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Personalised, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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ABSTRACT

Introduction: Managing nutrition is critical for reducing morbidity and mortality in patients on haemodialysis but adherence to the complex dietary restrictions remains problematic. Innovative interventions to enhance the delivery of nutritional care are needed. The aim of this phase II trial is to evaluate the feasibility and effectiveness of a semi-personalised mobile phone text messaging system to improve dietary and lifestyle behaviours in patients on long-term haemodialysis.

Methods and analysis: Single-blinded randomised controlled trial with six months of follow-up in 130 patients on haemodialysis who will be randomised to either standard care or KIDNEYTEXT. The KIDNEYTEXT intervention group will receive three text messages per week for six months. The text messages provide customised dietary information and advice based on renal dietary guidelines and general healthy eating dietary guidelines, and motivation and support to improve behaviours. The primary outcome is feasibility including: recruitment rate, drop-out rate, adherence to renal dietary recommendations, participant satisfaction and a process evaluation using semi-structured interviews with a subset of purposively sampled participants. Secondary and exploratory outcomes include a range of clinical and behavioural outcomes and a healthcare utilisation cost-analysis will be undertaken.

Ethics and dissemination: The study has been approved by the Western Sydney Local Health District Human Research Ethics Committee – Westmead. Results will be presented at scientific meetings and published in peer-reviewed publications.

Clinical trials registration number: ACTRN12617001084370

ARTICLE SUMMARY

Strengths and limitations of this study:

- Mobile phone technology is inexpensive and widely available, and has been found to be effective in improving clinical outcomes in some chronic diseases, including cardiovascular disease.
- This intervention will be evaluated in a randomised controlled study, with outcome assessors and statistician blinded to participant allocation
- The trial will be conducted in Australia and recruit participants from culturally diverse populations.
- Dietary intake will be measured using patients' self-report, using validated 24-hour dietary recall methodology to standardise dietary intake assessment and minimise bias

INTRODUCTION

Chronic kidney disease (CKD) is recognised as a global public health problem that affects approximately 13% of the population globally, and continues to increase (1, 2). Compared to the general population, people with CKD have an increased risk of mortality from 1.2 times higher in those with mild dysfunction in early CKD to 5.9 times higher in patients on dialysis (2).

In CKD, dietary management plays an important role in preventing the development and progression of CKD, improving clinical outcomes (e.g. proteinuria, hypertension), reducing symptom burden and managing electrolyte abnormalities frequently seen in end-stage kidney disease, particularly in people requiring haemodialysis (Ash 2014). Dietary management in patients on haemodialysis is particularly challenging because patients have to integrate complex and restrictive dietary requirements specific to CKD such as restricting protein, fluid, sodium, potassium, and phosphorus. In addition they may need to follow recommendations for co-morbidities such as diabetes, as well as following general healthy eating principles (3). Furthermore, dietary prescription can vary substantially among patients depending on age, co-morbidities and goals of treatment (4). In the haemodialysis population, educating patients about end-stage kidney disease fosters capacity for self-management and shared decision making, which can in turn contribute to improved health related behaviours (e.g. diet, exercise and smoking cessation) (5) and reduce burden on the healthcare system.

Patients and health professionals have identified lifestyle and nutrition as a high priority research topic (6, 7) and is an important clinical management intervention that reduces symptom burden and acute medical events due to electrolyte abnormalities, as well as enhancing patients' quality of life (8). However, dietary prescription on haemodialysis is often seen as restrictive and difficult for patients to adhere to (3). Patients have reported that one off didactic education sessions are

overwhelming and difficult to comprehend, particularly at the time of diagnosis (3). Dietary related behaviour change and self-management may be most effectively achieved through individualised education with a dietitian, frequent feedback and monitoring and longer duration of intervention (e.g. at least 6 months) (9, 10). Patient-centred interventions that are individualised and provide step-wise education over time to support and engage patients may help to improve outcomes in this population.

Electronic health interventions (eHealth) refers to "health services and information delivered or enhanced through the Internet and related technologies" (11). eHealth interventions improve consumer access to relevant health information, enhances the quality of care and encourages the adoption of healthy behaviours (11). Globally, the use of technology is increasing; with a median of 87% of people regularly using the internet in high-income countries and a median of 54% of people regularly use the internet in developing countries (12). It is estimated that 95% of people in the US own a mobile phone, with 77% owning a smart phone (13). Given this, there is increasing interest in the use of eHealth in healthcare. Systematic reviews have shown that eHealth interventions are effective in changing health-related behaviour and in improving outcomes in patients with diabetes and cardiovascular disease (14-18). Specifically, telehealth (i.e. the use of telecommunication techniques to provide health education remotely) (19) and mobile phone text messaging (20) have shown positive improvements in dietary behaviours and clinical outcomes when compared to usual care in people with chronic diseases (e.g. chronic lung disease, diabetes) and coronary heart disease, respectively.

There is a paucity of research using eHealth interventions targeting diet and lifestyle in the haemodialysis population (21). There is some indication that using electronic self-monitoring apps with additional dietary counselling may improve dietary sodium intake (22, 23), however these studies were small and of short duration. Mobile phone text messaging has been shown to improve

both dietary and clinical outcomes in patients with coronary heart disease, and to be well accepted, with more than 90% of participants reporting that the text messaging was useful and easy to understand (20). Given the complexity of dietary requirements in haemodialysis and the difficulty patients have in comprehending and integrating these requirements, text messaging offers an inexpensive and readily available way to motivate and help patients with managing their diet by providing frequent, short bursts of information over an extended period of time.

The aim of this study is to assess the feasibility and effectiveness of a mobile phone text message intervention to improve dietary and lifestyle behaviour in patients on haemodialysis. The results of this study will inform a larger trial.

METHODS AND ANALYSIS

Design

The design and development of KIDNEYTEXT has been underpinned by frameworks for the development of complex interventions (24) and a range of behaviour change frameworks (25). KIDNEYTEXT is a six month single-blinded randomised controlled trial, with a 2:1 allocation ratio (Figure 1) (ACTRN12617001084370).

Study setting

This study will be conducted in six dialysis units across three local health districts in Sydney, Australia that serves ethnically, culturally and socioeconomically diverse populations.

Study population

A total of 130 patients receiving maintenance haemodialysis will be included. Patients receiving maintenance haemodialysis in the three local health districts in Sydney, Australia will be eligible to enrol in the study. Eligibility criteria include: receiving maintenance haemodialysis for at least 90 days, aged 18 years and over, having sufficient English language skills to read and understand text messages, and having access to a mobile phone throughout the duration of the study. If patients do not have their own mobile phone, a partner or close family member involved in meal provision may consent to have their mobile phone number used throughout the trial. Patients will be ineligible if they are: prescribed a diet that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery), acutely unwell (e.g. septic), if they are not expected to be on haemodialysis for the forthcoming 6 months (e.g. change of dialysis modality or transplantation), if they have a life expectancy of less than 12 months, pregnant or breastfeeding or if they have significant cognitive impairment or intellectual disability that would inhibit their understanding of the text messages. A "screening log" containing basic demographic information and reason for non-participation will be kept for patients who are ineligible or decline to participate.

Interventions

Participants will be randomly allocated to either control or intervention group. The control group will continue to receive standard care provided by the dialysis unit that they attend. Standard care practices may differ between dialysis units; however, there will be no change to frequency of usual dietetic consultations or service delivery throughout the study.

The KIDNEYTEXT intervention group will receive standard care plus they will receive three text messages per week over a 6 month period. Text messages will be unidirectional, (i.e. one-way with

no response required from participants), and will act as reminders and reinforcements of various dietary components. The messages will provide advice, information, motivation and support to improve renal dietary behaviours (related to potassium, phosphorus, sodium, fluid) and general healthy eating and lifestyle behaviours (Table 1). From baseline to 3 months patients may receive messages relating to dietary modification of potassium, phosphorus and sodium and fluid (Figure 2). Participants will receive messages relating to potassium if one or both of the following guidelines is exceeded:

1. Dietary intake exceeds guidelines for potassium (1mmol per kilogram of ideal body weight per day) (26)
2. Two of three previous pre-dialysis serum potassium levels exceeds 5.5mmol/L (27)

Participants will receive messages relating to phosphorus if one or both of the following guidelines is exceeded:

1. Dietary intake exceeds guidelines for phosphorus (greater than 1000mg per day) (26)
2. Two of three previous pre-dialysis serum phosphate levels exceeds 1.78mmol/L (28)

Participants will receive messages relating to sodium and fluid if one or both of the following guidelines is exceeded:

1. Dietary intake exceeds guidelines for sodium (greater than 2300mg per day) (26)
2. An average of interdialytic fluid gains from the previous three dialysis sessions being more than 3.5% of body weight or more than or equal to 3kg (29)

If a participant satisfies all of these guideline criteria they will only receive general healthy eating and lifestyle messages from baseline to 3 months.

From 4 to 6 months all participants will receive general healthy eating and lifestyle messages that are congruent with renal dietary guidelines (Figure 2).

Table 1: Examples of text messages to be sent to the KIDNEYTEXT intervention group
Potassium • Did you know the way you cook your vegetables can change their potassium content? Boil vegetables in water to get rid of some potassium. • Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian. • How much dairy do you have? Limit to 250ml milk and milk products (e.g. yoghurt and custard) daily to help control your potassium and levels.
Phosphorus • Phosphate is added to pre-packaged foods and convenience foods. Choose fresh foods to reduce how much phosphate you eat. • Phosphate binders act like a magnet and stop you from absorbing some phosphate. Take your phosphate binders with your meals so that they work properly.
Sodium and Fluid • Make sure you know what is in your foods! Look for foods that contain less than 400mg per 100g of sodium. • To get more flavour into your food use pepper, chilli, herbs and spices in your cooking. • Use smaller cups to help reduce how much you drink.
General healthy eating and lifestyle • Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. • Include low potassium fruits and vegetables daily to make sure you get enough fibre. • Are you a bit off your food? Including small snacks can be a good way to keep up your nutrition. • The colour of vegetables gives a clue to what nutrients they contain. By including a variety of colours you will get more vitamins and nutrients.

Message delivery will be managed by computerised software ('TextQStream, Python v3.6 using Pycap version 1.02 library) that was developed and customised in-house for use in this trial. Computer software is run through the University of Sydney RedCap system. The program will keep a log of all messages sent to each participant. The messaging engine will send messages through a gateway interface that can be sent through Australian phone network at no cost to the participant. Data exports will be compliant with privacy legislation and held in strict privacy, centrally managed at Westmead Hospital. There will be no access to data by any third party, including the software developers.

A record of any text messages received from participants will be kept and managed by a researcher who is not involved in recruitment or outcome assessment. Participants will have the opportunity to withdraw via a text message and the researcher will contact the software manager in order to initiate the withdrawal.

KIDNEYTEXT intervention development

In total, 160 text messages have been systematically developed through an iterative process and based on renal dietary recommendations (26-29) and general healthy eating guidelines (30). Messages targeting renal-specific dietary components provide advice to assist participants in reducing their intake of potassium, phosphorus, sodium and fluid and provide prompts for self-monitoring and self-management behaviours. General healthy eating and lifestyle messages promote general healthy eating principles, such as increasing dietary fibre, encouraging physical activity and improving medication management.

The text message bank was developed in three stages. Initially text messages were developed using behaviour change frameworks including information-motivational-behavioural skills model, theory of reasoned action, theory of planned behaviour and social cognitive theory (25). Text message content was assessed for readability using Flesh-Kincaid, with an average Flesh-Kincaid score of 6

or less being deemed appropriate. An expert review panel including renal dietitians, nephrologists, renal nurses and social scientists then reviewed each message to ensure the content of the messages were accurate. The final draft of text messages were reviewed by people on haemodialysis, caregivers and public health researchers who rated the usefulness and understanding of the text messages on a five-point Likert scale with additional space for comments. Feedback from these ratings was incorporated into the final draft of text messages for the KIDNEYTEXT intervention.

Patient and public involvement

We sought feedback from people on haemodialysis during the design and development stages of KIDNEYTEXT. We conducted semi-structured interviews to elicit patient perspectives regarding the use of eHealth, particularly mobile phone technology to support current nutritional management. We incorporated feedback from these interviews into the design of KIDNEYTEXT. Once an initial bank of text messages was developed, we asked patients to review all message content for accuracy, relevancy and usability. Each message was reviewed by at least three consumers and we integrated their feedback into the final set of text messages for use in the trial. A process evaluation exploring the feasibility of the trial, including burdens and benefits to participants, will be undertaken at the completion of the trial. We will disseminate de-identified findings from the trial to study participants and dialysis units at the completion of the trial.

Study outcomes

The primary outcome will be the feasibility of the mobile phone text messaging intervention. Feasibility will be assessed as a composite outcome of: recruitment rate, retention rate, adherence to renal dietary recommendations, and participant satisfaction (Table 2). Adherence to dietary recommendations will be defined as participants meeting three of the four dietary guideline

recommendations with respect to protein, potassium, phosphorus and sodium (Table 2). Dietary intake will be assessed by two dietitians blinded to participant allocation, using the validated 24-hour pass methodology (31). Dietary intake will be assessed using an average of 2 days intake, including a dialysis day and a non-dialysis day. Dietary intake will be assessed at baseline, three months and six months, and will be taken assessed within two weeks a participant's scheduled review.

Table 2: Primary, secondary and exploratory outcome measures

Primary outcome (measured at baseline, 3 months and 6 months)

Feasibility will be measured using:

Adherence to dietary recommendations. This will be measured using the 24-hour pass methodology to assess dietary intake with particular focus on renal dietary components: protein, potassium, phosphorous and sodium intake compared to renal dietary guideline recommendations. Adherence will be defined as meeting three of the four nutrition guidelines.

