TITLE PAGE

Comparison of the JOURNEY II bi-cruciate stabilised and GENESIS II total knee arthroplasty for functional ability and motor impairment: the CAPAbility, blinded, randomised controlled trial

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ABSTRACT (300 words)

Objectives: To determine if a newer design of TKR (Journey II BCS) produces superior patient reported outcomes scores and biomechanical outcomes than the older, more established design (Genesis II).

Setting: Patients were recruited from an NHS University Hospital between July 2018 and October 2019 with surgery at two sites. Biomechanical and functional capacity measurements were at a University Movement and Exercise Laboratory.

Participants: 80 participants undergoing single-stage TKR.

Interventions: Patients were randomised to receive either the Journey II BCS or Genesis II TKR

Primary and secondary outcome measures: Primary outcome was the Oxford Knee Score (OKS), at six months. Secondary outcomes were: OKS Activity and Participation Questionnaire (OKS-APQ), EQ-5D-5L and UCLA Activity scores, Timed Up and Go Test (TUG), six-minute walk test (6MWT), lower limb kinematics and lower limb muscle activity during walking and balance.

Results: This study found no difference in the OKS between groups. The OKS scores for the JII-BCS and Genesis II groups were mean (SD) 42.97 (5.21) and 43.13 (5.20) respectively, adjusted effect size 0.35 (-2.01,2.71) p=0.771

In secondary outcome measures, the Genesis II group demonstrated a significantly greater walking range-of-movement (50.62 (7.33) versus 46.07 (7.71) degrees, adjusted effect size, 3.14 (0.61,5.68) p=0.02) and higher peak knee flexion angular velocity during walking (mean (SD) 307.69 (38.96) versus 330.38 (41.40) degrees/second, adjusted effect size was 21.75 (4.54,38.96), p=0.01) and better postural control

(smaller resultant centre of path length) during quiet standing than the JII-BCS group (mean (SD) 158.14 (65.40) versus 235.48 (176.94) mm, adjusted effect size, 59.91 (-105.98,-13.85) p=0.01.).

Conclusions: In this study population, the findings do not support the hypothesis that the Journey II BCS produces a better outcome than the Genesis II for the primary outcome of the OKS at six months after surgery.

Trial registration: ISRCTN32315753, 12 December 2017.

Key words: Total knee replacement**,** Genesis II, Journey II BCS, PROMS, biomechanical analysis

Strengths and limitations

Strengths:

- This is a two arm, superiority, observer-blind, participant-blind and clinical staff-blind, randomised control trial
- It uses a wide variety of patient reported outcomes measures and biomechanical measurements to determine if one implant is superior to the other
- the required sample size was achieved with only one person lost to follow-up.

Weaknesses

- A potential limitation is the relatively large number of secondary outcomes.
- The surgeons all had a much greater familiarity with the implantations of Genesis II implants.

ORIGINAL PROTOCOL FOR THE STUDY UPLOADED AS A SUPPLEMENTAL FILE

INTRODUCTION

Despite total knee replacement (TKR) being an recommended surgical treatment for end-stage knee osteoarthritis[1], up to 34% of all patients following TKR have poor functional outcomes [2–6]. With estimates of osteoarthritis of the knee affecting one in eight people in the USA [7] and 250 million individuals worldwide [8] the number of patients with intrusive symptoms after surgery is significant.

Multiple changes in implant design have been introduced to try to improve patient outcomes and whilst some implant design alterations have led to improvements in patient-reported outcome measures (PROMS) [9–11] and kinematics [12,13] not all have led to differences [14–20].

The Genesis II (Smith & Nephew, Memphis, TN) TKR has been reported to have good survivorship and patient satisfaction [13,21] and commonly used in the UK [22] An evolutionary design, the Journey II BCS (JII-BCS; Smith & Nephew, Memphis, TN), also manufactured by Smith and Nephew, has been developed with the aim of improving kinematic outcome compared to the Genesis II by using a bicruciate design [23] This design change has been supported by encouraging fluoroscopic studies. However, to date, no randomised controlled trials have been conducted to assess if there is a difference in the outcome compared to its predicate design. [24].

The aim of this trial was to assess whether the JII-BCS would produce better patient reported and movement outcomes than the Genesis II.

The published protocol included the aims for investigating: the rotational profile around the native knee and following TKR; and patients' experiences and surgeons' experiences [25]. These findings will be reported in subsequent manuscripts.

