

1 Title: CAPAbility: Comparison of the JOURNEY II Bi-Cruciate Stabilised
2 and GENESIS II total knee arthroplasty in performance and functional
3 ability: protocol of a randomised controlled trial.

4 Authors' Information

5 Dr Celia Clarke¹, Celia.Clarke@uea.ac.uk

6 Prof Valerie Pomeroy¹, V.Pomeroy@uea.ac.uk

7 Dr Allan Clark², Allan.Clark@uea.ac.uk

8 Mr Graham Creelman³, grahamcreelman97@gmail.com

9 Dr Nicola Hancock¹, N.Hancock@uea.ac.uk

10 Dr Simon Horton¹, S.Horton@uea.ac.uk

11 Dr Anne Killett¹, A.Killett@uea.ac.uk

12 Mr Charles Mann⁷, charles.mann@nnuh.nhs.uk

13 Dr Estelle Payerne⁴, E.Payerne@uea.ac.uk

14 Prof Andoni Toms^{2,5}, Andoni.Toms@uea.ac.uk

15 Mr Gareth Roberts³, Gareth.Roberts@lovell.co.uk

16 Dr Toby Smith^{1,6}, toby.smith@ndorms.ox.ac.uk

17 Prof Ann Marie Swart², A.Swart@uea.ac.uk

18 Prof Iain McNamara^{2,7}, iain.mcnamara@nnuh.nhs.uk

19 Affiliations

20 ¹ School of Health Sciences, University of East Anglia, Norwich, UK.

21 ² Norwich Medical School, University of East Anglia, Norwich, UK.

22 ³ Patient and Public Involvement.

23 ⁴ Norwich Clinical Trials Unit, UEA, Norwich, UK.

24 ⁵ Norwich Radiology Academy, Norfolk and Norwich University Hospital, Norwich UK.

25 ⁶ Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences,
26 University of Oxford, Oxford, UK

27 ⁷ Department of Trauma and Orthopaedics, Norfolk and Norwich University Hospital,
28 Norwich UK.

29 Trial registration

30 International Standard Randomised Controlled Trials Number Registration:

31 ISRCTN32315753, 12 December 2017. <http://www.isrctn.com/ISRCTN32315753>

32 Trial Status

33 Recruitment opened on 14th May 2018. First participant was recruited on 25th May 2018.

34 The current protocol is version 2.4 dated 27.02.2019 Recruitment is expected to be
35 completed by the 11th October 2019.

36

37

38 Abbreviations

39 ADEs: Adverse Drug Events; AEs: Adverse Events; BCS: Bi-Cruciate Stabilised; Co-CI: Co-
40 Chief Investigator; Consort: Consolidated Standards of Reporting Trials; CoP: Centre of
41 Pressure; CRF: Case Report Form; CT: Computerised Tomography; DMC: Data Monitoring
42 Committee; EMG: Electromyography; FJS: The Forgotten Joint Score; GCP: Good Clinical
43 Practice; GDPR: General Data Protection Regulation; GISP3: General Information Security
44 Policy 3; HADS: Hospital Anxiety and Depressions Score; HRA: Health Research Authority;
45 ICH: International Council for Harmonisation; ISRCTN: International Standard Randomised
46 Controlled Trials Number; MoveExLab: Movement Analysis Laboratory; mSEBT: Modified
47 Star Excursion Balance Test; NCTU: Norwich Clinical Trials Unit; NERP: Norwich Enhanced
48 Recovery Programme; NICE: National Institute for Health and Care Excellence; NNUH:
49 Norfolk and Norwich University Hospital NHS Foundation Trust; OKS: Oxford Knee Score;
50 OKS-APQ: Oxford Knee Score Activity & Participation Questionnaire; PI: Principle
51 Investigator; PIN: Participant Identification Number; PIS: Patient Information Sheet; PROMs:
52 Patient-Reported Outcome Measures; QA: Quality Assurance; QC: Quality Control; QMMP:
53 Quality Management and Monitoring Plan; ROMs: Range of Movement; SAEs: Serious
54 Adverse Events; SAP: Statistical Analysis Plan; TKR: Total Knee Replacement; TMG: Trial
55 Management Group; TTB: time to boundary; UKCRC: UK Clinical Research Collaboration

56 ABSTRACT

57 **Background:** Osteoarthritis of the knee is a common condition that is expected to rise in the
58 next two decades leading to an associated increase in total knee replacement (TKR)
59 surgery. Although there is little debate regarding the safety and efficacy of modern TKR, up
60 to 20% of patients report poor functional outcomes following surgery. This study will

61 investigate the functional outcome of two TKR; the JOURNEY II Bi Cruciate Stabilised knee,
62 a newer prosthesis designed to provide guided motion and improve knee kinematics by
63 more closely approximating a normal knee and the GENESIS II, a proven existing design.

64 **Aim:** To compare the change in patient reported outcome scores of the JOURNEY II BCS
65 and the GENESIS II from pre-operation to six months post-operation.

66 **Methods:** CAPAbility is a pragmatic, blinded, two-arm parallel, randomised controlled trial
67 recruiting patients with primary osteoarthritis due to have unilateral TKR surgery across two
68 UK hospitals. Eligible participants (n=80) will be randomly allocated to receive either the
69 JOURNEY II or the GENESIS II BCS knee prosthesis. Baseline measures will be taken prior
70 to surgery. Patients will be followed at one week, six to eight weeks and six months post-
71 operatively. Primary outcome is the Oxford Knee Score (OKS) at six months post-
72 operatively. Secondary outcomes include: other patient-reported outcome measures
73 (PROMs), biomechanical, radiological (computerised tomography, (CT)), clinical efficacy and
74 safety outcomes. An embedded qualitative study will also investigate patients' perspectives
75 via interview pre- and post-surgery on variables known to affect the outcome of TKR
76 surgery. A sub-sample (n=30) will have additional in-depth interviews to explore themes
77 identified. The surgeons' perspectives on the operation will be investigated by a group
78 interview after all participants have undergone surgery.

79 **Discussion:** This trial will evaluate two generations of TKR using PROMS, kinematic and
80 radiological analyses and qualitative outcomes from the patient perspective.

81 **Trial registration** ISRCTN32315753 (12 December 2017).

82 **Keywords:** Total knee arthroplasty; knee replacement; functional ability; knee prosthesis;
83 kinematics; primary osteoarthritis.

84 Introduction

85 Background and rationale

86 Osteoarthritis of the knee is a common musculoskeletal condition. The surgical management
87 of painful end-stage osteoarthritis is by total knee replacement (TKR) which should be
88 considered before there is prolonged and established functional limitation and severe
89 pain.[2] Over 100,000 TKRs were performed in the UK in 2019.[3] While TKR frequently
90 reduces pain and improves physical function in the majority of patients, 20% of patients
91 report poor functional outcomes post-operatively.[4,5] Such poor outcomes are of
92 importance to patients and have a considerable financial and service-provision impact on
93 NHS care. Research is needed to improve post-arthroplasty outcomes for those patients.

94 There is a paucity of literature regarding the kinematic outcomes of patients following TKR.
95 However, there is uncertainty as to whether good patient reported outcome measures
96 (PROMs) are associated with a return to normal kinematics of the TKR knee compared to
97 the native knee. Movement analysis can be used to examine the change in kinematics
98 before and after TKR by examining functional movements in activities of daily living.

99 The long-term success of TKR depends largely on correct component alignment and
100 accurate ligamentous balancing.[6] The impact of femoral and tibial component rotation on
101 flexion gap balance, patellofemoral tracking and normal kinematic function is well-known.[7-
102 9] Complications secondary to poor component alignment have been reported to lead to a
103 higher rate of revision surgery.[10,11] Computerised Tomography (CT) imaging is a valid
104 and reproducible technique for accurately measuring TKR component rotation.[12,13]
105 However, despite CT being widely used to examine implant rotation, the correlation between
106 rotational alignment, PROMs and kinematic function comparing pre- and post-operative
107 measurement is unclear.[14,15] It is hypothesised that patients with poor rotational profile

108 post-operatively compared to their pre-operative values will have significantly worse
109 PROMs, movement parameters and patient satisfaction.

