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The Healthy Hearts and Kidneys (HHK) study: Design of a 2 × 2 RCT of technology-supported self-monitoring and social cognitive theory-based counseling to engage overweight people with diabetes and chronic kidney disease in multiple lifestyle changes

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Abstract

Patients with complex chronic diseases usually must make multiple lifestyle changes to limit and manage their conditions. Numerous studies have shown that education alone is insufficient for engaging people in lifestyle behavior change, and that theory-based behavioral approaches also are necessary. However, even the most motivated individual may have difficulty with making lifestyle changes because of the information complexity associated with multiple behavior changes. The goal of the current Healthy Hearts and Kidneys study was to evaluate, different mobile health (mHealth)-delivered intervention approaches for engaging individuals with type 2 diabetes (T2D) and concurrent chronic kidney disease (CKD) in behavior changes. Participants were randomized to 1 of 4 groups, receiving: (1) a behavioral counseling, (2) technology-based self-monitoring to reduce information complexity, (3) combined behavioral counseling and technology-based self-monitoring, or (4) baseline advice. We will determine the impact of randomization assignment on weight loss success and 24-hour urinary excretion of sodium and phosphorus. With this report we describe the study design, methods, and approaches used to assure information security for this ongoing clinical trial.

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1. Introduction and background

T2D is an epidemic in the US with the prevalence expected to double between 2005 and 2050 [1]. CKD also is an epidemic in the US, affecting 14.8% of US adults [2]. CKD is a common microvascular complication of T2D. Diabetic CKD progresses more rapidly than other forms of kidney disease, and is responsible for 44% of incident end-stage renal disease (ESRD) [3]. According to the recent estimates, annual per person per year Medicare expenses for CKD (but not ESRD) were \$19,075 for stages 1–2, \$21,176 for stage 3, and \$28,541 for stages 4–5; with total spending of \$52.8 billion [4]. Furthermore, ESRD Medicare treatment costs rose from \$31.8 billion in 2013 to \$32.8 billion in 2014 [5]. Research on approaches to slow progression of CKD is urgently needed.

Multiple lifestyle behaviors (obesity, sedentary lifestyle, and excessive dietary sodium and phosphorus intake) appear to contribute to the development and progression of CKD. Obesity is an independent risk factor for CKD [6–9] and is associated with proteinuria [10] and progressive CKD [11]. A systematic review of 13 nonsurgical weight loss intervention studies in CKD patients showed that weight loss reduced proteinuria and blood pressure and seemed to prevent further decline in kidney function [12]. Sedentary behavior also has been shown to be an independent risk factor for the development of CKD [13] and total and light physical activity are positively associated with kidney function [14]. While the literature does not provide definitive evidence that exercise training will slow CKD progression, a recent review of 29 studies shows that physical activity improves cardiovascular fitness, physical performance and function; improves quality of life; has anabolic effects; and mediates cardiovascular risk factors that are predictors of CKD progression [15]. Concurrent hypertension is quite common in those with T2D [16–18] and is a powerful predictor of CKD progression. Excess dietary sodium intake contributes to hypertension and blunts the effectiveness of some antihypertensive agents [19–21]. A recent clinical trial showed that dietary sodium restriction reduced ambulatory blood pressure, extracellular volume, proteinuria, and albuminuria in CKD patients [22]. Finally, several epidemiological studies suggest that serum phosphorus promotes CKD progression [23–29]. To our knowledge, no studies have been performed to test behavioral lifestyle interventions involving restriction of dietary phosphorus in stage 1–4 CKD.

In order to slow the progression of CKD in overweight T2D patients with stage 1–4 CKD, it may be necessary to restrict calories, sodium, and phosphorus, and for them to engage in physical activity. Changing a single behavior is difficult and decades of research have shown that the most effective interventions employ behavioral methods that target psychological determinants of behavior (e.g., attitudes, risk perceptions, and self-efficacy). However, behavioral methods alone may be insufficient for engaging overweight T2D patients with CKD in changing the multiple behaviors identified above. Lifestyle change requires

vigilance regarding the targeted behaviors. Vigilance is cognitively burdensome and, as newly adopted behaviors become routine, the person may stop paying attention and regress to former behavioral patterns [30,31]. Normal cognitive limitations in short-term memory also sharply limit the complexity of problems that people can realistically manage (e.g., What can I eat for dinner now and remain under my ceiling for multiple nutrients, given what I have already consumed today?) [32,33]. Vigilance and information burden result in confusion, frustration, and failure that, in turn, may undermine patients' confidence (self-efficacy) in their ability to make appropriate lifestyle behavior changes.

New mobile health (mHealth) technologies make it possible to reduce vigilance and information burden. While mHealth applications have become available to assist CKD patients in lifestyle and medication management [34–36], to our knowledge no studies have been done to demonstrate their efficacy.

2. Objectives

The purpose of the Healthy Hearts and Kidneys (HHK) study is to evaluate, compared to usual care, the efficacy of 3 different technology-supported intervention modalities for engaging individuals with T2D and concurrent CKD in multiple behavior changes including weight loss, physical activity, dietary sodium restriction, and dietary restriction of phosphate additives. With this report we describe the design and methods and, because of the unique nature of intervention delivery (i.e., using mobile technology) we describe the measures taken to assure information security.