METHODS

Trial design, randomisation, blinding to intervention allocation, ethics and registration

A two-arm, superiority randomised controlled trial (RCT) comparing the JII-BCS knee implant (experimental intervention) to the Genesis II knee implant (control intervention) was performed. The trial was observer-blind, participant-blind and clinical staff-blind. Only the operating surgeon and theatre team knew which implant was used for an individual participant.

Trial participants were assigned to either the JII-BCS or Genesis II group using a computer-generated, 1:1 randomisation schedule stratified by site and age (<60 years = younger; ≥60 years = older) [26,27]. Group allocation was revealed using REDCap [28,29], the interactive web-randomisation system, to a member of the research team who was not involved in either the clinical care or assessments of any participant. Allocation was concealed from the surgical team until after the pre-operation baseline measures were completed.

Ethical approval

Ethical approval was given by the East of England – Cambridge Central Research Ethics Committee (reference 16/EE/0230). All participants provided informed consent prior to enrolment.

Sample size

The sample size was calculated from the Oxford Knee Score (OKS, primary outcome measure) [30]. The RCT was powered at 80% with a 5% significance level to detect a minimally important clinical difference of five points [31,32] with a standard deviation of 7.4 points [33]. Accounting for an estimated attrition rate of 10% at six months post-surgery the estimated sample size was 80 participants (40 per group).

Participants, setting and recruitment

Full eligibility criteria are provided in the published protocol [25]. In brief, participants were aged at least 18 years and met the clinical and radiological criteria for a single-stage TKR. People were excluded if they: had a fixed-flexion deformity of at least 15^{o} or non-correctable varus/valgus deformity of at least 15^{o}; had inflammatory arthritis or previous septic arthritis; had previous surgery to the collateral ligaments of the affected knee; had a contralateral TKR implanted less than one year earlier; had severe co-morbidity that could present an unacceptable safety risk or were pregnant; were a private patient; were likely to be living outside the clinical centre catchment area at six months post-surgery; or were enrolled on another clinical trial.

Patients were recruited at a university teaching hospital with surgery conducted at two sites. Outpatient physiotherapy was conducted in a single hospital. The Movement and Exercise Laboratory at the associated University (MoveExLab) was the setting for measures of functional capacity and biomechanics.

Interventions

All participants received routine NHS care for people with TKR irrespective of the implant received. This included following a standard post-operative rehabilitation of out-patient physiotherapy centred on knee strength and range of motion exercises within the first six weeks after surgery. Patients received the same physiotherapy protocols and classes.

Experimental intervention

Participants in the experimental group received the JII-BCS. The JII-BCS is a dual-cam post designed to substitute for both the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) to In addition the femoral component is asymmetric and the polyethylene insert is a medially concave and laterally convex shape. The device is designed to provide guided motion, and thus improve knee kinematics, and increase anteroposterior (AP) stability throughout knee flexion.

Control intervention

- Participants in the control group received the Genesis II (Smith and Nephew, Memphis TN), posterior stabilised (PS) TKR. The design features specific to the implant and a lateralized trochlear groove to improve patellar contact and tracking, an externally rotated femoral implant design and an anatomically-shaped tibial baseplates.

Surgical techniques

All four surgeons had extensive experience, at least five years, of the Genesis II implant. All undertook cadaveric training on the JII-BCS and declared that they were competent in the surgical technique having completed their operative learning curve before starting the trial. Both implants are uncoated, cemented implants. The surgical procedure followed the standard manual surgical approach and technique through a medial parapatellar approach in all cases with intramedullary femoral and tibial rods to provide the alignment of the components. Patella resurfacing was used in both groups.

Data collection schedule

Data collection timepoints for the primary outcome measure were: at least one day before surgery (baseline), 7±2 days after surgery (one-week post-operatively), 6-8±2 weeks after surgery (two months), six months ±4 weeks after surgery (outcome, primary time point). Secondary outcomes were collected at baseline, two months and six months. Any differences from these timepoints are provided in the outcome measures section.

Outcome measures

Primary outcome measure

The Oxford Knee Score (OKS) was the primary outcome measure. This is a 12-question patient self-assessment of knee function and pain [30] with values ranging from 0 (worst outcome) to 48 (best outcome.

