UK **F**ull Randomised Controlled Trial of **A**rthroscopic **S**urgery for **H**ip **I**mpingement versus best C**oN**ventional care

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CLINICAL TRIALS UNIT

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National Institute for Health Research

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Abbreviations

AE – Adverse Event

CA – Conversation analysis

CI – Chief Investigator

ConDuct – Collaboration and Innovation in Difficult and Complex Randomised Controlled Trials

CONSORT - Consolidated Standards of Reporting Trials

CRF – Clinical Reporting Form

CT – Computed Tomography

CTU – Clinical Trials Unit

DMC – Data Monitoring Committee

EQ-5D - EuroQol

FAI - Femoro-acetabular impingement

FASHIoN - Full of arthroscopic surgery for hip impingement compared with personalised hip therapy

HTA- Health Technology Assessment

iHOT-33 - International Hip Outcome Tool

HOS – Hip outcome score

IQR – Integrated Qualitative Research

MR – Magnetic Resonance

MRC – medical research council

NAHS – Non-arthritic Hip Scale

NHS – National Health Service

NICE – National Institute for Health and Clinical Excellence

PI – Principal Investigator

PIS – Patient information sheet

QA – Quality Assurance

QALY – Quality Adjusted Life Year

RCT- Randomised Controlled Trial

REC – Research Ethics Committee

RF – Research Fellow

SAE – Serious Adverse Event

SAP – Statistical Analysis Plan

SD – Standard Deviation

SOP – Standard Operating Procedures

SF -12 – Short form-12

TMG – Trial Management Group

TSC – Trial Steering Committee

UCLA – University of California, Los Angeles

UHCW – University Hospitals Coventry and Warwickshire

WOMAC – Western Ontario and Mcmaster University Osteoarthritis index

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Wrightington, Wigan and Leigh NHS Foundation Trust
Northumbria NHS Trust
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2. Background

2.1 Femoroacetabular impingement (FAI)

Until recently, there was little understanding of the causes of hip pain in young adults. A few of these patients had established osteoarthritis, inflammatory arthritis, avascular necrosis, fractures or childhood hip disease, but the majority had no specific diagnosis. In the last few years there has been increasing recognition of the syndrome of FAI, which seems to account for a large proportion of the previously undiagnosed cases of hip pain in young adults.[1,2] Subtle deformities in the shape of the hip (ball and socket joint) combine to cause impingement between femoral head (ball) or neck and the anterior rim of the acetabulum (socket), most often in flexion and internal rotation.[1,3] Excess contact forces lead to damage to the acetabular labrum (fibrocartilage rim of the socket) and the adjacent acetabular cartilage surface.[1] FAI seems to be associated with progressive articular degeneration of the acetabulum and may account for a significant proportion of so called idiopathic osteoarthritis, although this remains unproven.[3] The shape abnormalities of the hip joint are typically divided into three categories:[3]

- Cam-type, in which the femoral head is oval rather than round, or there is prominent bone on the femoral neck;
- Pincer-type, in which the rim of the acetabulum is too prominent, in one or more areas of its circumference;
- Mixed-type hip impingement, which is a combination of cam and pincer types.

Surgery can be performed to improve bone shapes in order to prevent impingement between the femoral neck and rim of the acetabulum. In the case of cam-type FAI this usually involves removal of bone at the femoral head-neck junction. In the case of pincer-type FAI, it may involve removal of bone at the rim of the acetabulum. At the same time as bony shape improvement, any soft tissue damage to the cartilage or labrum as a result of the FAI is debrided, repaired or reconstructed. Surgery can be undertaken using either keyhole (arthroscopic surgery) or more traditional open surgery to access the hip joint and correct the hip shape abnormalities associated with FAI.

Surgery for FAI has evolved more quickly than our understanding of the epidemiology or natural history of the condition[4-8], yet it is becoming an established treatment within the NHS. The risks of complications from open surgery are greater than those for arthroscopic surgery[9] and current evidence suggests that the outcomes of arthroscopic treatment for the symptoms of FAI are comparable to open surgery.[10] Consequently, hip arthroscopy for FAI is a rapidly growing new cost pressure for the NHS. Three systematic reviews have shown that no RCTs have been conducted to measure the clinical or cost effectiveness of either surgery or non-operative care for FAI[8,11-13], and we have recently confirmed this in a Cochrane systematic review (not yet published). In particular there is no RCT of hip arthroscopy compared with conventional care in patients with FAI.

Multi-centre randomised controlled trials (RCTs) are acknowledged to be the best design for evaluating the effectiveness of health care interventions as they provide robust evidence.[14,15] However, there are often major challenges in performing RCTs of surgical technologies,[16] and there have been concerns that an RCT of hip arthroscopy in FAI might not be feasible.

2.2 Feasibility and pilot studies

A feasibility and pilot study commissioned by HTA (HTA 10/41) has been completed. It comprised: (i) a pre-pilot phase including patient and clinician surveys and interviews, and a systematic review of non-operative care; (ii) a workload survey of hip arthroscopy for FAI; (iii) development of best conventional care and arthroscopic surgery protocols; (iv) a pilot RCT to measure recruitment rate; and (v) an integrated programme of qualitative research (IQR) to understand and optimise recruitment.
The feasibility study followed the commissioning brief and specifically addressed the following parameters to inform the design of the proposed full-scale RCT:

2.2.1 Define eligibility criteria

The eligibility criteria were initially designed in collaboration with the *Multicenter Arthroscopy of the Hip Outcomes Research Network* (MAHORN) - an academic group of highly experienced hip arthroscopists within the *International Society for Hip Arthroscopy* (www.isha.net). These criteria were then discussed with a further sample of 14 UK specialist hip surgeons with experience of treating patients with FAI. In

individual interviews, a variety of clinical scenarios were presented to them, and they were asked to describe decision making for treatment. Minor modifications were made to the eligibility criteria. These criteria were then tested during recruitment of real patients during the pilot RCT. They were found to be easy to apply, with little disagreement among clinicians.

2.2.2 Define a protocol for hip arthroscopy for FAI

A draft protocol for arthroscopic treatment of FAI was developed in a consensus conference with MAHORN members. This draft was circulated among the sample of 14 UK hip surgeons for feedback. After editing it was re-circulated, and agreed by all. The protocol was then tested in 21 participants randomised to surgery in the pilot trial. We also developed a method to measure fidelity by intra-operative photographs and post-operative MRI, assessed by a panel of independent international experts. We showed that this approach was acceptable to surgeons, and demonstrated complete adherence to protocol in 6 out of 7 operations at the first panel conference.

2.2.3 Define a protocol for best conventional care (comparator)

We performed a systematic review of non-operative care for FAI. This revealed little evidence of a standard for best conventional care, even though many NHS commissioners describe 'failure of conventional care' as a prerequisite for surgery.[17] There was some evidence that physiotherapy-led non-operative care is most frequently used.[11] This is complemented by established theory and evidence supporting treatment effects for physiotherapy in other painful musculoskeletal conditions including osteoarthritis and back pain.[18,19]

We used a combination of consensus methods (Delphi and Nominal Group techniques) among physiotherapists to agree a protocol for 'best conventional care'. We advertised to relevant networks of the Chartered Society of Physiotherapy (CSP) through their interactive communication system (iCSP) and in the *Frontline* magazine (twice monthly magazine posted to 52,000 CSP members in the UK). These advertisements invited physiotherapists to help develop a consensus for a best conventional care treatment protocol for FAI. Electronic invitations were also sent to physiotherapists in the United States and Australia known to us through previous collaborative work on FAI. To encourage a process of 'snowball sampling' within the international community, these therapists were encouraged to invite colleagues with experience and interest in managing FAI to join in the consensus process.

We developed a physiotherapy-led, four component protocol, to be delivered over 12 weeks with a minimum of 6 one-to-one treatment sessions. It includes: (i) a detailed patient assessment; (ii) education and advice about FAI; (iii) help with pain relief including hip joint steroid injections; and (iv) an exercise programme that has the key features of individualisation, supervision and progression. We used a patient focus group to choose the most acceptable name for this protocol of best conventional care. The group made it clear that we should express that this was a coherent and valid alternative to surgery and different to physiotherapy likely to have been received already, and recommended the name Personalised Hip Therapy (PHT).