110 We report the protocol of a two-group, parallel RCT comparing patient-reported, surgical and
111 biomechanical outcomes from a TKR of newer design (the JOURNEY II BCS) designed to
112 provide improved kinematic outcomes compared to an older design TKR implant (the
113 GENESIS II).

114 This protocol (version 2.4, dated 27 February 2019) has been written and reported according
115 to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)
116 guidance and Checklist[16] (see Additional file [1](#): SPIRIT 2013 Checklist).

117 Aims

118 The principal aim of the trial is to compare the change in PROMs scores of the JOURNEY II
119 BCS and the GENESIS II knee from pre-operation to six months post-operation. Additional
120 aims are as follows:

121 1. To determine if the temporal and spatial parameters of gait, the range of movement and
122 static and dynamic balance are closer to aged-matched normative data in those receiving
123 the JOURNEY II BCS compared to those receiving the GENESIS II knee.

124 2. To monitor the change in function (Aim 1 above) and PROMs of the JOURNEY II BCS
125 and the GENESIS II knee from post-operation to six months post-operation.

126 3. From CT scan measures, determine anatomical landmarks and rotational profile around
127 the native knee and following TKR to ascertain the component rotational position post-
128 operatively compared to anatomical landmarks.

129 4. Examine the relationship between rotational values determined by CT scanning with pre-
130 and post-operative PROMs and movement analysis.

131 5. To develop knowledge and understanding of patient and surgeon experiences,
132 perspectives and satisfaction when receiving or implanting the JOURNEY II BCS compared
133 with the GENESIS II knee, and their experiences of recovery and rehabilitation.

134 Methods: Participants, interventions, and outcomes

135 Trial design

136 This is a pragmatic, triple-blinded, parallel, superiority, randomised controlled trial of the
137 JOURNEY II BCS (Intervention) versus GENESIS II (Control) in patients with primary
138 osteoarthritis undergoing TKR. Embedded in the clinical trial is a qualitative investigation of
139 participants' confidence in the TKR received and their experiences of the recovery process
140 in the first six months after surgery. The aim of this is to identify any differences in the
141 experience of recovery between each type of TKR. Surgeons will also be interviewed to
142 investigate their perceptions of the surgery and patient's rehabilitation.

143 The trial outline is illustrated in **Figure 1**

144 **Figure 1:** CAPAbility trial outline.

145

146 Study setting

147 Trial sites were pre-selected on the basis of their locality to facilitate data collection (namely
148 the kinematic assessment). Sites include the Norfolk and Norwich University Hospital
149 (NNUH), where all patients recruited to the trial will be referred for consideration of TKR. The
150 NNUH refers a proportion of its TKR patients to Spire Norwich where the operation and
151 follow-up physiotherapy is delivered. Both hospital are participating in this trial. All CT scans

152 will be performed at NNUH. The biomechanical assessment will be undertaken in a
153 specialist movement analysis laboratory (MoveExLab) at the University of East Anglia
154 (UEA).

155 Eligibility criteria

156 To be eligible for the trial, patients must satisfy the surgeon's general requirements for a
157 TKR, meet all inclusion criteria and none of the exclusion criteria listed in **Table 1**.

158 Patients will be excluded if they are currently enrolled on an interventional trial involving
159 surgery, exercise or rehabilitation. Patients can be co-enrolled into studies given prior
160 agreement from the Trial Management Group (TMG) of both studies. Patients who enter the
161 study are eligible for entry onto the UK National Joint Registry.

162 **Table 1:** Eligibility criteria

Inclusion Criteria

- Listed for a primary TKR at the NNUH (may be referred to Spire Norwich for the operation)
- Indication for the TKR is primary osteoarthritis of the knee joint involving one or more compartments
- Aged 18 or over
- Patient willing to provide full informed consent to the trial including consent for any incidental findings to be communicated to their GP

Exclusion Criteria

- Listed for a single-stage bilateral TKR procedure
- Severe symptoms in the contralateral knee so as to require staged bilateral knee replacements within six months of the primary procedure
- Fixed flexion deformity of 15 degrees or greater or patients who may require excessive resection of the distal femur
- Clinically assessed uncorrectable varus/valgus deformity of 15 degrees or greater
- Any co-morbidity which, in the opinion of the investigator, is severe enough to present an unacceptable risk to the patient's safety
- Inflammatory arthritis
- Previous septic arthritis in the affected knee joint
- Previous surgery to the collateral ligaments of the affected knee
- A contralateral TKR that has been implanted less than one year from the date of consultation, or severely painful
- Patients on warfarin or Novel Oral Anti-Coagulants
- Will not be resident in the catchment area for NNUH for at least six months post-surgery
- Undertaking the surgery as a private (non-NHS) patient
- Patients who, in the opinion of the clinical staff, do not have capacity to consent
- Patients who are pregnant
- Unable to understand written and spoken English
- Patients currently enrolled on an interventional trial involving surgery, exercise or rehabilitation. Patients can be co-enrolled into studies not meeting the above criteria given prior agreement from the TMG of both studies. Patients who enter the study are eligible for entry onto the National Joint Registry and in terms of the Journey II BCS, into Beyond Compliance.

163
164

165 Screening

166 Potential participants will be approached via a single route. Potential participants will be
167 screened by a member of the clinical team in collaboration with research nurses after having
168 been added to the orthopaedic clinic waiting list. Potentially eligible patients who meet the

169 eligibility criteria, will either be handed a patient information sheet (PIS) if still at the clinic, or
170 be posted an invitation letter informing them that the trial is taking place and include the PIS.
171 After having been provided the trial PIS, potential participants will be telephoned by a
172 research nurse. To minimise the possibility of attrition, appointments for outcome measures
173 will be agreed with participants when they enter the trial. In addition, members of the
174 research team will maintain regular contact with participants to ensure attendance at follow
175 up visits and to monitor any adverse events.

176 Informed consent

177 Written informed consent to enter and be randomised into the trial will be taken by a member
178 of the clinical team and obtained from participants after explanation of the aims, methods,
179 benefits and potential hazards of the trial. Potential participants will be given as much time
180 as they need to consider whether or not to provide informed consent. Consent will take place
181 before any trial-related measures, at a time convenient to the potential participant, preferably
182 at a time to combine with one or more of the measures to reduce participant visits.

183 If a participant withdraws prior to surgery, an additional participant will be randomised to
184 ensure 80 participants complete the surgery.

185 Patients who, in the opinion of the clinical team, do not have capacity to consent, will be
186 ineligible. If a participant loses capacity during the course of the trial, they will be withdrawn
187 from any further assessments, but any data already collected will be retained. Consent will
188 be re-sought if new information becomes available that affects the participant's consent in
189 any way. This will be documented in a revision to the PIS and the participant will be asked to
190 sign an updated consent form. These will be approved by the ethics committee prior to their
191 use. A copy of the approved consent form is available from the Norwich Clinical Trials Unit
192 (NCTU).

193 Sample size

194 Eighty patients will be recruited onto this superiority trial. The sample size has been
195 calculated from the Oxford Knee Score (OKS).[17] The OKS ranges from a score of 12 to
196 60, with 12 being the best outcome. The minimally important clinical difference for OKS is
197 five[18,19] and a standard deviation of 7.4.[20] For an 80% power, and an assumed dropout
198 rate of 10%, 80 participants will be randomised to one of the two groups.

199 Participant timeline

200 The participant timeline is shown in **Figure 1**. Where possible trial visits will be combined
201 with standard clinic visits. Should additional visits be necessary, participants will be
202 reimbursed for travel costs.

203 Interventions

204 All participants will receive routine care provided by the NHS. Pre-operative and peri-
205 operative care is standardised irrespective of implant.