Secondary outcome measures

1. Patient reported outcome questionnaires
   a. The OKS Activity and Participation Questionnaire (OKS-APQ) which complements the OKS by assessing everyday activity and social participation [34]. The overall score is from 12 to 60 with 12 being the best outcome.
   b. The EQ-5D-5L is a self-report questionnaire consisting of five questions and a visual analogue scale (VAS). Higher values indicate better quality of life [35].
   c. The UCLA Activity score to assess physical activity self-rating scale ranged from 0 (complete inactivity) to 10 (participation in impact sport).
2. Walking and balance functional ability
   a. Timed Up and Go Test (TUG) – seconds to rise from chair, walk 3m and return to sitting; mean of three trials [36]. The reported minimal detectable change after TKR is 2.27 seconds [37]. A lower value indicates better function.
   b. Six-minute walk test - metres walked in six minutes around a 20-metre circuit [38,39]. The reported minimal detectable change from baseline after TKR is 26 metres [40]. A higher value indicates greater function.
   c. Modified Star-Excursion Test [41] (cm/leg length) where larger values indicate better balance.
3. Movement performance during walking and balance

   For these simultaneous measures, participants wore shorts and were bare-footed. Reflective sensors were placed in accordance with the Plug-In Gait model (Vicon) for the lower limb and 3D motion data were collected, at 100 HZ, with eight wall-mounted infrared cameras (Vicon Motion System, Oxford UK). Three embedded force plates (BERTEC, Ohio, USA) were used to collect kinetic

data at 2000Hz for walking tasks and 100hz for balance tasks. Surface electromyographic sensors (EMG: Delsys) were placed bilaterally on the Vastus Medialis, Vastus Lateralis, Tibialis Anterior, Bicep Femoris and lateral head of the Gastrocnemius following SENIAM guidance. EMG data was collected at 2000 Hz.

For walking tasks, participants were asked to walk in a straight line along a 10-metre walkway at their self-selected speed. For double stance balance activities, participants were instructed to stand with their feet shoulder-width apart. For single stance balance activities, participants were instructed to stand on one leg with hands-on-hips. Three trials of 10 seconds were recorded for each activity.

For the stair ambulation task, participants were asked to complete six ascents and six descents all unaided, leading with the operated limb for three trials and the non-operated limb for the remainder. The stairs had four steps. The first step was 16.5 cm, and the others were 15 cm high. Handrails were available if participants needed support.

Movement data were processed in accordance with the Vicon Plug-in Gait Model (Oxford Metrics, Oxford, UK). Raw EMG was filtered with pass bands at 10 and 500 Hz, rectified and low pass filtered using a 4^{th} order Butterworth with a 10 Hz cut off. Walking data were normalised to 101 data points for the gait cycle. Three trials of tasks were used to create a mean for each measure per participant. Values were extracted using a purpose-built MATLAB script. Data were processed by motion analysis experts in the research team.

a. Primary movement performance measures

   The JII-BCS is expected to provide more normal kinematics during knee movement than Genesis II due to the design changes discussed earlier. Other authors have indicated that the femo-tibial relationship may be more normal during deep knee bend [42]and more stable during walking [43] Accordingly, people with the Journey prosthesis may [44,45] or may [43] have

greater knee ROM, may walk faster [46,47], and may have a longer stride length[46,47] than people receiving a comparison knee replacement . In addition, greater stability of the femur on the tibia could produce greater knee flexion angular velocity as dynamic knee loading could be more normal. However, there is only one non randomised study of 18 patients comparing the JII-BCS directly with the Genesis II [45] . On the basis of the available literature, the hypothesis driving the kinematic investigation was that people receiving the Journey compared with those receiving the Genesis would have greater walking velocity, step-length symmetry (resulting from longer stride length), knee range of motion (ROM) and peak knee flexion angular velocity.

i. Walking speed (meters/second). A higher value indicates better performance
ii. Step length symmetry during walking. Step length ratio was calculated as ((2xOp)/Op+NOp))-1); where Op is the step length of the operated leg and NOp is the step length of the non-operated leg. Zero indicates perfect symmetry and best performance.
iii. Knee ROM during walking (degrees). Higher values indicate better performance.
iv. Peak knee flexion angular velocity during walking (degrees per second). This was inadvertently omitted from the statistical analysis plan. Higher value indicates better performance.

b. Secondary movement performance measures.

