Pre-operative exercise therapy in subgroups of patients with knee osteoarthritis: outcomes on pain and function after TKA/UKA – A protocol for an individual patient data systematic review

Protocol paper for website OA trial bank

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Abstract

Introduction Knee pain is considered as the most disabling OA symptom in people with knee joint osteoarthritis (OA). Several treatment options are available for different stages of OA. Exercise therapy (ET) is one of the non-surgical and non-pharmacological therapy intervention with beneficial effects, recommended by international clinical guidelines. Although, patients might have improvement of pain and function pre-operative due to pre-operative ET, the primary purpose is to have better outcomes on pain and function postoperatively. The overall effects of pre-operative ET are rather small and the population of patients with knee OA is heterogeneous, therefore it is still unknown which patients benefit from exercise therapy given pre-surgery. Individualized and targeted patient care should be approached in the management of OA to improve treatment and patient outcomes. This study aims to identify subgroups of patients with knee OA who have better outcome after pre-operative exercise therapy compared to usual care after total knee joint replacement.

Methods and analysis We will conduct an individual patient data (IPD) analysis by collecting IPD of relevant published randomized controlled trials (RCTs). A systematic literature search will be performed through Embase, Medline, Web of Science, CINAHL and Scopus. The primary outcome will be self-reported pain and knee function 3 months post-surgery on a WOMAC scale and the secondary outcomes are pain and physical function measured at other time points and scales, hospital stay duration, adverse events, analgesic use and quality of life.
Subgroups that will be evaluated, will be defined based on age, sex, body mass index (BMI), severity of pain and physical disability, muscle strength, mental health complaints, presence of comorbidities, daily physical activity, and radiographic involvement of patellofemoral compartment. IPD of RCTs containing homogenous exercise interventions will be pooled and analysed using a two-stage approach to evaluate the treatment effect in different subgroups.

Ethics and dissemination For this study no new data is collected and therefore research ethical or governance approval is exempted. Findings shall be presented and shared via national and international conferences, publications in peer-reviewed journals and summaries on websites, which are accessible by the public and professionals.

Keywords Osteoarthritis, knee joint, exercise therapy, pre-operative, individual patient data

Introduction

The knee joint is the most commonly affected joint by osteoarthritis (OA). (1) Knee OA is a clinical diagnosis, presented most often with pain and physical dysfunction. Pre-operative inactivity can lead to muscle atrophy (such as the quadriceps), loss of bone density, and lung capacity. These conditions are reversible with proper exercise therapy (ET). (2) ET is recommended by the international clinical guidelines as a core treatment for patients with knee OA, consisting of several types and forms. ET programs have been developed to strengthen physical function, reduce patient anxiety before a knee joint replacement surgery, and improve physical outcomes after surgery. (3) Several studies have suggested that ET pre-operatively has potential to accelerate the recovery period and have better outcomes on pain and function postoperatively. (3)
However, the effect sizes of pre-operative ET are moderate and have a wide dispersion (regarding the postoperative recovery), potentially due to suboptimal content of exercise programmes, and a heterogeneous knee OA population. Therefore treatment regimens should be considered at individual patient level to see which patient benefits from which type of intervention. Possibly more targeting of subgroups is needed to distinguish people who are most likely to respond to pre-operative ET. (4)

The aim of this study is to investigate moderators of the effect of pre-operative ET to pain and function postoperatively, compared to pre-operative usual care (no exercise controls). For this a subgroup analysis will be performed with individual patient data (IPD). We will follow the 'better in, better out' theory, where patients undergoing surgery are anticipated to have a better outcome post-surgery after undergoing pre-operative ET. In general, a patient's physical condition has been correlated with less complications and better recovery. (5)

Methods

We will perform an IPD analysis of randomized clinical trials (RCTs) studying the effectiveness of pre-operative ET in patients with knee OA and awaiting a surgery (total knee arthroplasty (TKA) or uni-compartmental knee arthroplasty (UKA)). This study will be conducted in collaboration with and adhering to the protocols of the OA Trial Bank (www.oatrialbank.com). The data sharing agreement is between the OA Trial Bank and data deliverer. All data of the included RCTs will be submitted and stored within the OA Trial Bank. This protocol is not registered in the PROSPERO database.