206 Explanation for choice of comparators (Genesis II versus JOURNEY II BCS)

207 The GENESIS II TKR system made by Smith and Nephew (Smith & Nephew plc, Watford,
208 UK) is frequently used in standard practice within the NHS.[3] It has been the standard TKR
209 within the NNUH and Spire Norwich hospitals for over 10 years. The Genesis II has a
210 survivorship of over 93% of implants at 15 years[3,21] and offers good health-related quality
211 of life outcomes.[22]

212

213 A newer device, JOURNEY II BCS, also manufactured by Smith and Nephew, has been
214 developed to theoretically provide improved kinematic outcomes compared to the GENESIS
215 II.[23] These improvements are proposed to include:

- 216 • Alteration in the dimensions of the femoral component to reduce soft-tissue strain
217 and maintain more natural translation and external rotation.
- 218 • Reduction in the thickness of the lateral and medial anterior flange of the femoral
219 component and edge tapering to reducing tension on the iliotibial band (ITB) and IT-
220 patellar bands (ITPB).
- 221 • Reduction in the width of the femoral component to limit implant overhang, and
222 reduction in the mid-flexion thickness of the medial condyle to maintain more
223 consistent strain on the medial-collateral ligament (MCL) throughout the flexion
224 range.
- 225 • A superior cam position, which serves to decrease femoral rollback in the targeted
226 ranges of motion, increase femoral external rotation, and lower the point of tibial
227 post-contact in deep-flexion.

228 Whilst there is fluoroscopic data to support normal kinematics in early and late flexion,[24]
229 there is a paucity of evidence exploring these hypotheses for this newer implant.

230 Surgical flow and training

231

232 Surgeons will be high-volume arthroplasty surgeons who work at both NNUH and Spire
233 Norwich Hospital. The standard implant at both sites is the Genesis II TKR system. All
234 surgeons have used this implant for many years and are very familiar with the surgical
235 technique. All surgeons and theatre staff have received training on the implantation of the

236 JOURNEY II BCS Implant. All surgeons have undergone training on the JOURNEY BCS II
237 implant in a cadaveric lab and also undertaken a learning curve with the device until they
238 were confident with the technique. This was supported by a Smith and Nephew
239 representative. There are minimal differences in the surgical cuts and technique between the
240 Genesis II and the JOURNEY BCS II. Participating surgeons felt there was a shallow
241 learning curve to the JOURNEY BCS II. Both devices are CE marked and will be used within
242 indication. Smith and Nephew are providing the JOURNEY II BCS at the same price as the
243 GENESIS II system for this study.

244 Surgical procedures

245 Devices will be identified and prepared for the operation by a surgical technician at the
246 surgery site.

247 Participants allocated to the intervention device will receive the JOURNEY II BCS prosthesis
248 while participants allocated to the control condition will receive the GENESIS II prosthesis.
249 The type of device implanted, and serial number will be recorded on the trial database, by an
250 unmasked member of the research team.

251 The surgical procedure will follow the standardised surgical approach and technique. It will
252 be undertaken through a medial parapatellar approach. In both implants and in every case to
253 ensure standardisation of technique, a posterior stabilised prosthesis with patella resurfacing
254 will be used.

255 It is possible that a decision will be taken prior to or during the operation not to use the
256 allocated device if, in the opinion of the surgeon, the patient is found to have become
257 unsuitable for continued participation in the trial. The reasons for an allocated device not
258 being used will be recorded on the trial database. In this case or if a participant chooses to
259 withdraw consent for treatment, or follow-up, all data collected up to the point of withdrawal

260 will be retained. The standard Norwich Enhanced Recovery Programme (NERP)[25,26] is
261 used for anaesthetic technique and post-operative recovery.

262 Post-operative rehabilitation

263 Post-operative rehabilitation will follow routine clinical care at NNUH and Spire
264 Norwich.[25,26] Whilst an inpatient, participants will be seen by a physiotherapist for routine
265 care at least twice daily to progress on a tailored gait re-education and exercise programme
266 during their hospital admission. This will be recorded in an in-patient hospital rehabilitation
267 log. Once safe for discharge, patients will be asked to continue a home exercise programme
268 and gait re-education. This will consist of daily (advised) knee flexion range of motion
269 exercises and quadriceps strengthening.

270 At Week 4 post-operatively, all participants will attend an exercise group-based intervention
271 delivered by a qualified physiotherapist and a physiotherapy assistant. These sessions will
272 be used to increase participant's knee range of motion, strength and overall confidence to
273 undertake more strenuous exercises. Participants will attend this class weekly for two to six
274 sessions depending on their need. All rehabilitation interventions will be recorded in a post-
275 discharge rehabilitation log. Participants will be encouraged to continue their exercises
276 which are prescribed within the group as part of a home-exercise programme.

277 No additional ancillary or post-trial care will be provided (in the absence of adverse event) to
278 trial participants.

279 Outcomes

280 The schedule of enrolment, interventions and assessment is shown in **Table 2**. The PROMs
281 will be administered by research nurses apart from the Week 1 follow-up telephone call
282 undertaken by the research associate performing the qualitative interview. The CT scans will

283 be performed at the NNUH by research radiographers and reported by a consultant
 284 radiologist. The biomechanical assessments and qualitative interviews will be performed at
 285 the MoveExLab at UEA. Participants who were unable to attend an assessment
 286 appointments were provided with an alternative appointment. If participants were unable to
 287 attend any alternative assessment appointments, PROMs data were collected during a
 288 telephone call to promotion participant retention and follow-up.

289 **Table 2: Schedule of enrolment, interventions, and assessments.**

	Consent Visit	Baseline	Pre-Op	Op	Discharge	1 week Post-op	6-8 weeks Follow Up	6 month Follow-Up
TIMEPOINT	Up to 4 months pre-operatively	-2 to -1 days pre-operatively	4 days (+/- 3 days) pre-operatively	Day 0	On discharge	7(+/-2) days	6-8 weeks (+2weeks)	6 months (+ 4 weeks)
Enrolment:								
Eligibility screen	X							
Informed consent	X							
Randomisation			X					
Interventions:								
Knee prosthesis implanted				X				
Assessments:								
Home Exercise Diary								
Oxford Knee Score (OKS)		X				X	X	X
OKS-APQ		X				X	X	X
Current Pain Medication		X			X	X	X	X
Knee Flexion/Extension ROM		X			X		X	X
Timed Get Up and Go		X					X	X
Timed 6 Minute Walk		X					X	X
3D Motion Capture with EMG		X					X	X
Static & Dynamic Balance		X					X	X
MVIC		X					X	X
EQ-5D-5L		X				X	X	X
UCLA Activity Score		X					X	X
Forgotten Joint Score							X	X
Charlson Comorbidity index		X					X	X
Complications (Efficacy and Safety)				X	X	X	X	X
Pain Self-efficacy Questionnaire		X						

HADS		X						
CT Study:								
CT Scan	←————→ Single scan within the consent to operation window					←————→ Single scan within the post op window		
Qualitative Study (Participant):								
Semi Structured Interview		X				X	X*	X*
Physiotherapy rehabilitation:								
Post-surgery rehabilitation log					←————→ Group sessions			

290 * subset of 30 patient; CT – computerised tomography; HADS – Hospital Anxiety and
291 Depression Score; MVIC - maximum voluntary isometric contraction; OKS – Oxford Knee
292 Score; OKS-APQ – Oxford Knee Score Activity and Participation Questionnaire; Pre-Op –
293 pre-operative; Post-Op – post-operative; ROM – range of motion; UCLA – University of
294 California Los Angeles
295

296 Primary Outcome

297 The OKS[17] will be used to assess patient-reported functional status at six months post-
298 surgery.

299 Secondary Outcomes: Patient Reported Outcome Measures

300 The Oxford Knee Score (OKS)[17] – Activity and Participation Questionnaire (OKS-
301 APQ),[27] EQ-5D-5L,[28] UCLA Activity score,[29] Hospital Anxiety and Depression Score
302 (HADS),[30] Forgotten Joint Score (FJS),[31] and 2-Item Pain Self-Efficacy
303 Questionnaire.[32]

304 Secondary Outcomes: Clinical Efficacy Outcomes

305 Clinical efficacy will be evaluated by:

- 306 • Surgical-related parameters: need for revision surgery; length of hospital stay and
307 change in pain medication will be collected during in-patient stay and at all the follow-
308 up time points.

