TRIAL PROTOCOL

Hand-2

Needle fasciotomy versus limited fasciectomy for the treatment of Dupuytren's contractures of the fingers: a randomised non-inferiority trial (Hand-2)

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1 Protocol development and sign off

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Protocol Amendments				
The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version				
Amendment number	Date of amendment	Protocol version number	Type of amendment	Summary of amendment
NSA01	17 Feb 2022	1.2	Non-substantial	1) Inclusion criteria updated -One or more fingers with a Dupuytren's contracture of ≥30° with functional problems' 2) Section 8.2 - '2PD sensation' removed as this measurement is not required. 3) Addition of pre-intervention assessment time point (up to 4 weeks prior to or on the day of surgery) to allow exploring the effect of any significant delays between randomisation and intervention (due to pandemic related increases in waiting list times). 4) Section 13.4 (Procedures for missing data) under 'missing baseline data' to include additional statement clarifying that where there are published methods for dealing with missing items in questionnaire outcome measures, these will be applied.

				5)Needle Aponeurotomy/Needle Fasciotomy Protocol added in the appendix. This document will be used to aid Health Care Professionals. 6)Statistical Methods and section 13.3 CACE analysis replaced with per protocol analysis.
NSA02	10 March 2022	1.2	Non-substantial	Basingstoke has been added as a site. This does not affect the protocol.
NSA03	22 March 2022	1.2	Non-substantial	Leicester has been added as a site. This does not affect the protocol.
NSA04	13 April 2022	1.2	Non-substantial	Winchester and Basingstoke merged sites to become Hampshire. This does not affect the protocol.
SA01	24 Jun 2022	2.0	Substantial Amendment	1. Addition of recruitment patient pathway in section 7.1.2. 2. Section 8.2- Allows treatment to be performed in independent sector. 3. Change to the time point of pre-operation clinics assessment up to 8 weeks prior to intervention/ surgery.
NSA05	13 Dec 2022	2.1	Non-substantial	1. Study duration corrected from 24 to 60 months 2. Update to co-ordinating centre contact details
NSA06	12 Apr 2023	2.2	Non-substantial	Removal of fax number for SAE reporting
SA02	05 May 2023	3.1	Substantial Amendment	1. Changes to SAE reporting guidance 2. Correction to table 1 table of assessments 3. Clarify inconsistent eligibility criteria 4. Clarify date of NSA01 on protocol 5. Insert reference to NSA02, NSA03 and NSA04 6. Update participant flow diagram to more accurately represent trial activities

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2 CI Signature Page	
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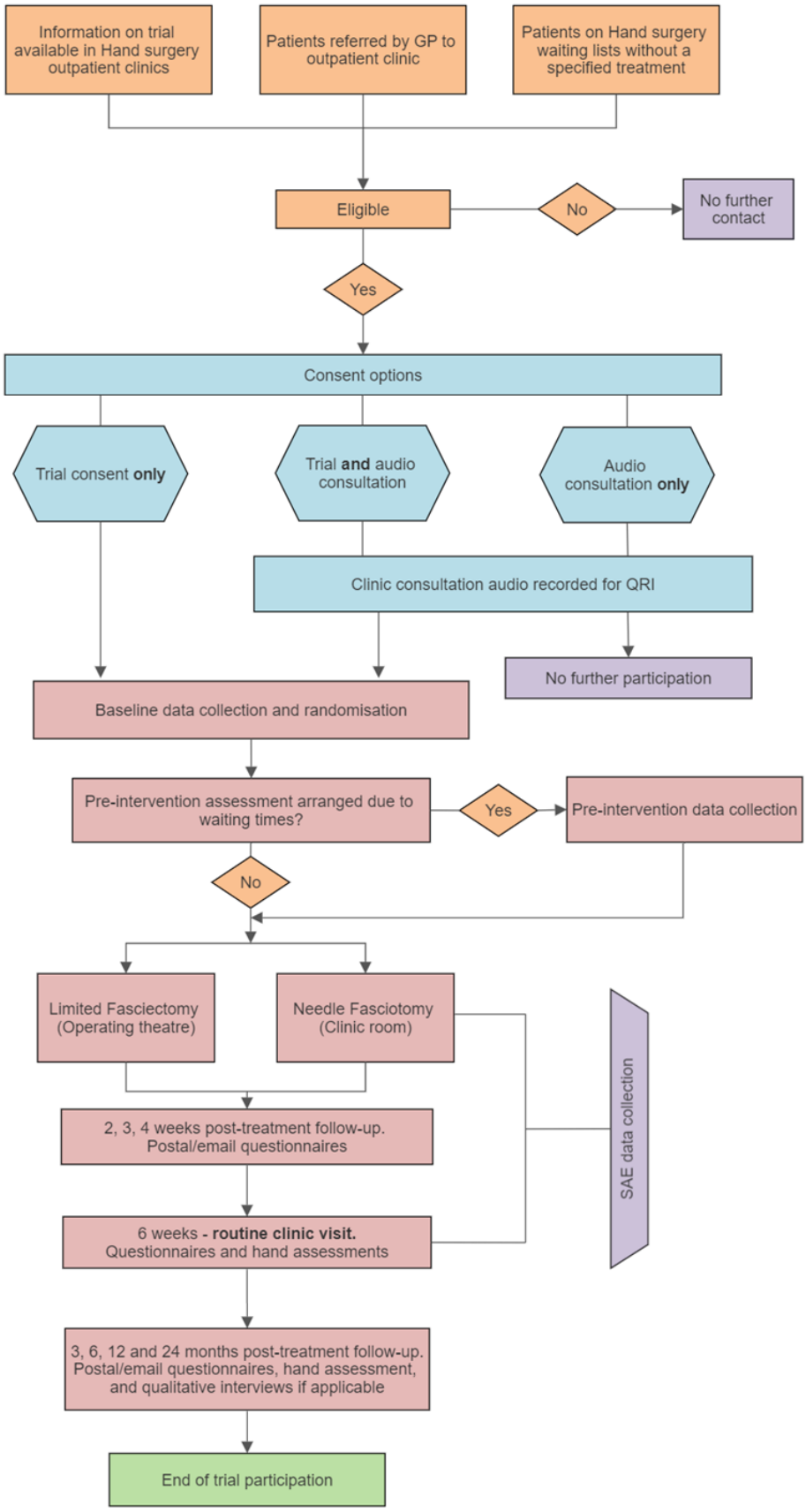
1. TRIAL SUMMARY