A systematic search strategy has been developed in collaboration with Erasmus MC librarian, W.M. Bramer. The purpose of this search strategy is to collect all relevant RCTs by using different databases, such as Embase, Medline, Web of Science, CINAHL and Scopus.(6) This literature search was performed on 13th June 2022. The full search strategy with all search terms for each specific online database are shown in online supplemental appendix 1.

The following criteria will be applied to identify all relevant RCTs for this study purpose.

Study design

We will include all peer-reviewed RCTs only, studying pre-operative ET in all adult patients with knee OA awaiting a primary knee replacement surgery.

Participants

Participants are all patients, men or women, awaiting a primary TKA or UKA for OA. Studies with other

surgery treatment than TKA or UKA or with patients having a previous prosthesis of the affected knee joint will be excluded. In case it is not mentioned in the study, the IPD will be screened on these criteria. RCTs studying subgroups will also be included, because individual patient data are collected.

Intervention

RCTs evaluating any form of pre-operative ET will be included in this study. ET will be defined as supervised, repetitive and structured therapy, regardless of the setting. Also it should be purposeful for the improvement or maintenance of a specific health condition, like OA.(4, 7) This definition is to ensure the dose, frequency and intensity of the intervention, which will not be considered as criteria to in- or exclude studies for this IPD analysis. As per the WHO definition ET is participation in physical activity, existing of many forms, land- or water based, e.g. aerobic, strength, flexibility, balance or body-region specific exercises. Education/self-management/ motivational techniques can be part of the interventions. In case exercise therapy is combined with other form of interventions (i.e. pharmacological treatment, other surgical treatment), these studies will be excluded. By excluding these combined interventions, treatments effects attributed to exercise therapy alone could be measured. (4)

Comparison

RCTs comparing pre-operative ET with usual care as the control group will be selected. The control group will consist of therapy which are not supervised, or repetitive or structured. Usual care can consist of no intervention (usual physical activity) or usual physician follow up, education and advice, non-surgical treatment (e.g. pharmacological treatment) or other surgical intervention (e.g. diagnostic arthroscopy pre-operative, post-exercise), unsupervised home-training (e.g. with a maximum of one physiotherapist consult), but not of exercise therapy.

Outcomes

At least one or more adequate patient-reported outcome measure (PROM) on pain or physical function of the knee should be included in the outcome of the RCTs. The measurements should have been taken at least at one time point, within a year after surgery. The measurements method should have been done with one of the following scoring systems: the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS).

Types of baseline assessments

As a minimum, studies need to have assessed at least one or more of the subgroup factors (see next paragraph). The potential RCTs should have baseline PROMs before or at start of pre-operative ET. At least the level of baseline pain or function, age and sex should be mentioned. Besides that, other important patient characteristics measured at baseline, including body mass index (BMI), comorbidities, occupation, radiological severity and duration of symptoms (i.e. how long on the waiting list), will be extracted if available. These characteristics will be used to classify the patients in the subgroups and taken into account for bias evaluation.

Subgroup definitions

The potential subgroups have been pre-defined by reviewing the literature and by expert opinion. A thorough search of the literature has been conducted to identify clinical important moderators. These possible moderators have been discussed with clinical experts (part of the project group, see author list) to get a definitive set of potential moderators for pre-operative ET.

