Knee arthroplasty compared with joint distraction for osteoarthritis: a phase III randomized controlled trial

From University of Leeds, Leeds, UK

Correspondence should be sent to H. Pandit H.Pandit@leeds.ac.uk

Cite this article:
Bone Jt Open 2025;6(8):
886–893.

DOI: 10.1302/2633-1462.68.BJO-2024-0120.R2

T. W. Hamilton,[1] B. Lineham,[2,3] D. D. Stocken,[4] H. Pandit,[2,3] KARDS Study Group

[1]Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK
[2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK
[3]Chapel Allerton Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK
[4]Clinical Trials Research Unit, Leeds Institute of Clinical Trials, University of Leeds, Leeds, UK

Aims

Knee joint distraction (KJD) has been proposed as a joint-preserving alternative to arthroplasty. The objective of this study was to evaluate the clinical and cost-effectiveness of KJD compared to arthroplasty for knee osteoarthritis.

Methods

This phase III multicentre, pragmatic, randomized controlled non-inferiority trial recruited adults aged ≤ 65 years with symptomatic osteoarthritis refractory to non-surgical treatment and suitable for knee arthroplasty. Patients were randomized to static, linear, KJD of 5 mm, produced with an external fixator construct for six-week duration, or total knee arthroplasty. The primary outcome measure was the Knee injury and Osteoarthritis Outcomes Score (KOOS) pain subscale 12 months post-surgery. The trial was terminated early due to failure to recruit following cessation of elective orthopaedic surgery during the COVID-19 pandemic.

Results

A total of 24 participants were randomized with baseline characteristics balanced between groups. Improved median KOOS pain scores at 12 months postoperatively were observed in both treatment groups. The median KOOS pain score in the KJD group improved from 38.9 (IQR 30.6 to 41.7) at baseline to 55.6 (IQR 41.7 to 94.4) at 12 months, while corresponding scores in the arthroplasty group improved from 30.6 (IQR 11.1 to 36.1) to 75.0 (IQR 66.7 to 88.9). Similar improvements following KJD were seen across other KOOS subdomains and pain VAS, range of motion, or timed up-and-go test. The small sample size does not provide sufficient information to make meaningful comparisons between treatment groups. Pin site infection was seen in two patients, and a fracture through a pin site after frame removal following trauma in one patient.

Conclusion

KJD appears to be associated with improved pain and function compared to baseline. The clinical and cost-effectiveness of KJD compared to arthroplasty remains uncertain.

Take home message

- Our small study in a UK population was impacted by the cessation of elective orthopaedic surgery secondary to the COVID-19 pandemic.
- Our results are in agreement with earlier studies of knee osteoarthritis where knee joint distraction performed well.

Introduction

Knee arthroplasty is a highly clinically and cost-effective treatment for patients with symptomatic advanced osteoarthritis refractory to non-surgical treatment.[1] While registry studies consistently report implant survival exceeding 95% at ten years, there is concern about the high lifetime risk of revision in younger patients,

particularly males, which has been reported to be around one in three across multiple studies.[2-4] Furthermore, in young patients arthroplasty may not meet expectations in terms of level of function or pain relief, and where composite endpoints including these factors are used, under two-thirds of arthroplasties may be considered successful in the mid term.[5]

Knee joint distraction (KJD) is thought to work by temporarily removing mechanical stress on the cartilage and permitting intrinsic joint repair mechanisms. Historically, it was considered that articular cartilage was incapable of spontaneous repair, but joint-offloading procedures such as osteotomies and joint distraction in different locations, including the ankle and knee joints, have demonstrated cartilage regeneration in experimental models.[6-9]

Current evidence on the comparative effectiveness of KJD is limited, with two small randomized controlled trials (RCTs) from a single Dutch centre.[10,11] The Knee Arthroplasty versus Distraction Study (KARDS) was a UK-based phase III multicentre, pragmatic, randomized controlled non-inferiority trial assessing the clinical and cost-effectiveness of KJD compared to knee arthroplasty in adults aged ≤ 65 years with symptomatic osteoarthritis of knee refractory to non-surgical treatment.

Methods

Design

A summary of the study protocol has been published previously.[12] The trial was terminated early due to failure to recruit, which was a result of the cessation of NHS elective orthopaedic surgery due to the COVID-19 pandemic.

Participant eligibility

Eligible participants were those aged between 18 and 65 years inclusively, with symptomatic knee osteoarthritis refractory to non-surgical treatment, who were considered suitable for knee arthroplasty. Participants had to have clinically intact collateral ligaments, leg alignment not requiring correction, and a fixed flexion deformity ≤ 10°. Patients were excluded if they had: complete joint space obliteration in the medial and lateral tibiofemoral compartments on weightbearing radiograph, isolated patellofemoral joint osteoarthritis, inflammatory arthritis, insufficient bone density to support pins for six weeks, prior joint arthroplasty in any limb, surgical treatment of the knee (excluding arthroscopy) within the prior six months, previous knee joint distraction, weight > 120 kg, pregnancy, active cancer, if they had been previously involved in the KARDS study, or were unable to complete all trial procedures or provide informed consent.