3. Methods

3.1. Design

The HHK study is a 2×2 factorial, randomized controlled trial of overweight adults with T2D and concurrent CKD. Participants are randomized into 1 of the 4 groups: (1) mobile self-monitoring of diet and physical activity (hereafter “MONITORING”), (2) Social Cognitive Theory-based group behavioral counseling delivered via mobile technology videoconferencing (hereafter “SCT”), (3) both SCT and MONITORING (hereafter “COMBINED”), or (4) baseline advice regarding weight loss, physical activity, and restriction of dietary sodium and foods containing phosphate additives but no mobile self-monitoring or group behavioral counseling (hereafter “ADVICE”). All participants receive usual care throughout the trial.

Prior to randomization, participants are stratified by recruitment site. Within strata they are randomized using computer-generated permuted blocks with equal allocation. Participants are randomized to SCT or no SCT and, within SCT and no SCT groups, re-randomized to MONITORING or no MONITORING. Group assignments are illustrated in Fig. 1.

3.1.1. Primary aims—We will determine the impact of randomization assignment on weight loss success and 24-hour urinary excretion of sodium and phosphorus. Hypotheses: We will test the null hypotheses of no difference versus the two-sided alternative. We expect that the proportion of participants losing at least 5% of their baseline weight at 3 months will

be ADVICE < SCT < COMBINED, and reductions in 24-hour urinary sodium and phosphorus excretion at 3 months will be ADVICE < SCT < COMBINED. We expect these differences to be sustained at 6 months.

3.1.2. Exploratory aims—We expect that weight losses, and reductions in urinary sodium and phosphorus in the MONITORING group will be comparable to or somewhat less than the SCT group. However, because research on technology-based self-monitoring and dietary advice without the use of behavioral methods is limited, aims pertaining to the MONITORING group are exploratory. We will describe the impact of MONITORING on primary outcomes at 3 and 6 months, and differences compared with results observed in the other randomization groups. At 3 and 6 months we will describe between-group differences in physical activity, blood pressure, lipids, medication requirements, and vascular stiffness. We will describe the mediating influence of self-efficacy on all outcomes.

3.2. Recruitment, screening and enrollment procedures

Recruitment for HHK began in January 2016, and is expected to conclude in 2019. The study has been reviewed and approved by the New York University School of Medicine Institutional Review Board. To-date, participants have been drawn from New York University Langone Medical Center (NYULMC) and its affiliates as well as New York City Health and Hospital Corporation's Bellevue Hospital. Study advertisements also have been placed in newsprint circulars (amNewYork and Metro) that are distributed at New York City subway station entrances. Other potential recruitment sources are under consideration.

3.3. Sample size requirements

The target population for this study is 300 overweight adults, living in the greater New York City area. Final sample size estimates were based upon the number of participants required to determine between group differences using 2-tailed z tests for two independent proportions, 80% power, and alpha of 0.008 (to account for 6 multiple comparisons among 4 groups), and taking into consideration an expected drop-out of 20%. The study was powered to determine whether or not the intervention conditions resulted in a weight loss of at least 5% of baseline, as weight losses as small as 5% have been shown to result in clinically significant improvements in this population [37]. In the SMART study which was performed in healthy participants, Burke et al. showed that an intervention similar to the COMBINED arm resulted in a 6-month weight loss of 7.3% (SD 6.6%) [38]. Because HHK participants are insulin resistant and sometimes prescribed medications (e.g. insulin) that result in weight gain, we conservatively assumed that 50% of COMBINED participants would achieve a weight loss of at least 5% at 6 mos. Also, in the absence of intervention, most patients with T2D would be expected to gain weight [39]. We conservatively assumed that 1% of ADVICE participants would achieve a weight loss of at least 5% at 6 months. Because we expected that, even the most motivated participant would have difficulty making multiple behavior changes due to information complexity, we conservatively assumed that 20% of the SCT group would achieve a weight loss of at least 5% at 6 mos. With a final retained sample of 240 (60 per group) we can detect the expected differences between ADVICE and COMBINED with > 90% power, ADVICE and SCT with 82% power, and COMBINED and SCT with 84% power. We expect that MONITORING group weight losses will be

comparable or less than SCT weight losses. However, we are unaware of studies showing the extent to which weight loss can be expected from self-monitoring alone (i.e. in the absence of behavioral intervention), and so analyses pertaining to the MONITORING group are exploratory.

In the TONE Study, compared to those randomized to groups not counseled about sodium, those counseled to reduce sodium intake to 1800 mg/day (higher than our recommended ceiling as discussed in Section 3.6 below) excreted 1072 mg/day less sodium at 9 mos, 1134 mg/day less at 18 mos, and 909 mg/day at 30 mos [40]. This level of dietary restriction was effective in significantly reducing the reoccurrence of hypertension in TONE participants. In our sample, we anticipate that the baseline sodium excreted in 24 h will be consistent with that observed in TONE (mean = 3594 mg/d SD = 1282). With a sample of 240 (60/group), using a 2-tailed two sample *t*-test and a significance level $\alpha = 0.008$, we can detect, with 80% power, differences from baseline in urine sodium excretion as small as 830 mg/day.

