DIDACT TRIAL PROTOCOL

University Hospitals of Leicester NHS Trust

Full Title: Surgery compared with sling immobilisation in the management of adults with a displaced fracture of the distal clavicle (DIDACT): a multi-centre, pragmatic, parallel group, non-inferiority, randomised controlled trial

Short Title / Acronym: DIsplaced DistAl Clavicle Trial - DIDACT

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Amendment history

Amendment number	Revised protocol version number and date	Details of key changes made (including if justification required)
Not applicable	Not applicable	Added text to Section 4.3.2 to summarise post-operative sling care for participants who receive surgery.
Not applicable	Not applicable	Added at baseline about a participant's satisfaction with their shoulder appearance so can be compared with this at 12 months.
Not applicable	Not applicable	Added at both baseline and 12 months whether for participants it is painful or sensitive to touch the area of the broken collarbone.
Not applicable	Not applicable	Modified the eligibility criteria so that the lower age limit is 18 rather than 16. This is because of requirements around consent and GDPR in 16 to 17 year olds. Being able/willing to consent and unable/willing to consent have been added. Additionally, that participants must not be related to any member of the local study team because of past experiences at the Sponsor site.
Substantial amendment 1	V2.0_2024.06.17	1. Inclusion of an A&E staff flyer. 2. Inclusion of reference to the Community Health Index for contacting patients for follow-up in Scotland. 3. Reference to a letter and flyer to encourage participant attendance at the 12 month follow-up. 5. Inclusion of an infographic to complement the Patient Information Sheet. 6. Added about how participant information at follow-up can be accessed using routine NHS mechanisms from hospitals other than the recruiting site. 7. Expanded obtaining patient consent to allow this to be done remotely. 8. Collection of fracture classification to be done after randomisation, if necessary.
Substantial amendment 2	V3.0_2024.11.11	(1) Include a flyer one month prior to the 12 month questionnaire is due (primary end-point) to prepare participants to expect it i.e. a pre-notification. (2) Clarified the wording of safety reporting around serious adverse events and deaths. (3) Addition of an animation to the Patient Information Sheet to communicate about the study.

List of abbreviations

AE	Adverse Event
API	Associate Principal Investigator
BESS	British Elbow and Shoulder Society
BOA	British Orthopaedic Association
BOTA	British Orthopaedic Trainee Association
CACE	Complier average causal effect
CC	Coracoclavicular
CDC	Centres for Disease Control
CONSORT	Consolidated Standards of Reporting Trials
CORNET	Collaborative Orthopaedic Research Network
DASH	Disability of Arm, Shoulder and Hand
eCRF	electronic Case Record Form
EFFORT	European Federation of National Associations of Orthopaedics and Traumatology
EUSSER	European Society for Shoulder and Elbow Rehabilitation
GCP	Good Clinical Practice
GIRFT	Getting It Right First Time
HEAP	Health economic analyses plan
HES	Hospital Episode Statistics
HRA	Health Research Authority
HRG	Healthcare Research Group
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
IDMC	Independent Data Monitoring Committee
ITT	Intention-to-treat
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Clinical Excellence
NRS	Numeric Rating Scale
PAG	Patient/Public Advisory Group
PI	Principal Investigator
PIS	Patient information sheet
QALY	Quality-adjusted Life Years
RoSPA	Royal Society of Prevention of Accidents
RCT	Randomised controlled trial
REC	Research Ethics Committee
ROM	Range of movement
SAC	Speciality Advisory Committees
SAE	Serious Adverse Event
SAP	Statistical Analyses Plan
SECEC	European Society for Surgery of the Shoulder and the Elbow
SWAT	Study Within A Trial
TMG	Trial Management Group
TSC	Trial Steering Committee
UK	United Kingdom
YTU	York Trials Unit

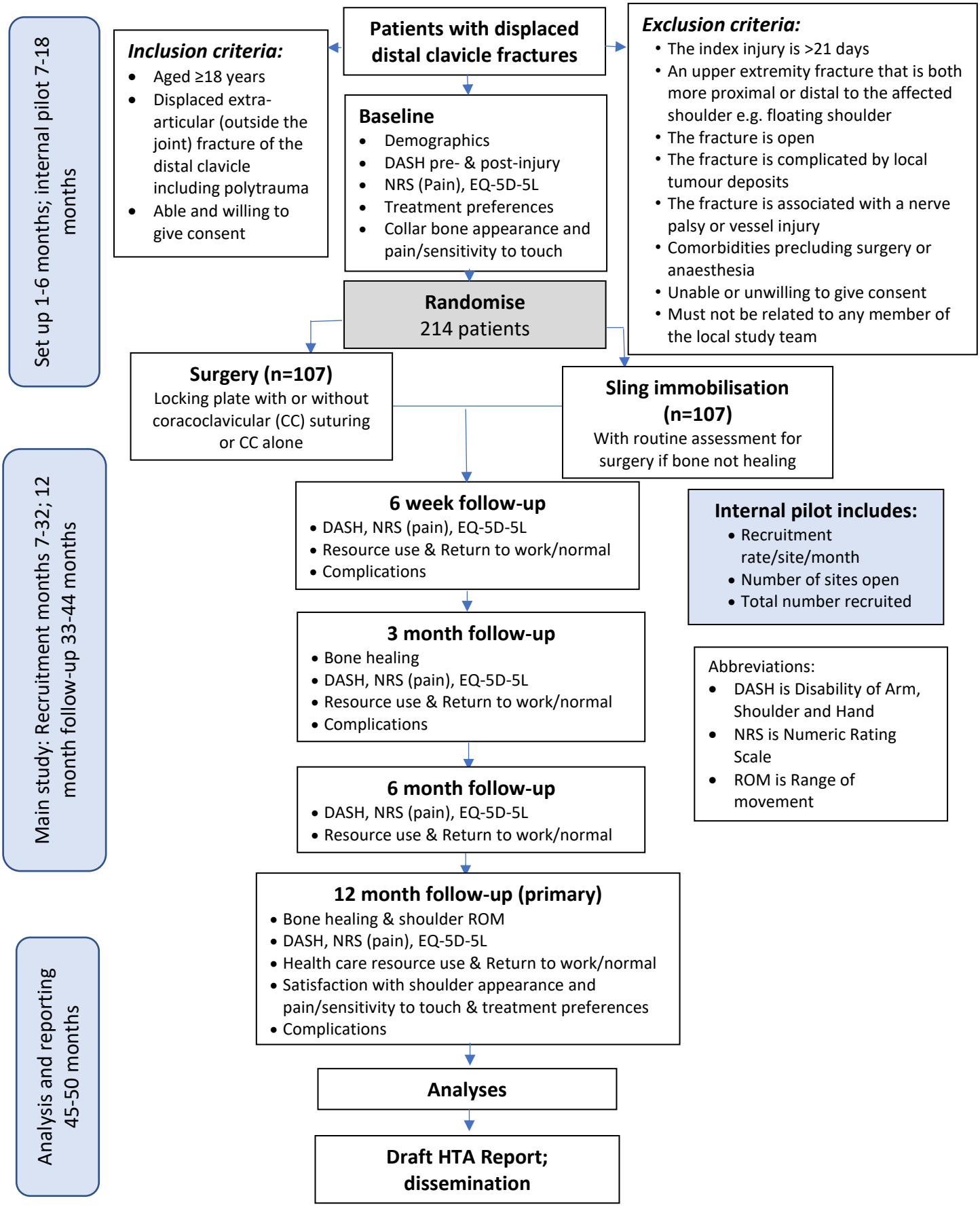
Contents

Trial Synopsis

Acronym	DIDACT
Full title	Surgery compared with sling immobilisation in the management of adults with a displaced fracture of the distal clavicle (DIDACT): a multi-centre, pragmatic, parallel group, non-inferiority, randomised controlled trial
Type of trial	Non-CTIMP
Trial design	A two-arm, pragmatic, multi-centre, randomised, non-inferiority trial with parallel groups, allocated on a 1:1 ratio and stratified by age (<65 or ≥65 years). It includes a 12 month internal pilot and a full health economic analysis.
Setting	Major Trauma Centres and Trauma Units within the United Kingdom. Patients will be identified either in the Emergency Department or Fracture Clinic and /or the orthopaedic trauma meeting and will attend for routine out-patient appointment at 6 weeks, 3 and 12 months.
Target population	Adults with a radiological diagnosis of a displaced fracture of the distal clavicle that does not involve the acromioclavicular joint.
Intervention	Surgery – locking plate fixation, with or without coracoclavicular (CC) sling, or CC reconstruction alone when the distal fragment is very small.
Comparator	Sling immobilization – upper limb support with a sling, typically for 2 to 4 weeks, followed by surgical fixation if symptomatic non-union of the fracture typically at the 3 month follow-up.
Primary outcome	Patient-reported functional outcome measured by the Disability of Arm, Shoulder and Hand (DASH) at 12 months.
Secondary outcomes	DASH score at 6 weeks, 3 and 6 months, and over 12 months; Shoulder pain, EQ5D-5L at 6 weeks, 3, 6, and 12 months; complications (e.g. infections, re-operations) at 6 weeks, 3 and 12 months; fracture healing at 3 and 12 months; patient preferences, satisfaction with appearance of their shoulder/sensitivity or pain to touch, and range of movement at 12 months.
Estimated recruitment period	26 months (1 May 2023 to 30 Jun 2025)
Duration per patient	12 months
Estimated total trial duration	50 months (1 November 2022 to 31 December 2026)
Planned trial sites	Minimum of 23 sites
Planned sample size	214 patients (107 in each group)
Eligibility criteria	**Inclusion criteria:** • Aged 18 years or older. • Displaced extra-articular (outside the joint) fracture of the distal clavicle based on routine radiographic assessment, with or without polytrauma. • Able and willing to give consent. **Exclusion criteria:** • The index injury is >21 days.

