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Synopsis

The Knee Arthroplasty versus Joint Distraction Study for Osteoarthritis (KARDS): lessons learnt from an internal pilot trial

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Abstract

Background: Patients with symptoms of pain and restricted function related to knee osteoarthritis are typically offered a knee replacement. However, a proportion remain dissatisfied with their outcomes, and the failure risk is disproportionately higher in the young. Knee joint distraction may be an intervention to postpone the time to knee replacement in this patient population.

Objective and main outcome measure: The primary objective of the Knee Arthroplasty versus Joint Distraction Study for Osteoarthritis (KARDS) was to evaluate the effectiveness of knee joint distraction compared to knee replacement based on patient-reported pain 12 months post surgery using the Knee Injury and Osteoarthritis Outcomes Score pain score as the primary outcome.

Design and methods: KARDS was an open-label, two-arm individually randomised controlled non-inferiority trial with an embedded 12-month internal pilot phase and process evaluation to evaluate recruitment feasibility. A hybrid expertise design was used to account for surgeon expertise and potential lack of individual equipoise. The trial was closed to recruitment early following cessation of elective orthopaedic surgery secondary to COVID-19 pandemic. Descriptive statistics are reported.

Setting: United Kingdom National Health Service Trusts.

Participants: Adult patients aged < 65 years with symptoms severe enough to warrant knee replacement, in the opinion of the treating clinician.

Interventions: Participants were randomised to receive either knee joint distraction (static distraction of 5 mm, using external fixator for 6 weeks) or knee replacement.

Results: Twenty-four participants were randomised from a single centre between March 2021 and October 2022 with minimum 3-month safety follow-up post surgery. Eleven participants were randomised to knee joint distraction and 13 to knee replacement. Seventeen patients were male (71%), median age 60 (47–65) years. One patient withdrew due to being medically unfit for surgery and two received a different treatment than which they were randomised

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(one crossover from each arm). The median Knee Injury and Osteoarthritis Outcomes Score pain score in the knee joint distraction group improved from 38.9 (22–50) at baseline to 55.6 (0–100) at 12 months, corresponding scores in the knee replacement improved from 30.6 (6–36) to 75.0 (50–100). Adverse events were more common with knee joint distraction, pin site infection being the commonest complications (n = 4, 58%).
As part of process evaluation, we conducted semistructured qualitative interviews with staff in secondary care and with study participants. Data were analysed using thematic content analysis. One overarching theme emerged: 'An unexpected journey', which encapsulates staff and participants' experiences.
Conclusion: Reduced research capacity and the suspension of elective surgery following the COVID-19 pandemic caused significant recruitment barriers. Despite early termination, KARDS demonstrated that patients were willing to be recruited to a trial investigating a novel treatment for knee osteoarthritis and the trial was feasible and implementable. The limited results indicated that the technique is safe with no safety concerns. Clinical and cost-effectiveness of knee joint distraction remains uncertain. The embedded KARDS process evaluation has provided helpful insights.
Limitations: Reduced research capacity at sites and suspension of elective surgery services within the United Kingdom following COVID-19 caused significant recruitment barriers to KARDS. All the recruited patients in both arms of the study were White.
Future work: As a commissioned piece of research with delivery significantly impacted by the National Health Service environment post-COVID and the impact on National Health Service surgical services, the research question remains highly relevant. Any future research in this field can be helped by the pilot data published here along with the lessons learnt.
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Background

Osteoarthritis (OA) is the most common musculoskeletal condition that affects joints, causing pain and joint dysfunction with significant impact on quality of life. In England alone, an estimated 8.75 million people aged 45 and over have sought treatment for OA, including 4.1 million with knee OA.[1] With rising obesity rates and an ageing population, the number of people presenting with knee OA is increasing.[1,2]

Beyond pain medications and physical therapy strategies, no pharmacological or surgical treatment currently available reliably cures or halts OA. Therefore, patients with knee OA and severe symptoms are typically offered a knee arthroplasty, also known as knee replacement (KR), to relieve pain and improve mobility. KR is a cost-effective and clinically proven technique.[3] However, a significant proportion of patients with a KR continue to be dissatisfied with their outcomes. Analysis of the England and Wales National Joint Registry data set showed that < 10% of patients after total KR report no problems with their knee while a significant proportion have major ongoing issues, such as problems with kneeling (57%), persistent pain (20%) and pain on walking (17%).[4] In addition, artificial joints have a finite life span and KRs fail over time, secondary to aseptic loosening, wear or instability, requiring them to be revised. Revision of a KR is complex, costly and associated with higher morbidity, mortality, and inferior outcomes.[5–7]

The number of young patients undergoing KR is increasing year on year.[5–7] The risk of failure of KR is disproportionately higher in the young and active. The age-adjusted estimate of lifetime risk of revision after KR is 35% in males between 50 and 54 years of age. The risk of re-revision in these cases is significantly higher, and associated morbidity (infection, cardio-respiratory problems, stroke, venous thrombo-embolism) and mortality increases with every subsequent surgical intervention.

The age at which a patient receives a KR is the most important factor affecting both implant survival as well as clinical outcomes, with patients younger than 60 years having the worst clinical outcomes and the highest revision rate.[5,7] Currently 40% of primary KRs and up to 44% of KR revisions in Europe are performed in patients aged < 65 years.[8–10] The risk of revision KR is < 5% if the first KR is performed at around the age of 70 years.

Rationale for research

There is a clear unmet need for a treatment which postpones the time to KR, particularly in the young population (< 65 years) with knee OA, thereby preventing or postponing revision KR.[8,9] To bridge this gap in treatment options, there is a need for cost-effective strategies that preserve the joint. Knee joint distraction (KJD) is one such treatment option to address the current problems associated with KR in the younger population. KJD is a joint-sparing technique not currently widely used in the UK but has shown good midterm outcomes in studies

conducted in the Netherlands.[10–12] It utilises the well-established orthopaedic practice of external fixators for fracture stabilisation, except that the stabilisation is across a synovial joint. KJD harnesses intrinsic joint repair potential, providing cartilage repair and normalisation of subchondral bone abnormalities.[11]

Knee joint distraction aims at mechanically unloading the damaged tibiofemoral joint surfaces of the arthritic knee and allowing 6 weeks of biomechanical joint homeostasis by distracting the femur from the tibia by approximately 5 mm. This distraction is achieved and maintained using an external fixator assembly.[10] This procedure can be performed in 30–45 minutes. To date, none of the patients receiving total knee replacement (TKR) after KJD treatment (16.6% at 5 years) have reported joint or deep wound infection (personal communication).

Knee joint distraction for treating knee OA has been reported to be safe and effective in studies carried out in the Netherlands[12,13] but no such studies had been conducted in the UK in an NHS setting. One small trial (n = 60) suggested KJD to be non-inferior to TKR in function and achieved good patient satisfaction from baseline to 5 years in the Western Ontario and McMaster Universities OA Index (WOMAC) functioning and pain scales.[11,14,15] It had also been shown to be non-inferior to tibial osteotomy (n = 69) in randomised clinical trials.[10] A relatively high pin tract infection rate has been reported (60%) in the KJD patients.

KJD was predicted to save over 100 TKRs and ~30 revision KRs over a 20-year period for patients < 55 years.[16] With a willingness to pay €20,000 per quality-adjusted life-year, KJD was estimated to be cost-effective in > 75% in all age groups and > 90% in young < 55 years (€1 = £0.87; conversion date: 28 July 2025).[17] In an update, Struik T, *et al.* published their experience in 2023. They reported on outcomes of 49 patients at 2 years: 1 patient did not complete treatment, 3 patients received arthroplasty in the first and 4 patients received arthroplasty in the second-year of follow-up.[18] Eight patients were lost to follow-up in the second year. The total WOMAC score showed a clinically relevant improvement at 1 and 2 years (+ 26 and + 24 points), as did all its subscales. Authors also reported on the changes in the minimum radiographic joint space width which improved over 1 (+ 0.5 mm; p < 0.001) and over 2 (+ 0.4 mm; p = 0.015) years, as did the physical Short-Form 36 (+ 10 points; p < 0.001). The results summarised above demonstrate the usefulness of KJD but are again from the 'designer' centre.

KJD could be an alternative therapy to KR for younger patients (< 65 years) where there is a large unmet treatment need. However, the current evidence base is small and outside of the UK NHS environment. Our patient and public involvement (PPI) feedback indicated that the single most important priority for patients in this age group is retaining their own knee, at the expense of some residual knee pain. If shown to be non-inferior in the NHS setting, KJD could be offered to patients aged 65 and under and thereby enable postponement of KR and further revision surgery.

Objectives

The overall aim of the Knee Arthroplasty versus Joint Distraction Study for Osteoarthritis (KARDS) was to investigate the clinical and cost-effectiveness of KJD compared to KR in the treatment of patients aged 65 years or under. The target population was patients with symptomatic knee OA refractory to non-surgical treatment that was severe enough to warrant KR (unicompartmental or TKR) and who had intact collateral ligaments and leg alignment not requiring correction.

The primary objective was to examine the effectiveness of KJD compared to KR based on patient-reported pain 12 months after surgery using the Knee Injury and Osteoarthritis Outcomes Score (KOOS) pain score as the primary outcome measure. KOOS is a patient-administered questionnaire validated for use in patients with knee OA or knee injury, consisting of 5 domains with a total of 42 items.[19] A normalised score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each KOOS domain.

Secondary objectives were:

1. Patient-reported outcomes and quality of life within 24 months after surgery measured using KOOS at the component level.
2. Pain visual analogue scale (VAS) unidimensional measure of pain intensity[20,21] ranging from 'no pain' (score 0) to 'pain as bad as it could be' or 'worst imaginable pain' (score 100). Please note that for VAS, the worst outcome would be a score of 100 and for KOOS, the best outcome would be a score of 100.
3. Oxford Knee Score (OKS) assessing outcomes of knee interventions[22–24] ranging from 0 (most symptoms) to 48 (least symptoms).
4. Objective assessment of knee function measuring the angles of the affected leg with a goniometer to determine the range of movement, timed-up-and-go test (TUG).
5. Rates of intraoperative and postoperative complications reported by their degree of severity using the Clavien–Dindo classification.[25] Surgical site infection was categorised based on the Centers for Disease Control and Prevention (CDC) classification and recorded with antibiotics use.[26]

6. The need for further intervention within 24 months after surgery.
7. Short- and long-term cost-effectiveness.
8. Intervention fidelity.
9. Participant experiences of the trial/interventions and possible facilitators or barriers to wider implementation.