- dietary protein intake more than or equal to 1.2 grams of protein per kilogram of ideal body weight per day
- dietary potassium intake less than or equal to 1mmol of potassium per kilogram of ideal body weight per day
- dietary phosphate intake less than or equal to 1000mg phosphorus per day
- dietary sodium intake less than or equal to 2300mg sodium per day

- Recruitment rate
- Drop-out rate
- Participant satisfaction (measured using a 7-point likert scale)
- Semi-structured interviews to describe perspectives on participating in the trial, use of the intervention information, self-monitoring behaviours, decision making, problem solving and behaviour change (only conducted in KIDNEYTEXT intervention group)

Secondary outcomes (measured at baseline, 3 months and 6 months)

- Serum electrolytes (potassium, phosphate)
- Interdialytic weight gains (average of the previous three haemodialysis sessions)
- Changes in nutritional status as measured using the Patient-Generated Subjective Global Assessment tool
- Change in quality of life scores measured using EQ-5D-5L
- Change in dietary quality measured using the Australian Healthy Eating Index
- The mean change in the intake of renal specific dietary components across all time points

Exploratory outcomes (measured at baseline and 6 months)

- Blood pressure within recommended targets for patients on haemodialysis
- Serum parathyroid hormone, urea, bicarbonate, albumin levels

- Glycaemic control, measured using glycated haemoglobin levels (HbA1c) (subgroup analysis for patients with diabetes)
- Healthcare utilisation

After completion of the 6 month follow-up a qualitative process evaluation (32) will be undertaken using semi-structured interviews conducted amongst a subset of 25 to 30 purposively sampled participants from the KIDNEYTEXT intervention group. Semi-structured interviews will elicit participants' perspectives regarding their satisfaction, acceptability and use of KIDNEYTEXT, and also their views and attitudes regarding changes in dietary behaviours, self-monitoring, decision-making, and problem solving as a result of the KIDNEYTEXT intervention. With the consent of the participants, all interviews will be audio-recorded and transcribed verbatim. The transcripts will be entered in the computer software package 'HyperRESEARCH 3.0' for storage, coding and searching of data. The audio recordings will be stored in a password protected computer drive and hardcopy transcripts will be stored in a locked cabinet.

Secondary outcomes (outlined in table 2) will be assessed by two dietitians blinded to participant allocation, and include changes in: serum potassium, serum phosphate, interdialytic weight gain, dietary quality and nutritional status. Dietary quality will be evaluated using the Australian Healthy Eating Index (33) which uses seven parameters to assess the quality of a person's diet. Nutritional status will be assessed using the Patient-Generated Subjective Global Assessment. Quality of life will be measured using the EQ-5D-5L instrument (34). All secondary outcomes will be measured at baseline, three months and six months, except for nutritional status which will be assessed at baseline and six months only.

Additional exploratory outcomes will also be measured at baseline and 6 months and comparisons made between the control and the KIDNEYTEXT intervention groups. Exploratory outcomes will include: biochemical parameters (urea, albumin, bicarbonate, parathyroid hormone, glycated haemoglobin), blood pressure (pre and post dialysis), and healthcare utilisation. Healthcare

utilisation will be estimated from participant self-reported records of their healthcare-related appointments (including general practitioner, medical specialists and allied health) using a calendar supplied by the research team. Any hospital and emergency department admissions will be collected from medical records. Data relating to dialysis prescription (e.g. dialysate composition, frequency and duration of dialysis) and dialysis-related medications (e.g. prescription details of phosphate binders, resonium and diuretics) will be collected at baseline, three months and six months. The cost of implementation of the intervention, including cost of sending the text messages and software development will be estimated.

An exploratory cost analysis from the perspective of the healthcare provider for the intervention compared to standard care, will be completed using costs estimated from the health service utilisation records and the cost of implementation of the intervention. The EQ-5D-5L scores will be used to calculate quality adjusted life years (QALYs) for the control and intervention groups. Although the main purpose is to determine the feasibility of collecting healthcare utilization and QOL in this patient population, should the data be sufficiently robust, a preliminary calculation of an incremental cost effectiveness ratio may be possible.

Randomisation

The random allocation sequence will be in a 2:1 (intervention: control) allocation ratio stratified by geographical location (Western Sydney, South Eastern Sydney). Randomisation will occur via a computerised randomisation program that will be accessible by study staff with username and password through a web interface. Allocation will be concealed from study personnel undertaking assessments until the completion of the trial. Participants will be notified of their allocation via text message and will be asked not to disclose their allocation to study personnel.

Blinding

Blinded assessments will be conducted by two dietitians at baseline, three months and six months in face-to-face or telephone interviews. Prior to three and six month reviews participants will be sent a text message reminding them not to reveal their allocation to the outcome assessors. A statistician analysing data will also be blinded to participant allocation.

Statistical analysis

A sample size of 129 participants, 86 in the intervention arm and 43 in the control arm, provide 80% power to detect an increase from 10% to 35% on adherence to dietary recommendations, with a significance level of 0.05. The analysis will follow an intention-to-treat principle. Balance across baseline characteristics (age, gender, haemodialysis type, dialysis vintage, dietary intake, biochemistry and interdialytic weight gains) will be checked. Continuous variables will be compared between groups using t-tests or Wilcoxon tests, according to their distribution. The chi-square test will be used to compare proportions. Logistic and linear mixed models will be used to analyse the longitudinal measurements of categorical and continuous outcomes, respectively. In particular the interaction between time and group will allow for overall comparison between the two groups. Adjustment for unbalanced baseline characteristics will be considered in the analysis. A significance level of 5% will be used.

Safety and monitoring

If a participant is found to have a serum potassium level greater than 6mmol/L study personnel will alert dialysis staff. If a participant is commenced on a long-term (i.e. longer than one month)

dietary regime that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery, total parenteral nutrition, complete enteral nutrition) during the study period the intervention will be ceased.

ETHICS AND DISSEMINATIOMN:

The findings of this study will be disseminated via scientific forums including peer-reviewed publications and presentations at international conferences. The study will be administered by the Westmead Clinical School, The University of Sydney, with the design and conduct overseen by a project management committee (authors). This committee has experience in large-scale clinical trials, qualitative research, health economics, renal medicine, renal dietetics and health policy implementation. Formal ethical approval for this study has been obtained by the Western Sydney Local Health District Human Research Ethics Committee (Westmead) approval number HREC/16/WMEAD/396) and will adhere to their guidelines for ethical human research. Written and informed consent will be obtained from all participants.

DISCUSSION

This study will evaluate a novel intervention to improve dietary behaviours in a haemodialysis population by using widely available and used mobile phone text messaging technology. Interventions using simple, inexpensive technology provide an opportunity to complement current dietary care and provide patients with more consistent support, particularly for those in resource poor settings and for those living in geographically isolated areas.

Rigorous studies are needed to evaluate the effectiveness of a mobile phone text message intervention targeting behaviour change in the haemodialysis population. No known studies have

used mobile phone text messaging to improve dietary behaviours in a CKD or haemodialysis population, however there is evidence that utilising mobile phone text messaging to improve dietary and clinical outcomes is feasible and effective in patients with coronary heart disease (20, 35, 36). Additionally, the content, level of individualisation, frequency and timing of text messages and level of interaction between healthcare professional and patient need to be determined. The current study will explore these important issues.

This KIDNEYTEXT trial will provide robust evidence about the feasibility of a semi-personalised text messaging intervention to improve dietary behaviours and clinical outcomes in a haemodialysis population. Interventions to improve patients' knowledge and motivation to alter their dietary behaviours in this population are needed to enhance patients' quality of life and clinical care and are seen as a high priority for both patients and clinicians. This intervention has the potential as a cost-effective, readily accessible and simple method to improve patients' dietary knowledge and behaviours.

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Contributions

VWL, KLC, JCC, AT, JS are the principle investigators who designed the study and drafted the manuscript. CC and ATh made substantial contributions to the conception and design of the project; ATh developed the software for use in the trial; CC, ATh, KH, MH, MB, KS, RK have been involved in drafting the manuscript and revising it critically for important intellectual content. ATP is in charge of the statistical analysis; KH and MH will lead the economic analysis. All authors have given final approval of the version to be published.

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Declaration of competing interests

A/Prof Kamal Sud has received speaker's honoraria from Baxter Healthcare, Roche, Amgen and Boehringer Ingelheim and conference or meeting sponsorships from Shire, Roche, Boehringer Ingelheim, Amgen, Sanofi and Novartis. Other authors do not have any competing interests of conflicts of interest to declare.

Figure 1: Study design and flow

Figure 2: Text message allocation

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Figure 1: Study design and flow

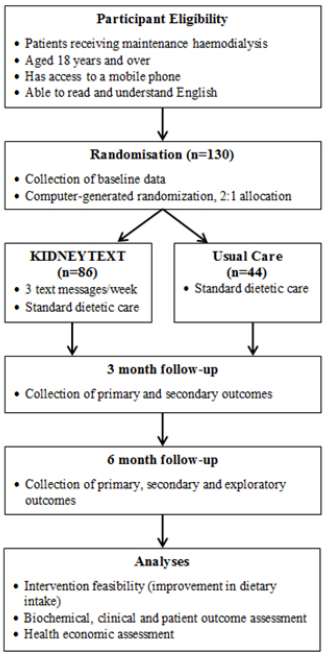

Figure 1: Study design and flow

254x190mm (96 x 96 DPI)

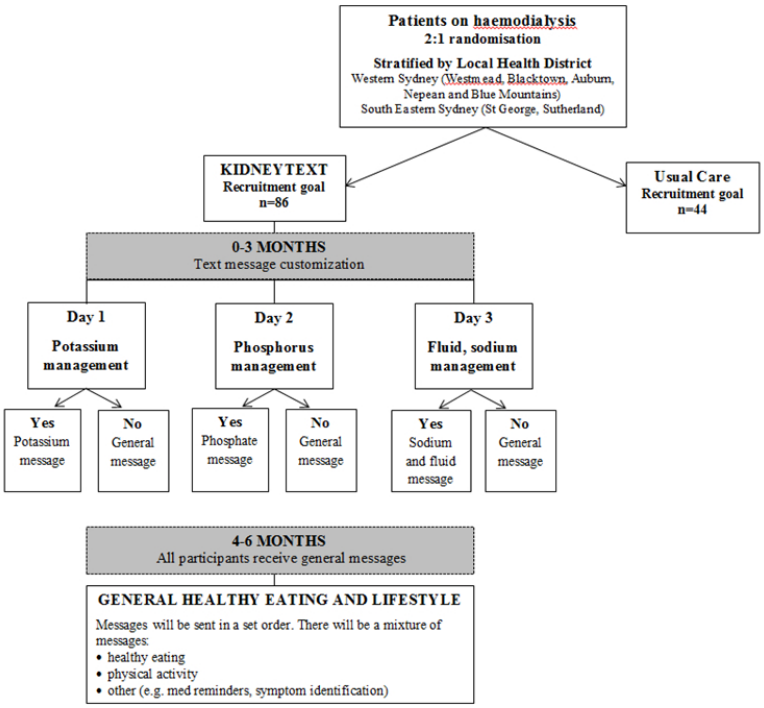

Figure 2: Text message allocation

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Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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ABSTRACT

Introduction: Managing nutrition is critical for reducing morbidity and mortality in patients on haemodialysis but adherence to the complex dietary restrictions remains problematic. Innovative interventions to enhance the delivery of nutritional care are needed. The aim of this phase II trial is to evaluate the feasibility and effectiveness of a targeted mobile phone text messaging system to improve dietary and lifestyle behaviours in patients on long-term haemodialysis.

Methods and analysis: Single-blinded randomised controlled trial with six months of follow-up in 130 patients on haemodialysis who will be randomised to either standard care or KIDNEYTEXT. The KIDNEYTEXT intervention group will receive three text messages per week for six months. The text messages provide customised dietary information and advice based on renal dietary guidelines and general healthy eating dietary guidelines, and motivation and support to improve behaviours. The primary outcome is feasibility including: recruitment rate, drop-out rate, adherence to renal dietary recommendations, participant satisfaction and a process evaluation using semi-structured interviews with a subset of purposively sampled participants. Secondary and exploratory outcomes include a range of clinical and behavioural outcomes and a healthcare utilisation cost-analysis will be undertaken.

Ethics and dissemination: The study has been approved by the Western Sydney Local Health District Human Research Ethics Committee – Westmead. Results will be presented at scientific meetings and published in peer-reviewed publications.

Clinical trials registration number: ACTRN12617001084370

ARTICLE SUMMARY

Strengths and limitations of this study:

- Mobile phone technology is inexpensive and widely available, and has been found to be effective in improving clinical outcomes in some chronic diseases, including cardiovascular disease.
- This intervention will be evaluated in a randomised controlled study, with outcome assessors and statistician blinded to participant allocation
- The trial will be conducted in Australia and recruit participants from culturally diverse populations.
- Dietary intake will be measured using patients' self-report, using validated 24-hour dietary recall methodology to standardise dietary intake assessment and minimise bias

INTRODUCTION

Chronic kidney disease (CKD) is recognised as a global public health problem that affects approximately 13% of the population globally, and continues to increase (1, 2). Compared to the general population, people with CKD have an increased risk of mortality from 1.2 times higher in those with mild dysfunction in early CKD to 5.9 times higher in patients on dialysis (2).

In CKD, dietary management plays an important role in preventing the development and progression of CKD, improving clinical outcomes (e.g. proteinuria, hypertension), reducing symptom burden and managing electrolyte abnormalities frequently seen in end-stage kidney disease, particularly in people requiring haemodialysis (3). Dietary management in patients on haemodialysis is particularly challenging because patients have to integrate complex and restrictive dietary requirements specific to CKD such as restricting protein, fluid, sodium, potassium, and phosphorus. In addition they may need to follow recommendations for co-morbidities such as diabetes, as well as following general healthy eating principles (4). Furthermore, dietary prescription can vary substantially among patients depending on age, co-morbidities and goals of treatment (5). In the haemodialysis population, educating patients about end-stage kidney disease fosters capacity for self-management and shared decision making, which can in turn contribute to improved health related behaviours (e.g. diet, exercise and smoking cessation) (6) and reduce burden on the healthcare system.