	• An upper extremity fracture both more proximal or distal to the same affected shoulder e.g. floating shoulder. • The fracture is open. • The fracture is complicated by local tumour deposits. • The fracture is associated with a nerve palsy or vessel injury. • Comorbidities precluding surgery or anaesthesia. • Unable or unwilling to give consent. • Must not be related to any member of the local study team.

DIDACT trial flowchart



Study Assessment Schedule

Assessment	**Baseline (Clinic)**	**Allocation (surgery)**	**6 weeks (Clinic / remote)**	**3 months (Clinic / remote)**	**6 months (remote/no clinic)**	**12 months (Clinic / remote) Primary**
Enrolment:						
Eligibility screen	X					
Informed consent	X					
Randomisation	X					
Treatment:						
Treatment allocation		X				
Assessments:						
Baseline demographics	X					
Operation Data		X				
DASH[1]	X		X	X	X	X
NRS[2] (shoulder pain)	X		X	X	X	X
EQ-5D-5L	X		X	X	X	X
Shoulder range of movement						X
Fracture union/non-union/malunion				X		X
Patient preferences	X					X
Patient satisfaction with appearance of shoulder and sensitivity/pain to touch	X					X
Complications e.g. infections, re-operations			X	X		X
Resource Use			X	X	X	X
Return to work and normal activities			X	X	X	X
Adverse events			X	X		X

[1] Disability of Arm, Shoulder and Hand
[2] Numeric Rating Scale

1 Background and rationale

1.1 General introduction

Fractures of the clavicle, primarily occur in young males, and constitute 2.6–5% of all fractures in adults.(1) Distal clavicle fractures account for 20-25% of all clavicle fractures.(1, 2) The outer part of the collarbone breaks and separates and these fractures can be called displaced, in that the bones fail to line up. This ruptures the ligaments connecting the collarbone to the shoulder blade (coracoclavicular complex) and can be classified as Neer's II and V.(3) These are currently treated with an operation involving fracture fixation or with sling immobilisation.(4, 5)

Surgery, where the bone fragments are realigned and fixed into place, may reduce the risk of the fracture not healing (non-union) and may lead to quicker recovery. However, patients treated with surgery are at risk of complication; (estimated at 48%)(6) including infection, plate breakage and refracture after metal removal. A second operation may be required to remove the metalwork due to prominence, (7) leading to a further impact on patients' lives including work activities and caring responsibilities. Non-operative treatment, using a sling, carries a low risk of complications (15%) and has a relatively low immediate treatment cost.(6, 8) Sling treatment requires a period of immobilization, typically between 2 and 4 weeks, to restrict activities whilst providing comfort during the early painful stages of healing. The risk of the bone not healing (non-union) with non-operative treatment is up to 35-40% but this appears to cause minimal functional deficits in most individuals.(7) If a non-union occurs following sling treatment, and surgical intervention is indicated, it can prolong the treatment period and increase costs.(9)

Hospital Episode Statistics (HES) for 2019 for patients who are operated on show that there were 9,410 finished consultant episodes for a fracture of the clavicle with 2,353 (25%) being a distal fracture and 1,176 (50%) of these being displaced. Therefore, in a typical year there are 1,176 patients who have surgery in our fracture population. Healthcare Research Group (HRG) codes estimate the cost of the index operation to be £3,725 and the cost of removing metalwork to be £2,551 which can apply to approximately 45% of patients. This is in contrast to the cost of £156 per patient for sling immobilization using HRG codes. The cost of surgical fixation in our fracture population to the NHS is approximately £6 million per annum.

At a time when the National Health Service (NHS) is under more pressure than ever to manage the impact of COVID-19, it is important to know whether a potentially cheaper, safe and non-surgical option can replace more costly and invasive surgery and to optimise the use of staff and theatre time for patients who do need surgery. This randomised controlled trial (RCT) will answer the question as to whether a non-surgical pathway is not inferior to surgery for the treatment of adults with a displaced fracture of the distal end of the clavicle. The concomitant health economic evaluation will identify which is the most cost-effective treatment option to the NHS.

1.2 Review of existing evidence

Routine fixation of fractures to the middle third of the clavicle can reduce the risk of non-union but is not cost-effective.(10, 11) However, displaced distal clavicle fractures are associated with rupture of coracoclavicular ligaments and considered unstable and therefore a different patient population.

A systematic review (search end date; 27 January, 2021)(12) identified no RCTs comparing surgery and sling immobilisation for displaced distal clavicle fractures. The highest level of evidence was 13 prospective studies, followed by 46 retrospective cohort studies. The limited evidence from this and other systematic reviews (7, 13, 14) have shown equivocal outcomes for patients who have developed a non-union of their distal clavicle fracture when compared to those patients who have healed.(15) Despite the lack of evidence, more distal clavicle fractures are now treated with surgery than non-surgical treatments with data suggesting a worldwide trend to increasing use of surgical fixation.(7, 8)

There is only one recent RCT(6) studying distal clavicle fractures from Canada where 57 patients were recruited and found that more patients in the surgical group went on to union (bone healing) within 12 months compared to sling immobilisation (95% vs 64%, p=0.02). Despite the significantly higher non-union in the non-operative group, only 6 patients (6/30, 20%) had further surgical procedures. Twelve patients in the operative group underwent a second operation for hardware removal (12/27, 44%). There were no significant differences between groups in patient reported outcomes. However, the study was underpowered and the surgical intervention included locking plates or hook plates; there is evidence that a hook plate may not be as effective as a locking plate.(12-15) Nor was there an economic evaluation.

The James Lind Alliance(16) and United Kingdom (UK) orthopaedic trauma network(17) have identified the treatment of distal clavicle fractures with or without surgery as a high priority research topic. The importance of this research question has further been confirmed in our national survey of shoulder surgeons from the British Elbow and Shoulder Society (BESS) who agree there is a need for this trial and a lack of consensus on how to manage this patient population. Almost half of the 152 surgeons who took part stated they manage 50% or more of these patients with surgery. The survey data also shows of the 152 responses, 63% (84 respondents) reported using the distal clavicle locking plate alone, 48% a locking plate with coracoclavicular reconstruction, 37% coracoclavicular reconstruction only, and 33% clavicle hook plate.

For the proposed trial the surgical arm will comprise of the locking plate (with or without coracoclavicular (CC) reconstruction) or CC reconstruction alone. Hook plate will not be included in either of the trial arms. The following explains our decision for this:

1. We have a minimum of 23 sites at which a surgeon has agreed to be a Principal Investigator (PI) of a study that compares the proposed surgical approach with sling immobilisation;
2. BESS, that includes surgeons who are trained in this type of shoulder surgery, have adopted the proposed trial into their portfolio of trials as they have agreed it is of clinical importance, methodologically sound in their opinion and should be useful to their membership in the care of these patients;
3. There is evidence that locking plate is superior to hook plate (7, 12);
4. Including the hook plate as a third trial arm would prohibitively increase the cost of the study. Furthermore, a detailed audit of 18 hospitals identified that centres either exclusively or predominantly use locking plates or hook plates. There is, therefore, likely to be a significant lack of surgeon equipoise to randomise between these two surgical approaches;
5. Including the hook plate in the surgical arm of the trial would not provide sufficient statistical power to compare the effectiveness of the two surgical approaches and would be a non-random comparison. The different surgical options could negate each other and lead to the false conclusion that the non-surgical approach is not inferior to surgery;
6. Focusing on locking plate or CC reconstruction should future proof the study as the BESS survey shows this is the most common approach and we expect this is likely to increase in use with the decline of hook plates;

7. Our patient representatives discouraged including hook plates as these need a further operation to be removed due to the risk of damage to the rotator cuff muscles which in the long term could slow the speed of recovery and be of more pain and burden to patients. The proposed trial design should be more acceptable to patients and is centred around what is important to them.