Methods

Full details of the proposed KARDS trial design and analysis plan were published as a protocol.[27] Protocol amendment history is recorded (see *Appendix 1*, *Table 1*). It was pre-specified that publication would be divided as process evaluation (PE), main trial results based on 12-month outcomes, health economic results, and subsequent publication of longer -term outcomes (24-month patient-reported outcomes and decision analytic cost-effectiveness).

Trial design summary

KARDS was an open-label, two-arm individually randomised controlled non-inferiority trial. It was planned that a total of 344 participants would be randomised on a 1 : 1 basis between KJD and KR, stratified by surgical delivery unit and OA severity. A hybrid expertise design was used to account for surgeon expertise in the surgical procedures and potential lack of individual equipoise. Surgeons were grouped into delivery units based on the interventions they were approved to deliver within the trial.

The trial had an embedded 12-month internal pilot phase (no fixed number of patients was allocated for the pilot phase, but this phase would last for 12 months to allow for the gathering of sufficient data to inform the main study) and PE with selected clinicians, participants and non-recruited patients to evaluate the feasibility of recruitment and address any barriers to recruitment. It was planned that all participants would be followed up for 24 months post surgery. The trial was not blinded to participants, medical staff or clinical trial staff. Progression at the end of the pilot phase will be based on (1) recruitment and dropout rates, (2) safety and (3) the PE.

KARDS was approved across NHS institutions in England and Scotland (reference number 19/YH/0368) and was overseen by an independent Trial Steering Committee (TSC) and a Data Monitoring and Ethics Committee (DMEC). The KARDS trial was prospectively registered on the International Standard Randomised Controlled Trial Number (ISRCTN) Register (reference number 14879004).

A trial flow diagram can be seen in *Appendix 1*, *Figure 2*.

Process evaluation and PPI: PE would be conducted using semistructured interviews in two key phases: (1) internal pilot phase and (2) main trial phase. The primary aim of the planned formative PE in the internal pilot phase (phase one) is to maximise participant recruitment to the trial and identify/minimise variation in intervention delivery that could affect outcomes. Specifically, the objectives in phase one are to (1) document individual sites care pathways (for context), (2) engage with key stakeholders (surgeons, recruiting staff, admin staff and patients) to understand their experiences of recruitment and (3) engage with surgical teams to explore their perceived facilitators and barriers to delivering the surgical interventions as per the protocol. In phase two, it is planned that further participant/non-participant interviews would be undertaken in the main phase of the trial. KARDS PPI group provided feedback on choice of primary outcome, minimally important difference used in sample size calculations and the decision to not blind participants. PPI representatives on the Trial Management Group provided feedback on the schedule of events for participants. The feedback continued through the life cycle of the study.

Early trial closure

The trial was closed to recruitment early, following cessation of NHS elective orthopaedic surgery secondary to the COVID-19 pandemic. The trial recruited participants from a single site. The closedown plan was ratified by the DMEC and the TSC and approved by the Sponsor and the Funder based on a 3-month postoperative follow-up period of all patients recruited.

Participants

Participants were adult patients aged < 65 years with symptoms (pain and/or reduced function) refractory to non-surgical treatment and severe enough to warrant KR, in the opinion of the treating clinician. Patients with bone density not sufficient to support pins for 6 weeks, in the opinion of treating clinician, were excluded. Patients were recruited from a single NHS hospital trust in the UK able to deliver both procedures (KJD and KR).

Interventions

Following confirmation of written informed consent and eligibility and completion of the baseline assessments, patients were randomised centrally using the Clinical Trials Research Unit's (CTRU's) automated secure 24-hour randomisation service to either KJD or KR. Randomisation

took place on the same day as the baseline visit which could be up to 6 weeks prior to the planned date of surgery. To facilitate the hybrid expertise-based design, surgeons were categorised into delivery units. A centre was eligible to participate if they had at least one complete delivery unit defined as: '*Single delivery unit:* At least one surgeon authorised to deliver only KJD and at least one surgeon authorised to deliver only KR' or '*Dual delivery unit:* At least one surgeon authorised to deliver both KJD and KR'. Randomisation was stratified by delivery unit and radiographic OA severity (Kellgren-Lawrence grade 2/3 vs. grade 4).

A surgical manual was provided to sites detailing the surgical procedures for both interventions and highlighting mandatory components. Briefly, KJD used a definitive external fixator construct which allowed for controlled linear distraction across the knee joint of 5 mm along the mechanical axis of the limb with further distraction applied postoperatively to create a total of 5 mm articular distraction at the frame. Distraction was maintained for 6 weeks. External fixators were removed under general anaesthetic with manipulation of the knee to achieve > 90° flexion. KR surgery (unicompartmental or TKR), implants used and alignment philosophy was performed in line with surgeons' usual practice and device instructions. Routine general postoperative care including the need for concomitant medication and further management of symptomatic knee OA was according to local surgical team discretion and protocol. The participants were free to withdraw from the trial at any time without explanation and without their further treatment or care being affected.

Statistical considerations

The trial originally planned to recruit 344 patients to be able to demonstrate non-inferiority within a threshold of 8 points[16] with 90% power, assumed variability of standard deviation (SD) = 21, assumed difference between groups of zero and allowing for 15% dropout. As a non-inferiority trial, the original analysis plan was to primarily analyse a per-protocol population with planned sensitivity analyses based on the intention-to-treat population.[28,29] Given the trial closed early with a small number of patients from a single centre, only descriptive statistics are presented.

Results

Right at the outset, we acknowledge that it was not possible to carry out the original analyses as planned in the published protocol. Relevant explanation and lessons learnt have been provided in the following sections.

Recruitment

The trial opened to recruitment in March 2021 at Leeds Teaching Hospitals NHS Trust. By the end of the internal pilot phase in March 2022, a total of three sites were open to recruitment (see *Appendix 1*, *Table 2*). The trial struggled to open sites due to the unprecedented challenges faced by surgical services during and after the COVID-19 pandemic. Reduced research capacity at sites and the suspension of elective surgery services within the NHS both caused significant recruitment barriers to the trial.

Details of patients screened and found to be ineligible are provided in the (see *Appendix 1*, *Table 14*). Three hundred and twelve patients were found to be ineligible and another 15 refused to participate (see *Appendix 1*, *Table 15*). The main reason for ineligibility was age above 65 years and symptoms not severe enough to warrant KR. The reasons for refusal to participate included lack of equipoise (n = 4) and not wanting to have surgery at the time of consultation (n = 4).

The Funder agreed with the trial team in October 2022 to close the trial to recruitment, given the inability to recruit sites and the trial's overall low recruitment rates at sites that were open. At that time five sites were formally open to recruitment (Leeds Teaching Hospitals NHS Trust, Royal Infirmary of Edinburgh, Hull University Teaching Hospitals NHS Trust, University Hospitals Southampton NHS Foundation Trust, and Imperial College Healthcare NHS Trust) although only one single site recruited any patients (Leeds Teaching Hospitals NHS Trust). The trial closed having recruited a total of 24 patients. It was evident that KARDS was not feasible to deliver in the foreseeable NHS climate.

A total of 13 patients were randomised to KR and 11 patients to KJR. All patients were recruited through the single delivery unit, that is at least one surgeon authorised to deliver only KJD and at least one surgeon authorised to deliver only KR. Patient characteristics across randomised groups were similar (see *Appendix 1*, *Table 3*) with median age of 60 years (range 47–65), predominantly male (n = 17, 71%), median body mass index (BMI) of 31 (range 22–44), all White.

Two patients in the KR group and two patients in the KJD group reported having relevant medical history. Of these, one patient had ischaemic heart disease, one had spinal stenosis or prolapsed intervertebral disc and two patients had diabetes mellitus. Ten patients (42%) had bilateral knee arthritis. Ten (42%) patients had Kellgren and Lawrence grade 3 OA and 14 (58%) grade 4 OA. No patients had an arthroscopy in previous 6 months. Overall, 11 (46%)

of patients classified their knee pain as moderate and 13 (54%) severe. Twenty (83%) patients reported taking oral narcotic analgesics or non-steroidal anti-inflammatories in the last week. Of these, nine (31%) took opioids. Three (12%) used gel or dermal analgesics in the previous week. One (4%) patient had received an intra-articular corticosteroid infection in the previous 6 months.

There were three participants with protocol violations: one withdrew being medically unfit for surgery, while two received a different treatment than which they were randomised; thus the per-protocol population consisted of 21 patients (12 KR, 9 KJD). The intention-to-treat population is 24 patients (13 KR, 11 KJD). The safety population consists of 23 patients (13 KR, 10 KJD) since one participant did not receive any surgical intervention.

Participant flow is shown in the Consolidated Standards of Reporting Trials (CONSORT) diagram (see *Appendix 1*, *Figure 3*, and *Tables 14* and *15*). Although various sites expressed willingness to participate in the study (with detailed knowledge of what was needed and expected), no site other than Leeds (which consistently recruited one patient per month) were able to recruit a single patient for the entire duration of the study. Indeed, the factors contributing to this anomaly are likely to be unique to the individual site (e.g. lack of suitable patients, long waiting lists for surgery as well as outpatient appointment, limited number of research staff) and it is impossible to ascertain the exact reasons for the same. It is possible that, as all research activities were significantly delayed across the UK during and after COVID-19 pandemic, each site decided to prioritise a study that was hosted by them. In future research readiness of an NHS organisation and its ability to adapt to changing circumstances may need further checks prior to recruitment in a research study.

Primary outcome

The primary outcome measure was the KOOS pain score within 12 months from surgery. KOOS is a patient-administered questionnaire validated for use in patients with knee OA or knee injury,[19] consisting of 5 domains with a total of 42 items. A normalised score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each KOOS domain.

The median KOOS pain score at baseline was 30.6 (range 6–36) for the KR arm and 38.9 (range 22–50) for the KJD arm (see *Appendix 1*, *Table 4*). At 12 months post surgery, the median KOOS pain score in the KR arm reached 75.0 (range 50–100) and 55.6 (range 0–100) in the KJD arm. A higher median KOOS pain score was observed in both treatment groups, indicating an improvement in symptoms. However, the low number of 12-month scores obtained (9 scores in KR, 7 scores in KJD) does not provide sufficient information to make meaningful comparisons between the two treatment groups. Similar improvements in KOOS pain scores were recorded (*Figure 1*).