Title	Hand-2: Needle fasciotomy versus limited fasciectomy for the treatment of Dupuytren's contractures of the fingers: a randomised, multi-centre non-inferiority trial.
Trial Design	Multi-centre, two-arm, parallel randomised, non-inferiority trial.
Objectives	**Primary:** To determine whether, in adults with Dupuytren's contractures of the fingers, treatment with needle fasciotomy (NF) is non-inferior to limited fasciectomy (LF) in terms of hand function 12 month post-intervention. **Secondary:** To compare NF and LF for short-term recovery and up to 24 months post-intervention for: complication and re-operation rates, health-related quality of life, healthcare resource, cost effectiveness and treatment acceptability.
Setting	Acute Care UK NHS Trusts
Participant population and Key eligibility criteria	Adults referred from primary to secondary care, or on hand surgery waiting lists, with a Dupuytren's contracture of a previously untreated finger which satisfies the NHS/CCG criteria for intervention and is suitable for treatment with either NF or LF. Inclusion Criteria 1. Age ≥18 years 2. One or more fingers with a Dupuytren's contracture of≥30°with functional problems 3. No previous treatment for Dupuytren's contracture on study finger 4. a) Well defined cord(s) and b) suitable for NF and LF 5. Able to comply with the requirements of the study up to 24 months post-intervention Exclusion Criteria 1. Dupuytren's contracture of the distal interphalangeal joints (DIP) only 2. Planned dermofasciectomy or very limited fasciectomy (excision of≤1cm cord segment) 3. Previously recruited into this study for treatment of either hand
Intervention	Intervention: Needle Fasciotomy This procedure can take place in an outpatient clinic room or operating theatre setting. The contracture is divided with a needle which pierces the skin (no skin incision). Control: Standard Care: Limited Fasciectomy This procedure takes place in an operating theatre
Study duration	60 months
Primary outcome	Participant reported assessment of hand function using the Hand Health Profile of the Patient Evaluation Measure (PEM) questionnaire at 12 months post intervention

Secondary outcome	a) Participant reported assessment of hand function and overall satisfaction using the Hand Health Profile PEM questionnaire 3 weeks, 6 weeks, 3 month, 6 months and 24 months post intervention. b) Participant-reported quality of life/health measures (MYMOP, SANE, EQ-5D-5L) c) Loss of finger extension d) Adverse effects of treatment (complications) e) Recurrence of DC f) Need for revision surgery g) Cost and cost utility h) Patient experiences and acceptability of treatment
Sample size	406 participants (203 each arm) are required to achieve 90% power to detect non-inferiority of NF compared to LF within a margin of 6.0 on the PEM at 12 months using SD of 16.6, based on 2.5% 1-sided alpha and allowing for 20%loss to follow-up.
Randomisation and blinding	Eligible patients who consent to participate will be individually allocated on the day of recruitment on a 1:1 ratio, minimised by treating centre, hand dominance, number of fingers to undergo treatment (1 or more than 1) and finger joint involvement and retaining a random element, to have their DC treated by either NF or LF. Blinding of clinicians and participants is not possible for this trials the treatments are very different. The non-clinical research team members, including the trial statisticians, will remain blind to treatment allocation until after database lock.
Statistical methods	The main approach to between-group comparisons will be based on intention-to-treat, analysing participants in the groups to which they were randomised. This will be supplemented by a per-protocol analysis. For the primary outcome, a two-sided 95% confidence interval (equivalently one-sided 97.5% interval) for the difference in mean PEM score at 12 months between the NF and LF arms will be constructed using a linear mixed-effect model adjusted for baseline PEM and minimisation variables. Non-inferiority of the NF will be inferred if the upper bound of this interval lies within the non-inferiority margin of 6.0 points. The mixed effects model will use all available follow-up outcome data and include a treatment-by-time interaction to estimate the between group difference at each follow-up time-point with 12 months being the primary treatment comparison.

