Trials

STUDY PROTOCOL

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Remote and In-person Supervised Exercise in Patients with Knee Osteoarthritis (RISE-KOA): study protocol for a non-inferiority randomized controlled trial

Maurício Tatsch Ximenes Carvalho[1*] and Cristine Lima Alberton[1]

Abstract

Background Knee osteoarthritis (OA) is a prevalent joint condition resulting in years lived with disability. A first-line treatment recommended by clinical guidelines is the therapeutic exercise to control pain and improve physical function. One possible approach for exercise supervision is telehealth using video calls, as it can be an effective alternative to in-person physical therapy for treating musculoskeletal conditions, expanding community access to physical rehabilitation. In this scenario, this study aims to investigate whether a muscle-strengthening exercise program for the lower limbs supervised remotely via video calls is as effective as the same exercise applied in person for improving pain, physical function, condition-specific patient-reported outcomes (PROMs), psychological well-being, sleep quality, functional performance, and quadriceps muscle architecture.

Methods A *R*emote and *I*n-person *S*upervised *E*xercise in Patients with *K*nee *O*steo*a*rthritis (RISE-KOA) study is a parallel, two-armed, single-blinded protocol for a non-inferiority randomized controlled trial. Forty-eight participants aged 45 years or more, with a symptomatic and radiographic diagnosis of unilateral or bilateral knee OA (grade II or III according to Kellgren and Lawerence) will be randomly assigned to a remote exercise group supervised by video calls or in-person exercise group supervised at a physiotherapy clinic. Both groups will receive the same muscle-strengthening exercises for the lower extremities for 12 weeks. Follow-ups will be conducted during treatment (6 weeks), after treatment (12 weeks), and 18 weeks after randomization. The primary outcomes will be pain intensity and physical function during (6 weeks) and after treatment (12 weeks). Secondary outcomes will be condition-specific PROMs, psychological well-being, sleep quality, functional performance, and quadriceps muscle architecture.

Discussion We hypothesize that muscle strengthening exercise supervised remotely via video calls will not be inferior to in-person exercise at a physiotherapy clinic in terms of primary and secondary outcomes in patients with knee OA.

Trial registration The study was prospectively registered at ClinicalTrials.gov (NCT06101797). Registered on Oct 26, 2023.

Keywords Musculoskeletal conditions, Telehealth, Physical exercise, Patient-reported outcomes, Muscle architecture

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Administrative information

Note: the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/).

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Trial registration {2a and 2b}.	Remote and In-person Supervised Exercise in Patients With Knee Osteoarthritis (RISE-KOA)—https://classic.clinicaltrials.gov/ct2/show/study/NCT06101797?term=NCT06101797&draw=2&rank=1 ClinicalTrials.gov: NCT06101797
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Introduction

Background and rationale {6a}

Knee osteoarthritis (OA) is a multifactorial joint condition with increased prevalence and global burden of the disease, which is one of the predictive factors for the years lived with disability [1, 2]. Specifically, the global prevalence of knee OA, standardized by age, in 2019 was 4376.0 per 100,000 individuals (95% CI −3793.0 to 5004.9), an increase of 7.5% between 1990 and 2019 [3]. OA is a disorder that manifests first as a molecular derangement, leading to cartilage degradation, bone remodeling, osteophyte formation, inflammation, and loss of normal joint function [4]. The main symptom of knee OA is joint pain, and other clinical manifestations include joint stiffness, reduced range of motion, functional decline, and muscle weakness [5]. Worse symptoms and functional disability can be associated with muscle quality loss, particularly in the vastus medialis muscle [6]. In addition, as well as repercussions on the knee joint and functional performance, sleep quality and psychological well-being are often impacted in people with knee OA, including increased pain catastrophizing and symptoms of depression, anxiety, and stress [7–10].

According to clinical guidelines, structured exercise and arthritis education are the core treatments for patients with knee OA [11, 12]. Interventions that include aerobic exercises, strength exercises, or a combination of them are considered effective ways to improve condition-specific patient-reported outcomes measures (PROMs), such as pain and physical function, with no superiority from one form of exercise compared to the other [12]. On the other hand, regarding psychological well-being, findings of a network meta-analysis showed that muscle-strengthening exercise is a superior treatment strategy for knee OA patients to improve overall mental health compared to other exercise modalities [13]. However, some barriers are recognized to patient engagement in traditional exercise programs, including physical (patients reporting pain and functional limitations), psychological (some patients believe that physical activities are ineffective, harmful, or of doubtful effectiveness, as well as reporting lack of motivation), and social-environmental factors (patients experience lack of advice and encouragement from health professionals and have lack of social support) [14]. To address these challenges, it is essential to develop alternative strategies that promote treatment engagement. One such strategy is implementing inclusive telehealth systems, such as video calls, which allow real-time supervision of exercise performance, and strengthening the facilitators for physical activity for patients with knee OA at home [14, 15]. Therefore, developing alternative strategies to promote treatment engagement for patients with knee OA is imperative, specifically in developing countries [15].

Knee OA treatment is traditionally delivered in a face-to-face modality with the supervision of a physiotherapist in the clinic or at home [16, 17]. On the other hand, there has been growing interest in exercise remotely supervised via telehealth, also known as telerehabilitation, as this mode of intervention uses information and communication technologies to improve exercise participation in patients with musculoskeletal conditions [18–23]. Several factors highlight the need to apply remote rehabilitation, including cost-effectiveness, delivered treatment for patients who live in rural and remote areas, patients' preferences or convenience, limited physiotherapy services, or other challenges to community access to physical rehabilitation [24, 25]. Tools used for this treatment approach include websites, mobile applications, phone calls, text messages, and video calls [26]. From patients' and physiotherapists' perspectives, video calls are considered viable and well-evaluated real-time therapeutic intervention tools [27, 28]. This resource is commonly

used for telehealth consultations and is considered as effective as face-to-face outpatient consultations for managing patients with knee OA [29]. In this context, adopting telerehabilitation into clinical practice is a promising way to reduce costs and expand access to treatment for patients with knee OA [26, 30].