The Kidney Stone Study (KSS), an epidemiologic investigation of the risk factors associated with the development of kidney stones, was conducted as an ancillary study to the Nurses' Health Study, Nurses' Health Study II, and the Health Professionals Follow-up Study. While the size of a clinically significant reduction is unknown, the KSS study showed the mean 24-hour urinary phosphorus excretion at baseline to range from 738 mg/day (SD = 221) to 1032 mg/day (SD = 300) [41]. Conservatively assuming the larger SD, with a sample of 240 (60/group), using a 2-tailed two sample *t*-test and a significance level $\alpha = 0.008$, we can detect differences from baseline in urinary phosphorus excretion as small as 194 mg/day with 80% power. Table 1 provides the smallest effects that we will be able to detect in other exploratory variables with the final sample of 240, $p = \alpha = 0.008$, and 80% power.

3.4. Eligibility

3.4.1. Inclusion criteria—Participants must be 40 years of age or older, overweight/obese [Body Mass Index (BMI) ≥ 27.0 kg/m²], with T2D and evidence of CKD. To recruit from clinical practice settings, we abstract the electronic medical records (EMRs) of individuals receiving care from participating providers via EMR platforms (e.g., Epic, Quadramed). We generate a list of potentially eligible patients, including those who have an ICD code consistent with T2D, and one or more of the following: an ICD code consistent with Stages 1–4 CKD or albumin-to-creatinine ratio (ACR) > 30 mg/g or 2+ proteinuria or an estimated glomerular filtration rate (eGFR) 15–89 ml/min. Clinicians also may make direct referrals to the study. Those who self-refer from community sources must report a diagnosis of T2D and a medication management regimen consistent with T2D, and report having been informed by their physician that they have CKD or proteinuria. If deemed eligible with telephone screening, physician clearance to participate in the study is subsequently obtained. Regardless of recruitment source, prior to enrollment, the physician of record must indicate that weight loss, sodium restriction, and 150 min/week of moderate intensity physical activity are not contraindicated for the participant.

3.4.2. Exclusion criteria—We exclude from participation those with the following characteristics: unable or unwilling to provide informed consent; unable to participate

meaningfully in an intervention that involves group sessions (e.g., due to uncorrected hearing impairment); unable to read or otherwise use an iPad to monitor dietary intake, physical activity, and weight using software that is available in English only (e.g., blind, illiterate, non-English-speaking); unwilling to accept randomization assignment; pregnant, or plans to become pregnant in the next 12 months, < 3 months postpartum, or nursing or within 6 weeks of having completed nursing; weight loss of > 10% in the past 6 months except for postpartum weight loss; unable to walk 0.25 miles in 10 min; planning gastric bypass surgery in the next 12 months, or individuals who are institutionalized (e.g., in a nursing home or personal care facility, or those who are incarcerated and have no control over their diet). We also will exclude from the study those with underlying diseases that would increase the risk of participating in an intervention involving caloric restriction and physical activity. Such individuals would include those requiring treatment for cancer, exclusive of skin cancer other than melanoma, in the past 2 years; infectious diseases including untreated AIDS and active tuberculosis; persistent, uncontrolled hypertension of > 190 mmHg systolic blood pressure or > 105 mmHg diastolic blood pressure despite treatment; stroke or transient ischemic attack in the past 6 months; conditions requiring the use of home oxygen; advanced congestive heart failure; other end-stage diseases; or other chronic disease or condition likely to limit life span to < 1 year.

3.5. Measurements

Data are collected during measurement visits through self-administered questionnaires and records, physical exams, and fasting blood and urine tests. Approximately four weeks prior to measurements, a phone screening questionnaire is conducted to determine the participant's overall eligibility. Those deemed preliminarily eligible during the phone screening are then scheduled for baseline assessments. Table 2 outlines the various measures obtained at each assessment time point. Baseline visits include two assessments within a 7–10 day interval. At the first assessment, eligibility is verified, informed consent is obtained, and weight, height, blood pressure, and pulse wave velocity are collected. Those deemed eligible receive a packet of questionnaires, a 3 day-food diary, and a urine container with instructions (verbal and written) for collecting a 24-hour urine sample. Videos demonstrating the correct approach to completing the food diary and collecting the 24-hour urine sample are shown. Prior to the second assessment, participants receive a phone call to remind them of their appointments, and to complete the food diary, and collect their urine. At the second assessment, completed self-administered questionnaires and food diaries are collected and reviewed for accuracy and completeness. Urine specimens and fasting blood samples are obtained. At 3 and 6 months, a single follow-up assessment visit is scheduled at which time similar measurements are obtained. The study questionnaires, 3-day food diaries and urine containers with instructions, as well as 3 and 6 month monitoring forms, are mailed to participants at least 2 weeks in advance. For the first 4 cohorts, participants received a \$20 incentive for completion of each of the 4 assessment visits. As a retention incentive, beginning with cohort 5, participants received a \$20 incentive for completion of the first baseline assessment visit, and \$50 for each of the 3 subsequent assessment visits for which they produce a 24-hour urine sample.