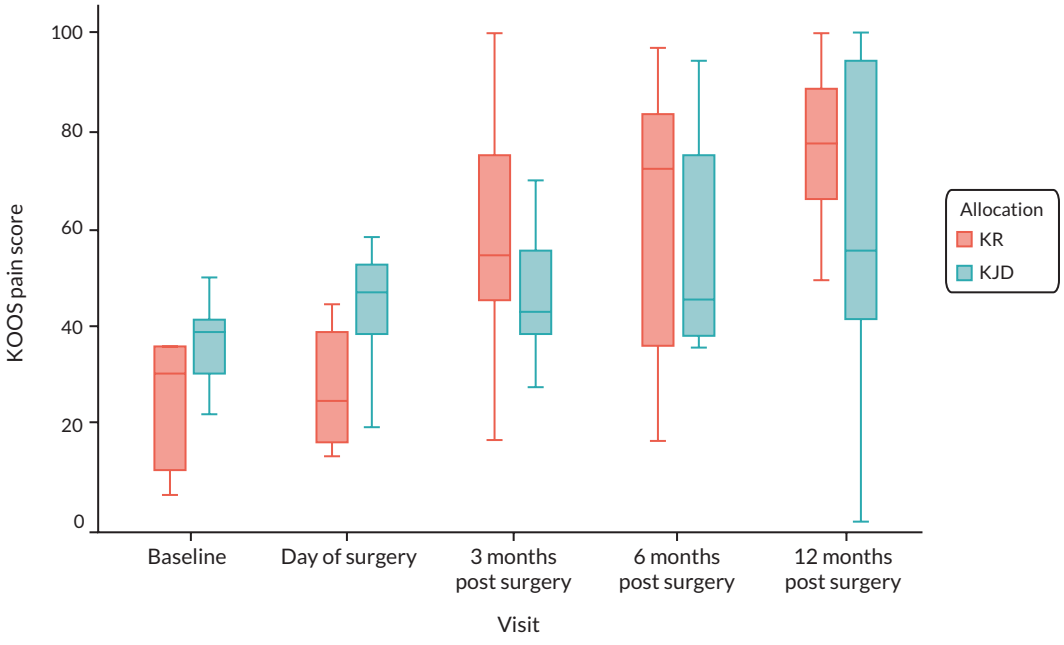

FIGURE 1 Knee Injury and Osteoarthritis Outcome Score pain scores by treatment allocation and visit. Median (line), IQR (box), range (whisker). IQR, interquartile range.

The median KOOS pain score at baseline for participants with OA severity grade 2–3 was 30.6 (range 6–42), and 36.1 (range 11–50) for participants with OA severity grade 4. At 12 months post surgery, the median KOOS pain score for participants with OA severity grade 2–3 was 55.6 (range 0–75) and 94.4 (range 56–100) for those with OA severity grade 4. Overall, the group with OA severity grade 4 saw a more substantial improvement in their symptoms than those with OA severity grade 2–3 (see *Appendix 1*, *Figure 4* and *Table 5*), although the number of scores in each grouping was still low.

Sensitivity analyses confirmed data were not substantially different when including the wider intention-to-treat population (see *Appendix 1*, *Tables 6* and *7*).

With the small sample size, it is difficult to be confident about the extent to which knee distraction actually contributed to the improvement in patient's symptoms. Indeed, for any future trial, it might be worthwhile to include a third group of patients who would receive physiotherapy and other conservative measures for managing knee arthritis.

Secondary outcomes

Patient-reported outcomes and quality of life within 24 months

The patient-reported secondary outcomes consisted of the other components of the KOOS score [Symptoms, activities of daily living (ADL), Sport and Recreation function and knee-related Quality of Life], a pain VAS measure of pain intensity[20,21] ranging from 'no pain' (score 0) to 'pain as bad as it could be' or 'worst imaginable pain' (score 100) and the OKS assessing outcomes of knee interventions[22–24] ranging from 0 (most symptoms) to 48 (least symptoms).

All of the patient-reported secondary outcomes indicate an improvement in the condition of the participants, with each of the KOOS components and the OKS increasing over time, while the pain VAS decreases over time for both intervention arms (see *Appendix 1*, *Tables 8* and *9* and *Figure 5*). Sensitivity analysis carried out on the intention-to-treat population did not produce substantially different results.

Objective assessment of knee function

The angles of the affected leg were measured with a goniometer to determine the range of motion (ROM). The TUG test measures, in seconds, show how long it took the participant to rise from a chair, walk 3 m, turn around, walk back to the chair, and sit down.

The ROM does not substantially differ between the trial arms across follow-up time-points. Participants in the KR arm did report a marked improvement in their TUG times from baseline to 12 months post surgery compared to the KJD arm, but there are only a small number of measurements in both arms to consider (see *Appendix 1*, *Tables 10* and *11*).

Sensitivity analyses confirmed data were not substantially different when including the wider intention-to-treat population.

Complications

Rates of intraoperative and postoperative complications reported by their degree of severity using the Clavien–Dindo classification. Twenty-four surgical site infection was categorised based on the CDC classification and recorded with antibiotics use.[26]

Day of surgery Two patients experienced complications reported on the day of surgery, with one in each randomised group. In one patient undergoing KR a drill pin broke with the tip retained in the patient. In one patient undergoing KJD a tube snapped loosening a pin which required replacement. No adverse event was associated with either of these patient's outcomes in relation to these complications.

Day of fixator removal Four patients had pin site infections identified at the time of fixator removal.

Three-month follow-up Five patients from KJD group (four residual pin site infection and one stiff knee) reported postoperative complications at 3-month follow-up (see *Appendix 1*, *Table 12*). Pin site infections were treated by a course of oral antibiotics, and the stiff knee by outpatient physiotherapy sessions.

Twelve-month follow-up In the KJD group one further complication (femoral fracture) was reported at 12-month follow-up. The patient, who had a residual pin site infection at 3 months post operatively, slipped on a wet floor at 3 months post-fixator removal sustaining a fractured femur that was found to be associated with stress riser around a previous pin tract. The fracture was managed surgically with an intramedullary nail and extended antibiotic cover.

Further intervention

One patient in the KJD group needed open reduction and internal fixation of fractured femur at 3 months post-fixator removal. The fracture has subsequently healed without any additional complications.

Intervention fidelity

Intervention fidelity was assessed on surgical case report forms for compliance with mandatory components of surgery and any deviations explained. For the KJD group of participants, radiographic assessment of joint space width (an indicator of intrinsic cartilage repair) was performed using standardised fixed flexion (210°) radiographs,[30] to assess the structural benefits of distraction. X-rays were assessed by blinded central review using KneeMorph (MatLab, Release 2015b, The MathWorks, Inc., Natick, MA, USA).

The median operating time for KR group was 84.5 minutes (range 52–131) and 96.0 minutes (range 43–165) for the KJD group. The median theatre time for KR group was 145.5 minutes (range 120–191) and 137.0 minutes (range 86–194) for the KJD group. All patients received surgery in laminar airflow theatre. Twenty out of 21 surgeries were performed by a consultant principal surgeon. All patients were administered perioperative intravenous antibiotic prophylaxis.

The participants in KR arm had traditional open surgery. They all received cruciate retaining TKR (10 Sphere and 2 Persona). For the KJD group, six patients received ArthroSave – Knee Reviver type of external fixator while three received Smith and Nephew – Ilizarov. For the knee reviver cases, half pins were used throughout. For the Ilizarov cases, a combination of half pins and tensioned fine wires was employed. None of the distraction pins had HA coating. No tourniquet was used on all KJD patients. All patients followed the pin site care advice.

The reviewers and surgeons agree that 5 mm distraction was achieved post surgery (excluding two KJD participants who did not receive a review). For all participants in the KR group, the KR was deemed acceptable by the reviewers.

Three protocol violations were recorded – two due to treatment group crossover (one from each trial arm) and one KR patient who was deemed medically unfit for surgery. There were a total of 16 other protocol deviations (from 10 participants – 6 participants in the KR group and 4 in the KJD group) (see *Appendix 1*, *Table 13*). Eight protocol deviations (five in KR group and three in KJD group) were due to surgery not being done within 42 days of randomisation. Two protocol deviations (one from each trial arm) were due to the use of radiographs more than 6 months old. Three deviations (in KR group) were questionnaire related where either a questionnaire was completed late or not completed at all. Two deviations (by one participant in KJD arm) were X-ray related.

Process evaluation

Given KJD is not currently used widely in the UK, the KARDS trial included an integrated PE, involving semi-structured interviews with site staff and patients, to identify barriers in order to maximise recruitment possibilities, as well as identify any challenges experienced in maintaining the integrity of the interventions to minimise variation in intervention delivery. The three objectives were:

1. to document the various care pathways at individual sites that potential participants are exposed to as they consider entry to the trial (context)
2. to engage with key stakeholders (surgeons, recruiting staff, admin staff and patients) at sites to understand their experiences of recruitment
3. to engage with the surgical teams and explore their perceived facilitators or barriers to delivering the surgical interventions as per the protocol.

During the internal pilot, 11 staff interviews were conducted with 8 staff members from 2 KARDS sites (these included 8 initial interviews and 3 follow-up interviews). Eleven participants took part in an initial interview (six of whom underwent KR and five of whom had KJD) and follow-up interviews were conducted with four KJD participants.

The full PE originally planned for KARDS was unable to be completed owing to the early trial closure. However, the information gathered from the work conducted highlighted that providing sufficient and comprehensive information about all elements of treatment, including estimated recovery timelines, in trials of novel interventions is essential. Another key learning was the need to incorporate a comprehensive rehabilitation package following KJD surgery.

We have published the full details of the PE and its findings. We have provided here a summary of key findings for reference. As part of PE, we conducted semistructured qualitative interviews with staff in secondary care and with study participants. Data were analysed using thematic content analysis. Key common themes emerged and are listed here. Eleven members of staff were interviewed from two KARDS sites (eight initial interviews just after site opening and three follow-up interviews at 12 months). Eleven KARDS participants (six KR and five KJD) were interviewed. One overarching theme emerged: 'An unexpected journey'. This incorporated subtheme including 'an important research question', 'a roller coaster ride', 'lessons learnt', 'managing expectations' and 'a slow recovery'. These encapsulate experiences of both staff and participants. The information that we were able to collect highlights that providing adequate and comprehensive information about all aspects

of treatment, including estimated timelines of recovery, is essential in clinical trials of novel interventions. Incorporating a comprehensive rehabilitation package following KJD was a key learning. PEs in these complex trials are essential to determine issues as early as possible so that appropriate changes can be made to ensure participants have a smooth journey through the trial experience.

