Supplementary Online Content

Buhagiar M, Naylor J, Harris I, et al. Effect of inpatient rehabilitation vs a monitored home-based program on mobility in patients with total knee arthroplasty - the HIHO study: a randomized clinical trial.

Supplement 1: Table of Contents

1. Final protocol
2. Statistical analysis plan

This supplementary material has been provided by the authors to give readers additional information about their work.

The HIHO Rehab Study Protocol

Version Number: 5

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SYNOPSIS

Protocol title: The HIHO Rehab Study Protocol

Protocol version: 5

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Summary

Study title: The HIHO Rehab Study

Protocol version: 5

Objectives Our over-arching aim is to establish whether inpatient rehabilitation is necessary after total knee replacement (TKR).

Primary objective: The aim of the proposed study is to determine whether 10 days of post-acute inpatient rehabilitation followed by a home programme is superior to a home programme alone.

Study design: Two arm, parallel randomised controlled trial with third observational group.

Planned sample size: A minimum of 140 participants, minimum of 70 in each arm.

Selection criteria: Patients presenting to Fairfield or Sutherland Hospital for a primary total knee replacement, and who can comprehend the protocol, and who are not predisposed (due to lack of social supports or multiple physical impairments) to be discharged to an inpatient facility.

Study procedure: Patients will be screened, consented and thus enrolled pre-operatively. Day 1 after surgery they will be randomized to 1 of the 2 treatment arms – inpatient rehabilitation at Braeside or Sutherland Hospital (10 days) or to usual care, a monitored home programme, provided by Fairfield, Sutherland or Campbelltown Hospitals.

Statistical considerations*: Sample size calculation:* The primary endpoint in this trial is function at 6 months post-surgery, measured using the outcome of a Six-Minute Walk Test (6MWT). A total minimum of 140 patients (minimum of 70 patients in each group) will provide 80% power and 95% confidence to detect a difference of 60m (SD 100m) in the in-hospital rehab group at 6 months when compared to the home based programme, and allows for 10% loss to follow-up.

Duration of the Study: 3.5 years

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BACKGROUND

1.1. DISEASE BACKGROUND*

TKR and associated costs Since 2003, the number of primary TKR procedures undertaken annually in Australia has increased 55.9%;[1] the increase in the private sector has outstripped the increase in the public sector (62.2 vs 44.4%). The private sector performs approximately 67.4% (22 822/33 884) of all primary TKRs.[1] The increasing surgical volume witnessed locally mirrors the increase seen internationally.[2,3] Demand is secularly increasing due to advances in surgical approach,[4] the ageing population, and because consumers, who are living longer, are opting for a surgical solution in order to reduce age-related disability in their latter years.[5,6] Further increases are expected in the foreseeable future,[1] thus, there is increasing concern regarding the sustainability and affordability of this type of intervention both in the public and private sector. Increased demand in the public sector cannot be readily met because the supply of services is not driven by demand, but rather, is dictated by governmental policy set within the context of a fixed proportion of GDP.[5] Whilst the private sector can adjust more readily to increases in demand owing to greater underutilised capacity, this inevitably puts upward pressure on private health insurance premiums.[4] Regardless of sector, current and future affordability is an issue.

Whilst the TKR procedure is viewed as highly cost-effective in light of the impressive gains in functional performance and health-related quality of life,[3,7] the acute-care and associated rehabilitative costs impose a significant burden on public and private hospital budgets.[8,9,10] Not surprisingly, a recent retrospective study from the US concluded that the cost-effectiveness of TKR is reduced if the procedure is associated with a stay in an inpatient rehabilitation facility.[3]

Evidence in support of inpatient rehabilitation after TKR Our own systematic search of key electronic healthcare databases (May 30, 2011) revealed that there was no high-level evidence to support the provision of inpatient rehabilitation after TKR. Specifically, no randomised trial has compared inpatient rehabilitation to any out-patient mode or a monitored or unmonitored home programme. Several studies undertaken in the US have concluded that inpatient rehabilitation is not superior to domiciliary rehabilitation (hospital services provided at home).[11,12] A non-randomised pilot study in Germany concluded that inpatient rehabilitation was not more cost-effective compared to out-patient rehabilitation.[13] Longitudinal data from an Australian cohort[9] observed that patient-reported outcomes were similarwhether or not TKR patients were discharged to inpatient rehabilitation. The authors concluded, therefore, that randomised trials were required to explore who benefits most - such as the older or more infirm patients - from inpatient rehabilitation.