3.6. Intervention

The intervention phase lasts 6 months. All participants continue to receive usual care throughout the duration of the study. All participants are provided with a baseline prescription for diet and physical activity. The Mifflin St. Jour equation [42] is used to estimate the resting metabolic rate of the participant, which we multiply by an activity factor of 1.4 and subtract 500 kcals/day to create an energy deficit, but maintain a minimum threshold of 1200 kcals/day. Participants also are encouraged to reduce their dietary sodium to 1500 mg/day. They are advised to read food labels and avoid consumption of foods containing phosphate additives in their ingredients lists. They are instructed in how to safely and gradually increase the duration of physical activity to 150 min/week and, once they achieve that goal, to increase physical activity intensity to moderate. The manner in which these targets are conveyed to participants varies by randomization group as described below. Aside from advising participants of all groups that the proposed lifestyle changes may reduce medication requirements, no counseling regarding medication management is offered.

3.6.1. MONITORING—Participants in the MONITORING group are provided with an iPad and a 4G connection service plan (iPad Air 2; Apple Inc., Cupertino CA, USA). These participants use iPads to: (1) attend, via WebEx® video-conference, group educational sessions regarding the nature of CKD and lifestyle changes that may slow progression of the disease, and (2) engage in daily electronic self-monitoring of all meals and snacks, physical activity (daily), and weight (at least once/week), and (3) receive self-monitoring feedback from study dietitians, which is sent directly to a study-assigned email address linked to their device. After randomization, participants attend 1–2 face-to-face training sessions with a research assistant on the operation of the iPad and use of the study applications described below.

WebEx® (Cisco Systems Inc., San Jose CA, USA) is used to deliver 14 educational modules (outlined in Table 3). These modules are delivered weekly during the first 4-weeks, and every other week thereafter. Sessions last approximately 1 h or less, and are presented by the study dietitian. A brief video (~10 min) summarizing the content of each session is placed on the study website for participants to view if they miss or wish to review the content following the session. Videos are configured using Brainshark® (Brainshark Inc., Waltham MA, USA), which records per-participant time devoted to viewing the videos.

Participants are provided a MyNetDiary® (hereafter MND®; MyNetDiary Inc., Cherry Hill NJ, USA) account, programmed with their dietary prescription as described above, which they use to record meals and snacks, physical activity, and weight. MND® provides real-time feedback about the nutrient content of meals and snacks consumed, % of dietary targets consumed with each entry, and chart and line graph interfaces for tracking trends over time. Participants are encouraged to enter food and exercise in real time, and record their body weight at least once per week. Participants are provided bathroom scales if they do not have one. Study dietitians review participants' MND® records weekly during the first 4 weeks, and every other week thereafter. At each of these time points, participants receive standardized feedback messages that are tailored to reflect the individual participant's

adherence to the intervention protocol and progress made toward study goals. Email content and example messages are shown in Table 4.

3.6.2. SCT—Participants in the SCT arm also receive an iPad, training, and the same WebEx® educational sessions as the MONITORING arm, but no subscription to MND®. Immediately following the educational session, SCT participants are exposed to dietitianled, WebEx® group behavioral counseling sessions that are based on Bandura's Social Cognitive Theory. This theory postulates that behavior change is influenced by the individual's perceived self-efficacy, or belief in their capacity to overcome conflicting demands to achieve the desired outcomes [43]. Self-efficacy is derived from four major sources of information: mastery experiences, social modeling, verbal persuasion, and physiological states. **Mastery experiences** include emphasizing past successes; setting incremental, easily achievable goals; identifying modifiable barriers to healthy behavior; receiving positive feedback on goal achievement; and practicing problem solving skills around barriers to adherence. With **social modeling**, mastery is enhanced when participants share with each other their successes and help each other problem-solve around barriers. **Verbal persuasion** includes emphasizing the participant's previous successes to demonstrate their capability (e.g., "As a result of your effort, you lost a pound last week. You can do it again.") We encourage participants to share their observations regarding **physiologic benefits** that they experience from the intervention (e.g. looser clothing, more energy, better sleep, better glucose or blood pressure control). Short videos summarizing the SCT content are uploaded to a study web site and configured with Brainshark®. Each SCT session lasts approximately 1 h.

3.6.3. COMBINED—Participants in the COMBINED arm receive all of the elements of the MONITORING and SCT arms, with 14 group videoconferencing sessions lasting approximately 1 h. The intervention components for each of the four groups are summarized in Table 5.

3.6.4. ADVICE—Participants randomized to the ADVICE arm are sent information about the above-described targets via US mail, which is then followed by a telephone call to discuss these recommendations. As a retention tool, ADVICE participants receive monthly newsletters, sent to them via US mail. At the end of the study, ADVICE participants are provided with a flash drive or DVD (per their preference) containing video summaries of educational and SCT-based sessions delivered to the COMBINED group as described above.

3.7. Safety

Participants are monitored to assure that weight losses do not exceed an average of 2 lb/week or BMI does not fall below 24 kg/m². Participants with excessive weight loss receive 1:1 evaluation by the study dietitians to assure proper nutritional intake and are advised to either slow the rate of weight loss or, when a BMI of 24 kg/m² is achieved, change the weight goal to one of maintenance.

