# END OF TRIAL REPORT

| Trial Identification and Report Information | |
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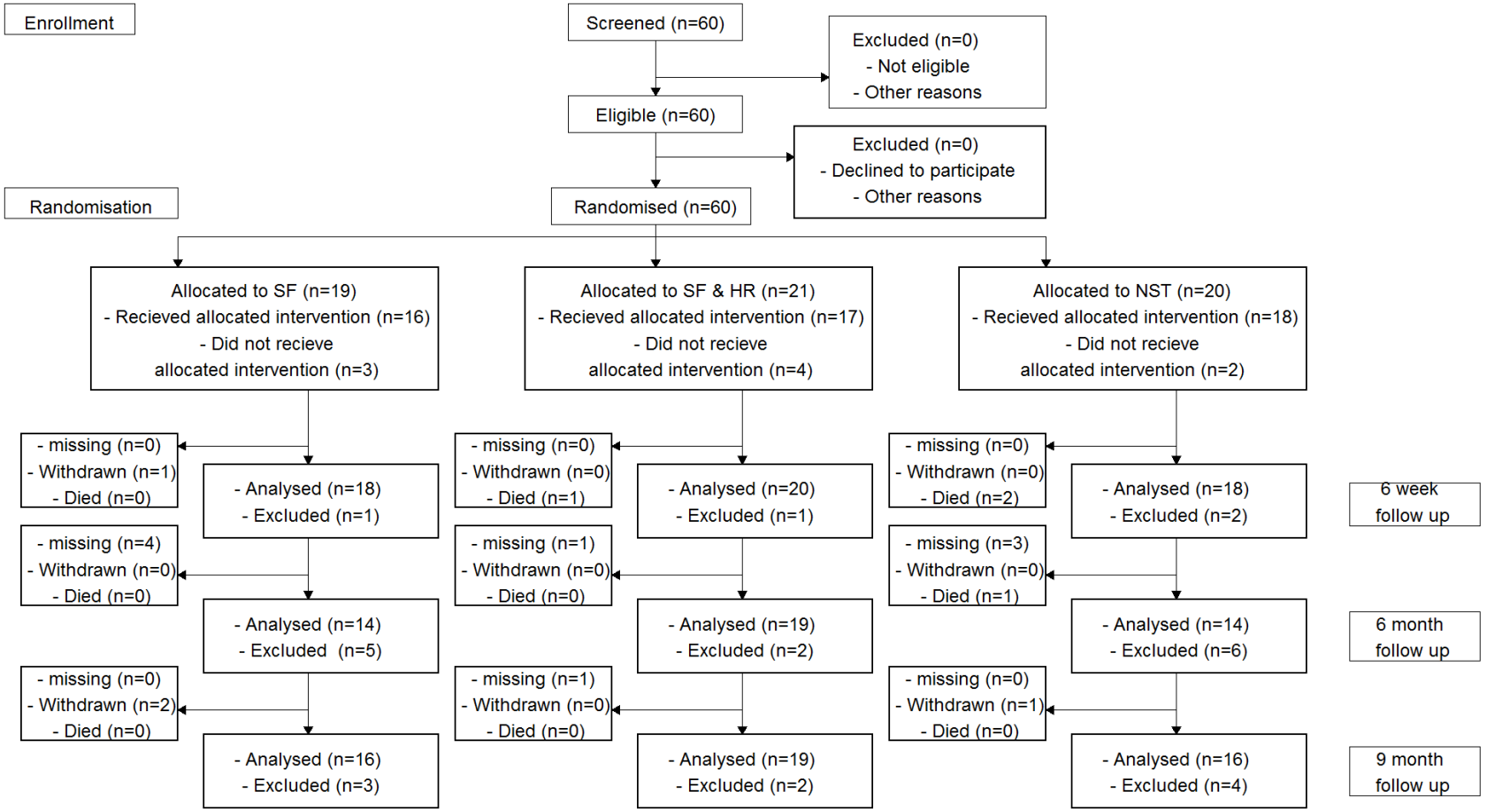
| **Title** | AceFIT – Acetabular Fractures in older patients Intervention Trial. A feasibility study comparing three methods of treatment of acetabular fractures in older patients; surgical fixation versus surgical fixation and hip replacement versus non-surgical treatment. |
| **Chief Investigator:** | Mr Andrew Carrothers |
| **EudraCT no.:** | N/A |
| **REC Ref no.:** | 17/EE/0271 |
| **R&D no.:** | A094243 |
| **Sponsor:** | Cambridge University Hospitals NHS Foundation Trust |
| **Sponsor's Address:** | Addenbrooke's Hospital<br>Hill Road, Cambridge CB2 0QQ |
| **Trial Statistician:** | Dr Simon Bond |
| **Final Data Analysis carried out by:** | Simon Bond<br>Rachel Donegan |
| **Author of the report:** | Simon Bond<br>Rachel Donegan |