Evidence in support of non-inpatient modes of rehabilitation A recent systematic review concluded that there was insufficient evidence to support any specific type or mode of outpatient rehabilitation over any other outpatient mode or even a home programme.[14] This included the use of hydrotherapy, 1-to-1 or group-based therapy, and even different exercise types such as those targeting function versus isolated muscle groups. Notably, most of the studies to date have been small ($n \leq 160$) and none have simultaneously compared group-based, 1-to-1 and home-based programmes. Our own recently completed, comparatively large RCT (n =249) provides strong evidence that 1-to-1 centre-based therapy is not superior to a group-based programme or a monitored home programme at 10 and 52 weeks post surgery.[15] The similar recovery patterns observed was despite the fact that access to centre-based interventions for the outpatient groups was optimised through the use of transport and parking concessions. Thus, lack of access or poor attendance did not explain a lack of superiority of the 1-to-1 mode.

1.2. Rationale for Performing the Study*

In Australia, inpatient rehabilitation is a costly and commonly utilised treatment option after TKR surgery, particularly in the private sector. A 12-day inpatient stay in a private facility costs approximately $7000[16], and utilization of inpatient rehabilitation by private patients post TKR is estimated to be as high as 43% in NSW and 29% Australia-wide (compiled data from AROC and AOA). As the majority of TKR procedures are performed in the private sector,[1] the question of whether inpatient rehabilitation is cost-effective is of considerable interest to private health insurers and governments alike. Inevitably, the cost of inpatient services is reflected in private insurance premiums and costly premiums negatively affect rates of private health insurance.

Based on our recent RCT and the lack of research evaluating the necessity of inpatient rehabilitation, we contend that a trial comparing the effectiveness of the most resource-intensive form of rehabilitation delivery after TKR – inpatient rehabilitation - to one with comparatively little resource use – a monitored home programme – is readily justified. The definitive study will be a landmark study in this area. It will provide conclusive evidence which either supports or refutes the need for resource-intensive inpatient rehabilitation after TKR.

Rationale for cohort selection and setting: From our previous RCTs conducted in this area[15,17] and discussions with representatives from the private sector (Australia Private Hospital Association and members), we know that private patients are less willing to partake in randomised trials that compare the effectiveness of different rehabilitation interventions given participation removes their automatic 'right' to be discharged home via an inpatient rehabilitation facility. *We therefore propose to answer this most significant question 'Is inpatient rehabilitation necessary after TKR?' by researching a private sector model within a public sector setting.*

Working hypothesis: The hypothesis for the definitive study is that inpatient rehabilitation after TKR is more cost-effective and associated with superior outcomes – in terms of recovery of function, mobility and quality of life – compared to a monitored home programme. If superiority is shown, a cost-effectiveness analysis will be undertaken.

2. STUDY OBJECTIVES*

2.1. Primary Objectives*

The primary objective of this study is to establish whether inpatient rehabilitation is necessary after TKR for patients with osteoarthritis (OA) who could otherwise be discharged directly home.

The main hypothesis to be tested by the proposed study is that TKR recipients who receive inpatient rehabilitation in addition to participating in a home programme, compared to patients who participate in a home programme only, will achieve a superior level of mobility at 6 months post surgery. If superiority is shown, a cost-effectiveness analysis will be undertaken.

Primary outcome

The primary outcome variable is walking distance at 6 months post surgery, measured using the Six-Minute Walk Test (6MWT) [17, 19]. Function measured by this test is a composite of several factors targeted in rehabilitation programmes after TKA such as lower limb strength, knee range of motion, and balance[17, 18, 19, 20, 21]. The test is highly reproducible within the individual[22], is likely to be less susceptible to misinterpretation and less culturally sensitive

than patient-reported outcomes, and does not appear to suffer from the floor or ceiling effects associated with many patient-reported outcomes[23] Together, these attributes mean the results for our primary outcome should be readily translatable to any TKA cohort. Finally, a functional outcome based on a physical test is a novel choice as a primary outcome in this field with most TKA rehabilitation studies focusing on patient-reported outcomes[12, 17, 18, 20, 24].