Patient characteristics

All KARDS patients were recruited from a single centre in England (Leeds Teaching Hospitals NHS Trust). Between March 2021 and October 2022, 354 participants were assessed for eligibility for the trial. A total of 326 were excluded before randomization, with the remaining 24 participants randomized between two groups (11 KJD, 13 arthroplasty) (Figure 1). Despite knee osteoarthritis (OA) being a common condition, the number of patients assessed for eligibility and excluded was high (326 of 350). The vast majority of these were due to not meeting the inclusion criteria (308 of 326) with the main reason for exclusion being age under 18 or over 65 years at the time of consent (n = 185). Other common reasons for exclusion were prior joint arthroplasty in the upper or lower limbs, and symptoms (pain and/or reduced function) not severe enough to warrant knee arthroplasty in the opinion of the treating surgeon. Of those patients, eligible recruitment was high, with 24 of 41 eligible patients recruited.

The median age of participants was 60 years (range 47 to 65), BMI 31 kg/m^2 (range 22 to 44), 17 (71%) were male, and 14 (58%) had Kellgren-Lawrence grade 4 OA.[13] In total, 20 patients (83%) reported taking oral narcotic analgesics or non-steroidal anti-inflammatories in the preceding week, of whom nine (31%) used oral opioids prior to surgery. All participants identified as being of white ethnicity. Baseline characteristics were balanced between groups (Table I).

Surgeon eligibility

Surgeries were completed either by a consultant orthopaedic surgeon (HP, PH), or under their direct supervision. To deliver KJD a surgeon must have performed ≥ ten external fixations procedures as primary surgeon during their career, or completed a limb reconstruction fellowship. To deliver arthroplasty, a surgeon must have performed ≥ ten knee arthroplasties in the past 12 months as the primary surgeon.

Randomization

Patients were randomized 1:1 to KJD or knee arthroplasty groups centrally using a secure online system. Randomization was based on a minimization algorithm with random component balanced for delivery unit and osteoarthritis severity (Kellgren-Lawrence 2/3 vs grade 4). Randomization occurred at the time of baseline visit, within six weeks of the planned surgery date.

Interventions

For KJD, a definitive external fixator construct that allowed controlled linear distraction across the knee joint of 5 mm was used. Aside from the requirement that external fixator constructs were licensed for spanning a joint, no restriction was placed on the construct used. Pins were placed under fluoroscopic control with between 2 mm and 5 mm of axial distraction applied. Postoperatively, further distraction at a maximum of 1 mm/day was applied until radiological confirmation of 5 mm distraction. Full weightbearing was allowed through the external fixator construct. External fixators were removed under general anaesthesia with manipulation under anaesthesia of the knee to achieve ≥ 90° flexion at six weeks with pin site care, as per local protocol. For arthroplasty, the surgical technique, implants used, and alignment philosophy were in line with surgeons' usual practice and device instructions for use.

Outcomes

The primary outcome measure was the Knee injury and Osteoarthritis Outcomes Score (KOOS) pain score 12 months postoperatively, transformed to a 0 to 100 scale with zero representing extreme knee problems.[14] The study planned to collect data at week six (KJD only), and months three, 12, and 24 postoperatively; however, as the trial was closed early, minimum safety follow-up of all patients was conducted at three months postoperatively.