The physical activity goal involves a conservative, stepped approach that focuses on slow progression to safely reach an activity goal of 150 min/week of moderately intense activity

similar to that successfully used in national clinical trials of sedentary individuals at high risk for diabetes (e.g., the Diabetes Prevention Program) [50] or who have diabetes (Look AHEAD) [51]. This goal is also in line with the 2008 Physical Activity Guidelines for Americans [52] as well as current American College of Sports Medicine and American Heart Association recommendations pertaining to those who are elderly and/or have chronic diseases [53]. Participants who experience myocardial infarction, unstable angina, symptoms suggesting angina pectoris, a percutaneous transluminal coronary angioplasty or a coronary artery bypass graft procedure during the study will be referred back to their physician of record for re-evaluation of their ability to safely participate in the exercise component of the study. The participant will be advised to discontinue the exercise program until the study team receives additional clearance from their physician of record. In the interim, participants may continue to participate in dietary intervention activities. The participant's physician of record is alerted when laboratory values listed in Table 6 are observed.

3.8. Intervention protocol adherence

Study staff personnel monitor attendance to the MONITORING, SCT, and COMBINED sessions. Participants who miss sessions are sent emails containing web links to Brainshark® videos that summarize the intervention content delivered. As noted above, Brainshark® permits quantification of the amount of time each participant devotes to reviewing intervention videos.

For those using MND®, adherence to self-monitoring is abstracted remotely from the MND® electronic record. As noted above, emails are generated for MONITORING and COMBINED participants who are using MND®. The emails note the participant's adherence to self-monitoring. Participants who monitor most days of the week (4 days) receive encouraging messages to continue with their frequency of self-monitoring. Participants who monitor some days of the week (1–3 days) are encouraged to increase the frequency of self-monitoring to achieve the goals of the intervention. Participants who are not monitoring (0 days) are encouraged to begin tracking to increase their likelihood of successfully meeting behavioral targets. All participants are offered the opportunity to ask questions, request assistance, or schedule retraining to encourage adherence to self-monitoring using the tools of the program.

Protocol adherence in the first 3 cohorts completing the study to-date appear in Table 7. Attendance at WebEx® sessions and adherence to dietary self-monitoring using MND® were lower than expected. To minimize the possibility that nonadherence may have been due to participants' confusion regarding use of the technology, we redesigned our training materials to include colored, hard copies of iPad screen-shots. The screenshots illustrate the sequence of using the technology, from the point of entering the security code to using the email, WebEx®, and MND® applications. Participants leave the training session with these materials which they can reference at home when using the iPad. Adherence rates of subsequent cohorts appear to have improved. However, these cohorts have not yet completed final measurements and efforts to evaluate adherence are ongoing.

3.9. Planned statistical analyses

An “intent-to-treat” (ITT) approach will be used to address the specific aims. We will first test the interaction effect between SCT and MONITORING at 3 months and 6 months using the primary outcomes separately. The test will be performed using the 2-way ANOVA model through PROC GLM SAS procedure in which other covariates will be adjusted. To investigate specific group differences, we will conduct the following longitudinal analyses between the 4 randomization groups.

The statistical modeling of the baseline, 3 month, and 6 month outcome variables will be based on linear mixed models (for continuous outcomes), logistic generalized linear mixed models (for binary outcomes), and random effects multinomial models (for outcomes with > 2 levels, such as adherence). In all models, clinical site, stage of CKD, time (3 dummy variables), and treatment allocation will be included as fixed effects, and the participant will be the random effect. The intervention effect of interest is the treatment X time interaction in this model. Identified predictors of missing data will be included as covariates in this random effects framework, to provide unbiased estimates of the intervention effect under an assumption of missing at random (i.e., missingness depends on observed covariates but not on unobserved covariates). We will conduct sensitivity analyses to assess plausible departures from this assumption. Other demographic and clinical covariates will be included as necessary in adjusted analyses. In particular, medications will be recoded as 6 dummy variables reflecting the expected impact on primary outcomes (i.e., whether or not the medications could result in weight loss, weight gain, reduced urinary sodium excretion, increased urinary sodium excretion, reduced urinary phosphorus excretion, increased urinary phosphorus excretion). These variables will be used to characterize the medication regimen at baseline and follow-up measurement visits. We will check the balance of these features of the medication regimen across intervention arms and incorporate these variables as time varying covariates in our models. Model assessment will be conducted using appropriate regression diagnostics. Post hoc multiple comparison tests, such as Tukey or Tukey-Kramer method, will be applied to adjust the pairwise comparisons across different treatment groups at single measurement time. For the longitudinal modeling, we will use the resampling method to adjust the post hoc testing to address the correlated comparisons [44].

3.10. Information security

Those who intend to use mHealth approaches in research with or without delivery of care to clinical populations must be aware of potential information security risks and take necessary precautions. Mobile carriers and cloud-based applications generally require End User Licensing Agreements (EULAs). EULAs specify the terms of the contract, maintenance, use restrictions, and indemnifications. Particularly relevant for the our study, EULAs often permit licensors to use and share the purchaser’s data with third parties, usually for marketing purposes. Additionally, mobile devices are increasingly the target of cyber attacks. In particular, use of a mobile device on an unsecure WiFi network increases the likelihood of being hacked. A lost or stolen device, or a device that has been hacked can be used to steal identity or credit card information, make unauthorized purchases, or result in exposure of personal information. Some apps are designed specifically to steal, spy, or destroy. To eliminate concerns regarding sharing of personal information as part of a

licensing agreement and otherwise minimize security risks, the following steps were taken by the Healthy Hearts and Kidneys study.

