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Study Title: *NEAT!2* Sedentary Behavior Reduction Intervention for Individuals with Past or Present Knee Symptoms, Injuries, or Surgeries*

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*Study stopped due to COVID-19 pandemic

A. SPECIFIC AIMS

The purpose of this proposed project is to conduct a randomized controlled trial to evaluate the effect of an mHealth sedentary reduction program (*NEAT!2)* over a 6 month period of time in adults with past or present knee symptoms, injuries, or surgeries. The specific aims of the project are:

Aim 1: To compare the change in sedentary behavior from baseline to 1 and 3 months between a smartphone app delivered sedentary reduction intervention with (*NEAT!2+Calls)* or without (*NEAT!2)* coaching calls and a delayed control (*Delayed NEAT!2)* in adults with past or present knee symptoms, injuries, or surgeries.

Aim 2: To examine the changes in physical function after participating in the *NEAT!2* or *NEAT!2+Calls* mHealth sedentary reduction interventions as compared to control from baseline to 1 and 3 months in adults with past or present knee symptoms, injuries, or surgeries.

Aim 3: To examine the maintenance in changes in sedentary behavior and physical function during the follow-up period between 3- and 6- months with no intervention contact in those who were initially randomized to *NEAT!2* or *NEAT!2+Calls.*

B. BACKGROUND AND SIGNIFICANCE

Sedentary behavior is defined as "any waking behavior characterized by an energy expenditure of ≤ 1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture."[1] Excess sedentary behavior is associated with numerous health consequences[2-4] including poor physical function.[5] Older adults with symptomatic knee pain spend the majority of waking hours engaged in sedentary behaviors.[5] To reduce the risk of disability, improve quality of life, and prevent deterioration in physical function,[6,7] it is critical to develop ways to decrease sedentary time. Several studies have started to explore preliminary ways to reduce sedentary time in older adults,[8-10] however, to our knowledge, few studies have been done in older adults with current or past knee symptoms. Smartphone ownership among older adults is increasing and may provide a scalable opportunity to disseminate a sedentary reduction intervention. Therefore, this study aims to evaluate and compare changes in sedentary behavior between an mHealth sedentary reduction, mHealth intervention plus coaching, and delayed control group.

C. PRELIMINARY STUDIES

Using data obtained from the Osteoarthritis Initiative, we evaluated physical activity levels and sedentary behavior in adults with or at risk of developing knee osteoarthritis (KOA). Adults with KOA spend at least 2/3 of waking hours in sedentary behaviors.[11] We have found that greater amounts of time engaged in sedentary behaviors are associated with functional decline, lower quality of life, and weight gain.[7,11,12] We have previously identified barriers and facilitators to physical activity in adults with KOA prior to having knee replacement. Barriers for activity included pain, physical limitations, and lack of motivation, whereas facilitators included having motivation to improve knee symptoms/outcomes, personal commitment to activity, and monitoring activity levels.[13]

Although this population is interested in being active, they are limited by knee pain. It is unclear how willing this population would be to decrease sedentary time, which may be a more feasible approach for those with knee pain. Additionally, those with end-stage KOA who recently had knee replacement are engaging in sedentary behavior ~69% of the day (manuscript in preparation).

Nine adults (53.1±10.7 years, BMI 37.4±9.9kg/m^2) with diabetes used the *NEAT!* app on 21.9±8.0 days/month. *NEAT!* interrupted continuous bouts (≥20 minutes) of sitting by providing prompts on the smartphone to engage in light-intensity activity for ≥2 minutes. Prompts to interrupt sedentary time were given 5.8±3.5 times/day. Participants reduced their sedentary time by 8.1±4.5% (156.4±75.0 min/day) between baseline and 1 month.[14] Nearly 88% of participants indicated they would use *NEAT!* again in the future, suggesting high acceptability of the first iteration of the technology.

To inform the development of our *NEAT!2* sedentary reduction intervention and update the *NEAT!* smartphone application, we surveyed 42 participants (61.8±7.6 years, 67% female) on their beliefs about sedentary behavior and preferences for participating in a sedentary behavior reduction program. Nearly 80% of participants were located within the Columbia, SC region. Additionally, 88% of participants own a smartphone and 80% indicated they would be interested in participating in a sedentary reduction program.