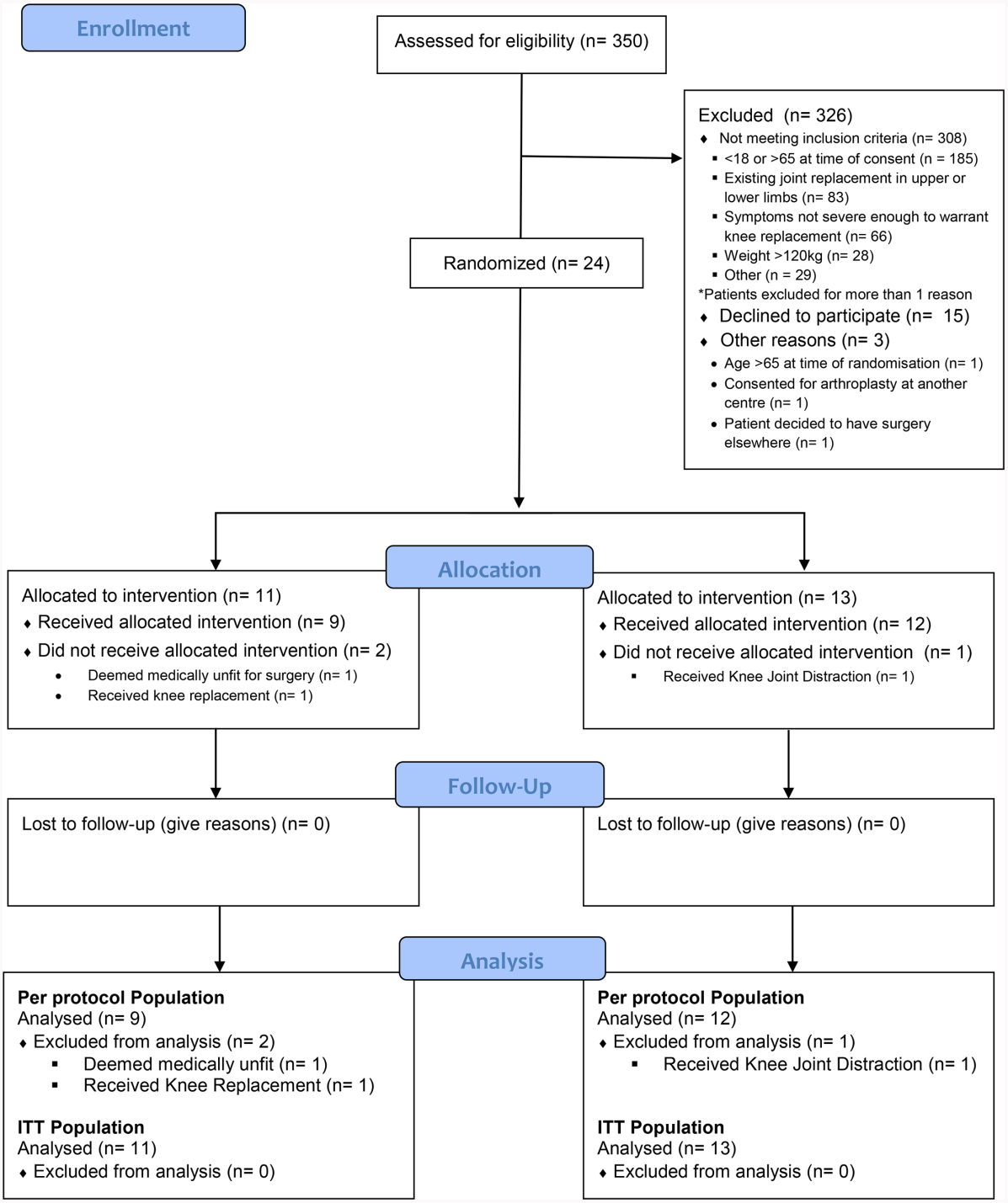

Fig. 1
PRISMA flowchart. ITT, intention to treat.

Predefined secondary outcomes included: patient-reported outcome measures (PROMs; KOOS, pain visual analogue scale (VAS), Oxford Knee Score (OKS)),[15,16] objective assessments of knee function (active range of motion, timed up-and-go test), complications (intraoperative and postoperative), further surgery, and a cost-effectiveness analysis.

Health economic analysis

The objective of the health economic evaluation was to estimate the costs of KJD with arthroplasty over 12 months after the initial surgical intervention from the perspectives of the NHS, the Personal Social Services, and Society. A cost-effectiveness analysis was conducted using available individual participant data. Given the low number of participants, the health economic evaluation was reduced to estimate costs and average EuroQol five-dimension three-level questionnaire (EQ-5D-3L) utility score of each surgical intervention. As with the statistical plan, economic data were analyzed according to a per protocol population.

Table I. Patient characteristics.

Characteristic	Knee arthroplasty (n = 13)	KJD (n = 11)	Total (n = 24)
Median age, yrs (range)	57.0 (47 to 64)	61.0 (52 to 65)	60.0 (47 to 65)
Sex, n (%)			
Male	10 (76.9)	7 (63.6)	17 (70.8)
Female	3 (23.1)	4 (36.4)	7 (29.2)
White ethnicity, n (%)	13 (100.0)	11 (100.0)	24 (100.0)
Median BMI, kg/m^2 (range)	32.9 (22 to 44)	29.0 (24 to 40)	31.3 (22 to 44)
KL OA grade, n (%)			
2 to 3	6 (46.2)	4 (36.4)	10 (41.7)
4	7 (53.8)	7 (63.6)	14 (58.3)

KL, Kellgren-Lawrence; OA, osteoarthritis.

Ethical approval and consent to participate

KARDS obtained approval from the National Research Ethics Service, Yorkshire & The Humber Leeds East Research Ethics Committee on 9 January 2020 (REC reference 19/YH/0368). The University of Leeds was the sponsor. The trial was registered with the International Standard Randomized Controlled Trials database (ISRCTN reference number 14879004). Written informed consent was obtained from all participants prior to their involvement in the study.

Statistical analysis

Statistical analysis was according to a Statistical Analysis Plan. As the trial ended early, with a small number of patients from a single centre, only descriptive statistics are reported. As a non-inferiority trial, the original analysis plan was primarily to analyze a per-protocol population with planned sensitivity analyses based on the intention-to-treat population.[17,18] The original target sample size for the trial was 344 patients. A total of 172 patients randomized in each group were required to detect an eight-point non-inferiority margin in KOOS pain score at a one-sided 0.025 significance level with 90% power, assuming a SD of 21 allowing for a 15% loss to follow-up rate.[11]

Results

Withdrawals, ITT, and PP populations

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

Surgical procedures

Of 21 surgeries, 20 were performed by a consultant principal surgeon (HP, PH). All patients were administered perioperative intravenous antibiotic prophylaxis. The median operating time for KJD was 96.0 minutes (range 43 to 165) and 84.5 minutes (range 52 to 131) for arthroplasty.