Enrollment
Screened (n=60)
Excluded (n=0)
- Not eligible
- Other reasons
Eligible (n=60)
Excluded (n=0)
- Declined to participate
- Other reasons
Randomisation
Randomised (n=60)
Allocated to SF (n=19)
- Recieved allocated intervention (n=16)
- Did not recieve allocated intervention (n=3)
Allocated to SF & HR (n=21)
- Recieved allocated intervention (n=17)
- Did not recieve allocated intervention (n=4)
Allocated to NST (n=20)
- Recieved allocated intervention (n=18)
- Did not recieve allocated intervention (n=2)
- missing (n=0)
- Withdrawn (n=1)
- Died (n=0)
- Analysed (n=18)
- Excluded (n=1)
- missing (n=0)
- Withdrawn (n=0)
- Died (n=1)
- Analysed (n=20)
- Excluded (n=1)
- missing (n=0)
- Withdrawn (n=0)
- Died (n=2)
- Analysed (n=18)
- Excluded (n=2)
6 week follow up
- missing (n=4)
- Withdrawn (n=0)
- Died (n=0)
- Analysed (n=14)
- Excluded (n=5)
- missing (n=1)
- Withdrawn (n=0)
- Died (n=0)
- Analysed (n=19)
- Excluded (n=2)
- missing (n=3)
- Withdrawn (n=0)
- Died (n=1)
- Analysed (n=14)
- Excluded (n=6)
6 month follow up
- missing (n=0)
- Withdrawn (n=2)
- Died (n=0)
- Analysed (n=16)
- Excluded (n=3)
- missing (n=1)
- Withdrawn (n=0)
- Died (n=0)
- Analysed (n=19)
- Excluded (n=2)
- missing (n=0)
- Withdrawn (n=1)
- Died (n=0)
- Analysed (n=16)
- Excluded (n=4)
9 month follow up

| **Trial Summary** | |
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| **Final Protocol version:** | 2.1 |
| **Study Design:** | This is a randomised controlled prospective study, to assess the feasibility of performing a full scale randomised control trial comparing three different treatment methods of acetabular fractures in older patients; non-surgical treatment (NST), surgical fixation (SF) or surgical fixation combined with hip replacement (SF+HR).<br><br>A feasibility randomised controlled trial is required to inform the design and the sample size calculation for a larger trial - specifically to understand how the characteristics of the target population (older patients, high incidence of cognitive impairment and medical comorbidities) will affect the study process and documentation. We wish to ensure that patient recruitment, follow-up and data collection is practical and will provide appropriate outcome data to inform a sample size calculation for a definitive trial.<br><br>Background:<br>Approximately 2,000 older people break the pelvic part of their hip joint (acetabulum) each year in the UK. This is a vulnerable patient group; pre-existing medical conditions are common, one year mortality is 25% and a recent study of older patients with similar fractures found that 30% have cognitive impairments. Based on hip fracture data, we estimate that the annual cost to the NHS and the wider UK economy is over £80 million.<br><br>Acetabular fractures occur in a similar patient population to that of hip fracture patients. They also have similar comorbidities such as cognitive impairment and osteoporosis. NICE guidelines for the management of hip fractures state that interventions should be undertaken with the aim of facilitating early mobilisation to optimise recovery and clinical outcomes. Despite the similarity to the hip fracture population, current treatment principles for acetabular fractures however are very different to those of hip fractures. There is no guidance in place for acetabular fractures with minimal evidence available to inform best practice. Surgeons worldwide are uncertain how best to treat these fracture with significant variance in treatment occurring between different institutions who treat these injuries.<br><br>Currently there are two main options available; nonsurgical treatment and surgical treatment. Non-surgical (NST) treatment involves the patient keeping the weight off the affected leg until the fracture has healed. This often means patients are immobile for a prolonged period, have a prolonged rehabilitation and exhibit difficulty returning to their pre-injury level of function and independence. Furthermore, as the hip joint anatomy has not been restored patients may also have compromised function and quality of life in the long term.<br><br>Surgical treatment involves surgical fixation (SF) using a plate and screws to hold the fractured pieces of bone in the correct position until the fractures has healed. This has the advantage of restoring the hip joint anatomy and is |