Trial Flow Diagram



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Abbreviations and Definitions

Abbreviation	Definition
AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
CRPS	Complex Regional Pain Syndrome
DASH	Disabilities of the Arm, Shoulder and Hand Questionnaire
DC	Dupuytren's Contractures
DIP	Distal Interphalangeal joint
EQ-5D	EuroQol - 5 Dimension
GCP	Good Clinical Practice
GP	General Practitioner
GRI	Guyatt's Responsiveness Index
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ISF	Investigator Site File
LF	Limited Fasciectomy
LPLV	Last patient last visit
MCIP	Minimal Clinically Important Difference
MCP	Metacarpophalangeal joint
MYMOP	Measure Yourself Medical Outcome Profile
NCTU	Nottingham Clinical Trials Unit
NF	Needle Fasciotomy
NUH	Nottingham University Hospitals NHS Trust
PEM	Patient Evaluation Measure
PIS	Participant Information Sheet
PIP	Proximal Interphalangeal joint
PPI	Public Patient Involvement
PROM	Patient Reported Outcome Measures
QRI	QuinteTRecruitment Intervention
R&D	Research and Development
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SANE	Single Assessment Numeric Evaluation
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SRM	Standardised Response Mean
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMG	Trial Management Group
UAR	Unexpected Adverse Reaction
URAM	Unité Rhumatologique des Affections de la Main Questionnaire

Definitions

Term	Description
Adverse Event (AE)	Any untoward medical occurrence in a clinical trial participant which does not necessarily have a causal relationship with the treatment received. Comment: An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory findings), symptom or disease temporally associated with the use of a treatment, whether or not related to the treatment.
Related Event	An event which resulted from the administration of any of the research procedures.
Serious Adverse Event (SAE)	An untoward occurrence that: **1.** Results in death **2.** Is life-threatening* **3.** Requires hospitalisation or prolongation of existing hospitalisation **4.** Results in persistent or significant disability or incapacity **5.** Consists of a congenital anomaly/ birth defect **6.** Or is otherwise considered medically significant by the Investigator** Comments: The term severe is often used to describe the intensity (severity) of a specific event. This is not the same as serious, which is based on participants/event outcome or action criteria. * Life threatening in the definition of an SAE refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe. ** Medical judgment should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should be considered serious
Unexpected and Related Event	An event which meets the definition of both an Unexpected Event and a Related Event
Unexpected Event	The type of event that is not listed in the protocol as an expected occurrence.
Source data	All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial

2. Background and Rationale

2.1. Background

Dupuytren's contractures are fibrous cords under the skin of the palm of the hand. They typically occur in men and women over 50. They have a strong genetic tendency and increased incidence associated with diabetes and epilepsy (1).

The contractures are painless but cause one or more fingers to gradually and irreversibly curl into the palm, resulting in loss of hand function for day-to-day tasks such as washing, grooming and shaking hands. It increasingly becomes difficult to put on a glove, hold large objects or put the hand in a pocket. Disabilities experienced are diverse and include difficulties with for example, computer use, baking, piano playing, carpentry, gardening, cycling and sports such as golf and tennis (2, 3). The standard treatment is surgery to remove or divide the Dupuytren's contractures, allowing the finger to straighten (extend) again. Surgery, however, does not cure Dupuytren's contractures, and recurrent contractures may occur and require further treatment.

Approximately 16,700 procedures costing £36 million were performed for Dupuytren's contractures in operating theatres in England in 2016-17 (4). An increased longevity in an aging population may cause a 77% increase in demand for treatment by 2030 (5).

There are no agreed guidelines for surgical treatment of Dupuytren's contractures. One option is an operation **"limited fasciectomy" (LF)**, in which the fibrous cords preventing the finger(s) from straightening are cut out of the hand through a long skin incision. This procedure is done under general or regional anaesthesia in an operating theatre and has a minimum of4-6-week recovery period. Around 13,000 LFs were done in England in 2016-2017 (4). Another treatment is a surgical procedure called **"needle fasciotomy" (NF)**. In this procedure the fibrous cords preventing the finger(s) from straightening are divided with the sharp tip of a hypodermic needle. The needle is passed through the skin into the underlying fibrous cord. NF can be done in an outpatient clinic room and has a one-two week recovery period. About 1200 needle fasciotomies were performed in operating theatres during 2016/7 (4) and more will have been performed in outpatient rooms (not accurately captured by Hospital Episode Statistics).

Compared with LF, NF is less expensive for the NHS, less disruptive for patients, and probably carries a lower risk of complications that restrict hand function (temporarily or permanently) (6). Contractures can reform in the operated fingers after either treatment, causing the finger to bend up into the palm again, but recurrence is quicker and more frequent with NF, resulting in a need for further treatment (7). Both procedures successfully straighten fingers with a Dupuytren's contracture involving only the metacarpophalangeal joint. However, fingers with contractures involving the proximal interphalangeal joint cannot always be fully straightened with either treatment.