For KJD (6 ArthroSave Knee Reviver (Netherlands), 3 Smith and Nephew (UK), Ilizarov Construct) no tourniquet was used. For the knee reviver cases, half-pins were used throughout. For the Ilizarov cases, a combination of half-pins and tensioned fine-wires were employed. None of the pins were hydroxyapatite (HA)-coated. The required 5 mm distraction was achieved postoperatively in all patients.

All arthroplasty patients received a total knee arthroplasty (TKA) (10 Medacta Sphere (Switzerland), 2 Zimmer Biomet Persona (USA)). Radiographs were reviewed by independent orthopaedic surgeons (TWH, BL), blinded and in duplicate, with implant sizing and position confirmed as acceptable.

Primary outcome

The low number of 12-month scores obtained (seven scores in KJD and nine scores in arthroplasty) does not provide sufficient information to make meaningful comparisons between the treatment groups. Higher median KOOS pain scores at 12 months postoperatively, compared to baseline, were observed in both treatment groups, indicating an improvement in symptoms (Table II, Figure 2). The median KOOS pain score in the KJD group improved from 38.9 (IQR 22.2 to 41.7) at baseline to 55.6 (IQR 44.4 to 93.1). The median KOOS pain score in the arthroplasty group improved from 31.9 (IQR 18.1 to 36.1) at baseline to 75.0 (IQR 66.7 to 88.9).

Secondary outcomes

For both KJD and arthroplasty groups, KOOS scores across all domains, pain VAS scores, and the OKS improved from baseline to 12 months (Table II). The small number of patients does not allow for meaningful comparison between groups.

Range of motion did not appear to differ substantially between randomized groups across follow-up timepoints. Participants randomized to arthroplasty reported improvements in their 'timed up-and-go' times from baseline to 12 months postoperatively, whereas this was not seen in the KJD group.

Adverse events

Two patients experienced complications related to their index surgery. In one patient undergoing KJD, a component jammed during application and attempts at removal to replace it resulted in one of the pins becoming loose. This was replaced during the same surgery. In one patient undergoing arthroplasty a drill pin broke, with the tip retained in the patient. At a six-week fixator removal visit, two infected pin sites were reported (one of them being the same patient in whom one of the pins needed replacing). This patient slipped on a wet floor at three months post fixator removal, sustaining a fractured femur that was found to be associated with stress riser around a previous pin-track. The fracture was managed surgically with retrograde intramedullary nail and extended antibiotic cover, and healed without complication. No other participant reported any additional secondary procedures.