A systematic review found that remote exercise programs were not less effective than in-person physical therapy in patients with knee OA [19]. A non-inferiority randomized controlled trial showed that periodized circuit training via recording videos or face-to-face resulted in equivalent effects for pain intensity, physical function, muscle strength, pain catastrophizing, thigh composition, intermuscular adipose tissue, and muscle architecture [18]. Another study found that remote exercise supervised by video calls for patients with knee OA is more effective than self-management exercise programs for outcomes such as physical performance and emotional status [31]. In this context, a gap in the literature is whether fully supervised muscle-strengthening exercises by video calls are non-inferior to in-person in condition-specific PROMs, psychological well-being (including pain catastrophizing, symptoms of depression, anxiety, and stress) sleep quality, functional performance, and quadriceps femoris architecture. In addition, increasing literature has highlighted the changes in quadriceps muscle architecture in patients with knee OA, including alterations in muscle thickness, pennation angle, fascicle length, and muscle echo intensity [32–35]. In this context, investigating the effects of exercise on these parameters will assist clinicians in adopting remote supervision methods to address changes in quadriceps muscle architecture. Current studies indicate that the primary changes in the quadriceps muscle are related to muscle quality rather than muscle structure [6, 36]. Future results from this trial will enhance our understanding of how exercise influences changes in muscle quality, particularly in relation to reducing intramuscular fat infiltration. Therefore, the present randomized clinical trial aims to answer the question: Does a remote exercise program have comparable responses to the in-person exercise program regarding condition-specific PROMs, psychological well-being, sleep quality, functional performance, and quadriceps muscle architecture in patients with knee OA?

Objectives {7}

The primary aim of this non-inferiority randomized controlled trial is to determine if a muscle-strengthening exercise program for the lower limbs supervised remotely is as effective as the same exercise applied in person for improving pain and physical function (primary outcomes).

The secondary aim of this study is to determine if a muscle-strengthening exercise program for the lower limbs supervised remotely is as effective as the same exercise applied in person for improving condition-specific PROMs, psychological well-being, sleep quality, functional performance, and quadriceps muscle architecture (secondary outcomes).

Trial design {8}

The *R*emote and *I*n-person *S*upervised *E*xercise in *P*atients with *K*nee *O*steo*a*rthritis (RISE-KOA) study protocol, designed as a noninferiority trial, is an investigator-blinded randomized clinical trial aiming to assess whether a remotely supervised intervention of muscle-strengthening exercises is non-inferior to an in-person intervention in patients with knee OA. This study will be conducted in a single center, using a 1:1 allocation ratio, two-armed, with parallel groups. The RISE-KOA protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and OARSI Clinical Trials Recommendations and was registered at www.ClinicalTrial.gov (NCT06101797).

Methods: participants, interventions and outcomes

Study setting {9}

The clinical trial is being conducted in the city of Bagé, located in the southern region of Brazil. The study assessments occur in person at the University Hospital of the Center of Campaign Region at the Physiotherapy School Clinic and remotely via *WhatsApp* video calls. The Physiotherapy School Clinic treats community patients with musculoskeletal conditions, such as low back and neck pain, hand, hip, or knee osteoarthritis, and rheumatological diseases. In this study, the exercise intervention is supervised by a physiotherapist, either in the remote exercise group via video calls, or in the in-person exercise group at the physiotherapy clinic.

Eligibility criteria {10}

Volunteers, both male and female patients with knee OA diagnosis, are recruited from the waiting list for physiotherapy treatment at the Physiotherapy School Clinic and through a social media invitation. Subsequently, a researcher contacts the volunteers via telephone to check their initial eligibility based on the following criteria:

- Age $\geq$ 45 years.
- History of pain lasting more than 3 months.
- History of reduced knee function.

Eligible patients are invited for an in-person consultation, and a screening process is performed based on the clinical manifestations and recent radiographic exam. Participants without an exam with the radiographic classification, or if the X-ray was carried out over 12 months,

are required to undergo a new exam at the radiology department of the University Hospital. The exam is conducted bilaterally and involves standard anteroposterior weight-bearing and lateral radiographs. The radiographs are evaluated by a blinded, experienced radiologist using the Kellgren and Lawrence grading, in which 0 means no OA and 4 refers to severe OA [37].

Specific inclusion and exclusion criteria for enrollment in this trial are as follows:

Inclusion criteria

1. Patients with a radiographic diagnosis of unilateral or bilateral knee OA, classified as grades II or III according to the Kellgren and Lawrence criteria [37].
2. Symptomatic patients meeting the following American College of Rheumatology criteria: average pain score ≥ 3 in the last week on the numerical rating scale (0–10), morning stiffness <30 min, and joint crepitus [38].
3. Independent walking and internet access.

Exclusion criteria

1. Patients with systemic inflammatory diseases, including rheumatoid arthritis, ankylosing spondylitis, and systemic lupus erythematosus.
2. Neurological diseases with motor disability.
3. Unstable heart diseases.
4. History of total knee arthroplasty or lower extremity surgery.
5. Body mass index (BMI) ≥ 35 kg/m^2.
6. Physical therapy treatment or participation in a supervised exercise program in the last 6 months.

Who will take informed consent? {26a}

The researcher conducts a detailed explanation of in-person consultation for eligible patients about all study stages, including information about the objectives, outcome measures, intervention characteristics, risks, benefits, and the confidentiality of data management. Data collection only begins after signing the informed consent form.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

It is not applicable since this trial does not involve collecting biological specimens for storage. The study's primary and secondary outcomes use PROMs, physical functional tests, and ultrasound measurements.

