APPENDIX 1: Outcomes

Primary outcome

The pain subscale of the WOMAC Osteoarthritis Index LK3.0\textsuperscript{74} questionnaire will be used for the assessment of pain severity. The Knee injury and Osteoarthritis Outcome Score (KOOS)\textsuperscript{75} includes WOMAC Osteoarthritis Index LK3.0\textsuperscript{74} in its complete and original format (with permission). WOMAC (and therefore the pain and symptoms subscale of the KOOS) is a valid tool for subjects with KOA. The KOOS is proven to generate valid and reliable scores\textsuperscript{76,77}. The KOOS shows adequate content validity, internal consistency, reliability, content validity and responsiveness for age and condition relevant subscales\textsuperscript{77}.

Secondary outcomes

Different subtypes of pain (online)

Different subtypes of pain, such as intermittent pain, constant pain, and central sensitization will be measured using various short and easily applicable self-reported measures. The nominated visual analogue scale (VAS) measures pain in the activity that most aggravates the pain (nominated by the patient)\textsuperscript{62}. The intermittent and constant pain (ICOAP) will be used to evaluate the constant and intermittent pain experience\textsuperscript{122}. The ICOAP is believed to generate reliable and valid data\textsuperscript{123,124}. The Central Sensitization Inventory (CSI) aims to assess central sensitization. The total score of the CSI ranges from 0 to 100. A score of 40 or higher indicates the presence of central sensitization pain\textsuperscript{117}. The psychometric strength, clinical utility, and initial construct validity of the CSI in chronic pain patients with CS-related symptoms were demonstrated\textsuperscript{116}.

Function in daily living (online)

Function in daily living will be measured using self-reported measures\textsuperscript{72}. The KOOS function in daily living (ADL) subscale and functioning in sports and recreation subscale are reliable and valid scales to measure function in people with osteoarthritis\textsuperscript{75,77,125}. The patient global assessment measures the improvement or deterioration of their condition since baseline\textsuperscript{55} on a 7-point Likert scale.

Treatment adherence/compliance

Patients’ attendance at treatment sessions will be recorded. Patient adherence for the treatment sessions will be calculated as the ratio of the number of treatment sessions that were carried out versus the number of prescribed sessions. For the home sessions, patients will be asked to record the sessions’ content in a personal log book. Treatment adherence will be calculated as a ratio of the number of training/activity sessions that were carried out at home versus the total number of prescribed home sessions. Compliance will be calculated as the ratio of the total training duration (recorded in the logbooks) versus the prescribed total training duration, multiplied by 100. Patient drop-out and the reason for withdrawal will be registered. In addition, co-interventions will be closely monitored.

Health care cost effectiveness
Medical consumption, the type, dose, method of administration and frequency of analgesic, NSAID or symptom-modifying medication, as well as surgeries (total or partial knee replacements) will be recorded. Health care use will be evaluated using three questionnaires: (1) the Medical Consumption Questionnaire; and (2) the Productivity Cost Questionnaire. These two questionnaires are understandable, easy-to-use and generate valid data. (3) Third, the EuroQol EQ-5D will be used to calculate quality adjusted life years in the cost-utility analysis.

**Explanatory outcomes**

Possible treatment mediators to be measured include pain catastrophizing, pain hypervigilance, illness perceptions and dietary intake.

**Pain catastrophizing**

The Dutch translation of the Pain Catastrophizing Scale (PCS-DV) has demonstrated adequate to excellent internal consistency (Cronbach’s alphas between 0.85 and 0.91). Construct and concurrent validity were demonstrated good. Previous research indicated that a total PCS score of 30 represents a clinically relevant level of catastrophizing.

**Pain hypervigilance**

The Pain Vigilance and Awareness Questionnaire (PVAQ) comprises 16 items and investigates awareness, consciousness, vigilance, and observation of pain in persons with chronic pain. The items have demonstrated good internal consistency reliability (Cronbach’s alpha = .86) in a population of chronic pain.

**Illness perceptions**

The illness perception questionnaire-revised (IPQ-R) addresses the patient’s perceptions of pain and illness. The IPQ-R has good construct and criterion validity and discriminates clearly between acute and chronic pain populations. It has been demonstrated to be a reliable questionnaire, except for illness coherence. Furthermore, the internal consistency is good, except for the causal domain.

**Dietary intake**

As high-fat, high-energy and ketogenic diets are known to affect inflammation, patients’ food intake can potentially confound the study findings. Therefore, dietary intake will be assessed online using the Food Frequency Questionnaire, an easy-administered tool generating valid data.