We have identified the following possible effect modifiers: age, sex, pain severity, severity of physical disability, muscle strength, mental health (anxiety or depression) and radiographic involvement of patellofemoral compartment. In case any of the primary effect modifiers data is not available, we will use other available variables as secondary effect modifiers, such as comorbidities (arthrosis/arthritis elsewhere, cardiovascular, respiratory diseases, neurologic (not able to perform exercise therapy)), daily usual physical activity, working status, use of a walking aid, use and need of analgesics and length of stay in the hospital.(8-11) The hypothesized direction of the effect for some potential moderators is variable due to lack of evidence, as Holden et al. have shown. (4) To identify potential relevant subgroups with clinical implications, we will dichotomize some of these moderators, before analysing the data. This will be performed by determining cut-off values based on the distribution of the data, the prevalence and consensus within the project group.

IPD analysis

For this IPD analysis, studies regarding animal studies will be excluded and there will be no language restriction. Inclusion criteria of the population, intervention and comparison are based on the criteria for the RCTs.
In contrast to the study of STEER OA (4) and Quicke et al. (12) we will investigate patients on the waiting list for knee arthroplasty for OA. Also, whereas previous studies have investigated hip osteoarthritis along to knee OA, we only investigate knee osteoarthritis. Criteria for the intervention and control groups are the same as in the previous mentioned studies (exercise vs non-exercise).

Outcome measures

The Cochrane Musculoskeletal Review Group (13) created a hierarchy of the outcome measures. However, a recent IPD review of Georgopoulos et al. (OARSI 2022 (14)) showed that caution is required in harmonization of PROMs for IPD analysis as they found substantial heterogeneity within data of individuals. Therefore they should be selected according to the clinical population and research question. All trials will be clustered based on their outcomes (e.g. patient reported outcome measures (PROMs) or performance-based outcome). Outcomes measured on different scales will be standardized in order to pool the data.

Primary outcome postoperative

The primary outcome for this IPD analysis is the difference of self-reported pain and physical function score (e.g. WOMAC/KOOS) at three months post-surgery between the subgroups. If there is no three months measurement, then any outcome measure closest to three months post-surgery will be the primary outcome.

We follow the 'better in, better out' theory for pre-operative exercise therapy, which means that patients on the waiting list, following pre-operative ET, should have improvement of the (pre-operative) medical condition to obtain better outcome post-surgery without necessarily pain reduction. Pre-operative pain reduction is not a compulsory aim of the pre-operative ET.

Secondary outcomes pre-operative

The secondary outcomes, measured post ET and pre-operatively, will be:

- Self-reported pain (measured on VAS/NRS),
- Self-reported physical function score (WOMAC/KOOS)
- Range of motion
- Performance-based score

The OARSI guidelines recommended a core set of performance-based tests of physical function (30-second chair stand test, 4x10 m fast-paced walk test and stair climb test), which also was assessed by Tolk et al. (15, 16). We will consider the change in these performance-based outcome measures, if two or more studies have analysed one of these.

- Quality of life (measured by KOOS, Quality adjusted life years (QALY), 36-Item Short Form Health Survey (SF-36))

Secondary outcomes postoperative

Additional secondary outcomes will be those measured at any other time point post-surgery (e.g. after 8 weeks, 6 months or 12 months of follow-up)

- Self-reported pain (measured on VAS/NRS),
- Self-reported physical function score (WOMAC/KOOS)
- Range of motion
- Performance-based score
- Hospital stay duration
- Adverse events
- (reduction of) analgesic use
- Quality of life (measured by KOOS, QALY, SF-36)

If due to pre-operative ET, no surgery was required (e.g. pain reduction or function improvement), the patient data will be extracted and presented as a descriptive analysis.

Data collection

Multiple reviewers will independently select studies based on titles and abstracts. These will be imported into EndNote 20.0.1. Secondly, full articles are obtained for those citations which might fulfill the inclusion criteria and will be screened by the same reviewers, independently. A third author will be consulted if consensus is not reached. Then, the first author and/or corresponding author of the included RCTs will be contacted following the procedures of the OA Trial Bank. If the corresponding author cannot be reached, we will contact the other authors or institutes in which the trials have taken place. They will be requested to participate and consequently share anonymized IPD of the RCTs. Full protocol details for the IPD meta-analysis are pre-specified in the data delivery license agreement, that was approved by all members of the OA trial Bank Steering Committee.