Interventions

Explanation for the choice of comparators {6b}

In-person supervised exercise is a well-established and effective treatment method in patients with knee OA [17]. However, there is a need for more research to establish whether remote exercise is non-inferior to in-person training. There is also an increasing interest in telerehabilitation strategies to treat patients with musculoskeletal disease, particularly in developing countries where socioeconomic reality limits community access to specialized healthcare. Therefore, this study was designed to provide a supervised muscle-strengthening exercise program for the lower extremities, with both groups receiving the same level of supervision. The aim of this protocol is to improve the strength of the quadriceps femoris and, functionally, strengthen the lower limb muscles. The only difference between the two groups will be the supervision format, with one group participating in in-person sessions and the other in remote sessions.

Intervention description {11a}

Patients in this study are randomly assigned to receive one of two modes of supervised exercise programs. One group is supervised by a physical therapist remotely via video calls in *WhatsApp* (remote supervised exercise group), while the other receives in-person supervision (in-person supervised exercise group). The treatment will last for 12 weeks and consists of approximately 40-min sessions, twice a week for the first 2 weeks and three times from the third week until the end of the protocol.

The treatment protocol consists of six guided muscle-strengthening exercises for the lower extremities, performed in alternating muscle groups based on exercise programs of previous randomized controlled trials [39–43]. In the first treatment block, the exercise sequence addresses the knee extensors, hip adductors, and plantar flexors, and in the second block, the knee extensors, hip abductors, and knee flexors. The exercises encompass weight-bearing (with body weight support through the affected lower limb) and no-weight-bearing exercises (where participants do not support their body weight through the affected lower limb). Stationary walking precedes the first training block and concludes the exercise program.

Supervision is conducted in an individualized format, so the professional responsible for the intervention supervises a patient at each meeting, and the physiotherapist can make adaptations according to the functional characteristics of each participant. The physiotherapist responsible for the intervention records the entire exercise program, describing any necessary adaptations throughout the training weeks. The study participants

are encouraged to perform movements in both open and closed kinetic chains, encompassing a full range of motion. In those subjects who report pain ≥ 3 during the movement on the numerical pain scale, the exercises are adapted and guided toward a smaller range of motion.

During the first 2 weeks of treatment, exercise intensity is monitored for each participant to complete two sets of 8–12 repetitions in dynamic exercises and 5–8 repetitions of 20 s in isometric exercises. From the third week onward, participants are instructed to include one additional set. The interval is set at 1 min between sets and 30 s between exercises. In addition, an interval of 1 min is maintained between the first and second blocks in the initial 6 weeks, followed by an interval of 30 s in the subsequent weeks. An additional file presents the full exercise periodization of the study in more detail (see Additional file 1).

The patient completes the sets and repetitions of the exercises for each muscle group within the block before proceeding to the next one. In all exercises, the physiotherapists responsible for the intervention guide the progression. Adjustments to weight-bearing, the external load imposed by the elastic band (low to moderate), and exercise position throughout the protocol are performed to maintain the target participant's level of effort. Perceived exertion is monitored using the rating of perceived exertion by the Borg scale—index five on week one to 7 weeks and index seven on week eight to 12 weeks [44].

Once the 12-week supervised treatment period is over, all study participants, regardless of group allocation, will be encouraged to continue exercising at home without the supervision of a physiotherapist. All participants will receive reference material for independent performance (a booklet with photos depicting the exercises) to maintain consistency in treatment. The material will instruct participants to continue with the same treatment program as carried out during 12 weeks of the exercise protocol.

Remote supervised exercise group or in-person supervised exercise group

Following pre-intervention assessments and randomization, all subjects included in the study undergo a face-to-face familiarization session with the exercise program. This session includes specific guidance on the format for providing the intervention (either remote or in-person), and instructions on using the modified Borg effort rating scale during treatment.

In the remote exercise group, participants will receive guidance on video calls, emphasizing positioning the mobile device to ensure the quality of real-time supervision. Subsequently, each exercise will be carried out with safe home performance guidelines. For example, keep a chair and a broom nearby to carry out standing movements to prevent falls and avoid moving near rugs that could slip. At this same meeting, elastic bands will be made available to participants. The physiotherapist conducts all sessions in an individualized format using video calls from *WhatsApp*.

In the in-person supervised exercise group, participants will also be familiarized with each exercise under the supervision of the physiotherapist and guided about the weekly meetings scheduled at the physiotherapy clinic for treatment.

Criteria for discontinuing or modifying allocated interventions {11b}

Participants in the study are free to discontinue the treatment at any time and for any reason without penalty. Participation in the study may be interrupted for safety reasons, such as medical advice, complications related to pre-existing illnesses, or worsening of a clinical condition that makes participation in the exercise program contraindicated.

Strategies to improve adherence to interventions {11c}

One of OARSI's recommendations for developing the best therapeutic exercise practices for people with knee OA is to motivate patients to engage in and adhere to exercise programs [45]. To ensure participants maintain adherence to their exercise regimens, regardless of remote or in-person supervised exercise format, the researcher responsible for delivering the intervention explains relevant education content throughout the treatment process. Physiotherapists provide real-time instructions remotely (via video call) or in person, based on group allocation, for approximately 10 min preceding selected exercise sessions. Three educational sessions will focus on the clinical characteristics of knee OA and exercise treatment. These sessions are scheduled for the initial week of supervised exercise, the third week, and the eighth week. The researcher presents a brief illustrated presentation according to the following approach.

1. Guidance about knee OA and the importance of treatment-based exercises.
2. Patient-centered approach, facilitating an understanding of the symptomatic presentation of knee OA.
3. Positive and simple communication to explain OA, aiming to prevent kinesiophobia.
4. Explanation of long-term exercise benefits and their repercussions on pain and function. The physiotherapist emphasizes that exercise is an effective way for managing OA.

