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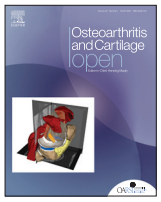

Clinical Study Protocol

KArAT (Knee Arthroplasty Activity Trial): Rationale and design features of a multicenter randomized controlled trial

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ABSTRACT

Background: Total knee arthroplasty (TKA) is commonly performed to relieve pain in persons with severe knee osteoarthritis. Despite substantial pain reduction and functional improvements, physical activity (PA) does not necessarily increase post TKA. The premise for this randomized trial is that a behavioral intervention invoking internal and external motivators could lead to improvement in PA uptake post TKA.
Methods: KArAT (the Knee Arthroplasty Activity Trial) is a three-arm multi-center randomized controlled trial designed to establish the efficacy and sustainability of a personalized behavioral intervention in improving PA among TKA recipients with a primary diagnosis of knee osteoarthritis. The three arms include: 1) usual care, 2) attention control with Fitbit activity trackers, and 3) health coaching and financial incentives for reaching personalized PA goals. The primary outcome is defined as the proportion of participants engaged in at least 150 min of moderate-to-vigorous physical activity over a given week after the 6-month intervention. We also plan to conduct a cost-effectiveness analysis to establish the value and affordability of the KArAT interventions.
Discussion: This paper aims to outline the rationale, study design, and implementation of KArAT.
Trial Registration: Clinicaltrials.gov NCT04107649.

1. Background and rationale for KArAT

Total knee arthroplasty (TKA) is a common intervention for advanced knee osteoarthritis (OA), with an annual US incidence of over 843,000 surgeries [1]. Over 80% of individuals report satisfaction with outcomes as well as improvements in knee pain post-knee arthroplasty [2–5]. For TKA recipients, increasing physical activity (PA) levels could help to maximize health benefits of TKA. PA is associated with higher health-related quality of life (QoL) and lower levels of depression and other physical and mental comorbidities [6–10]. For individuals with knee OA, increases in daily PA are associated with lower risks of the onset and progression of disability [11], and even moderate levels of PA are associated with substantial improvement in health-related QoL compared to inactivity [12]. However, only 44% of men and 22% of women with or at risk for knee OA currently meet the Center for Disease Control's (CDC) Physical Activity Guidelines, defined as 150 min of moderate-to-vigorous

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PA (MVPA) per week [13,14]. TKA recipients may have an opportunity to increase PA post-surgery, given reductions in pain and improvements in knee function. Despite these benefits, PA levels tend to stagnate post-joint arthroplasty, with a study of knee and hip arthroplasty recipients finding only a 0.7% increase in PA 6 months after surgery [15].

Interventions designed to increase PA for TKA recipients or individuals with knee OA can effectively incorporate behavioral strategies, such as goal-setting and personalized feedback from activity trackers and health coaches, to improve PA levels [16,17]. Such strategies can be implemented virtually or over the phone, and can continue to provide PA benefits even after study contact is complete [18–20]. Health coaching interventions grounded in motivational interviewing principles have been shown to promote PA, help weight management, and improve physical and mental health measures for individuals with chronic health conditions, including diabetes and heart disease [21–25]. Behavioral economics-based interventions can also promote activity, often by incorporating immediate financial rewards that offset the delayed gratification inherent in PA. Financial incentives have been shown to increase exercise adherence, walking and PA levels, and weight loss for adults who are sedentary or have chronic disease [26–28].

Our motivational interviewing and financial incentives intervention invokes both internal and external motivators for greater physical activity and is adapted from the previous SPARKS study that showed their efficacy in this population [16]. KArAT is aimed at confirming SPARKS' findings using multiple study centers.

In this report, we describe the details of a three-arm multicenter randomized controlled trial (RCT) to establish the efficacy and sustainability of a personalized intervention, with components built upon behavioral science and behavioral economics, in improving PA among individuals who have undergone primary TKA.

2. Methods

We divide the methods into two sections: Study Design, which describes the structural and statistical considerations in planning KArAT, and Trial Implementation, which details components of day-to-day trial execution.