2 Research question and objectives

2.1 Research question

In adults with a radiological diagnosis of a displaced fracture of the distal clavicle that does not involve the acromioclavicular joint is sling immobilisation non-inferior to surgical fixation using a patient self-reported functional outcome at 12 months?

2.2 Primary objective

To determine whether self-reported functional outcome, measured by the Disability of Arm, Shoulder and Hand (DASH) at 12 months, following sling immobilisation is not inferior to surgical fixation in adults with a displaced fracture of the distal clavicle.

2.3 Secondary objectives

- Confirm the feasibility of the study in a 12 month internal pilot to obtain robust estimates of site set up and recruitment.
- Determine the effectiveness of surgery versus sling immobilisation in adults with a displaced fracture of the distal clavicle.
- Determine the cost-effectiveness of the two treatments to inform the most efficient provision of future care and to describe the resource impact on the NHS.

3 Trial design

DIDACT is a two-arm, pragmatic, multi-centre, randomised, non-inferiority trial with parallel groups, allocated on a 1:1 ratio using random permuted blocks of random block size and stratified by age (<65 or ≥65 years).(18) There will be a 12 month internal pilot to assess the assumptions about site set up and recruitment. The trial will include a full health economic evaluation. As with many surgical trials, it will not be feasible to blind patients, surgeons, or outcome assessors to the treatment allocation.

3.1 Internal pilot

We will undertake a 12 month internal pilot study to test our assumptions about recruitment to confirm whether the trial is feasible (see Table 1). The aim is to have set up all 23 sites, which we believe is realistic due to efficiencies in using remote Site Initiation Visits. The monthly recruitment projections are adjusted to account for a phased set-up of study sites. Setting up these sites during the pilot will allow us to recruit 60 patients i.e. 27% of the overall target. The key progression criteria are presented below where “Green” is continue to main trial, “Amber” is review and implement methods to meet the target and “Red” is stop, unless mitigating circumstances.

Table 1: Progression criteria for the internal pilot

Progression criteria	**Red**	**Amber**	**Green**
% Threshold			
Trial recruitment	<50%	50-99%	100%
Recruitment rates per site per month	<0.25	0.25-<0.5	0.5
Number of sites opened	<12	12-22	23
Total number of participants recruited	<30	30-59	60

Secondary reasons for undertaking the internal pilot are to closely monitor: a) the number of eligible patients; b) that all eligible patients are being approached to take part; c) reasons for patients being excluded; d) the length of time spent discussing with a patient their consent into the study, reasons for not consenting and the consent rate; e) cross-overs between trial arms when participants do not receive their originally assigned treatment, and the need to inflate the sample size, if necessary; f) the extent to which participants in the sling immobilization group go on to have subsequent surgery as part of that established pathway of care and the reasons why this decision has occurred; g) follow-up rates of participant completed questionnaires; h) ensuring the participating sites are provided with enough training and documentation; i) ensuring that all suitable surgeons at a site are actively taking part in the trial and to find out if not why not. Reviewing screening logs (for the numbers screened, eligible, approached and randomised) including variability between sites in the proportion of undisplaced versus displaced distal clavicle fractures,(19) Case Record Forms and following up with sites will allow us to monitor the above during the pilot.(20)

At the end of the pilot phase, data required to assess the trial against the pre-specified progression criteria will be summarised descriptively. No formal hypothesis testing will be undertaken, nor will this involve looking at any primary or secondary outcome data. Our independent oversight committees will review progress and recommend that the trial continue without amendments, continue with major/minor amendments (for example, increase the number of participating sites), or discontinue.

4 Methods

4.1 Setting

We will recruit from a minimum of 23 Major Trauma Centres and Trauma Units within the UK. Patients will be identified in hospital when presenting with their index shoulder fracture, either in the Emergency Department or Fracture Clinic and /or the orthopaedic trauma meeting. Trial participants will attend for routine out-patient appointment at 6 weeks, 3 and 12 months.

4.2 Target population

Adults with a radiological diagnosis of a displaced fracture of the distal clavicle that does not involve the acromioclavicular joint.

4.2.1 Inclusion criteria

- Patients aged 18 years or older.
- Displaced extra-articular (outside the joint) fracture of the distal clavicle based on routine radiographic assessment, with or without polytrauma.
- Able and willing to give consent.

4.2.2 Exclusion criteria

Patients will be excluded if any of the following apply:

- The index injury is >21 days.
- An upper extremity fracture both more proximal or distal to the same affected shoulder e.g. floating shoulder.
- The fracture is open.
- The fracture is complicated by local tumour deposits.
- The fracture is associated with a nerve palsy or vessel injury.
- Comorbidities precluding surgery or anaesthesia.
- Unable or unwilling to give consent.
- Must not be related to any member of the local study team.

4.3 Trial treatments

4.3.1 Eligible and consenting patients will be randomly allocated to either sling immobilisation or surgical fixation. Sling immobilization (comparator)

Upper limb support is provided with a sling that is applied in the emergency department to relieve pain, allow for swelling and to provide comfort. A sling is typically worn for between 2 and 4 weeks, as was the preferred length of complete immobilisation in the BESS survey (n=84, 46%)(21), and can be discarded when pain resolves or when there is evidence of fracture union. Overall, however, this can take from 6 to 8 weeks.(21) Each recruiting centre will be provided with a standardized protocol for the application and management of sling immobilization. The type of sling used will be the clinician's decision. Trial participants will also be provided with a standardised "Sling Use and Initial Self-care" leaflet and video to manage their sling care. The type of sling and duration of use will be recorded. Patients' progress and bone healing in the non-operative pathway will be assessed clinically and radiographically when they attend hospital visits as would occur during routine clinical practice. Finally, surgeons will consider the need for surgery for patients who are immobilised in a sling if there is evidence of symptomatic non-union(22) using established indicators e.g. no callus, fracture movement, patient symptoms.(23) Therefore, the need for surgery, when clinically indicated, and which will typically occur at the three month visit, is part of an already established pathway of care in the sling immobilization group as a shared decision between the patient and surgeon.

4.3.2 Surgical fixation (intervention)

Plates are inserted through an incision at the top of the shoulder and applied to the end of the clavicle with screws into the distal end of the fracture. Some surgeons prefer to put a coracoclavicular sling to the fractured bone to provide additional stability(13) or perform CC reconstruction alone when the distal fragment is very small.(24) The exact technique of surgical approach and insertion of the type of plate and coracoclavicular sling will be recorded and will be the surgeon's decision. The principles of fixation with a plate are the

same for all types of plate, the choice of plate type, size and screw positions will be the surgeon's decision. The exact techniques and metalwork used will be recorded.

Post-operatively, the arm will be placed in an appropriately sized sling with guidance provided to participants on how to manage the sling and aftercare, including about axillary (armpit) hygiene and exercises. Movement of the arm will be expected to be encouraged from day one, with sling use initially for comfort, and to be discarded by the participant typically by two weeks after surgery. The type of sling used will be the health care professional's decision and recorded.

4.3.2.1 Surgeon's level of experience

To reflect the pragmatic design the level of experience of the operating surgeon will not be defined. All surgeons performing surgery on patients within the trial will be required to be familiar with the techniques and equipment that they are using. We will record the number of operations the surgeon has previously performed on this fracture population.

4.3.3 Physiotherapy

All participants will receive physiotherapy that may be delivered in person or remotely. Each centre will be provided with a "Physiotherapist Guidance" document about undertaking the physiotherapy. The frequency and timing of the physiotherapy will be a shared decision between the patient and physiotherapist. Participants will be provided with a standardised "Advice and early exercise" leaflet and video about undertaking home exercises. The use and acceptability of the home exercises, and frequency and setting within which the physiotherapy is performed, will be collected from participants.

4.4 COVID-19 mitigation

We have planned data collection methods to mitigate against any ongoing COVID-19 disruption. This includes hospital follow-up being aligned with routine appointments and data collection to be captured electronically. Both out-patient appointments and physiotherapy will be undertaken remotely if necessary as encouraged by our PAG and will follow government and NHS guidance. Training of hospital site staff, including ensuring sites are following relevant clinical and government guidelines, and monitoring of sites will be done remotely. Therefore, neither participants nor hospital staff will be at additional risk to COVID-19 exposure beyond that of normal clinical practice. Finally, whilst patients testing positive for coronavirus on admission are not specifically excluded from the study, it may be that these patients will not be considered suitable for surgery. The decision will be that of the treating surgeon in line with any local restrictions.