In the development of PHT we struck a balance between the need for a meaningful comparator for hip arthroscopy, the need to ensure PHT is different to previous physiotherapy that FAI patients may have experienced and the need for PHT to be deliverable in the NHS outside a trial. UK physiotherapists and patients felt that PHT was 'best' in that not all patients currently receive such a comprehensive package, but 'conventional' in that all its elements are widely used and the package is deliverable within usual constraints in the NHS. We tested the protocol, and a logbook approach to assessing fidelity, in 21 participants randomised to PHT in the pilot trial. The protocol was acceptable to patients and physiotherapists, and we demonstrated complete adherence in 7 of the first 8 participants.

2.2.4 Define willingness of centres and patients to be recruited to an RCT

We performed a survey of all orthopaedic surgery departments in NHS hospital trusts in the UK. Clinical directors of those departments reported that 120 consultant surgeons were treating FAI. We contacted all of these surgeons, who reported having performed 2399 operations for FAI in 2011/2012; 1908 were performed by hip arthroscopy compared to 491 open surgery.[20] Thirty-four hospital trusts had a workload of 20 or more hip arthroscopies for FAI in a year. We interviewed 18 of the highest volume surgeons to explore their views about a trial comparing hip arthroscopy and best conventional care in patients with

FAI. One surgeon felt that he could not participate in a trial because he was certain that surgery worked; five had a bias toward surgery but recognised the need for a trial and were prepared to randomise patients; 12 expressed equipoise and were keen to take part in a trial.

We purposively sampled 18 patients who had been treated for FAI. Fourteen of them had received arthroscopic surgery and five had received physical therapy and steroid injections (one had both). These patients had a semi-structured interview with a qualitative researcher who had not been involved in their care, to explore their experiences of diagnosis and treatment, and their views on the proposed trial. The majority of the patients were young and physically active. Symptoms of FAI had affected their work, recreation and day-to-day activities: many reported a great sense of relief when a diagnosis was made. Patients said that both surgical and conventional care would be acceptable. The majority saw surgery as the solution for a condition that they perceived as mainly caused by abnormal bone shapes. On the other hand, non-operative care was perceived as attractive if it might be successful and could avoid the risks of surgery. Some commented that they had not been offered a non-operative option and saw this as a positive addition to available treatments. Patients were enthusiastic about research in this field, and about being involved, but had reservations about some of the language involved: to them, 'trial', 'random' and '50:50 chance' implied a lack of personalised care. All of these patients said that they would have been prepared to take part in an RCT as long as the treatment options and uncertainty around them had been fully explained, the treatment they received had been personalised for them, and they were assured that their care would be continued whatever happened in the research.

Our findings in these in-depth interviews are broadly consistent with a questionnaire survey of 30 surgeons who performed FAI surgery, and 31 patients with a diagnosis of FAI.[21] In that study, 71% of surgeons and 90% of patients felt that a trial of this question was appropriate.

We concluded that surgeons in most centres in the UK that perform hip arthroscopy for FAI, and their patients, would be willing to be included in a RCT.

2.2.5 Understand and optimise recruitment

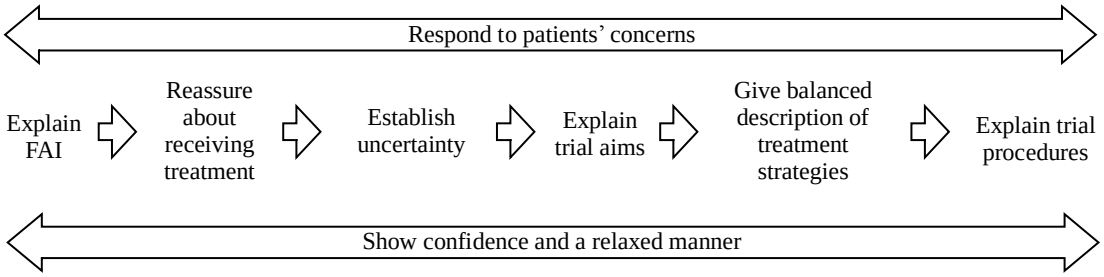
An important objective of the pilot trial was to explore likely issues in recruitment and to develop optimum procedures for the full trial.

We interviewed all principal investigators and research associates during the pilot trial to ensure that the study was being described, and recruitment procedures followed, according to the study protocol, and to identify where they were not. We developed training packages to correct common problems. We identified structural features associated with successful recruitment, such as running targeted clinics, having a dedicated research associate in attendance, and ensuring referred patients arrived with expectations of receiving *treatment* for FAI rather than being told they had been referred for surgery. This learning was shared across all sites.

We recorded and analysed 87 diagnostic and recruitment consultations with 60 new patients during the pilot trial. We identified where improvements could be made in presenting trial information and in engaging patients to consider participation, guided by our previous work.[22,23] The analysis was targeted at the recruitment levels at specific sites, with individual confidential feedback for recruiters on good practice and areas for improvement, and with anonymised findings being fed back to all sites.

Common difficulties with recruitment that were identified included: poorly balanced presentations of treatment options, where surgery was presented at greater length and more favourably compared than PHT; graphic descriptions of surgery that may have put patients off that option or discouraged participation; presenting trial information in an order that was confusing for patients; and surgeons going beyond their protocol brief, to explain the trial rather than referring patients to the trial recruiter for this information. Analysis of the consultations led to the development of a six-step model for presentation of trial information (Figure 1) to optimise recruitment.

Figure 1: Six-step model for recruitment to the FASHIoN trial



2.2.6 Estimate recruitment rate

Ten clinical centres participated in the pilot trial; nine opened to recruitment within 6 months. At one site, local R&D approval was delayed until just before the end of the pilot, so no patients were recruited. Recruitment rates are shown in Table 1.

Table 1: Recruitment rates for ten sites involved in the pilot trial

Site	Recruitment duration (months)	Eligible patients	Recruited patients	Eligible patients per month	Recruited patients per month	Recruitment %
1	9.3	24	19	2.6	2.1	79
2	7.1	7	3	1.0	0.4	42
3	4.4	3	2	0.7	0.5	66
4	5.0	6	3	1.2	0.6	50
5	4.1	4	4	1.0	1.0	100
6	3.1	4	4	1.3	1.3	100
7	3.0	1	1	0.3	0.3	100
8	2.8	10	5	3.6	1.8	50
9	2.2	1	1	0.5	0.5	100
10	n/a	n/a	n/a	n/a	n/a	n/a
Mean	4.6	6.7	4.7	1.5	1.0	**70 (95%CI 58-81)**

Of 144 potentially eligible patients with hip problems identified at pre-clinic screening of referral letters, 60 met the inclusion criteria after assessment, and were approached for randomisation. The most frequent reasons for exclusion were a diagnosis other than FAI (53/84) and a judgement that the patient would not benefit from arthroscopic surgery (21/84). Forty-two patients (70% of those eligible) consented to take part in the pilot RCT. Among those who declined (18), the most common reasons were a preference for surgery (11/18) and a preference not to have surgery (3/18). The mean duration and recruitment rate across all sites was 4.5 months and 1 patient per centre per month respectively. The lead site recruited for the longest period (9.3 months) and recruited the largest number of patients (2.1 patients per month).

2.2.7 Selection of appropriate outcome measures

A variety of outcome measures have been used to study patients with FAI. Some, such as the Western Ontario and McMaster Universities Arthritis Index (WOMAC)[24] and the Harris Hip Score[25], were intended for older patients with symptoms of severe arthritis, and are most suitable to measure the effect of hip replacement surgery. These measures tend to exhibit ceiling effects and are not sensitive to change after treatment in patients with FAI.[25,26]

The Non-Arthritic Hip Score (NAHS) is a self-administered instrument to measure hip-related pain and function in younger patients without arthritis. The score is valid compared to other measures of hip

performance, internally consistent and reproducible.[27] However, it is not patient-derived, raising concern that it may not measure what is most important to patients.