5. Highlights regarding the role of exercise as a treatment, considering it is not associated with an increased risk of joint injury or replacement.
6. Guidance about the difference between pain as an OA symptom and pain after exercise. The physiotherapist emphasizes that short-term pain does not indicate joint damage.
7. Addressing patients' reported fear of exercise by ensuring treatment safety and dispelling any misconceptions about the effectiveness of therapeutic exercise.

Relevant concomitant care permitted or prohibited during the trial {11 d}

Participants are encouraged not to participate in a simultaneous physiotherapeutic treatment program, including any therapeutic modality such as manual therapy, electrophysical agents, or another supervised exercise program. Participants can maintain usual care treatment for knee OA, including pharmacological treatment for other health conditions. However, the researcher advises them to avoid treatment through intra-articular injections of glucocorticoids for symptomatic management of knee OA.

Provisions for post-trial care {30}

Our goal is to ensure that all participants receive the highest level of care and support throughout the trial. After completing the RISE-KOA study, patients will receive a report of the results. In addition, during the trial, participants will be provided with a description of the X-ray exam.

At the end of the supervised exercise treatment, all participants will receive reference material (a booklet with photos depicting the exercises) for independent exercise performance in the following weeks to maintain consistency in treatment and encourage self-efficacy. The material will instruct participants to continue the same treatment program during the 12 weeks of the exercise protocol.

Outcomes {12}

Primary outcome measure

The primary outcomes are pain intensity and physical function in the sixth week (during treatment), 12 th week (after treatment). These outcomes were selected as they are strongly recommended in clinical trials involving patients with knee OA [46].

Pain intensity The average pain intensity in the last week is measured using an 11-point Pain Intensity Numerical Rating Scale (NRS), in which 0 corresponds to "no pain," and 10 represents "worst possible pain." NRS is a PROM for assessment and clinical decision-making in patients with knee OA with good psychometric properties [47].

Physical function Physical function is measured by Knee Injury and Osteoarthritis Outcome Score (KOOS) using an Activities of Daily Living subscale. The KOOS is a PROM comprising 42 items divided into five subscales: Pain, other Symptoms, Activities of daily living, Sport and Recreation Function, and Knee-related Quality of Life. Its score ranges from 0 (extreme problem) to 100 (no problems) separately in each subscale [48]. The Brazilian version of the KOOS questionnaire was recently validated, consisting of an instrument with validity, reliability, and responsiveness in patients with knee OA [49].

Secondary outcome measures

The secondary outcomes involve PROMs related to joint condition, psychological well-being, sleep quality, functional performance, and quadriceps muscle architecture.

Condition-specific PROMs Pain intensity is measured using NRS, and physical function using KOOS Activities of Daily Living subscale as secondary outcomes after 18 weeks (follow-up). Pain score, other symptoms (hear clicking, swelling, catching, restricted range of motion, and stiffness), sport and recreation function, and knee-related quality of life before and after 6 (during treatment), 12 (after treatment), and 18 weeks (follow-up) are measured by each KOOS subscale which ranges from 0 (extreme problem) to 100 (no problems).

Psychological well-being Pain catastrophizing; symptoms of depression, anxiety, and stress; are measured before, after 6 (during treatment), 12 (after treatment), and 18 weeks (follow-up) with the following instruments, respectively:

1. The Pain Catastrophizing Scale is an instrument validated and translated into Brazilian Portuguese used to classify subjects with chronic pain as potentially catastrophic patients [50, 51]. Catastrophizing is a maladaptive reaction to pain and can be considered one of the factors that contribute to the chronicity of some pain syndromes. The scale comprises 13 items involving self-reported catastrophic thoughts, feelings, and behaviors. Items are rated on a 5-point Likert scale, ranging from 0 to 4, and the total score is generated by summing the scores of all items (0–52). Higher values indicate catastrophic thoughts about pain.

2. Depression, Anxiety, and Stress Scale is a self-reported instrument validated and translated into Brazilian Portuguese [52]. It consists of 21 items ranging from 0 (did not apply at all) to 3 (applied very much or most of the time), divided into subscales of seven questions each. The highest score on each subscale represents more significant symptoms severity of depression, anxiety, and stress.

Sleep quality Sleep quality is measured before, after 6 (during treatment), 12 (after treatment), and 18 weeks (follow-up) with the following instrument:

The Pittsburgh Sleep Quality Index Self-report Questionnaire, validated for the Brazilian population, assesses sleep quality over a 1-month period through questions related to sleep habits [53]. The questionnaire consists of 19 self-reported questions and five questions that should be answered by bedmates or roommates. The study will not consider the last questions as they are used to obtain clinical information. In this sense, 19 questions will be graded on a score ranging from 0 to 3 and categorized into seven components: (1) subjective sleep quality; (2) sleep latency; (3) sleep duration; (4) habitual sleep efficiency; (5) sleep disturbances; (6) use of sleeping medication, and (7) daytime dysfunction. The sum of the scores of the seven components will result in a global score (0 to 21), with the highest value indicating worse sleep quality.

Functional performance The functional tests recommended by OARSI for knee OA patients assess the participants' functional profiles [54]. Sit-to-stand, ambulatory transition, short-distance walking, and stair negotiation activities are measured before and after 12 weeks of treatment with the following instruments, respectively: the 30-s chair-stand test, the Timed Up and Go test, the 40-m fast walk test, and the Stair Climb test. The assessor applies the functional tests described below in random order.

1. In the 30-s chair-stand test, patients are instructed to sit in the center of the chair 42 cm high from the seat, positioned against the wall, without the aid of the upper limbs, and perform the test movements for familiarization. Subsequently, sit down and get up from the chair as quickly as possible within 30 s. Thus, the measurement result will consist of a total number of complete chair stands in 30 s (up and down represent one stand).
2. In the Timed Up and Go test, patients are instructed to move from a seated position to standing, walking to a mark 3 m away, turn around, and return to the seated position. The measurement result will be expressed in seconds, corresponding to the time taken to complete the task.
3. In the 40-m fast walk test, patients are instructed to walk as quickly but as safely as possible without running. They walk to the 10-m mark, turn around, and return, repeating for a total distance of 40 m. The measurement of walking time only includes the 10-m walking period, excluding turns. The speed measurement will be expressed in m/s, dividing the 40 m by the time (seconds) needed to travel through the test area.
4. In the Stair Climb Test, patients are instructed to ascend and descend stairs as quickly as possible while wearing their usual shoes. The measurement will be expressed in seconds, corresponding to the total time taken to complete both ascending and descending the stairs.