2.1. Study design

2.1.1. Trial design and structure

The Knee Arthroplasty Activity Trial (KArAT) is a multicenter, three-arm, parallel assessor-blinded RCT. It is designed to establish the efficacy of behavioral interventions, that are based on invoking both internal (perception of importance) and external (financial incentives) motivators, in improving PA behavior among primary TKA recipients. Health coaches facilitate internal motivators for reaching personalized weekly physical activity goals and external motivators are invoked by sending financial rewards for reaching personalized adaptive PA goals that are monitored using Fitbit trackers. The three arms include: 1) usual post-surgical care (UC); 2) Fitbit wear as attention control (AC); and 3) telephonic active coaching via motivational interviewing with financial incentives (TAC(MI) + FI), where data from Fitbit trackers are used for assigning financial incentives. The primary outcome is the percentage of participants performing at least 150 min/week of MVPA at 6 months post-TKA (end of intervention). This study is registered at Clinicaltrials.gov (NCT04107649) and was approved by a Single Institutional Review Board (sIRB) hosted at MGB overseeing all sites. In this paper, we describe KArAT according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [29].

2.1.2. Study sample

We plan to recruit 600 participants across geographically diverse clinical sites: Mass General Brigham (MGB), Boston, Massachusetts; University at Buffalo Jacobs School of Medicine and Biomedical Sciences (UB-SMBS), Buffalo, New York; Northwestern Memorial Hospital, Chicago, Illinois; and University of Kansas Medical Center, Kansas City, Kansas.

2.1.3. Inclusion/exclusion criteria

To be eligible, participants must be 40–85 years old, scheduled for a primary, unilateral TKA for OA and 'pass' a pre-TKA run-in period by wearing an ActiGraph accelerometer (ActiGraph GT3X-BT, ActiGraph Corp, Pensacola, FL) for at least four out of seven days for at least 10 h each day. In addition, their average daily step count should not exceed a pre-specified amount to ensure the intervention is offered to only those with low PA uptake. Participants with inflammatory arthritis and those who report using a wheelchair for ambulation during the screening process are not eligible to participate in the study. Those with another elective musculoskeletal or inpatient surgery scheduled within six months following the index primary TKA, including planned staged bilateral TKA, are also ineligible. While slower recovery rates and TKA complications are possible (rates are low), it is hard to know with high certainty prior to TKA who will encounter these events. Therefore, we did not include these factors as an exclusion criterion. The randomization ensures that these events are similarly distributed across the study arms. The full list of KArAT inclusion and exclusion criteria is displayed in Table 1.

2.1.3.1. Screening. Research Coordinators (RCs) at each site perform an electronic medical record review for participants scheduled for surgeries with recruiting surgeons from 21 days (3-weeks) to 90 days (3 months) from the date of pre-screening. RCs conduct these reviews in accordance with the KArAT inclusion and exclusion criteria (Table 1). Those patients deemed eligible based on electronic medical records are advanced to the next level of screening conducted by phone. These phone calls further assess health conditions that may preclude enrollment into KArAT. Once interested patients are deemed safe to participate in the study, RCs administer a set of brief phone questionnaires to understand their current attitudes and perceptions toward physical activity and motivation to exercise. At the end of the screening call, participants interested in enrolling are scheduled for the baseline KArAT visit.

2.1.3.2. Baseline visit. Prior to the baseline visit, RCs send potential participants the baseline questionnaire and an accompanying fact sheet about the study. Completion of the questionnaire after reading the fact sheet is considered implied consent to the questionnaire. At the enrollment visit, the RC reviews the informed consent form with participants, giving adequate time for participants to read the document and ask questions. Physical assessment activities only occur after the RC has received written consent to participate in the KArAT study.

Table 1
KArAT study inclusion and exclusion criteria.