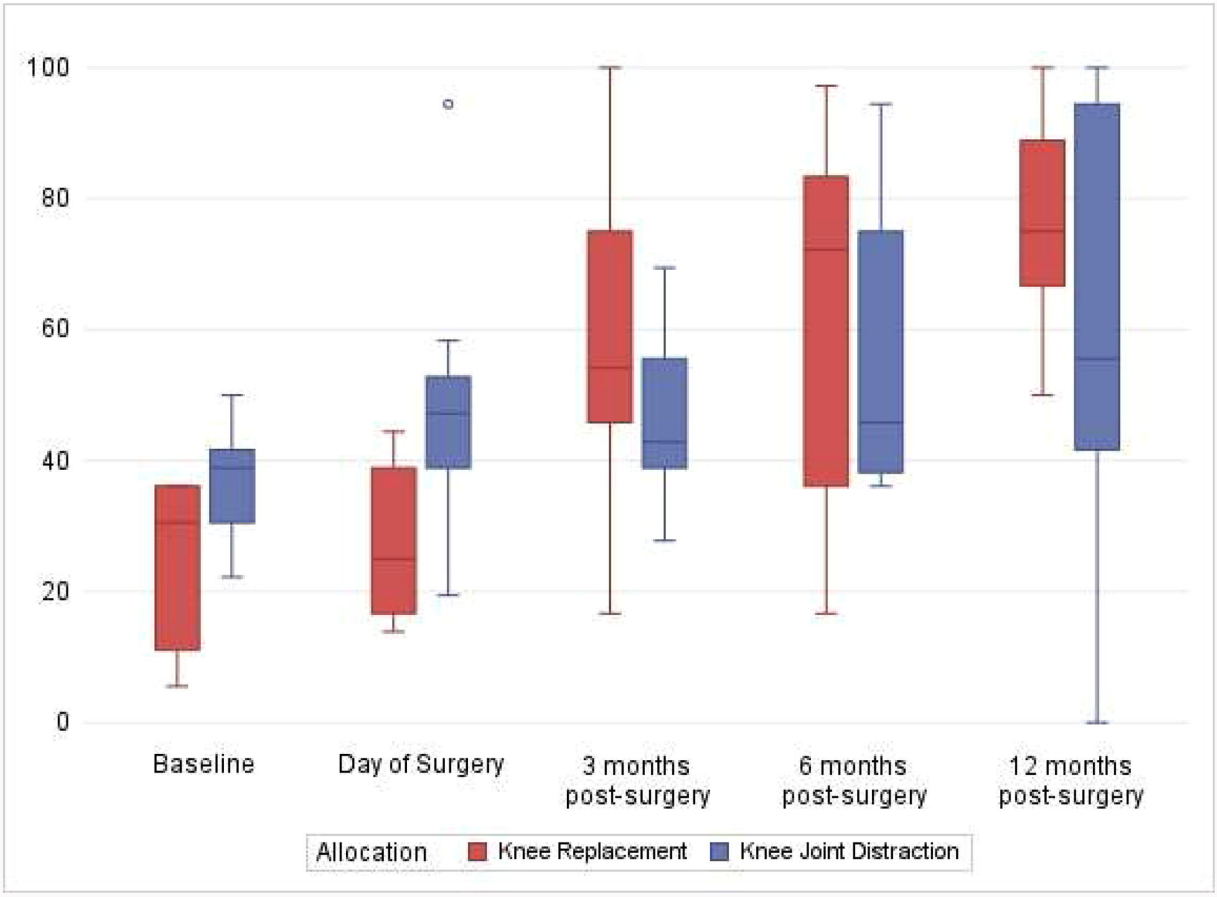

Fig. 2
Knee injury and Osteoarthritis Outcome Score (KOOS) pain scores by treatment allocation and visit. Median (line), IQR (box), range (whisker).

Patients with infected pin-track were treated with debridement and antibiotics at the time of fixator removal. At three months, three patients from the KJD group reported events (two residual pin site infections and one stiff knee). Pin site infections were treated by a further course of oral antibiotics, and the stiff knee by outpatient physiotherapy sessions.

Sensitivity analyses

Sensitivity analyses confirmed results were not substantially different when including the wider ITT population. Planned analysis was performed based on stratification factors. As recruitment was from a single centre, only radiological OA grade based on standing anteroposterior radiographs, Kellgren-Lawrence Grade 2/3 versus Grade 4, was assessed. KOOS pain scores at follow-up were higher, representing less pain, in those with more advanced structural disease (Grade 4). The median KOOS pain score in the severity Grade 2/3 group improved from 30.6 (IQR 27.8 to 36.1) at baseline to 55.6 (IQR 47.2 to 66.7). The median KOOS pain score in the severity Grade 4 group improved from 36.1 (IQR 22.2 to 38.9) at baseline to 94.4 (IQR 75.0 to 100.0). Similar results were seen across secondary outcomes.

Health economic analysis

The median change in EQ-5D-3L index utility score at three months was 0.35 (IQR 0.08 to 0.62) in KJD and 0.69 (IQR 0.62 to 0.76) in arthroplasty patients. The respective figures at six months, with one KJD and two arthroplasty patients having missing data, were 0.52 (IQR 0.19 to 0.59) and 0.76 (IQR 0.62 to 0.88). The mean and median costs of KJD were £1,0441 (SD 2,697) and £1,0494 (IQR 7,299 to 13,350) and for arthroplasty £6,101 (SD 816) and £6,032 (IQR 5,650 to 6,340).

The median NHS costs of hospital service use, outpatient attendance and inpatient admissions, were £463 (IQR 363 to 845) and £421 (IQR 161 to 1,083), respectively, at the three-month clinical follow-up. Use of narcotic and nonsteroidal anti-inflammatory drugs (NSAIDs) was associated with £13.13 (IQR 1 to 22) at post-surgical assessment, and £3.95 (IQR 0 to 11) at three months post-surgery in the KJD group and £13.27 (IQR 9 to 13) and £2.80 (IQR 0 to 7) in the arthroplasty group.

Ten KJD patients reported median out-of-pocket costs of £55 (IQR 0 to 700) and incurred an estimated £0 (IQR 0 to 7,646) of productivity costs (time off work due to health or receiving care) at three months; the corresponding figures for 13 arthroplasty patients were £4 (IQR 0 to 125) and £0 (IQR 0 to 4,588).

Discussion

The purpose of the KARDS trial was to demonstrate non-inferiority of KJD as an alternative to knee arthroplasty for OA in a phase III trial conducted in a UK population. Unfortunately, KARDS was closed to recruitment due to the impact of the

Table II. Patient-reported outcome measures (PROMs) by treatment allocation and visit.