4.5 Outcomes

4.5.1 Baseline

At baseline we will record participant demographics and treatment preferences, the DASH to assess pre- and post-injury functioning, shoulder pain in the past 24 hours using a 11-point numeric rating scale (NRS) and the EQ-5D-5L. Patient satisfaction with appearance of shoulder and sensitivity/pain to touch will also be recorded. The surgeon or authorised staff will confirm the classification of the fracture, where necessary, after randomisation.(3, 15, 25)

4.5.2 Primary outcomes

The primary outcome measure will be the DASH (a 30-item self-administered outcome measure of upper extremity disability and symptoms, scored 0 (no disability) to 100) at 12 months.(26) This is when patients in both trial arms will have completed their treatment pathways. This will also be collected at 6 weeks, 3 and 6 months. All time-points are post-randomisation.

4.5.3 Secondary outcomes

- **Upper extremity disability and symptoms:** measured by DASH at 6 weeks, at 3, 6 and 12 months, and over 12 months.
- **Shoulder pain:** measured using an 11-item unidimensional numerical rating scale of pain intensity in adults (27) with 0 representing 'no pain' and 10 representing 'worst imaginable pain' in the past 24 hours at 6 weeks, and at 3, 6 and 12 months.(28)
- **Health-related quality of life:** measured at 6 weeks, and at 3, 6 and 12 months using the EQ-5D-5L, a validated measure of health-related quality of life in terms of 5 dimensions (mobility, ability to self-care, ability to undertake usual activities, pain and discomfort, anxiety and depression) each with 5 levels of severity.(29) The EQ-5D-5L will be scored according to the User Guide(30) and to calculate quality-adjusted life years (QALYs) according to National Institute for Clinical Excellence (NICE) best practice at the time of the analysis.
- **Complications:** This will include (but not be limited to) deep wound infection, (using Centres for Disease Control (CDC) and Prevention definition (31) superficial infection (using CDC definition), rehospitalisation (e.g. repeat surgery to remove metalwork), nerve and skin problems and collected at 6 weeks, and 3 and 12 months.
- **Health care resource use and impact on return to work and activities:** An accurate record of procedures at hospital level will be put in place in order to record the cost of surgery and complications via bespoke forms designed for this trial. Patient-reported questionnaires and hospital forms will be designed to collect information on hospital stay (initial and subsequent inpatient episodes, outpatient hospital visits and A&E admissions); primary care consultations (e.g. GP, nurse and physiotherapy); and return to work and to normal activities. These data will be collected from participants and hospital records at 6 weeks, and at 3, 6 and 12 months.

At 12 months, data will be collected from participants on:

- **Satisfaction with the appearance of their shoulder and pain/sensitivity to touch:** Participants will rate their satisfaction with the appearance of their shoulder using a 5-item unidimensional Likert scale that ranges from 'Very satisfied' to 'Very dissatisfied'. A 5-item unidimensional Likert scale will also be used to record how sensitive or painful to touch is the area where the collarbone is broken.
- **Shoulder range of movement (ROM):** Participants will self-assess both their shoulder ROM (32, 33) using a diagram based questionnaire (34, 35) that is proven to be reliable.
- **Treatment preferences:** a single question will ask whether the participant at this time has no treatment preference, or prefers surgery or sling.

Bone healing (i.e. union, non-union and malunion): This will be assessed and recorded using routine radiographs (typically anteroposterior and axial views) by the participating surgeons in clinic at the 3 and 12 month follow-up post-randomisation. If radiographs are not routinely available at these time-points, or the participant does not attend, then the most routinely available radiographs will be used. However, if at 12 months a hospital would not routinely take radiographs, these will be requested to be done. Radiographic union will be

defined as complete cortical bridging between the medial and lateral fragments on radiographs. Non-union will be defined as a lack of radiographic healing with clinical evidence of pain and motion at the fracture site.(25) Radiographic malunion will be defined as loss of the anatomic contour of the clavicle and whether it is symptomatic or not.(36)

Imaging will be performed at participating sites and may be undertaken at a different hospital site (including non-NHS sites) to the recruiting hospital in line with any changes to the routine imaging pathway at the recruiting site. Although to review patient eligibility and bone healing there are no additional radiographs required to be taken to that as part of standard care, under Ionising Radiation (Medical Exposure) Regulations (2017), appropriate approvals will be obtained to ensure risk is minimised. For hospitals that may not take routine radiographs at 12 months to assess bone healing, which will be an additional research exposure, this has been addressed in the IRAS application and explained to patients in the information sheet.

4.6 Sample size

This was calculated using a standard deviation value of 20 as estimated from the Canadian trial(6) in this patient population (personal communication). Minimal clinical important differences for the DASH are around 10 points from individual studies using anchor-based methods(26, 37). A 10-point difference on the DASH at 12 months represents the threshold at which treatment differences become important to patients and clinicians, and which would represent an appropriate noninferiority margin. This is the approach that has been taken in other surgical Health Technology Assessment (HTA) funded trials: DISC HTA - 15/102/04; HAND2 NIHR127393; SOFFT NIHR127739. For 90% statistical power, 170 participants are required to establish noninferiority of sling immobilisation compared with surgical fixation within a margin of 10 points on the DASH (SD=20), based on the upper limit of a 95% two-sided confidence interval (equivalent to a one-sided 97.5% confidence interval). Assuming 20% attrition at 12 months follow-up, gives the total target sample size 214. This rate of attrition should be feasible as was found with the SWIFFT trial (HTA 13/26/01) in a similar patient population that compared similar treatment options and the completion of a patient-reported outcome measure as the primary outcome at 12 months.

An audit of 18 hospitals and a survey of surgeons identified Principal Investigators at 23 sites and allowed us to estimate that sites would see an average of 1.5 cases per centre per month; therefore, 414 cases per year from 23 sites. Patients willingness to consent is estimated to be 50% based on three UK-wide upper limb, trauma surgical trials that compared surgery with a non-operative pathway i.e. ProFHER (displaced humeral fractures; HTA 06/404/53) consent rate of 250/560, 45%; SWIFFT (scaphoid waist factures; HTA 13/26/01) consent rate of 439/875, 50%; Ahrens et al (displaced midshaft clavicle fractures) consent rate of 302/533, 57%. ProFHER reported exclusions in eligibility criteria of 687/1250, 55% and the more recently conducted SWIFFT trial excluded 272/10147, 26%. Ahrens et al did not report this.(10) We expect the exclusions will align more with the recently conducted SWIFFT trial. Therefore, we conservatively estimate a further third lost to exclusions. This will provide an estimated maximum of 138 patients per year, on average 0.5 per site per year. Set up of the 23 sites will be staggered during the first year. Using these estimates, our sample size will be achieved after a 26 month recruitment period. We will start high-volume sites early and will constantly monitor recruitment and take appropriate mitigating action involving the PAG and our independent oversight committees where appropriate.

4.7 Participant recruitment

4.7.1 Screening and identification of patients for the study

Participating sites will record in REDCap the number of ineligible or non-consenting patients. This will allow the trial team to identify potential areas to target to improve recruitment rates. All distal clavicle fracture cases treated during the recruitment period will be recorded. Monitoring variability between sites in the proportion of undisplaced versus displaced fractures will be done at least during the pilot phase to check whether this is affecting recruitment at sites. For those patients with displaced fractures it will be recorded as to their age (years in bands), sex, ethnicity and postcode (first part) (to monitor inclusivity of recruitment into the trial), whether eligible to take part or not (with reasons for ineligibility), whether the patient has been approached to take part and whether recruited or not into the trial (reasons for unwilling to consent will be recorded if the patient provides this when seeking consent).

The identification of potential patients will be by the direct care team and will occur in the emergency department, fracture clinics and /or the orthopaedic trauma meeting of participating NHS hospitals. Posters will also be available to display about the study for patients, generic staff and specifically for staff in the emergency department. Radiographs taken as part of routine care will be used to assess eligibility (typically anteroposterior and axial views). A surgeon delegated to perform this task, will confirm eligibility and they, or other member of the direct team will invite the patient to consider joining the study.

4.7.2 Obtaining informed consent

After the initial identification of the patient by the direct care team and invitation to take part it will be a delegated member of the study team, for example, Research Nurse who will explain the study in more detail and seek to obtain consent. To help with seeking informed consent the patient will be provided with a participant information sheet (PIS) and complementary infographic sheet in an appropriate language either in person or via post or email and have the opportunity to ask questions of the surgeon and authorised staff at the site before deciding on taking part. The PIS will include a link to an animation which are commonly being used to communicate about a study in a more engaging and accessible way.(38) Potential participants may also be contacted by telephone by the direct care team to determine interest, and whether the patient would be willing to discuss the study in more detail with a delegated member of the study team either over the telephone or in clinic. The detailed PIS, will outline the study and clearly explain the risks and benefits of trial participation. Potential participants will be given contact details so they have the opportunity to ask questions of hospital staff and to discuss the trial with friends/family prior to agreement to take part. The patient will be asked when approached whether they have had sufficient time to consider participation and whether they agree to consent at that time; if required, they will be given further time to decide on whether to take part. Specific consent will be sought to enable the sharing of identifiable data with YTU in order to facilitate data collection. All members of staff involved in the informed consent process must have training in Good Clinical Practice (GCP).