Health economic evaluation

The objective of the health economic evaluation was to estimate the costs of KJD with KR over 12 months after the initial surgical intervention from an NHS and Personal Social Services and societal perspectives.[31] A cost-effectiveness analysis was conducted using individual participant data. Resource use data on the initial surgery, complications and follow-up visits in secondary care were collected using trial case report forms collected at baseline, 3 and 12 months. Additional health and social care, out of pocket costs, and productivity costs to patients and their carers were collected through patient questionnaires at baseline 3, 6 and 12 months. Patients also completed the EuroQol-5 Dimensions, three-level version (EQ-5D-3L) within the patient questionnaires.

Given the low number of participants, the health economic evaluation was reduced to estimate costs and average EQ-5D-3L utility score of each surgical intervention. Results need to be treated with caution due to the small sample sizes. Patients were analysed according to the surgery received (per-protocol analysis).

EuroQol-5 Dimensions, three-level version patient-reported outcome

EuroQol-5 Dimensions, three-level version comprises five dimensions of health: mobility, ability to self-care, ability to undertake usual activities, pain/discomfort and anxiety/depression. The EuroQol-5 Dimensions VAS scale records the patients' self-rated health on a vertical VAS from 0 ('Best imaginable health state') to 100 mm ('Worst imaginable health state').

The median [interquartile range (IQR)] EQ-5D-3L index utility score at 3 months was 0.69 (0.62–0.76) in KR and 0.35 (0.08–0.62) in KJD patients. The respective figures at 6 months, with two KR patients and 1 KJD patient having missing data, were 0.76 (0.62–0.88) and 0.52 (0.19–0.59). The respective median changes from baseline at 6 months were 0.15 (−0.54 to 0.43) and 0.14 (0.00–1.07).

Health resource utilisation and private costs questionnaire

This trial-specific questionnaire measured participant-reported healthcare use, days off work and private costs due to knee OA using a bespoke short self-reported schedule. Healthcare use included the number of contacts with clinical staff (occupational health, primary care staff, rheumatologists etc.) and medications as a result of knee OA.

The mean (SD) and median (IQR) costs of KR, all of which were total, were £6101 (816) and £6032 (5650–6340). The respective costs for knee distraction were £10,441 (2697) and £10,494 (7299–13,350). The median (IQR) NHS costs of hospital service use over (outpatient attendance and inpatient admissions) was £421 (161–1083) and £463 (363–845) at the 3-month clinical follow-up, respectively in the KR and KJD groups. At baseline, use of narcotics and non-steroidal anti-inflammatory drugs (NSAIDs) in the previous week amounted to a median cost of £3.01 (IQR: 0–4) in the KR group, and £0.85 (0–9) in the knee distraction group. From surgery to the time of post-surgical assessment, narcotic and NSAIDs use was associated with median costs of £13.27 (9–13) and £13.13 (1–22), respectively. During the week preceding the 3-month follow-up, use of these medications had an associated median cost of £2.80 (0–7) in the KR group and £3.95 (0–11) in the KJD group.

Thirteen KR patients reported median (IQR) out of pocket costs of £4 (0–125) and incurred an estimated £0 (0–4588) of productivity (time off work due to health or receiving care) costs at 3 months; the corresponding figures for 10 KJD patients were £55 (0–700) and £0 (0–7646).

Patient and public involvement

Aim

The aim of PPI in KARDS was to ensure that the voices of patients were heard and shaped the trial design and study conduct, ensuring the trial results would be relevant and of direct benefit to the target population.

Methods

The KARDS trial had PPI throughout its duration, from the grant application development onwards. Meetings were held with a PPI group during the work-up of the grant application, and once funding was secured, PPI representatives were members of the Trial Management Group and TSC and attended and participated in trial meetings. Our PPI representatives input to the design of the protocol and played a key role in helping to draft and review participant information resources, providing invaluable feedback on the suitability of these documents from a patient and public perspective.

Results of patient and public involvement input

Patient and public involvement ensured that the trial design and patient-facing resources were fit for purpose, and met the needs of the patient population whom the trial set out to benefit. PPI input also fed into developing recruitment strategies when the trial was recruiting slower than anticipated.

Discussion of patient and public involvement input

Patient and public involvement was integral throughout the trial with PPI representatives providing feedback and shaping the design and ongoing recruitment. These discussions occurred throughout the study set-up and delivery. There were some key learning points, which would be useful to consider in future studies. Regular input from physiotherapy colleagues (as part of the study) was a key consideration for patients in both groups but more relevant to the KJD group. The COVID pandemic affected the ability to arrange face-to-face visits, but this should be a key point for future studies if KJD needs to be assessed in an NHS setting. Participants views about further follow-up (including up to 2 years and beyond) post intervention were also helpful. All participants suggested further annual follow-up (even if virtual) but due to the financial restraints and decision to close the study this was not feasible.

It is clear that PPI input has driven the study, and these discussions have helped the researchers enormously in understanding potential barriers to run a complex study especially when the COVID-19 pandemic impacted the ability to deliver the study effectively.

Reflections and critical perspective

Patient and public involvement input was vital in making sure patient voices were heard and embedded into all elements of the trial, ensuring that the results would be of direct relevance to the very people the trial aimed to benefit. PPI has been a very positive experience.

This study although ending with premature closure, has allowed us to reflect on various matters in particular around the PPI and PE. The intervention (KJD) is not routine practice and the results so far (prior to start of this study) were primarily from a single centre in Holland. It was not possible to develop an international consensus of the key items to report to enhance the quality, transparency and consistency of the evidence base. The PPI group contributed to the development of research method, including contribution to the PE methodology. On reflection, it would have been helpful to engage with patients from Holland (who have the lived experience of KJD) and ask them to liaise with KARDS PPI group as well as provide ongoing online support to the study participants.

Both the researchers as well as the study participants had limited understanding of the complexity of day-to-day support needed post distraction. In particular, it became obvious that face-to-face consultations by the physiotherapy team would have proven useful but was not possible due to the COVID-19 pandemic. Setting up a social media group for current and previous KJD patients would have helped them to exchange views and share techniques that they employed for coping with a stiff knee and an additional burden of an external fixator, which was cumbersome to many. In addition, the time taken to recover after the external fixator was removed, varied across patients, and this information could have been provided in more detail to the PPI group to enable better guidance for future patients. Having a video diary of day-to-day experiences with the KJD could have also been helpful. Whether this fits within the governance structure is another matter as it would potentially breach confidentiality. Indeed, the interactions could contribute to the patient's well-being but the discussions among patients should not be treated as advice.

Equality, diversity and inclusion

The research target of OA is generalisable to a wide patient group affecting multiple populations. Patients were screened in general routine clinics and thereby matched the intended patient group. Reimbursement was available for travel to overcome barriers due to geographical areas. The majority of patients were in full term employment (or seeking future employment) and were young and active. Their willingness to consider an alternative treatment to KR confirmed the general perception among patients, their carers and clinicians that often a patient with a TKR may not be able to indulge in all the social and recreational activities that they would like to. Indeed, someone managed with knee distraction had this potential advantage (as patient's own joint was retained and not replaced) along with the advantage of delaying subsequent need for a KR. This could have a potential financial impact as the costs of future care: revision surgery (costs associated with which are significantly higher) need would be less. In addition, these patients could possibly retain their future employment for longer (if treated with knee distraction) thereby having a positive impact. Indeed, these questions remain unanswered due to early study closure.

Impact and learning

Clinical impact

It is clear that patients with knee distraction needed more support and two interventions (one for application of

the frame and one for removal) rather than one (in the KR group), but the surgical procedure was less invasive. Although return to activities of daily living would be delayed in the knee distraction group, overall, they regained good function with the added advantage of retaining their own knee joint. This is likely to be of consequence in the mid-term to long term. Qualitative interviews and detailed information about prolonged rehabilitation for patients undergoing KJD could help improve recruitment for future studies.

Research impact

Lessons were also learnt about the barriers to study delivery, which were largely related to the impact of the COVID-19 pandemic. There have been significant delays in the ability to surgically treat patients with knee OA in the NHS due to complete shutdown of the elective work for a significant time period. This led to worsening of conditions, less likelihood of patients and clinicians participating in a research study of this nature and therefore overall patient and centre recruitment.

Policy implications

Indeed, there is a need for patients participating in a research study to be prioritised for their treatment to ensure effective study delivery of any translational research that is carried out/planned in the NHS. Although this could be a potentially contentious point, it is important for research and innovation and improving patient outcomes that this is discussed at a national level.

Research recommendations

As a commissioned piece of research, the research question remains highly relevant. Until further, high-quality, evidence is produced there remains uncertainty about the role of KJD for knee OA. We advocate that patients considering KJD should be counselled regarding the uncertainties associated with the outcomes of joint distraction and be part of a clinical trial (or evaluation) where possible. Further research should embrace the insight from the KARDS PE.

It is difficult to recommend actual study design for a future trial. Although a superiority design might be preferable, addition of a third arm assessing the outcomes of conservative treatment and comparing these with KJD and KR would be essential to make a meaningful comparison. Indeed, there are other factors, which will play a role in delivery of such a trial. The inclusion criteria will need to be broad enough to include patients undergoing other types of joint preserving surgery (such as high tibial osteotomy and focal cartilage replacement).

Future studies of a similar nature should consider mechanisms to mitigate future barriers through effective support mechanisms, international recruitment and a reserve fund for extending studies, particularly those which are part of a commissioned call.

Conclusion

Reduced research capacity at sites and the suspension of elective surgery services within the UK following the COVID pandemic caused significant recruitment barriers to KARDS. Despite early termination KARDS demonstrated that patients were willing to be recruited to a trial investigating a novel treatment for knee OA, a disease where knee arthroplasty is a well-established treatment. KARDS demonstrated that the trial was feasible and implementable, and the limited results indicated that the technique is safe with no safety concerns. To our knowledge this is the only independent study of KJD for the management of knee OA refractory to non-surgical treatment. While KARDS was closed early, it has contributed to our improved understanding of KJD as a potential treatment of knee OA. The clinical and cost-effectiveness of KJD remains uncertain. The research question remains highly relevant, and the embedded KARDS PE has provided helpful insights.