Inclusion Criteria
- Age 40–85 years
- English-speaking
- Scheduled to undergo primary, unilateral TKA at one of the 4 recruitment centers
- OA is principal underlying indication for TKA
- During an accelerometer run-in period lasting one week at baseline (prior to surgery), participants must show that they can comply with ActiGraph protocols: o Participant wears the ActiGraph for ≥4/7 days of the week for ≥10 h/day
- Regular access to a tablet or smartphone for Fitbit syncing
- Regular access to a device capable of receiving e-mail and/or text messages
- Average baseline steps/day (calculated from ActiGraph data from the run-in period) less than a prespecified threshold
Exclusion Criteria
- Non-English speaking
- Residence in nursing home
- Diagnosis of dementia
- Diagnosis of epilepsy, Parkinson's Disease, or diabetes with peripheral neuropathy with documented gait or balance disturbance of falls related to the condition
- Inflammatory arthritis (rheumatoid arthritis, reactive arthritis, systemic lupus erythematosus, polymyalgia)
- Psychological issues that preclude participation
- Inpatient or other musculoskeletal surgery scheduled within six months following index primary TKA
- Uses a wheelchair to ambulate
- Surgeon-documented other reason for study exclusion

2.1.3.3. ActiGraph run-in period. Following the baseline visit physical assessment, the RC instructs participants on proper wear and data uploading procedures for the ActiGraph accelerometer. KArAT participants are asked to wear the ActiGraph for a minimum of 10 h/day for one week. Wear compliance is defined as ActiGraph wear for at least an average of 10 h/day for four days of wear during that one week period [30]. Participants are given the option to receive reminders to wear their device throughout their wear week via email or text message. Those who prefer to receive text messages must also provide written consent to receive unencrypted text messages.

To monitor ActiGraph wear compliance, RCs use a website to view each participant's upload status. If by the beginning of day three of the participant's wear period, they have not yet established a day of wear compliance, the RC calls the participant to remind them of the wear criteria and addresses any questions or concerns the potential participant may have about ActiGraph wear and uploads. To be randomized to one of the three KArAT arms, participants must be ActiGraph wear compliant, have PA levels below a prespecified threshold and have evidence in their medical record of having undergone a TKA.

2.1.4. Randomization and blinding

Participants who meet all eligibility criteria and undergo TKA are randomized to one of the three arms in a 1:2.3:2.3 ratio (UC:AC:TAC(MI) + FI) within four weeks post TKA. The randomization is stratified by BMI (<30 kg/m^2 vs. ≥ 30 kg/m^2) and recruitment site, using randomly permuted blocks. After ensuring compliance with all inclusion criteria, the arm assignment is done at the coordinating site (MGB), to assure allocation concealment, using the randomization schema developed by the KArAT lead statistician and implemented in the KArAT REDCap (Research Electronic Data Capture) data system. Study referring surgeons, outcomes assessors, principal investigator, and any research personnel involved in collection of the outcome data are blinded to participant arm assignment. The nature of the intervention delivery precludes blinding of the KArAT study participants.

2.1.5. Post-randomization procedures

About four weeks post TKA, participants are informed of their randomization assignment. At this time, participants in all arms receive a Memorandum of Understanding via mail and email that explains the tasks for which they are responsible and the monetary rewards they can earn for completing those tasks. Additionally, those in the AC and TAC(MI) + FI arms are mailed a Fitbit and setup instructions.

2.1.6. Procedures and activities

The activities across the three KArAT arms are displayed in Table 2 and are described below in accordance with the Template for Intervention Description and Replication (TiDIER) guidelines [31]. The intervention period begins six weeks after randomization and lasts for 26 weeks, ending at about 8–9 months post TKA.

2.1.6.1. Check-in calls (all arms). Participants in all arms receive brief check-in phone calls from local site research coordinators (RCs) from weeks 1–3 post-randomization. Participants in Arms 1 (UC) and 2 (AC) continue to receive brief check-in phone calls from RCs located centrally at MGB throughout the intervention period, on a schedule parallel to that of TAC(MI) calls. The goal of these calls is to 1) identify if adverse events have occurred, 2) assess participants' pain levels, and 3) provide participants with regular contact with study staff. Staff do not share any health advice, but instead ask participants about specific adverse events and knee pain levels according to a prespecified script.

Table 2
Intervention components by arm.