i. Double stance support (% of gait cycle). It was planned to measure cadence, (steps/min), step length (m), and stride length (m). However, there is redundancy with the temporal-spatial gait parameters of walking speed and step length symmetry which are included in the primary movement performance measures.
ii. Peak extension and flexion moments of operated knee during the gait cycle (Nm/kg).

iii. Hip and ankle ROM during walking.
iv. Peak knee flexion angular velocity during stepping up onto a stair.
v. Percentage of gait cycle for peak activation of Vastus Medialis, Vastus Lateralis, Tibialis Anterior, Biceps Femoris and Lateral head of Gastrocnemius (% of gait cycle).
vi. Balance measures were derived from kinetic data (from force plates) during standing still: single stance on the operated lower limb for 10 seconds with eyes open (yes/no) and duration maintained; resultant centre of pressure path length (COP cm) in double stance with eyes closed; and resultant COP velocity (cm/s) in double stance with eyes closed.

Clinical context and adverse events

Data on length of hospital stay and complications related to the surgery (e.g. anaesthesia-related problems, bleeding, morbidities) was collected from a notes review. At each visit, participants were asked about their pain medication and if they had received additional treatment since their surgery/previous visit and what this entailed. Any need for revision surgery was recorded. All adverse events identified were tracked until resolution.

Analysis

The statistical analysis plan (SAP) was finalised and agreed prior to database lock and analysis was completed blinded to group allocation (Supplementary file). For all outcomes the hypothesis tests and 95% confidence intervals (CI) were two-sided; and a p-value of <0.05 was considered significant. An intention-to-treat analysis was conducted i.e., all randomised participants regardless of their eligibility or

adherence were analysed according to the treatment they were randomised to receive. The analysis was undertaken by the Trial Statistician using Stata version 16.

For the primary outcome, the mean OKS at six months was compared between the control and experimental groups using a general linear model adjusting for site and age (<60years/≥60years). An adjusted analysis was conducted using the same model but adjusting for the OKS at baseline. The model assumptions were checked graphically, and sensitivity analysis done using a non-parametric bootstrap using 5,000 repetitions.

All the other outcomes were analysed separately at two months and six months using the same general linear model specified above and a corresponding adjusted analysis. The exception was ability to balance for 10 seconds. This was analysed using a logistic regression model adjusting for site and age.

Patient and public involvement

A patient representative, who had previously undergone knee replacement surgery, was involved in the protocol development, assessment of the burden of the intervention and time taken to participate in the research and oversight of the trial as a member the trial management group. The representative also contributed to the planning and writing of research dissemination materials.

RESULTS

Participants were recruited between July 2018 and October 2019. Last follow-up visits were in October 2020 with some impact and delayed visits due to COVID-19.

In the published protocol [25] the analysis plan included a per-protocol and safety analysis. This was not undertaken as the implants were used as intended so these populations would be the same as the intention-to-treat population.

Flow of participants through the trial

In total, 105 of 153 people screened were eligible to take part, 16 declined participation and eight were excluded for other reasons. Therefore, 81 of 153 people (53%) were recruited. All participants in the Genesis II group (n=40) received their allocated intervention. In the JII-BCS group (n=41) one participant withdrew prior to surgery (post-randomisation exclusion). Full details are in the CONSORT Flowchart (Figure I).

Participant characteristics

There were no discernible baseline differences between the groups. (Table 1) .

Table 1. The baseline characteristics of participants

	JII-BCS (n=40)	**Genesis II (n=40)**
Age, mean (SD)	69.28 (7.50)	67.95 (6.28)
Sex, female, number (%)	24 (60.0%)	20 (50.0%)
Body Mass Index, mean (SD)	28.77 (4.25)	29.86 (4.29)
Operated knee, right, number (%)	23 (57.0%)	14 (35.0%)
Intraoperative Am Soc Anaesthesiologists		
Score 1, number (%)	4 (10%)	2 (5%)
Score 2, number (%)	35 (88%)	36 (90%)
Score 3, number (%)	1 (3%)	2 (5%)
Previous contralateral knee implant		
yes, number (%)	7 (17.5%)	6 (15.0%)