First, we minimize reliance on WiFi connections by providing participants with 4G iPads and Verizon data plans. Factory-installed apps are grouped in one folder labelled “Restricted”, and placed in a separate page on the iPads. Participants are informed, during trainings, not to use factory-installed apps. iPads, apps, and accounts (MND[®], WebEx[®], and Brainshark[®]) are purchased by and registered to NYULMC rather than the individual participant. A single Apple ID, belonging to the program coordinator, is used to purchase and download study-required apps to the iPad (i.e. the participant is unable to download additional, potentially malicious, apps). To further circumvent unauthorized app purchases, updates (which could jeopardize security of personal information) and app deletions, “App Store” and “Safari” (internet browser) apps are hidden and fully locked. Email addresses are created for each iPad and contain no personal identifiers; personal email addresses are neither used nor linked to the iPad and all email communications occur via the account registered to the iPad. In addition, the iPad account feature is also fully locked, therefore the participant is unable to change or add his/her personal email address. Identifiers are not used (e.g., full name is replaced with first name only or study ID, birthdays are standardized to “1-1-XXXX” format, etc.). For the first 4 cohorts enrolled in the study, staff created Gmail[®] email accounts. To further secure the information communicated, in subsequent cohorts, the study employed institutional email addresses on a server dedicated to clinical trials (i.e., behind the NYULMC firewall so that emails never “touch” the internet). The security settings on the new email system allow participants to send emails to NYUMC-only email domains. A 4-digit security code is required when the iPad is first turned-on and after the iPad is idle for 5 min. iPads are secured with MaaS360[®], a mobile device management program that is used to remotely review security settings and locate or scrub iPads that are lost or stolen. In January 2017, the study began using AirWatch[®], an alternative to MaaS360[®]. After a participant completes the trial, all the applications on the iPads are reset and all data stored in the device are wiped-out before the iPad is re-deployed for the next participant.

3.11. Limitations and strengths

The HHK study has several limitations. In particular, the study is not powered to determine the impact of the interventions on CKD progression. The sample is drawn from a single geographic region. While it is not possible to blind study staff to randomization group assignment, bias is minimized by excluding interventionists from follow-up measurement visits. Due to budget constraints, it is not possible to hire different interventionists for each of the 3 randomization arms. Crossover effects are minimized by: 1) having a separate interventionist generate tailored MND[®] feedback, 2) using PowerPoint slides to guide discussion content, and 3) videorecording all sessions with investigator review of 10% to monitor fidelity.

HHK also has several strengths. In particular it addresses an understudied problem, namely to determine the efficacy of alternative approaches for engaging those with complex disease in multiple behavior changes. The study design is a randomized clinical trial. Behavior

change is evaluated using measures that do not rely on self-report. Participants are able to attend group counseling sessions from a location convenient to them. Participants who self-monitor using MND[®] obtain immediate feedback regarding their dietary intake and energy expenditures, and the MND[®] is used to provide tailored feedback about adherence and achievement of study goals. The study provides iPads to all participants which minimizes sampling bias that would occur from requiring participants to own and use their own technology. It also permits study staff to standardize the appearance, operation, and participant training materials, and minimize information security risks. If determined to be efficacious, the frequency of intervention contacts is consistent with Medicare coverage for intensive weight loss counseling which enhances the potential for downstream dissemination.

4. Conclusion

mHealth technologies provide new opportunities to improve the management of complex chronic disease, in a manner that does not require participants to travel to a central location. Although there is considerable interest in adopting mHealth into healthcare systems, evidence is limited regarding how best to implement these technologies. The HHK study will evaluate the independent effects of SCT and MONITORING, and their interaction effects compared to ADVICE. The findings from this study will provide valuable information for researchers and healthcare systems interested in implementing mHealth technologies into clinical practice. Steps used by the study to maintain the security of personal health information may be useful for others planning to implement counseling interventions using mHealth technology.

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Fig. 1.
Randomization scheme for the Healthy Hearts and Kidneys study.

Table 1

Smallest detectable effects in exploratory outcomes of the Healthy Hearts and Kidneys study.

Exploratory outcomes	SD	d
LDL (mg/dl)	38.6	25
HDL (mg/dl)	13.8	8.9
Triglycerides (mg/dl)	96.8	62.7
Systolic BP (mmHg)	18.8	12.2
Diastolic BP (mmHg)	10.0	6.5
Carotid-femoral pulse wave velocity (cm/s)	280.0	181.3
Brachial-ankle pulse wave velocity (cm/s)	920.5	596.1

Table 2

Measurement summary and data collection time-points for the Healthy Hearts and Kidneys study.