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| | commonly used in younger patients. However as the bone is generally of poor quality in older patient groups due to osteoporosis, accurate reconstruction of the hip joint is challenging. Consequently this method of surgical treatment has a much poorer outcome in older patients than in younger patients.<br><br>Furthermore, this surgical fixation means that these patients are not permitted to bear weight on the affected leg until the fracture has healed. This may mean a period of non-weight bearing on the affected limb for up to three months post fracture. As older patients who sustain acetabular fractures have similar demographic characteristics and comorbidities to hip fracture patients and are likely to suffer the same complications if they undergo a period of prolonged immobilisation, it may be appropriate to adopt the NICE hip fracture management philosophy for acetabular fractures in older patients and aim for early mobilisation.<br><br>With this in mind, a third method of treatment for acetabular fractures in older patients is gaining popularity in some centres and involves replacing the hip joint at the time of fixation of the fracture (SF+HR). This has the advantage of allowing patients to weight bear immediately which would bring care in line with NICE guidelines for the management of hip fractures. This may enable patients to regain function earlier and consequently have a shorter hospital stay and possibly a quicker return to their usual place of residence. The downside to SF+HR is longer surgery, increased blood loss and the risks of hip dislocation, early failure of the hip replacement and increased initial cost of treatment.<br><br>Deciding which of these treatment options will give the best outcome is often difficult with no clear evidence or guidelines. There is limited evidence available that assesses the above described treatment options for acetabular fractures in older patients. A recent systematic review from 2014 found no randomised controlled trials in this area. It identified 15 studies consisting of retrospective case series. Only one study assessed the outcome of non-surgical treatment (NST) within 9-52 months post-surgery demonstrating that 30% of patients did poorly and were unable to weight bear without severe pain.<br><br>For patients who had surgical fixation (SF) only; pooled data from eight studies demonstrated satisfactory surgical fixation being achieved in only 45.3% of patients. 23.1% of patients had significant pain and reduced function to the point where they had to undergo a hip replacement. This is a significant procedure for an older patient and represents a considerable setback to their rehabilitation with increased risks of complications such as infection, hip dislocation and reduced hip function.<br><br>In the studies that assessed surgical fixation combined with a hip replacement (SF+HR), no increase in complications such as mortality or other complications was found , when compared to patients who underwent surgical fixation (SF) alone. It was not possible to reliably determine which patients had better function as the studies used different functional scores at different intervals after surgery. |

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| | As demonstrated above, the evidence base describing the treatment of acetabular fractures in older patients is of poor quality consisting entirely of retrospective case series. There are significant differences between these studies in terms of which outcomes are assessed, making meaningful comparison between treatments unreliable. To address the above identified deficiencies in the evidence base, high quality research in the form of a randomised controlled trial comparing the different treatment options for acetabular fractures in older patients is now warranted.<br><br>In summary, the problem being addressed is which of three treatments is best for older patients sustaining an acetabular fracture – non-surgical treatment (NST), surgical fixation (SF) or surgical fixation combined with hip replacement (SF+HR). An adequately powered randomised controlled trial is required to determine which is the optimal treatment. However, there are several potential difficulties with implementing such a trial. The aim of this study is to assess the feasibility of performing a larger scale trial and if found to be feasible then we will seek support to undertake a full scale randomised clinical trial. |
| **No. of participants:** | Aim: 60.<br>Final number of recruited participants: 60<br>Following informed consent, confirmation of eligibility and collection of baseline data, patients were randomised into one of the three groups: the non-surgical treatment (NST) group, surgical fixation (SF) group or fixation combined with hip replacement (SF+HR) group with each group containing 20 patients each. The randomisation was performed using stratified blocked randomisation, using capacity status (with and without) as a stratification factor. |
| **Investigational Medicinal Products:** | N/A |
| **Date of End of Trial:** | LPLV: 12/10/2020<br>Last TSC meeting: 10/03/2021<br>End of trial report sent to funder: 30/09/2021 |
| **Reported Serious Breaches:** | N/A |
| **Significant deviations identified during the trial:** | - 2 protocol non-compliances for missed visit (6months). Local teams took corrective actions to improve follow-up of trial participants<br>- 1 global non-compliance for all follow-ups during COVID-19 pandemic. Local teams were advised to follow-up participants with phone call and to schedule a visit as soon as possible to collect 9 months follow-up X-Ray. X-rays for these participants were collected out of window. |

| **Statistical Analysis and Main Findings** | |
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| **Trial objectives and endpoints:** | As this is a feasibility study, our objectives are to measure:<br>• Willingness of patients to participate and clinicians to recruit participants<br>• Drop-out rates<br>• Ability to capture all specified data<br>• Estimates of standard deviation of the primary outcome measure to inform the sample size calculation for the main RCT trial |