no, number (%)	26 (65.0%)	22 (55.0%)
Missing, number (%)	7 (17.5%)	12 (30.0%)
Previous hip surgery, yes, number (%)	5 (13.0%)	5 (13.0%)
Employment, retired, number (%)	25 (63.0%)	24 (60.0%)
Pain Self-Efficacy-2 Questionnaire, median (IQR)	8.0 (6.0,10.0)	6.0 (3.0,9.5)
Hospital Anxiety & Depression Scale		
Anxiety total, mean (SD)	6.32 (3.54)	7.43 (3.05)
Depression total, mean (SD)	6.03 (2.37)	8.05 (3.55)
Oxford Knee Score, mean (SD)	20.25 (5.69)	19.05 (5.28)
EQ-5D utility score, mean (SD)	0.52 (0.16)	0.47 (0.20)
EQ-5D visual analogue score, mean (SD)	59.78 (17.70)	51.30 (17.71)
Timed Up and Go time (seconds), mean (SD)	11.34 (3.40)	11.04 (3.33)
Six-minute walk distance (metres), mean (SD)	304.03 (79.75)	299.09 (85.69)
Walking speed, mean (SD)	0.95 (0.21)[a]	0.93 (0.20)
Step length ratio, mean (SD)	-0.00 (0.04)[a]	-0.00 (0.04)
Operated knee range-movement (degrees), mean (SD)	42.11 (9.90)[a]	44.35 (8.56)
Operated leg single stance eyes open (secs), mean (SD)	5.60 (3.44)[b]	5.58 (3.28)[b]

[a] = 39 participants; [b] = 38 participants.

EQ-5D is a measure of health-related quality of life, in the range of -0.109 (worst possible state) and 1.0 (perfect health), anchored at 0 (death).

EQ-VAS is a health state assessment ranging between 0 and 100, in which zero is worst imaginable health state and 100 is best imaginable health state.

OKS is a 12-item knee function assessment, ranging from 0 (worst score) to 48 (best score).

Timed Up and Go Test (TUG) – seconds to rise from chair, walk 3m and return to sitting; mean of three trials. A lower value indicates better function.

Six-minute walk test - metres walked in six minutes around a 20-metre circuit A higher value indicates greater function.

The UCLA Activity score to assess physical activity self-rating scale ranged from 0 (complete inactivity) to 10

Primary outcome comparison – six months post-operatively (Table 2)

The OKS scores for the JII-BCS and Genesis II groups were mean (SD) 42.97 (5.21) and 43.13 (5.20) respectively. There was no significant difference between the groups: adjusted effect size 0.35 (-2.01,2.71) p=0.771 (Table 2).

Table 2. Oxford Knee Scores (OKS, primary outcome), OKS-APQ, EQ5D-5L and UCLA from baseline to six months after surgery (primary timepoint)

	Means (SDs) (number of participants)			Between groups comparison							
				Two months				Six months			
	Baseline	Two months after surgery	Six months after surgery	Unadjusted effect size (95% CI)	p-value	Adjusted[a] effect size (95% CI)	p-value	Unadjusted effect size (95% CI)	p-value	Adjusted[a] effect size (95% CI)	p-value
OKS											
JII-BCS	20.25 (5.69) (n=40)	34.10 (7.10) (n=39)	42.97 (5.21) (n=39)	1.97 (-1.37,5.32)	0.24	2.5 (-0.71,5.71)	0.12	0.24 (-2.10,2.58)	0.84	0.35 (-2.01,2.71)	0.77
Genesis II	19.05 (5.28) (n=40)	36.00 (7.61) (n=40)	43.13 (5.20) (n=40)								

[a] adjusted for strata used in randomisation and for baseline scores, [b] median (IQR)

OKS is a 12-item knee function assessment, ranging from 0 (worst score) to 48 (best score).

The OKS Activity and Participation Questionnaire (OKS-APQ) which complements the OKS by assessing everyday activity and social participation. The overall score is from 12 to 60 with 12 being the best outcome.

EQ-5D is a measure of health-related quality of life, in the range of -0.109 (worst possible state) and 1.0 (perfect health), anchored at 0 (death).

EQ-VAS is a health state assessment ranging between 0 and 100, in which zero is worst imaginable health state and 100 is best imaginable health state.

The UCLA Activity score to assess physical activity self-rating scale ranged from 0 (complete inactivity) to 10 (participation in impact sport)

Secondary outcome comparisons – six months post-operatively

Patient-reported outcome questionnaires

There were no differences between the two groups for any of the secondary patient reported outcomes (online supplement Tables S1).