309 • Performance-related parameters: knee flexion and extension ranges of movement,
310 measured at six to eight weeks and six months post-operatively by the research
311 associate in the MoveExLab (and by the research physiotherapist at baseline as part
312 of routine care); timed-up-and-go (TUG)[33] and timed six-minute walk test[34]
313 recorded at the six to eight weeks and six month time-points by the research associate
314 in the MoveExLab.

315 Secondary Outcomes: Clinical Safety Outcomes

316 Complications related to the surgery (e.g. anaesthesia-related problems, bleeding,
317 morbidities) will be collected from a notes review, prior to discharge, post-discharge,
318 rehabilitation and follow-up. Additionally, at each visit, participants will be asked if they have
319 received additional treatment since their surgery/previous visit and what that consisted of.

320 Secondary Outcomes: Biomechanical Outcomes

321 All biomechanical measures will be collected in the MoveExLab by the research associate.
322 3D motion capture using eight cameras (Vicon Motion System, Oxford UK), three built in
323 force plates (Bertec Corporation, Columbus, Ohio, USA) and surface electromyography
324 (EMG) (Delsys, Natick, Massachusetts, USA). Participants will be unshod and asked to
325 walk at their self-selected speed. A minimum of three heel strikes from each foot will be
326 used to construct an average.

327 1. Overground walking: Unshod and walking at self-selected speed:

328 a. Spatiotemporal parameters; speed, cadence, step length, stride length and symmetry

329 b. Kinematics of bilateral hip, knee and ankle joints

330 c. Kinetics: moments of bilateral hip, knee and ankle joints and ground reaction forces during
331 the stance phase

332 d. EMG parameters: recruitment patterns of quadriceps: rectus femoris, vastus medialis and
333 vastus lateralis, hamstrings: semitendinosus, biceps femoris, tibialis anterior, medial and
334 lateral gastrocnemius.

335 2. Stair ascent and descent:

336 a. Spatiotemporal parameters; speed, cadence, symmetry

337 b. Kinematics of bilateral hip, knee and ankle joints

338 c. Kinetics: moments of bilateral hip, knee and ankle joints and ground reaction forces from
339 the bottom step

340 Static balance measures will be completed on a single in-built force plate (Bertec
341 Corporation, Columbus, Ohio, USA). Participants will be instructed to stand with their feet
342 shoulder width apart for double stance with their eyes closed and then open for 10 seconds.
343 Three attempts will be recorded. Participants will then be instructed to stand on one leg in
344 centre of the force plate with their hands on their hips with their eyes open and closed for 10
345 seconds. Each limb will be tested. Three trials of 10 seconds will be recorded. The time will
346 be stopped if the participant places the other foot on the floor. Each participant will be given
347 six attempts at each position.

348 3. Static balance; measures of Centre of Pressure (CoP) from single and double leg
349 standing

350 a. Anterior-Posterior (AP), Medial-Lateral (ML) and COP path length

351 b. AP, ML and COP velocity

352 c. AP, ML and COP range and SD

353 4. Time-To-Boundary (TTB)[35]

354 a. TTB minimum, mean and SD

355 5. Modified Star Excursion Balance Test (mSEBT)[36]

356 a. Anterior, Posteromedial and Posterolateral distance (mm) on both limbs

357 Secondary Outcomes: Radiological Outcomes

358 Radiographs

359 Pre-operative and post-operative conventional semi-flexed AP and lateral radiographs of the
360 knee will be acquired.

361 Computerised Tomography

362 A rotational profile CT protocol will be acquired at the NNUH radiology department under
363 standard operating procedure.

364 This will consist of three separate axial acquisitions through the femoral necks, knees and
365 ankles reconstructed on bone and soft tissue algorithms. The images through the knee will
366 be split into two acquisitions according to the Berger protocol.[37] The pre-operative CT will
367 be performed in the time after consent for the study and before TKR. The post-operative CT
368 is not time sensitive and will be performed any time following surgery.

369 Two independent observers, radiologists under direct supervision of a senior
370 musculoskeletal radiologist, will obtain the following measurements from the CT. In the case
371 of disagreement between the two independent observers, through discussion, the senior
372 musculoskeletal radiologist will act as adjudicator to ensure agreement is met.

373 Measurements will include:

374 Pre-operative

375 1. Femoral ante-torsion (degrees)

376 2. Tibial tubercle-trochlear groove distance (TT-TG) (mm)

377 3. Tibial torsion (degrees)

378 Post-operative

379 1. Femoral ante-torsion (degrees)

380 2. Femoral component version (degrees)

381 3. Tibial component version (degrees)

382 4. Tibial torsion (degrees)

383

384 In the event of an incidental finding being reported, the Clinical Chief Investigator will
385 organise the necessary clinical follow-up which may include referral to an appropriate
386 clinician and the organisation of further investigations.

387 Secondary Outcomes: Qualitative Study

388 Interviews will be completed either via a telephone call or face-to-face by the research
389 associate. This flexibility was adopted to promote participant retention and complete follow-
390 up. These will be audio-recorded and transcribed for analysis.

391 All TKR participants will be invited to take part in an interview and complete a self-efficacy
392 questionnaire and the HADS at baseline and a telephone call interview at the seven days
393 (+/- two days) surgery.

394 Two additional post-surgery interviews will be carried out with a purposive sample of
395 participants (N=30), drawn equally from intervention and control groups. Sampling decisions
396 will be based on the following factors: age; sex; ethnicity; socioeconomic status; OKS; self-
397 efficacy; expectations, mood and symptom management (as ascertained from inspection of
398 baseline interviews).

399 The aims of the interviews are to gain in-depth understanding of patient perspectives on
400 important variables known to affect outcomes of TKR surgery.[5,38-40] Specific themes will
401 be:

- 402 1. To explore patients' expectations of and hopes for surgery (pre-operative only).
- 403 2. To explore patients' experiences and perspectives on: mood, pain and function –
404 everyday mobility, participation in work, social roles and activities; surgery and post-
405 operative clinical management; rehabilitation and recovery, and social support.

406 All surgeons will be invited to consent to a face-to-face interview after the last participant's
407 surgery to explore their perspective on using each prostheses and their overall experience of
408 surgery.

409 **Methods: Assignment of interventions**

410 **Allocation**

411 An interactive web randomisation system will be used by a member of the research team
412 who is not blinded to the intervention. Participants will be randomly assigned to either control
413 or experimental group with a 1:1 allocation as per a computer-generated randomisation
414 schedule. Randomisation will occur after the completion of all baseline tests. This will take
415 place four days (+/- three days) prior to the operation to allow the correct TKR to be made

416 available. Randomisation will be stratified by: (a) site (i.e. hospital where surgery is to take
417 place); and (b) age (<60 years = younger; equal or 60+ years = older).[41,42]

418 Blinding (masking)

419 It is not possible to blind the surgeon to the trial intervention. However, the participants, the
420 physiotherapists, and all staff involved in assessing outcomes will be blinded. Processes will
421 be in-place to maintain blinding. These will include concealment in a sealed envelope of the
422 surgery notes mentioning the prosthesis implanted in the patient file.

423 In the unlikely event of a research nurse accidentally becoming unmasked, the contacts,
424 assessments, and data entry for that participant will be undertaken by another member of
425 the research team for the remaining period of trial participation for that participant.

426 Accidental unmasking will be logged and monitored to ensure appropriate steps are taken to
427 prevent a re-occurrence.

428 The clinical staff providing usual care will also be blinded. The decision to unmask a case
429 will be made when knowledge of an individual's allocated treatment is required to enable
430 treatment of a serious adverse event (SAE) which is likely to be caused by the type of device
431 implanted.

432 Where possible, requests for emergency unmasking of individuals will be made via the Trial
433 Manager in agreement with the Clinical Chief Investigator. However, in circumstances where
434 there is insufficient time to make this request or for agreement to be sought, the treating
435 clinician can make the decision to unmask immediately. This can be done via the trial
436 database.