2.2. SECONDARY OBJECTIVE

Secondary hypotheses to be tested relate to patient-reported knee pain and function, health-related quality of life, and knee joint mobility. Superiority in these outcomes will be evident at six months after surgery.

3. STUDY DESIGN*

3.1. DESIGN*

Two-arm, parallel randomised controlled trial with third observational group.

3.2. STUDY GROUPS

Two study groups (treatment arms).

1) HI – Hospital inpatient rehabilitation group
2) HO – Home-based rehabilitation group

Description of the interventions

(HI): Those allocated to the HI will be admitted to Braeside or Sutherland Hospital's Rehabilitation Unit for 10 days. Informed by the private sector,[25] HI patients will receive twice-daily supervised physiotherapy. Supervised therapy will comprise 1-1.5 hr of class-based exercises and 1-1.5 hr of 1-to-1 therapy. After discharge, patients will be provided with a home programme (described below). Monitored Home Programme (HO) (standard care): Approximately 2 weeks post-surgery, patients allocated to HO will attend 1 group-based exercise session at Fairfield, Sutherland or Campbelltown Hospitals where the home programme will be rehearsed and exercises individualised as per extant co-morbidities. Patients will be encouraged to attend a 2nd class within the first 2-8 post-operative weeks to encourage exercise progression and discuss any ongoing issues with the therapist. *Patients in both groups will receive a booklet (see attached) detailing the home programme, and will be permitted to contact the therapist by phone in this period for advice.* Any patient can be reviewed at any time by the therapist within the first 8 weeks of surgery if there are any concerns raised by either the patient or the therapist. All patients will be required to complete a diary detailing programme adherence and healthcare utilisation.[8,9]

Treating therapists will be required to complete a study proforma detailing therapy provided and therapy attendance and any complications.

Therapy provided to those who do not consent to participate

Patients who do not consent to participate in the study will receive standard care, i.e. the HO programme. Due to unforeseen circumstances, some may be discharged to inpatient rehabilitation.

3.3. NUMBER OF PARTICIPANTS*

A minimum of 140 participants will be assigned to either the HI or HO groups with a minimum of 70 in each group.

3.4. NUMBER OF CENTRES

- There are two recruitment centres and four treatment sites.
- Fairfield and Sutherland Hospitals are the recruiting sites. Fairfield, Sutherland and Campbelltown Hospitals will oversee the monitored home programme.
- Braeside and Sutherland Hospitals will provide the inpatient rehabilitation.

3.5. DURATION

The study is expected to take approximately 48 months including 30 months for recruitment, 12 months from enrolment of the last participant, and 6 months for analysis.

4. PARTICIPANT SECTION

4.1. INCLUSION CRITERIA*

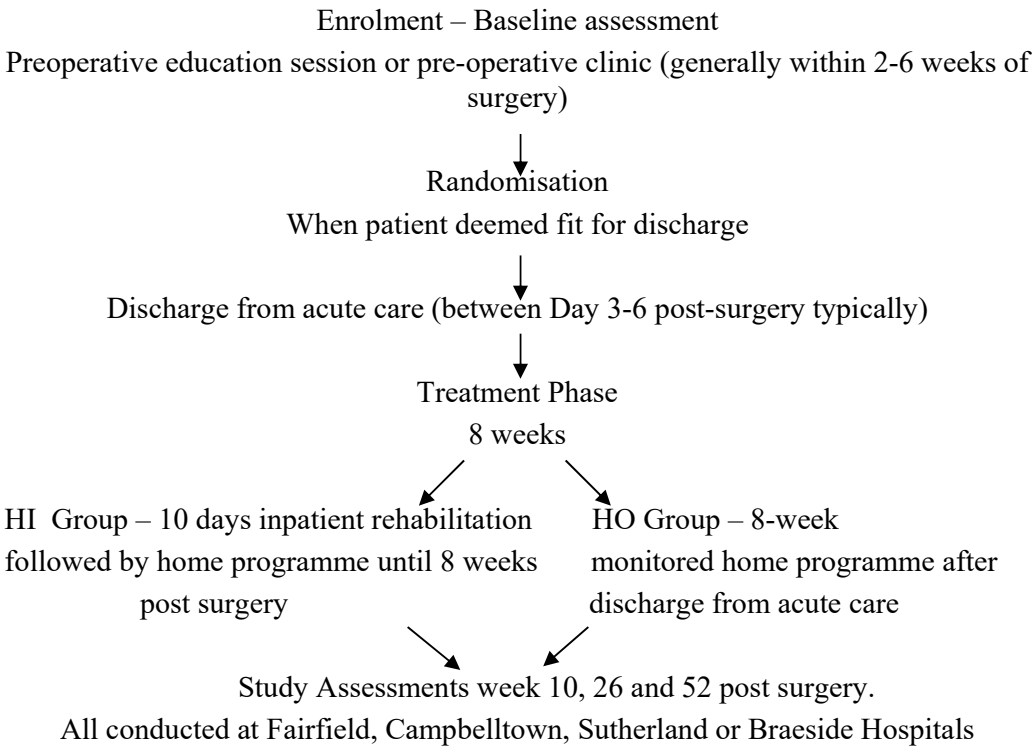
- Undergoing primary unilateral TKR at Fairfield or Sutherland Hospital
- Having a primary diagnosis of osteoarthritis
- Willingness to give written informed consent and willingness to participate to and comply with the study.
- Age 40 years or over