Walking and balance functional ability

There was no difference between the JII-BCS and Genesis II groups in the time to complete the TUG Test or the distance covered in the six-minute walk test (Online supplement Table S2). The Star-Excursion Test was attempted by all participants but 59% of participants at baseline, 59% at follow up and 63% at outcome were unable to complete it. (Online supplement Table S3). Therefore, statistical analysis was not undertaken.

Movement performance during walking and balance

The primary movement performance measures are reported in Table 3. In summary at six months post-surgery the Genesis II group had a significant advantage for knee ROM and peak knee flexion angular velocity during walking. There were no differences between the groups for walking speed or peak flexion angular knee velocity on stair climbing.

Table 3. Movement performance primary measures during walking from baseline to six months post-surgery (primary timepoint): walk speed, step length symmetry, knee range of motion (ROM) and peak knee flexion angular velocity.

	Means (SDs) (number of participants)			Between groups comparison							
				Two months				Six months			
	Baseline	Two months after surgery	Six months after surgery	Unadjusted effect size (95% CI)	Unadjusted p-value	Adjusted[a] effect size (95% CI)	Adjusted[a] p-value	Unadjusted effect size (95% CI)	Unadjusted p-value	Adjusted[a] effect size (95% CI)	Adjusted[a] p-value
Walking speed (ms/sec)											
JII-BCS	0.95 (0.21)	0.90 (0.23)	1.09 (0.22)	0.08	0.11	0.09	**0.03**	0.05	0.34	0.03	0.40

	(n=39)	(n=37)	(n=35)	(-0.02,0.17)		(0.01,0.17)		(-0.05,0.15)		(-0.04,0.09)	
Genesis II	0.93 (0.20) (n=40)	0.97 (0.17) (n=37)	1.13 (0.18) (n=34)								
Step length symmetry (ratio)											
JII-BCS	-0.00 (0.04) (n=40)	0.03 (0.04) (n=37)	0.02 (0.04) (n=35)	-0.02 (-0.04,0.00)	**0.02**	-0.02 (-0.04,0.00)	**0.02**	-0.01 (-0.03,0.00)	0.10	-0.01 (-0.03,0.00)	**0.05**
Genesis II	-0.00 (0.04) (n=40)	0.01 (0.04) (n=37)	0.00 (0.04) (n=34)								
Knee ROM (degrees)											
JII-BCS	42.11 (9.90 (n=39)	37.87 (7.73) (n=38)	46.07 (7.71) (n=35)	4.51 0.39,8.64)	**0.03**	3.42 (-0.41,7.24)	0.08	4.77 (1.11,8.43)	**0.01**	3.14 (0.61,5.68)	**0.02**
Genesis II	40.31 (5.93) (n=40)	42.25 (9.75 (n=38)	50.62 (7.33) (n=34)								
Peak knee flexion angular velocity – walking (degrees/second											
JII-BCS	283.10 (53.83) (n=39)	269.65 (36.75) (n=38)	307.69 (38.96) (n=35)	23.15 (-0.84,47.14)	0.06	16.47 (-6.21,39.14)	0.15	31.00 (10.34,51.66)	**0.01**	21.75 (4.54,38.96)	**0.01**
Genesis II	300.36 (55.56) (n=40)	321.65 (43.31) (n=38)	330.38 (41.40) (n=35)								
Peak knee flexion angular velocity – stairs (degrees/second)											
JII-BCS	283.10 (53.83) (n=39)	198.09 (62.56) (n=34)	271.84 (95.48) (n=32)	54.31 (16.67,91.96)	**0.01**	51.63 (15.36,87.89)	**0.01**	50.01 (5.97,94.04)	**0.03**	35.15 (-3.09,73.39)	0.07
Genesis II	300.36 (55.56) (n=40)	251.04 (87.88) (n=34)	318.82 (71.32) (n=30)								

[a] adjusted for strata used in randomisation and for baseline scores

Step length symmetry – step length ratio calculated as ((2xOp)/Op+NOP))-1); where Op is the step length of the operated leg and NOP is the step length of the non-operated leg. Zero indicates perfect symmetry and best performance.

Data for all secondary movement performance measures are provided in the online supplement (Tables S4 – S8). The only difference between groups that reached statistical significance was for COP path length in double stance with eyes closed (On line supplement table S7). The mean (SD) values for the Genesis II and JII-BCS groups were 158.14 (65.40) mm and 235.48 (176.94) mm, respectively. Adjusted effect size was -59.91 (-105.98,-13.85) p=0.01 in favour of the Genesis II group.