The International Hip Outcome Tool (iHOT) is a patient-derived, hip specific, patient-reported instrument, which measures health-related quality of life in young, active patients with hip disorders.[18] It was developed by a large international collaboration of patients and clinicians led by MAHORN over five years. It comprises 33 items, each measured on a visual analogue scale, to assess functional limitations, sports activities, job related and emotional concerns. Importantly, these items were generated and refined by patients, reflecting their most important concerns. The instrument generates a single score in the range 0-100. People with no hip complaints usually score 95 or more; a diverse international population of younger adults with a variety of hip pathologies had a mean score of 66 with a standard deviation of 19.3.

iHOT has been validated for use in patients with FAI, and is sensitive to change after treatment for FAI. The minimum clinically important difference (MCID) has been determined using an anchor and distribution-based approach in a group of 27 young active patients that were independent of the development population. Clinical change was determined using a global rating scale that asked patients whether their hip condition had improved, had deteriorated, or had not changed since the previous assessment, using a single VAS. The MCID was 6.1points[28-30]. This is equivalent to...
iHOT and EQ-5D have been adopted as the principal outcome measures by the UK Non-Arthritic Hip Registry. This Registry is led by the British Hip Society; its use in all patients having arthroscopic FAI surgery is required by the National Institute for Health and Care Excellence (NICE)[31].
In our pilot study we tested NAHS and iHOT-33 as potential primary outcome measures, and found both to be easy to use and acceptable to patients. The extensive patient involvement in item generation, the availability of an independently determined MCID and the use of iHOT as the principal outcome measure for the UK Non-Arthritic Hip Registry led us to choose iHOT-33 as the most appropriate primary outcome measure for a full trial.

2.2.8 Estimate effect size and standard deviation of the primary outcome

The standard deviation (SD) of iHOT-33 has been reported to be 19.3 in a population of patients undergoing hip arthroscopy for a variety of conditions.[26] In our pilot study, the baseline iHOT-33 data of patients who were suitable for inclusion had a SD of 16.0, suggesting that the population of patients with FAI is more homogenous. This is consistent with an observational study over several years by one of our team (Griffin), which showed an SD of 14 iHOT points among FAI patients who had no radiographic signs of arthritis.

Observational studies have measured clinical improvement after hip arthroscopy in FAI patients and a recent systematic review suggests that the effect size in these studies is between 0.67 and 2.95.[13] However, these are descriptions of the mean change in a group of patients before and after one treatment rather than the difference between two groups of patients having two different treatments. In addition an effect size of 2 has also reported in the literature for hip arthroscopy, but not specifically for arthroscopic FAI surgery.[26] We anticipate that conventional care is likely to provide some benefit, and suggest that the real effect size of arthroscopy compared to best conventional care might be around 0.5.

2.2.9 Develop and test trial procedures

Protocols, eligibility criteria, patient information material and case report forms were designed for the pilot RCT and will be available for the full trial. We interviewed 18 patients who had been treated for FAI to develop patient information sheets. These were scrutinised by a panel of expert patients with FAI, who helped to improve the content and presentation so that they addressed patients' key concerns and information needs, and provided explanations with appropriate language and detail. 28 clinicians, including surgeons, physicians and physiotherapists, also contributed to developing these procedures and documents.
Research Ethics Committee (REC) and National Research and Development (R&D) approvals were granted for the pilot trial promptly and without any significant concerns. The majority of the recruitment sites were then able to complete local approval within a month of our site initiation visits. Typical causes for a delay to approval were identified within the first few sites allowing these to be addressed in

subsequent sites at a much earlier stage. This will help considerably to ensure further sites in a full trial can obtain local R&D approval more quickly.

2.2.10 Calculate sample size for a definitive study

We designed a definitive study; the sample size calculation is presented in paragraph 3.7 below.

2.2.11 Conclusion of the feasibility study and pilot trial

We showed that a robust RCT of hip arthroscopy versus best conventional care for patients with FAI is feasible, that patients and clinicians were willing to participate, that we were able to obtain ethics and R&D approval at multiple sites, and that the trial procedures we developed work well. The pilot trial recruited successfully (70% recruitment rate) to the protocol that will be used for the full trial; these patients can therefore be included in the full trial analysis.

2.3 Relevance of project

Young adults with hip pain are now often aware of the diagnosis of FAI. There are many descriptions in the scientific literature, popular press, and on the internet, but there is an overwhelming focus on the benefits of surgery with little regard to other treatments.[1,11] With limited evidence of effectiveness and a significant increase in the cost of arthroscopic surgery (NHS tariff for hip arthroscopy £5200), a number of NHS care commissioners have begun to limit the funding for this procedure. In some areas, hip arthroscopy is not commissioned at all, in others, only patients who have failed to respond to non-operative treatment are allowed access to arthroscopic surgery.[17] Provision of non-operative alternatives to surgery for FAI is inconsistent, and the evidence and guidance for this conventional care is weak.[11] PHT is a credible physiotherapy-led “best conventional care” protocol for FAI, developed for the pilot trial through clinical consensus informed by existing literature. The proposed full trial will establish the best treatment for patients with FAI, taking into account clinical effectiveness, costs and risks. This will allow clinicians within the NHS to offer treatment for FAI that is in patients’ best interests. Establishing the comparative cost-effectiveness of arthroscopy and PHT will help NHS commissioners to make funding decisions based on robust evidence and to avoid the current situation of unjustified variation in provision.

3. Study design

3.1 Research Question

What is the clinical and cost-effectiveness of hip arthroscopy for femoroacetabular impingement compared to best conventional care?

3.2 Primary objective

To measure the clinical effectiveness of hip arthroscopy compared with best conventional care for patients with femoroacetabular impingement, assessed by patient-reported hip-specific quality of life after one year.

3.3 Secondary objective

- To compare differences in general health status and in health-related quality of life after 12 months between treatment groups.
- To compare, in a longitudinal analysis, the pattern of clinical change over 12 months.
- To compare patient satisfaction with treatment and outcome after one year.
- To compare the number and severity of adverse events after treatment.
- To compare the need for further procedures up to three years.
- To compare the cost-effectiveness of hip arthroscopy for FAI with best conventional care, within the trial, and for a patient's lifetime.
- To develop and report processes to optimise recruitment in an RCT or surgery versus non-operative care.
- To measure fidelity of delivery of interventions.

3.4 Study summary

This is a pragmatic, multi-centre, randomised controlled trial of hip arthroscopy versus best conventional care for femoroacetabular impingement (FAI).

In patients with symptoms of FAI, we will determine whether arthroscopic surgery provides a beneficial effect in patient-reported quality of life compared with personalised hip therapy (PHT, a protocol for best conservative care). We will also compare patient satisfaction, need for further procedures, risk of complications and cost-effectiveness for the two treatment strategies.

We have performed a feasibility study and pilot trial, which demonstrated that patient recruitment is possible and that the patient eligibility criteria, trial procedures, follow-up and outcome assessment processes that we developed are working well. The internal pilot trial has already recruited 42 patients. In this proposal we intend to recruit a further 302 patients (344 including pilot patients) from 25 hospitals throughout the UK over 20 months.

Patients will be randomly allocated to one of the two trial treatments. The primary outcome, the International Hip Outcome Tool-33 (iHOT-33) score, will be measured at 12 months post-randomisation. iHOT-33 is a patient reported quality of life tool specifically designed for young adults with hip disorders. Secondary outcome measures include number and type of adverse events, need for further procedures, health-related quality of life and patient satisfaction. The incremental cost and cost-effectiveness of hip arthroscopy compared with best conventional care will be evaluated from NHS and societal perspectives; with cost-effectiveness being calculated using both within trial and lifetime horizons.

An integrated programme of qualitative research will monitor and facilitate recruitment, and explore patients' experiences of both treatment strategies and of their outcomes.

3.5 Eligibility Criteria

Patients are eligible to be included in the trial if they meet the following criteria:

3.5.1 Inclusion criteria

- Age ≥16 (no upper age limit);
- Symptoms of hip pain - patients may also have symptoms of clicking, catching or giving way;
- *Radiographic evidence of pincer- and/or cam-type FAI morphology on plain radiographs and cross-sectional imaging, defined as:*
  i Cam morphology - an alpha angle >55º;
  ii Pincer morphology - a lateral centre edge angle of >40 degrees or a crossover sign on the anteroposterior radiograph of the pelvis;[32]
- The treating surgeon believes the patient would benefit from arthroscopic FAI surgery;
- The patient is able to give written informed consent and to participate fully in the interventions and follow-up procedures.