It has been thought that Collagenase Injections (CI) might replace LF and NF as the treatment of choice for DC. However, recent, small, low quality RCTs suggest CI is no more effective than NF (18-21). CI is currently being compared to LF in a high-quality NIHR-funded study (DISC; ISRCTN18254597). Hand-2 has been designed to allow a comparison of outcomes after CI and NF, through an individual participant data network meta-analysis with DISC. This will be of value, even though CI has now been withdrawn from the European (including UK), but not the USA, market by its manufacturer, Pfizer. This is as CI may be reintroduced into the European market in the future and other companies are developing/may develop alternative CIs, especially once Pfizer's patent expires.

2.2. Trial Rationale

There are five systematic reviews of the surgical treatment for DC (22-27). The first in 2010 highlighted that previous studies had varying outcomes (both in terms of definition and time points) which made comparison impossible. It found the reported recurrence rates ranged from 0% to 71%. The majority of studies used "angular correction of contracture" or "contracture recurrence" as the primary outcome. However, these do not fully capture the impact of DC on hand function. A recurrent contracture is often not as severe as the original DC and may not cause loss of hand function or require treatment. In addition, neither outcome fully captures the impact of surgical complications on hand function (e.g. finger numbness, pain and inability to fully flex the finger to the palm). These complications can often cause greater loss of function than the original or recurrent DC. The frequency of these complications can differ between treatments and is less after NF than LF.

Researchers involved in this study conducted a Cochrane review(8)into the effects of surgery for people with DC (search date May 2015). Thirteen studies (described in 14 publications) were identified that met the inclusion criteria, but only one compared LF and NF (7, 9). This study presented low-quality evidence that LF had better outcomes (straightening fingers, hand function and recurrence rate) than NF, but there was no assessment of hand function using a Patient Reported Outcome Measure (PROM) at follow-up of more than 5 weeks, nor of the immediate or long-term costs and cost-effectiveness of the treatments. A re-run of the search strategy in July 2018 found four further publications from three small RCTs comparing treatment with CI and NF. These showed similar outcomes for NF and CI at one(18, 19, 21) and two(20) years.

The lack of well-designed and conducted trials means that the choice of treatment for Dupuytren's contractures of the fingers mainly depends on surgeon and patient preference. A survey of 116 hand surgeons showed marked variations in treatments advised for Dupuytren's contractures (10). A survey (11, 12) of 110 patients awaiting surgery found that 38% of them thought the recurrent contracture rate was the most important factor in deciding which treatment to undergo. For 25% the most important factor was the speed of recovery following surgery, andfor 37% it was the recommendation of the surgeon. Thus, there is an urgent need for robust evidence to guide decision making.

NHS England produced guidance for CCGs on intervention for Dupuytren's contracture in 2018 (published 28.11.18 (13)). The above uncertainties prevented this from providing advice on which procedure is best to first consider for NHS patients with DC (13). This is reflected in the "Summary of Intervention" section of the guideline: *"No-one knows which interventions are best for restoring and maintaining hand function throughout the rest of the patient's life, and which are the cheapest and most cost-effective in the long term. Ongoing (DISC) and planned (i.e. radiotherapy) National Institute for Health Research studies aim to answer these questions."* This study will assist future revisions of this and other guidelines, and is thus important to patients, the taxpayer and the NHS.

In summary LF, NF and CI are the most widely used treatment options for DC (14) in the NHS, but there is no consensus on their roles. The research question: ***"In patients with Dupuytren's disease, what techniques give the best results in terms of function, recurrence and cost?"*** was a top 10 priority in the recent James Lind Alliance Priority Setting Partnership for Hand Surgery(15). Robust data from high quality studies are needed to advise patients, surgeons and commissioners of the relative benefits and disadvantages of the treatment options.

This study will answer some of the many uncertainties regarding the optimum treatment of Dupuytren's contractures. The RCT comparing NF and LF will demonstrate their relative values in terms of clinical outcome, costs and acceptability to patients over a two year follow-up period. Also,

an indirect comparison of CI and NF will be provided by the Network Meta-analysis which will use individual patient data from Hand-2 and the DISC studies.

Surgery, predominantly NF and LF, and maybe CI in the future, are likely to be the mainstays of treatment for established DC for many years. Thus a comparison of the effectiveness of CI, NF and LF is of immediate benefit to the NHS, and will ensure optimal patient treatment and/or cost benefit for many years.

2.2.1. Participant population

Adults referred from primary to secondary care with DC of a hand. The inclusion/exclusion criteria have been developed to allow a broad patient population reflecting current NHS practice.

2.2.2. Justification for design

Hand-2 is a multi-centre two-arm, parallel, randomised, non-inferiority trial comparing the outcomes of NF with LF among adults eligible for the treatment of DC in the UK NHS.

The trial design for Hand-2 was guided by a randomised feasibility study (HAND-1 NIHR Project Number PB-PG-0613-31083) which demonstrated that Hand-2 can be successfully performed.

This:

a. showed it is possible to recruit and retain participants to a trial of two very different treatments (NF and LF) for DC
b. allowed selection of appropriate outcome measures which patients consider relevant to this experience
c. demonstrated through qualitative interviews the acceptability of this trial to patients and health professionals

An integrated QuinteT Recruitment Intervention will be used to optimise recruitment in the current study(16).