Measures	Months		
	0	3	6
Primary outcomes			
Weight: % of baseline weight lost	X	X	X
Dietary sodium intake: 24-hour urinary sodium excretion	X	X	X
Dietary phosphorus intake: 24-hour urinary phosphorus excretion	X	X	X
Secondary outcomes			
Physical activity: International Physical Activity Questionnaire Short Form [45].	X	X	X
Blood pressure: right arm, resting, recumbent position	X	X	X
Serum lipids (fasting): Total cholesterol, triglycerides, HDL-cholesterol, and derived LDL-cholesterol	X	X	X
Vascular stiffness: pulse wave velocity (AtCor Medical, Itasca, IL)	X	X	X
Changes in medication regimen: medication inventory	X	X	X
Changes in dietary patterns: 3 day diet diary records analyzed with Nutrition Data System for Research (Version 2.91, University of Minnesota, Minneapolis MN)	X	X	X
Mediators			
Self-efficacy for weight loss: Weight Efficacy Lifestyle Questionnaire [46].	X	X	X
Self-efficacy for reducing dietary sodium intake: Selected items from the BalanceWise Dietary Self-Efficacy Scale [47].	X	X	X
Self-efficacy for physical activity: Self-Efficacy for Exercise (SEE) Scale [48].	X	X	X
Covariates			
Sociodemographic characteristics and health habits: Investigator-developed instrument to assess ethnicity, gender, age, income, education, employment, and insurance, smoking, and use of alcohol	X		
Body Composition: bioelectrical impedance analysis beginning with cohort 3 (Omron Healthcare, Inc., Lake Forest, Illinois)	X		
Glomerular filtration: creatinine clearance and eGFR	X		
Nephropathy: 24-hour microalbuminuria	X		
Comorbidities: Self-reported Charlson Comorbidity Index [49].	X		
Glycemic control: HbA1c	X		
Medication regimen	X		

Table 3

Summary of topics for the education and Social Cognitive Theory components of the Healthy Hearts and Kidneys Study.

Week	Education content delivered to MONITORING, SCT, and COMBINED groups	Behavioral counseling content delivered to SCT and COMBINED groups
1	Study goals and rationale: <ul style="list-style-type: none"> Effect of obesity, sedentary lifestyle, and sodium- and phosphorus-based food additives on CKD Being a good group member 	Goals for life: <ul style="list-style-type: none"> Establishing relevance of goals Clarifying personal values
2	Being a calorie detective: <ul style="list-style-type: none"> Major contributors to energy intake Role of portion sizes and empty calories in excess energy intake 	Where am I?: <ul style="list-style-type: none"> Establishing baseline behavior Identifying discrepancies between actual and ideal behavior
3	Move those muscles: <ul style="list-style-type: none"> Introducing physical activity into your life Choosing the right type of exercise 	Setting goals: <ul style="list-style-type: none"> How and why to set goals Short-versus long-term goals Engage the group in goal setting for energy intake and physical activity
4	Being a fat detective: <ul style="list-style-type: none"> Identifying fat in the diet (e.g., hidden fats, reading nutrition facts panel) Types of dietary fats, and their relation to CVD risk 	Taking credit for your success: <ul style="list-style-type: none"> Recognizing the emotional, social, economic and physiological benefits of successful behavior change Turning behaviors into healthy habits to reach goals with self-reward
5	Sodium and blood pressure: <ul style="list-style-type: none"> Processed foods and sodium intake Using the nutrition facts panel to assess sodium content of processed foods Knowing your numbers and when medical evaluation for a change in blood pressure management is needed 	Would a partner or social support help?: <ul style="list-style-type: none"> Why social support can be important How to develop and work with your social support network
6	Changing seasons, special occasions and life events <ul style="list-style-type: none"> Impact of life events and special occasions on lifestyle behavior 	Problem solving: barriers and challenges: <ul style="list-style-type: none"> Using the problem-solving model to identify potential challenges and identify facilitators to healthy behaviors
7	Phosphorus and Blood Vessel Disease: <ul style="list-style-type: none"> Effect of excess phosphorus on bones and blood vessels in CKD Using the ingredients list to identify phosphorus additives in processed food 	Problem Solving - Behavioral Triggers: <ul style="list-style-type: none"> Stimulus control, identifying behavioral triggers, avoiding cues to unhealthy behavior, and altering response to behavioral cues
8	Aerobic exercise: <ul style="list-style-type: none"> Finding aerobic exercise that you enjoy Achieving moderate intensity exercise 	Problem solving - stress management: <ul style="list-style-type: none"> Role of stress in successfully establishing healthy habits and achieving goals

Week	Education content delivered to MONITORING, SCT, and COMBINED groups	Behavioral counseling content delivered to SCT and COMBINED groups
	<ul style="list-style-type: none"> Knowing your limits and staying safe 	<ul style="list-style-type: none"> Strategies for responding to stressful situations/ events
9	Eating out of cans, bags and boxes: <ul style="list-style-type: none"> Limiting processed foods (e.g., low-cost solutions for healthy eating) Using food labels to choose healthier processed foods 	Problem solving - emotional eating: <ul style="list-style-type: none"> Difference between emotional eating and physical hunger Strategies to prevent and deal with emotional eating
10	Starting the day right: <ul style="list-style-type: none"> Role of breakfast and meal frequency in managing energy intake 	Problem solving - self-talk: <ul style="list-style-type: none"> How negative self-talk can interfere with your efforts to establish healthy habits and achieve goals Strategies for establishing positive self-talk
11	Healthy snacking and sugar-sweetened beverages: <ul style="list-style-type: none"> Contribution of mindless snacking and sugar-sweetened beverages to empty calorie intake Choosing healthy snacks and beverages 	Problem solving - habitual overeating: <ul style="list-style-type: none"> Habit versus hunger Strategies to avoid overeating
12	Building muscle with strength training: <ul style="list-style-type: none"> How and why to incorporate strength training into your physical activity routine 	Problem solving – high-risk situations: <ul style="list-style-type: none"> High-risk situations that interfere with efforts to establish healthy habits and achieve goals Strategies to anticipate and deal with high-risk situations
13	Adding more color to your diet: <ul style="list-style-type: none"> How and why to incorporate many colorful fruits and vegetables into your diet 	Lapses, relapses and collapses: <ul style="list-style-type: none"> How to avoid a continuation of relapses that result in a final collapse
14	Putting it all together: <ul style="list-style-type: none"> Review of study goals and tools to use moving forward 	Changing lifestyle behavior to achieve study goals: <ul style="list-style-type: none"> Review of progress made, problems encountered and plans moving forward

Table 4

Examples of email messages sent to MONITORING and COMBINED participants of the Healthy Hearts and Kidneys study.