D. RESEARCH DESIGN AND METHODS AND DATA ANALYSIS

Design Overview: This study is a three-group randomized controlled trial comparing changes in sedentary behavior between the *NEAT!2* intervention with or without coaching calls and a control group in adults with past or present knee symptoms, injuries, or surgeries. A total of 90 participants will be randomized into one of three groups 1) *NEAT!2* 2) Delayed *NEAT!2* or 3) *NEAT!2*+Calls. Data will be collected at baseline and months 1, 3, and 6.

Screening: Potential participants will complete an online screener to assess initial eligibility. Eligible patients will be invited to an in-person session where staff will review full details of the study and answer any questions. An equipoise induction will be conducted to review the pros and cons of being randomized to either condition to help prevent differential attrition.[15] Interested and eligible participants will provide informed consent, approved by the University of South Carolina's Institutional Review Board. Participants will complete the baseline assessment and wear an accelerometer for 7 days. Participants will need to have 4 valid days of accelerometer data to be eligible for randomization. They will not receive any feedback on sedentary time and will be encouraged to engage in typical behavior during this period. In addition, to ensure compatibility and eliminate the potential of technological issues following randomization, all participants will download a test version of *NEAT!2* app on their phone. The test version of *NEAT!2* app will remain idle, and participants will not receive notifications about their sedentary time until after randomization.

Randomized Conditions:

1) *NEAT!2*: *NEAT!2* is guided by the Dual-Process Theory[16] and targets both automatic and controlled processes.[17] Participants randomized to *NEAT!2* will have their *NEAT!2* app turned on after randomization. Using the smartphone's internal accelerometers, *NEAT!2* detects periods of movement vs. non-movement. When 30 minutes of continuous non-movement or sedentary time is detected, the *NEAT!2* app will initiate a reminder notification via vibration or audio as well as display a reminder on the phone's lock/home screen. This novel approach will take advantage of the frequent number of times an individual looks at his/her phone.[18] If and when the app detects activity/movement, the 30-minute timer will restart; thus, the app will only provide notifications when prolonged bouts of inactivity are objectively detected. Further, the app will only trigger notifications during participants waking hours. Each notification will consist of a different message. Participants will be asked to use the app for the 3 months of the intervention. Participants will be given an initial goal to reduce total sedentary time by 30 minutes/day, ultimately progressing to a 90 minute/day reduction by 3 months. After the 3-month assessment, participants randomized to *NEAT!2* will have the option to continue using the app until 6 months.

2) *Delayed NEAT!2:* Participants randomized to the delayed control condition will not receive any contact or app between baseline and 3 months. However, after completing the 3-month assessment, participants in the delayed condition will receive the *NEAT!2* application. Participants will then have the option to use the app between 3 and 6 months.

3) *NEAT!2+Calls*: *NEAT!2+Calls* participants will have their *NEAT!2* app turned on after randomization. In addition, to receiving the identical app and given the same goals as participants randomized to *NEAT!2*, *NEAT!2+Calls* participants will receive bi-weekly coaching calls. Coaching calls will be completed by trained coaches, be semi-scripted, and last approximately 10-15 minutes. During calls, coaches will use motivational interviewing techniques, discuss goal progression and educational handouts, problem solve, and set a SMART (specific, measurable, attainable, realistic/reward, timely) goal related to reducing sedentary time. All calls will be recorded and timed to allow the assessment of treatment fidelity. After the 3-month assessment, participants randomized to *NEAT!2+Calls* will have the option to continue using the app until 6 months. During this time, participants will not receive any coaching calls.

Treatment Fidelity: Telephone sessions will be audiotaped, and a 15% sample rated for treatment fidelity on a quarterly basis. If fidelity falls below 80%, coaches will be retrained. Fidelity checklists will assess intended session content (e.g., app usage, SMART goal setting). Dr. Pellegrini will train the coaches on the intervention and will oversee the fidelity evaluation. Coaches will meet with Dr. Pellegrini once a month to review treatment delivery.