3.5.2 Exclusion criteria

- Evidence of pre-existing osteoarthritis, defined as Tonnis grade >1[33], or more than 2mm loss of superior joint space width on AP pelvic radiograph[34];
- Previous significant hip pathology such as Perthes' disease, slipped upper femoral epiphysis, or avascular necrosis;
- Previous hip injury such as acetabular fracture, hip dislocation or femoral neck fracture;
- Previous shape changing surgery (open or arthroscopic) in the hip being considered for treatment;

3.6 Recruitment

See Figure 2 – Flow Diagram

Participants will be recruited from amongst the patients presenting to young adult hip clinics in each of the centres.

Screening of referrals

Possible FAI patients (younger adults with hip pain) will be identified by collaborating surgeons from referral letters. These patients will be invited to a diagnostic consultation with one of the collaborating surgeons. Prior to their appointment, these patients will be approached to seek consent for recording of their clinic consultations.

Diagnostic consultation

Surgeons will assess patients as usual, taking a history, examining the patient, and performing appropriate imaging investigations. Patients in whom a diagnosis of FAI is made, and who meet the eligibility criteria, will receive a description of the condition from their surgeon and an explanation that there are two possible treatments: an operation or a package of personalised hip therapy. They will be given patient information about FAI and the trial. Patients will be invited to a trial information consultation to discuss what action they would like to take.

Trial information consultation

Patients will attend a Trial Information Consultation with a trained clinical researcher. Information will again be provided about FAI and its possible treatments, and about the trial. Patients will be given an opportunity to ask questions. Patients will then be invited to give their consent to become participants in the trial. Patients who wish to take more time to consider will be given an opportunity to do so. Patients who agree to take part will complete baseline questionnaires at this consultation.

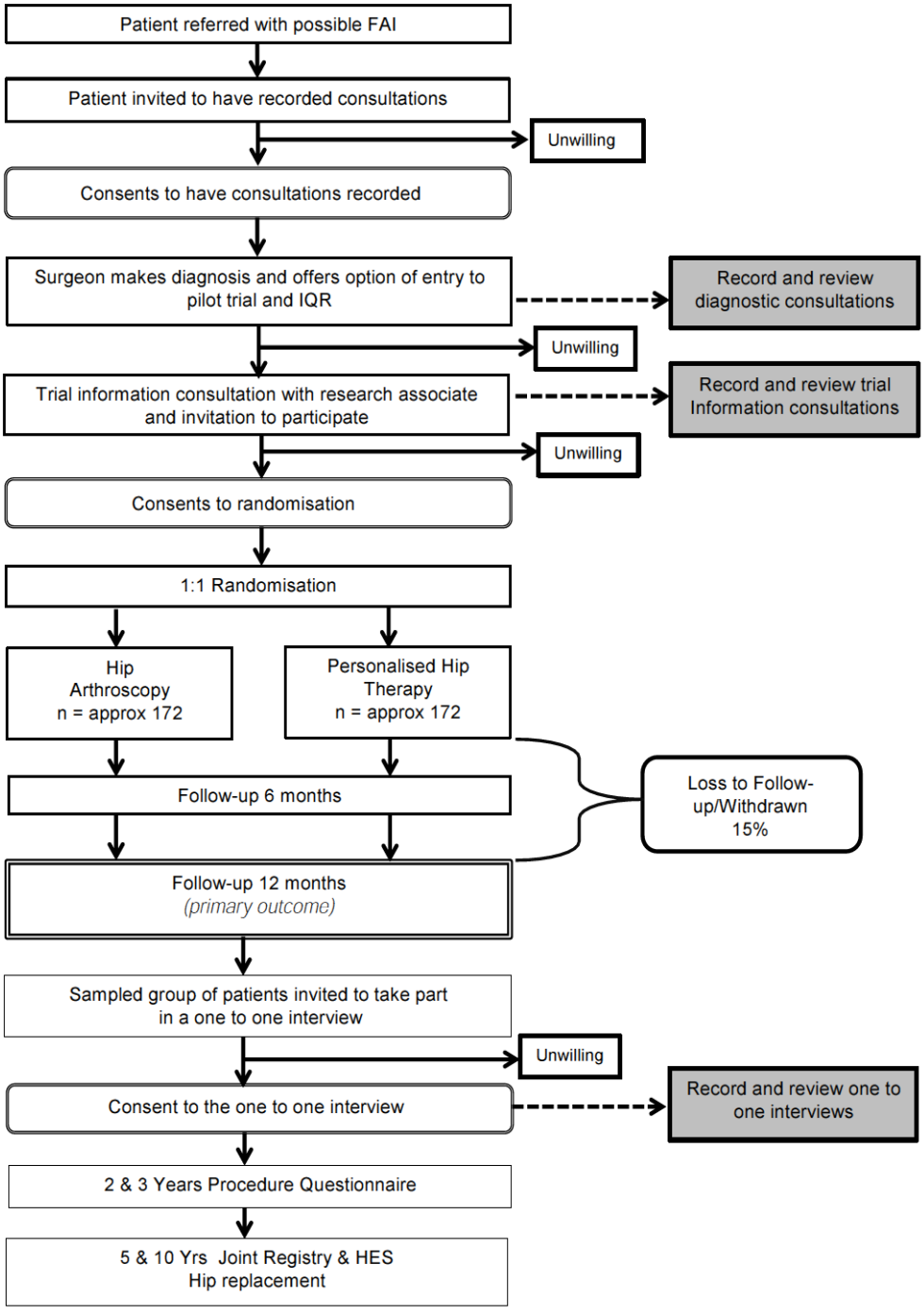
Treatment allocation

Participants will be randomly allocated to arthroscopic surgery and post-operative rehabilitation or personalised hip therapy using 1:1 secure centralised telephone randomisation provided by Warwick CTU. Patients will usually be informed of their allocation at the Trial Information Consultation, and plans for delivery of the intervention will begin to be made there. The recruiting centre and FAI type will be used as stratifying factors when randomising.

Post randomisation withdrawals

Participants may withdraw from the trial treatment and/or the whole trial at any time without prejudice. If a participant decides to change from the treatment to which they were allocated, they will be followed-up and data collected as per the protocol until the end of the trial. However, every effort will be made to minimise crossovers from both intervention arms. It will be made clear to study participants and clinicians that it is important for the integrity of the trial that everyone follows their allocated treatment. For those participants who do decide to move to the other intervention arm, the numbers, direction and reasons for moving will be recorded and reported in line with CONSORT guidance. The IQR will investigate how and why the participant made their decision. The IQR team will provide training for physiotherapists and surgeons, so that they are equipped to answer patients' questions about the trial during treatment. During the pilot trial, we found that this reduced the risk of participants losing confidence in the trial and breaching protocol.

Figure2–Flow diagram



3.6.1 Blinding

The patients cannot be blind to their treatment. The treating surgeons will, of course, not be blind to the treatment, but will take no part in outcome assessment for the trial. The functional outcome data will be collected and entered onto the trial central database via postal questionnaire by a research assistant who will be blind to the treatment allocation. The statistical analysis will also be performed blind.

3.6.2 Consent

Written informed consent will be obtained by a researcher delegated and trained by the research team. In general, patients will have at least one month from initial consultation to the day of surgery or start of personalised hip therapy so there will be sufficient time for the patients to consider taking part in the trial. Any new information that arises during the trial that may affect patients' willingness to take part will be reviewed by the Trial Management Group; if necessary this will be communicated to all participants by the Study Manager. A revised patient information sheet (PIS) will be provided and revised consent form will be completed if necessary.

3.7 Sample size

The development work for iHOT-33 reported a mean iHOT-33 score of 66 and a standard deviation of 19.3 in a heterogeneous population with a variety of hip pathologies. The baseline iHOT-33 data from our pilot trial suggests the target population of patients being considered for hip arthroscopy for FAI in the UK have lower scores with less variability, with a mean of 33 and SD of 16.