Email content	Examples
Frequency of self-monitoring	<ul style="list-style-type: none"> • Wonderful job keeping up with tracking everything you eat and drink daily! Research shows frequency of self-monitoring is associated with weight loss success. Your commitment to tracking has contributed to your own success! Great job! • Good job using MyNetDiary to record the days you were physically active! This week's lesson was on aerobic activity. Work on incorporating what you've learned into your daily routine to help meet your weight loss goals. Keep in mind, the goal is to gradually achieve 30 min per day of brisk intensity (makes you huff and puff, comparable to a brisk walk) on at least 5 days during the week. • Great job continuing to enter your weight into MyNetDiary! Remember to enter your weight at least one time per week – frequency of self-monitoring is associated with successful weight loss!
Reinforce efforts to continue, resume, or begin self-monitoring	<ul style="list-style-type: none"> • It looks like you missed tracking some days during this period. We encourage you to resume use of MyNetDiary to track your food and drinks daily. Studies show that recording everything you eat and drink is associated with weight loss success! • We encourage you to consider logging any activity in your day, for example, walking during lunch, or taking the stairs. Remember, the goal is to reach 30 min per day, most days per week, to meet your weight loss goals! • You've done a great job so far! You're in the home stretch! Even if you haven't been using MyNetDiary, it's not too late to resume. We encourage you to take full advantage of the tools of the program during your final weeks.
Progress made toward intervention goals	<ul style="list-style-type: none"> • Good job getting started with physical activity and recording the time in MyNetDiary! Physical activity helps with weight loss, blood sugar control, and makes you feel good! Keep in mind that the goal is to gradually achieve 30 min/day on at least 5 days a week to help meet your weight loss goal. • Continue to review your MyNetDiary food record to identify the foods that are contributing to your sodium intake. Processed meat, like deli ham, is a high contributor. The goal is to reach the 1500 mg sodium limit by the end of the program. • You've lost 12 lb since starting the program! This exceeds your original weight goal for the duration of the study – amazing job! Celebrate your success!
Tip of the week	<ul style="list-style-type: none"> • Special occasions can still be fun while making healthy choices! Have a healthy snack before you arrive to take the edge off hunger so you can focus on the company and conversation! • Identifying phosphorus in processed foods can require some detective work. Be sure to check nutrition labels for any ingredient containing the word "phos." • Breakfast can set the tone for your entire day. Be sure to eat a healthy breakfast that includes fiber from fresh fruit, vegetables, or whole grains to control blood sugar and avoid overeating later in the day.

Table 5

Intervention components for the Healthy Hearts and Kidneys study.

Intervention components	Groups			
	ADVICE	MONITORING	SCT	COMBINED
Baseline advice regarding recommended lifestyle behavior changes, videos summarizing content delivered to COMBINED shared after the study concludes	X			
Educational sessions regarding T2D and strategies for limiting CKD progression, delivered via WebEx® weekly in weeks 1–4, and biweekly in weeks 5–24		X	X	X
MND® self-monitoring of diet, physical activity and weight with standardized feedback emails sent weekly in weeks 1–4, and biweekly in weeks 5–24		X		X
Behavioral counseling based on principles of Social Cognitive Theory, delivered via WebEx® weekly in weeks 1–4, and biweekly in weeks 5–24			X	X

Table 6

Critical laboratory alert values that trigger notification of the physician of record in the Healthy Hearts and Kidneys study.

Laboratory values	Alert levels
Serum calcium (mg/dl)	< 6.1 or > 12.0
Serum sodium (mEq/l)	< 120 or > 159
Serum potassium (mEq/l)	< 2.8 or > 6.1
Serum carbon dioxide (mEq/l)	< 11 and > 40
Serum glucose (mEq/l)	< 50 or > 500 ^a
Blood urea nitrogen (mg/dl)	> 75
Serum creatinine (mg/dl)	Increase > 25% of baseline

^a Study participant is contacted if serum glucose > 300 mg/dl.

Table 7

Adherence to the intervention protocol in the Healthy Hearts and Kidneys study.

Adherence	MONITORING (<i>n</i> = 12)	SCT (<i>n</i> = 12)	COMBINED (<i>n</i> = 14)
Median attendance at WebEx [®] sessions: % (IQR)	62.2 (51.9–91.7)	53.3 (32.8–66.7)	50.0 (44.4–57.6)
Median proportion of days entering at least 1 meal/day in MND [®] : % (IQR)	71.4 (27.6–81.7)	NA	68.0 (28.6–92.9)
Median number of meals/day entered into MND [®] : Meals (IQR)	2.3 (0.9–2.7)	NA	2.1 (0.9–3.2)