437 Methods: Data management and analysis

438 Data management

439 Each participant will be given a unique trial Participant Identification Number (PIN). Data will
440 be entered under the participant's PIN number onto the central database stored on the
441 servers based at NCTU. Access to the database will be via unique, individually assigned (i.e.
442 not generic) usernames and passwords, and only accessible to members of the CAPAbility
443 trial team at NCTU, and external regulators if requested. The servers are protected by
444 firewalls and are patched and maintained according to best practice. The physical location of
445 the servers is protected physically and environmentally in accordance with UEA's General
446 Information Security Policy 3 (GISP3: Physical and environmental security).

447 The database and associated code have been developed by NCTU Data Management, in
448 conjunction with the CAPAbility trial team. The database software provides a number of
449 features to help maintain data quality, including; maintaining an audit trail, allowing custom
450 validations on all data, allowing users to raise data query requests and search facilities to
451 identify validation failure/missing data. After completion of the trial, the database will be
452 retained on the servers of NCTU for on-going analysis of secondary outcomes.

453 The identification, screening and enrolment logs, linking participant identifiable data to the
454 pseudoanonymised PIN, will be held locally by the trial site. This will either be held in written
455 form in a locked filing cabinet or electronically in password protected form on hospital
456 computers. After completion of the trial, the identification, screening and enrolment logs will
457 be stored securely by the sites for 15 years unless otherwise advised by NCTU. The consent
458 form will explain that if a participant wishes to withdraw from the study the data acquired
459 prior to that point will be retained. Reason for withdrawal will be recorded, if given, as will
460 loss to follow-up.

461 Statistical analysis

462 A full Statistical Analysis Plan (SAP) will be developed between the Trial Statistician and
463 Chief Investigators and agreed with the trial's governance committees. All analysis will be
464 based on the intention-to-treat principle in which all participants will be analysed according to
465 the group they were allocated, regardless of compliance.

466 Baseline factors will be summarised by group. All continuous variables will be summarised
467 by the mean and standard deviation, or if appropriate, the median and interquartile range.
468 Categorical variables will be summarised with the number and percentage, in each category.

469 The primary comparison for OKS will be made using a general linear model with the
470 stratification factors included as fixed-effects. The difference between arms will be
471 summarised using the mean difference, with 95% confidence intervals presented. A similar
472 analysis will be undertaken for all other outcome measures.

473 For the temporal gait parameters and kinematic outcomes, each participant's 'closeness' to
474 age-matched normative data will be calculated. This will then be compared between-groups
475 using a general linear model with the stratification factors included as fixed-effects. This data
476 will also be presented graphically via scatter and distributional graphs to describe the
477 deviations from the normative data.

478 For all the measures of movement listed, a general linear model with the stratification factors
479 included as fixed-effects will be used to assess for between-group differences. If
480 appropriate, adjusted analyses will be undertaken by including baseline factors and fixed-
481 effects in the above models.

482 Assumptions and sensitivity analysis

483 All the assumptions will be checked via distribution graphs and tests. If the assumptions are
484 not valid, transformation will be considered. If none are found, a non-parametric approach
485 will be used. The pattern of missing or incomplete data will be assessed. If appropriate,
486 missing data will be imputed. The baseline comparability of the groups will be assessed. If
487 appropriate, any factor found to be imbalanced and important, will be adjusted for in the
488 analysis.

489 Exploratory subgroup analysis will be undertaken by including an interaction in the model to
490 assess if the effectiveness of the prosthesis is dependent on age or gender.

491 All analyses will be conducted using Stata and the full SAP will be produced, and approved,
492 before any comparative analysis is undertaken.

493 Additional Analyses – CT Scans

494 All rotational profile measurements will be performed at NNUH under standard operating
495 procedure on a full diagnostic workstation (Synapse DICOM viewer, Fujifilm, Japan, High
496 resolution 2K monitors, Radiforce RX340 Eizo, Germany) in the BioImaging Laboratory and
497 under the supervision of a consultant musculoskeletal radiologist (AT).

498 Reproducibility

499 Inter-rater reliability will be assessed using intra-class correlation coefficients and 95% limits
500 of agreement derived from Bland-Altman plots.

501 TKR alignment versus native landmarks

502 The difference between the post-operative component rotational alignment and the pre-
503 operative native landmarks will be assessed using Bland-Altman plots.

504 Correlation with PROMS

505 The correlation between the PROMs and the difference between the post-operative
506 component rotational alignment and the pre-operative native landmarks will be assessed
507 using a correlation coefficient. A regression model will also be fitted including the
508 randomisation group to allow for a potential between-group difference in PROMs.

509 Correlation with movement analysis

510 A similar analysis will be undertaken for the correlation between movement analysis and the
511 difference between the post-operative component alignment and the pre-operative native
512 landmarks.

513 Additional Analyses – Qualitative Study

514 Interview transcripts will be organised using NVivo qualitative data management software
515 (QSR International, Burlington, Massachusetts, USA). Analysis will follow qualitative content
516 analysis procedures.[43] Coding and thematic analysis will be carried out independently by
517 two experienced qualitative researchers. Trustworthiness strategies[44] will be used to
518 increase the credibility, dependability and transferability of analysis and interpretation. This
519 will include cross-checking and review of codes and themes; constant comparative method
520 (hypothesis testing within and across the data set) and deviant case analysis (the use of
521 'outliers' as a resource for understanding and interpretation of data).[45]

522 Analysis Population and Missing Data

523 The analysis population are defined as:

524 a) intention-to-treat: all randomised individuals

525 b) per-protocol: all randomised individuals who do not have an alternative TKR during the
526 follow-up period. Individuals will be included up to the point of the alternative TKR.

527 c) safety population: all randomised individuals who receive the TKR.

528 Missing outcomes data will be multiple imputed to increase precision of the treatment effect
529 estimates. Sensitivity analyses will be conducted to assess the impact of the multiple
530 imputations and a complete case analysis will also be conducted. All imputations will be
531 examined to ensure sensible values are being generated. Imputation models will contain
532 baseline measures, outcome measures and factors predictive of missing data.

533 No Interim analysis is planned for this study.

534 **Methods: Monitoring**

535 **Data monitoring**

536 A TMG has been convened to assist with developing the design, co-ordination and strategic
537 management of the trial. A Safety Committee will review safety data and act in place of a
538 Data Monitoring Committee (DMC). Monitoring activities will be undertaken both centrally
539 and on-site. The frequency, type and intensity of routine and triggered monitoring are
540 detailed in the Quality Management and Monitoring Plan (QMMP). Ongoing central
541 monitoring will ensure quality and consistency of data thorough the trial. Details about data
542 collection and cleaning are described in the Data Management Plan (DMP)

543 **Harms**

544 **Safety**

545 Definitions of harm of the EU Directive 2001/20/EC Article 2 based on the principles of
546 International Council for Harmonisation (ICH) guideline for good clinical practice (GCP)
547 apply to this trial. A record of all study-related SAEs, including details of the nature, onset,
548 duration, severity, relationship to the device, relationship to the operative procedure,
549 outcome and expectedness will be made on the relevant section(s) of the trial-specific SAE
550 Form to be sent to the Trial Manager for onward reporting where required. SAEs resulting
551 from surgery or arthroplasty complications (clinical and safety outcomes) will be reported in
552 the relevant section of the case report form (CRF).

553 All non-serious adverse events (AEs) and adverse drug events (ADEs), whether expected or
554 not, should be recorded in the participant's medical notes and also reported in the relevant
555 section of the CRF.

556 Adverse events do NOT include:

- 557 • Readmissions for revision surgery
- 558 • Mild (i.e. not lasting more than five days) anaesthetics related complications:
559 Nausea, vomiting, dizziness, drowsiness, vaso-vagal drop, hypotension and constipation.
- 560 • Medical or surgical procedures; the condition that led to the procedure is the adverse
561 event
- 562 • Pre-existing disease or a condition present that was diagnosed before trial entry and
563 does not worsen
- 564 • Hospitalisation where no untoward or unintended response has occurred e.g.
565 elective surgery, social admissions

566 The Safety Committee will be provided with safety data for each treatment arm including
567 related AEs. The committee will advise on the continuation or early stoppage of the trial in
568 the unlikely event that there are concerns over harm to participants. The medical care in
569 response to any harm from the trial participation will be managed by routine NHS care.