Patients and health professionals have identified lifestyle and nutrition as a high priority research topic (7, 8) and is an important clinical management intervention that reduces symptom burden and acute medical events due to electrolyte abnormalities, as well as enhancing patients' quality of life (9). However, dietary prescription on haemodialysis is often seen as restrictive and difficult for

patients to adhere to (4). Patients have reported that one off didactic education sessions are overwhelming and difficult to comprehend, particularly at the time of diagnosis (4). Dietary related behaviour change and self-management may be most effectively achieved through individualised education with a dietitian, frequent feedback and monitoring and longer duration of intervention (e.g. at least 6 months) (10, 11). Patient-centred interventions that are individualised and provide progressively simple to more complex education over time to support and engage patients may help to improve outcomes in this population.

Electronic health interventions (eHealth) refers to "health services and information delivered or enhanced through the Internet and related technologies" (12). eHealth interventions improve consumer access to relevant health information, enhances the quality of care and encourages the adoption of healthy behaviours (12). Globally, the use of technology is increasing; with a median of 87% of people regularly using the internet in high-income countries and a median of 54% of people regularly use the internet in developing countries (13). Australia has one of the highest rates of mobile phone ownership, with 88% of Australians owning a smart phone (14). Given this, there is increasing interest in the use of eHealth in healthcare. Systematic reviews have shown that eHealth interventions are effective in changing health-related behaviour and in improving outcomes in patients with diabetes and cardiovascular disease (16-20). Specifically, telehealth (i.e. the use of telecommunication techniques to provide health education remotely) (21) and mobile phone text messaging (22) have shown positive improvements in dietary behaviours and clinical outcomes when compared to usual care in people with chronic diseases (e.g. chronic lung disease, diabetes) and coronary heart disease, respectively.

There is a paucity of research using eHealth interventions, particularly interventions utilising mobile phone technologies, to target diet and lifestyle in the haemodialysis population (23). There is some indication that using electronic self-monitoring apps with additional dietary counselling may

improve dietary sodium intake (24, 25) in haemodialysis and peritoneal dialysis populations, however these studies were small and of short duration. In coronary heart disease mobile phone text messaging has been shown to improve both dietary and clinical outcomes in patients, and to be well accepted, with more than 90% of participants reporting that the text messaging was useful and easy to understand (22). Given the complexity of dietary requirements in haemodialysis and the difficulty patients have in comprehending and integrating these requirements, text messaging offers an inexpensive and readily available way to motivate and help patients with managing their diet by providing frequent, short bursts of information over an extended period of time.

The aim of this study is to assess the feasibility and effectiveness of a mobile phone text message intervention to improve dietary and lifestyle behaviour in patients on haemodialysis. The results of this study will inform a larger trial.

METHODS AND ANALYSIS

Design

The design and development of KIDNEYTEXT has been underpinned by frameworks for the development of complex interventions (26) and a range of behaviour change frameworks (27). KIDNEYTEXT is a six month single-blinded randomised controlled trial, with a 2:1 allocation ratio (Figure 1) (ACTRN12617001084370).

Study setting

This study will be conducted in six dialysis units across three local health districts in Sydney, Australia that serves ethnically, culturally and socioeconomically diverse populations.

Study population

A total of 130 patients receiving maintenance haemodialysis will be included. Patients receiving maintenance haemodialysis in the three local health districts in Sydney, Australia will be eligible to enrol in the study. Eligibility criteria include: receiving maintenance haemodialysis for at least 90 days, aged 18 years and over, having sufficient English language skills to read and understand text messages, and having access to a mobile phone throughout the duration of the study. If patients do not have their own mobile phone, a partner or close family member involved in meal provision may consent to have their mobile phone number used throughout the trial. Patients will be ineligible if they are: prescribed a diet that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery), acutely unwell (e.g. septic), if they are not expected to be on haemodialysis for the forthcoming 6 months (e.g. change of dialysis modality or transplantation), if they have a life expectancy of less than 12 months, pregnant or breastfeeding or if they have significant cognitive impairment or intellectual disability that would inhibit their understanding of the text messages. A "screening log" containing basic demographic information and reason for non-participation will be kept for patients who are ineligible or decline to participate.

Interventions

Participants will be randomly allocated to either control or intervention group. The control group will continue to receive standard care provided by the dialysis unit that they attend. Standard care practices may differ between dialysis units; however, there will be no change to frequency of usual dietetic consultations or service delivery throughout the study.

The KIDNEYTEXT intervention group will receive standard care plus they will receive three text messages per week over a 6 month period. Text messages will be unidirectional, (i.e. one-way with no response required from participants), and will act as reminders and reinforcements of various dietary components. The messages will provide advice, information, motivation and support to improve renal dietary behaviours (related to potassium, phosphorus, sodium, fluid) and general healthy eating and lifestyle behaviours (Table 1). From baseline to 3 months patients may receive messages relating to dietary modification of potassium, phosphorus and sodium and fluid (Figure 2). Participants will receive messages relating to potassium if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for potassium (1mmol per kilogram of ideal body weight per day) (28)
2. Two of three previous pre-dialysis serum potassium levels exceeds 5.5mmol/L (29). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to phosphorus if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for phosphorus (greater than 1000mg per day) (28)
2. Two of three previous pre-dialysis serum phosphate levels exceeds 1.78mmol/L (30). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to sodium and fluid if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for sodium (greater than 2300mg per day) (28)
2. An average of interdialytic fluid gains from the previous three dialysis sessions being more than 3.5% of body weight or more than or equal to 3kg (31)

If a participant satisfies all of these guideline criteria they will only receive general healthy eating and lifestyle messages from baseline to 3 months.

From 4 to 6 months all participants will receive general healthy eating and lifestyle messages that are congruent with renal dietary guidelines (Figure 2).

Table 1: Examples of text messages to be sent to the KIDNEYTEXT intervention group

Potassium • Did you know the way you cook your vegetables can change their potassium content? Boil vegetables in water to get rid of some potassium. • Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian. • How much dairy do you have? Limit to 250ml milk and milk products (e.g. yoghurt and custard) daily to help control your potassium and levels.
Phosphorus • Phosphate is added to pre-packaged foods and convenience foods. Choose fresh foods to reduce how much phosphate you eat. • Phosphate binders act like a magnet and stop you from absorbing some phosphate. Take your phosphate binders with your meals so that they work properly.
Sodium and Fluid • Make sure you know what is in your foods! Look for foods that contain less than 400mg per 100g of sodium. • To get more flavour into your food use pepper, chilli, herbs and spices in your cooking. • Use smaller cups to help reduce how much you drink.
General healthy eating and lifestyle • Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. • Include low potassium fruits and vegetables daily to make sure you get enough fibre. • Are you a bit off your food? Including small snacks can be a good way to keep up your nutrition. • The colour of vegetables gives a clue to what nutrients they contain. By including a variety of

colours you will get more vitamins and nutrients.

Message delivery will be managed by computerised software ('TextQStream, Python v3.6 using Pycap version 1.02 library) that was developed and customised in-house for use in this trial. Computer software is run through the University of Sydney RedCap system. The program will keep a log of all messages sent to each participant. The messaging engine will send messages through a gateway interface that can be sent through Australian phone network at no cost to the participant. Data exports will be compliant with privacy legislation and held in strict privacy, centrally managed at Westmead Hospital. There will be no access to data by any third party, including the software developers.

A record of any text messages received from participants will be kept and managed by a researcher who is not involved in recruitment or outcome assessment. Participants will have the opportunity to withdraw via a text message and the researcher will contact the software manager in order to initiate the withdrawal.

KIDNEYTEXT intervention development

In total, 160 text messages have been systematically developed through an iterative process and based on renal dietary recommendations (28-31) and general healthy eating guidelines (32). Messages targeting renal-specific dietary components provide advice to assist participants in reducing their intake of potassium, phosphorus, sodium and fluid and provide prompts for self-monitoring and self-management behaviours. General healthy eating and lifestyle messages promote general healthy eating principles, such as increasing dietary fibre, encouraging physical activity and improving medication management.

The text message bank was developed in three stages. Initially text messages were developed using behaviour change frameworks including information-motivational-behavioural skills model, theory of reasoned action, theory of planned behaviour and social cognitive theory (27). Table 2 outlines behavior change techniques with examples of text messages used in KIDNEYTEXT.

Table 2: Behavioural frameworks used to develop text messages

Technique (Theoretical Framework)	Definition	Examples
Provide information about behaviour link (Information-motivational-behavioural skills model)	General info re: behavioural risk (e.g. susceptibility to poor health outcomes or mortality risk in relation to behaviour)	*Look out for symptoms of high potassium levels. Nausea, tiredness, muscle weakness and an irregular heartbeat. Check your blood tests regularly.*
Provide information on consequences (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Information about the benefits and costs of action or inaction, focusing on what will happen if the person does / does not perform the behaviour	*Did you know that having a low or high potassium can cause a heart attack? Aim for a potassium level between 4-6mmol/L.* *Having high blood phosphate levels for a long time causes your bones to become weak and fragile. To keep them strong follow a low phosphate diet.*
Prompt intention formation (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Encouraging the person to decide to act or set a general goal (E.g. make behavioural resolutions "I will exercise more this week")	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*
Prompt barrier identification (Social Cognitive Theory)	Identify barriers to performing the behaviour and plan ways of overcoming them	*A high salt diet will make you thirstier and harder to stick to your fluid restriction. Avoid adding salt to your meals and limit takeaways and processed foods.*
Set graded tasks (Social Cognitive Theory)	Set easy tasks and increase difficulty until target behaviour is performed	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*

Provide instruction (Social Cognitive Theory)	Telling person how to perform a behaviour and/or preparatory behaviours	*Did you know the way you cook your vegetables will change their potassium content? Boil vegetables in water to get rid of potassium.*
Prompt self-monitoring of behaviour (Control theory)	Person is asked to keep a record of specified behaviours (e.g. a diary)	*Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian.*
Teach to use prompts / cues (Operant Conditioning)	Teach person to identify environ cues which can be used to remind them to perform behaviour, including times of day, contexts	*Having trouble sticking to your fluid restriction? Drink only out of a water bottle so you can measure how much you are drinking!*
Relapse prevention (Relapse prevention theory)	Following initial change, help identify situations likely to result in re-adopting risk behaviours or failure to maintain new behaviours and help the person plan to avoid or manage these situations	*Had a lapse in exercise? This is normal, but it is important to get back on track. Plan exercise into your day. Park your car further away or take the stairs.*
Time management	Helping person make time for the behaviour (e.g. to fit it into daily schedule)	*Aim for 30 minutes of exercise most days. You can break your daily exercise into smaller 10-15 minute blocks.*

Text message content was assessed for readability using Flesh-Kincaid, with an average Flesh-Kincaid score of 6 or less being deemed appropriate. An expert review panel including renal dietitians, nephrologists, renal nurses and social scientists then reviewed each message to ensure the content of the messages were accurate. The final draft of text messages were reviewed by people on haemodialysis, caregivers and public health researchers who rated the usefulness and understanding of the text messages on a five-point Likert scale with additional space for comments. Feedback from these ratings was incorporated into the final draft of text messages for the KIDNEYTEXT intervention.

Patient and public involvement

We sought feedback from people on haemodialysis during the design and development stages of KIDNEYTEXT. We conducted semi-structured interviews with 35 patients on haemodialysis to elicit their perspectives regarding the use of eHealth, particularly mobile phone technology to support current nutritional management. Based on these interviews three text messages per week was indicated as an acceptable frequency of receiving text messages. We incorporated feedback from these interviews into the design of KIDNEYTEXT. Once an initial bank of text messages was developed, we asked patients to review all message content for accuracy, relevancy and usability. Each message was reviewed by at least three consumers and we integrated their feedback into the final set of text messages for use in the trial. A process evaluation exploring the feasibility of the trial, including burdens and benefits to participants, will be undertaken at the completion of the trial. We will disseminate de-identified findings from the trial to study participants and dialysis units at the completion of the trial.

Study outcomes

The primary outcome will be the feasibility of the mobile phone text messaging intervention. Feasibility will be assessed as a composite outcome of: recruitment rate, retention rate, adherence to renal dietary recommendations, participant satisfaction and changes in dietary knowledge, attitude and behaviours (Table 3). Adherence to dietary recommendations will be defined as participants meeting three of the four dietary guideline recommendations with respect to protein, potassium, phosphorus and sodium (Table 2). Dietary intake will be assessed by two dietitians blinded to participant allocation, using the validated 24-hour pass methodology (33). Dietary recalls will be conducted in-person, or if this is not possible, on the telephone with food models to assist with portion size estimations. Dietary intake will be assessed using an average of 2 days intake, including a dialysis day and a non-dialysis day to ensure we are capturing any differences in dietary

intake on these days. Dietary intake will be assessed at baseline, three months and six months, and will be taken assessed within two weeks a participant's scheduled review. Dietary intake data will be analysed using Xyris Software Foodworks version 9 Pty Ltd.

Table 3: Primary, secondary and exploratory outcome measures

Primary outcome (measured at baseline, 3 months and 6 months)

Feasibility will be measured using:

Adherence to dietary recommendations. This will be measured using the 24-hour pass methodology to assess dietary intake with particular focus on renal dietary components: protein, potassium, phosphorous and sodium intake compared to renal dietary guideline recommendations. Adherence will be defined as meeting three of the four nutrition guidelines.