Arm	Check-in Calls[a]	Fitbit wear	TAC(MI)	FI
UC	✓	–	–	–
AC	✓	✓	–	–
TAC(MI) + FI	✓ (first 5 weeks post TKA only)	✓	✓	✓

UC: Usual Care.
AC: Attention Control.
TAC(MI) + FI: Telephonic Active Coaching based on Motivational Interviewing with Financial Incentives.
[a] Schedule of AC and UC check-in calls is consistent with coaching calls in TAC(MI) + FI arm.

2.1.6.2. Fitbit wear (arms 2 & 3). Participants in the AC and TAC(MI) + FI arms receive a Fitbit Inspire 3 (Fitbit Inc., San Francisco, CA) to wear throughout the 6-month intervention period and until 24-month follow-up. During the intervention period, participants receive weekly reminders via text or email to wear the Fitbit. Those in the TAC(MI) + FI arm who wear the Fitbit for $\geq$4/7 days of the week for $\geq$10 h/day receive a $5 reward each week during the intervention period. Participants in the AC arm do not receive a weekly incentive for wearing their Fitbit, but they are eligible to win $25 for each week that they wear their Fitbit at least 10 h a day for 4 days throughout the duration of the study. At the end of the intervention period, TAC(MI) + FI participants who wear their Fitbit for the required time are also entered into the weekly $25 lottery through two years post-randomization.

2.1.6.3. Motivational interviewing (TAC(MI), arm 3). Participants in the TAC(MI) + FI arm receive calls from a TAC(MI) interventionist (health coach) at prespecified time intervals. The TAC(MI) intervention is based on the four key aspects of MI Spirit (partnership, acceptance, compassion, and evocation) [32]. These aspects are implemented by using the key MI processes (engaging, focusing, evoking, and planning) to form the flow of MI during each call [33]. MI based health coaching calls are related to PA goal-setting: coaches review the participant's Fitbit data from the prior week, help the participant identify days when PA levels were consistent with goals, and reflect on days with particularly low or high PA. The coaches use MI skills, such as reflective listening, to help participants voice reasons for changing PA and to elicit participants' motivations for change. The coaches help participants develop a commitment to change and formulate concrete plans of action. The frequency and content of TAC(MI) coaching is described below:

- 6–13 weeks post-randomization: weekly – the coach uses MI skills to help the participant set PA-related goals and elicit internal motivation to improve PA.
- 14–31 weeks post-randomization: every other week – the coach uses MI skills to help the participant set PA goals of longer duration and/or greater intensity (e.g., longer and/or faster walks) and to return to activities previously limited by OA-related pain or TKA recovery.

2.1.6.4. Financial incentives (FI, arm 3). Those assigned to the TAC(MI) + FI arm are eligible for FI awards if they achieve step and/or MVPA goals.

The 6-month intervention period is divided into three FI phases corresponding to TKA recovery milestones. Walking based PA goals focus on incrementally increasing average daily step counts and weekly minutes of MVPA. FI earned each week are determined based on step counts and MVPA minutes as measured by Fitbit. We define the threshold for MVPA as 3 metabolic equivalents of task (METs) [34,35].

During the three phases of the intervention, participants can earn financial rewards for achieving escalating step and MVPA goals and/or meeting CDC PA guidelines (>150 min/week MVPA) [14]. The specific phases and the corresponding step and MVPA levels sufficient for receiving financial incentives are shown in Table 3. Finally, additional bonuses are available for participants who reach their step goals for 4 consecutive weeks; this bonus is equal to the amount earned for meeting the step goal at the end of the fourth consecutive week. Participants can

receive six of these bonuses during the 6-month intervention. Participants receive weekly e-mails outlining the amount of money they did and did not earn for meeting their step and/or MVPA reward goals (Table 3).