4.2. EXCLUSION CRITERIA*

- Patients with a history of a psychological illness or condition such as to interfere with the patient's ability to understand the requirements of the study. This may include, but is not limited to a history of dementia or short-term memory impairment secondary to a cerebrovascular accident.
- Patients predisposed to be discharge to an inpatient rehabilitation (or hostel) facility due to lack of social support or multiple physical impairments
- Patients unable to read English
- Patients unable to perform a home exercise programme without hands-on support from another person or who are unable to perform the programme without supervision (that is, observation) from another person.
- Patients restricted to partial or nil weight-bearing through the operated limb post surgery.
- Patients experiencing a catastrophic complication post surgery (e.g. suffer a stroke or periprosthetic fracture) which precludes participation in the planned rehabilitation programmes.
- Pregnancy

5. STUDY OUTLINE*

5.1. STUDY FLOW CHART



5.2. INVESTIGATION PLAN*

Consenting participants will undergo a baseline assessment prior to surgery. Participants will be reassessed (followed up) at 10, 26 and 52 weeks post surgery. The assessments which will be conducted are summarised in the table below. As well as obtaining measures commonly used to assess recovery after knee replacement [six minute walk, 15 metre walk (distance and gait speed), Knee Injury and Osteoarthritis Outcome Score (KOOS), EQ-5D, Oxford knee], patient adherence to the home programme and physiotherapy attendance, patient healthcare utilisation costs and carer burden will be monitored. Physiotherapy attendance will be directly obtained from the treating therapists. Patients experiencing any catastrophic complaints that affect their capacity to engage in the allocated rehabilitation programme will still be followed-up as per the planned schedule. Patients allocated to the Inpatient arm will also be assessed using the Functional Independence Measure (FIM) on entry and exit to Braeside and Sutherland Hospitals as this is a tool commonly utilised by inpatient rehabilitation providers and will allow future comparisons with other rehabilitation datasets.

List	Enrolment	Week 10	Week 26	Week 52

Interventions	Visit			(Final)
Informed Consent	✓			
Inclusion / Exclusion critieria	✓			
Nomination of preferred Rx method	✓	✓		
Obtain demographic and anthropometric data	✓	Weight only	Weight only	Weight only
Complete KOOS, EQ5D, Oxford surveys	✓	✓	✓	✓
Six minute walk test (gait speed and distance)	✓	✓	✓	✓
15 metre walk test	✓	✓	✓	✓
SF12 or EQ-5D	✓	✓	✓	✓
Patient-reported adverse event		✓	✓	✓
Postacute healthcare utilisation costs		✓	✓	✓

Each test or survey will be completed according to standardised protocols, and conducted by an assessor blinded to the treatment allocation. The assessments will take place at Fairfield Hospital (Whitlam Joint Replacement Centre or the Pre-Admission Clinic), Sutherland Hospital (Preadmission Clinic) or Campbelltown Hospital (Physiotherapy Department). Occasionally it may be necessary for a follow-up assessment to be conducted at a participant's home, in the event that this is deemed the only way that an outcome measure may be collected for a participant, for example when participants are unable to come to the designated hospital for follow-up due to transportation or other issues. Patients will be given diaries to complete their record of healthcare utilisation after discharge from acute care or from inpatient rehabilitation. Acute care costs will be ignored as they will be assumed to be the same for all patients. Length of stay will not be dictated by the study as

the normal criteria for discharge from acute care will apply independent of which study arm the patient is in. Costs of rehabilitation will commence from either discharge to inpatient rehabilitation or discharge home. The inpatient rehabilitation costs will be estimated from known costs of TKR inpatient episodes in a private facility. Other healthcare costs will be derived from the standard Medicare Schedule and Pharmaceutical Benefits Schedule for the study time period.