- dietary protein intake more than or equal to 1.2 grams of protein per kilogram of ideal body weight per day
- dietary potassium intake less than or equal to 1mmol of potassium per kilogram of ideal body weight per day
- dietary phosphate intake less than or equal to 1000mg phosphorus per day
– dietary sodium intake less than or equal to 2300mg sodium per day

- Recruitment rate
- Drop-out rate
- Participant satisfaction (measured using a 7-point likert scale)
- Semi-structured interviews to describe perspectives on participating in the trial, use of the intervention information, self-monitoring behaviours, decision making, problem solving and behaviour change (only conducted in KIDNEYTEXT intervention group). Interviews will be conducted in-person or on the telephone within eight weeks of completing the trial.

Secondary outcomes (measured at baseline, 3 months and 6 months)

- Serum electrolytes (potassium, phosphate)
- Interdialytic weight gains (average of the previous three haemodialysis sessions)
- Changes in nutritional status as measured using the Patient-Generated Subjective Global Assessment tool
- Change in quality of life scores measured using EQ-5D-5L
- Change in dietary quality measured using the Australian Healthy Eating Index
- The mean change in the intake of renal specific dietary components across all time points

Exploratory outcomes (measured at baseline and 6 months)

- Blood pressure within recommended targets for patients on haemodialysis
- Serum parathyroid hormone, urea, bicarbonate, albumin levels
- Glycaemic control, measured using glycated haemoglobin levels (HbA1c) (subgroup

analysis for patients with diabetes)
- Healthcare utilisation

After completion of the 6 month follow-up a qualitative process evaluation (34) will be undertaken using semi-structured interviews conducted amongst a subset of 25 to 30 purposively sampled participants from the KIDNEYTEXT intervention group. Semi-structured interviews will elicit participants' perspectives regarding their satisfaction, acceptability and use of KIDNEYTEXT, and also their views and attitudes regarding changes in dietary behaviours, self-monitoring, decision-making, and problem solving as a result of the KIDNEYTEXT intervention. With the consent of the participants, all interviews will be audio-recorded and transcribed verbatim. The transcripts will be entered in the computer software package 'HyperRESEARCH 3.0' for storage, coding and searching of data. The audio recordings will be stored in a password protected computer drive and hardcopy transcripts will be stored in a locked cabinet.

Secondary outcomes (outlined in table 2) will be assessed by two dietitians blinded to participant allocation, and include changes in: serum potassium, serum phosphate, interdialytic weight gain, dietary quality and nutritional status. Dietary quality will be evaluated using the Australian Healthy Eating Index (35) which uses seven parameters to assess the quality of a person's diet. Nutritional status will be assessed using the Patient-Generated Subjective Global Assessment. Quality of life will be measured using the EQ-5D-5L instrument (36). All secondary outcomes will be measured at baseline, three months and six months, except for nutritional status which will be assessed at baseline and six months only.

Additional exploratory outcomes will also be measured at baseline and 6 months and comparisons made between the control and the KIDNEYTEXT intervention groups. Exploratory outcomes will include: biochemical parameters (urea, albumin, bicarbonate, parathyroid hormone, glycated haemoglobin), blood pressure (pre and post dialysis), and healthcare utilisation. Healthcare

utilisation will be estimated from participant self-reported records of their healthcare-related appointments (including general practitioner, medical specialists and allied health) using a calendar supplied by the research team. Any hospital and emergency department admissions will be collected from medical records. Data relating to dialysis prescription (e.g. dialysate composition, frequency and duration of dialysis) and dialysis-related medications (e.g. prescription details of phosphate binders, resonium and diuretics) will be collected at baseline, three months and six months. The cost of implementation of the intervention, including cost of sending the text messages and software development will be estimated.

An exploratory cost analysis from the perspective of the healthcare provider for the intervention compared to standard care, will be completed using costs estimated from the health service utilisation records and the cost of implementation of the intervention. The EQ-5D-5L scores will be used to calculate quality adjusted life years (QALYs) for the control and intervention groups. Although the main purpose is to determine the feasibility of collecting healthcare utilization and QOL in this patient population, should the data be sufficiently robust, a preliminary calculation of an incremental cost effectiveness ratio may be possible.

Randomisation

The random allocation sequence will be in a 2:1 (intervention: control) allocation ratio stratified by geographical location (Western Sydney, South Eastern Sydney). Randomisation will occur via a computerised randomisation program that will be accessible by study staff with username and password through a web interface. Allocation will be concealed from study personnel undertaking assessments until the completion of the trial. Participants will be notified of their allocation via text message and will be asked not to disclose their allocation to study personnel.

Blinding

Blinded assessments will be conducted by two dietitians at baseline, three months and six months in face-to-face or telephone interviews. Prior to three and six month reviews participants will be sent a text message reminding them not to reveal their allocation to the outcome assessors. A statistician analysing data will also be blinded to participant allocation.

Statistical analysis

A sample size of 129 participants, 86 in the intervention arm and 43 in the control arm, provide 80% power to detect an increase from 10% to 35% on adherence to dietary recommendations, with a significance level of 0.05. The analysis will follow an intention-to-treat principle. Balance across baseline characteristics (age, gender, haemodialysis type, dialysis vintage, dietary intake, biochemistry and interdialytic weight gains) will be checked. Continuous variables will be compared between groups using t-tests or Wilcoxon tests, according to their distribution. The chi-square test will be used to compare proportions. Logistic and linear mixed models will be used to analyse the longitudinal measurements of categorical and continuous outcomes, respectively. In particular the interaction between time and group will allow for overall comparison between the two groups. Adjustment for unbalanced baseline characteristics will be considered in the analysis. A significance level of 5% will be used.

Safety and monitoring

If a participant is found to have a serum potassium level greater than 6mmol/L study personnel will alert dialysis staff. If a participant is commenced on a long-term (i.e. longer than one month)

dietary regime that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery, total parenteral nutrition, complete enteral nutrition) during the study period the intervention will be ceased.

ETHICS AND DISSEMINATIOMN:

The findings of this study will be disseminated via scientific forums including peer-reviewed publications and presentations at international conferences. The study will be administered by the Westmead Clinical School, The University of Sydney, with the design and conduct overseen by a project management committee (authors). This committee has experience in large-scale clinical trials, qualitative research, health economics, renal medicine, renal dietetics and health policy implementation. Formal ethical approval for this study has been obtained by the Western Sydney Local Health District Human Research Ethics Committee (Westmead) approval number HREC/16/WMEAD/396) and will adhere to their guidelines for ethical human research. Written and informed consent will be obtained from all participants.

DISCUSSION

This study will evaluate a novel intervention to improve dietary behaviours in a haemodialysis population by using widely available and used mobile phone text messaging technology. Interventions using simple, inexpensive technology provide an opportunity to complement current dietary care and provide patients with more consistent support, particularly for those in resource poor settings and for those living in geographically isolated areas.

Rigorous studies are needed to evaluate the effectiveness of a mobile phone text message intervention targeting behaviour change in the haemodialysis population. No known studies have

used mobile phone text messaging to improve dietary behaviours in a CKD or haemodialysis population, however there is evidence that utilising mobile phone text messaging to improve dietary and clinical outcomes is feasible and effective in patients with coronary heart disease (22, 37, 38). Additionally, the content, level of individualisation, frequency and timing of text messages and level of interaction between healthcare professional and patient need to be determined. The current study will explore these important issues.

This KIDNEYTEXT trial will provide robust evidence about the feasibility of a targeted text messaging intervention to improve dietary behaviours and clinical outcomes in a haemodialysis population. Interventions to improve patients' knowledge and motivation to alter their dietary behaviours in this population are needed to enhance patients' quality of life and clinical care and are seen as a high priority for both patients and clinicians. This intervention has the potential as a cost-effective, readily accessible and simple method to improve patients' dietary knowledge and behaviours.

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Contributions

VWL, KLC, JCC, AT, JS are the principle investigators who designed the study and drafted the manuscript. CC and ATh made substantial contributions to the conception and design of the project; ATh developed the software for use in the trial; CC, ATh, KH, MH, MB, KS, RK have been involved in drafting the manuscript and revising it critically for important intellectual content. ATP is in charge of the statistical analysis; KH and MH will lead the economic analysis. All authors have given final approval of the version to be published.

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Declaration of competing interests

A/Prof Kamal Sud has received speaker's honoraria from Baxter Healthcare, Roche, Amgen and Boehringer Ingelheim and conference or meeting sponsorships from Shire, Roche, Boehringer Ingelheim, Amgen, Sanofi and Novartis. Other authors do not have any competing interests of conflicts of interest to declare.

Figure 1: Study design and flow

Figure 2: Text message allocation

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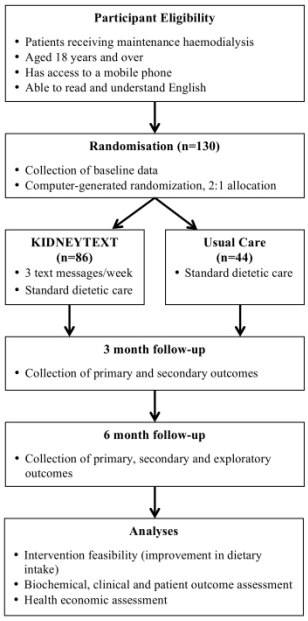

Figure 1: Study design and flow

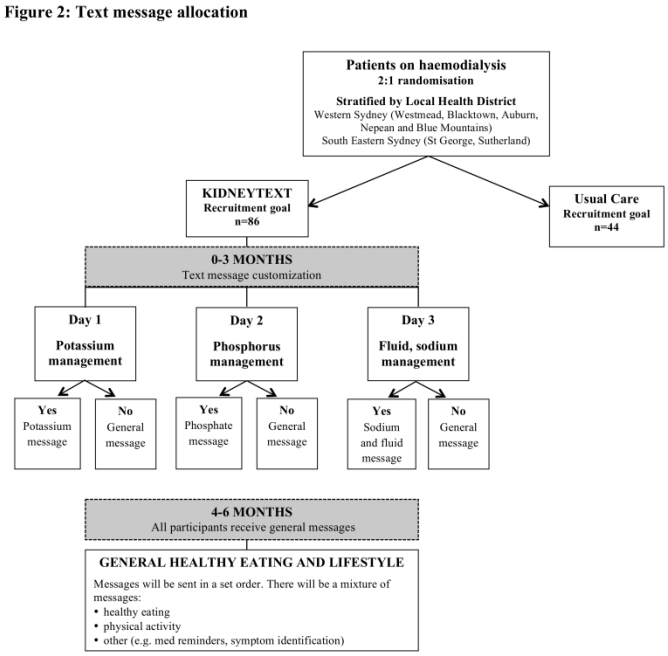

Figure 2: Text message allocation

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 4
	2b	All items from the World Health Organization Trial Registration Data Set	
Protocol version	3	Date and version identifier	October 2017, protocol
Funding	4	Sources and types of financial, material, and other support	Page 20
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 2, 3, 20
	5b	Name and contact information for the trial sponsor	N/A
	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	N/A
	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)	N/A

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	Page 6-8
	6b	Explanation for choice of comparators	Page 9
Objectives	7	Specific objectives or hypotheses	N/A
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)	Page 9
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	Page 9
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)	Page 9
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 9
	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)	Page 9 and 17
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Page 9
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	Page 13-14
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)	Page 14

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	Page 17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 9
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	Page 16
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	Page 16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 16
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 17
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 12
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	Page 14 and protocol
	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	Page 17

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	Protocol
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	Page 17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 17
	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)	Page 17
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	Protocol
	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	Protocol
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	Protocol
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 18
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)	Page 18

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 18
	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	Protocol
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 20
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	Protocol
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	Protocol
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	Page 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendix
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

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Citations

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-207.

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BMJ Open

Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Nutrition and metabolism
Keywords:	Dialysis < NEPHROLOGY, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, Nutrition < TROPICAL MEDICINE, dietary intervention

Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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ABSTRACT

Introduction: Managing nutrition is critical for reducing morbidity and mortality in patients on haemodialysis but adherence to the complex dietary restrictions remains problematic. Innovative interventions to enhance the delivery of nutritional care are needed. The aim of this phase II trial is to evaluate the feasibility and effectiveness of a targeted mobile phone text messaging system to improve dietary and lifestyle behaviours in patients on long-term haemodialysis.

Methods and analysis: Single-blinded randomised controlled trial with six months of follow-up in 130 patients on haemodialysis who will be randomised to either standard care or KIDNEYTEXT. The KIDNEYTEXT intervention group will receive three text messages per week for six months. The text messages provide customised dietary information and advice based on renal dietary guidelines and general healthy eating dietary guidelines, and motivation and support to improve behaviours. The primary outcome is feasibility including: recruitment rate, drop-out rate, adherence to renal dietary recommendations, participant satisfaction and a process evaluation using semi-structured interviews with a subset of purposively sampled participants. Secondary and exploratory outcomes include a range of clinical and behavioural outcomes and a healthcare utilisation cost-analysis will be undertaken.

Ethics and dissemination: The study has been approved by the Western Sydney Local Health District Human Research Ethics Committee – Westmead. Results will be presented at scientific meetings and published in peer-reviewed publications.

Clinical trials registration number: ACTRN12617001084370

ARTICLE SUMMARY

Strengths and limitations of this study:

- Mobile phone technology is inexpensive and widely available, and has been found to be effective in improving clinical outcomes in some chronic diseases, including cardiovascular disease.
- This intervention will be evaluated in a randomised controlled study, with outcome assessors and statistician blinded to participant allocation
- The trial will be conducted in Australia and recruit participants from culturally diverse populations.
- Dietary intake will be measured using patients' self-report. Self-reported dietary intake may not accurately reflect an individual's actual intake, however we are using validated 24-hour dietary recall methodology to standardise dietary intake assessment and minimise bias

INTRODUCTION

Chronic kidney disease (CKD) is recognised as a global public health problem that affects approximately 13% of the population globally, and continues to increase (1, 2). Compared to the general population, people with CKD have an increased risk of mortality from 1.2 times higher in those with mild dysfunction in early CKD to 5.9 times higher in patients on dialysis (2).