Quadriceps femoris architecture Quadriceps femoris architecture is measured before and after 12 weeks of treatment. For this measurement, quadriceps femoris images are generated through a B-mode imaging device (Versana Balance Ultrasound—GE Healthcare) equipped with a 12 MHz linear-array probe with optimized ultrasound settings (image depth: 4 to 6 cm, 60-dB general gain, time gain compensation at neutral position) [55]. The sonographer considers the symptomatic lower limb for measurement, and the more symptomatic side will be in bilateral OA. The same evaluator with expertise in musculoskeletal ultrasound generates the images.

For image acquisition, participants remain rested in the supine position for 5 min with the lower limbs at the neutral position, extended and relaxed, preventing muscle activation [56]. The transducer is coated with a generous amount of water-soluble transmission gel and positioned perpendicularly, applying the minimum pressure at each point of the quadriceps femoris to visualize the ultrasound image.

Three transverse images are obtained for all quadriceps femoris muscles: rectus femoris (RF), vastus intermedius (VI), vastus medialis (VM), and vastus lateralis (VL). Additional longitudinal images of VL are also acquired to visualize muscle fascicules. Similar to a previous study [57], RF and VI capture occurs by transducer positioning between the anterior superior iliac spine and the proximal end of the patella (a midpoint). For VL, the transducer is positioned midway between the greater trochanter and the lateral epicondyle of the femur. To identify the VM, the transducer is positioned at a 30% distal between the greater trochanter and the lateral epicondyle of the femur. To ensure a similar probe position in

subsequent tests, the assessment site of each muscle is marked on transparent paper and used for probe repositioning. After image acquisition, a second investigator will measure quadriceps femoris architecture using ImageJ software (National Institutes of Health, USA, version 1.53) according to the following outcomes.

1. Quadriceps femoris muscle thickness

The quadriceps muscle thickness is measured considering the distance between muscle fascia or at the fascia and bone structure interface [57]. The muscle thickness will be expressed in centimetres and presented as the sum of the measurements of each quadriceps femoris muscle (i.e., RF + VL + VM + VI), with individual muscle values also shown separately.

2. Quadriceps femoris muscle quality

Quadriceps muscle quality, expressed as muscle echo intensity (EI), is measured using a greyscale function in ImageJ software. The EI is an echo or brightness reflected by the muscular structure. It will be calculated based on a region of interest in each muscle, including as much of the muscle as possible, and shown in arbitrary units, with values ranging between 0 (black) and 255 (white) [58]. The highest value represents decreased muscle quality and deposition of non-contractile tissue within the muscle. Subsequently, a researcher will correct the EI data according to subcutaneous fat thickness; thus, the correction of echo intensity will be calculated as uncorrected EI + (subcutaneous fat thickness (cm) × 40.5278). Data will be presented as the mean of the quadriceps femoris EI corrected ((RF + VL + VM + VI)/4), with individual muscle values also shown separately [59, 60].

3. Pennation angle

Due to the alignment of the fascicles, the pennation angle is measured using only images of the vastus lateralis [61]. The pennation angle is formed between the muscle fascicle line and the deep aponeurosis. It will be expressed in degrees. The data analysis will include the mean of three measurements for pennation angle.

4. Fascicle length

Fascicle length is measured using only images of the VL [62]. Fascicle length (cm) is the length of the fascicle insertion between the superficial and deep aponeurosis. When the fascicle extends out of the acquired ultrasound image, the length of the missing portion will be estimated by linear extrapolation of both the fascicular path and the aponeurosis. In addition, an experienced evaluator will normalize the data by analyzing the ratio between the fascicle length of the VL and the femur length. Femur length is the distance (cm) between the lateral femoral condyle and trochanter major.

Other outcomes

Number of medications The number of analgesic and anti-inflammatory medications ingested is being registered considering information reported by the patient before, after 6, 12, and 18 weeks of treatment.

Participant timeline {13}

The schedule of trial enrolment, interventions and assessments is presented in Fig. 1.

Sample size {14}

The sample size calculation was performed using the Sealed Envelope Power (sample size) calculators [63]. We based our sample size calculation on a previous study [64], considering an alpha level of 0.05, power of 0.80, standard deviation of 2 in pain level, and a non-inferiority margin of −1.6 points. The minimum required sample size was determined to be at least 40 participants. Considering an expected sample loss of ≈20% between baseline and follow-up, 48 participants are needed, 24 per group. According to previous recommendations [65, 66], we established a non-inferiority margin in primary outcome pain level, measured by NRS, of −1.6 points (20% less than the minimum clinically significant difference reported for the NRS [67]).

Recruitment {15}

The recruitment period started in December 2023 and will be completed in October 2024. Subjects for Bagé, Brazil, will be recruited through notes shared in local newspapers and social media, as well as the waiting list of the Physical Therapy School Clinic.

Assignment of interventions: allocation

Sequence generation {16a}

Each participant is assigned an internal code (ID) for de-identification purposes (i.e., RISE-KOA-256), and a randomization process is implemented using an allocation ratio 1:1. The randomization sequence is generated by a single researcher using a specific Excel random function.