2.2.3. Choice of treatment

Intervention. Needle fasciotomy (NF)is a surgical technique in which the Dupuytren's cord is divided mechanically through repeated perforations using a needle. This is performed in a clinic room under regional anaesthesia or sometimes in an operating theatre under general anaesthetic using a standard 19G-23G hypodermic needle on a syringe. The DC cord is divided at one or more levels by performing side to side movement of the needle tip across the cord or multiple needle punctures, in order to prevent the cord from tethering the finger. Rehabilitation after NF will be according to local practice and individual patient need. It may involve supervised therapy, a formal instruction sheet and/or night splints.

Comparator. Limited fasciectomy (LF) is a surgical technique to excisethe fibrous band (cord) in the palm of the hand and/ or finger and is standard care. This is performed in an operating theatre under general or regional anesthetic, using the surgeon's favored skin incision. For contractures involving the metacarpophalangeal (MCP) joint, the cord will be excised proximally at least to the proximal margin of the transverse fibres of the palmar aponeurosis. Digital cords will be excised completely from their origin. In all cases the distal margin of the cord excision will be the insertion of the cord

onto the flexor sheath (or other structure). Rehabilitation after LF will be according to local practice and individual patient need. It may, or may not, include supervised therapy, a formal instruction sheet and/or night splints.

Please see Appendix for mandated, prohibited and flexible components of both needle fasciotomy and limited fasciectomy

3. Aims, Objectives and Outcome Measures

3.1. Aims and Objectives

Aim

To establish the clinical and cost effectiveness of needle fasciotomy (NF) versus limited fasciectomy (LF) for treatment of DC in the NHS in terms of patient reported hand function and symptoms and resource utilisation.

Primary Objective:

To determine whether, in adults with symptomatic DC of the hand, treatment with NF is non-inferior to LF in terms of hand function (assessed with the Hand Health Profile of the PEM) at 12 months post-intervention.

Secondary Objectives:

To compare NF and LF with respect to:

a) Participant reported hand function and overall satisfaction at 3 weeks, 6 weeks, 3 months, 6 months and 24 months using the Hand Health Profile PEM questionnaire.

b) Participant reported assessment of location specific health (the hand) using the Single Assessment Numeric Evaluation (SANE) tool at 2 weeks, 3 weeks, 4 weeks, 6 weeks, 3 months,6 months,12 months and 24 months and the Measure Yourself Medical Outcome Profile (MYMOP) tool at 3 weeks, 6 weeks, 3 months, 6 months and 24 months.

c) Loss of finger extension at 6 weeks, and 6, 12 and 24 months

d) Adverse events and complications, recurrence of DC, and revisions or salvage surgery up to 24 months

e) Health related quality of life, health resource use, and cost effectiveness at 2 weeks, 3 weeks 6 weeks, 6 months, 12 and 24 months

f) Treatment acceptability (qualitative study)

Perform an individual participant data network meta-analysis to compare outcome of NF and CI with respect to:

a) PEM scores at 3, 6, 12 and 24 months

b) SANE scores at 2 and 6 weeks and 3, 6, 12 and 24 months

c) Revision of surgery rates at 12 and 24 months

d) Cost and cost utility at 24 months

3.2. Outcome Measures

Primary Outcome: Participant reported assessment of hand function using the PEM questionnaire at 12 months post treatment intervention.

Secondary Outcomes:
Participant reported assessment of hand function and overall satisfaction using the Hand Health Profile PEM questionnaire at 3 weeks, 6 weeks, 3 months, 6 months and 24 months post intervention.

- Participant reported quality of life/ health measures (MYMOP, SANE, EQ-5D5L)
- Loss of finger extension
- Recurrence of DC
- Revision surgery
- Cost and cost utility

Safety outcomes:

- Adverse effects of treatment

Timelines associated with collection of the above secondary outcomes are detailed in Table 1 (summary of assessment by timepoint).

4. Trial Design and Setting

4.1. Trial Design

A multi-centre, two-arm, parallel, randomised, non-inferiority trial comparing the outcome of NF and LF among adults eligible for treatment of DC within the NHS. An internal pilot phase with an integrated QuinteT Recruitment Intervention (QRI) will be used to optimise trial design.

The sample size required to detect non-inferiority of needle fasciotomy compared to limited fasciectomy is 406 participants. This allows for a 20% loss to follow-up at 12 months.

4.2. Trial Setting

12 UK secondary care centres. Participants can be transferred between surgeons within a centre to ensure treatment by those with suitable expertise.

4.3. Internal pilot phase and progression criteria

Internal pilot phase and progression criteria: Recruitment and retention will be continuously monitored throughout the trial. A formal review of recruitment will occur 10 months after randomisation of the first participant. Recruitment will be measured against the overall recruitment target. Due to the initial staggered recruitment, little data will be available on retention and particularly the 12-month primary outcome. Therefore, a further formal review of retention will occur 18 months after first person randomised. Retention will be assessed as the proportion of participants attending 6 week and 12-month follow-up visits. We propose the following criteria, although final agreement on stop/go criteria will take place after discussion with HTA.

Progression guidance	Recruitment	Retention
Continue: No action needed	100%	100%
Continue: Action needed	80-99%	80-99%
Continue: Recovery Strategy	50-79%	50-79%
Stop trial	<50%	<50%

If recruitment at 10 months from the first participant randomised is GREEN (100%), no action is needed.