During our feasibility study, we estimated the likely effect size of hip arthroscopy compared to best conventional care for FAI to be 0.5. (see paragraph 2.2.8, above). The MCID for iHOT-33 in this population is 6.1 points.

Our sample size calculation is therefore based on a SD of 16 and MCID of 6.1: a standardised effect difference between groups at 12 months of 0.38. Table 2 shows the expected sample size for scenarios with 80% and 90% power to detect an effect of this size, at a 5% significance level, assuming an approximately normal distribution of the iHOT-33 score. The table also shows sample sizes for small to moderate (0.32) and moderate (0.47) effect differences, which are broadly consistent with other pragmatic RCTs measuring clinical effectiveness.

Table 2: Total sample size (n) for MCID = 6.1

Standard deviation	Power		Standardised effect difference
	80%	90%	
13.3	144	192	0.47
16.0	218	**292**	0.38
19.3	316	422	0.32

A recent systematic review of observational studies have reported effect sizes of hip arthroscopy for FAI of between 0.67 and 2.95 up to 5 years after surgery, but these are likely to be overestimates of the real effect we might measure in this trial.[13] They were uncontrolled studies, and we anticipate that our best conventional care protocol will provide some benefit.

We have, therefore, adopted a conservative approach, seeking to demonstrate an effect difference between groups equal to the MCID. We propose to recruit sufficient patients to be able to analyse 292 at 12 months follow-up. Allowing for 15% loss to follow-up, we will recruit a sample of 344 participants (172 in each group). This will provide 90% power to detect a difference of 6.1 iHOT-33 units, if that is the true difference. As 42 eligible patients have already been recruited from the internal pilot RCT, an additional 302 patients are required in the full trial.

3.8 Trial treatments

3.8.1 Arthroscopic hip surgery

An operative protocol was established during and implemented in the pilot trial. The agreed protocol is typical of the surgical techniques used by the majority of surgeons around the world, and representative of those used widely in the UK. The surgeons delivering the intervention are all NHS consultants specialising in hip arthroscopy.

Pre-operative.

Patients will all undergo routine preoperative care, which will include an assessment of their general health and suitability for a general anaesthetic.

Peri-operative.

Arthroscopic hip surgery will be performed under general anaesthesia in a lateral or supine position. Arthroscopic portals will be established in the central and peripheral compartment under radiographic guidance according to the surgeon's usual practice. Shape abnormalities and consequent labral and cartilage pathology will be treated. Bony resection at the acetabular rim and at the head-neck junction will be assessed by intraoperative image intensifier radiograph and/or satisfactory impingement free range of movement of the hip.

Post-operative.

Patients will be allowed home when they can walk safely with crutches (usually within 24h hours). On discharge all patients will be referred to outpatient physiotherapy services for a course of rehabilitation as per usual care for that surgeon. We will not specify a protocol for this post-operative physiotherapy, but will record it using a treatment log. These post-operative physiotherapists will be distinct from those providing PHT to avoid contamination between groups. Patients will also have a post-op MRI.

3.8.2 Personalised Hip Therapy

PHT is a package of physiotherapy-led best conventional care for FAI. It was developed during the feasibility study and 'road-tested' during the pilot trial. Although the name for this intervention is new, the care being offered represents a consensus of what physiotherapists, physicians and surgeons in the NHS currently provide, and regard as 'best conventional care' for FAI. PHT will be delivered by at least one qualified physiotherapist at each site, who will be trained in a FASHIoN PHT workshop. We developed and tested this one-day workshop during our pilot trial.

***Pre-treatment*.**

Participants will receive a PHT information pack that describes what to expect during the course of their treatment. The first core component of PHT is an assessment of pain, function and range of hip motion.

***Treatment*.**

PHT has three further core components: (i) an exercise programme that has the key features of individualisation, progression and supervision; (ii) education; and (iii) help with pain relief (which may include one X-ray or ultrasound guided intra-articular steroid injection where pain prevents performance of the exercise programme). The intervention is delivered over a minimum of 12 weeks with a minimum of 6 patient contacts. Some of the patient contacts are permissible using either telephone / email for whom geographical distance prevents all contacts being carried out face-to-face.

Post-treatment.

Typically, PHT will be delivered over a minimum of 12 weeks. However, in situations where the patient needs additional review, support or guidance, a further two booster sessions with the physiotherapists are permitted between 12 weeks and 6 months.

3.8.3 Timing of intervention

The two interventions will commence as soon as possible after randomisation. In our pilot trial, participants allocated to hip arthroscopy usually had surgery within 10 weeks, and those allocated to

PHT usually commenced treatment within a month, according to usual waiting list and capacity constraints. We will record dates of randomisation and of the start of allocated treatment.

3.9 Quality assurance of treatments

Assessing the fidelity of the intervention and control

The conclusions we can draw from this trial will depend on the fidelity with which the two treatment strategies are implemented during the trial. Fidelity is also important because we need to be clear at the end of the trial about exactly what strategy we recommend the NHS to adopt. We developed our fidelity assessments during the feasibility study and tested them during the pilot study.

3.9.1 Hip arthroscopy

Each participant will have post-operative 3-D shape imaging with a single sequence MR proton density volume acquisition. The anonymised encrypted scan will be sent by electronic transfer to Clinical Graphics B.V. based in the Netherlands. The sequence will then be surface rendered to create a 3-D shape model of the hip joint. Alpha and lateral centre edge angles will be measured on radial reconstructions. Hips that have evidence of continued abnormal shape (alpha angle >55° or lateral centre edge angle >40°) would may be deemed to not have undergone adequate shape modifying surgery depending upon the majority decision amongst an international expert panel who review this data along with a qualitative assessment of operation notes and intraoperative photographs to judge fidelity. This panel will include: Mark Philippon (USA; chairman of the Research Committee of the International Society for Hip Arthroscopy), Martin Beck (Switzerland; one of the investigators credited with developing the early understanding of FAI), John O'Donnell (Australia; President of the International Society of Hip Arthroscopy), and Professor Charles Hutchinson (UK; an expert in musculoskeletal radiology).

3.9.2 Personalised hip therapy

Physiotherapists will record full details of the advice and treatments, number and mode of treatment sessions, any non-attendance, and any adverse events for each patient on specifically designed case report forms. These case report forms will be reviewed for accuracy in comparison to the usual physiotherapy records at each treatment site and then assessed for fidelity by a panel comprising members of the core group who developed the protocol for PHT including: Foster (co-investigator), Hughes and Robinson (UK; senior extended scope musculoskeletal physiotherapists) and Wall (co-investigator).

3.9.3 Overall fidelity

The IQR team will observe a sample of clinicians and patients in each arm to record how the treatment interventions are delivered. Findings will be fed back to the CI and TMG so that practice can be reviewed and any necessary training or changes implemented. This research will be linked, through Donovan, to the programme of research within the MRC ConDuCT-II (Bristol) Trial Methodology Hub to investigate the complexity of surgical interventions and their fidelity

3.10 Outcome Measures

The primary outcome measure for this study is the International **Hip Outcome Tool-33 (iHOT-33)** at 12 months. iHOT-33 is a validated hip specific patient-reported outcome tool which measures health-related quality of life in young, active patients with hip disorders.[18] We chose it after work during our feasibility and pilot studies: it is more sensitive to change than other hip outcome tools and does not show evidence of floor or ceiling effects in patients undergoing hip arthroscopy[26]; patients were involved extensively in item generation, so we can be confident that it measures what is most important to patients; there is an independently determined MCID; and it is used as the principal outcome measure for the UK Non-Arthritic Hip Registry mandated for arthroscopic FAI surgery by NICE.

The secondary outcome measures in this trial are:

EuroQol EQ-5D

This is a validated measure of health-related quality of life, consisting of a five dimension health status classification system and a separate visual analogue scale. EQ-5D is applicable to a wide range of health conditions and treatments and provides a simple descriptive profile and a single index value for health status.[35] EQ-5D is primarily designed for self-completion by respondents

and is ideally suited for use in postal surveys, in clinics and face-to-face interviews. It is cognitively simple, taking only a few minutes to complete.[36]

Short Form-12.