PROM	Baseline		Day of surgery		3 mths post-surgery		6 mths post-surgery		12 mths post-surgery	
	KA (n = 12)	KJD (n = 9)	KA (n = 12)	KJD (n = 9)	KA (n = 12)	KJD (n = 9)	KA (n = 12)	KJD (n = 9)	KA (n = 12)	KJD (n = 9)
Median KOOS Pain (IQR)*	30.6 (11.1 to 36.1)	38.9 (30.6 to 41.7)	25.0 (16.7 to 38.9)	47.2 (19.0 to 94.0)	54.2 (45.8 to 75.0)	42.9 (38.9 to 55.6)	72.2 (36.1 to 83.3)	45.8 (38.2 to 75.0)	75.0 (66.7 to 88.9)*	55.6 (41.7 to 94.4)*
Median KOOS Symptoms (IQR)	39.3 (25.0 to 46.4)	39.3 (32.1 to 50.0)	35.7 (28.6 to 50.0)	46.4 (35.7 to 67.9)	60.7 (35.7 to 66.1)	41.1 (32.1 to 57.1)	55.4 (39.3 to 67.9)	37.5 (32.1 to 62.5)	57.1 (50.0 to 64.3)	57.1 (32.1 to 71.4)
Median KOOS ADL (IQR)	33.8 (25.0 to 42.6)	45.3 (33.8 to 48.5)	36.8 (26.5 to 48.5)	45.6 (41.2 to 66.2)	69.9 (50.7 to 80.1)	50.0 (35.9 to 51.6)	78.7 (44.1 to 88.2)	39.3 (34.1 to 71.3)	88.2 (73.5 to 94.1)	48.5 (36.8 to 92.6)
Median KOOS Sport & Rec (IQR)	5.0 (0.0 to 65.0)	25.0 (5.0 to 30.0)	10.0 (0.0 to 35.0)	17.5 (5.0 to 47.5)	50.0 (25.0 to 87.5)	5.0 (5.0 to 25.0)	60.0 (41.7 to 75.0)	20.0 (10.0 to 75.0)	70.0 (55.0 to 100.0)	25.0 (0.0 to 90.0)
Median KOOS QoL (IQR)	6.3 (0.0 to 18.8)	12.5 (6.3 to 25.0)	6.3 (0.0 to 18.8)	18.8 (12.5 to 31.3)	43.8 (25.0 to 59.4)	18.8 (6.3 to 18.8)	56.3 (43.8 to 62.5)	12.5 (12.5 to 43.8)	56.3 (56.3 to 81.3)	25.0 (12.5 to 68.8)
Median Pain VAS, (IQR)	66.5 (55.0 to 78.0)	56.0 (50.0 to 64.0)	N/A†	N/A†	23.0 (7.0 to 58.5)	52.0 (40.0 to 79.5)	31.5 (7.0 to 56.0)	57.0 (22.0 to 68.5)	12.0 (3.0 to 33.0)	50.0 (10.0 to 69.0)
Median OKS overall (IQR)	16.0 (11.0 to 26.0)	20.0 (12.0 to 22.0)	N/A†	N/A†	28.0 (22.5 to 38.0)	16.0 (11.0 to 20.0)	34.0 (25.0 to 41.0)	20.0 (12.5 to 35.5)	37.0 (36.0 to 46.0)	27.0 (14.0 to 44.0)

*Primary outcome measure.
†Outcome not assessed at this timepoint.
ADL, activities of daily living; KA, knee arthroplasty; KJD, knee joint distraction; KOOS, Knee injury and Osteoarthritis Outcome Score; N/A, not available; OKS, Oxford Knee Score; QoL, quality of life; VAS, visual analogue scale.

COVID-19 pandemic on UK NHS surgical services. Despite early termination KARDS contributes to the literature on knee joint distraction as a treatment for knee OA in patients aged 65 years or younger. While the small number of participants mean that results must be interpreted with caution, our data indicate that KJD is likely to be associated with improvements in knee joint function as assessed by KOOS and, to a lesser extent, OKS. However, we must also acknowledge that KJD may also be associated with complications such pin site infection (two cases; 22%) and fracture (one case; 11%), which, in addition to their immediate effects, may compromise future arthroplasty.

As OA is a chronic condition, with an increasing life expectancy the advantages to delaying the time of index knee arthroplasty, potentially through KJD, will become increasingly important, and thus the research question remains highly relevant. In our small sample, better function with less pain was seen in the knee arthroplasty group; however, it remains unclear whether these results indicate inferiority of KJD. Complications of both surgical treatments were rare, with the most common complication in the KJD group being pin site infection, which is an endemic issue with the use of external fixators. KJD appeared to be associated with less improvement in quality of life at a higher cost, but small numbers means that there remain uncertainty around these findings. Furthermore, these findings do not take into account the benefits of delaying arthroplasty in this age group where the lifetime risk of revision is around one in three,[2-4] with under two-thirds being considered successful in the mid-term.[5]

We are aware of two previous RCTs, both from the same Dutch centre, assessing the outcomes of KJD as a treatment for knee OA,[10,11] one comparing KJD with high tibial osteotomy, and one with knee arthroplasty. Both studies were conducted in patients aged under 65 years with similar inclusion criteria to KARDS. Like KARDS, both studies reported improvements across all KOOS subdomains between baseline and 12 months. In the Dutch RCTs, KJD was also associated with significant improvements in pain as assessed by pain VAS, although baseline pain scores were higher than in KARDS.

Compared to knee arthroplasty, van der Woude et al[10] reported that, aside from the KOOS quality of life subdomain (which was better following knee arthroplasty), at 12 months no difference in KOOS or WOMAC subdomains, pain VAS, or quality of life assessed by EQ-5D or 36-Item Short-Form Health Survey questionnaire (SF-36) was observed between treatment groups. These results differed from the small KARDS patient group, where all early results from our small sample favoured knee arthroplasty. While acknowledging that our results are severely underpowered, it is interesting to note a difference in response to knee arthroplasty (control arm) between studies. In both studies, knee arthroplasty was associated with improvements in outcomes; however, these were more marked in KARDS than the Dutch study, indicating that differences in patient or disease characteristics or surgical technique likely exist between study populations.