If AMBER (80-99%): continued detailed completion and examination of screening logs, streamlining of patient pathways, interviews with site staff and audio-recording all consultations with regular feedback meetings as part of the QuinteT Recruitment Intervention (QRI).

If there is evidence of nearing RED (50-79%) or RED (<50%) itself: increased frequency of investigators meetings with QRI feedback and training, intensive QRI investigations and tailored actions in sites with particularly low recruitment rate. Also consideration of opening additional centres.

Non-adherence with allocated treatment will be monitored and recorded. Review will be undertaken by the TMG and the TSC.

Retention will be monitored at all timepoints throughout the trial. Our primary method of patient retention is to send participants a high street voucher (of modest value) as a token of appreciation for completion and return of the questionnaires at 12 and 24 months. Data arising from the QRI and participant interviews that addresses issues relating to retention will be reviewed and actions implemented based on this.

5. Eligibility

5.1. Inclusion Criteria

1. Age ≥18 years
2. One or more fingers with a Dupuytren's contracture of 30 degrees or greater in the MCP and/or PIP joints with functional problems
3. No previous treatment for Dupuytren's contracture on study finger
4. a) Well-defined cord(s) and
   b) suitable for treatment with NF and LF
5. Able to comply with the requirements of the study up to 24 months post-intervention

5.2. Exclusion Criteria

1. Dupuytren's contracture of the distal interphalangeal joints (DIP) only
2. Planned dermofasciectomy or very limited fasciectomy (excision of≤1cm cord segment)
3. Already recruited into this study for treatment of DC of either hand

6. Consent

Written informed consent for each participant must be obtained prior to performing any trial related procedure. The potential participant will be given the opportunity to ask questions throughout the process. Written informed consent can be obtained by Investigators or delegated members of the local research team (as captured on the Site Delegation Log). It remains the responsibility of the Principal Investigator to ensure informed consent is obtained appropriately. A Participant Information Sheet (PIS) will be provided to facilitate this process. Investigators or their delegate(s) will ensure that they adequately explain the aim, trial treatment, anticipated benefits and potential hazards of taking part in the trial to the participant. They will also stress that participation is voluntary and so the potential participant is free to decline participation and may withdraw from the trial at any time. The

patient will be given adequate time to read the trial information, ask any questions and discuss their participation with others (i.e. family members, GP or other healthcare professionals outside of the site research team), if they wish.

If the potential participant expresses an interest in participating in the trial they will be asked to sign and date the latest version of the Informed Consent Form (ICF). The Investigator or delegate(s) will then sign and date the form. A copy of the ICF will be given to the participant, a copy will be filed in the medical notes, and the original placed in the Investigator Site File (ISF). Once the participant is entered into the trial, the participant's unique trial identification number will be entered on the Informed Consent Form maintained in the ISF. In addition, if the participant has given explicit consent for this to occur, a copy of the signed Informed Consent Form will be sent to the Coordinating Centre for review.

Details of the informed consent discussions will be recorded in the participant's medical notes. This will include date of discussion, the name of the trial, summary of discussion, version number of the PIS given to participant and version number of ICF signed and date consent received. Where consent is obtained on the same day that the trial related assessments are due to start, a note will be made in the medical notes as to what time the consent was obtained and what time the procedures started.

Throughout the trial the participant will have the opportunity to ask questions about the trial. Any new information that may be relevant to the participant's continued participation will be provided. Where new information becomes available which may affect the participants' decision to continue, participants will be given time to consider and, if happy to continue, will be re-consented. Re-consent will be documented in the medical notes. The participant's right to withdraw from the trial will remain.

Electronic copies of the PIS and ICF will be available from the Coordinating Centre and for UK trials will be printed or photocopied onto the headed paper of the local institution.

Details of all participants approached about the trial will be recorded on the Participant Screening/Enrolment Log. Following randomisation and with the participant's prior consent, their General Practitioner (GP) will also be informed that they are taking part in the trial.

The 24 month follow-up will capture early DC recurrences, but it is anticipated that, subject to funding and necessary approvals, this will be extended to 5 years and participants will be asked to consent to this at the outset.

Study staff/healthcare professional consent for QRI

Recruiting staff and TMG member consent will be obtained through a 'master' consent form that covers all aspects of the QRI (audio-recording of patient consultations and staff qualitative interviews). Study staff need only sign one consent form that covers all future recordings of appointments and/or interviews. Staff can withdraw their permission at any point for the audio-recording of consultations and/or interview, although they will be informed that any information collected before withdrawal may still be retained and used anonymously.

Patient consent for QRI

Information about the QRI is provided to patients in a separate sheet – 'The Hand-2 Study – Information about audio-recording your consultations'. Recruiters will check if the patient has any questions about the audio-recording process prior to recording. Patients who agree will sign an audio-

recording consent form that seeks permission to record all discussions about the trial with the surgeon and local research team in the lead up to them making their decision about participation. If patients have not yet been given an information sheet about the audio-recordings, then verbal consent for audio-recording will be taken at the start of the consultation and written consent sought after they have had time to read the separate information sheet. It will be explained to patients that recordings are undertaken to explore how treatment and study information is conveyed to potential study participants, and that they have the option to have the recording erased if they wish once they have had sufficient time to read and discuss the relevant information sheet. It will be made clear to patients that they are free to change their mind at any time about the recordings and without any adverse effects on their care, although any information collected before their withdrawal may still be retained and used anonymously. Patients may agree to the audio-recordings regardless of whether they agree to participate in the trial or not.