For any future studies in this field, this trial and its findings could serve as a formal pilot, and the lessons learnt could be employed to ensure successful recruitment at multiple sites in a timely fashion. One cannot predict whether there will be another pandemic like COVID-19 and if there is one, how the NHS (particularly the research and Innovation departments in each Trust) would cope. The data presented in the current study could help determine sample size, recruitment rates, retention and patient acceptability.

The research question remains very relevant. There have been further updates from the Dutch investigators regarding KJD.[18] However, an independent assessment of clinical and cost-effectiveness of knee distraction in an NHS setting is needed.

Additional information

CRediT contribution statement

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Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that those are stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation

Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Ethics statement

The KARDS trial was granted national ethics approval by the Yorkshire and The Humber Leeds East Research Ethics Committee on 9 January 2020 (REC reference 19/YH/0368).

Information governance statement

The University of Leeds (UoL) is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679.

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Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/ANDK1124.

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Hamish Simpson – Chair DMB of ORIF: NIHR funded multicentre, Chair STC of PART: NIHR funded multicentre, Editor-in Chief of Bone and Joint Research and Editorial board member of Bone and Joint Journal.

Thomas Hamilton – HTA Prioritisation Committee B (in hospital) 1 November 2020–30 November 2024.

Deborah Stocken – NIHR EME Funding Committee member 1 August 2020–10 August 2024.

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This synopsis was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Trial registration

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Award publications

This synopsis provided an overview of the research award *Knee Arthroplasty versus Joint Distraction Study for Osteoarthritis (KARDS)*. Other articles published as part of this thread are:

Arnold S, Pandit H, Croft J, Stocken DD, Ellard DR; KARDS Trial Team. 'The unexpected journey': a qualitative interview study exploring patient and health professionals experiences of participating in the knee arthroplasty versus joint distraction study (KARDS). *BMJ Open* 2024;**14**:e083069. https://doi.org/10.1136/bmjopen-2023-083069

Hamilton TW, Lineham B, Stocken DD, Pandit H, KARDS Study Group. Knee arthroplasty compared with joint distraction for osteoarthritis: a phase III randomized controlled trial. *Bone Jt Open* 2025;**6**(8):886–93. https://doi.org/10.1302/2633-1462.68.BJO-2024-0120.R2

For more information about this research please view the award page www.fundingawards.nihr.ac.uk/award/17/122/06.

Additional output

Tassinari CJ, Higham R, Smith IL, Arnold S, Mujica-Mota R, Metcalfe A, *et al.* Clinical and cost-effectiveness of Knee Arthroplasty versus Joint Distraction for Osteoarthritis (KARDS): protocol for a multicentre, phase III, randomised control trial. *BMJ Open* 2022;**12**:e062721. https://doi.org/10.1136/bmjopen-2022-062721

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List of abbreviations

ADL	activities of daily living
BMI	body mass index
CDC	Centers for Disease Control and Prevention
COVID	coronavirus disease
CTRU	Clinical Trials Research Unit
DMEC	Data Monitoring and Ethics Committee
EQ-5D-3L	EuroQol-5 Dimensions, three-level version
FU	follow-up
HTA	Health Technology Assessment
ISRCTN	International Standard Randomised Controlled Trial Number
KARDS	The Knee Arthroplasty versus Joint Distraction Study for Osteoarthritis
KJD	knee joint distraction
KOOS	Knee Injury and Osteoarthritis Outcome Score
KR	knee replacement
NSAID	non-steroidal anti-inflammatory drug
OA	osteoarthritis
OKS	Oxford Knee Score
PE	process evaluation
PPI	patient and public involvement
ROM	range of motion
TKR	total knee replacement
TSC	Trial Steering Committee
TUG	timed-up-and-go
VAS	visual analogue scale
WOMAC	Western Ontario and McMaster Universities OA Index

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Appendix 1

TABLE 1 Changes made to the protocol during the lifetime of the trial

Version and date	Summary of changes
V1.0, dated 27 September 2019	N/A – original protocol submitted for ethical review
V2.0, dated 29 September 2020	• Participants can return consent form by post if a face-to-face visit is not possible. • Initial trial discussion, baseline and follow-up visit to be conducted remotely if face to face consultations not possible. • Sites to post the self-completion questionnaires (patient-reported outcome measures) to the participant to complete at home and return by post if not possible to complete the questionnaires in clinic. • Staff interviews and informed consent for the PE to be conducted either by telephone or video call if face-to-face interviews are not possible. • Focus groups with site staff added as an alternative to one-to-one interviews. • Sites to scan CRFs and return to CTRU by secure file transfer if return by post is not possible. • Removal of requirement for baseline anteroposterior/lateral view X-ray to be repeated if more than 6 months old. • Change to surgical procedure to allow surgeons the option of applying up to the full 5 mm distraction during initial surgery, or at any point up to Day 7 after surgery. • Questionnaires completed by participants in clinic to be placed in a sealed envelope before being given to site staff to return to CTRU. • Details of which participants take part in the qualitative interviews to be provided to CTRU by the University of Warwick. • Assumed difference for sample size clarification added to the protocol. • Other minor changes throughout protocol for example typographical.

CRFs, case report forms; N/A, not applicable.

TABLE 2 Participating sites

Participating site	Date opened to recruitment
Leeds Teaching Hospitals NHS Trust	31 March 2021
Royal Infirmary of Edinburgh	21 January 2022
Hull University Teaching Hospitals NHS Trust	11 March 2022
University Hospitals Southampton NHS Foundation Trust	29 April 2022
Imperial College Healthcare NHS Trust	19 May 2022

TABLE 3 Patient characteristics

	KR (*n* = 13)	KJD (*n* = 11)	Total (*n* = 24)
Age	57.0 (47–64)	61.0 (52–65)	60.0 (47–65)
Sex			
Male	10 (76.9%)	7 (63.6%)	17 (70.8%)
Female	3 (23.1%)	4 (36.4%)	7 (29.2%)

TABLE 3 Patient characteristics (*continued*)

	KR (*n* = 13)	KJD (*n* = 11)	Total (*n* = 24)
Ethnicity			
White	13 (100.0%)	11 (100.0%)	24 (100.0%)
BMI (kg/m^2)	32.9 (22–44)	29.0 (24–40)	31.3 (22–44)
OA severity score			
2–3	6 (46.2%)	4 (36.4%)	10 (41.7%)
4	7 (53.8%)	7 (63.6%)	14 (58.3%)

Note
Values are median (range) or *n* (%).

TABLE 4 Knee Injury and Osteoarthritis Outcome Score pain domain score, per-protocol population

	KR (*n* = 12)	KJD (*n* = 9)	Total (*n* = 21)
Baseline			
Mean (SD)	26.3 (11.61)	36.7 (9.99)	31.0 (11.90)
Median (range)	30.6 (6–36)	38.9 (22–50)	34.7 (6–50)
IQR	11.1–36.1	30.6–41.7	23.6–37.5
Missing	1	0	1
Day of surgery			
Mean (SD)	28.0 (11.28)	49.4 (20.45)	37.6 (19.02)
Median (range)	25.0 (14–44)	47.2 (19–94)	37.5 (14–94)
IQR	16.7–38.9	38.9–52.8	23.6–45.8
Missing	1	0	1
3 months post surgery			
Mean (SD)	60.4 (24.41)	48.0 (14.56)	55.1 (21.26)
Median (range)	54.2 (17–100)	42.9 (28–69)	52.8 (17–100)
IQR	45.8–75.0	38.9–55.6	41.7–69.4
Missing	0	0	0
6 months post surgery			
Mean (SD)	63.5 (29.70)	56.1 (23.38)	60.2 (26.58)
Median (range)	72.2 (17–97)	45.8 (36–94)	59.1 (17–97)
IQR	36.1–83.3	38.2–75.0	37.5–83.3
Missing	2	1	3
12 months post surgery			
Mean (SD)	76.2 (17.68)	56.3 (33.74)	67.5 (26.95)
Median (range)	75.0 (50–100)	55.6 (0–100)	70.8 (0–100)
IQR	66.7–88.9	41.7–94.4	52.8–91.7
Missing	3	2	5

TABLE 5 Knee Injury and Osteoarthritis Outcome Score pain domain score by OA severity, per-protocol population

	OA 2–3 (*n* = 10)	OA 4 (*n* = 11)	Total (*n* = 21)
Baseline			
Mean (SD)	30.2 (11.24)	31.6 (12.93)	31.0 (11.90)
Median (range)	30.6 (6–42)	36.1 (11–50)	34.7 (6–50)
IQR	27.8–36.1	22.2–38.9	23.6–37.5
Missing	1	0	1
Day of surgery			
Mean (SD)	39.2 (24.23)	36.4 (14.62)	37.6 (19.02)
Median (range)	36.1 (14–94)	38.9 (14–58)	37.5 (14–94)
IQR	25.0–44.4	22.2–47.2	23.6–45.8
Missing	1	0	1
3 months post surgery			
Mean (SD)	43.6 (16.72)	65.5 (20.05)	55.1 (21.26)
Median (range)	41.7 (17–75)	66.7 (42–100)	52.8 (17–100)
IQR	33.3–55.6	47.2–75.0	41.7, 69.4
Missing	0	0	0
6 months post surgery			
Mean (SD)	46.4 (21.10)	71.3 (26.12)	60.2 (26.58)
Median (range)	45.8 (17–81)	81.9 (36–97)	59.1 (17–97)
IQR	30.6–60.5	37.5–94.4	37.5–83.3
Missing	2	1	3
12 months post surgery			
Mean (SD)	51.9 (22.74)	87.7 (16.81)	67.5 (26.95)
Median (range)	55.6 (0–75)	94.4 (56–100)	70.8 (0–100)
IQR	47.2–66.7	75.0–100.0	52.8–91.7
Missing	1	4	5

TABLE 6 Knee Injury and Osteoarthritis Outcome Score pain domain score, intention-to-treat population

	KR (*n* = 13)	KJD (*n* = 11)	Total (*n* = 24)
Baseline			
Mean (SD)	28.2 (13.02)	35.4 (10.98)	31.6 (12.36)
Median (range)	31.9 (6–50)	38.9 (17–50)	36.1 (6–50)
IQR	18.1–36.1	22.2–41.7	22.2–41.7
Missing	1	0	1
Day of surgery			
Mean (SD)	30.6 (13.86)	45.8 (22.31)	37.5 (19.35)
Median (range)	27.8 (14–58)	45.8 (14–94)	37.5 (14–94)