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| | • Completion rates and the main cost-drivers, to inform the decision as to how costs and benefits should be measured in a definitive trial |
| **Trial Analysis Population:** | The analysis was performed on an intention-to-treat basis and included all eligible patients that received any study treatment and had at least one post-baseline assessment. |
| **Statistical Methods:** | No formal hypothesis testing was performed, as this was a feasibility trial. A pooled estimate of the standard deviation of the primary outcome was calculated in order to inform the sample size required for a full-scale trial. |
| **Results:** | During the trial period 333 patients were screened, of which 60 patients were recruited and randomised at 7 sites to one of the interventions. 4 patients withdrew from the study and 8 patients changed their randomised treatment. 56 patients were followed up for 9 months and completed 3 monthly EQ5D, DRI and OHS.<br><br>Baseline demographics: 66% of the patients were male, medium age 76, 87% had full mental capacity, 77% were admitted from their own home. There was no significant difference between the groups in age, BMI, alcohol or smoking habits. 59 of the 60 recruited patients had clinically significant medical comorbidities prior to their injury.<br><br>Median surgery time was 2.25 hours for fixation surgery and 4.2 hours for fix and replace (including changing the patient's operative position on the operating table). The majority of operations were performed by a consultant: 61% for fixation and 79% for fix and replace. Surgery safety data provided by this trial indicates that there is no significant difference in renal function deterioration after the 2 types of surgeries. In addition, regarding blood loss and transfusion, there was no significant difference between the 2 surgical groups: median blood loss was 550ml for fixation and 600ml for fix and replace; 33% of patients required blood transfusion in the fixation group and 37% in the fix and replace group. There was no significant difference in the change of haemoglobin between the 2 surgical procedures: -19.5 for fixation and -15.5 for fix and replace.<br><br>The 9 months radiographic evaluation showed a 100% evidence of hip osteoarthritis progression in the conservatively managed group, with 27% having femoral head collapse and only 53% showing fracture union. In the fixation group, 89% had evidence of hip osteoarthritis progression, with 22% having femoral head collapse and 69% showing fracture union. In addition,14% had evidence of metalwork failure. In the fix and replace, there was no loosening of the hip prosthesis with no acetabular cup migration. There was no metalwork failure at the 9 months point.<br><br>There were 5 registered deaths in the 3-year trial period. 3 unrelated to the trial, 2 with hospital acquired pneumonia, 1 in the conservative arm and 1 in the fix and replace.<br><br>In terms of treatment arm complications:<br>1) Conservative group:<br>- 1 fractured neck of femur converted to fix and replace<br>- 1 DVT<br>- 2 early severe hip arthritic pain converted to hip replacement |

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| | 2) Fixation group:<br>- 1 massive blood loss during surgery<br>- 1 fractured neck of femur converted to fix and replace<br>- 1 early severe hip arthritic pain converted to hip replacement<br>- 1 ongoing hip arthritic pain<br>- 1 fracture malunion<br>3) Fix and replace:<br>- 2 early hip dislocations (day 6, 13) both treated with a single manipulation under anaesthetic hip reduction<br>- 1 superficial wound infection debrided in theatre |
| **Conclusion:** | We have shown feasibility for a full randomised controlled trial in the future to confirm the results obtained in this pilot study. We have shown this patient cohort to be medically complex with a true need for multidisciplinary care; surgeon, anaesthetist and orthogeriatrician input.<br><br>Current data seems to indicate that fixation and replacement managements have a better "signalled outcome" in the short term (EQ5D5L at 6 months) follow-up of the trial participants. In addition this trial has provided safety data on the larger surgical treatment arm of fix and replace strategies. Further research will be needed on both these findings.<br><br>The conservative management arm anecdotally struggled for this injury pattern.<br><br>Results from this trial have informed for the design of an RCT fixation vs fix and replace study with 1400 patients to have a power of 80 and a MCID of 0.06 on the EQ5D5L.<br><br>We expect that this future trial with the learnings from this feasibility study will provide conclusive answers to the scientific question proposed in this project. |

| **Dissemination of Research Findings and Publications** | |
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| **To participants:** | A newsletter will be prepared with the results of the trial to all the participants. |
| **Publications:** | Plans are for a published manuscript in the American JBJS or British BJJ. Podium presentations are planned in the Brittish Orthopaedic Association Congress and the North American Orthopaedic Trauma Association. This study has already been presented at the Brittish Hip Society 2021 |

| **Chief Investigator's Signature** | |
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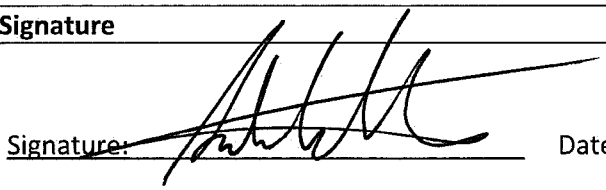
| | Signature:  Date: 7/10/21 |