This is a validated and widely-used health-related quality of life measure particularly including hip conditions and treatments.[37] SF-12 is able to produce the physical and mental component scales originally developed from the SF-36 with considerable accuracy and but far less respondent burden.[38]

Patient satisfaction

Using questions that our team (Foster) has used in previous trials with musculoskeletal pain patients[39], we will measure two distinct dimensions of satisfaction in all participants during follow-up: '*Overall, how satisfied are you with the treatment you received?'* and *'Overall*, *how satisfied are you with the results of your treatment?'* Responses are on a 5-point Likert scale. These questions are in line with previous studies of patient satisfaction which show that the majority of patients express overall satisfaction with the care they received, but fewer express overall satisfaction with the clinical outcomes resulting from their care.

Qualitative assessment of outcome

We will conduct in-depth interviews with a purposively selected sample of 25-30 participants in each of the study arms, including older and younger, male and female, more and less active, and more and less satisfied participants recruited at different locations, to explore their experiences of the treatments and outcomes, particularly focusing on aspects of treatment and outcome that are important to patients and may not necessarily be measured by the formal instruments. While face to face interviewing is usually better, telephone or skype may be more practical due to the geographical spread of the sites. Participants will be invited to and informed consent will be sought for an interview at the end of the trial.

Need for further procedures

We will record any further treatments performed in both arms, such as hip arthroscopy, open hip preservation surgery, hip replacement, or additional non-protocol physiotherapy. Observational evidence suggests that for patients who have hip arthroscopy for mild arthritis but whose symptoms subsequently deteriorate and require further surgery in the form of hip replacement, the mean time between the two operations is 2.2 years (range 0.2-5 years).[40] This is not precisely the situation for our patients being treated for FAI, but it provides the only available rationale for the duration of further follow-up for this outcome. We propose to ascertain the need for further procedures by questionnaire at two and three years. We also propose a 5 and 10-year no-cost ascertainment of hip replacement by linkage to the UK National Joint Registry and Hospital Episode Statistic (HES) databases.

Adverse Events

We will record number and type of adverse events up to 12 months (detailed in section 3.15).

Resource utilisation

Information on health care resource use (detailed in economic analysis, below) will be collected by incorporating questions within the patient follow-up questionnaires. We confirmed the feasibility and acceptability of this approach in our pilot trial, and patient self-reported information on service use has been shown to be accurate in terms of the intensity of use of different services.[41]

Follow-up

We will use techniques common in long-term cohort studies to ensure minimum loss to follow-up, such as collection of multiple contact addresses and telephone numbers, mobile telephone numbers and email addresses. Considerable efforts will be made by the trial team to keep in touch with patients throughout the trial by means of newsletters etc.

Follow-up questionnaires will be administered by post or email with 3 reminders and a final telephone call for minimum data collection.

Table 3: Data collection, Follow-up measures and time points.

Time point	*Data collection*
Baseline	Demographics, physical activity (UCLA Activity Scale), iHOT-33, SF-12,EQ-5D
	Preoperative imaging, economics questionnaire.
Intervention	Operation notes and photographs; or PHT log. Complications records 6 weeks post start of intervention. Post-op MRI (surgery intervention only)
6 months	iHOT-33, SF-12, EQ-5D, resource utilisation, adverse events
12 months (primary outcome)	**iHOT-33, SF-12, EQ-5D, patient satisfaction, resource utilisation, adverse events**
2 years	Further procedures questionnaire
3 years	Further procedures questionnaire
5 & 10 years	Linkage to National Joint Registry and HES to identify need for hip replacement

3.11 Good Clinical Practice

The trial will be conducted in accordance with the Medical Research Council's Good Clinical Practice (MRC GCP) principles and guidelines, the Declaration of Helsinki, Warwick Clinical Trials Unit SOPs, relevant UK legislation and the Protocol. GCP-trained personnel will conduct the trial.

3.12 Consort

The trial will be reported in line with the CONSORT statement.

3.13 Integrated qualitative study of recruitment (IQR)

Purpose

The IQR team will observe a sample of clinicians and patients in each arm to record how the treatment interventions are delivered. Findings will be fed back to the CI and TMG so that practice can be reviewed and any necessary training or changes implemented. This research will be linked, through Donovan, to the programme of research within the MRC ConDuCT-II (Bristol) Trial Methodology Hub to investigate the complexity of surgical interventions and their fidelity

Evaluation

Numbers of eligible patients, and the percentages of these that are approached about the RCT, consent to be randomised and immediately accept or reject the allocation will be assessed before the plan of action is implemented, and regularly afterwards to check whether rates are improving.

3.14 Risks and benefits

Both interventions are thought to provide benefit in patients with FAI. There is thought to be a long-term risk of osteoarthritis in patients with FAI. It is not known whether conservative care or arthroscopic surgery have an effect on this risk. The short-term risks of this study relate to the two interventions. These risks are described below:

3.14.1 Operative

Hip arthroscopy requires a general anaesthetic. The risk of complications from hip arthroscopy is about 1-2%[45]. These include:

- Infection – thought to be less than 1in 1000. If the infection occurred deep within the joint it may require more procedures to wash out the hip joint.
- Bleeding – possibly causing bruising or a local haematoma.

- Traction related – to allow the small arthroscopy instruments into the hip joint, traction is required to separate the hip joint surfaces. Sometimes after the procedure the pressure from the traction can cause some numbness in the groin, leg or foot. The numbness usually resolves within a few hours or days.
- Osteonecrosis – during surgery the blood supply to the hip joint could be damaged. However, there are no reported cases of osteonecrosis following arthroscopic hip impingement surgery so this is a very small risk.
- Femoral neck fractures - This is also a very rare complication. This complication would require a further procedure to fix the fracture.

3.14.2 Non-operative

There are some small risks with pain medications and joint injection. However, the main risk is muscle soreness and transient increases in pain from the exercises that will be undertaken.

3.15 Adverse events

Adverse events (AE) are defined as *any untoward medical occurrence in a clinical trial patient and which do not necessarily have a causal relationship with the treatment*. All AEs will be listed on the appropriate Case Report Form for routine return to the 'FASHIoN' central office.

Serious adverse events (SAE) are defined as any *untoward and unexpected medical occurrence that:*

1. *Results in death*,
2. *Is life-threatening*
3. *Requires hospitalisation or prolongation of existing inpatients´ hospitalisation*,
4. *Results in persistent or significant disability or incapacity*,
5. *Is a congenital anomaly or birth defect*
6. *Any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed*.

All SAEs will be entered onto the reporting form and faxed to dedicated fax at WMSCTU within 24 hours of the investigator becoming aware of them. Once received, causality and expectedness will be confirmed by the CI. SAEs that are deemed to be unexpected and related to the trial will be notified to the Research Ethics Committee (REC) within 15 days. All such events will be reported to the Trial Steering Committee and Data Monitoring Committee at their next meetings.

SAEs that may be expected as part of the surgical interventions, and that do not need to be reported to the main REC are: complications of anaesthesia or surgery (wound infection, bleeding or damage to adjacent structures such as nerves, tendons and blood vessels, delayed wound healing, and thromboembolic events, hip fracture, osteonecrosis and traction related neuropathies). SAEs that may be expected as part of the conservative care interventions and that do not need to be reported to the main REC are: transient increase in pain, delayed onset muscle soreness or mild bleeding at injection or acupuncture needle sites. All participants experiencing SAEs will be followed-up as per protocol until the end of the study period i.e. 12 months from study entry.

3.16 End of trial

The end of the trial will be defined as the collection of 10 year outcome data from the last participant.

The primary end point will be defined as the collection of 12 month outcome data from the last participant.

The trial will be stopped prematurely if:

- Mandated by Ethics Committee
- Following recommendations from the Data Monitoring and Ethics Committee (DMEC)
- Funding for the trial ceases

The Main Research Ethics committee (MREC) will be notified in writing within 15 days if the trial has been concluded or terminated early.

4. Data Management

Personal data collected during the trial will be handled and stored in accordance with the 1998 Data Protection Act. Post-op MRI data will be stored in accordance with the Netherlands 2001 Personal Data Protection Act.