TABLE 6 KOOS pain domain score, ITT population (*continued*)

	KR (*n* = 13)	KJD (*n* = 11)	Total (*n* = 24)
IQR	19.4–41.7	36.1–52.8	22.2–47.2
Missing	1	1	2
3 months post surgery			
Mean (SD)	60.9 (23.43)	51.0 (16.65)	56.6 (20.93)
Median (range)	55.6 (17–100)	49.2 (28–78)	55.6 (17–100)
IQR	47.2–75.0	38.9–66.7	41.7–71.9
Missing	0	1	1
6 months post surgery			
Mean (SD)	65.5 (28.99)	58.5 (23.04)	62.4 (26.05)
Median (range)	80.6 (17–97)	47.2 (36–94)	62.5 (17–97)
IQR	36.1–86.1	38.9–77.8	38.2–84.7
Missing	2	2	4
12 months post surgery			
Mean (SD)	76.1 (16.68)	60.8 (33.64)	69.3 (25.98)
Median (range)	75.0 (50–100)	55.6 (0–100)	75.0 (0–100)
IQR	66.7–88.9	44.4–93.1	55.6, 91.7
Missing	3	3	6

TABLE 7 Knee Injury and Osteoarthritis Outcome Score pain domain score by OA severity, intention-to-treat population

	OA 2–3 (*n* = 10)	OA 4 (*n* = 14)	Total (*n* = 24)
Baseline			
Mean (SD)	30.2 (11.24)	32.5 (13.36)	31.6 (12.36)
Median (range)	30.6 (6–42)	36.1 (11–50)	36.1 (6–50)
IQR	27.8–36.1	22.2–41.7	22.2–41.7
Missing	1	0	1
Day of surgery			
Mean (SD)	39.2 (24.23)	36.3 (16.14)	37.5 (19.35)
Median (range)	36.1 (14–94)	38.9 (14–58)	37.5 (14–94)
IQR	25.0–44.4	22.2–47.2	22.2–47.2
Missing	1	1	2
3 months post surgery			
Mean (SD)	43.6 (16.72)	66.5 (18.62)	56.6 (20.93)
Median (range)	41.7 (17–75)	66.7 (42–100)	55.6 (17–100)
IQR	33.3–55.6	52.8–75.0	41.7–71.9
Missing	0	1	1

continued

TABLE 7 KOOS pain domain score by OA severity, ITT population (*continued*)

	OA 2–3 (*n* = 10)	OA 4 (*n* = 14)	Total (*n* = 24)
6 months post surgery			
Mean (SD)	46.4 (21.10)	73.0 (24.06)	62.4 (26.05)
Median (range)	45.8 (17–81)	81.9 (36–97)	62.5 (17–97)
IQR	30.6–60.5	49.3–91.7	38.2–84.7
Missing	2	2	4
12 months post surgery			
Mean (SD)	51.9 (22.74)	86.7 (15.26)	69.3 (25.98)
Median (range)	55.6 (0–75)	91.7 (56–100)	75.0 (0–100)
IQR	47.2–66.7	75.0–100.0	55.6–91.7
Missing	1	5	6

TABLE 8 Patient-reported outcome measures by visit

	Baseline	Day of surgery	3 months post surgery	6 months post surgery	12 months post surgery
KOOS symptoms					
Mean (SD)	40.0 (11.27)	44.8 (16.81)	50.1 (18.89)	49.2 (17.56)	54.1 (18.92)
Median (range)	39.3 (21–57)	37.5 (25–71)	50.0 (18–86)	53.6 (18–71)	57.1 (14–86)
IQR	32.1–48.2	32.1–60.7	33.9–64.3	32.1–64.3	40.2–67.9
Missing	1	1	1	3	5
KOOS ADL					
Mean (SD)	37.3 (13.71)	44.0 (21.39)	56.7 (22.92)	61.0 (28.39)	69.3 (29.33)
Median (range)	39.0 (7–66)	41.9 (1–100)	52.9 (14–100)	70.6 (12–100)	74.3 (0–100)
IQR	26.5–47.1	28.7–55.9	43.8–70.6	34.4–86.8	46.1–93.4
Missing	1	1	0	3	5
KOOS Sport&Rec					
Mean (SD)	24.8 (30.20)	23.9 (27.47)	40.5 (34.69)	49.8 (33.31)	56.1 (37.46)
Median (range)	12.5 (0–100)	10.0 (0–90)	25.0 (0–100)	57.5 (0–100)	62.5 (0–100)
IQR	0.0–35.0	0.0–35.0	10.0–70.0	17.5–75.0	22.5–92.5
Missing	1	2	5	5	5
KOOS QoL					
Mean (SD)	14.1 (15.02)	16.6 (17.36)	32.7 (24.12)	41.9 (25.65)	50.3 (27.97)
Median (range)	9.4 (0–56)	12.5 (0–69)	25.0 (0–88)	43.8 (6–81)	56.3 (0–88)
IQR	3.1–18.8	6.3–18.8	18.8–50.0	12.5–56.3	28.1–75.0
Missing	1	1	0	4	5
Pain VAS (mm)					
Mean (SD)	60.6 (13.82)		43.8 (31.45)	41.4 (28.20)	29.3 (26.60)
Median (range)	60.0 (27–81)		50.0 (1–91)	40.5 (2–87)	26.0 (0–77)

TABLE 8 Patient-reported outcome measures by visit (*continued*)

	Baseline	Day of surgery	3 months post surgery	6 months post surgery	12 months post surgery
IQR	53.0–72.0		14.0–69.5	17.0–59.0	4.0–54.0
Missing	3		1	3	5
OKS overall[a]					
Mean (SD)	18.1 (8.03)		23.7 (11.65)	28.3 (13.15)	33.5 (12.66)
Median (range)	17.5 (7–33)		21.0 (5–48)	29.0 (10–46)	36.0 (5–47)
IQR	11.5–24.5		16.0–33.0	13.0–41.0	24.5–45.0
Missing	1		0	3	5

QoL, quality of life.
a OKS is continuous on scale of 0–48.

TABLE 9 Patient-reported outcome measures by visit and treatment allocation

	Baseline		Day of surgery		3 months post surgery		6 months post surgery		12 months post surgery	
	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)
KOOS symptoms										
Mean (SD)	39.0 (12.42)	41.3 (10.28)	39.3 (13.83)	51.6 (18.39)	53.8 (20.25)	44.6 (16.31)	52.9 (17.96)	44.6 (17.07)	56.0 (14.06)	51.8 (24.89)
Median (range)	39.3 (21–57)	39.3 (29–57)	35.7 (25–71)	46.4 (25–71)	60.7 (18–86)	41.1 (25–71)	55.4 (18–71)	37.5 (25–68)	57.1 (29–71)	57.1 (14–86)
IQR	25.0–46.4	32.1–50.0	28.6–50.0	35.7–67.9	35.7–66.1	32.1–57.1	39.3–67.9	32.1–62.5	50.0–64.3	32.1–71.4
Missing	1	0	1	0	0	1	2	1	3	2
KOOS ADL										
Mean (SD)	32.5 (12.76)	43.3 (13.07)	35.2 (16.08)	54.7 (22.95)	64.4 (24.45)	46.3 (16.78)	67.5 (30.53)	52.9 (24.97)	80.6 (20.87)	54.8 (33.68)
Median (range)	33.8 (7–49)	45.3 (24–66)	36.8 (1–60)	45.6 (24–100)	69.9 (14–100)	50.0 (19–76)	78.7 (12–97)	39.3 (33–100)	88.2 (34–100)	48.5 (0–97)
IQR	25.0–42.6	33.8–48.5	26.5–48.5	41.2–66.2	50.7–80.1	35.9–51.6	44.1–88.2	34.1–71.3	73.5–94.1	36.8–92.6
Missing	1	0	1	0	0	0	2	1	3	2
KOOS Sport&Rec										
Mean (SD)	22.7 (31.17)	27.2 (30.63)	20.5 (24.44)	28.8 (32.27)	52.8 (32.20)	20.0 (30.66)	56.3 (28.59)	41.4 (39.23)	70.6 (30.46)	37.6 (39.49)
Median (range)	5.0 (0, 75)	25.0 (0, 100)	10.0 (0, 70)	17.5 (0, 90)	50.0 (15, 100)	5.0 (0, 80)	60.0 (0, 95)	20.0 (0, 100)	70.0 (20, 100)	25.0 (0, 95)
IQR	0.0–65.0	5.0–30.0	0.0–35.0	5.0–47.5	25.0–87.5	5.0–25.0	41.7–75.0	10.0–75.0	55.0–100.0	0.0–90.0
Missing	1	0	1	1	2	3	3	2	3	2
KOOS QoL										
Mean (SD)	10.2 (8.96)	18.8 (19.76)	8.5 (8.96)	26.4 (20.44)	43.8 (23.54)	18.1 (16.37)	54.2 (19.01)	28.1 (26.09)	63.2 (18.87)	33.6 (30.13)
Median (range)	6.3 (0–25)	12.5 (0–56)	6.3 (0–25)	18.8 (6–69)	43.8 (0–88)	18.8 (0–56)	56.3 (19–81)	12.5 (6–81)	56.3 (31–88)	25.0 (0–81)

continued

TABLE 9 Patient-reported outcome measures by visit and treatment allocation (*continued*)

	Baseline		Day of surgery		3 months post surgery		6 months post surgery		12 months post surgery	
	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)
IQR	0.0–18.8	6.3–25.0	0.0–18.8	12.5–31.3	25.0–59.4	6.3–18.8	43.8–62.5	12.5–43.8	56.3–81.3	12.5–68.8
Missing	1	0	1	0	0	0	3	1	3	2
Pain VAS (mm)										
Mean (SD)	65.6 (12.93)	54.4 (13.00)			35.0 (33.54)	57.0 (24.18)	36.6 (28.62)	47.5 (28.32)	19.7 (20.54)	41.7 (29.78)
Median (range)	66.5 (44–81)	56.0 (27–68)			23.0 (1–91)	52.0 (23–90)	31.5 (2–87)	57.0 (4–81)	12.0 (0–58)	50.0 (0–77)
IQR	55.0–78.0	50.0–64.0			7.0–58.5	40.0–79.5	7.0–56.0	22.0–68.5	3.0–33.0	10.0–69.0
Missing	2	1			0	1	2	1	3	2
OKS overall										
Mean (SD)	16.9 (7.46)	19.6 (8.90)			29.2 (11.01)	16.5 (8.32)	31.7 (12.59)	24.0 (13.36)	38.3 (8.17)	27.3 (15.23)
Median (range)	16.0 (7-27)	20.0 (7–33)			28.0 (11–48)	16.0 (5–33)	34.0 (12–46)	20.0 (10–46)	37.0 (22–47)	27.0 (5–47)
IQR	11.0–26.0	12.0–22.0			22.5–38.0	11.0–20.0	25.0–41.0	12.5–35.5	36.0–46.0	14.0–44.0
Missing	1	0			0	0	2	1	3	2

QoL, quality of life.