Patients who are consented on-site will have the option to provide consent electronically using the REDCap study database or as an alternative a paper consent form will be provided. Consent obtained electronically will be held on a General Data Protection Regulation (GDPR) compliant secure software platform which will be password protected with access limited to named members of the study team. Copies of consent forms will be automatically generated following online completion and submission by patients. A copy will be provided to participants and available to the recruiting site in REDCap.

Patients may attend virtual fracture clinics, or staff may not be available to consent a patient in clinic at hospital. Therefore, in addition to on-site consent, this can be done remotely with the patient via telephone or videoconference. The same methods will be used to obtain consent and baseline data electronically using the REDCap study database or via post to the patient as a paper consent form along with a paper copy of the baseline CRF that will be returned back to the hospital. The patient should where possible sign the paper consent form, which on receipt will be uploaded by site staff to REDCap, or complete electronically, in the presence of the authorised person taking consent who are GCP trained. The authorised staff should also record in the patient's case notes and in the "Comments" eCRF in REDCap to explain any discrepancies in dates between when the patient and the staff member signed for consent. As above, a copy of consent will be provided to participants and be available to the recruiting site in REDCap which will also record whether it was on-site or remote consent that was obtained.

4.7.3 Associate Principal Investigators

An Associate Principal Investigator (API) scheme will be utilised at participating sites to involve aspiring researchers to coordinate study recruitment. The APIs will be trained in study processes and will be supervised by the PI at the site. Participating centres will be encouraged to involve local Trauma Co-ordinators and Specialty Trainees in Trauma and Orthopaedic Surgery, particularly "out of hours" (evenings and weekends) when Research Nurses or APIs may not be available. APIs will be acknowledged on the main publications.

4.7.4 Equality, diversity and inclusion of study participants

We have designed our eligibility criteria to be as inclusive as possible to reflect our target population of people experiencing a distal clavicle fracture. From the limited epidemiological data available on clavicle fractures we expect the injury to be substantially more common in men than women under 50 years old but similar incidence by sex in the over 50s. Clinical experience is that this is a fracture that can be experienced by anyone but is a more common injury amongst younger physically active people, particularly men of working age.(39) A key barrier to participation of this group can be data collection burden and hospital visits. We have timed the majority of our data collection around standard hospital visits and with all other data collected electronically. We appreciate that not all participants will be comfortable with electronic data collection and can offer alternatives such as collecting data by telephone or postally and then entered into the electronic system. This will ensure that participants are not at a digital disadvantage. The proposed financial incentives to participants at each time-point should ensure they are not out-of-pocket for taking part and are ethically acceptable incentives.

We will aim to ensure every person eligible has the same opportunity to take part and not to exclude underserved or vulnerable groups whether by demographic factors (e.g. age, sex, ethnicity, education) or social, economic and health factors.(39) Both the trial team and our independent oversight committees will monitor screening data to ensure patients are not being excluded for these reasons. We will also investigate whether deprived areas are adequately represented using the participant's postcode and also collect age (years), sex and ethnicity data at screening to monitor recruitment into the trial. We will also ensure awareness on all aspects of equality, diversity and inclusivity by embedding advice in our site training visits and provide site staff with resources about this with input from our PAG. We will have ongoing discussions about this with sites throughout the trial.

We anticipate that geography will be addressed by having a minimum of 23 sites distributed across the UK. We have collated the most up to date regional level data from multiple national sources to identify areas with high proportions of young males (40), alongside the index of multiple deprivation (41), index of health deprivation (41) and ethnicity (42). These

data have been linked and combined to ensure we recruit from geographic populations with high disease burden which have been historically underserved by research activity in this field. Examining this data shows that the 23 sites already identified to recruit to the DIDACT trial includes one in three of the top 5% of regions with the most vulnerable and underserved populations, and just under half of the top 10% of regions at the highest risk from a clavicle fracture. In addition, we will use this data to target recruitment at additional sites should those be needed during the trial.

We will consult throughout the study with our PAG to ensure inclusivity which will have a broad representation of people of different ages, ethnic and socioeconomic backgrounds and gender who have experienced collarbone injuries; and people with experience of supporting vulnerable patients with a shoulder problem. Our PAG will help us to prepare patient facing material using plain, simple language and to advise the trial team of any unforeseen barriers to recruitment or retention by particular sections of populations served that can feasibly be overcome. Capturing, evaluating and reporting this activity will be supported by our patient representative lead who will attend TMG meetings. We will also provide translations of the PIS to facilitate potential participants' understanding of the study; translate our newsletters to participants; and have budgeted for a translator to assist with data collection where necessary. Our primary outcome, DASH, is now available in 54 languages and dialects. We will also produce a recruitment video and infographic along with the sling care leaflet/video, the home exercise leaflets/video for participants with input from our PAG. These materials will also be translated and there will be translator support for the treatment guidance materials.

4.8 Randomisation

Allocation will be on a 1:1 ratio, using random permuted blocks of random block size, and stratified by age (<65 or ≥65 years) as a surrogate for the fragility of the fracture.(18) The allocation schedule will be generated by a trial statistician, otherwise not involved in the recruitment or randomisation of participants. It will be implemented using a secure web-based randomisation service managed by YTU, ensuring allocation concealment. The hospital staff at the site will confirm patient eligibility and consent and access the online service to perform the randomisation within 21 days of the index injury. As with many surgical trials, it will not be feasible to blind patients, surgeons, or outcome assessors to the treatment allocation.

5 Data management

5.1 Data collection methods

Trial participants will complete electronic Case Record Forms (eCRFs) at baseline and the follow-up time-points (6 weeks, 3, 6 and 12 months post-randomisation) with supplemental telephone/video follow-up for non-responders that will be entered directly into the study database. Postal completion of paper follow-up CRFs will also be permissible by participants who do not have ready access to devices to provide data electronically or when the questionnaires are provided in languages other than English. Paper completed CRFs by participants will be entered directly into the study database. Contact details will be provided to participants for if they need support with completing questionnaires. Delegated staff at participating sites will also complete eCRFs as shown in the study assessment schedule and will be offered a tablet to do this.

The trial database to manage this data is REDCap (Research Electronic Data Capture) and is hosted on a secure cloud-server in Amazon Web Services, in the UK region. A CRF

specification plan will be completed for all the instruments to be included in the database with the respective questions, responses and validation rules. A project specification form will also be completed that details the requirements of the project such as what events are due and who has access to the system and their role. The randomisation system will be hosted outside of REDCap, it will take data from and feed back into REDCap.

As a duty of care, participant data will be reviewed to check for anything that indicates that the participant could be at risk of harm. Where this occurs, the hospital team will be notified of this and their General Practitioner as necessary.

YTU will develop the study database in REDCap and manage the data collection. All reporting of data collection will be undertaken in line with the Consolidated Standards of Reporting Trials (CONSORT).(43)

5.1.1 Access to data

Data will be held securely on the cloud-hosted REDCap server. Access to the study interface will be restricted to named authorised individuals granted user rights by a REDCap administrator at YTU. Authorised users will be required to set passwords in line with University of York's policy and enable 2 factor authentication. Study documents (paper and electronic) held at the University of York will be retained in a secure (kept locked when not in use) location for the duration of the trial. All work will be conducted following University of York's data protection policy which is publicly available.

The sponsor, University Hospitals of Leicester NHS Trust, are data controller for this study which will be detailed in a collaboration agreement between the sponsor and the University of York. There will also be an agreement between the sponsor and each of the participating sites (within the model Non-Commercial Agreement (mNCA)) that will include data sharing responsibilities with YTU.

The Investigator(s)/institution(s) will permit authorised representatives of the sponsor and applicable regulatory agencies direct access to source data/documents to conduct trial related monitoring, audits and regulatory inspection. Trial participants are informed of this during the informed consent discussion. Participants will consent to provide access to their medical notes.