2.1.7. Data collection, analytic procedures, and statistical considerations

2.1.7.1. Overview of data collection. Study outcomes are assessed via accelerometry (ActiGraph model GT3X-BT), self-report questionnaires, and physical examination, including strength and performance tests (Table 4). Study questionnaires are administered at baseline and at 3-, 6-, 12-, 18-, and 24-months post-randomization. Participants are given an ActiGraph accelerometer to wear for one week at baseline, 6-, 12-, 18-, and 24-months. A musculoskeletal (MSK) exam and quantitative sensory test (QST) are performed at baseline and at 6 months by a study-certified assessor. Performance tests for the MSK exam are carried out according to the Osteoarthritis Research Society International (OARSI) recommendations [36]. Study staff performing the exams, data entry and sending questionnaires are blinded to participant arm assignment after randomization. The trial statistician will remain blinded to participant arm assignment.

2.1.8. Statistical considerations

2.1.8.1. Primary outcome. The primary outcome of this trial is the proportion of participants that have ≥150 min/week MVPA measured at the end of intervention (EoI) (~32 weeks post randomization). We will use thresholds from Barnett et al. [34] and Hall et al. [35] to identify the proportion of KArAT participants reaching >150 min/week of PA at ≥ 3 METs.

2.1.8.2. Secondary outcomes. The key secondary outcome is the proportion of participants that have ≥150 min/week MVPA measured at 12 months post randomization (included in the power estimation). Additional secondary outcomes include: (1) change in weekly minutes engaged in MVPA between pre-TKA and EoI, (2) change in average daily steps between pre-TKA and EoI, and (3) change in average daily amount of sedentary time (defined by uniaxial cut-point<100 counts per minute) between pre-TKA and EoI. All secondary outcomes will be measured using the ActiGraph. We repeat the PA assessment with the ActiGraph at 12-, 18-, and 24-months post-randomization to examine whether PA levels remain the same, increase or decrease over time.

2.1.8.3. Tertiary outcomes. Tertiary outcomes include changes in global physical functional status, knee pain and function, changes in physical performance (quadriceps and hamstrings strength tests, balance tests, and 40-m walk), QST, generic health status, QoL, and costs associated with healthcare utilization.

Table 3
Financial incentive goal by study phase.

Phase: Weeks post-randomization	Weekly step goal	FI	Weekly MVPA goal	FI
1: Weeks 6–13	2000 steps/day and 15% increase from the average of previous 4 weeks	$10/ week	–	N/A
2: Weeks 14–25	5000 steps/day and 15% increase from the average of previous 4 weeks	$15/ week	100 min MVPA and 15% increase from the average of previous 4 weeks	$15/ week
3: Weeks 26–31	7500 steps/day and 15% increase from the average of previous 4 weeks	$20/ week	150 min MVPA and the average of previous 4 weeks	$20/ week

Table 4
Study outcomes.

Form of Assessment	Outcome Measure
ActiGraph accelerometer (baseline, 6[a], 12, 18, and 24 months)	% of participants performing PA ≥ 150 min/ week at ≥ 3 METs[a] Mean daily steps Weekly MVPA Minutes of sedentary time
Questionnaire	Knee Injury and Osteoarthritis Outcome Score (KOOS) [49] EuroQol-5D [50] PROMIS-10 Global Health Measure [51] PROMIS Sleep Disturbance [51] Healthcare Utilization Work Productivity and Activity Impairment Index [52]
Performance Tests	Quadriceps and hamstring strength 40-m walk [36] 30s sit-to-stand [36] Mini-BESTest [53] Quantitative Sensory Testing: Pressure Pain Threshold, Conditioned Pain Modulation, Mechanical Temporal Summation [54–56]

[a] Primary outcome.

2.1.8.4. Hypothesis and sample size. This study will address the following main hypotheses:

Hypothesis 1a. TAC(MI) + FI will lead to a greater likelihood of compliance with 2018 CDC PA guidelines (≥150 min/week of MVPA) compared to UC, at the end of intervention. This hypothesis will address the 'total treatment' effect.

Hypothesis 2a. TAC(MI) + FI will lead to a greater likelihood of compliance with 2018 CDC PA guidelines (≥150 min/week of MVPA) compared to AC, at the end of intervention. This hypothesis will address the 'treatment specific' effect.

Hypothesis 1b. TAC(MI) + FI will lead to a greater likelihood of compliance with 2018 CDC PA guidelines (≥150 min/week of MVPA) compared to UC, 12 months post randomization.