		STUDY PERIOD								
	Enrolment	Baseline	Allocation	Post-allocation 12 weeks				End-points		
TIMEPOINT**	$-t_1$	*0*	*0*	*1 w*	*3w*	*8w*	*12w*	*6w*	*12w*	*18w*
ENROLMENT:										
Eligibility screen (by telephone)	X									
Eligibility screen (In-person)	X									
Informed consent	X									
Allocation			X							
INTERVENTIONS:										
Remote supervised exercise group				♦—	—	—	—♦			
In-person supervised exercise group				♦—	—	—	—♦			
ASSESSMENTS:										
Primary outcomes										
Pain intensity (NRS)		X						X	X	X
Physical function (KOOS - physical function subscale)		X						X	X	X
Secondary outcomes										
Pain (KOOS - pain subscale)		X						X	X	X
Other symptoms (KOOS - symptoms subscale)		X						X	X	X
Sport and recreation function (KOOS - sport and recreation function subscale)		X						X	X	X
Knee-related quality of life (KOOS - knee-related quality of life subscale)		X						X	X	X
Pain catastrophizing		X						X	X	X
Symptoms of depression, anxiety, and stress		X						X	X	X
Sleep quality		X						X	X	X
Performance-based tests		X							X	
Quadriceps architecture		X							X	
Other measures										
Age		X								
Sex		X								
Height		X								
Weight		X								
Body mass index		X								
Educational level		X								
Work status		X								
Fear of movement		X								
Medication consumption		X								
Radiographic screening		X								
Comorbidities		X								
Blood pressure		X								

Fig. 1 The schedule of trial enrolment, interventions and assessments

Concealment mechanism {16b}

The researcher responsible for participant matching and randomizing is not involved in the study's recruitment and intervention stages. Exclusive access to the age variable is granted solely for the purpose of randomizing participants into study groups. Following randomization, the team responsible for the intervention is informed via text messages regarding the group assignment of each patient.

Implementation {16c}

After participants sign the informed consent form and complete baseline measurements, a randomization sequence is carried out by a researcher not involved in any other study step. Patients will be assigned to either the remote or in-person exercise groups. The sociodemographic characteristic of age will be used as stratification to balance the groups (in the categories of participants aged 45 to 54 or 55 to 80). The age was selected because it impacts the symptomatic presentation of patients with knee OA and the years lived with disability [1, 68].

Assignment of interventions: blinding

Who will be blinded {17a}

Outcome assessors will remain unaware of the intervention assignment (remote or in-person). Participants are instructed not to discuss their interventions during evaluation outcomes to ensure evaluator masking. However, due to the nature of the intervention, neither the participants nor the team conducting the exercise sessions can be blinded.

Procedure for unblinding if needed {17b}

RISE-KOA is a single-blind study, with only the outcome assessors being blinded. For this reason, unblinding will not be anticipated; however, in the case of unintentional unblinding, the study coordinator will be contacted.

Data collection and management

Plans for assessment and collection of outcomes {18a}

The study assessment is conducted over 2 days. On the first day, assessments take place in-person at the Physiotherapy School Clinic and the Radiology Department within the University Hospital of the Center of Campaign Region. On the second day, assessments are conducted remotely via video call using *WhatsApp*.

On the first day, a research team conducts a physical therapy anamnesis, followed by ultrasound measures and functional assessments performed by independent assessors. Ultrasound scanning and functional assessments are conducted at two time points (baseline and after 12 weeks).

Anamnesis comprises an evaluation of the clinical profile (inspection, palpation, ligament integrity, blood pressure, past medical history, medication consumption, intraarticular injection therapy, fear of movement, the wait list for knee arthroplasty surgery) and a sociodemographic characterization (age, sex, height, weight, body mass index, educational level, and work status).

On the second day, condition-specific PROMs, psychological well-being, sleep quality, and medication use are assessed by another researcher who conducts the evaluation remotely via WhatsApp video calls. These measurements occur at three time points: after 6 (during treatment), 12 (after treatment), and after 18 weeks (follow-up). Even if participants withdraw from the study or do not adhere to treatment, they are invited to participate in all assessment time points. After completing all evaluations, the intervention team contacts patients to schedule a familiarization session and subsequent treatment.

The research team underwent comprehensive training on the assessment and intervention methods prior to the study. The training process started with the provision of illustrated materials in a virtual environment, covering the essential themes of the intervention. Subsequently, in-person training was conducted in several stages. During the initial meeting, the assistant researcher explained the concepts related to the joint condition, and the intervention program was thoroughly discussed. This explanation encompassed the definition of knee OA, the crucial role of exercises in physiotherapeutic treatment, elucidating methods for conducting this therapeutic approach both in person and remotely, and the topics related to the educational approach to OA.

In the subsequent meeting, the study team received training on how to conduct the protocol in both modalities. They experienced one session of the intervention program exercises, both in person and via video calls. In addition, the team responsible for the assessment received training related to each outcome and measurement. Training sessions for both intervention and assessment teams were conducted in focal groups.

Furthermore, each topic of the educational approach was discussed from a theoretical and practical perspective. Decision-making related issues were emphasized concerning possible challenges encountered during video calls, such as connectivity loss or transmission quality concerns. During the third meeting, a pilot study involving real patients was conducted to train the team.

Plans to promote participant retention and complete follow-up {18b}

During the recruitment period, patients receive thorough explanations regarding the importance of participating

in all assessment time points. In weeks one, three, and eight, education strategies aimed at enhancing adherence to exercise programs are implemented to promote patient engagement with study assessments. Additionally, all patients receive regular follow-ups from staff and are provided priority access to schedule appointments at the clinic or remotely to address any concerns or manage worsening joint symptoms.

Data management {19}

The collected data will be stored in a digital file on the responsible researcher's drive, with the names of the participants coded as IDs, thus allowing more accessible access to the information collected for future data analysis. Therefore, to maintain participants' safety and resolve any doubts about the research, the information collected will be stored for 5 years after the end of the study.

Confidentiality {27}

All data collected will be anonymous and identified by ID. The data will be stored in a secure drive accessible only by the research team.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

There is no need to collect any specimens as it is not applicable.