TABLE 10 Objective assessment of knee function by visit

	Baseline	3 months post surgery	12 months post surgery
ExtSign			
Plus	19 (90.5%)	20 (95.2%)	15 (71.4%)
Minus	2 (9.5%)	1 (4.8%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	6 (28.6%)
ROM (degrees)			
Mean (SD)	102.1 (13.92)	96.1 (21.98)	103.0 (22.90)
Median (range)	105.0 (70–125)	100.0 (20–120)	100.0 (35–130)
IQR	100.0–110.0	85.0–110.0	95.0–120.0
Missing	0	0	6
TUG time (seconds)			
Mean (SD)	13.0 (3.32)	13.0 (4.12)	11.4 (4.73)
Median (range)	13.0 (7–21)	12.0 (7–23)	10.0 (6–24)
IQR	11.0–15.0	10.0–16.0	8.0–13.0
Missing	0	1	6

TABLE 11 Objective assessment of knee function by visit and treatment allocation

	Baseline		3-month FU		12-month FU	
	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)	KR (*n* = 12)	KJD (*n* = 9)
ExtSign						
Plus	11 (91.7%)	8 (88.9%)	12 (100.0%)	8 (88.9%)	8 (66.7%)	7 (77.8%)
Minus	1 (8.3%)	1 (11.1%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (33.3%)	2 (22.2%)
ROM (degrees)						
Mean (SD)	101.3 (13.99)	103.3 (14.58)	99.8 (13.26)	91.2 (30.31)	105.6 (13.74)	100.0 (31.36)
Median (range)	103.5 (70–120)	105.0 (75–125)	100.0 (85–120)	103.0 (20–120)	102.5 (90–130)	100.0 (35–125)
IQR	95.0–109.0	100.0–110.0	87.5–110.0	85.0–110.0	95.0–115.0	95.0–125.0
Missing	0	0	0	0	4	2
TUG time (seconds)						
Mean (SD)	13.0 (3.25)	13.1 (3.62)	11.4 (3.41)	15.0 (4.18)	9.5 (2.20)	13.6 (6.02)
Median (range)	13.0 (8–21)	13.0 (7–18)	10.0 (7–17)	13.0 (11–23)	9.0 (7–14)	12.0 (6–24)
IQR	11.0–14.0	11.0–16.0	8.0–13.0	12.0–17.0	8.0–10.5	10.0–19.0
Missing	0	0	1	0	4	2

FU, follow-up.

TABLE 12 Postoperative complication summaries

	KR (*n* = 12)	Joint distraction (*n* = 9)	Total (*n* = 21)
3-month FU complications			
Yes	1 (8.3%)	2 (22.2%)	3 (14.3%)
No	11 (91.7%)	7 (77.8%)	18 (85.7%)
12-month FU complications			
Yes	0 (0.0%)	2 (22.2%)	2 (9.5%)
No	9 (75.0%)	5 (55.6%)	14 (66.7%)
Missing	3 (25.0%)	2 (22.2%)	5 (23.8%)

FU, follow-up.

TABLE 13 Line listing of other protocol deviations

Pat no	Other deviation further information	Details of remedial action	Allocation
7	Date of surgery > 42 days since randomisation (patient preference)	N/A	KR
8	Patient's surgery was cancelled (postponed) as there was a medical emergency to be sorted. SEC: Date of operation was more than 42 days after baseline visit IW 02/11/2021	Another date for surgery arranged	KR
10	KOOS questionnaire was not completed on day of surgery	Not required – communication error	KR

continued

TABLE 13 Line listing of other protocol deviations (*continued*)

Pat no	Other deviation further information	Details of remedial action	Allocation
14	Randomisation was based upon > 6-month-old radiograph	We will obtain up to date AP and lateral radiograph prior to surgery	KR
14	Date of surgery > 42 days since randomisation (patient preference)	N/A	KR
14	Patient not able to attend planned consultant outpatient appointment 7 February 2022, patient stated due to having COVID-19		KR
14	Participant agreed to complete the 12-month questionnaire but does not want to come in person; therefore, the study assessments were not done	Patient is aware that he can come and see Prof Pandit if he wishes to. Patient is happy to be contacted for 24-month review	KR
14	Baseline questionnaire not completed/participant took the form to be completed at home and did no return it	Protocol violation form completed and sent to CTRU	KR
22	Study participant 00022 communicated to us that their circumstance have changed; therefore, estimated surgery date has been moved to January 2023		KR
23	Surgery date is more than 42 days after randomisation. Delay is due to lack of theatre availability		KR
12	Radiographs > 6 months old; however, they show gr IV cA (which can't get worse) > 6 months prior to randomisation	N/A	KJD
12	Date of surgery > 42 days since randomisation (patient preference)	N/A	KJD
13	Date of surgery > 42 days since randomisation (patient preference)	N/A	KJD
17	Post-surgery lateral new X-ray not done, only AP-X-ray taken dated 26 November 2021	Pt has X-rays on table (intra-op) including lateral X-ray. No further distortion performed, hence cannot taken to minimise rotation	KJD
17	Patient developed COVID and fixator was left on for additional 9 days. Also, due to COVID, patient could not get a pre-sacral X-ray	Surgery delayed by 1 week, surgery performed at Leeds Gen Infirmary to follow IPC advice	KJD
21	Surgery date is more than 42 days after randomisation. After randomisation patient informed us about an unplanned urgent social commitment, which meant delaying participant 00021 surgery by 5 weeks		KJD

AP, anteroposterior; IPC, infection prevention and control; N/A, not applicable.

TABLE 14 Details of patients not meeting the inclusion criteria

Reasons for ineligibility	
Is aged under 18 years or above 65 years at the time of signing the informed consent form.	185 (60.1%)
Does not have symptoms (pain and/or reduced function) severe enough to warrant KR.	66 (21.4%)
Does not have intact collateral knee ligaments	3 (1.0%)
Does not have a fixed flexion deformity ≤ 10° of the involved knee.	1 (0.3%)
Has an isolated patello-femoral OA	1 (0.3%)
Does not have complete joint space obliteration in both medial and lateral tibio-femoral compartments	11 (3.6%)
Has a known diagnosis of inflammatory arthritis	7 (2.3%)

TABLE 14 Details of patients not meeting the inclusion criteria (*continued*)

Reasons for ineligibility	
Has an existing joint replacement in either of the upper or lower limbs	83 (26.9%)
Weighs > 120 kg	28 (9.1%)
Has an active cancer making them unsuitable for the study intervention	2 (0.6%)
Is not expected to complete all the trial procedures	3 (1.0%)
Is unable to provide informed consent	1 (0.3%)
Other	4 (1.3%)
Total	**312**

TABLE 15 Details of reasons for refusal to participate

Reasons did not wish to take part	
Does not want to take part in any research	2 (13.3%)
Refused without a reason	2 (13.3%)
Expressed a preference to not have KJD	3 (20.0%)
Expressed a preference to not have KR	1 (6.7%)
Does not want surgery	4 (26.7%)
Personal vreasons	3 (20.0%)
Total	**15**

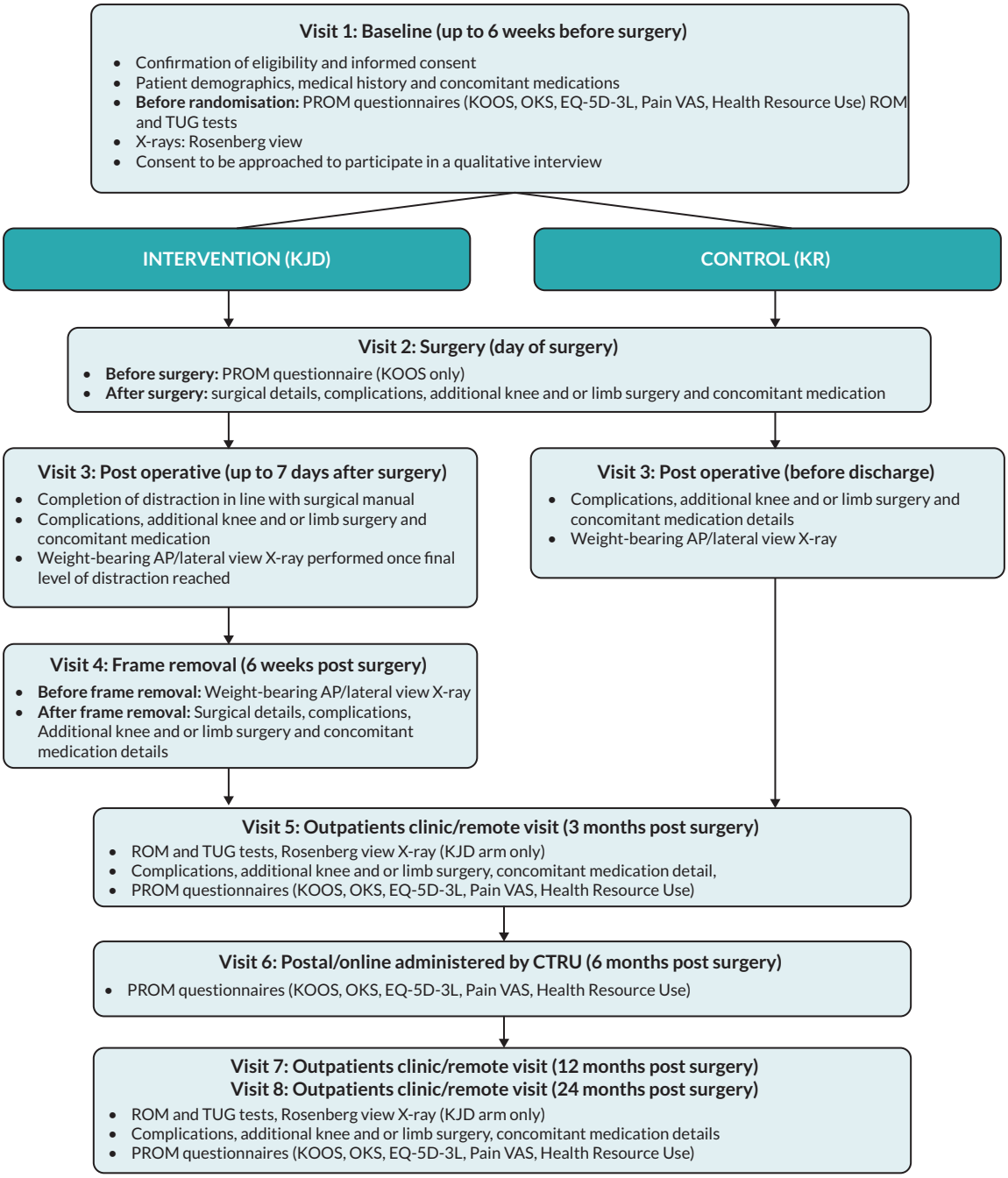

FIGURE 2 Trial flow diagram. AP, anteroposterior; PROM, patient-reported outcome measure.