Hypothesis 2b. TAC(MI) + FI will lead to a greater likelihood of compliance with 2018 CDC PA guidelines (≥150 min/week of MVPA) compared to AC, 12 months post randomization.

2.1.8.5. Sample size considerations. Our sample size estimation for the primary outcome of achieving ≥150 min of PA at 3+METs per week was informed by the SPARKS trial [16]. We calculated sample size for the four hypotheses stated above and selected the maximum required sample size across all contrasts for a given group. We assumed 25% attrition rate, alpha = 0.0125, and 80% power. 110 subjects are required in Arm 1 (UC) in order to achieve sufficient power of at least 80% for each of the contrasts, including Arm 1 (15% vs 38% for EoI and 20% vs 50% for 12 months). Similarly, Arm 2 (AC) and Arm 3 (TAC(MI) + FI) will need 245 subjects each to achieve 80% power for all contrasts involving these arms (22% vs 38% for EoI and 25% vs 50% at 12 months). Based on these considerations, we will need to recruit 110 subjects for UC arm and 245 subjects for each AC and TAC(MI) + FI arms, for a total of 600 study participants.

We will analyze the primary outcome– achieving ≥150 min/week of MVPA measured by ActiGraph – with logistic regression. We will perform linear regression analyses to assess the following continuous secondary outcomes: change from pre-TKA to EOI in average daily step count, total weekly minutes of MVPA, and average daily sedentary time. We will perform repeated measures analysis (when data are collected over multiple time points) using mixed-effects linear regression analyses to assess continuous secondary and tertiary outcomes including: MVPA time, pain, PROMIS Global Health, EQ-5D, and physical performance tests [17–19, 37–39]. All models will adjust for the stratification factors BMI group and study site. Sensitivity analysis will use multiple imputation for missing data.

2.1.9. Data management

Study timeline and procedures are depicted in Figs. 1 and 2.

ActiGraph data are managed in CentrePoint, a cloud-based platform that specializes in clinical investigations [40]. Fitbit data are downloaded weekly from the Fitabase platform [41]. All other study data are managed using REDCap, a secure web-based platform designed for research studies [42].

2.1.10. Staff training

We developed a detailed manual of operations and procedures (MOOP) to standardize the daily practices involved in KArAT. The MOOP covers topics including the enrollment process, physical assessment performance, proper data entry, and ActiGraph accelerometer management. The Mass General Brigham (MGB) team serves as the coordinating center for all study activities, including study training.

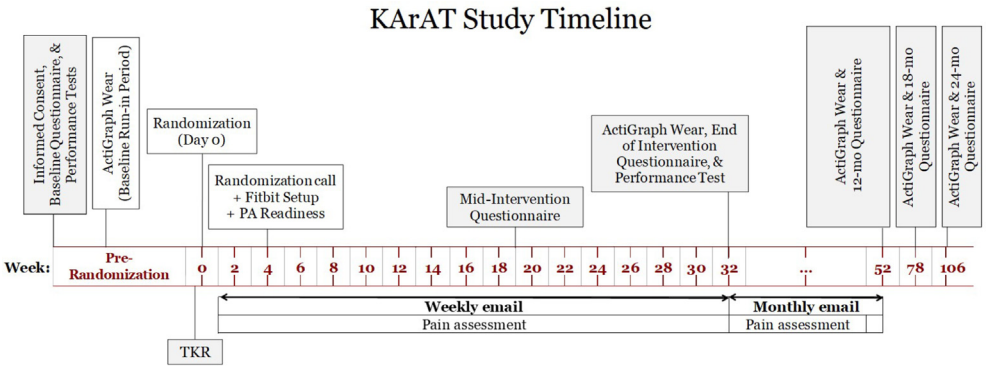

Fig. 1. Depicts the study timeline. The numbers shown represent the weeks since randomization which also correspond to the study week.