5.1.2 Plans to promote retention

To minimise attrition, we will use multiple methods to keep in contact with patients. We will ask patients for full contact details (including mobile phone number and email address). Patients will also be asked to consent to agree to their General Practitioner being contacted for their address and using NHS Digital (the Spine portal) to help stay in contact in England and Wales or the Community Health Index in Scotland. For all follow-up data collections, two reminders (at 2 weeks and 4 weeks) will be sent to non-responding participants, with a final attempt to obtain data by a telephone/video call at 6 weeks. Around a month before the 12 month questionnaire is due (primary end-point), the participant will receive by post/electronically a flyer to expect the questionnaire as there is evidence that pre-notification can improve response rates.(44) Participants will receive a gift voucher for completing questionnaires at 6 weeks (£5), 3 months (£5), 6 months (£20) and 12 months (£20).(44) The increase at 6 months is because the data collection is not aligned to a clinic and at 12 months as this is the primary end-point. We will text participants to prompt completion as part of the embedded SWAT and non-responders will be contacted via text, email or mobile when necessary about being available to complete the questionnaire over the telephone or video.(44) Regular newsletters will be sent to participants during the trial to keep them informed and engaged with the trial.(45) In addition, we will underpin data collection based on our experience and stakeholder engagement when completing another

orthopaedic surgical RCT in a primarily young, male population (SWIFFT HTA – 11/36/37).(46, 47)

Imaging and reports from peripheral sites can be directly accessed by the participating site to help with assessment of bone union, imaging can also be retrieved by the participating hospital for local area/regional hospitals using Picture Archiving Communication Systems (PACS). Furthermore, if a participant moves away from the participating site and is followed-up at a hospital not taking part in the trial, follow-up data (e.g. re-operations, complications, infections) can be requested securely through NHSmail. Both these mechanisms for capturing data are available as would occur in routine clinical practice. A bespoke letter and flyer is also available to hospital staff to encourage participant attendance at the 12 month clinic which is the primary end-point for the study.

5.2 Proposed time period for retention of relevant trial documentation

Essential Trial documentation (i.e. the documents which individually and collectively permit evaluation of the conduct of a clinical trial) will be kept with the Trial Master File and Investigator Site Files. The sponsor will ensure that this documentation will be retained for a minimum of five years after the conclusion of the trial to comply with standards of GCP. They will then be securely destroyed as per York Trial Unit Standard Operating Procedures and/or that of the Sponsor.

Data that is collected on paper will be stored for a minimum of 10 years after the conclusion of the trial in a secure University managed storage facility or off-site and similarly then destroyed securely. Data that is stored electronically will also be stored for a minimum of 10 years on secure, password-protected University computers. We plan to indefinitely store de-identified data, with the unique study ID removed, that is truly anonymous.

5.3 Embedded Study Within A Trial (SWAT)

An electronic prompt compared with no prompts may improve patient follow-up (RR 1.03 (0.98 to 1.08)).(44)

An embedded SWAT, not yet being undertaken from a search of the Northern Ireland SWAT repository, will be conducted to evaluate whether including a timeframe to complete the questionnaire has an effect on questionnaire return. Participants will be randomly allocated on a 1:1 ratio to get a prompt at each follow-up that either will or will not ask for the questionnaire to be completed within the next 7 days. Our PAG has informed the wording of the text message.

Generation of the SWAT allocation will be undertaken independently by a statistician at York Trials Unit not involved with the DIDACT follow-up process. Block randomisation stratified by the main trial treatment allocation using randomly permuted block sizes will be used. Allocation will take place at the time of allocation to the main trial. The sending of text messages will be hosted outside of REDCap and will be sent using a secure UK-based text message gateway software, for example, Intelli Software.

The primary outcome of this embedded SWAT is the response rate to the participant follow-up questionnaire at 12 months. Secondary outcomes include: response rates to the participant follow-up questionnaire at 6 weeks, 3 months and 6 months; whether the participant required a reminder; completeness of the primary outcome for the main trial (defined as providing sufficient data to produce a valid summary score); and time to response.

Analysis of dichotomous outcomes will be via a mixed-effect logistic regression model adjusting for main trial allocation, and site as a random effect. Time to response will be analysed using a Cox proportional hazard model with shared centre frailty and adjusting for main trial allocation.

6 Statistical methods

6.1 Internal pilot

The recruitment rate and 95% confidence interval (CI) will be estimated from the data collected. A CONSORT diagram will be constructed to show the flow of participants through the study and the following outcomes calculated: number of eligible patients; proportion of eligible patients approached for consent; proportion of eligible patients not approached and reasons why; proportion of patients approached who provide consent; proportion of patients approached who do not provide consent; proportion of patients providing consent who are randomised; proportion of patients randomised who do not receive the randomly allocated treatment; proportion of patients dropping out between randomisation and follow-up; proportion of patients for whom a primary outcome is recorded. Data will be summarised on the reasons why eligible patients were not approached, reasons for patients declining to participate in the study; reasons why randomised patients did not receive their allocated treatment and reasons for drop-out, if available. Results will be compared against the study's recruitment assumptions and progression targets.

6.2 Statistical analysis full trial

For the analysis of the full trial (assuming continuation) a CONSORT flow diagram will be provided to display the flow of participants through the study. Baseline characteristics will be presented descriptively by group. All outcomes will be reported descriptively at all collected time points. Continuous data will be presented using means and standard deviations or medians and ranges as appropriate, and categorical data will be presented using frequencies and percentages. The primary analysis will be on an intention-to-treat (ITT) basis, analysing patients in the groups to which they were randomised. A mixed-effects linear regression model will be used to compare groups, adjusting for stratification factors and relevant baseline covariates as fixed effects and centre as a random effect. Non-inferiority will be accepted if the upper bound of the two-sided 95% confidence interval (equivalent to a one-sided 97.5% CI) lies within the non-inferiority margin of 10 at the 12 month time point.

Completeness of data at follow-up will be reported by group. In non-inferiority comparisons in the presence of treatment switching the ITT analysis could bias towards the null, which may lead to false claims of non-inferiority, hence we will undertake both ITT and CACE (complier average causal effect) analyses. Full analyses will be detailed in the trial's statistical analysis plan (SAP), which will be reviewed and approved by the trial steering and data monitoring committees and finalised before the end of patient follow-up. All analyses will be conducted in STATA v17 (StataCorp LP, College Station, TX, USA), or later (to be confirmed in the final report).(48)

7 Economic analysis

The embedded health economic evaluation assesses the relative cost-effectiveness of surgery compared with sling immobilisation in the management of adults with a displaced fracture of the distal clavicle in order to determine which treatment offers the best value for

money for the NHS. The methods will be consistent with the NICE Guide to the Methods of Technology Appraisal.(49)

An NHS and personal social services (PSS) costing perspective will be taken in the base case analysis; relevant costs will include participant level NHS resource use, medication use and related social services. The time horizon of the analysis will be 12 months. A secondary analysis will explore the wider societal perspective.

The costs of providing the treatments will be based on national tariff data. Applying national average costs makes the results more generalisable when cost-effectiveness results are considered for wider adoption by policy-makers. We will also include the cost of the operation to remove metalwork implanted in the surgery arm and the necessary surgery following non-union in the sling immobilisation arm. These costs represent key extra costs of the respective treatment arm and are an important resource implication which is factored into the economic evaluation.

Health care utilisation data for contacts with the NHS and PSS are recorded using a bespoke service use questionnaire. The healthcare resource data will be collected using patient self-administered questionnaires and hospital forms. Quantities recorded are multiplied by national average unit costs in the appropriate year at the time of analysis (50, 51) to derive a cost profile for each participant in each arm of the trial.

We will also collect costing data to inform a cost-utility analyses from a societal perspective. The trial will assess the impact of both treatments on days of lost employment by participants and their unpaid carers, and any paid additional care required. In addition to the base-case analysis conducted from the perspective of the NHS and PSS, we will conduct a secondary analysis to explore the impact of productivity costs and extra personal spending on cost effectiveness results. The wider cost data does not form part of the base case but can be submitted as supplementary evidence.

Health related quality of life (HRQoL) will be quantified using EQ-5D-5L(52) administered at baseline, six weeks, 3, 6 and 12 months. The UK social tariff is applied to EQ-5D-5L responses to derive utility values from patient responses at each data point. We will use the valuation method as recommended by NICE at the time of analysis to calculate Quality Adjusted Life Years (QALYs)(53) using the area under the curve approach.(54) QALYs will be the primary outcome for the economic evaluation.

Regression methods, adjusted for key covariates, will be used to estimate incremental costs and QALYs (on an ITT basis) by treatment allocation. Patient costs are combined with QALYs to estimate the incremental cost per QALY of the surgery comparing to the sling immobilisation over the follow-up.

If deemed appropriate the short-term cost-effectiveness will be extrapolated beyond the trial follow-up.

Underlying uncertainty around the decision to adopt the intervention is assessed using non-parametric bootstrap re-sampling. Bootstrapping is an efficient method for calculating the confidence limits for the ICER as its validity does not depend on any specific form of underlying distribution. We perform the bootstrap to produce 5,000 replications and construct the cost-effectiveness plane based on the bootstrapping results. Cost-effectiveness acceptability curves (CEAC) will be constructed based on the bootstrap iterations(55) to illustrate the probability that the surgery is more cost-effective than sling immobilisation at different acceptable ICER threshold values. The probability that surgery is more cost-effective than sling immobilisation will be marked specifically at the NICE

maximum acceptable ICER threshold range of £20,000 to £30,000/QALY and also £13,000/QALY by empirical studies.(49, 56)

A range of sensitivity analyses is undertaken to assess the impact of missing data. In the main analysis, missing data will be imputed using multiple imputation method and analysed following Rubin's rule.(57) As part of the sensitivity analysis, we will conduct an additional set of analyses using the complete case analysis (CCA), whereby results are analysed only for those participants who had both the completed cost and outcome data at the same time. We will also examine the assumption of missing data pattern using pattern mixture modelling.(58) Given the implication of the painful shoulder for the patient in terms of loss of earnings, as well as private care costs, a sensitivity analysis from a broader perspective will also be conducted.