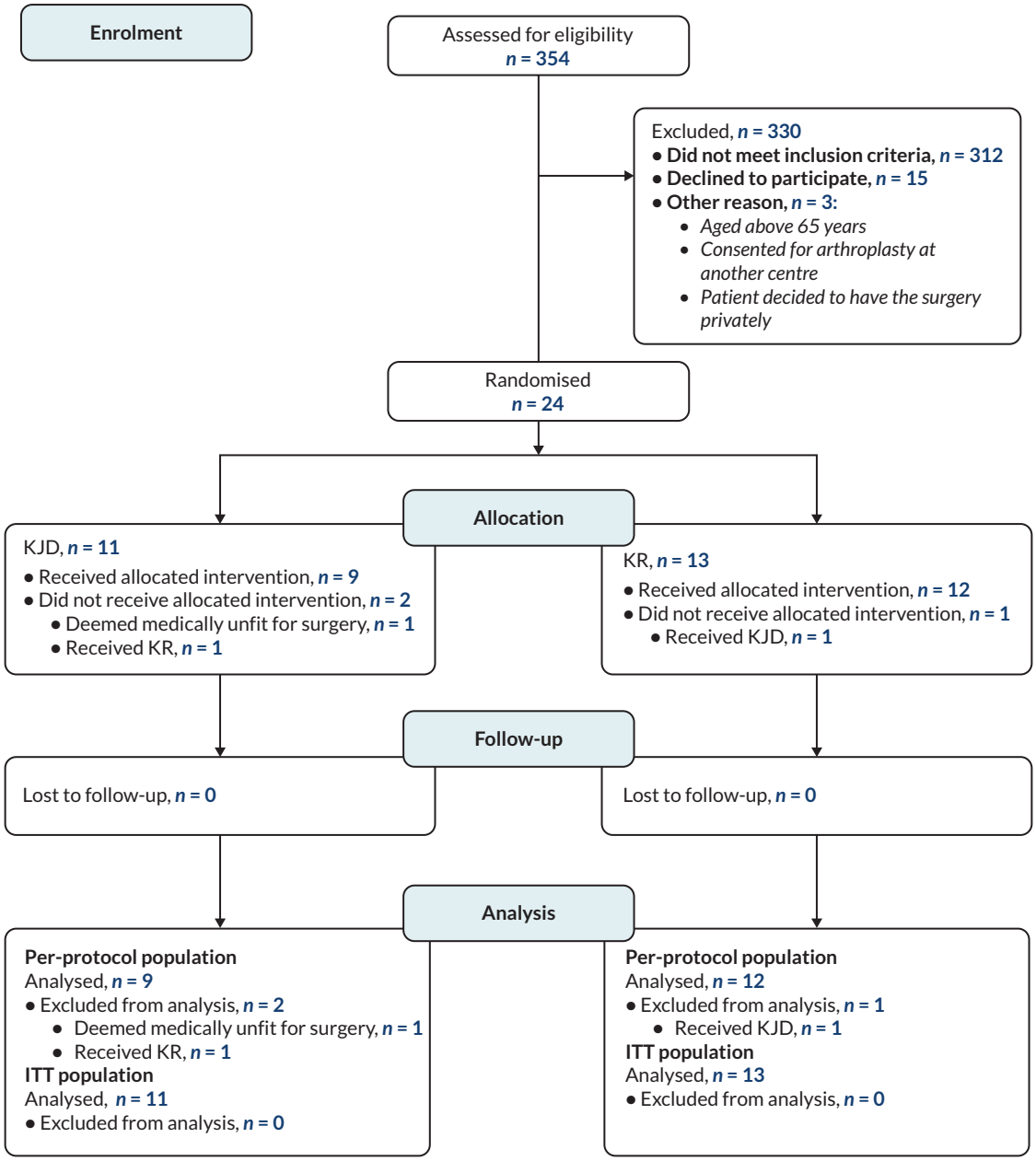

FIGURE 3 Consolidated Standards of Reporting Trials diagram. ITT, intention to treat.

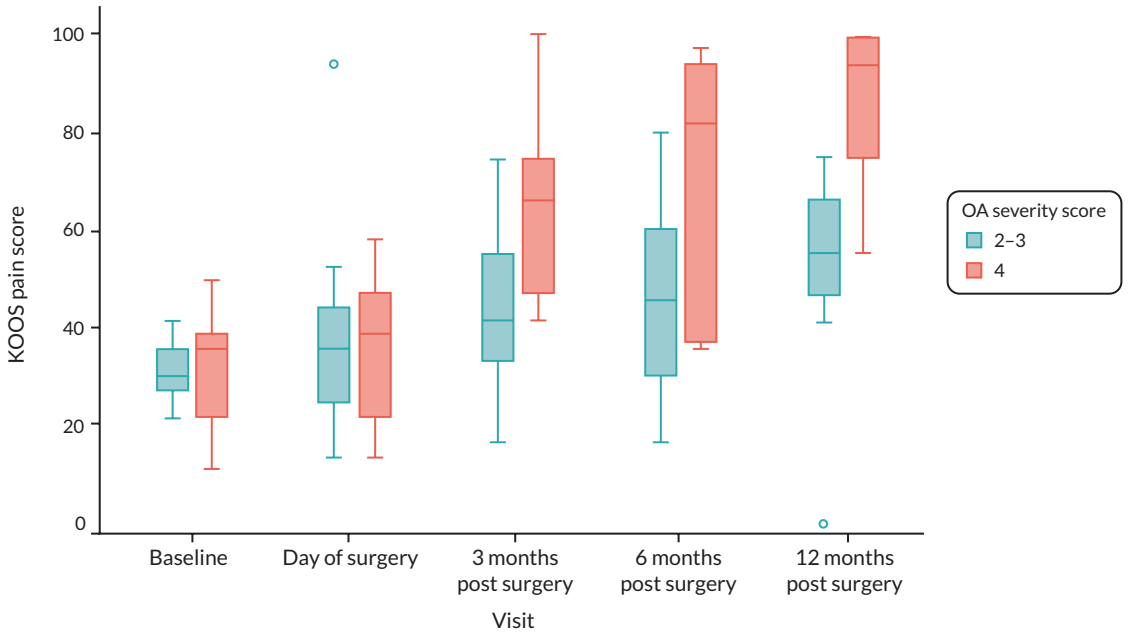

FIGURE 4 Knee Injury and Osteoarthritis Outcome Score pain scores by OA severity and visit. Median (line), IQR (box), range (whisker).

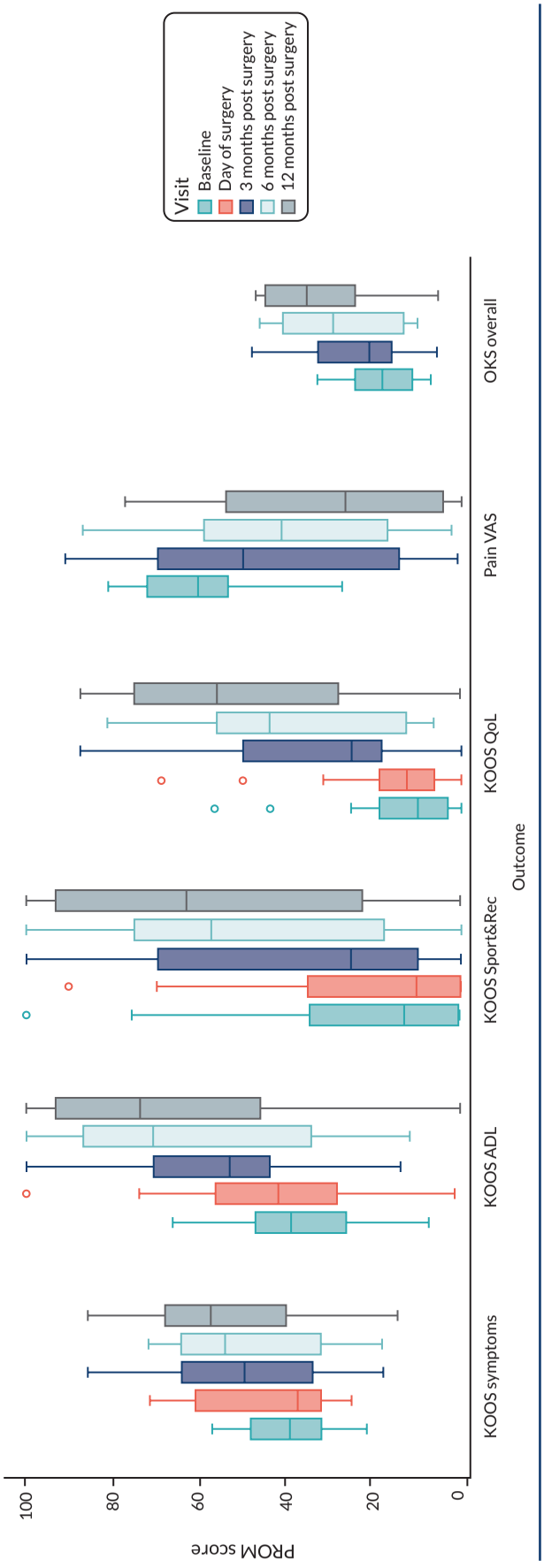

FIGURE 5 Patient-reported outcome measures by visit. Median (line), IQR (box), range (whisker).PROM, patient-reported outcome measure; QoL, quality of life.