KARDS suggested that, for both KJD and knee arthroplasty, despite similar baseline KOOS pain score, outcomes were better in the small subset of patients with more advanced structural disease (Grade 4). This finding is consistent with the two published RCTs, where improvements in PROMs following KJD were greater in the knee arthroplasty study, which likely represented greater structural disease, than the high tibial osteotomy (HTO) study, despite KJD being performed by the same surgeons in both studies.[10,11] Degree of structural disease is known to influence outcomes following knee arthroplasty, with more variable outcomes seen in lower Kellgren-Lawrence grades (representing less severe structural disease). Thus, imbalances in baseline degree of structural disease may influence the results seen. While in our study Kellgren-Lawrence grade was well balanced between

randomized groups, with around 60% in both having Grade 4 changes, in the published RCT 17% in the arthroplasty group had Grade 4 changes compared to 55% in the KJD group.[10]

Despite early termination, this study 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. During both trial development and implementation, patients had a strong desire to pursue joint-preserving options, if feasible. This was particularly true in younger, often male, patients who wanted to get back to manual occupations. KARDS demonstrated that this trial was feasible and implementable; the limited results indicated that the technique is safe with no safety concerns.

To our knowledge, this is the only independent study of KJD knee OA. Although KARDS was closed early, it has contributed to our improved understanding of KJD as a potential treatment. As a commissioned piece of research, with delivery greatly impacted by the NHS environment post-COVID-19 pandemic and the impact on NHS surgical services, the research question remains highly relevant. The embedded KARDS process evaluation has provided helpful insight into research delivery for the future.

In addition to the limitations following early closure, KARDS was a pragmatic RCT, so while it positively reflects the real-world experience, a consequence is variation in surgical practice, implant selection, and surgical technique, which will influence outcomes of both the intervention and control groups. Despite this, we would advocate that any future trials are pragmatic in design, stratifying randomization and adjusting for potential cofounders, such that the results of this trial represent the outcomes of the population studied as a whole.

In conclusion, clinical conclusions are limited due to small sample size as a result of the suspension of elective surgery services within the UK following the COVID-19 pandemic and early closure of the trial. Our small randomized clinical trial of 24 UK patients demonstrated improved pain scores at 12 months postoperatively in both treatment groups. KJD was a deliverable treatment for knee OA, and our data are in agreement with prior studies where KJD performed well. The clinical and cost-effectiveness of KJD, and whether it achieves longer-term equivalent outcomes to knee arthroplasty, remains uncertain and 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 these uncertainties, and procedures carried out as part of a clinical trial where possible.

Social media

Follow T. W. Hamilton on X @hamilton_tw

References

1. **Yapp LZ**, **Scott CEH**, **MacDonald DJ**, **Howie CR**, **Simpson AHRW**, **Clement ND**. Primary knee arthroplasty for osteoarthritis restores patients' health-related quality of life to normal population levels. *Bone Joint J*. 2023;105-B(4):365–372.
2. **Stone B**, **Nugent M**, **Young SW**, **Frampton C**, **Hooper GJ**. The lifetime risk of revision following total knee arthroplasty. *Bone Joint J*. 2022;104-B(2):235–241.
3. **Yapp LZ**, **Clement ND**, **Moran M**, **Clarke JV**, **Simpson A**, **Scott CEH**. The estimated lifetime risk of revision after primary knee arthroplasty is influenced by age, sex, and indication. *Bone Joint J*. 2022;104-B(12):1313–1322.
4. **Bayliss LE**, **Culliford D**, **Monk AP**, **et al**. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. *Lancet*. 2017;389(10077):1424–1430.
5. **Price AJ**, **Longino D**, **Rees J**, **et al**. Are pain and function better measures of outcome than revision rates after TKR in the younger patient? *Knee*. 2010;17(3):196–199.
6. **Wiegant K**, **Intema F**, **van Roermund PM**, **et al**. Evidence of cartilage repair by joint distraction in a canine model of osteoarthritis. *Arthritis Rheumatol*. 2015;67(2):465–474.
7. **McGonagle D**, **Baboolal TG**, **Jones E**. Native joint-resident mesenchymal stem cells for cartilage repair in osteoarthritis. *Nat Rev Rheumatol*. 2017;13(12):719–730.
8. **Baboolal TG**, **Mastbergen SC**, **Jones E**, **Calder SJ**, **Lafeber F**, **McGonagle D**. Synovial fluid hyaluronan mediates MSC attachment to cartilage, a potential novel mechanism contributing to cartilage repair in osteoarthritis using knee joint distraction. *Ann Rheum Dis*. 2016;75(5):908–915.
9. **Jansen MP**, **Mastbergen SC**. Joint distraction for osteoarthritis: clinical evidence and molecular mechanisms. *Nat Rev Rheumatol*. 2022;18(1):35–46.
10. **van der Woude JAD**, **Wiegant K**, **van Heerwaarden RJ**, **et al**. Knee joint distraction compared with total knee arthroplasty: a randomised controlled trial. *Bone Joint J*. 2017;99-B(1):51–58.
11. **van der Woude JAD**, **Wiegant K**, **van Heerwaarden RJ**, **et al**. Knee joint distraction compared with high tibial osteotomy: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(3):876–886.
12. **Tassinari CJ**, **Higham R**, **Smith IL**, **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(6):e062721.
13. **Kellgren JH**, **Lawrence JS**. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16(4):494–502.
14. **Rolfson O**, **Wissig S**, **van Maasakkers L**, **et al**. Defining an international standard set of outcome measures for patients with hip or knee osteoarthritis: Consensus of the International Consortium for Health Outcomes Measurement Hip and Knee Osteoarthritis Working Group. *Arthritis Care Res (Hoboken)*. 2016;68(11):1631–1639.
15. **Dawson J**, **Fitzpatrick R**, **Murray D**, **Carr A**. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br*. 1998;80-B(1):63–69.
16. **Murray DW**, **Fitzpatrick R**, **Rogers K**, **et al**. The use of the Oxford hip and knee scores. *J Bone Joint Surg Br*. 2007;89-B(8):1010–1014.
17. **Rehal S**, **Morris TP**, **Fielding K**, **Carpenter JR**, **Phillips PPJ**. Non-inferiority trials: are they inferior? A systematic review of reporting in major medical journals. *BMJ Open*. 2016;6(10):e012594.
18. **Piaggio G**, **Elbourne DR**, **Pocock SJ**, **Evans SJW**, **Altman DG**, **CONSORT Group**. Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. *JAMA*. 2012;308(24):2594–2604.