A data delivery license agreement has been set up by the OA Trial Bank, including items on input data, obligations, ownership of data, terms, authorship, statistical analyses and publications. All data deliverers will be asked to sign this agreement. Data-entry mistakes and consistency will be checked to ensure the quality of the data. Also all individual patient results will be compared with the published summary results of the primary studies. If there will be differences, authors will be contacted to resolve the discrepancies.

Risk of bias

The risk of bias will be evaluated for every included trial, by two independent authors, using the revised version of the Cochrane Risk of Bias (RoB) tool, known as RoB 2.0(17)**.** The criteria can be scored as 'yes' (low risk of bias), 'no' (high risk of bias) or 'unclear'. If a trial fulfilled six or more criteria items, the trial will be considered having a low risk of bias, which is supported by empirical evidence.(18) A disagreement between the reviewers will be discussed with input from a third reviewer.

Data extraction

The following data will be extracted from the published RCTs as per the availability: list of authors,

target population, country of study, publication year, patient characteristics (age, sex, BMI), disease-specific characteristics (clinical criteria, radiographic information, duration of complaints, on-going treatments), details of the intervention (e.g. exercise therapy and surgery) and intervention measures, comparator groups, and all outcome measures of pain or function on all time-points that are available. Interventions will be categorized by frequency, intensity, type, duration, setting, and exercise deliverer.(4)

To create one complete and homogeneous dataset, all datasets will be converted into a common format with IBM SPSS statistics software 28.0 (or any latest version). A new variable will be then created to allocate and identify all trials with an individual random trial number. All the randomized patients with a database record will be entered in the pooled database.

Data analysis

After receiving the datasets, an IPD analysis will be performed. We will follow an intention-to-treat analysis. For this study, a two-stage approach will be performed, where from each trial all IPD will be analysed separately in the first stage to obtain aggregate data of effect estimates of interest, which are then pooled in the second stage to produce summary meta-analysis results based on a random effect model. A subgroup analysis will be done if at least two or more studies have investigated a moderator, to have a better power for the subgroup analysis. The mixed-effect regression model (or hierarchical) method is particularly suitable for investigating interaction effects between the subgroups. In order to avoid aggregation bias and estimate the treatment-covariate interactions, these interactions will be estimated in each trial separately, and then synthesized in the second stage. The model will include the baseline and follow-up measures of dependent variables (i.e. pain intensity or physical function score), independent variables (i.e. treatment (intervention or control)), the effect modifier (different subgroups), and an interaction term (subgroup x treatment). A single covariate will be included in the regression model to adjust for possible residual confounding by study differences. The pooled subgroup effect of pre-operative ET will be estimated by the mean difference (for continuous outcomes) and odds ratio (for binary outcomes). A p-value of <0.05 is regarded as statistically significant. When obtaining too few studies (i.e. less than 3 RCTs or < 100 patients in total), an one-stage approach will be performed by combining all individual patient data in a single meta-analysis based on a regression model stratified by trial. (19, 20) If there will be more than three RCTs with a total of > 100 patients for one type of control group, then we will analyse subgroups per control group. The control groups will be divided into non-surgical (e.g. pharmacological) treatment and no treatment.

It is important to note that the population of both surgery methods differ. Therefore at first an overall analysis will be performed, to then look for interaction between ET and type of surgery method, within the different type of surgery groups.

If more than 10% of the data is missing, we assume it to be missing at random. Therefore observed patient characteristics will be used to impute missing data (potential covariates and outcomes) by means of multiple imputation. Missing data will be imputed within each original study, before data of the individual studies are pooled.(18)

Heterogeneity

During selection of the trials, the interventions will be screened on clinical heterogeneity. We expect the types of interventions, in the several trials, to be heterogeneous with different rehabilitation protocols. Details of the interventions will be specified in order to see if interventions are homogenous and can be

clustered, if possible. The between-study differences will be assessed by a descriptive comparison.