In CKD, dietary management plays an important role in preventing the development and progression of CKD, improving clinical outcomes (e.g. proteinuria, hypertension), reducing symptom burden and managing electrolyte abnormalities frequently seen in end-stage kidney disease, particularly in people requiring haemodialysis (3). Dietary management in patients on haemodialysis is particularly challenging because patients have to integrate complex and restrictive dietary requirements specific to CKD such as restricting protein, fluid, sodium, potassium, and phosphorus. In addition they may need to follow recommendations for co-morbidities such as diabetes, as well as following general healthy eating principles (4). Furthermore, dietary prescription can vary substantially among patients depending on age, co-morbidities and goals of treatment (5). In the haemodialysis population, educating patients about end-stage kidney disease fosters capacity for self-management and shared decision making, which can in turn contribute to improved health related behaviours (e.g. diet, exercise and smoking cessation) (6) and reduce burden on the healthcare system.

Patients and health professionals have identified lifestyle and nutrition as a high priority research topic (7, 8) and is an important clinical management intervention that reduces symptom burden and acute medical events due to electrolyte abnormalities, as well as enhancing patients' quality of life (9). However, dietary prescription on haemodialysis is often seen as restrictive and difficult for

patients to adhere to (4). Patients have reported that one off didactic education sessions are overwhelming and difficult to comprehend, particularly at the time of diagnosis (4). Dietary related behaviour change and self-management may be most effectively achieved through individualised education with a dietitian, frequent feedback and monitoring and longer duration of intervention (e.g. at least 6 months) (10, 11). Patient-centred interventions that are individualised and provide progressively simple to more complex education over time to support and engage patients may help to improve outcomes in this population.

Electronic health interventions (eHealth) refers to "health services and information delivered or enhanced through the Internet and related technologies" (12). eHealth interventions improve consumer access to relevant health information, enhances the quality of care and encourages the adoption of healthy behaviours (12). Globally, the use of technology is increasing; with a median of 87% of people regularly using the internet in high-income countries and a median of 54% of people regularly use the internet in developing countries (13). Australia has one of the highest rates of mobile phone ownership, with 88% of Australians owning a smart phone (14). Given this, there is increasing interest in the use of eHealth in healthcare. Systematic reviews have shown that eHealth interventions are effective in changing health-related behaviour and in improving outcomes in patients with diabetes and cardiovascular disease (15-19). Specifically, telehealth (i.e. the use of telecommunication techniques to provide health education remotely) (20) and mobile phone text messaging (21) have shown positive improvements in dietary behaviours and clinical outcomes when compared to usual care in people with chronic diseases (e.g. chronic lung disease, diabetes) and coronary heart disease, respectively.

There is a paucity of research using eHealth interventions, particularly interventions utilising mobile phone technologies, to target diet and lifestyle in the haemodialysis population (22). There is some indication that using electronic self-monitoring apps with additional dietary counselling may

improve dietary sodium intake (23, 24) in haemodialysis and peritoneal dialysis populations, however these studies were small and of short duration. In coronary heart disease mobile phone text messaging has been shown to improve both dietary and clinical outcomes in patients, and to be well accepted, with more than 90% of participants reporting that the text messaging was useful and easy to understand (21). Given the complexity of dietary requirements in haemodialysis and the difficulty patients have in comprehending and integrating these requirements, text messaging offers an inexpensive and readily available way to motivate and help patients with managing their diet by providing frequent, short bursts of information over an extended period of time.

The aim of this study is to assess the feasibility and effectiveness of a mobile phone text message intervention to improve dietary and lifestyle behaviour in patients on haemodialysis. The results of this study will inform a larger trial.

METHODS AND ANALYSIS

Design

The design and development of KIDNEYTEXT has been underpinned by frameworks for the development of complex interventions (25) and a range of behaviour change frameworks (26). KIDNEYTEXT is a six month single-blinded randomised controlled trial, with a 2:1 allocation ratio (Figure 1) (ACTRN12617001084370).

Study setting

This study will be conducted in six dialysis units across three local health districts in Sydney, Australia that serves ethnically, culturally and socioeconomically diverse populations.

Study population

A total of 130 patients receiving maintenance haemodialysis will be included. Patients receiving maintenance haemodialysis in the three local health districts in Sydney, Australia will be eligible to enrol in the study. Eligibility criteria include: receiving maintenance haemodialysis for at least 90 days, aged 18 years and over, having sufficient English language skills to read and understand text messages, and having access to a mobile phone throughout the duration of the study. If patients do not have their own mobile phone, a partner or close family member involved in meal provision may consent to have their mobile phone number used throughout the trial. Patients will be ineligible if they are: prescribed a diet that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery), acutely unwell (e.g. septic), if they are not expected to be on haemodialysis for the forthcoming 6 months (e.g. change of dialysis modality or transplantation), if they have a life expectancy of less than 12 months, pregnant or breastfeeding or if they have significant cognitive impairment or intellectual disability that would inhibit their understanding of the text messages. A "screening log" containing basic demographic information and reason for non-participation will be kept for patients who are ineligible or decline to participate.

Interventions

Participants will be randomly allocated to either control or intervention group. The control group will continue to receive standard care provided by the dialysis unit that they attend. Standard care practices may differ between dialysis units; however, there will be no change to frequency of usual dietetic consultations or service delivery throughout the study.

The KIDNEYTEXT intervention group will receive standard care plus they will receive three text messages per week over a 6 month period. Text messages will be unidirectionall, (i.e. one-way with no response required from participants), as they are intended to function as reminders and reinforcements of various dietary components. Unidirectional text messages have improved dietary and lifestyle behaviours in patients with coronary heart disease (21) and are more time and cost effective compared with in-person interventions. The messages will provide advice, information, motivation and support to improve renal dietary behaviours (related to potassium, phosphorus, sodium, fluid) and general healthy eating and lifestyle behaviours (Table 1). From baseline to 3 months patients may receive messages relating to dietary modification of potassium, phosphorus and sodium and fluid (Figure 2). Participants will receive messages relating to potassium if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for potassium (1mmol per kilogram of ideal body weight per day) (27)
2. Two of three previous pre-dialysis serum potassium levels exceeds 5.5mmol/L (28). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to phosphorus if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for phosphorus (greater than 1000mg per day) (27)
2. Two of three previous pre-dialysis serum phosphate levels exceeds 1.78mmol/L (29). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to sodium and fluid if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for sodium (greater than 2300mg per day) (27)
2. An average of interdialytic fluid gains from the previous three dialysis sessions being more than 3.5% of body weight or more than or equal to 3kg (30)

If a participant satisfies all of these guideline criteria they will only receive general healthy eating and lifestyle messages from baseline to 3 months.

From 4 to 6 months all participants will receive general healthy eating and lifestyle messages that are congruent with renal dietary guidelines (Figure 2). Feedback regarding participants' biochemical and clinical parameters will continue to be provided as per the standard care of each dialysis unit (e.g. via nursing and medical staff).

Table 1: Examples of text messages to be sent to the KIDNEYTEXT intervention group

Potassium • Did you know the way you cook your vegetables can change their potassium content? Boil vegetables in water to get rid of some potassium. • Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian. • How much dairy do you have? Limit to 250ml milk and milk products (e.g. yoghurt and custard) daily to help control your potassium and levels.
Phosphorus • Phosphate is added to pre-packaged foods and convenience foods. Choose fresh foods to reduce how much phosphate you eat. • Phosphate binders act like a magnet and stop you from absorbing some phosphate. Take your phosphate binders with your meals so that they work properly.
Sodium and Fluid • Make sure you know what is in your foods! Look for foods that contain less than 400mg per 100g of sodium. • To get more flavour into your food use pepper, chilli, herbs and spices in your cooking. • Use smaller cups to help reduce how much you drink.
General healthy eating and lifestyle

- Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps.
- Include low potassium fruits and vegetables daily to make sure you get enough fibre.
- Are you a bit off your food? Including small snacks can be a good way to keep up your nutrition.
- The colour of vegetables gives a clue to what nutrients they contain. By including a variety of colours you will get more vitamins and nutrients.

Message delivery will be managed by computerised software ('TextQStream, Python v3.6 using Pycap version 1.02 library) that was developed and customised in-house for use in this trial. Computer software is run through the University of Sydney RedCap system. The program will keep a log of all messages sent to each participant. The messaging engine will send messages through a gateway interface that can be sent through Australian phone network at no cost to the participant. Data exports will be compliant with privacy legislation and held in strict privacy, centrally managed at Westmead Hospital. There will be no access to data by any third party, including the software developers.

Whilst participants are asked not to respond to text messages, a record of any text messages received from participants will be kept and managed by a researcher who is not involved in recruitment or outcome assessment. Participants will have the opportunity to withdraw via a text message and the researcher will contact the software manager in order to initiate the withdrawal.

KIDNEYTEXT intervention development

In total, 160 text messages have been systematically developed through an iterative process and based on renal dietary recommendations (27-30) and general healthy eating guidelines (31). Messages targeting renal-specific dietary components provide advice to assist participants in reducing their intake of potassium, phosphorus, sodium and fluid and provide prompts for self-

monitoring and self-management behaviours. General healthy eating and lifestyle messages promote general healthy eating principles, such as increasing dietary fibre, encouraging physical activity and improving medication management.

The text message bank was developed in three stages. Initially text messages were developed using behaviour change frameworks including information-motivational-behavioural skills model, theory of reasoned action, theory of planned behaviour and social cognitive theory (26). Table 2 outlines behavior change techniques with examples of text messages used in KIDNEYTEXT.

Table 2: Behavioural frameworks used to develop text messages

Technique (Theoretical Framework)	Definition	Examples
Provide information about behaviour link (Information-motivational-behavioural skills model)	General info re: behavioural risk (e.g. susceptibility to poor health outcomes or mortality risk in relation to behaviour)	*Look out for symptoms of high potassium levels. Nausea, tiredness, muscle weakness and an irregular heartbeat. Check your blood tests regularly.*
Provide information on consequences (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Information about the benefits and costs of action or inaction, focusing on what will happen if the person does / does not perform the behaviour	*Did you know that having a low or high potassium can cause a heart attack? Aim for a potassium level between 4-6mmol/L.* *Having high blood phosphate levels for a long time causes your bones to become weak and fragile. To keep them strong follow a low phosphate diet.*
Prompt intention formation (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Encouraging the person to decide to act or set a general goal (E.g. make behavioural resolutions "I will exercise more this week")	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*
Prompt barrier identification (Social Cognitive Theory)	Identify barriers to performing the behaviour and plan ways of overcoming them	*A high salt diet will make you thirstier and harder to stick to your fluid restriction. Avoid adding salt to your meals and limit takeaways and processed*

		foods.
Set graded tasks (Social Cognitive Theory)	Set easy tasks and increase difficulty until target behaviour is performed	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*
Provide instruction (Social Cognitive Theory)	Telling person how to perform a behaviour and/or preparatory behaviours	*Did you know the way you cook your vegetables will change their potassium content? Boil vegetables in water to get rid of potassium.*
Prompt self-monitoring of behaviour (Control theory)	Person is asked to keep a record of specified behaviours (e.g. a diary)	*Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian.*
Teach to use prompts / cues (Operant Conditioning)	Teach person to identify environ cues which can be used to remind them to perform behaviour, including times of day, contexts	*Having trouble sticking to your fluid restriction? Drink only out of a water bottle so you can measure how much you are drinking!*
Relapse prevention (Relapse prevention theory)	Following initial change, help identify situations likely to result in re-adopting risk behaviours or failure to maintain new behaviours and help the person plan to avoid or manage these situations	*Had a lapse in exercise? This is normal, but it is important to get back on track. Plan exercise into your day. Park your car further away or take the stairs.*
Time management	Helping person make time for the behaviour (e.g. to fit it into daily schedule)	*Aim for 30 minutes of exercise most days. You can break your daily exercise into smaller 10-15 minute blocks.*

Text message content was assessed for readability using Flesh-Kincaid, with an average Flesh-Kincaid score of 6 or less being deemed appropriate. An expert review panel including renal dietitians, nephrologists, renal nurses and social scientists then reviewed each message to ensure the content of the messages were accurate. The final draft of text messages were reviewed by people on haemodialysis, caregivers and public health researchers who rated the usefulness and understanding of the text messages on a five-point Likert scale with additional space for comments. Feedback

from these ratings was incorporated into the final draft of text messages for the KIDNEYTEXT intervention.

Patient and public involvement

We sought feedback from people on haemodialysis during the design and development stages of KIDNEYTEXT. We conducted semi-structured interviews with 35 patients on haemodialysis to elicit their perspectives regarding the use of eHealth, particularly mobile phone technology to support current nutritional management. Based on these interviews three text messages per week was indicated as an acceptable frequency of receiving text messages. We incorporated feedback from these interviews into the design of KIDNEYTEXT. Once an initial bank of text messages was developed, we asked patients to review all message content for accuracy, relevancy and usability. Each message was reviewed by at least three consumers and we integrated their feedback into the final set of text messages for use in the trial. A process evaluation exploring the feasibility of the trial, including burdens and benefits to participants, will be undertaken at the completion of the trial. We will disseminate de-identified findings from the trial to study participants and dialysis units at the completion of the trial.

Study outcomes

The primary outcome will be the feasibility of the mobile phone text messaging intervention. Feasibility will be assessed as a composite outcome of: recruitment rate, retention rate, adherence to renal dietary recommendations, participant satisfaction and changes in dietary knowledge, attitude and behaviours (Table 3). Adherence to dietary recommendations will be defined as participants meeting three of the four dietary guideline recommendations with respect to protein, potassium, phosphorus and sodium (Table 2). Dietary intake will be assessed by two dietitians blinded to

participant allocation, using the validated 24-hour pass methodology (32). Dietary recalls will be conducted in-person, or if this is not possible, on the telephone with food models to assist with portion size estimations. Dietary intake will be assessed using a 24-hour recall, of both a dialysis day and a non-dialysis day, to ensure that we are capture any differences in dietary intake on these days. Dietary intake will be assessed at baseline, three months and six months, and will be taken assessed within two weeks a participant's scheduled review. Dietary intake data will be analysed using Xyris Software Foodworks version 9 Pty Ltd (using food databases AUSNUT 2011-2013, Aus Foods 2017, Aus Brands 2017).