We will maintain the integrity and neutrality of the heath economic analysis by presenting a detailed *a priori* health economics analysis plan. The plan will pre-specify the methods used for the health economic analysis, the data-sources and the outcomes for analysis.

8 Project management

DIDACT will be sponsored by University Hospitals of Leicester NHS Trust. Each site will have a site PI who will be responsible locally for the study and an API who will be a trainee surgeon. The day-to-day running of the project will be undertaken by the Trial Manager based at YTU, supported by YTU senior staff. The Trial Manager at YTU will be responsible for all aspects of trial management. They will be supported by a Trial Co-ordinator, who will be responsible for the day-to-day support to trial sites, data handling, and the management of the administrative trial team. The team at YTU will meet on a weekly basis during the study and will work closely with the Chief Investigator throughout, including regular meetings to ensure that all aspects of preparation of study material, study site setup and the start of recruitment progress smoothly and throughout the trial. YTU staff will keep in close contact via email, telephone or videoconferencing throughout.

The trial team is experienced in working with local investigators at recruitment sites to ensure ethical and efficient delivery of trials in compliance with the trial protocol. In addition to regular TMGs, the trial team will keep in regular contact with sites and use joint local investigator meetings, newsletters and other forms of communication to monitor progress, support any struggling sites, and to share good practice across sites.

8.1 Trial Management Group

A Trial Management Group (TMG) will monitor the day-to-day management (e.g. protocol and ethics approvals, set-up, recruitment, data collection, data management) of the study chaired by the Chief Investigator. Membership will include the Chief Investigator, co-investigators and research staff on the project. Throughout the project there will be regular video/teleconference contact supplemented by face-to-face meetings where required. Frequency of meetings will vary depending on the stage of the trial but at least monthly during the early stages and pilot.

8.2 Trial Steering and Independent Data Monitoring Committee

A Trial Steering Committee (TSC) will monitor progress of the study, provide independent advice and the independent chair will make recommendations to the funder. An Independent Data Monitoring Committee (IDMC) will monitor the data arising from the trial and recommend to the TSC on whether there are any ethical or safety reasons why the trial

should not continue. The TSC and IDMC will meet regularly to provide oversight to the study. The project will also be monitored by the sponsor and a representative will be invited to attend the TSC meetings.

9 Safety monitoring

Participants will be allocated to routinely delivered treatments in the NHS and therefore the risks are not increased through trial participation.

9.1 Definitions

Adverse events (AE) are defined as any untoward medical occurrence in a trial participant and which do not necessarily have a causal relationship with the treatment. Only medical occurrences specific to the participants' clavicle fracture that are 'unexpected' and up until the 12-month follow-up will be classified as events when non-serious. This is because 'expected' events are well known complications for the two routine treatment options which the specialist clinical care teams will be experienced in managing.

Serious adverse events (SAEs) will be defined as any untoward medical occurrence that:

- Results in death.
- Is life threatening (that is it places the participant, in the view of the Investigator, at immediate risk of death).
- Requires hospitalisation or prolongation of existing inpatients' hospitalisation (unplanned refers to emergency hospitalisations resulting in an inpatient stay; prolonged hospitalisation is deemed to be where a patient's stay is longer than expected).
- Results in persistent or significant disability or incapacity.
- 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.

Medical occurrences about the participant's clavicle fracture that are serious and up until the 12 month follow-up will all be reported as SAEs (including deaths for any reason) whether expected or not.

9.2 Collection, recording and reporting of adverse events

A delegated member of staff at the hospital will record all AEs or SAEs on the appropriate eCRF in REDCap. In addition, sites should follow their own local procedures for the reporting of any adverse events.

AEs and SAEs will be reported to YTU within five days or 24 hours respectively of the site investigator becoming aware of them. Once received, causality (or 'relatedness') and expectedness will be confirmed by the Chief Investigator. SAEs that are deemed to be unexpected and related to the trial treatment will be notified to the Research Ethics Committee (REC) and sponsor within 15 days.

Expected events that do not need reporting are: complications of anaesthesia or surgery (59) (e.g. wound complications, infection, damage to a nerve or blood vessel, frozen shoulder, coracoid fracture, metalwork failure and thromboembolic events) and secondary operations for or to prevent infection, malunion, non-union or for symptoms related to the metalwork.(59, 60) Nor does any of the above that may arise from sling immobilisation pathway need reporting, including swelling, bruising, discomfort or stiffness from sling use.(6, 8)

Follow-up reports a month later of all AEs and SAEs will be reviewed by the Chief Investigator to ensure that adequate action has been taken and progress made.

AEs and SAEs will be monitored regularly at TMG meetings and reported to the TSC and IDMC when they meet.

10 Research governance

10.1 Ethical considerations and approval

The trial will be conducted to protect the human rights and dignity of the patients as reflected in the Declaration of Helsinki.(61)

Formal NHS REC approval and that of the Health Research Authority (HRA) will be sought and will include all the documentation to be given to patients. Local R&D approvals (confirmation of capacity and capability) and the Sponsor green light will be obtained for participating sites prior to recruitment starting. Any further amendments to the trial protocol will be submitted and approved by the appropriate regulatory authorities where required.

The PIS will be developed with the involvement of our PAG and will give a balanced account of the possible benefits and known risks of the interventions. It will state explicitly that quality of care will not be compromised if the participant decides to a) not enter the trial or b) withdraw their consent. Informed consent will be obtained from all trial participants after they have had sufficient time to read the study materials and ask any questions.

In the context of the lack of robust evidence to determine the best treatment for displaced clavicle fractures and comparing routine treatment pathways the risks to patients are not increased through trial participation. Therefore, we do not anticipate major ethical concerns with this study.

10.2 Proposed action to comply with the medicines for human use (clinical trials) regulations 2004

The techniques under investigation are well-recognized and international accepted surgical procedures using CE-marked implants and medical devices. We do not therefore require prior authorisation by the UK Competent Authority, the MHRA, under the Medical Devices Regulations (2002).(62)

10.3 Regulatory compliance

The trial will comply with the approved protocol and adhere to the HRA and the UK Health Department policy framework (63) and MRC Good Clinical Practice Guidance.(64) An agreement will be in place between the site PI and the sponsor, setting out respective roles and responsibilities.

All deviations from the protocol or GCP will be reported by PIs or designated site staff to YTU. The site must inform the PI as soon as they are aware of a possible serious breach of compliance, so that the sites can report this breach to the trial sponsor (via YTU) with onward reporting to ethics and regulatory bodies as necessary. For the purposes of this regulation, a 'serious breach' is one that is likely to affect to a significant degree:

- The safety, physical or mental integrity of the participants in the trial, or
- The scientific value of the trial.

Processing of all trial data will comply with GDPR as implemented in the Data Protection Act 2018.(65)

Monitoring of sites to ensure that the trial is complying with the approved protocol and regulatory requirements will also be undertaken by YTU. The monitoring plan will be kept in the Trial Master File.

10.4 Patient confidentiality

The researchers and clinical care teams must ensure that patient confidentiality will be maintained and that their identities are protected from unauthorised parties. Patients will be assigned a unique participant identification number which will be used on eCRFs. Sites will securely keep and maintain the patient Enrolment Log showing participant identification numbers and names of the patients. This unique participant number will identify all eCRFs and other records.

All records will be kept in locked locations. All paper copies of consent forms will be secured safely in a separate compartment of a locked cabinet. Electronic copies will be stored separately to clinical information and access restricted to study personnel. Clinical information will not be released without written permission, except as necessary for monitoring purposes.

10.5 Trial Closure

The end of the trial will be defined as the last patient's last contact at 12 month follow-up and all their data are entered, checked and queries resolved.

An end of study declaration form will be submitted to the REC and sponsor within 90 days of trial completion and within 15 days if the trial is discontinued prematurely. A summary of the trial report and/or publication will be submitted to the REC, sponsor and Funders within 12 months of the end of the trial.

10.6 Annual progress reports

An Annual Progress Report will be submitted to the REC that gave the favourable ethics opinion 12 months after the date on which the favourable opinion was given and thereafter until the end of the trial (if applicable). The Sponsor will also be provided with a copy of these reports.