Patient public involvement

In this trial, we did not plan for direct involvement of patients in the study design. However, the study manager (MTXC), a physical therapist at the Physical Therapy Clinic of the University Hospital, regularly interacted with knee OA patients who had similar expectations regarding physical therapy treatment. Based on gaps identified in the available literature and the main concerns reported by patients, the study was designed by the study manager (MTXC) and the principal investigator (CLA).

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

The study will use descriptive statistics to present the baseline characteristics of the participants. The between-groups difference and 95% confidence interval (95% CI) after 6, 12, and 18 weeks of treatment will be calculated using linear mixed models using interaction terms of treatment group versus time. A non-inferiority of the remotely supervised exercise would be demonstrated if the lower bound of the two-sided 95% CI for the between-group difference (remotely supervised exercise minus in-person supervised exercise) would be above -1.6 points for pain and -6.4 points for physical function (KOOS Activities of daily living subscale) (corresponding to 20% less than the minimum clinically significant difference reported by these outcome) [67, 69]. Effect sizes (Cohen's d) between groups will be calculated and classified as small (0.2 to 0.5), moderate (0.5 to 0.8) or large (above 0.8). The significance level adopted in this study will be $\alpha = 0.05$. All statistical analyses will be performed on SPSS statistical software (Statistical Package for Social Science), version 20.0 for Windows (IBM corporation, Somers, NY, USA).

Interim analyses {21b}

No interim analyses are planned for this study because it was designed to assess the effect of interest according to a predefined non-inferiority margin for the primary outcome pain level, based on a prior sample size calculation. In addition, given that the international guidelines strongly recommend the intervention proposed in the study, we do not anticipate any issues that could be detrimental to participants, which would necessitate an interruption of the trial.

Methods for additional analyses (e.g., subgroup analyses) {20b}

None planned.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

The study's primary and secondary outcomes will be analyzed using two methods: intention-to-treat analysis, which involves all patients randomized into the study, and per-protocol analysis, which focuses only on patients who followed the intervention with an adherence rate of more than 85%. Multiple imputations will be used to impute missing data using a specific function on SPSS software.

Plans to give access to the full protocol, participant level data and statistical code {31c}

The full study protocol, participant-level data, and statistical code can be made available by the Trial Coordinator upon reasonable request.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

Due to the study's single-center nature, a specific monitoring committee was not considered. However, the main researcher (CLA) supervises all trial steps through continuous communication with the study manager (MTXC), who coordinates the research team. The study manager is responsible for training the work team, providing constant support, and taking all the necessary precautions to avoid unmasking treatment allocation.

Composition of the data monitoring committee, its role and reporting structure {21a}

A data monitoring committee was not considered as this study will be conducted in one center and adopts a low-risk intervention.

Adverse event reporting and harms {22}

In the context of knee osteoarthritis patients, adverse events encompass any increase in pain intensity during the trial or other joint symptoms presentation (such as clicking, swelling, catching, restricted range of motion, and stiffness) during assessments or intervention periods. In this sense, adverse events will be monitored and categorized according to the severity of pain, classified as mild (1–3), moderate (4–7), or severe (8–10). In addition, the research team will monitor predictability (expected or unexpected) and possible association with the timing of outcome measures, the exercise protocol, and the mode of supervision (associated, possibly associated, or not associated). All potential adverse events will be discussed by at least two researchers (the principal investigator and study manager) and, if necessary, consultants and experts in the field.

Frequency and plans for auditing trial conduct {23}

The research team meets weekly to discuss the trial development, any necessary adaptations, and the quality of delivering the exercise protocol for knee OA participants. Study documents are constantly checked for an independent researcher not involved with the present study to guarantee the accuracy of data tabulation at all time points. If any records are missing, the research team will report it to the local ethics committee. The research team will contact the patient if any information needs consistency. The composition of the research team that discusses the trial development and delivery of exercise consists of the main researcher (CLA) and the study manager (MTXC), who maintains periodic contact with the intervention and evaluation team, providing support weekly while maintaining blinding. As detailed in the "Composition of the data monitoring committee, its role, and reporting structure" section, we did not establish a data monitoring committee because the intervention poses a low risk to patients.

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees) {25}

All possible amendments to the Protocol are primarily discussed between the study manager and main researcher, and subsequently communicated and approved by the Human Research Ethics Committee from the Federal University of Pelotas—RS. After Ethical approval, the researcher adjusted the ClinicalTrials.gov register to maintain public any amendments in the protocol. All deviations from the Protocol will be documented thoroughly using a breach report form or described in the future publication of the original article of the randomized controlled trial. Possible amendments did not include changes in intervention, delivery format, or assessment instruments. Changes may include some adaptations in data analysis that did not affect the quality of intervention delivery.

Dissemination plans {31a}

We planned to disseminate our results in three ways:

1. Through the Scientific community by submitting papers to journals,
2. Through our future randomized patients, and
3. Through social media and local newspapers.

All positive and negative results will be disseminated, ensuring transparency in research.

Discussion

The RISE-KOA study aims to investigate whether a muscle-strengthening exercise program for the lower limbs, supervised remotely, is as effective as in-person exercise for patients with knee OA. We hypothesized that the supervised training remotely via video call is no inferior to supervised in-person training, and it will equally improve condition-specific PROMs, psychological well-being, sleep quality, functional performance, and quadriceps architecture of patients with knee OA.

Video calls are a relatively simple and common way to promote teleconsultations, increasing community access to rehabilitation services [70]. Previously published studies or those in development have explored the effectiveness of remote exercises for patients with knee OA using video calls for the prescription; however, the supervision throughout the entire treatment in this format remains

underinvestigated [71–73]. Thus, although telerehabilitation is an attractive mode and cost-effective strategy for delivering treatment equal to traditional face-to-face rehabilitation, studies focusing primarily on the comparability of supervised exercise remotely using video calls or in-person in patients with knee OA are scarce [29]. In this sense, our study aims to fill this gap in the literature, offering alternative ways for delivering the core treatment for knee OA. Furthermore, by confirming our hypothesis, the study findings will contribute to changing a "hands-on" care culture, offering other forms to deliver recommended treatment beyond the conventional face-to-face physiotherapeutic consultation in clinical settings.