Assessments: Participants will be asked to complete four in-person assessments at baseline, 1 month, 3 months, and 6 months. All in-person assessments will take place

at the TecHealth Center at the University of South Carolina (915 Greene Street, Suite 403) and each session will be last approximately 45 minutes in length. Table 1 provides an overview of what outcomes will be assessed, how they will be assessed, and at what time points.

Table 1. Study Outcomes and Measures				
Concept	**Variable**	**Measure**	**Data Collection**	**Time Points**
Aim 1 Outcomes				
Sedentary Behavior	Objectively measured sedentary behavior	Sitting minutes/day and Sitting bouts >30 minutes during waking hours	ActivPal worn on thigh for 7 days for 24 hours/day	0, 1, 3, & 6 months
	Daily diary	Times monitor on/off, awake/sleep	Paper log for 7 days	0, 1, 3, & 6 months
Aim 2 Outcomes				
Physical Function	Objectively measured physical function	Timed up and go; 30-second chair stands, 6-minute walk test based on OARSI recommended procedures[19]	In-Person Assessment	0, 1, 3, & 6 months
Demographic, Health Status, and Process Variables				
Demographics	Age, Sex, Race, Ethnicity, Marital Status, Education	Demographic Questionnaire	REDCap survey	0 (baseline)
Health Status	Height, Weight, Waist Circumference BMI	Stadiometer, electric scale, and tape measure	In-Person assessment	0, 1, 3, & 6 months
	Medical History	Brief medical history	REDCap Survey	0 (baseline)
Knee Symptoms	Self-reported knee symptoms	Knee injury and Osteoarthritis Outcome Score (KOOS)[20]	REDCap Survey	0, 1, 3, & 6 months
	Pain intensity, pain interference, & mobility	Patient-Reported Outcomes Measurement Information System (PROMIS)[21,22]	REDCap Survey	0, 1, 3, & 6 months
Habit Strength	Self-reported habit strength	Adapted Self-Report Habit Index[23]	REDCap Survey	0, 1, 3, & 6 months
Domain specific sedentary behavior	Self-reported	Total sitting time and domain specific sitting time	SIT-Q[26] and the Sedentary Behavior Questionnaire[27]	0, 1, 3, & 6 months
Behavioral Beliefs	Self-reported beliefs on	TPB Survey[24] and Elicitation Interview[25]		0,1,3, & 6 months

	physical activity and sedentary behavior		REDCap Survey and In-Person Interview	(interview only 0 months)
Personal Environment Changes	Self-reported change in use of activity monitor	Physical Activity Monitor Changes Questionnaire	REDCap Survey	1, 3, & 6 months

Primary Outcomes:

- Sedentary behavior will be measured using ActivPALTM (PAL Technologies Ltd, Glasgow, UK), a small lightweight (15 g) uni-axial accelerometer. The time spent sitting/lying, standing, and stepping. The ActivPAL summarizes data in 15 second intervals over 24 hours at a sampling frequency of 10 Hz.[24] During assessments, participants will be asked to wear the ActivPAL on their thigh for 7 days. The monitor will be secured to the participants leg with medical grade waterproof adhesive tape. Participants will also be asked to complete a log indicating times the ActivPAL was worn and taken off over the 7-day assessment period in addition to what times they went to sleep and woke up.

Secondary and Exploratory Outcomes:

- Physical function measures will include the chair stand, timed up and go, and 6-minute walk test. All physical function tests will be completed following Osteoarthritis Research Society International (OARSI) recommendation procedures.[19] During the chair stand test, patients are asked to complete as many chair stand repetitions as possible during a 30-second period. The Timed Up and Go Test assesses the time in seconds taken to rise from a chair, walk 3-meters, turn, walk back to the chair, and sit down. The Six Minute Walk Test evaluates the maximal distance a patient can cover during a 6-minute period.
- Knee symptoms will be assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS).[20] Participants will self-report on symptoms, stiffness, pain, daily function, and active function of their knee from the past week. Patient-Reported Outcomes (pain intensity, pain interference, and mobility) will be assessed using Patient-Reported Outcomes Measurement Information System (PROMIS).[21] PROMIS utilizes a computer adaptive test via RedCap.[25]
- Adapted Self-Report Habit Index[23] assesses habit strength related to sitting. Participants answer the questions on a 1-7 Likert scale ranging from “Strongly Disagree” to “Strongly Agree”.
- Sedentary behavior will also be assessed with the SIT-Q.[26] This will be assessed as part of the web screening to estimate how many hours individuals spent sitting on an average day. The survey assesses time spent sleeping and sitting time during multiple domains (e.g., meals, transportation, work, leisure). The survey will also be administered at each assessment to explore changes in domain specific sedentary time. The Sedentary Behavior Questionnaire[27] will also be assessed to examine specific activities done while sitting (9 behaviors such as TV watching, reading, and using the phone on weekends vs. weekdays).

- Participants' control, normative, and behavioral beliefs toward sedentary behavior and physical activity will be assed with (1) a modified Theory of Planned Behavior (TPB) survey[24] - The survey includes 37 questions about the participants beliefs towards sedentary behavior and physical activity utilizing a 1-7 Likert scale. (2) An elicitation interview modified from Speed-Andrews et al.[25] will be administered at baseline. The interview contains 12 open-ended questions and elicits participants beliefs related to sedentary behavior and physical activity.
- Waist Circumference will also be assessed as a predictor of abdominal visceral fat. Measurement will be done twice during expiration, taking the average for analyses, by positioning an anthropometric tape midway between the palpated iliac crest and the palpated lowest rib margin in the mid-axillary lines (smallest part of the waist).

Evaluation: Following completion of the 3 or 6 month assessment, participants will be asked to complete a short evaluation form asking about their feelings and attitudes regarding the NEAT!2 program and the NEAT!2 application. The evaluation will aid in future research utilizing the *NEAT!2* application or research directed at reducing sedentary behavior in this population.

Statistical Analysis: Baseline participant characteristics will be described. Mixed ANCOVA's will be conducted to examine differences in sedentary behavior, physical function, and patient-reported outcomes across time by group. Additionally, we will control all sedentary time analyses for moderate intensity physical activity. All analyses will be performed using SAS 9.2 and SPSS.

E. PROTECTION OF HUMAN SUBJECTS

1. TARGET POPULATION:
We will aim to recruit 90 participants from Columbia, SC and surrounding areas. The target population will consist of adults over the age of 40 who identify with past or present knee pain, injury, or surgery.

Inclusion criteria: Eligible participants will 1) be at least 40 years of age, 2) own an Android or iOS smartphone, 3) have their smartphone near them (in their pocket, in their hand, or within 10 feet of them for >50% of their waking day 4) be willing to download the study application on their smartphone and have the application be compatible with their device, 5) spend at least 7 hours/day sitting, assessed by the SIT-Q, 6) have at least 4 days of valid accelerometer data at baseline, 7) have knee pain (at least one knee with pain, aching, or stiffness on most days for one month of the last 12 months), knee injury, or knee replacement within the last 5 years, and 8) read, speak, and understand English.

Exclusion criteria: Participants will only be excluded if they 1) have any contraindications to activity, 2) have a mobility limiting comorbidity (e.g. spinal stenosis), or 3) have a scheduled surgery (i.e., total knee replacement) within the next 6 months.

2. RECRUITMENT PLANS:
We will target recruitment channels including: 1) promotions in publications with low or no advertising cost (i.e., Craig's List); 2) electronic and social media recruitment blurbs (i.e., Facebook, Twitter, website, email newsletter, electronic billboard, etc.); 3) posting flyers around USC campus area and local Columbia businesses, health centers, rehabilitation or orthopedic centers; 4) word of mouth; and 5) emails to individuals from previous studies who expressed interest in participating in future trials.

All recruitment material will list study eligibility criteria and requirements and include a phone number, email address, and website where participants can reach staff if they have any general questions regarding study participation.