10.7 Urgent safety measures

The site PI may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. These safety measures should be taken immediately and may be taken without prior authorisation from the REC.

10.8 Indemnity

This trial will be sponsored by University Hospitals of Leicester NHS Trust. If there is negligent harm during the trial, when the NHS Trust owes a duty of care to the person harmed, NHS Indemnity covers NHS staff and medical academic staff with honorary contracts only when the feasibility of the trial has been approved by the R&D department. NHS indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm.

11 Patient and public involvement

Our research is addressing a James Lind Alliance Priority Setting Partnership priority topic of whether clavicle fractures should be managed with or without surgery.(16) We have undertaken a consultation with our PAG to inform the design and delivery of the study. This included the PAG recommendation that they would agree to be randomised between sling versus surgery on the understanding that surgery would be possible if indicated at a later date. Therefore, we will explain to patients that their progress and bone healing will be assessed clinically and radiographically when they attend hospital visits as would occur during routine clinical practice. Any decision to operate will be a structured and shared decision between the surgeon and patient. Our PAG also discouraged including hook plates as these need a further operation to be removed due to the risk of damage to the rotator cuff muscles which in the long term could slow the speed of recovery and be of more pain and burden to patients. The proposed trial design should be more acceptable to patients and is centred around what is important to them. Our PAG also recommended the use of electronic data collection where possible and the need for and amount of financial incentives for patients.

During the trial, our PAG will contribute to the development of study materials, advise on optimising the inclusion of patients with respect to our aims for EDI and we will discuss with them any challenges that arise in the delivery of the study. We will engage with trial participants through regular newsletters and Twitter and the wider population by updating the Wikipedia page about clavicle fractures and informing the Royal Society of Prevention of Accidents (RoSPA) about our research. We will work closely with our PAG to develop various outputs: a leaflet that summarises the findings in plain, simple English; an infographic and animation; and a booklet about the condition. We will use press releases and social media to publicise these outputs (e.g. Twitter, LinkedIn, YouTube) and will seek to upload these on various websites (e.g. sponsor and YTU, BESS, Wikipaedia, RoSPA, Cycling UK) with input from our PAG about the most appropriate channels of communication. Research comms support and advice will be available from the Sponsor on keeping in contact with participants during the trial through appropriate channels. All participants will be offered to complete the NIHR Participant in Research Experience Survey.

12 Plan of investigation and timetable

The project duration is 50 months with a proposed contractual start date of 1 November 2022. The timetable is summarised below.

Activity	Duration	Time period
Preparing study set up including relevant approvals	1-6 months	1 Nov 2022 to 30 Apr 2023
Recruitment for internal pilot phase	7-18 months	1 May 2023 to 30 Apr 2024
Recruitment for main trial phase	19-32 months	1 May 2024 to 30 Jun 2025
Final follow-up	33-44 months	1 Jul 2025 to 30 Jun 2026
Statistical/health economic analyses and write up of HTA report	45-50 months	1 Jul 2026 to 31 December 2026

13 Finance

The financial arrangements for the trial will be as contractually agreed between the funder (HTA), and the Sponsor (University Hospitals of Leicester NHS Trust). There will be a separate collaboration agreement between the Sponsor and the collaborating organisations.

14 Dissemination policy

This trial has the potential to improve joint decision making about the management of a displaced, distal clavicle fracture. DASH as the primary outcome, will allow a clear discussion between surgeons and patients regarding the benefits of one approach over the other. We will develop a dissemination strategy at the outset of the project which will be reviewed and adjusted by the TMG as required during the study. This will provide established pathways for the dissemination of the results when they are available. BESS has adopted the trial for inclusion in their research portfolio which will facilitate dissemination of findings to relevant stakeholders. A number of dissemination channels will be used to inform clinicians, patients and the public about the project and the results of the study. The projected outputs are listed below:

- The study protocol will be published in a peer-reviewed, open access journal, before the end of recruitment.
- A HTA monograph will be produced.
- On completion of the study, the findings of the trial will be presented at national and international meetings of organisations that will target orthopaedic surgeons such as the British Orthopaedic Association (BOA) Annual Congress, the British Shoulder and Elbow Society (BESS), European Federation of National Associations of Orthopaedics and Traumatology (EFORT), European Society for Surgery of the Shoulder and the Elbow (SECEC) and American Academy of Orthopaedic Surgeons. We will also target physiotherapists at BESS, The Chartered Society of Physiotherapy: Physiotherapy UK Conference, Allied Health Professional roadshows, BOA Annual Congress, and European Society for Shoulder and Elbow Rehabilitation (EUSSER).
- The study findings and patient-focused outputs will be cascaded to trainee surgeon networks (e.g. BOTA, CORNET) and we will seek to upload these outputs on their websites. The study findings will also be cascaded to Industry who produce the implants and also to Getting It Right First Time (GIRFT) which is a national programme designed to improve medical care within NHS by reducing unwarranted variations.
- The executive summary and copy of the trial report will be sent to NICE and other relevant bodies, including Integrated Care Systems, so that the study findings can inform their deliberations and be translated into clinical practice nationally. We will also work with the relevant National Clinical Director in the Department of Health to help ensure the findings of the trial are considered when implementing policy and will work with the Speciality Advisory Committees (SAC) to incorporate the findings into the training curriculum for clinicians who undertake surgical fixation of these fractures.
- The study report will be published in peer reviewed high impact general medical and orthopaedic journals, such as Lancet, the BMJ, the Bone and Joint Journal or similar.
- The study results will be shared with relevant evidence synthesis teams (including within the Cochrane Collaboration) in order to ensure that results are incorporated in future systematic reviews.
- A plain English summary leaflet of the study findings, will be produced and made available to participants, members of our user group and relevant patient-focused websites. In conjunction with the PAG we will develop an infographic and an animation to disseminate the findings.
- During the study webpages will be hosted on the Be Part of Research/YTU websites as an information resource for participants and we will work with the PAG to map the relevant websites who may be willing to make the information available. For example, distal clavicle fractures are common amongst cyclists and Cycling UK currently has an information page on clavicle fractures so are likely to be interested in the results of our trial.

- As part of the trial an information booklet on the condition, treatment options, the likely recovery process and physiotherapy exercises will be produced. We will explore making this more widely available to patients following the trial, with the inclusion of the study findings. This could be through hospitals as well as websites identified for the infographic and animation.
- The findings of the SWAT will be disseminated in a relevant journal read by trialists such as BMC Trials or BMJ Open and disseminated at relevant conferences such as the International Clinical Trials Methodology Conference.
- The study will be publicised at the start of the study, to help engage with different audiences and promote the study, and also to disseminate findings using press releases at the collaborating institutions and social media e.g. Twitter, LinkedIn, YouTube.
- These outputs will also be uploaded to various webpages (e.g. Sponsor, YTU, BESS, Wikipedia, ISRCTN registry).

The various outputs that we produce will be freely available to the NHS and public and is likely to only require IP protection with the use of a copyright statement from the Sponsor.

Access to fully anonymised trial dataset to a third party may be granted following review with the TMG. Participants will be informed that information collected about them may be shared anonymously with other researchers and will be asked to consent to this.

14.1 Anticipated impact of the research

The impact of our research is to benefit patients, surgeons and healthcare professionals by establishing an evidence-based treatment pathway for the management of this fracture that will facilitate shared decision-making. This should improve patients' wellbeing and ensure the efficient delivery of NHS services. There is growing evidence that orthopaedic surgical trials conducted in the UK can have a significant impact on clinical practice.(66, 67) We can achieve this too with our proposed plans.

In order to analyse the reach of our dissemination the journals that we will publish in are likely to provide an Altmetric score which includes citations in other journals and Twitter demographics. Similarly sharing the infographic and animation using social media such as Twitter and YouTube will allow us to record activity about its use. When we upload the infographic, animation and information booklet on various websites we will seek to allow the number of downloads to be recorded.

The trial team will engage with our PAG and the IP/Contracts Manager at the Sponsor to develop and implement an impact realisation plan. The aim of our impact is as follows.

(a) Short term:
- for the dissemination of the study findings to have real influence in informing treatment pathways and shared decision-making about the management of adult patients in our target population as illustrated using an infographic and animation;
- to provide a resource for our target population with an information booklet on the condition, the treatment options, the likely recovery process, physiotherapy exercises and study findings.

(b) in the short to medium term:
- to monitor access to the above outputs on appropriate websites.

(c) in the medium to long term:

- to use a dataset such as HES, potentially involving another NIHR workstream (e.g. CLAHRC), as has been done for other orthopaedic surgical trials(66) to assess whether there has been a change in the management of patients in our target population in terms of the number of operations being performed and explore the cost consequences of this.
- to follow-up with users of the infographic, animation and information booklet on the various websites as to how useful they have found this with input from our PAG about how to most effectively achieve this.

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