Should the nested pilot study indicate poor questionnaire completion rates, we will revise the breadth of the outcomes collected and simplify the questionnaire survey content to improve participant acceptability.

To minimise the risk of bias (selection, performance, and detection), the study is a single-blind randomised control trial (RCT). Whilst a higher level of blinding is often preferred to further reduce the risk of bias[49], due to the nature of the intervention being tested in this study, it is not possible to blind participants to the intervention. However, one method that can be used to reduce selection bias in an RCT is adequate allocation concealment[50] to prevent intentional and unintentional assignment of participants to either of the study groups[49]. Group allocation will be random and stratified by age.

An improvement of '4-points' in PAM-13 score is considered the minimal clinical important difference (MCID)[45-47], thus we used the required power to detect this alongside previous published data by our group on PAM-13. The MCID of PAM-13 is generic and not specific to CKD, however, we aim to identify the MCID of PAM-13 in CKD using data from the full RCT if feasible. Whilst there is evidence to suggest patient activation has important associations with health outcomes, including in CKD[51-53] and, interventions aiming to improve patient activation are meagre[4]. Interventions aimed at increasing patient activation are often designed for people other long-term conditions such as diabetes and hypertension, and to our knowledge, there are no published interventions designed to specifically target patient activation, particularly assessed using the PAM-13, in those living with CKD.

ETHICS AND DISSEMINATION

To carry out this study, we will consider the Good Clinical Practice (GCP) guidelines of the local governance organisations (University of Leicester and University Hospitals of Leicester NHS Trust) thus guaranteeing the protection of the rights, the safety, and the well-being of the participants of the trial in compliance with the principles of the Declaration of Helsinki, as well as the credibility of the data obtained in the clinical trial. All participant data entered into the 'My Kidneys & Me' will be managed through the MyDESMOND platform. Data entered as part of the online outcomes is managed by Jisc Online Surveys under a University of Leicester license. A full informative sheet explaining the study in detail, the voluntary nature of the research, and the procedure for the protection of their personal data will be provided along with the online consent form. Patients will be given the opportunity to contact the researchers with any questions prior to the informed consent. The informed consent obtained from study participants will be online.

This study was fully approved by the Research Ethics Committee (REC)-Leicester South and Health Research Authority (HRA) on the 19/11/2020 (reference: 17/EM/0357). The results are expected to be published in scientific journals and presented at clinical research conferences in 2024. Findings will be disseminated to patients and the wider kidney and healthcare community via social media platforms, interest groups, recruiting sites, and institutions associated with the research team. Any subsequent changes to the study protocol will reviewed by the REC and HRA through appropriate amendments. Any significant protocol changes will be stated on the ISRCTN Registry. The study was prospectively registered as ISRCTN18314195.

SUMMARY

'My Kidneys & Me', an online self-management and lifestyle education programme, aims to increase patient activation and promote self-management behaviours. If this is achieved, it is anticipated that the intervention will achieve its distal aims of improving patient QoL, physical function, and symptom burden whilst experiencing fewer hospital admissions and saving costs to the NHS.

DECLARATIONS

Ethics approval and consent to participate

This study was fully approved by the Research Ethics Committee-Leicester South on the 19/11/2020 (reference: 17/EM/0357). All participants will provide consent either online or face-to-face (sub-study). All participants will be given the opportunity to ask questions before completing the consent process. The trial is sponsored by the University of Leicester (rgo@le.ac.uk).

Consent for publication

N/A

Availability of data and materials

N/A

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors (CJL, TJW, TY, MJD, ACS) contributed to the design of the SMILE-K trial protocol. CJL, TJW and ACS are responsible for data collection. Analyses will be conducted by CJL, TJW and ACS. CLJ and TJW drafted the manuscript contributing equally. All authors read and approved the final manuscript.

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LIST OF ABBREVIATIONS

BIA	Bioelectrical Impendence Analysis
BMI	Body Mass Index
CKD	Chronic Kidney Disease
CKD-SMKT	Chronic Kidney Disease Self-Management Knowledge Tool
COVID-19	Coronavirus Disease-2019
DXA	Dual-Energy X-Ray Absorptiometry
eGFR	Estimated Glomerular Filtration Rate
EPQ	Modified Economic Patient Questionnaire
EWGSOP	European Working Group on Sarcopenia in Older People
GCP	Good Clinical Practice
GP	General Practitioner
GPPAQ	General Practice Physical Activity Questionnaire
HGS	Handgrip Strength
HRA	Health Research Authority
IPQ-R	Illness Representations Questionnaire
ITT	Intention-To-Treat
KSQ	Kidney Symptom Questionnaire
MARS-5	Medication Adherence Report Scale
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PAI	Physical Activity Index
PAM-13	Patient Activation Measure
QoL	Quality of Life
RCT	Randomised Control Trial
REC	Research Ethics Committee
SF-12	12-Item Short Form Health Survey
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
STS	Sit-To-Stand
TUAG	Timed-Up-And-Go
UKDDQ	UK Diabetes and Diet Questionnaire
UKRR	UK Renal Registry