Table 3: Primary, secondary and exploratory outcome measures

Primary outcome (measured at baseline, 3 months and 6 months)

Feasibility will be measured using:

Adherence to dietary recommendations. This will be measured using the 24-hour pass methodology to assess dietary intake with particular focus on renal dietary components: protein, potassium, phosphorous and sodium intake compared to renal dietary guideline recommendations. Adherence will be defined as meeting three of the four nutrition guidelines.

- dietary protein intake more than or equal to 1.2 grams of protein per kilogram of ideal body weight per day

- dietary potassium intake less than or equal to 1mmol of potassium per kilogram of ideal body weight per day

- dietary phosphate intake less than or equal to 1000mg phosphorus per day

– dietary sodium intake less than or equal to 2300mg sodium per day

- Recruitment rate
- Drop-out rate
- Participant satisfaction (measured using a 7-point likert scale)
- Semi-structured interviews to describe perspectives on participating in the trial, use of the intervention information, self-monitoring behaviours, decision making, problem solving and behaviour change (only conducted in KIDNEYTEXT intervention group). Interviews will be conducted in-person or on the telephone within eight weeks of completing the trial.

Secondary outcomes (measured at baseline, 3 months and 6 months)

- Serum electrolytes (potassium, phosphate)
- Interdialytic weight gains (average of the previous three haemodialysis sessions)
- Changes in nutritional status as measured using the Patient-Generated Subjective Global Assessment tool

• Change in quality of life scores measured using EQ-5D-5L • Change in dietary quality measured using the Australian Healthy Eating Index • The mean change in the intake of renal specific dietary components across all time points
Exploratory outcomes (measured at baseline and 6 months) • Blood pressure within recommended targets for patients on haemodialysis • Serum parathyroid hormone, urea, bicarbonate, albumin levels • Glycaemic control, measured using glycated haemoglobin levels (HbA1c) (subgroup analysis for patients with diabetes) • Healthcare utilisation

After completion of the 6 month follow-up a qualitative process evaluation (33) will be undertaken using semi-structured interviews conducted amongst a subset of 25 to 30 purposively sampled participants from the KIDNEYTEXT intervention group. Semi-structured interviews will elicit participants' perspectives regarding their satisfaction, acceptability and use of KIDNEYTEXT, and also their views and attitudes regarding changes in dietary behaviours, self-monitoring, decision-making, and problem solving as a result of the KIDNEYTEXT intervention. With the consent of the participants, all interviews will be audio-recorded and transcribed verbatim. The transcripts will be entered in the computer software package 'HyperRESEARCH 3.0' for storage, coding and searching of data. The audio recordings will be stored in a password protected computer drive and hardcopy transcripts will be stored in a locked cabinet.

Secondary outcomes (outlined in table 2) will be assessed by two dietitians blinded to participant allocation, and include changes in: serum potassium, serum phosphate, interdialytic weight gain, dietary quality and nutritional status. Dietary quality will be evaluated using the Australian Healthy Eating Index (34) which uses seven parameters to assess the quality of a person's diet. Nutritional status will be assessed using the Patient-Generated Subjective Global Assessment. Quality of life will be measured using the EQ-5D-5L instrument (35). All secondary outcomes will be measured at baseline, three months and six months, except for nutritional status which will be assessed at baseline and six months only.

Additional exploratory outcomes will also be measured at baseline and 6 months and comparisons made between the control and the KIDNEYTEXT intervention groups. Exploratory outcomes will include: biochemical parameters (urea, albumin, bicarbonate, parathyroid hormone, glycated haemoglobin), blood pressure (pre and post dialysis), and healthcare utilisation. Healthcare utilisation will be estimated from participant self-reported records of their healthcare-related appointments (including general practitioner, medical specialists and allied health) using a calendar supplied by the research team. Any hospital and emergency department admissions will be collected from medical records. Data relating to dialysis prescription (e.g. dialysate composition, frequency and duration of dialysis) and dialysis-related medications (e.g. prescription details of phosphate binders, resonium and diuretics) will be collected at baseline, three months and six months. The cost of implementation of the intervention, including cost of sending the text messages and software development will be estimated.

An exploratory cost analysis from the perspective of the healthcare provider for the intervention compared to standard care, will be completed using costs estimated from the health service utilisation records and the cost of implementation of the intervention. The EQ-5D-5L scores will be used to calculate quality adjusted life years (QALYs) for the control and intervention groups. Although the main purpose is to determine the feasibility of collecting healthcare utilization and QOL in this patient population, should the data be sufficiently robust, a preliminary calculation of an incremental cost effectiveness ratio may be possible.

Randomisation

The random allocation sequence will be in a 2:1 (intervention: control) allocation ratio stratified by geographical location (Western Sydney, South Eastern Sydney). Randomisation will occur via a

computerised randomisation program that will be accessible by study staff with username and password through a web interface. Allocation will be concealed from study personnel undertaking assessments until the completion of the trial. Participants will be notified of their allocation via text message and will be asked not to disclose their allocation to study personnel.

Blinding

Blinded assessments will be conducted by two dietitians at baseline, three months and six months in face-to-face or telephone interviews. Prior to three and six month reviews participants will be sent a text message reminding them not to reveal their allocation to the outcome assessors. A statistician analysing data will also be blinded to participant allocation.

Statistical analysis

A sample size of 129 participants, 86 in the intervention arm and 43 in the control arm, provide 80% power to detect an increase from 10% to 35% on adherence to dietary recommendations, with a significance level of 0.05. The analysis will follow an intention-to-treat principle. Balance across baseline characteristics (age, gender, haemodialysis type, dialysis vintage, dietary intake, biochemistry and interdialytic weight gains) will be checked. Continuous variables will be compared between groups using t-tests or Wilcoxon tests, according to their distribution. The chi-square test will be used to compare proportions. Logistic and linear mixed models will be used to analyse the longitudinal measurements of categorical and continuous outcomes, respectively. In particular the interaction between time and group will allow for overall comparison between the two groups. Adjustment for unbalanced baseline characteristics will be considered in the analysis. A significance level of 5% will be used.

Safety and monitoring

If a participant is found to have a serum potassium level greater than 6mmol/L study personnel will alert dialysis staff. If a participant is commenced on a long-term (i.e. longer than one month) dietary regime that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery, total parenteral nutrition, complete enteral nutrition) during the study period the intervention will be ceased.

ETHICS AND DISSEMINATIOMN:

The findings of this study will be disseminated via scientific forums including peer-reviewed publications and presentations at international conferences. The study will be administered by the Westmead Clinical School, The University of Sydney, with the design and conduct overseen by a project management committee (authors). This committee has experience in large-scale clinical trials, qualitative research, health economics, renal medicine, renal dietetics and health policy implementation. Formal ethical approval for this study has been obtained by the Western Sydney Local Health District Human Research Ethics Committee (Westmead) approval number HREC/16/WMEAD/396) and will adhere to their guidelines for ethical human research. Written and informed consent will be obtained from all participants.

DISCUSSION

This study will evaluate a novel intervention to improve dietary behaviours in a haemodialysis population by using widely available and used mobile phone text messaging technology. Interventions using simple, inexpensive technology provide an opportunity to complement current

dietary care and provide patients with more consistent support, particularly for those in resource poor settings and for those living in geographically isolated areas.

Rigorous studies are needed to evaluate the effectiveness of a mobile phone text message intervention targeting behaviour change in the haemodialysis population. No known studies have used mobile phone text messaging to improve dietary behaviours in a CKD or haemodialysis population, however there is evidence that utilising mobile phone text messaging to improve dietary and clinical outcomes is feasible and effective in patients with coronary heart disease (21, 36, 37). Additionally, the content, level of individualisation, frequency and timing of text messages and level of interaction between healthcare professional and patient need to be determined. The current study will explore these important issues.

This KIDNEYTEXT trial will provide robust evidence about the feasibility of a targeted text messaging intervention to improve dietary behaviours and clinical outcomes in a haemodialysis population. Interventions to improve patients' knowledge and motivation to alter their dietary behaviours in this population are needed to enhance patients' quality of life and clinical care and are seen as a high priority for both patients and clinicians. This intervention has the potential as a cost-effective, readily accessible and simple method to improve patients' dietary knowledge and behaviours.

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Contributions

VWL, KLC, JCC, AT, JS are the principle investigators who designed the study and drafted the manuscript. CC and ATh made substantial contributions to the conception and design of the project; ATh developed the software for use in the trial; CC, ATh, KH, MH, MB, KS, RK have been involved in drafting the manuscript and revising it critically for important intellectual content. ATP is in charge of the statistical analysis; KH and MH will lead the economic analysis. All authors have given final approval of the version to be published.

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Declaration of competing interests

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Figure 1: Study design and flow

Figure 2: Text message allocation

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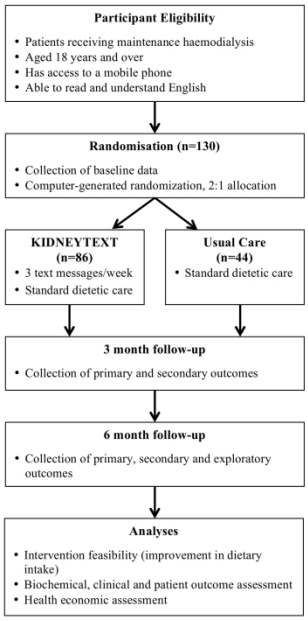

Figure 1: Study design and flow

296x209mm (300 x 300 DPI)

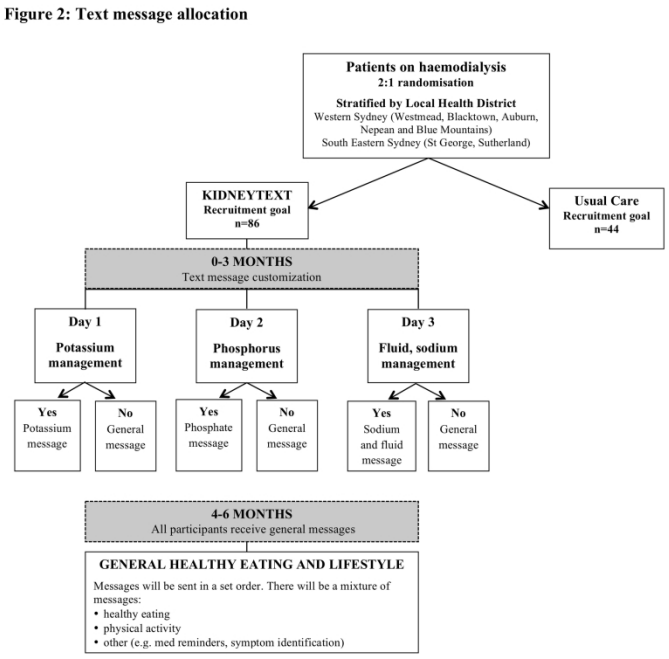

Figure 2: Text message allocation

209x296mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 4
	2b	All items from the World Health Organization Trial Registration Data Set	
Protocol version	3	Date and version identifier	October 2017, protocol
Funding	4	Sources and types of financial, material, and other support	Page 20
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 2, 3, 20
	5b	Name and contact information for the trial sponsor	N/A
	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	N/A
	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)	N/A

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	Page 6-8
	6b	Explanation for choice of comparators	Page 9
Objectives	7	Specific objectives or hypotheses	N/A
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)	Page 9
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	Page 9
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)	Page 9
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 9
	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)	Page 9 and 17
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Page 9
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	Page 13-14
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)	Page 14

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	Page 17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 9
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	Page 16
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	Page 16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 16
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 17
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 12
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	Page 14 and protocol
	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	Page 17

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	Protocol
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	Page 17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 17
	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)	Page 17
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	Protocol
	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	Protocol
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	Protocol
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 18
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)	Page 18

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 18
	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	Protocol
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 20
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	Protocol
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	Protocol
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	Page 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendix
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

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Citations

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-207.

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.

BMJ Open

Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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Primary Subject Heading:	Renal medicine
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Targeted, structured text messaging to improve dietary and lifestyle behaviours for people on maintenance haemodialysis (KIDNEYTEXT): study protocol for a randomised controlled trial

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ABSTRACT

Introduction: Managing nutrition is critical for reducing morbidity and mortality in patients on haemodialysis but adherence to the complex dietary restrictions remains problematic. Innovative interventions to enhance the delivery of nutritional care are needed. The aim of this phase II trial is to evaluate the feasibility and effectiveness of a targeted mobile phone text messaging system to improve dietary and lifestyle behaviours in patients on long-term haemodialysis.

Methods and analysis: Single-blinded randomised controlled trial with six months of follow-up in 130 patients on haemodialysis who will be randomised to either standard care or KIDNEYTEXT. The KIDNEYTEXT intervention group will receive three text messages per week for six months. The text messages provide customised dietary information and advice based on renal dietary guidelines and general healthy eating dietary guidelines, and motivation and support to improve behaviours. The primary outcome is feasibility including: recruitment rate, drop-out rate, adherence to renal dietary recommendations, participant satisfaction and a process evaluation using semi-structured interviews with a subset of purposively sampled participants. Secondary and exploratory outcomes include a range of clinical and behavioural outcomes and a healthcare utilisation cost-analysis will be undertaken.

Ethics and dissemination: The study has been approved by the Western Sydney Local Health District Human Research Ethics Committee – Westmead. Results will be presented at scientific meetings and published in peer-reviewed publications.