The exercise protocol implemented in the RISE-KOA study exhibits some relevant characteristics. Firstly, the exercise program was designed to be pragmatic, employing straightforward exercises that can be easily performed in both scenarios at home (remotely) or the clinic (in-person). Secondly, the protocol includes weight-bearing and non-weight-bearing quadriceps exercises. This approach aims to improve the strength of the quadriceps femoris while simultaneously strengthening the lower limb muscles functionally, progressing through weight-bearing exercises (i.e., squat on the wall, wall push, and chair stand), with instructions provided to the patients distributing the weight during movements onto the arthritic leg or the more symptomatic knee. Thirdly, this exercise protocol does not only focus on quadriceps femoris function but also on entire lower limb muscles, with patients guided in each session to alternating muscular groups. Finally, a detailed periodization and prescription of exercise protocol is a positive characteristic of this study, given that many other studies need more accurate information about exercise protocol.

Knee OA is a highly prevalent condition that continues to rise with implications for physical disability and psychological well-being [2]. In this sense, patients experience changes in the quadriceps femoris muscle characterized by loss of muscle quality [35]. Also, some patients self-reported symptoms of anxiety, depression, stress, pain catastrophizing, and reduced sleep quality [74–76]. Considering these particular characteristics, a RISE-KOA study will provide a relevant social impact, addressing gaps in the literature concerning the comparability of exercises remotely supervised by video call or in-person in clinical, physical, and psychological outcomes.

High-quality studies with large samples are necessary to increase knowledge concerning telerehabilitation for patients with knee OA [77]. In this sense, our study will improve evidence about telerehabilitation using video calls, providing insights into the comparable effects of remote and in-person rehabilitation. It will help physiotherapists make better treatment options, particularly for patients who cannot attend in-person sessions. Also, our future findings can increase community access to exercise and empower people to choose the better a supervision modality (remote or in-person), considering patient preferences.

The study has a few limitations that need to be taken into consideration. Initially, patients participating in the remote exercise group, just like those in the in-person exercise group, will be invited to attend an in-person familiarization session before the intervention period. This familiarization session is crucial for learning exercises and adherence to the program. However, it does not accurately represent a completely remote intervention. Moreover, the study will investigate muscle architecture at only one site in each muscle; in this sense, future morphological changes obtained with this study will not reflect changes in the entire muscle volume. While recognizing these limitations, one of the strengths of this study is that it examines the effectiveness of two exercise delivery methods that will contribute to expanding access to therapeutic exercise for patients with knee OA in developing countries.

Trial status

This protocol was initially approved by ClinicalTrials.gov on October 26, 2023 (Version 1). An update was published on December 21, 2023 (Version 2). A new update was published on February 18, 2025 (Version 3). The most recent update involved a revision of the sample size calculation. This adjustment was necessary because we initially established a very strict non-inferiority margin for the primary outcome, pain level, which led us to update the sample size calculation. We estimated a new sample size considering a non-inferiority margin of 20% less than the minimum clinically significant difference for pain level according to CONSORT recommendations to conduct non-inferiority clinical trials. The first sample size calculation estimated 68 patients for the study, and the new sample size was 48 patients. Recruitment started on December 4, 2024, and ended on October 15, 2024. Study completion was estimated on March 8, 2025. The study protocol was submitted to Trials for publication in the initial recruitment on April 12, 2024.

Abbreviations

OA	Osteoarthritis
PROMs	Patient-reported outcomes measures
RISE-KOA	Remote and In-person Supervised Exercise in Patients with Knee Osteoarthritis
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
OARSI	Osteoarthritis Research Society International
BMI	Body mass index
NRS	Numerical rating scale
KOOS	Knee Injury and Osteoarthritis Outcome Score
RF	Rectus femoris
VI	Vastus intermedius
VM	Vastus medialis
VL	Vastus lateralis
EI	Echo intensity
ID	Internal code

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-025-08884-w.

Additional file 1: Box 1. Training periodization for weeks one and two of supervised lower limb muscle-strengthening exercises. Box 2. Training periodization for weeks three to seven of supervised lower limb muscle-strengthening exercises. Box 3. Training periodization for weeks eight to twelve of supervised lower limb muscle-strengthening exercises. Box 4. Exercise description, bearing, and progression. Box 5. Exercise illustration.

Additional file 2: SPIRIT 2013 Checklist.

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Authors' contributions {31b}
MTXC and CLA conceived the study idea. MTXC took the lead in writing the manuscript. CLA revised the manuscript. All authors read and approved the final manuscript.

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The authors declare that they have not received any assistance from any funding sources, such as funding agencies in public, commercial, or non-profit sectors. The study manager provides the materials used in this clinical trial. The Physiotherapy School Clinic and Radiology Department of the University Hospital of Campaign Region provide educational support, such as the availability of equipment and consumables.

Data availability {29}
The datasets analyzed during the current study will be made available from the corresponding author upon reasonable request after study completion.

Declarations

Ethics approval and consent to participate {24}
The RISE-KOA study procedures were performed according to the Declaration of Helsinki and approved by the Human Research Ethics Committee of the Physical Education School of the Federal University of Pelotas (Brazil) (CAAE: 74411723.0.0000.5313). Recruited participants are informed about all study stages, including information about the objectives, outcome measures, intervention characteristics, risks, benefits, and the confidentiality of data management. Data collection only begins after participants accept to participate in the study and sign the informed consent form.

Consent for publication {32}
Not applicable: no identifying images or other clinical and demographic data that could identify participants.

Competing interests {28}
The authors declare that they have no competing interests.

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