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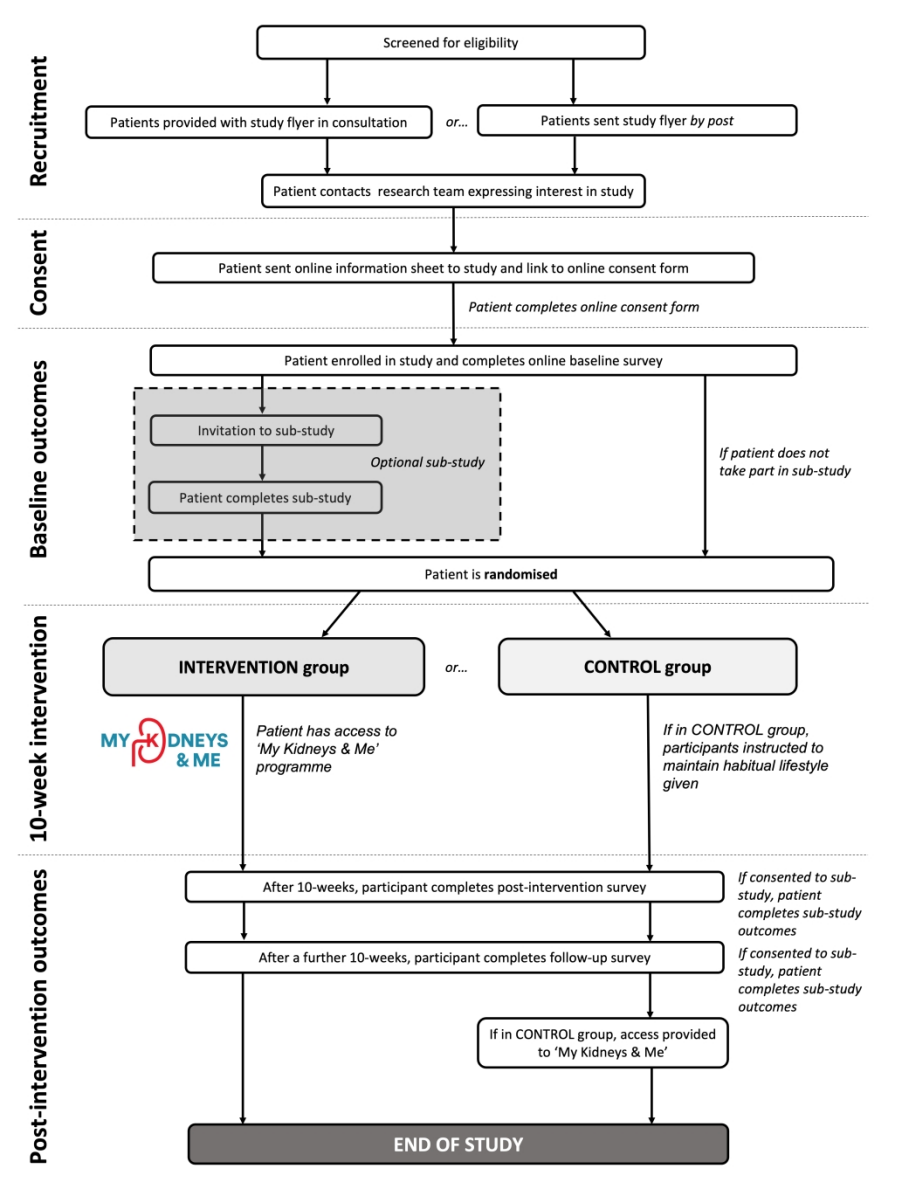
FIGURES

Figure 1. Study flow diagram

Figure 2. 'My Kidneys & Me' dashboard page



SMILE-K study flow diagram

300x398mm (330 x 330 DPI)

My Kidneys & Me dashboard

181x87mm (330 x 330 DPI)

Supplementary material S1. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents

Section/item	Item No.	Description	Page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	24
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	24
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	24
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 2 and Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	24
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	24
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A – online form
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A