Post-operative clinical context

There were no between-group significant differences for: length of stay, change in pain medication from randomisation or physiotherapy received (online supplement Tables S9 and S10).

Adverse events

One patient with a JII-BCS developed acute swelling and pain in the knee and was systemically unwell at 4 months post operatively. The joint aspiration demonstrated turbid fluid and an exchange of the polyethylene spacer and retention of the femoral and tibial components (Debridement And Implant Retention, (DAIR)) was performed with post operative antibiotic treatment. Subsequent microbiology was negative so infection was never conclusively demonstrated. The numbers and type of complications are reported in Table S11.

DISCUSSION

The findings do not support the hypothesis that the JII-BCS produces a better outcome than the Genesis II for the primary outcome of the OKS at six months after surgery. No differences between groups were also found for: other patient reported outcomes; measures

of balance and walking function; hip and ankle range-of-motion; knee moments during walking; double support time during walking and percentage of gait cycle for peak muscle activation. However, significant advantages for the control group (Genesis II) were found for: operated knee range-of-movement and peak knee flexion angular velocity during walking, and postural control (COP path length).

Whilst some investigators have demonstrated differences between generations of knee designs [12] not all modern generation TKR designs have demonstrated an improvement in outcomes when compared to their predecessors. [15–20,48]. One possible reason for this is that the predecessor is already producing good results and therefore is difficult to improve upon. Regarding the JII-BCS, at the time of writing, only Bialy et al [45] have directly compared the Genesis II and the JII-BCS. Their study was non randomised and consisted of 18 patients between the two groups. They reported a greater supine range of movement of the JII-BCS compared to the Genesis II when measured with a long arm goniometer. They also reported an improvement in functional knee scores and stability when balancing. Their conclusions were that the JII-BCS restores more normal anatomy and kinematics which is correlates into the improvements that they found. None of the other papers reporting outcomes of the JII-BCS compared the JII-BCS to the Genesis II, all none used a randomised design and none used methodology or outcomes that could be compared to the methodology used in this trial [42-46]. However, on the basis of the available literature this we measured outcomes that would be expected to be difference on the basis of the available literature, walking velocity, step-length symmetry (resulting from longer stride length), knee range of motion (ROM) and peak knee angular velocity.

Within our trial we found differences in some biomechanical measures of motor impairment but not for others; patient-reported outcomes; and, walking and balance function. It is possible that knee range-of-movement during walking, walking symmetry, peak knee flexion angular velocity during walking, and postural control (COP path length) are detecting motor impairment improvement for the Genesis II group and/or because statistical significance was a result of testing multiple outcomes. The latter explanation is clearly possible but knee range-of-movement is greater for people reporting good outcome after knee replacement than

for those reporting poor outcome [49]. Moreover, knee range-of-movement has been found to be the main biomechanical effect of TKR [50] and to improve over time whilst other biomechanical measures do not [50,51]. Likewise, postural control improves over time [52,53] and approaches healthy control values [52]. Importantly, gait symmetry is an indicator of walking control [54] and, whilst of borderline statistical significance ($p=0.05$) can possibly detect differences following insertion of different prostheses. Peak knee angular velocity during walking is also an indicator of walking control [55] and has been found to change beneficially after insertion of the Genesis II prosthesis [50]. These findings indicate that secondary, in-depth, analysis of the biomechanical data should be undertaken.

A potential limitation is the relatively large number of secondary outcomes. However, this is also a strength as it ensured comprehensive examination of the potential impact of TKR on functional ability, motor impairment and health-related quality of life. Another potential limitation is that the surgeons all had a much greater familiarity with the Genesis II implants. However, all surgeons were very experienced with the Genesis implant with at least 10 years of experience implanting the device. All surgeons received thorough training with the JII-BCS and the surgical technique and instrumentation are similar for both devices with only one additional femoral cut being necessary for the JII-BCS compared to the Genesis II. A key strength of this trial is that the required sample size was achieved with only one person lost to follow-up. Other strengths include minimisation of selection bias through a robust randomisation procedure and use of double blinding to minimise interpretation bias.