The Case Report Forms and outcome questionnaires have been designed by the Study Manager in conjunction with the Chief Investigator and Statistician and have already been tested in the pilot RCT. Original CRFs must be sent to the co-ordinating team based at the CSRL and copies retained on site.

4.1 Database

The database will be set up by the Programming Team at WCTU and all specifications (i.e. database variables, validation checks, screens) will be agreed between the programmer, statistician and study manager.

4.2 Data Storage

All of the data collected in this trial will be entered into a secure trial database held at the Clinical Sciences Research Laboratories (CSRL) within the Clinical Sciences Building, University Hospitals Coventry and Warwickshire. All electronic patient-identifiable information will be held on a secure, password-protected database accessible only to essential personnel. Paper forms with patient-identifiable information will be held in secure, locked filing cabinets within a restricted area of the CSRL. Patients will be identified by a trial number only.

4.2.1 Post-op MRI Scans

Anonymised encrypted post-op MRI scans will be sent by electronic transfer to:-
Clinical Graphics B.V
Molengraaffsingel 12-14
2629 JD Delft,
The Netherlands.

Anonymised encrypted data will be stored on the company's website. Patients will be identified by a trial number only. On completion of the MRI quality review all data will be transferred for electronic storage to the Clinical Sciences Research Laboratories (CSRL).

4.3 Data Access & Data Quality Monitoring

All data collected will be anonymised after the collection of baseline demographic data, and all participants given a unique trial number. Identifiable participant data will be held in a locked filing cabinet and coded with a trial participant number to tag identifiable data to the outcome data. Names and addresses will not be disclosed to anyone other than staff involved in running the trial**.**

We will institute a rigorous programme of quality control. The senior trial manager in conjunction with the study manager will be responsible for ensuring adherence to the trial protocols at the trial sites. Quality assurance checks will be undertaken by Warwick CTU to ensure integrity of randomisation, study entry procedures and data collection. The Warwick CTU has a quality assurance manager who will monitor this trial by conducting regular (yearly or more if deemed necessary) inspections of the Trial Master File. Furthermore the processes of consent taking, randomisation, registration, provision of information and provision of treatment will be monitored. Written reports will be produced for the TSC, informing them if any corrective action is required.

4.4 Confidentiality

The personal data recorded on all documents will be regarded as strictly confidential. To preserve the patient's anonymity, only their initials date of birth and trial number will be recorded on the CRFs. With the patient's permission, their name and date of birth, address and health service (NHS) number /Community Health Index (CHI) number, if applicable, will be collected to allow flagging with the Office of National Statistics and to allow sample tracking.

For reference, the participants GP will be informed by letter that the patient is/has taken part in this clinical trial. Participants may deny the research team to inform the GP of their trial involvement by not initialing the appropriate box on the consent form.

Disclosure of confidential information will be permitted should the study team feel there is information that may jeopardise the safety of the participant or another person.

4.4 Archiving

Trial documentation and data will be archived for at least ten years after completion of the trial in accordance with WCTU SOPs.

5. Statistical Analysis

5.1 Descriptive analysis

Data will be checked for outliers and missing values, and validated using the defined score ranges for all outcome measures. Standard statistical summaries (e.g. medians and ranges or means and variances, dependent on the distribution of the outcome) and graphical plots showing correlations will be presented for the primary outcome measure and all secondary outcome measures. Baseline data will be summarized to check comparability between treatment arms, and to highlight any characteristic differences between those individuals in the study, those ineligible, and those eligible but withholding consent.

It seems likely that some data may not be available due to voluntary withdrawal of patients, lack of completion of individual data items or general loss to follow-up. Where possible the reasons for missing data will be ascertained and reported. If judged appropriate, missing data will be imputed using the multiple imputation facilities (mice package) available in R. Any imputation methods used for scores and other derived variables will be carefully considered and justified, and analysis of imputed datasets used to assess the sensitivity of the analysis to the missing data.

Although every effort will be made to minimise crossovers from both intervention arms, the numbers, direction and reasons for participants moving between arms will be recorded and reported in line with CONSORT guidance.

5.2 Main analysis

The primary analysis will be of differences in hip-related quality of life (iHOT-33) at 12 months between the two treatment groups, on an intention-to-treat basis, presented as the mean difference between the trial groups with a 95% confidence interval. iHOT-33 data will be assumed to be normally distributed; possibly after appropriate variance-stabilising transformation.

The stratified randomisation procedure should ensure treatment group balance across recruiting centres. We have no reason to expect that clustering effects will be important for this study, but the possibility of such effects will be explored as part of the analysis.[33] We plan to account for clustering by generalizing a conventional linear (fixed-effects) regression approach to a mixed-effects modelling approach; where patients are naturally grouped by recruiting centres (random-effects) and, if amenable to analysis, also by therapist and surgeon. This model will formally incorporate terms that allow for possible heterogeneity in responses for patients due to the recruiting centre, in addition to the fixed effects of the treatment groups, and patient characteristics that may prove to be important moderators of the treatment effect such as age, gender and FAI type. This analysis will be conducted using specialist mixed-effects modelling functions available in the software package R (http://www.r-project.org/).

Secondary analyses will be performed using the above strategy for other approximately normally distributed outcome measures including iHOT-33 at 6 months, SF-12 (and computed sub-scales) and EQ-5D. Differences in dichotomous outcome variables such as adverse events, complications related to the trial interventions and the need for further procedures will compared between groups using chi-squared tests (or Fisher's exact test) and mixed effects logistic regression analysis will be undertaken, adjusting for the stratifying variables, with differences between trial intervention groups quantified as odds ratios (and 95% confidence intervals). The temporal patterns of any complications will be presented graphically and if appropriate a time-to-event analysis (Kaplan-Meier survival analysis) will be used to assess the overall risk and risk within individual classes of complications. Ordinal scores for patient satisfaction will be compared between intervention groups using proportional odds logistic regression analysis, assuming that the estimated intervention effect between any pair of categories is equivalent.

Although our inferences will be drawn from the intention to treat-analysis, we will perform per protocol analyses to place these in context. We plan to perform a subgroup analysis by FAI type because it is likely that treatment effect is moderated by type: in our pilot trial there were a significant number of participants in each group (cam, 27; pincer, 6; mixed, 9). We do not anticipate that crossovers (i.e. participants moving between intervention arms) will be a major issue for this study. Therefore we expect the main ITT and PP analyses to provide definitive results. However, if not completing (adhering to) or following (complying with) the PHT proves to be more problematic than we expect, we will augment the planned analysis with a Complier Average Causal Effect (CACE) analysis. The Data Monitoring

Committee will monitor crossovers and adherence to treatment and advise on appropriate modifications to the statistical analysis plan as the full trial progresses.

The initial pilot study was designed explicitly to measure recruitment rates and assess feasibility, and not to estimate treatment efficacy. Data from the pilot stage will be pooled with data from the full trial, and analysed together. No issues are raised in this setting concerning type I error rate inflation, as treatment efficacy data from the pilot study were not used to decide whether to proceed to the full study. We do not anticipate that, and can see no reason why, outcomes might be different for participants recruited in the pilot phase to those recruited in the main phase of the study. However, as a routine part of the primary analysis the moderating effects of study phase (pilot versus main study) on the treatment group effect will be investigated, in an analogous manner to the other planned subgroup analysis for FAI type.

A statistical analysis plan (SAP) will be agreed with the Data Monitoring Committee (DMC) at the start of the study and published in a trial protocol paper. Any subsequent amendments to this initial SAP will be clearly stated and justified. Interim analyses will be performed only where directed by the DMC. The routine statistical analysis will mainly be carried out using R (http://www.r-project.org/).