Statistical heterogeneity of the eligible studies will be determined for the primary outcomes, using a two-stage meta-analysis approach in Review Manager V.5.3. A sensitivity analyses will be done without data from trials causing the heterogeneity, in case of high heterogeneity (I^2 index >50).

Status of project

Currently, the search strategy has been completed. We expect the study selection to be finished in February 2023. Data collection is expected to be finished by December 2023.

Ethics and dissemination

Ethical research approval or governance approval is exempted for this IPD analysis, as no new data will be collected. To secure the confidentiality and secure transfer of IPD, existing protocols of previous OA Trial Bank projects will be used. All data will be stored in a secured digital research environment of the OA Trial Bank. Results and finding of this IPD analysis will be shared via national and international meetings, conferences, publications in peer-reviewed journals. Also summaries will be posted on websites (including our institutional patient platform) accessed by the public, clinicians and patients. Our aim is to inform all professionals involved with (all type/non-surgical and non-pharmacological) treatment modalities of knee OA.

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Disclaimer The funder will have no input on results or publication of the results.
Competing interests None declared
Patient and public involvement statement The Dutch Arthritis Society aims to improve treatment in patients with OA being a patient-driven foundation. The advisory board of the OA Trial Bank includes researchers in the field, a delegate of the Dutch Arthritis Foundation, and Patient Involvement (PPI). Patient members advise the Steering Committee of the OA Trial Bank on their activities. Given the nature of the study design, there is no patient involvement in the recruitment and conduct phase of this study. The generated results and conclusions however will be translated into laymen text and spread to patients and the general public through regular meetings of patient-oriented organisations and info-bulletins on Artrose Gezond, an OA patient oriented webbased platform.
Patient consent for publication Not applicable.

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Supplemental appendix 1: Search strategy

embase.com

('knee osteoarthritis'/de OR 'total knee arthroplasty'/de OR (('knee pain'/de OR 'patellofemoral joint'/de OR knee/de OR 'lower limb'/de) AND osteoarthritis/de) OR (((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial* OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) NEAR/6 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*):ab,ti) AND (kinesiotherapy/de OR physiotherapy/exp OR physiotherapist/de OR 'aerobic exercise'/exp OR 'anaerobic exercise'/exp OR 'aquatic exercise'/exp OR 'dynamic exercise'/exp OR 'exercise intensity'/exp OR 'high intensity exercise'/exp OR 'isokinetic exercise'/exp OR 'leg exercise'/exp OR 'low intensity exercise'/exp OR 'moderate intensity exercise'/exp OR 'muscle exercise'/exp OR 'preoperative exercise'/exp OR 'static exercise'/exp OR 'isometric exercise'/de OR 'movement therapy'/de OR 'muscle training'/de OR 'stretching exercise'/de OR (kinesiotherap* OR kinesitherap* OR (exercise* NEAR/3 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) NEAR/3 (exercise* OR training)) OR (movement NEAR/3 therap) OR ((muscle OR strength) NEAR/3 trainin*)):ab,ti) AND ('knee arthroplasty'/exp OR arthroplasty/de OR 'orthopedic surgery'/de OR 'joint surgery'/de OR 'preoperative period'/de OR 'postoperative period'/de OR 'osteoarthritis'/exp/dm_su OR (preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) NEAR/3 (arthroplast* OR replacement*))):Ab,ti) NOT [conference abstract]/lim NOT ([animals]/lim NOT [humans]/lim)