570 Auditing

571 The Quality Assurance (QA) and Quality Control (QC) considerations for the CAPAbility trial
572 are based on the standard NCTU Quality Management Policy that includes a formal risk
573 assessment, and that acknowledges the risks associated with trial conduct and proposals of
574 how to mitigate them through appropriate QA and QC processes. Risks are defined in terms
575 of their impact on: the rights and safety of participants; project concept including trial design,
576 reliability of results and institutional risk; project management; and other considerations.

577 NCTU staff will review CRF data for errors and missing key data points. The trial database
578 will also be programmed to generate reports on errors and error rates. Essential trial issues,
579 events and outputs, including defined key data points, will be detailed in the trial DMP. The
580 frequency, type and intensity of routine and triggered on-site monitoring will be detailed in
581 the QMMP. The QMMP will also detail the procedures for review and sign-off of monitoring
582 reports. In the event of a request for a trial site inspection by any regulatory authority, NCTU
583 must be notified as soon as possible.

584 Ethics and dissemination

585 Research Ethics Approval

586 The trial is being conducted in accordance with CODEX rules and guidelines for research
587 and the Helsinki Declaration as well as the ICH Guideline for GCP. The study protocol was
588 approved by the East of England - Cambridge Central Research Ethics Committee

589 (reference 17/EE/0230) prior to the start of the trial. The trial is registered on the
590 International Standard Randomised Controlled Trials Number (ISRCTN) registry (reference
591 ISRCTN32315753). Approval was granted by the Health Research Authority (HRA) and
592 Confirmation of Capacity and Capability to conduct the trial has been provided by the NNUH
593 Research and Development office.

594 The NNUH is the trial sponsor and has delegated responsibility for the overall management
595 of the trial to the Co-Chief Investigators and NCTU including the trial design, coordination,
596 monitoring and analysis and reporting of results. The standard procedures and policies at
597 NCTU, a UK Clinical Research Collaboration (UKCRC)-registered trial unit and the study's
598 QMMP are followed. A TMG, including lay membership, has been formed to assist with the
599 design, coordination and strategic management of the trial. An independent safety
600 committee has also been set up to provide oversight on the trial and to safeguard the
601 interests of the participants

602 Protocol amendments

603 The protocol was amended in August 2017 (before trial start at sites) to improve consistency
604 and clarity. To that effect, an additional inclusion criterion was added to match the consent
605 form requiring participants to agree to any incidental findings to be reported to their General
606 Practitioner. The exclusion criteria relating to the use of the warfarin was also improved by the
607 addition of novel anti-coagulants therapies which are increasingly used. As part of this
608 amendment we also changed the stratification criteria from American Society of
609 Anesthesiologists (ASA) grade[46] and age to site and age as we became aware that ASA
610 grading is highly subjective and has poor inter-rater reliability. We added the UCLA Activity
611 Scale[29] as a secondary outcome measure to provide valuable information on the participant
612 activity levels pre-and post-operatively. The HADS[30] was also added to be taken at baseline

613 to inform the purposive sampling for the embedded qualitative study. Symptoms of anxiety
614 and depression can impact the experience and perception of recovery. The embedded
615 qualitative study was also simplified by the removal of the physiotherapists' interview after
616 agreeing that these would not add relevant information towards the outcome measure due to
617 recall biases that would be introduced by practical aspects of running these interviews.

618 Further changes were made in June 2018 allowing further clarifications. This was done
619 following the removal of the BMI requirement enforced by one of our surgery sites. The
620 associated exclusion criteria could therefore be removed opening the recruitment to a wider
621 population and thus improving the representativeness of the study sample as many patients
622 have a BMI greater than 35. In addition to this, the criteria excluding prior knee surgery was
623 refined to exclude only previous surgery of the collateral ligaments of the knee as previous
624 surgery on the cruciate ligaments would not affect the trial outcome as these ligaments are
625 to be removed during surgery. The clarification of this exclusion criteria also permitted for
626 previous non-intra-articular knee surgery (e.g. minor procedures around the knee) which
627 were excluded despite not affecting the trial outcome. The visit windows were also reviewed
628 as part of these changes to increase the baseline window from - 21 days to - 42 days up to
629 surgery and to change the six month visit time-frame from +/- two weeks to + four weeks.
630 The former ensuring enough time for the assessments to take place before randomisation
631 and the latter that all participants would have a full six months rehabilitation period before
632 undertaking the last follow-up visits. Additional changes included the addition of the learning
633 curve details for surgeon training to perform the intervention, the addition of the process for
634 participants to be informed of their knee allocation at the end of the trial as part of the result
635 dissemination, the clarification of the non-adherence and non-retention section to confirm
636 that any data collected up to a participant withdrawal will be retained and the clarification of
637 the safety reporting period and responsibilities. This amendment also allowed us to update
638 the compliance section to add the General Data Protection Regulation (GDPR).[47]

639 Following on the previous amendment additional modifications were made in August 2018
640 after the agreement that the recruitment of patients with previous TKR could be allowed as
641 long as they are over a year old at the time of the consultation and painless, mildly or
642 moderately painful. This was agreed to create a more representative data set while ensuring
643 that these participants' mobility will not be affected by contralateral pain.

644 Additional changes were made in December 2018 to include the maximum voluntary
645 isometric contraction (MVIC) of the hamstring and quadriceps muscles on both limbs to
646 assess the known issue of muscle strength loss after TKR.[48] This biomechanical measure
647 evaluates post-operative quadriceps and hamstring muscle strength loss and subsequent
648 recovery in both the non-operative legs and healthy control legs for comparison. The
649 inclusion criteria were also amended to remove "Patient willing to provide full informed
650 consent to the trial, including consent for any incidental findings to be communicated to their
651 General Practitioner". This does not need to be an inclusion criteria as a potential participant
652 would not be enrolled on the trial if the consent form, which includes a statement about
653 communicating findings with the General Practitioner, was not initialled and signed. In
654 addition the PIS was amended to clarify that baseline data collected for participants that may
655 not progress to randomisation or surgery, for reasons other than withdrawal, will be retained
656 and used as observational data.

657 Furthermore, the protocol was amended in March 2019 to extend the six to eight week visit
658 window to six to ten weeks to ensure all participants can be seen within the appropriate
659 window. An additional time point for collecting changes in pain medication was also added to
660 the participant timeline at discharge from surgery. This will allow for a comparison between
661 the participant reported pain medications at the Week 1 phone call and what was prescribed
662 at discharge.

663 Consent or assent

664 Potential participants will be provided with a PIS and given time to read it fully. Following a
665 discussion with a medical qualified investigator or suitable trained and authorised delegate,
666 any questions will be satisfactorily answered and if the participant is willing to participate,
667 written informed consent will be obtained. During the consent process it will be made clear
668 that the participant is free to refuse to participate in all or any aspect of the trial, at any time
669 and for any reason, affecting their treatment.

670 Potential participants who, in the opinion of the clinical team do not have capacity to consent
671 will be ineligible for this study. If a participant loses capacity during the course of the trial,
672 they will be withdrawn from the any further assessments but, the data which has already
673 been collected will be retained.

674 Consent will be re-sought if new information becomes available that affects the participant's
675 consent in any-way. This will be documented in a revision to the patient information sheet
676 and the participant will be asked to sign an updated consent form. These will be approved by
677 the ethics committee prior to their use. A copy of the approved consent form is available
678 from the NCTU trial team.

679 No additional consent will be sought for the collection or use of additional participant data or
680 biological specimens as no such studies are planned.