Study endpoints

The data collection phase of the study will end when the last randomised patient has their 12-month assessment. The entire study will end after the analysis involving all participants is complete.

5.3. Study Procedure Risks*

We do not anticipate that the patient is exposed to any further risk than they would otherwise be exposed to when participating in a typical rehabilitation programme after TKR. There is a risk of falling or muscle or joint soreness (in either treatment arm), however, we believe the risk of falling to be low and the joint or muscle soreness experienced is generally well tolerated. We have conducted two rehabilitation RCTs involving TKR patients (351 patients in total) and not one adverse event has occurred or been reported as a result of the programmes under investigation (home, gym or one-to-one programme or hydrotherapy).[15,17] The assessments to be undertaken are also low or negligible risk and again have been the same tests conducted without mishap in the previous TKR rehabilitation trials.

5.4. Recruitment and Screening*

Patients booked for TKR surgery at Fairfield or Sutherland hospitals and presenting to the pre-operative education session or the pre-operative clinic will be screened for eligibility by an investigator (MB) and a research officer (if funding is obtained). Screening will occur through discussion with the potential patient and carer, and review of the joint replacement assessment undertaken by a musculoskeletal coordinator who prioritises patients for surgery at Fairfield and Sutherland Hospitals.

Enrolment Procedure*

The participant will be enrolled into the study after the informed consent process has been completed and the participant has met all inclusion criteria and none of the exclusion criteria. The participant will receive a study enrolment number and this will be documented in the participant's medical record and on all study documents. On enrolment, each participant will be asked their preferred treatment method.

Patients who do not wish to take part in the study will be invited to participate in a non randomised observational arm, to be followed up at 6 months.

5.5. Informed Consent Process*

Eligible patients who express an interest in the study will be required to read a study information sheet. Those agreeing to participate will be required to sign a Consent Form which in turn will be witnessed by an independent person. It is anticipated that a carer, friend or relative will be present during this process.

5.6. Randomisation Procedure

Randomisation will take place in the days following surgery, once it has been confirmed that participants have come through surgery without suffering any relevant adverse outcomes (see exclusion criteria) and are progressing towards discharge. If it is determined

that there is a need for rehabilitation at this time, patients are no longer eligible to participate in the study due to exclusion criteria.

The University of Sydney Randomisation service will be used for participant randomisation (1:1 ratio). This is a centralised service providing secure, coded randomisation via a telephone. The randomisation service will generate and hold the randomisation schedule. Allocation will be concealed until the point of randomisation. Randomisation will occur as close to the time of intervention as possible, by waiting 3-4 days post-surgery for clearance to participate.

Participants will be randomised to one of the two intervention groups using the method of minimisation stratified for age (≤70, >70 y), gender and height.

6. SAFETY*

6.1. Adverse Event Reporting*

Adverse events experienced by the patient during the acute period will be monitored to ensure the patient remains eligible for the study. Monitoring will occur via the ward-based physiotherapist who will inform the investigators of the patient progress.

Adverse events post discharge from acute care will be monitored, whether they be related or unrelated to the study intervention. This will occur via communication with the physiotherapists providing therapy (jnpatient or monitored home programme) and at the follow-up assessments with the patient. Adverse events include any post-surgical complication, falls or instances of greater than expected muscle or joint soreness.

If the treating therapist detects a complication, then, as per standard practice, they will advise the treating surgeon and any relevant registrar or GP of their concern and also record this information in the study proforma and patient record. If the patient simply informs the treating therapist about a known complication, then the therapist will record the complication in the study proforma and the patient's record. The study investigator will be informed as soon as possible by the physiotherapist of any complication that the therapist considers may interfere with the patient's capacity to continue with either programme.