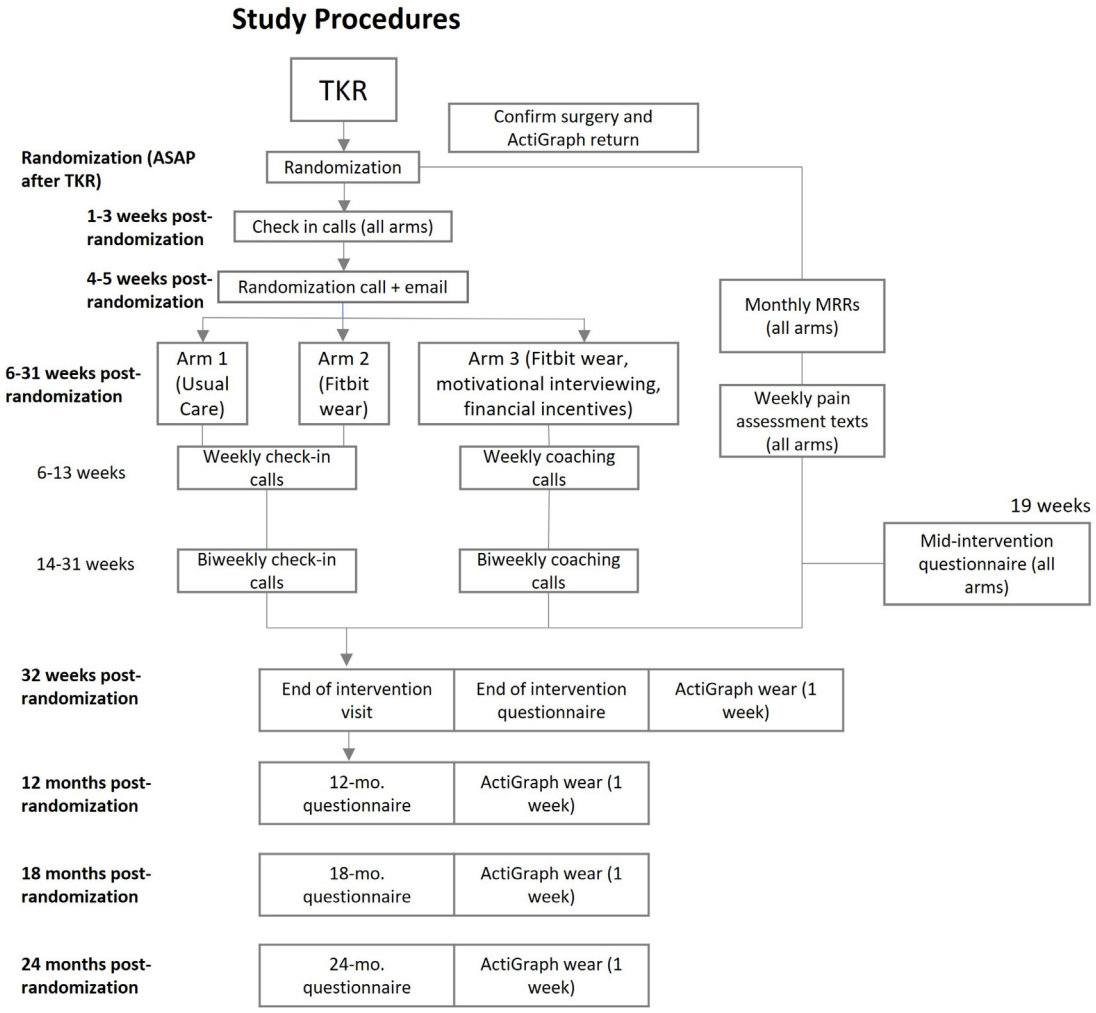

Fig. 2. Depicts recruitment procedures, activities by study arm, and follow-up timelines. KArAT (Knee Arthroplasty Activity Trial): rationale and design features of a multicenter randomized controlled trial.

KArAT clinical site staff undergo multidimensional training with support from the MGB team.

2.1.10.1. Data management training. To ensure fidelity in the data entry process, we developed a REDCap data entry manual and 18 training scenarios through which research coordinators learn about common issues that may arise. Successful use of REDCap to depict each of these scenarios results in KArAT REDCap certification.