681 Confidentiality

682 Any paper copies of personal trial data will be kept at the participating site in a secure
683 location with restricted access. Following consent, identifiable data will be kept on the trial
684 database to allow the MoveExLab staff to contact participants to arrange appointments. Only
685 authorised trial team members will have password access to this part of the database.

686 Confidentiality of participant's personal data is ensured by not collecting participant names
687 on CRFs and limiting access to personal information held on the database at NCTU. At trial
688 enrolment, the participant will be issued a participant identification number and this will be
689 the primary identifier for the participant, with secondary identifiers of month and year of birth
690 and initials.

691 The participant's consent form will carry their name and signature. These will be kept at the
692 trial site, and a copy sent to NCTU for monitoring purposes. They will not be kept with any
693 additional participant data.

694 Declaration of interests

695 The investigators named on the protocol have no financial or other competing interests that
696 impact on their responsibilities towards the scientific value or potential publishing activities
697 associated with the trial.

698 Access to data

699 Requests for access to trial data will be considered, and approved in writing where
700 appropriate, after formal application to the TMG. Considerations for approving access are
701 documented in the TMG Terms of Reference. The Co-Chief Investigators and Trial
702 Statistician at NCTU will have access to the full trial dataset.

703 Dissemination policy

704 The results of the trial will be disseminated regardless of the direction of effect and will be
705 reported following the Consolidated Standards of Reporting Trials (CONSORT)
706 Statement.[49] Ownership of the data arising from the trial resides with the trial team. The
707 publication policy will be in line with rules of the International Committee of Medical Journal

708 Editors.[50] The TMG will decide on the dissemination strategy including presentations,
709 publications and authorship.

710 Discussion

711 This protocol describes a trial that will explore the performance and functional ability of two
712 types of total knee implants by comparing them on multiple levels.

713 The use of validated PROMs as both primary and secondary outcomes will allow the
714 comparison of the Journey II BCS and the Genesis II TKR implants in a standardised
715 manner widely used in the literature. The addition of biomechanical, radiological, clinical
716 efficacy and safety outcomes will permit an in-depth comparison of the implants and to fully
717 assess the performance of both implants' design in a comprehensive way. This will also
718 highlight any relationships between each of these individual aspects and inform future study
719 designs. The biomechanical outcome using everyday movement and detailed anatomical
720 information from the rotational profile will both provide invaluable and pragmatic information
721 on the knee implants in situ which will help clinicians in the investigation and management of
722 participants before and after TKR. Additionally, the embedded qualitative study will
723 investigate not only participant related constructs associated with both their TKR and
724 rehabilitation but also provide surgeon's perspectives.

725 One of the challenges linked with the collection of varied outcome measures is the
726 participant visit burden. This has been considered very carefully and the trial has been
727 designed for study visits to be combined with routine clinical visits or to be undertaken over
728 the telephone

729 **Declarations**

730 **Ethics approval and consent to participate**

731 The study protocol was approved by the East of England - Cambridge Central Research
732 Ethics Committee (reference 17/EE/0230) prior to the start of the trial. The trial is registered
733 on the International Standard Randomised Controlled Trials Number (ISRCTN) registry
734 (reference: ISRCTN32315753). Approval was granted by the Health Research Authority
735 (HRA) and Confirmation of Capacity and Capability to conduct the trial has been provided by
736 the NNUH Research & Development office. Informed consent will be obtained from all study
737 participants.

738 **Consent for publication**

739 Not applicable

740 **Availability of data and materials**

741 Public access to the full trial protocol, trial-related documents, participant-level dataset and
742 statistical code may be made on request to the TMG.

743 **Competing interests**

744 The authors declare that they have no competing interests.

745 **Funding**

746 The CAPAbility trial is an investigator-initiated trial funded by Smith and Nephew (JOURNEY
747 BCS II and GENESIS II implant manufacturer) apart from the embedded radiological study

748 (radiological outcomes measures from rotational CT scans) which is funded by the Gwen
749 Fish Orthopaedic Trust.

750 Authors' contributions

751 CC, EP, TS and IMN drafted this paper. All authors contributed to revisions of the
752 manuscript, read and approved the final manuscript. All authors contributed to the research
753 funding application and development of the trial protocol. All authors read and approved the
754 final manuscript.

755 CC is the corresponding author.

756 Acknowledgements

757 The authors are thankful for the ongoing support from the trial participants, site staff and
758 NCTU team undertaking various aspect of the CAPAbility trial. We would also like to express
759 our gratitude to the Trial Management Group for their review of the protocol and the Safety
760 Committee members (Professor Simon Donell and Professor Marcus Flathers) for their
761 oversight of the trial.

762 References

763 1. Baker PN, van der Meulen JH, Lewsey J, Gregg PJ. National Joint Registry for
764 England and Wales. The role of pain and function in determining patient satisfaction after
765 total knee replacement: data from the National Joint Registry for England and Wales. J Bone
766 Joint Surg. 2007;89-B:893-900. Balke B. A simple field test for the assessment of physical
767 fitness. Rep Civ Aeromed Res Inst US. 1963;53:1-8.
768

- 769 2. NICE. Osteoarthritis: care and management. Clinical Guideline [CG177]. Available
770 at: <https://www.nice.org.uk/guidance/cg177> Accessed: 26 June 2019.
771
- 772 3. National Joint Registry. StatsOnline Available at: <http://www.njr.statsonline.org.uk>
773 Accessed: 26 June 2019
774
- 775 4. Beswick AD, Wylde V, Goberman-Hill R, Blom A, Dieppe P. What proportion of
776 patients report long-term pain after total hip or knee replacement for osteoarthritis? A
777 systematic review of prospective studies in unselected patients. *BMJ Open*. 2012;2:e000435
778
- 779 5. Judge A, Arden NK, Kiran A, Price A, Javaid MK, Beard D, Murray D, Field RE.
780 Interpretation of patient-reported outcomes for hip and knee replacement surgery:
781 identification of thresholds associated with satisfaction with surgery. *J Bone Joint Surg*.
782 2012;94:412-8.
783
- 784 6. Zanasi S. Innovations in total knee replacement: new trends in operative treatment
785 and changes in peri-operative management. *Eur Orthop Traumatol*. 2011;2:21–31
786
- 787 7. Barrack RL, Schrader T, Bertot AJ, Wolfe MW, Myers L. Component rotation and
788 anterior knee pain after total knee arthroplasty. *Clin Orthop*. 2001;392:46-55.
789
- 790 8. Hofmann S, Romero J, Roth-Schiffel E, Albrecht T. Rotational malalignment of the
791 components may cause chronic pain or early failure in total knee arthroplasty. *Orthopade*.
792 2003;32:469-76.
793

- 794 9. Torga-Spak R, Parikh SN, Stuchin SA. Anterior knee pain due to biplanar rotatory
795 malalignment of the femoral component in total knee arthroplasty: case report. J Knee Surg.
796 2004;17:113-16.
797
- 798 10. Berger RA, Rubash HE, Seel MJ, Thompson WH, Crossett LS. Determining the
799 rotational alignment of the femoral component in total knee arthroplasty using the
800 epicondylar axis. Clin Orthop. 1993;286:40-7.
801
- 802 11. Longstaff LM, Sloan K, Stamp N, Scaddan M, Beaver R. Good alignment after total
803 knee arthroplasty leads to faster rehabilitation and better function. J Arthroplasty.
804 2009;24:570-8.
805
- 806 12. Van Houten AH, Kosse NM, Wessels M, Wymenga AB. Measurement techniques to
807 determine tibial rotation after total knee arthroplasty are less accurate than we think. Knee.
808 2018;25:663-8.
809
- 810 13. Cho Y, Lee MC. Rotational alignment in total knee arthroplasty. Asia Pacific J Sport
811 Med Arthroscopy, Rehabil Technol. 2014;1:113-8.
812
- 813 14. Hirschmann MT, Konala P, Amsler F, Iranpour F, Friederich NF, Cobb JP. The
814 position and orientation of total knee replacement components: a comparison of
815 conventional radiographs, transverse 2D-CT slices and 3D-CT reconstruction. J Bone Joint
816 Surg. 2011; 93:629-33.
817