Clinical trials registration number: ACTRN12617001084370

ARTICLE SUMMARY

Strengths and limitations of this study:

- Mobile phone technology is inexpensive and widely available, and has been found to be effective in improving clinical outcomes in some chronic diseases, including cardiovascular disease.
- This intervention will be evaluated in a randomised controlled study, with outcome assessors and statistician blinded to participant allocation
- The trial will be conducted in Australia and recruit participants from culturally diverse populations.
- Dietary intake will be measured using patients' self-report. Self-reported dietary intake may not accurately reflect an individual's actual intake, however we are using validated 24-hour dietary recall methodology to standardise dietary intake assessment and minimise bias

INTRODUCTION

Chronic kidney disease (CKD) is recognised as a global public health problem that affects approximately 13% of the population globally, and continues to increase (1, 2). Compared to the general population, people with CKD have an increased risk of mortality from 1.2 times higher in those with mild dysfunction in early CKD to 5.9 times higher in patients on dialysis (2).

In CKD, dietary management plays an important role in preventing the development and progression of CKD, improving clinical outcomes (e.g. proteinuria, hypertension), reducing symptom burden and managing electrolyte abnormalities frequently seen in end-stage kidney disease, particularly in people requiring haemodialysis (3). Dietary management in patients on haemodialysis is particularly challenging because patients have to integrate complex and restrictive dietary requirements specific to CKD such as restricting protein, fluid, sodium, potassium, and phosphorus. In addition they may need to follow recommendations for co-morbidities such as diabetes, as well as following general healthy eating principles (4). Furthermore, dietary prescription can vary substantially among patients depending on age, co-morbidities and goals of treatment (5). In the haemodialysis population, educating patients about end-stage kidney disease fosters capacity for self-management and shared decision making, which can in turn contribute to improved health related behaviours (e.g. diet, exercise and smoking cessation) (6) and reduce burden on the healthcare system.

Patients and health professionals have identified lifestyle and nutrition as a high priority research topic (7, 8) and is an important clinical management intervention that reduces symptom burden and acute medical events due to electrolyte abnormalities, as well as enhancing patients' quality of life (9). However, dietary prescription on haemodialysis is often seen as restrictive and difficult for

patients to adhere to (4). Patients have reported that one off didactic education sessions are overwhelming and difficult to comprehend, particularly at the time of diagnosis (4). Dietary related behaviour change and self-management may be most effectively achieved through individualised education with a dietitian, frequent feedback and monitoring and longer duration of intervention (e.g. at least 6 months) (10, 11). Patient-centred interventions that are individualised and provide progressively simple to more complex education over time to support and engage patients may help to improve outcomes in this population.

Electronic health interventions (eHealth) refers to "health services and information delivered or enhanced through the Internet and related technologies" (12). eHealth interventions improve consumer access to relevant health information, enhances the quality of care and encourages the adoption of healthy behaviours (12). Globally, the use of technology is increasing; with a median of 87% of people regularly using the internet in high-income countries and a median of 54% of people regularly use the internet in developing countries (13). Australia has one of the highest rates of mobile phone ownership, with 88% of Australians owning a smart phone (14). Given this, there is increasing interest in the use of eHealth in healthcare. Systematic reviews have shown that eHealth interventions are effective in changing health-related behaviour and in improving outcomes in patients with diabetes and cardiovascular disease (15-19). Specifically, telehealth (i.e. the use of telecommunication techniques to provide health education remotely) (20) and mobile phone text messaging (21) have shown positive improvements in dietary behaviours and clinical outcomes when compared to usual care in people with chronic diseases (e.g. chronic lung disease, diabetes) and coronary heart disease, respectively.

There is a paucity of research using eHealth interventions, particularly interventions utilising mobile phone technologies, to target diet and lifestyle in the haemodialysis population (22). There is some indication that using electronic self-monitoring apps with additional dietary counselling may

improve dietary sodium intake (23, 24) in haemodialysis and peritoneal dialysis populations, however these studies were small and of short duration. In coronary heart disease mobile phone text messaging has been shown to improve both dietary and clinical outcomes in patients, and to be well accepted, with more than 90% of participants reporting that the text messaging was useful and easy to understand (21). Given the complexity of dietary requirements in haemodialysis and the difficulty patients have in comprehending and integrating these requirements, text messaging offers an inexpensive and readily available way to motivate and help patients with managing their diet by providing frequent, short bursts of information over an extended period of time.

The aim of this study is to assess the feasibility and effectiveness of a mobile phone text message intervention to improve dietary and lifestyle behaviour in patients on haemodialysis. The results of this study will inform a larger trial.

METHODS AND ANALYSIS

Design

The design and development of KIDNEYTEXT has been underpinned by frameworks for the development of complex interventions (25) and a range of behaviour change frameworks (26). KIDNEYTEXT is a six month single-blinded randomised controlled trial, with a 2:1 allocation ratio (Figure 1) (ACTRN12617001084370).

Study setting

This study will be conducted in six dialysis units across three local health districts in Sydney, Australia that serves ethnically, culturally and socioeconomically diverse populations.

Study population

A total of 130 patients receiving maintenance haemodialysis will be included. Patients receiving maintenance haemodialysis in the three local health districts in Sydney, Australia will be eligible to enrol in the study. Eligibility criteria include: receiving maintenance haemodialysis for at least 90 days, aged 18 years and over, having sufficient English language skills to read and understand text messages, and having access to a mobile phone throughout the duration of the study. If patients do not have their own mobile phone, a partner or close family member involved in meal provision may consent to have their mobile phone number used throughout the trial. Patients will be ineligible if they are: prescribed a diet that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery), acutely unwell (e.g. septic), if they are not expected to be on haemodialysis for the forthcoming 6 months (e.g. change of dialysis modality or transplantation), if they have a life expectancy of less than 12 months, pregnant or breastfeeding or if they have significant cognitive impairment or intellectual disability that would inhibit their understanding of the text messages. A "screening log" containing basic demographic information and reason for non-participation will be kept for patients who are ineligible or decline to participate.

Interventions

Participants will be randomly allocated to either control or intervention group. The control group will continue to receive standard care provided by the dialysis unit that they attend. Standard care practices may differ between dialysis units; however, there will be no change to frequency of usual dietetic consultations or service delivery throughout the study.

The KIDNEYTEXT intervention group will receive standard care plus they will receive three text messages per week over a 6 month period. Text messages will be unidirectionall, (i.e. one-way with no response required from participants), as they are intended to function as reminders and reinforcements of various dietary components. Unidirectional text messages have improved dietary and lifestyle behaviours in patients with coronary heart disease (21) and are more time and cost effective compared with in-person interventions. The messages will provide advice, information, motivation and support to improve renal dietary behaviours (related to potassium, phosphorus, sodium, fluid) and general healthy eating and lifestyle behaviours (Table 1). From baseline to 3 months patients may receive messages relating to dietary modification of potassium, phosphorus and sodium and fluid (Figure 2). Participants will receive messages relating to potassium if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for potassium (1mmol per kilogram of ideal body weight per day) (27)
2. Two of three previous pre-dialysis serum potassium levels exceeds 5.5mmol/L (28). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to phosphorus if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for phosphorus (greater than 1000mg per day) (27)
2. Two of three previous pre-dialysis serum phosphate levels exceeds 1.78mmol/L (29). Baseline blood values will be based on the previous 3 routine dialysis blood tests.

Participants will receive messages relating to sodium and fluid if one or both of the following guidelines is exceeded:

1. Baseline dietary intake exceeds guidelines for sodium (greater than 2300mg per day) (27)
2. An average of interdialytic fluid gains from the previous three dialysis sessions being more than 3.5% of body weight or more than or equal to 3kg (30)

If a participant satisfies all of these guideline criteria they will only receive general healthy eating and lifestyle messages from baseline to 3 months.

From 4 to 6 months all participants will receive general healthy eating and lifestyle messages that are congruent with renal dietary guidelines (Figure 2). Feedback regarding participants' biochemical and clinical parameters will continue to be provided as per the standard care of each dialysis unit (e.g. via nursing and medical staff).

Table 1: Examples of text messages to be sent to the KIDNEYTEXT intervention group

Potassium • Did you know the way you cook your vegetables can change their potassium content? Boil vegetables in water to get rid of some potassium. • Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian. • How much dairy do you have? Limit to 250ml milk and milk products (e.g. yoghurt and custard) daily to help control your potassium and levels.
Phosphorus • Phosphate is added to pre-packaged foods and convenience foods. Choose fresh foods to reduce how much phosphate you eat. • Phosphate binders act like a magnet and stop you from absorbing some phosphate. Take your phosphate binders with your meals so that they work properly.
Sodium and Fluid • Make sure you know what is in your foods! Look for foods that contain less than 400mg per 100g of sodium. • To get more flavour into your food use pepper, chilli, herbs and spices in your cooking. • Use smaller cups to help reduce how much you drink.
General healthy eating and lifestyle

- Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps.
- Include low potassium fruits and vegetables daily to make sure you get enough fibre.
- Are you a bit off your food? Including small snacks can be a good way to keep up your nutrition.
- The colour of vegetables gives a clue to what nutrients they contain. By including a variety of colours you will get more vitamins and nutrients.

Message delivery will be managed by computerised software ('TextQStream, Python v3.6 using Pycap version 1.02 library) that was developed and customised in-house for use in this trial. Computer software is run through the University of Sydney RedCap system. The program will keep a log of all messages sent to each participant. The messaging engine will send messages through a gateway interface that can be sent through Australian phone network at no cost to the participant. Data exports will be compliant with privacy legislation and held in strict privacy, centrally managed at Westmead Hospital. There will be no access to data by any third party, including the software developers.

Whilst participants are asked not to respond to text messages, a record of any text messages received from participants will be kept and managed by a researcher who is not involved in recruitment or outcome assessment. Participants will have the opportunity to withdraw via a text message and the researcher will contact the software manager in order to initiate the withdrawal.

KIDNEYTEXT intervention development

In total, 160 text messages have been systematically developed through an iterative process and based on renal dietary recommendations (27-30) and general healthy eating guidelines (31). Messages targeting renal-specific dietary components provide advice to assist participants in reducing their intake of potassium, phosphorus, sodium and fluid and provide prompts for self-

monitoring and self-management behaviours. General healthy eating and lifestyle messages promote general healthy eating principles, such as increasing dietary fibre, encouraging physical activity and improving medication management.

The text message bank was developed in three stages. Initially text messages were developed using behaviour change frameworks including information-motivational-behavioural skills model, theory of reasoned action, theory of planned behaviour and social cognitive theory (26). Table 2 outlines behavior change techniques with examples of text messages used in KIDNEYTEXT.

Table 2: Behavioural frameworks used to develop text messages

Technique (Theoretical Framework)	Definition	Examples
Provide information about behaviour link (Information-motivational-behavioural skills model)	General info re: behavioural risk (e.g. susceptibility to poor health outcomes or mortality risk in relation to behaviour)	*Look out for symptoms of high potassium levels. Nausea, tiredness, muscle weakness and an irregular heartbeat. Check your blood tests regularly.*
Provide information on consequences (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Information about the benefits and costs of action or inaction, focusing on what will happen if the person does / does not perform the behaviour	*Did you know that having a low or high potassium can cause a heart attack? Aim for a potassium level between 4-6mmol/L.* *Having high blood phosphate levels for a long time causes your bones to become weak and fragile. To keep them strong follow a low phosphate diet.*
Prompt intention formation (Theory of reasoned action, Theory of planned behaviour, Social cognitive theory, Information-motivational-behavioural skills model)	Encouraging the person to decide to act or set a general goal (E.g. make behavioural resolutions "I will exercise more this week")	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*
Prompt barrier identification (Social Cognitive Theory)	Identify barriers to performing the behaviour and plan ways of overcoming them	*A high salt diet will make you thirstier and harder to stick to your fluid restriction. Avoid adding salt to your meals and limit takeaways and processed*

		foods.
Set graded tasks (Social Cognitive Theory)	Set easy tasks and increase difficulty until target behaviour is performed	*Getting enough physical activity? Set regular goals to help you get to your target. Start small and build up over time. Every bit helps. Get on the move!*
Provide instruction (Social Cognitive Theory)	Telling person how to perform a behaviour and/or preparatory behaviours	*Did you know the way you cook your vegetables will change their potassium content? Boil vegetables in water to get rid of potassium.*
Prompt self-monitoring of behaviour (Control theory)	Person is asked to keep a record of specified behaviours (e.g. a diary)	*Not sure what is causing high potassium levels? Write down everything you are eating and drinking and discuss with your dietitian.*
Teach to use prompts / cues (Operant Conditioning)	Teach person to identify environ cues which can be used to remind them to perform behaviour, including times of day, contexts	*Having trouble sticking to your fluid restriction? Drink only out of a water bottle so you can measure how much you are drinking!*
Relapse prevention (Relapse prevention theory)	Following initial change, help identify situations likely to result in re-adopting risk behaviours or failure to maintain new behaviours and help the person plan to avoid or manage these situations	*Had a lapse in exercise? This is normal, but it is important to get back on track. Plan exercise into your day. Park your car further away or take the stairs.*
Time management	Helping person make time for the behaviour (e.g. to fit it into daily schedule)	*Aim for 30 minutes of exercise most days. You can break your daily exercise into smaller 10-15 minute blocks.*

Text message content was assessed for readability using Flesh-Kincaid, with an average Flesh-Kincaid score of 6 or less being deemed appropriate. An expert review panel including renal dietitians, nephrologists, renal nurses and social scientists then reviewed each message to ensure the content of the messages were accurate. The final draft of text messages were reviewed by people on haemodialysis, caregivers and public health researchers who rated the usefulness and understanding of the text messages on a five-point Likert scale with additional space for comments. Feedback

from these ratings was incorporated into the final draft of text messages for the KIDNEYTEXT intervention.