Medline ALL Ovid

(Osteoarthritis, Knee/ OR Arthroplasty, Replacement, Knee/ OR ((Patellofemoral Joint/ OR Knee Joint/ OR Knee/ OR Lower Extremity/) AND Osteoarthritis/) OR (((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial* OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) ADJ6 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*).ab,ti.) AND (exercise therapy/ OR exp Physical Therapy Modalities/ OR Physical Therapists/ OR High-Intensity Interval Training/ OR Preoperative Exercise/ OR Muscle Stretching Exercises/ OR (kinesiotherap* OR kinesitherap* OR (exercise* ADJ3 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) ADJ3 (exercise* OR training)) OR (movement ADJ3 therap) OR ((muscle OR strength) ADJ3 trainin*)).ab,ti.) AND (Arthroplasty, Replacement, Knee/ OR Arthroplasty, Replacement/ OR Orthopedic Procedures/ OR Surgical Procedures, Operative/ OR Preoperative Period/ OR Postoperative Period/ OR Waiting Lists/ OR exp Osteoarthritis/su OR (preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) ADJ3 (arthroplast* OR replacement*))).ab,ti.) NOT (exp animals/ NOT humans/)

Web of science

TS=(((((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial* OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) NEAR/5 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*)) AND ((kinesiotherap* OR kinesitherap* OR (exercise* NEAR/2 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) NEAR/2 (exercise* OR training)) OR (movement NEAR/2 therap) OR ((muscle OR strength) NEAR/2 trainin*))) AND ((preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) NEAR/2 (arthroplast* OR replacement*))))) AND DT=(article)

Scopus

TITLE-ABS-KEY(((((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial* OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) W/5 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*)) AND ((kinesiotherap* OR kinesitherap* OR (exercise* W/2 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) W/2 (exercise* OR training)) OR (movement W/2 therap) OR ((muscle OR strength) W/2 trainin*))) AND ((preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) W/2 (arthroplast* OR replacement*))))) AND DocType(ar)

CINAHL EBSCOhost

(MH Osteoarthritis, Knee OR ((MH Knee Joint OR MH Knee OR MH Lower Extremity) AND MH Osteoarthritis) OR TI(((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial*

OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) N5 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*) OR AB(((knee* OR femorotibial* OR tibiofemoral* OR tibio-femoral* OR femoro-tibial* OR patellofemor* OR patell*-femor* OR lower-limb* OR lower-extremit*) N5 (osteoarthr* OR osteo-arthr* OR arthrosis* OR arthroses* OR arthroplast*)) OR gonarthro*)) AND (MH Therapeutic Exercise OR MH Lower Extremity Exercises OR MH Physical Therapy + OR MH Physical Therapists OR MH High-Intensity Interval Training OR TI(kinesiotherap* OR kinesitherap* OR (exercise* N2 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) N2 (exercise* OR training)) OR (movement N2 therap) OR ((muscle OR strength) N2 trainin*)) OR AB(kinesiotherap* OR kinesitherap* OR (exercise* N2 (therap* OR treatment*)) OR physiotherap* OR physi*-therap* OR ((aerobic* OR anaerobic* OR aquatic* OR dynamic* OR intensity* OR isokinetic* OR leg* OR muscle* OR preoperative* OR static* OR isometr* OR stretching OR walking OR strengthen* OR postoperat*) N2 (exercise* OR training)) OR (movement N2 therap) OR ((muscle OR strength) N2 trainin*))) NOT (MH animals+ NOT MH humans+) AND (MH Arthroplasty, Replacement, Knee OR MH Arthroplasty, Replacement OR MH Arthroplasty OR MH Orthopedic Surgery OR MH Surgery, Operative OR MH Preoperative Period OR MH Postoperative Period OR MH Waiting Lists OR TI(preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) N2 (arthroplast* OR replacement*))) OR AB(preoperati* OR pre-operati* OR presurg* OR pre-surg* OR postoperati* OR post-operati* OR postsurg* OR post-surg* OR waiting-list* OR surger* OR surgical* OR waitinglist* OR ((knee OR joint*) N2 (arthroplast* OR replacement*))))