- 818 15. Brunner A, Eichinger M, Hengg C, Hoermann R, Brenner E, Kralinger F. A simple
819 method for measurement of femoral anteversion Validation and assessment of
820 reproducibility. *J Orthop Trauma*. 2016;30:273-8.
821
- 822 16. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krleza-Jeric K,
823 Hrobjartsson A, Mann H, Dickersin K, Berlin J, Dore C, Parulekar W, Summerskill W, Groves
824 T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D, SPIRIT 2013 Statement: Defining
825 standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-7.
826
- 827 17. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of
828 patients about total knee replacement. *J Bone Joint Surg*. 1998;80:63-9.
829
- 830 18. Bohm ER, Loucks L, Tan QE, Turgeon TR. Determining minimum clinically important
831 difference and targeted clinical improvement values for the Oxford 12. American Academy of
832 Orthopaedic Surgeons 2012 Annual Conference. February 9 2012.
833
- 834 19. Beard DJ, Harris K, Dawson J, Doll H, Murray DW, Carr AJ, Price AJ. Meaningful
835 changes for the Oxford hip and knee scores after joint replacement surgery. *J Clin Epidemiol*
836 2015;68:79-90.
837
- 838 20. Williams DP, O'Brien S, Doran E, Price AJ, Beard DJ, Murray DW, Beverland DE.
839 Early postoperative predictors of satisfaction following total knee arthroplasty. *Knee*.
840 2013;20:442-6.
841
- 842 21. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR.
843 How long does a knee replacement last? A systematic review and meta-

844 analysis of case series and national registry reports with more than 15 years of follow-up.
845 Lancet. 2019;393:655-63.

846

847 22. Pennington M, Grieve R, Black N, van der Meulen JH. Cost-
848 effectiveness of five commonly used prosthesis brands for total knee replacement in the UK:
849 A study using the NJR dataset. PLoS One. 2016;11:e0150074.

850

851 23. Moore C, Lenz N. The evolution of guided motion total knee arthroplasty – The
852 JOURNEY II Bi-Cruciate Stabilized knee system. Bone Joint Sci 2012;03:1-8.

853

854 24. Grieco TF, Sharma A, Dessinger GM, Cates HE, Komistek RD.
855 In vivo kinematic comparison of a bicruciate stabilized total knee arthroplasty and the normal
856 knee using fluoroscopy. J Arthroplasty. 2018;33:565-71.

857

858 25. Smith TO, McCabe C, Lister S, Christie SP, Cross J. Rehabilitation implications
859 during the development of the Norwich Enhanced Recovery Programme (NERP) for patients
860 following total knee and total hip arthroplasty. Orthop Traumatol Surg Res. 2012;98:499-505.

861

862 26. Arshad H, Royan S, Smith TO, Barker L, Chirodian N, Wimhurst J. Norwich
863 Enhanced Recovery Programme vs. non-enhanced recovery following hip and knee
864 replacement: A matched-cohort study. Int J Orthop Trauma Nurs. 2014;18:227-34.

865

866 27. Dawson J, Beard DJ, McKibbin H, Harris K, Jenkinson C, Price AJ. Development of a
867 patient-reported outcome measure of activity and participation (the OKS-APQ) to
868 supplement the Oxford knee score. Bone Joint J. 2014;96-B:332-8.

869

- 870 28. EuroQol Group. EuroQol—a new facility for the measurement of health-related
871 quality of life. *Health Policy*. 1990;16:199–208.
872
- 873 29. Zahiri CA, Schmalzried TP, Szuszczewicz ES, Amstutz HC. Assessing activity in joint
874 replacement patients. *J Arthroplasty*. 1998;13:890–5.
875
- 876 30. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta*
877 *Psychiatrica Scandinavica*. 1983;67:361–70.
878
- 879 31. Behrend H, Giesinger K, Giesinger JM, Kuster MS. The "forgotten joint" as the
880 ultimate goal in joint arthroplasty: validation of a new patient-reported outcome measure. *J*
881 *Arthroplasty*. 2012;27:430-6.
882
- 883 32. Nicholas MK, McGuire BE, Asghari A. A 2-item short form of the Pain Self-efficacy
884 Questionnaire: development and psychometric evaluation of PSEQ-2. *J Pain*. 2015;16:153-
885 63.
886
- 887 33. Podsiadlo D, Richardson S. The Timed "Up & Go": a test of basic functional mobility
888 for frail elderly persons. *J Am Geriatr Soc*. 1991;39:142–8.
889
- 890 34. Balke B. A simple field test for the assessment of physical fitness. *Civ Aeromedical*
891 *Res Inst*. 1963;63:1-8.
892
- 893 35. Hertel J, Olmsted-Kramer LC, Challis JH. Time-to-boundary measures of postural
894 control during single leg quiet standing. *J Appl Biomech*. 2006;22:67-73.
895

- 896 36. Kinzey SJ, Armstrong CW. The Reliability of the Star-Excursion Test in Assessing
897 Dynamic Balance. *J Orthop Sport Phys Therap.* 1998;27:356-60.
898
- 899 37. Berger RA, Crossett LS, Jacobs JJ, Rubash HE. Malrotation causing patellofemoral
900 complications after total knee arthroplasty. *Clin Orthop Relat Res.* 1998;356:144-53.
901
- 902 38. Jones CA, Voaklander DC, Suarez-Alma ME. Determinants of function after total
903 knee arthroplasty. *Phys Ther.* 2003;83:696-706.
904
- 905 39. Johnson EC, Horwood J, Gooberman-Hill R. Patients' journeys through total joint
906 replacement: patterns of medication use. *Musculoskeletal Care.* 2014;12:92-102.
907
- 908 40. Johnson EC, Horwood J, Gooberman-Hill R. Trajectories of need: understanding
909 patients' use of support during the journey through knee replacement. *Disability Rehab*
910 *2016;38:2550-63.*
911
- 912 41. Merle-Vincent F, Couris C M, Schott AM, Conrozier T, Piperno M, Mathieu P, Vignon
913 E. Factors predicting patient satisfaction 2 years after total knee arthroplasty for
914 osteoarthritis. *Joint Bone Spine.* 2011;78:383-6.
915
- 916 42. Singh JA, O'Byrne M, Harmsen S, Lewallen D. Predictors of moderate-severe
917 functional limitation after primary Total Knee Arthroplasty (TKA): 4701 TKAs at 2-years and
918 2935 TKAs at 5-years. *Osteoarthritis Cartilage.* 2010;18:515-21.
919

- 920 43. Graneheim UH, Lundman B. Qualitative content analysis in nursing research:
921 concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*.
922 2004;24:105-12.
- 923
- 924 44. Lincoln YS, Guba EG. *Naturalistic Inquiry*. 1985. Newbury Park, CA: Sage
- 925
- 926 45. Silverman D. *Doing qualitative research: A practical handbook*. 2000. Thousand
927 Oaks, CA: Sage
- 928
- 929 46. Saklad M. Grading of patients for surgical procedures. *Anesthesiology*. 1941;2:281–
930 4.
- 931
- 932 47. Information Commissioner's Office. *Guide to the General Data Protection Regulation*.
933 Available at: [https://www.gov.uk/government/publications/guide-to-the-general-data-](https://www.gov.uk/government/publications/guide-to-the-general-data-protection-regulation)
934 [protection-regulation](https://www.gov.uk/government/publications/guide-to-the-general-data-protection-regulation) Accessed: 13 December 2019.
- 935
- 936 48. Moon, Y.W., Kim, H.J., Ahn, H.S. and Lee, D.H. Serial changes of quadriceps and
937 hamstring muscle strength following total knee arthroplasty: a meta-analysis. *PloS One*.
938 2016;11:e0148193.
- 939
- 940 49. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010. *BMJ*.
941 2010;340:c332.
- 942
- 943 50. ICMJE Recommendations Defining the Role of Authors and Contributors. Available
944 at: [http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-](http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html)
945 [role-of-authors-and-contributors.html](http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html) Accessed: 26 June 2019