6.2. Data Safety and Monitoring Board

An independent DSMB will be established to monitor the trial safety and where appropriate provide advice on issues regarding the scientific aspects of study conduct (eligibility, recruitment rates, and compliance/cross-overs) study safety (serious adverse events) and any emerging evidence as it relates to the trial. This board will comprise at least a rehabilitation physician, physiotherapist and a statistician/epidemiologist.

Early Termination

The study will be terminated early if access block to Braeside hospital becomes unmanageable because of the study. The primary investigator will inform the HREC if the study is terminated early. All enrolled patients will be notified of study termination by the primary investigator and future follow-ups will only be completed if the patient wishes.

7. BLINDING AND UNBLINDING

Any investigator or research officer involved in the follow-up assessments will be blinded to the treatment allocation. Patients and carers will be asked not to disclose their treatment allocation at the follow-up assessments. Blinding will not be possible for the treating physiotherapists, or the participants.

8.STATISTICAL CONSIDERATIONS

The primary endpoint in this trial is function at 6 months post surgery, measured using the outcome of a Six-Minute Walk Test (6MWT). A total minimum of 140 patients (minimum of 70 patients in each group) will provide 80% power and 95% confidence to detect a difference of 60m (SD 120m) in the in-hospital rehab group at 6 months when compared to the home based programme, and allows for 10% loss to follow-up.

9. CONFIDENTIALITY AND STORAGE AND ARCHIVING OF STUDY DOCUMENTS*

As per 2.2.2 in the Australian Code for the Responsible Conduct of Research,[27] the study data will be stored in the researcher's own department. That is, in the office of Mark Buhagiar at Braeside Hospital. The paper data will be stored in a locked cabinet in office which is locked when no research personnel are present and the database will be stored on Mr Buhagiar's M drive and be password protected. As per 2.2.3,[27] the researchers and the physiotherapists involved in providing therapy for the patients at Braeside, Sutherland, Campbelltown and Fairfield Hospitals have agreed that: the researchers will store study assessment data (such as KOOS surveys, six minute walk distances, exercise diaries) in the office of Mr Buhagiar; the physiotherapists will store their documentation relating to their treatment in the medical records at the two sites.

Once the data is entered into a computer database, the data will be coded, but will be re-identifiable. This is to permit future matching of data from a patient across time (pre-operative, at follow-up). At the conclusion of the analysis, the data will be non-identifiable.

The paper-based and electronic data will be stored in the researchers' department for 15 years as per 2.1.1 in Code.[27]

As stated in the NEAF (Section 8), confidentiality and patient privacy will be protected a variety of ways:

- Data will be coded once entered into the computer and the file will be password protected and only viewed by investigators. Paper copies of study documents and audio tapes will be stored in a locked filling cabinet in the researchers' office.
- Information collected will not be used for any other purpose beyond that stated.
- When disseminating the results, no individuals will be identified or identifiable.

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The Study Protocol was published in 2013 -

Buhagiar M et al. Hospital Inpatient versus HOme-based rehabilitation after knee arthroplasty (The HIHO study): study protocol for a randomized controlled trial. Trials 2013; 14:432.

The study was registered prospectively in April 2012 on a clinical trials registry - U.S. National Institutes of Health Clinical Trials Registry ref: NCT01583153.

eMethods1. Statistical analysis plan

HIHO STATISTICAL ANALYTICAL PLAN (SAP) – JANUARY 2014

Background

HIHO is a 2-armed parallel randomised controlled trial comparing 10 days on inpatient rehabilitation followed by a hybrid home program (usual care) to a hybrid program alone in people who have undergone a TKA. A third observational arm provides the opportunity to assess the effect of preference on the measured outcomes as well as assess generalisability of the randomised cohort.

Participants are randomly assigned via a central randomisation process to 1 of 2 arms. A centralised randomisation service will be used for participant randomisation using a 1:1 ratio, providing secure, coded randomisation via telephone. Group allocation, therefore, will be concealed from all parties until the result of the randomisation is known. Participants will be randomised to one of the two intervention groups using the method of minimisation stratified for variables that affect the primary outcome (distance walked in the 6MWT - age (≤68 y, >68 y), height (≤163 cm, >163 cm), and gender.

Participants are followed up by an assessor blind to treatment allocation at 10, 26 and 52 weeks.

Neither therapists or participants are blind to the intervention received.