Patient consent for interviews

Patients may be invited to participate in a discussion (interview) about their experiences and acceptability of treatment within the Hand-2 study. The trial consent form includes a question that asks if patients agree to being contacted by a researcher to discuss this aspect of the study. Patients who consent to this may then be contacted by the qualitative researcher who will explain more about the interview and obtain permission to post them an interview consent form (if the interview is to be conducted by phone), and arrange a convenient time for interview. Patients will be informed that the interview is optional.

7. Enrolment and Randomisation

7.1. Participant identification

7.1.1. Recruitment Pathway 1.

The Main recruitment pathway will be via secondary care elective outpatient Hand Clinics. Potential participants will be identified before their NHS clinic appointment by screening of GP referral letters and clinic lists by the local clinical care and/ or local research team at sites. A short patient information leaflet will be sent to potentially eligible patients explaining Dupuytren's contractures and the study before their clinic appointment. The leaflet will also explain that if they are potentially suitable for the study they may be asked for permission to audio-record consultations with the surgeon and local research team during the clinic visit.
All potentially eligible patients will be asked during their clinic visit if they are happy to be approached about the study and, if so, if they also willing to give permission to audio-record their consultations with the surgeon and local research team. They will be provided with an audio recording information sheet and they will be asked to sign an audio-recording consent form if they agree to audio recording (not necessary for recruitment into the study).

7.1.2. Recruitment Pathway 2.

An alternative recruitment pathway will identify potential eligible participants who have been placed on a waiting list awaiting surgery for "surgery for Dupuytren's contracture" but not for a specific procedure such as LF or NF by the local clinical care and/ or local research team at sites.

Potential recruits will be sent a short Patient Information Leaflet at least 4 weeks before the intervention date. They will then be contacted/seen at least 2 weeks before day of surgery for a discussion of trial by someone trained in trial recruitment and competent to explain benefits and drawbacks of both limited fasciectomy and needle fasciotomy. Those willing to participate in Hand-2 will be seen face to face before the day of surgery to confirm suitability for either procedure, confirm their willingness to participate in the trial and obtain consent and collect baseline data.

7.1.3 Patients considered for the study but found to be ineligible and those who are eligible but decline participation will be recorded on a screening log along with the reasons for this.

It will be recorded in the patient's records by a member of the treating clinical team that the patient has been screened for the study and found to be ineligible or declined participation.

7.2. Recruitment

Patients with a Dupuytren's contracture who have been identified as above and wish to have surgical treatment for their condition will have the trial explained to them during their initial consultation with the surgeon. If the patient is willing to consider participation, they will be given the participant information leaflet and asked to sign a consent form as described in section 6.

If a patient presents with two or more fingers on the same hand that require treatment, then both/all fingers will be treated in the same manner (i.e. both/all with limited fasciectomy or both/all with needle fasciotomy). For study outcomes the finger causing the most difficulties according to the patient will be termed "the study finger".

7.3. Randomisation

Eligible patients who consent to participate will be individually allocated on the day of recruitment on a 1:1 ratio, minimised by treating centre, hand dominance, number of fingers to undergo treatment (1 or more than 1) and finger joint involvement and retaining a random element, to have their DC treated by either NF or LF.

7.4. Blinding and concealment

Allocation will be concealed using a web-based minimisation algorithm developed and maintained by the Nottingham Clinical Trials Unit and held on a secure server, accessed via a secure website. Access to the system will be granted by the NCTU in accordance with the roles delegated by the Principal Investigator on the site signature and delegation log. Blinding of clinicians and participants is impossible as the treatments are very different. The non-clinical research team members, including the trial statisticians, will remain blind to treatment allocation until after database lock.

7.5. Protection against risk of bias

To minimise the potential for bias in this trial we will take the following steps:

a. **Selection bias** at recruitment will be avoided by separating the processes of determining patient eligibility and treatment allocation by using web-based randomisation operated by NCTU, not allowing clinicians assessing and treating patients to predict the next allocation in their clinic. Blinding of patients and clinicians is not possible.
b. **Detection bias:** Treating clinicians will have no role in outcome assessment. Primary and secondary outcomes will be collected both directly from participants through patient-

reported outcome measures, and clinical measurements at the clinic visits performed by trained research staff who are independent of the treating clinical team. Blinding of research staff will not be feasible due to the differing nature of the two surgery procedures. Further, any attempt to cover scars in the affected hand (i.e. via latex gloves) can impact on the clinical outcome measurements performed.

c. **Attrition bias:** Although the sample size has been inflated to allow for up to 20% non-collection of primary outcome data, we aim to obtain outcome data for every participant. Where possible, information will be collected around the reasons for attrition or withdrawal.
d. **Selective reporting bias:** To avoid selective reporting of outcomes, the trial will be registered before recruitment of the first participant and the protocol will be published before recruitment closes. Planned analyses will be clearly described, and all data collected will be reported

8. Trial procedures and assessments

Outcomes will be collected at specific times post-treatment, many of which are the same as in DISC(17). Time zero for follow up for this study will be the time of the intervention not time of randomisation. Post-treatment, rather than post-randomisation, time points are necessary as treatment cannot be provided immediately due to NHS waiting lists which are longer for LF than NF. In Hand-1 the median waiting time for treatment was longer for LF (97 days) than NF (41 days) (18). The PEM (primary outcome measure), the SANE and selected objective measurements will also be collected at pre-intervention on either the day intervention, or at a pre-operative assessment within 8 weeks of the actual intervention date. This is to determine whether there has been change (i.e. Progression of contracture or development of a comorbidity impacting on hand function) between baseline and the intervention while on the waiting list for treatment.