The lack of difference between implant designs is important for patients, surgeons, healthcare providers and implant companies. For the patient and surgeons, reassurance can be gained that older designs, with proven track record of function and survivorship, can provide the same patient reported and functional outcome as more modern designs. For the healthcare providers, older implants are often less expensive and, in the absence of clinical benefit with and demonstrable longevity, if the additional expenditure on more modern designs is avoided for the hundreds of thousands of patients undergoing surgery worldwide the cost savings are potentially significant. Finally, for the implant companies, it is more likely than not than implant design has reached a point when non-implant

related factors play a more important role in patient outcome. The future of design and innovation may come in the form of more modern surgical techniques such as robotic assisted implantation to assist in placing the knee in a more kinematically sympathetic position which in turn may allow the newer design philosophies to positively influence outcome. It is possible, only then in combination with modern surgical techniques, that improvements in patient outcomes can be realised but well-constructed surgical trials will need to answer such questions.

Conclusion

This study demonstrated no difference between the Genesis II and its successor the JII-BCS for patient reported outcome measures, walking function, temporal-spatial gait parameters, balance ability and lower limb kinematic results at 6 months follow up. However, significant advantages were seen in for the Genesis II in the operated knee range-of-movement, peak knee flexion angular velocity during walking, and postural control.

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Authors' contributions

IM and VP drafted this paper. All authors contributed to revisions of the manuscript, read and approved the final manuscript. All authors contributed to the development of the trial protocol.

- **Declaration of interest** *"All authors have completed the ICMJE uniform disclosure form at www.icmje.org/ coi_disclosure.pdf and declare: all authors had financial support from Smith and Nephew for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work."*

  All authors must download and complete a copy of the ICMJE COI disclosure form and send a copy to the corresponding author.

DATA SHARING STATEMENT

Requests for access to individual participant data will be considered by the Chief Investigators. Requests can be made to dm.norwichctu@uea.ac.uk. The trial protocol and Statistical Analysis Plan (SAP) will also be made available as supplementary files.

Trial governance and quality assurance

The trial was managed by the Norwich Clinical Trials Unit (NCTU). Study data were collected and managed using REDCap electronic data capture tools. Quality assurance was undertaken by the NCTU according to their usual processes.

The trial was overseen by the Trial Management Group. This was chaired by the Chief Investigators and included expert advisors, members of the research team and Patient and Public Involvement (PPI) representatives. A safety committee (Prof Marcus Flather and Prof Simon Donell) periodically reviewed adverse events and relevant safety data by treatment group to monitor for potential harm.

Abbreviations

ADEs: Adverse Drug Events; AEs: Adverse Events; BCS: Bi-Cruciate Stabilised; Co-CI: Co-Chief Investigator; Consort: Consolidated Standards of Reporting Trials; CoP: Centre of Pressure; CRF: Case Report Form; CT: Computerised Tomography; DMC: Data Monitoring Committee; EMG: Electromyography; FJS: The Forgotten Joint Score; GCP: Good Clinical Practice; GDPR:

General Data Protection Regulation; GISP3: General Information Security Policy 3; HADS: Hospital Anxiety and Depressions Score; HRA: Health Research Authority; ICH: International Council for Harmonisation; ISRCTN: International Standard Randomised Controlled Trials Number; MCL: Medial Collateral Ligament; MoveExLab: Movement Analysis Laboratory; mSEBT: Modified Star Excursion Balance Test; NCTU: Norwich Clinical Trials Unit; NERP: Norwich Enhanced Recovery Programme; NICE: National Institute for Health and Care Excellence; NNUH: Norfolk and Norwich University Hospital NHS Foundation Trust; OKS: Oxford Knee Score; OKS-APQ: Oxford Knee Score Activity & Participation Questionnaire; PI: Principle investigator; PIN: Participant Identification Number; PIS: Patient information sheet; PROMs: Patient-reported outcome measures; QA: Quality Assurance; QC: Quality Control; QMMP: Quality Management and Monitoring Plan; REDCap Research Electronic Data Capture ROMs: Ranges of Movement; SAEs: Serious Adverse Events; SAP: Statistical Analysis Plan; TKR: Total knee replacement; TMG: Trial Management Group; TTB: time to boundary; UKCRC: UK Clinical Research Collaboration

Ethical approval: The CAPAbility trial was conducted in accordance with the ethical principles outlined in the latest version of the Declaration of Helsinki and the Guideline for Good Clinical Practice related to experiments on humans. Ethical approval was given by the East of England – Cambridge Central Research Ethics Committee (reference 16/EE/0230). All participants provided informed consent prior to enrolment.

The lead authors (the manuscript's guarantors) affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Figure legends

Figure 1. Consort diagram

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