3. EXISTING DATA/SAMPLES:
Not applicable

4. CONSENT/ASSENT:
Written informed consent will be obtained in person. Full disclosure will be made of the nature and potential risks of participating in the study. Prior to starting, all participants will be asked if they have any questions about their participation to ensure they understand the procedures. The consent form has been developed according to the requirements of the University of South Carolina Institutional Review Board. All participants will receive a copy of their signed consent form. A copy of all signed IRB-approved consent forms will be kept in a locked file.

5. POTENTIAL RISKS:
Risks associated with interrupting sedentary time with brief bouts of light-intensity physical activity such as standing or light ambulation are minimal. Participants may experience skin irritation from wearing the activPAL accelerometer for 7 days at each assessment. In the event the participant experiences skin irritation, we will ask the participant to remove the device. We will provide them with additional tape, with multiple options available to accommodate individual reactions and preferences to medical grade tape, to reaffix to the other leg.

6. POTENTIAL BENEFITS:
Participants may or may not directly benefit from participating in this study, however the risks of participating in either randomized group are considered minimal. Participants may gain skills and knowledge regarding how to decrease sedentary behavior. Participants who are adherent to the intervention and reduce sedentary time may have greater reductions in pain and improvements in physical function. If the intervention is acceptable, safe, and effective, it may provide an innovative approach to reduce sedentary time among adults with previous or past knee symptoms, injuries, or surgeries.

7. CONFIDENTIALITY
A number will be assigned to the participant who agrees to be a part of the study. This number will be used on the project records rather than their name, and no one other

than the researchers will be able to link the data with the name. Study records/data will be stored in locked filing cabinets and protected computer files at the University of South Carolina.

8. COMPENSATION:
Participants will be given two raffle tickets for completing the assessments at 1, 3, and 6 months. They will receive 1 ticket for the in-person assessment; 1 ticket for wearing the activPAL. These tickets will be placed into a bi-monthly drawing. Every two months of the study, 2 winners will be drawn and receive a $25 prepaid Visa debit card.

9. WITHDRAWAL:
Participants will be informed they can leave the research at any time without penalty. If a participant decides to withdraw, no more information will be collected. The participants will be made aware of this during the consent process.

Any data collected during your participation in this research study prior to the date the participant chooses to withdraw consent may continue to be used by the investigators for the purposes described above.

Choosing not to be in the study will not result in any penalty or loss of benefit to which participants are entitled. Specifically, the choice not to be in this study will not negatively affect a participant's right to any present of future medical treatment or his/her present or future employment (for employees at USC or its affiliates).