Author information

T. W. Hamilton, FRCS, DPhil, NIHR Academic Clinical Lecturer, Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK.

B. Lineham, FRCS, MSc, Senior Clinical Research Fellow
H. Pandit, FRCS, DPhil, Consultant Orthopaedic Surgeon
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK; Chapel Allerton Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK.

D. D. Stocken, PhD, CStat, Professor of Clinical Trials Research, Clinical Trials Research Unit, Leeds Institute of Clinical Trials, University of Leeds, Leeds, UK.

Author contributions

T. W. Hamilton: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – original draft, Writing – review & editing.
B. Lineham: Investigation, Validation, Writing – original draft, Writing – review & editing.
D. D. Stocken: Funding acquisition, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.
H. Pandit: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

T. W. Hamilton and B. Lineham are joint first authors.

D. D. Stocken and H. Pandit are joint senior authors.

Funding statement

The author(s) received no financial or material support for the research, authorship, and/or publication of this article.

ICMJE COI statement

This paper presents independent research funded by the National Institute for Health and Care Research (NIHR) under its Health Technology Assessment (HTA) commissioned call programme, reference HTA 17/122/06. T. W. Hamilton reports a NIHR Academic Clinical Lectureship, unrelated to this study. H. Pandit reports an institutional industry grant from iSMART and an institutional NIHR HTA grant (PERISCOPE), consulting fees from Medacta International, Microport, MAT Ortho, Depuy Synthes, Invibio, Paradigm Pharma, Allay Therapeutics, and Zimmer Biomet, two patents with iSMART, and stock or stock options in Allay Therapeutics, all of which are unrelated to this study. D. D. Stocken's salary is funded by a NIHR Research Professorship (NIHR302439), and is an Independent Chair for NIHR DMC & TSC Committees and a NIHR EME committee member.

Data sharing

The data collected for the trial, including anonymized participant data and a data dictionary defining each field in the set, can be made available to researchers on request to the trial team with defined research question when accompanied by a peer-reviewed protocol and signed data access agreement.

Acknowledgements

This paper presents independent research funded by the National Institute for Health and Care Research (NIHR) under its Health Technology Assessment (HTA) commissioned call programme, reference HTA 17/122/06. The views and opinions expressed are those of the authors and do not necessarily reflect those of the UK National Institute of Health and Care Research (NIHR), the NIHR Health Technology Assessment (HTA) Programme, the NIHR Leeds Biomedical Research Centre (BRC), the National Health Service or Department of Health and Social Care. We would like to thank the participants and their families, principal investigators and their teams at each of the KARDS sites and the Trial Steering and Data Monitoring and Ethics Committee for their time and support throughout the trial. Professor Pandit is a NIHR Senior Investigator, Professor Stocken is an NIHR Research Professor and Thomas Hamilton an NIHR Academic Clinical Lecturer. Professor Pandit has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
The sponsor, University of Leeds, took overall responsibility for proportionate, effective arrangements being in place to set up, run and report this study. The sponsor and funders reviewed, and approved, the study design but neither the sponsor, nor funders, were involved with the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethical review statement

Approved by National Research Ethics Service, Yorkshire & The Humber Leeds East Research Ethics Committee on 9th January 2020 (REC reference 19/YH/0368). The University of Leeds was the sponsor.

Open access funding

The open access fee for this article was self-funded.

Trial registration number

Trial Registration: ISRCTN 14879004, registered on 11 January 2020. http://www.isrctn.com/ISRCTN14879004