2.1.10.2. Physical assessment training. Mobility, strength, function, and balance are key components of physical activity. As such, KArAT aims to understand each of these physical systems at baseline and EoI follow-up via the physical assessment. The physical assessment includes the assessment of index versus contralateral limb quadricep and hamstring strength. Additionally, knee flexion and extension range of motion is measured with handheld goniometers. Given the importance of balance in physical activity, RCs perform three of four Mini-Balance Evaluation Systems Test (Mini-BEST) assessments including the Anticipatory, Sensory Orientation, and Dynamic Gait tests [43]. Lastly, research staff administer QST to each participant including Pressure-Pain Threshold, Conditioned Pain Modulation, and Temporal Summation [44].

We established a two-pronged approach to training for the physical assessment: MSK/Mini-BEST training and certification, and QST training and certification. The Coordinating Center personnel provides each study site with a series of videos developed by a certified physical therapist and KArAT co-investigator (CSN). Along with the MOOP, RCs at each site correspond with their physical therapy (PT)/rehabilitation trainers to practice assessments of strength, motion, and balance. Upon mastery of the assessments, the PT trainers at each site certify the competency of the research staff in performing the assessments.

QST training initially involves watching a comprehensive training video along with a review of the MOOP covering QST. Coordinating Center personnel lead six weekly 1-h training sessions with site staff via video call. Once trainees demonstrate mastery of the QST procedures, they are certified via video call by Dr. Robert Edwards, a KArAT co-investigator with an extensive background in QST and pain psychology research [45–47].

2.1.11. Intervention fidelity

Health coaches are trained and certified (by LE-J) prior to interacting with KArAT participants. Coaching calls are recorded and 10% are reviewed monthly to ensure that all TAC(MI) coaches follow the appropriate skills and to identify discrepancies between the different coaches. Re-training of coaches will occur, if needed, throughout the duration of the KArAT study.

2.1.12. Optimizing engagement

All participants receive KArAT-branded promotional products, such as water bottles and small tote bags, and are provided with parking vouchers, where appropriate, for study visits. Participants in arm 2 receiving Fitbits are entered into a lottery for a monetary reward each week that they meet their wear-time goal. Monetary rewards are also provided for successfully completing questionnaires and study visits, as well as wearing and returning ActiGraph monitors. The study team sends periodic materials by mail, including holiday cards and newsletters.

2.1.13. Follow-up

When the 6-month intervention is complete, participants return to the study site for a follow-up visit with an assessor blinded to their arm assignment. Participants undergo a physical assessment similar to the one they underwent at the baseline visit and QST, and if they have not yet completed their 6-month questionnaire, then they do so at this time. Questionnaires are sent via email or mail, based on participant preference, at 19 weeks and 6-, 12-, 18-, and 24-months after randomization. Study staff perform questionnaire reminder calls to maximize response rate.

2.1.14. Adverse events

Adverse events (AEs) are defined as untoward medical incidents that occur during the conduct of a research study that may or may not be related to study procedures [48]. AEs can be considered serious (serious adverse event, or SAE) or non-serious. In KArAT, SAEs include: 1) death due to any cause; 2) overnight hospitalization for any reason; 3) any surgical procedure related to the TKA (e.g., revision TKA on index knee, manipulation under anesthesia, infection leading to washout); 4) events leading to disability; and 5) other important medical events that jeopardize the participant, as judged by the principal investigator. Non-serious adverse events include: 1) emergency department visits for any reason and 2) new walking/activity limitations that, per the participant's medical provider, should result in removal from the KArAT study.

All AEs are reported to the Data and Safety Officer semi-annually, and additionally, SAEs are reported to the Safety Officer within 48 h of study staff discovering the event. SAEs that are deemed 'probably or definitely related' to the trial activities are also reported to the sIRB within 5 working days/7 calendar days.

3. Summary

We have designed KArAT to establish the efficacy of a behavioral intervention based on the principals of motivational interviewing and behavioral economics in increasing PA post TKA. The necessity of this trial has been governed by the data showing that despite pain and function improving following TKA, patients do not improve their physical activity [15]. Results of this trial could identify a practical means of improving the long term outcomes of total knee arthroplasty.

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