Different therapists are involved in the delivery of the inpatient and home-based programs.

Data management

Data will be sent by blinded assessors to blinded data entry staff for collation and data entry, with range checks for data values. All databases will be password protected and stored in secure areas. Data will be checked for accuracy against the source documents by the study coordinator after all participants are randomized and then when all participants have had their final follow-up.

Statistical plan

Outcome measures: The primary outcome and most secondary outcomes will be measured pre-operatively, at week 10 (the time when the home program formally ceases), and then at 6 and 12 months post-randomisation. Assessments will be performed by an observer blinded to the participants' study allocation.

The primary endpoint in this trial is functional mobility at 6 months post-surgery measured using the distance walked during a 6MWT. Seventy participants in each group (140 in total) will provide 80% power at a significance level of 5%, to detect an increase in walking capacity from 400 m to 460 m between the Home and Inpatient groups respectively in the six-minute walk test at six months post-surgery, assuming a SD of 120 m and a drop-out rate of < 10%. With the addition of a second recruitment site, the definitive sample is expected to be approximately 160 participants, allowing us to increase the power of the study.

In the absence of data describing the minimum clinically important difference (MCID) for the 6MWT, a sub-study is now included to evaluate the MCID/MID for measured mobility in this population.

Descriptive analyses at baseline

Comparability of intervention groups will be investigated at baseline. Descriptive statistics will be presented, including summary statistics of potential confounding variables.

Analyses subsets

Data analysis will be completed using the principle of intention-to-treat (ITT) [1]. We will include all randomised participants regardless of level of compliance with the protocol. The primary outcome variable is distance measured using the outcome of a 6MWT at 26 weeks.

Analysis of covariance will be used for this primary outcome, with treatment group as the main study factor and walking distance at baseline, weight, co-morbidities and patient preference as covariates. For participants with a missing outcome measure at 26 weeks, an imputation method will be used [1,2].

The secondary outcome variables include the 6MWT at 10 and 52 weeks post-surgery, the 15 metre walk test, EQ5D, Oxford Knee Score, KOOS and knee ROM at most post-surgery time points.

Mixed model analyses will be used for the continuous variables measured repeatedly at 10, 26 and 52 weeks to estimate the treatment group by time effects. These analyses incorporate the missing data that may occur at the follow up occasions. Baseline measurements of the outcome variables, together with factors, such as weight, co-morbidities and patient preference, will be included as covariates. For the binary outcome measured 10, 26 and 52 weeks (knee flexion $> 100^{o}$ or $\leq 100\ ^{o}$), a Generalised Estimating Equation model will be used to test the treatment effect, with the adjustment of the covariates as above.

For the sensitivity analysis, we will also perform a per protocol analysis including only patients who complied with the treatment protocol. Compliance for HI group will be defined as attendance of a minimum of 7 days of inpatient rehabilitation, along with attendance at no less than two outpatient sessions and no more than five. Compliance for the HO group will be defined as attendance at no less than two outpatient sessions and no more than five.

There will be procedures put in place to minimise loss to follow-up, such as obtaining multiple contact details at time of consent and reminders that assessments are due. The age, gender and height of participants will be used as stratification variables in the randomisation procedure via a minimisation algorithm. The mixed model analysis indicated above will include these three variables as additional covariates to incorporate the possible within treatment group correlation associated with by stratification [3].

For the analyses involving the observational arm, the change score in the primary outcome will be compared between the observational group and those in the randomised home group adjusting for other covariates. A lack of significant difference in scores between the two groups will suggest there is no strong preference effect in this trial and we may not need to include preference as a covariate in the RCT analyses. To be consistent with the two RCT groups, we will aim for a minimum 64 participants in the observational group.

Cost-effectiveness analysis will be undertaken if the inpatient arm is shown to be superior. Due to limited funding, we will no longer utilize data from the PBS or Medicare. Costs will be based on standardized unit prices and based on patient diaries of expenses.

References

1. Sterne J, White I, Carlin J et al: Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009; 338: b2393.
2. Donders R, van der Heijdenc G, Stijnend T, Moonsc K: Review: A gentle introduction to imputation of missing values. *J Clin Epi* 2006 59: 1087e-1091.
3. Additional analyses [http://www.consort-statement.org/consort-statement/3-12---methods/item12b_additional-analyses/]