F. REFERENCES/LITERATURE CITATIONS

1. Tremblay MS, Aubert S, Barnes JD, et al. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act.* 2017;14(1):75.
2. Katzmarzyk PT, Church TS, Craig CL, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Medicine and science in sports and exercise.* 2009;41(5):998-1005.
3. Carson V, Wong SL, Winkler E, Healy GN, Colley RC, Tremblay MS. Patterns of sedentary time and cardiometabolic risk among Canadian adults. *Prev Med.* 2014;65:23-27.
4. Healy GN, Winkler EA, Brakenridge CL, Reeves MM, Eakin EG. Accelerometer-derived sedentary and physical activity time in overweight/obese adults with type 2 diabetes: cross-sectional associations with cardiometabolic biomarkers. *PLoS One.* 2015;10(3):e0119140.
5. Lee J, Chang RW, Ehrlich-Jones L, et al. Sedentary behavior and physical function: objective evidence from the Osteoarthritis Initiative. *Arthritis care & research.* 2015;67(3):366-373.
6. Dunlop DD, Song J, Arnston EK, et al. Sedentary time in US older adults associated with disability in activities of daily living independent of physical activity. *J Phys Act Health.* 2015;12(1):93-101.
7. Pinto D, Song J, Lee J, et al. Association Between Sedentary Time and Quality of Life From the Osteoarthritis Initiative: Who Might Benefit Most From Treatment? *Arch Phys Med Rehabil.* 2017.
8. Rosenberg D, Bellettiere J, Villareal V, Crist K, Kerr J. Independent Associations Between Sedentary Behaviors and Mental, Cognitive, Physical, and Functional Health Among Older Adults in Retirement Communities. *J Gerontol A Biol Sci Med Sci.* 2016;71(1):78-83.
9. Barone Gibbs B, Brach JS, Byard T, et al. Reducing Sedentary Behavior Versus Increasing Moderate-to-Vigorous Intensity Physical Activity in Older Adults. *J Aging Health.* 2017;29(2):247-267.
10. Gardiner PA, Eakin EG, Healy GN, Owen N. Feasibility of reducing older adults' sedentary time. *American journal of preventive medicine.* 2011;41(2):174-177.
11. Semanik PA, Lee J, Song J, et al. Accelerometer-monitored sedentary behavior and observed physical function loss. *Am J Public Health.* 2015;105(3):560-566.
12. Pellegrini CA, Song J, Chang RW, et al. Change in Physical Activity and Sedentary Time Associated With 2-Year Weight Loss in Obese Adults With Osteoarthritis. *J Phys Act Health.* 2016;13(5):461-466.
13. Pellegrini CA, Ledford G, Chang RW, Cameron KA. Understanding barriers and facilitators to healthy eating and physical activity from patients either before and after knee arthroplasty. *Disability and Rehabilitation.* 2017:1-7.
14. Pellegrini CA, Hoffman SA, Daly ER, Murillo M, Iakovlev G, Spring B. Acceptability of smartphone technology to interrupt sedentary time in adults with diabetes. *Translational behavioral medicine.* 2015;5(3):307-314.
15. Goldberg JH, Kiernan M. Innovative techniques to address retention in a behavioral weight-loss trial. *Health Educ Res.* 2005;20(4):439-447.

16. Groves PM, Thompson RF. Habituation: a dual-process theory. *Psychol Rev.* 1970;77(5):419-450.
17. Conroy DE, Maher JP, Elavsky S, Hyde AL, Doerksen SE. Sedentary behavior as a daily process regulated by habits and intentions. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* 2013;32(11):1149-1157.
18. Andrews S, Ellis DA, Shaw H, Piwek L. Beyond Self-Report: Tools to Compare Estimated and Real-World Smartphone Use. *PLoS One.* 2015;10(10):e0139004.
19. Dobson F, Hinman RS, Roos EM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. *Osteoarthritis and Cartilage.* 2013;21(8):1042-1052.
20. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes.* 2003;1:64.
21. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): Progress of an NIH Roadmap Cooperative Group During its First Two Years. *Medical care.* 2007;45(5 Suppl 1):S3-S11.
22. Hung M, Clegg DO, Greene T, Saltzman CL. Evaluation of the PROMIS physical function item bank in orthopaedic patients. *Journal of Orthopaedic Research.* 2011;29(6):947-953.
23. Verplanken B, Orbell S. Reflections on Past Behavior: A Self-Report Index of Habit Strength1. *Journal of Applied Social Psychology.* 2003;33(6):1313-1330.
24. Courneya KS, Friedenreich CM, Sela RA, Quinney HA, Rhodes RE. Correlates of adherence and contamination in a randomized controlled trial of exercise in cancer survivors: an application of the theory of planned behavior and the five factor model of personality. *Ann Behav Med.* 2002;24(4):257-268.
25. Speed-Andrews AE, McGowan EL, Rhodes RE, et al. Identification and evaluation of the salient physical activity beliefs of colorectal cancer survivors. *Cancer Nurs.* 2014;37(1):14-22.
26. Lynch BM, Friedenreich CM, Khandwala F, Liu A, Nicholas J, Csizmadi I. Development and testing of a past year measure of sedentary behavior: the SIT-Q. *BMC public health.* 2014;14:899.
27. Rosenberg DE, Norman GJ, Wagner N, Patrick K, Calfas KJ, Sallis JF. Reliability and validity of the Sedentary Behavior Questionnaire (SBQ) for adults. *J Phys Act Health.* 2010;7(6):697-705.