Patient and public involvement

We sought feedback from people on haemodialysis during the design and development stages of KIDNEYTEXT. We conducted semi-structured interviews with 35 patients on haemodialysis to elicit their perspectives regarding the use of eHealth, particularly mobile phone technology to support current nutritional management. Based on these interviews three text messages per week was indicated as an acceptable frequency of receiving text messages. We incorporated feedback from these interviews into the design of KIDNEYTEXT. Once an initial bank of text messages was developed, we asked patients to review all message content for accuracy, relevancy and usability. Each message was reviewed by at least three consumers and we integrated their feedback into the final set of text messages for use in the trial. A process evaluation exploring the feasibility of the trial, including burdens and benefits to participants, will be undertaken at the completion of the trial. We will disseminate de-identified findings from the trial to study participants and dialysis units at the completion of the trial.

Study outcomes

The primary outcome will be the feasibility of the mobile phone text messaging intervention. Feasibility will be assessed as a composite outcome of: recruitment rate, retention rate, adherence to renal dietary recommendations, participant satisfaction and changes in dietary knowledge, attitude and behaviours (Table 3). Adherence to dietary recommendations will be defined as participants meeting three of the four dietary guideline recommendations with respect to protein, potassium, phosphorus and sodium (Table 2). Dietary intake will be assessed by two dietitians blinded to

participant allocation, using the validated 24-hour pass methodology (32). Dietary recalls will be conducted in-person, or if this is not possible, on the telephone with food models to assist with portion size estimations. Dietary intake will be assessed using a 24-hour recall, of both a dialysis day and a non-dialysis day, to ensure that we are capture any differences in dietary intake on these days. Dietary intake will be assessed at baseline, three months and six months, and will be taken assessed within two weeks a participant's scheduled review. Dietary intake data will be analysed using Xyris Software Foodworks version 9 Pty Ltd (using food databases AUSNUT 2011-2013, Aus Foods 2017, Aus Brands 2017).

Table 3: Primary, secondary and exploratory outcome measures

Primary outcome (measured at baseline, 3 months and 6 months)

Feasibility will be measured using:

Adherence to dietary recommendations. This will be measured using the 24-hour pass methodology to assess dietary intake with particular focus on renal dietary components: protein, potassium, phosphorous and sodium intake compared to renal dietary guideline recommendations. Adherence will be defined as meeting three of the four nutrition guidelines.

- dietary protein intake more than or equal to 1.2 grams of protein per kilogram of ideal body weight per day

- dietary potassium intake less than or equal to 1mmol of potassium per kilogram of ideal body weight per day

- dietary phosphate intake less than or equal to 1000mg phosphorus per day

– dietary sodium intake less than or equal to 2300mg sodium per day

- Recruitment rate
- Drop-out rate
- Participant satisfaction (measured using a 7-point likert scale)
- Semi-structured interviews to describe perspectives on participating in the trial, use of the intervention information, self-monitoring behaviours, decision making, problem solving and behaviour change (only conducted in KIDNEYTEXT intervention group). Interviews will be conducted in-person or on the telephone within eight weeks of completing the trial.

Secondary outcomes (measured at baseline, 3 months and 6 months)

- Serum electrolytes (potassium, phosphate)
- Interdialytic weight gains (average of the previous three haemodialysis sessions)
- Changes in nutritional status as measured using the Patient-Generated Subjective Global Assessment tool

• Change in quality of life scores measured using EQ-5D-5L • Change in dietary quality measured using the Australian Healthy Eating Index • The mean change in the intake of renal specific dietary components across all time points
Exploratory outcomes (measured at baseline and 6 months) • Blood pressure within recommended targets for patients on haemodialysis • Serum parathyroid hormone, urea, bicarbonate, albumin levels • Glycaemic control, measured using glycated haemoglobin levels (HbA1c) (subgroup analysis for patients with diabetes) • Healthcare utilisation

After completion of the 6 month follow-up a qualitative process evaluation (33) will be undertaken using semi-structured interviews conducted amongst a subset of 25 to 30 purposively sampled participants from the KIDNEYTEXT intervention group. Semi-structured interviews will elicit participants' perspectives regarding their satisfaction, acceptability and use of KIDNEYTEXT, and also their views and attitudes regarding changes in dietary behaviours, self-monitoring, decision-making, and problem solving as a result of the KIDNEYTEXT intervention. With the consent of the participants, all interviews will be audio-recorded and transcribed verbatim. The transcripts will be entered in the computer software package 'HyperRESEARCH 3.0' for storage, coding and searching of data. The audio recordings will be stored in a password protected computer drive and hardcopy transcripts will be stored in a locked cabinet.

Secondary outcomes (outlined in table 2) will be assessed by two dietitians blinded to participant allocation, and include changes in: serum potassium, serum phosphate, interdialytic weight gain, dietary quality and nutritional status. Dietary quality will be evaluated using the Australian Healthy Eating Index (34) which uses seven parameters to assess the quality of a person's diet. Nutritional status will be assessed using the Patient-Generated Subjective Global Assessment. Quality of life will be measured using the EQ-5D-5L instrument (35). All secondary outcomes will be measured at baseline, three months and six months, except for nutritional status which will be assessed at baseline and six months only.

Additional exploratory outcomes will also be measured at baseline and 6 months and comparisons made between the control and the KIDNEYTEXT intervention groups. Exploratory outcomes will include: biochemical parameters (urea, albumin, bicarbonate, parathyroid hormone, glycated haemoglobin), blood pressure (pre and post dialysis), and healthcare utilisation. Healthcare utilisation will be estimated from participant self-reported records of their healthcare-related appointments (including general practitioner, medical specialists and allied health) using a calendar supplied by the research team. Any hospital and emergency department admissions will be collected from medical records. Data relating to dialysis prescription (e.g. dialysate composition, frequency and duration of dialysis) and dialysis-related medications (e.g. prescription details of phosphate binders, resonium and diuretics) will be collected at baseline, three months and six months. The cost of implementation of the intervention, including cost of sending the text messages and software development will be estimated.

An exploratory cost analysis from the perspective of the healthcare provider for the intervention compared to standard care, will be completed using costs estimated from the health service utilisation records and the cost of implementation of the intervention. The EQ-5D-5L scores will be used to calculate quality adjusted life years (QALYs) for the control and intervention groups. Although the main purpose is to determine the feasibility of collecting healthcare utilization and QOL in this patient population, should the data be sufficiently robust, a preliminary calculation of an incremental cost effectiveness ratio may be possible.

Randomisation

The random allocation sequence will be in a 2:1 (intervention: control) allocation ratio stratified by geographical location (Western Sydney, South Eastern Sydney). Randomisation will occur via a

computerised randomisation program that will be accessible by study staff with username and password through a web interface. Allocation will be concealed from study personnel undertaking assessments until the completion of the trial. Participants will be notified of their allocation via text message and will be asked not to disclose their allocation to study personnel.

Blinding

Blinded assessments will be conducted by two dietitians at baseline, three months and six months in face-to-face or telephone interviews. Prior to three and six month reviews participants will be sent a text message reminding them not to reveal their allocation to the outcome assessors. A statistician analysing data will also be blinded to participant allocation.

Statistical analysis

A sample size of 129 participants, 86 in the intervention arm and 43 in the control arm, provide 80% power to detect an increase from 10% to 35% on adherence to dietary recommendations, with a significance level of 0.05. The analysis will follow an intention-to-treat principle. Balance across baseline characteristics (age, gender, haemodialysis type, dialysis vintage, dietary intake, biochemistry and interdialytic weight gains) will be checked. Continuous variables will be compared between groups using t-tests or Wilcoxon tests, according to their distribution. The chi-square test will be used to compare proportions. Logistic and linear mixed models will be used to analyse the longitudinal measurements of categorical and continuous outcomes, respectively. In particular the interaction between time and group will allow for overall comparison between the two groups. Adjustment for unbalanced baseline characteristics will be considered in the analysis. A significance level of 5% will be used.

Safety and monitoring

If a participant is found to have a serum potassium level greater than 6mmol/L study personnel will alert dialysis staff. If a participant is commenced on a long-term (i.e. longer than one month) dietary regime that is incongruent with standard renal dietary education (e.g. immediately post bariatric surgery, total parenteral nutrition, complete enteral nutrition) during the study period the intervention will be ceased.

ETHICS AND DISSEMINATIOMN:

The findings of this study will be disseminated via scientific forums including peer-reviewed publications and presentations at international conferences. The study will be administered by the Westmead Clinical School, The University of Sydney, with the design and conduct overseen by a project management committee (authors). This committee has experience in large-scale clinical trials, qualitative research, health economics, renal medicine, renal dietetics and health policy implementation. Formal ethical approval for this study has been obtained by the Western Sydney Local Health District Human Research Ethics Committee (Westmead) approval number HREC/16/WMEAD/396) and will adhere to their guidelines for ethical human research. Written and informed consent will be obtained from all participants.

DISCUSSION

This study will evaluate a novel intervention to improve dietary behaviours in a haemodialysis population by using widely available and used mobile phone text messaging technology. Interventions using simple, inexpensive technology provide an opportunity to complement current

dietary care and provide patients with more consistent support, particularly for those in resource poor settings and for those living in geographically isolated areas.

Rigorous studies are needed to evaluate the effectiveness of a mobile phone text message intervention targeting behaviour change in the haemodialysis population. No known studies have used mobile phone text messaging to improve dietary behaviours in a CKD or haemodialysis population, however there is evidence that utilising mobile phone text messaging to improve dietary and clinical outcomes is feasible and effective in patients with coronary heart disease (21, 36, 37). Additionally, the content, level of individualisation, frequency and timing of text messages and level of interaction between healthcare professional and patient need to be determined. The current study will explore these important issues.

This KIDNEYTEXT trial will provide robust evidence about the feasibility of a targeted text messaging intervention to improve dietary behaviours and clinical outcomes in a haemodialysis population. Interventions to improve patients' knowledge and motivation to alter their dietary behaviours in this population are needed to enhance patients' quality of life and clinical care and are seen as a high priority for both patients and clinicians. This intervention has the potential as a cost-effective, readily accessible and simple method to improve patients' dietary knowledge and behaviours.

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Contributions

VWL, KLC, JCC, AT, JS are the principle investigators who designed the study and drafted the manuscript. CC and ATh made substantial contributions to the conception and design of the project; ATh developed the software for use in the trial; CC, ATh, KH, MH, MB, KS, RK have been involved in drafting the manuscript and revising it critically for important intellectual content. ATP is in charge of the statistical analysis; KH and MH will lead the economic analysis. All authors have given final approval of the version to be published.

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Declaration of competing interests

A/Prof Kamal Sud has received speaker's honoraria from Baxter Healthcare, Roche, Amgen and Boehringer Ingelheim and conference or meeting sponsorships from Shire, Roche, Boehringer

Ingelheim, Amgen, Sanofi and Novartis. Other authors do not have any competing interests of conflicts of interest to declare.

Figure 1: Study design and flow

Figure 2: Text message allocation

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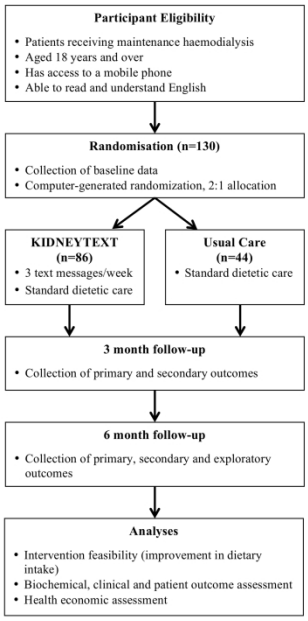

Figure 1: Study design and flow

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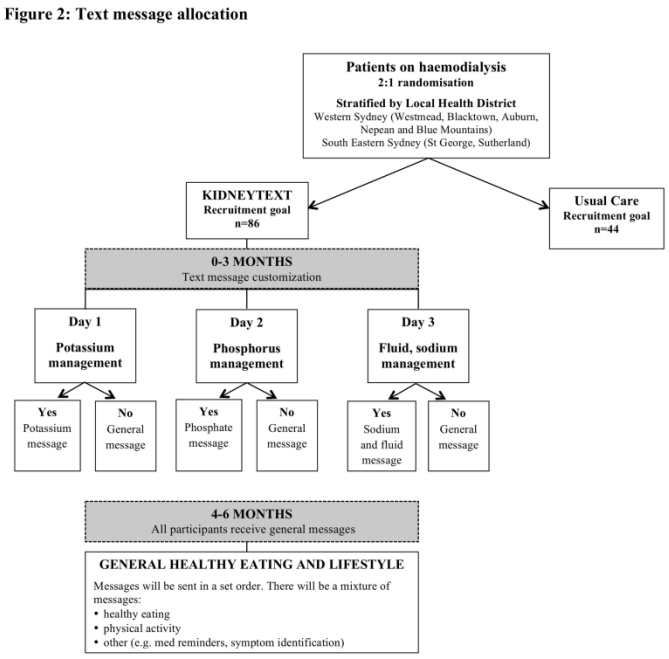

Figure 2: Text message allocation

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 2
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 4
	2b	All items from the World Health Organization Trial Registration Data Set	
Protocol version	3	Date and version identifier	October 2017, protocol
Funding	4	Sources and types of financial, material, and other support	Page 20
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 2, 3, 20
	5b	Name and contact information for the trial sponsor	N/A
	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	N/A
	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)	N/A

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	Page 6-8
	6b	Explanation for choice of comparators	Page 9
Objectives	7	Specific objectives or hypotheses	N/A
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)	Page 9
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	Page 9
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)	Page 9
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 9
	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)	Page 9 and 17
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Page 9
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	Page 13-14
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)	Page 14

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	Page 17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 9
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	Page 16
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	Page 16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 16
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 17
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 12
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	Page 14 and protocol
	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	Page 17

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	Protocol
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	Page 17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 17
	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)	Page 17
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	Protocol
	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	Protocol
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	Protocol
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 18
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)	Page 18

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 18
	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	Protocol
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 20
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	Protocol
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	Protocol
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	Page 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendix
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

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Citations

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-207.

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