5.3 Qualitative analysis

Recordings of interviews with participants and clinicians, and recruitment consultations, will be transcribed whole or in selected parts. Transcripts (or parts) will be coded using NVivo software[42], then cross-checked by a second researcher; inconsistencies will be resolved by discussion. Interview transcripts will be analysed thematically, using methods of constant comparison derived from grounded theory.[43] Emerging themes will be explored, looking for shared or disparate views among patients about their experiences, and among clinicians about their experiences of delivering the trial interventions. Focused conversation analysis will be undertaken on sections of recruitment appointments, and compared with the six-step good recruitment model developed in the pilot study to identify aspects of RCT presentation that are unclear, disrupted or hinder recruitment.[44]

Patient interviews will be used to supplement the outcome questions about satisfaction, exploring experiences of the trial processes and the treatment they received, and the consequences of that treatment for their lives, health and wellbeing. These will be analysed thematically, as above. Observations of the implementation of interventions will be recorded with detailed substantive and theoretical field-notes, supplemented by audio-recorded interviews with patients and clinicians. These will analysed according to methods being developed in the MRC ConDuCT-II Hub by Donovan and will aim to understand the fidelity of the implementation of the trial interventions.[45]

5.4 Economic evaluation

An economic evaluation will be integrated into the trial design and will be conducted from the recommended NHS and personal social services (PSS) perspective.[46] Cost-effectiveness will be calculated using both within-trial and lifetime horizons. Data will be collected on the health and social service resources used in the treatment of each trial participant until 12 months, when the primary outcome will be assessed. Trial data collection forms will record the duration of each form of hospital care, surgical procedures, adjunctive interventions, medication profiles, tests, procedures, and contacts with professionals for rehabilitation and follow-on care. Observational research may be required to detail additional staff and material inputs associated with clinical complications. In the follow-up questionnaires at 6 and 12 months, participants will be asked to complete economic questionnaires profiling hospital (inpatient and outpatient) and community health and social care resource use and, for the purposes of sensitivity analysis, out-of-pocket expenditures and costs associated with lost productivity. In addition, routinely collected HES data will document all hospital health service activity during the trial. HES data cover hospital inpatient, outpatient, and accident & emergency attendances. Current UK unit costs will be applied to each resource item to value total resource use in each arm of the trial. Per diem costs for hospital care, delineated by level or intensity of care, will be calculated using secondary national tariffs. The unit costs of clinical events that are unique to this trial will be derived from the hospital accounts of the trial participating centres, although primary research that uses established accounting methods may also be required. The unit costs of community health and social services will largely be derived from national sources, although some calculations from first principles using established accounting methods may also be required.[47] Responses to the EQ-5D and SF-12 will be converted into health utility scores using established algorithms.[48,49]

An incremental cost-effectiveness analysis, expressed in terms of incremental cost per quality-adjusted life year (QALY) gained, will be performed. Results will be presented using incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves (CEACs) generated via non-parametric bootstrapping. This accommodates sampling (or stochastic) uncertainty and varying levels of willingness to pay for an additional QALY. Due to the known limitations of within-trial economic evaluations, we will also construct a decision-analytical model to explore the cost-effectiveness of hip arthroscopy in FAI patients beyond the time horizon of the proposed trial.[50] The model will be informed partly by data collected as part of the proposed trial (including resource utilisation data collected within the follow-up study at two and three years), but also by data collected from other primary and secondary sources, including observational datasets held by the research team. Long term costs and health consequences will be discounted to present values using discount rates recommended for health technology appraisal in the United Kingdom.[46] A series of probabilistic sensitivity analyses will be undertaken to explore the implications of parameter uncertainty on the incremental cost-effectiveness ratios. Probabilistic sensitivity analyses will also explore the effects of extending the study perspective, target population, time horizon and decision context on the incremental cost-effectiveness ratios. In addition, cost-effectiveness acceptability curves will be constructed using the net benefits approach.

6. Trial Organisation

6.1 Trial Management Group (TMG)

The TMG will oversee the study and includes a multidisciplinary team of clinicians and researchers who have considerable expertise in all aspects of design, running, quality assurance and analysis of the trial. The TMG team will meet monthly to assess the study progress.

6.2 Trial Steering Committee (TSC)

A TSC will have an independent Chairperson as well as a 'lay' representative. Meetings will be held at regular intervals determined by need but not less than once a year.

The remit of the TSC is to:

- Monitor and supervise the progress of the trial towards its interim and overall objectives
- Review at regular intervals relevant information from other sources
- Consider the recommendations of the DMC
- Inform the funding body on the progress of the trial.

6.3 Data Monitoring Committee (DMC)

A DMC charter will be compiled detailing the members of the committee, their individual responsibilities and the overall responsibility of the DMC. The main roles of the DMC will be to review/approve the Statistical Analysis Plan (SAP), and to review trial progress, interim data and safety aspects of the study. Any recommendations will be fed back to the TSC by the DMC chair.

6.4 Essential Documentation

A Trial Master File will be set up according to WCTU SOPs and held securely at the coordinating centre.

6.5 Insurance and Indemnity Arrangements

NHS indemnity (Clinical Negligence Scheme for Trusts) covers negligent harm caused to patients whenever they are subjects of clinical research. NHS indemnity covers NHS staff and staff with honorary contracts with the NHS conduction the trial in the UK. The University of Warwick provides indemnity for any harm caused to participants by the design of the research protocol.

6.6 Dissemination

The results of this trial will substantially inform clinical practice on the clinical and cost effectiveness of the treatment of these injuries. The results of this project will be disseminated through peer-reviewed journals, conference presentations, the National Library for Health and through local mechanisms at all participating centres.

6.7 Regulatory Issues

The trial has obtained approval from the NRES Committee West Midlands - Edgbaston in the UK and has been registered with the International Standard Randomised Controlled Trial Number Register (ISRCTN64081839). The local investigator must submit the approved protocol, and supporting documentation and any amendments to the R&D Office at the Trust as appropriate in accordance with local requirements and recommendations made by REC.

6.8 Financial Support

This trial is funded through the Health Technology Programme, part of the National Institute of Health Research**.**

6.9 Project Timetable and Milestone

We propose a 5 year study starting in April, 2014

Study Month	Date	Activity	Milestone	Responsibility
-3-0	Mar 14	Ethics submission	MREC approval	CI/TM/RF
	Mar 14	Set-up main contract	Signed contract	CI/TM/RF
0-3	Apr 14	Finalise protocol & CRF's; Start trial		TMG
	Apr 14	Compose TSC/DMC	1st TSC/DMC meeting	CI/TM
	May 14	Start set-up		CI/TM
3-23	Jul 14	Start recruitment lead centre	Start recruitment	CI/TM
	Sep 14	First 10 centres open and recruiting		CI/TM
	Jan 15	All 25 centres open and recruiting		CI/TM
	Feb 15		2nd TSC/DMC	CI/TM
	Feb 16	Final patient recruited	Recruitment complete	
	Feb 16		3rd TSC/DMC	CI/TM
24-37	Mar 16	Outcome assessment begins for final patients		TM/DC
	Apr 17	Outcome assessment complete for primary outcome measure		TM/DC
38-40	May 17	Final analysis begins		STAT/HE
			4th TSC/DMC	CI/TM
	Jun 17	Close down of recruitment centres		TM
	Jul 17	Report to HTA	HTA report	CI/TMG
41-64	May 18	Central assessment of need for further procedures year 2		TM/DC
	Jul 18	Cross check of HES and Joint registry databases for evidence of further procedures/ analysis 2 year data	2 year data collection/analysis complete	STAT, RF, CI
	May 19	Central assessment of need for further procedures year 3		TM/DC
	Jul 19	Cross check of HES and Joint registry databases for evidence of further procedures/ analysis 3 year data	3 year data collection/analysis complete	STAT, RF, CI
	Aug 19		Supplementary HTA report	CI/STAT

Key: CI Chief Investigator, RF Research Fellow, STAT Statistician, HE Health economist, TMG Trial management group, TM Trial manager, TSC trial steering committee, DMEC Data monitoring committee, DC Data Clerk

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8. Summary of Protocol Amendments

Amendment No. 1
Date of Amendment: 20/06/2014
Date of Approval: 05/08/2014
Summary of Changes: Updated TSC membership
Amend the number of permissible PHT steroid injections from two to one.

Amendment No.2
Date of Amendment: 27/07/2015
Date of Approval: 01/12/2015
Summary of Changes: Updated Contacts, TMG & TSC membership.
Amendment to the inclusion criteria to clarify further the definition of Pincer impingement.
SAE to be collected for 12 months following patient study entry.

Amendment No. 3
Date of Amendment: 20/01/2016
Date of Approval: 02/03/2016
Summary of Changes: Section 1.1 collaborators centres updated