8.1. Summary of assessments

Table1

				Follow-up post Intervention							
TIME POINT	***Baseline[1]***	***At intervention or during 8 weeks before intervention***	***Intervention***	***2 weeks***	***3 weeks***	***4 weeks***	***6 weeks***	***3 months***	***6 months***	***12 months***	***24 months***
ENROLMENT											
Eligibility	*X*										
Informed consent	*X*										
Informed consent audio recording	*X*										
Audio recording of	*X*										

consultation											
Hand assessment	*X*										
Interviews with consented individuals (staff and patients)	*X*			*X*	*X*	*X*		*X*	*X*	*X*	*X*
INTERVENTION											
Conduct allocated procedure			*X*								
Record details of procedure performed			*X*								
PATIENT COMPLETED QUESTIONNAIRES (ideally self-completed by the participant but can be completed by a carer/member of staff reading them out aloud to the patient face-to-face or on a phone or video link)											
SANE	*X*	*X*		*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*
PEM (Part 2)	*X*	*X*			*X*		*X*	*X*	*X*	*X*	*X*
MyMOP	*X*				*X*		*X*	*X*	*X*	*X*	*X*
EQ-5D-5L	*X*	*X*		*X*	*X*		*X*		*X*	*X*	*X*
NHS Resource Use	*X*				*X*		*X*		*X*	*X*	*X*
Complications							*X*				
CLINICAL ASSESSMENTS											
Study Finger extension and flexion	*X*	*X*					*X*		*X*	*X*	*X*
Objective measurements	*X*	*X*					*X*				

[1]Participant consent for the trial, baseline assessment, and randomisation may take place at the first clinic visit or at a future visit arranged with the research nurse/ assistant

8.2 Schedule of Assessments

The following assessments will be performed at each time point indicated

Baseline – Clinic visit

- Check eligibility criteria
- Obtain written consent for audio recording consultation
- Audio recording of consultation

- Obtain trial consent
- Participant completed questionnaires:
    - SANE
    - PEM
    - MyMOP
    - EQ-5D-5L
- NHS Resource use
- Hand assessment:
    - Extension and flexion in study[1]finger
    - Objective measurements, Grip strength, active and passive study finger joint measurements, 2PD sensation
- Interviews with consented individuals (staff)
- Randomise

Pre-operative assessment (if occurs as part of standard care and within8 weeks of the day of intervention/surgery)

- Patient completed questionnaires
    - PEM
    - SANE
    - EQ-5D-5L

- Hand assessment prior to intervention:
    - Objective measurements, Grip strength, active and passive study finger joint measurements,
    - Extension and flexion in study finger

Intervention

- Patient completed questionnaires (if not completed already during 8 weeks before surgery)
    - PEM (if not completed already during 8 weeks before surgery)
    - SANE (if not completed already during 8 weeks before surgery)
    - EQ-5D-5L (if not completed already during 8 weeks before surgery)
- Perform allocated procedure
- Record details of procedure performed
- Hand assessment prior to intervention (if not completed already during the8 weeks before surgery):
    - Objective measurements, Grip strength, active and passive study finger joint measurements
    - Extension and flexion in study finger

Two weeks post-intervention – Remote collection

- Patient completed questionnaires:
    - SANE
    - EQ-5D-5L

[1] If treatment is planned for only one finger, then this finger is the study finger. If treatment of two or more fingers is planned, then it is the finger ***to undergo treatment*** that is causing the participant the greatest problems. It is never a finger for which treatment with NF or LF is not planned.

Three weeks post-intervention – Remote collection

- Patient completed questionnaires:
    - SANE
    - PEM
    - MyMOP
    - EQ-5D-5L
- NHS Resource use

Four weeks post-intervention – Remote collection

- Patient completed questionnaires:
    - SANE

Six weeks post-intervention (routine NHS clinic visit)

- Patient completed questionnaires:
    - SANE
    - PEM
    - MyMOP
    - EQ-5D-5L
- NHS Resource use
- Complications
- Hand assessment:
    - Extension and flexion in study finger
    - Objective measurements, Grip strength, active and passive study finger joint measurements, 2PD sensation

3 months post-intervention – Remote collection

- Patient completed questionnaires:
    - SANE
    - PEM
    - MyMOP

Six months post-intervention (Remote collection)

- Patient completed questionnaires:
    - SANE
    - PEM
    - MyMOP
    - EQ-5D-5L
    - NHS Resource use
- Hand assessment:
    - Extension and flexion in study finger
- Interviews with consented individuals (staff)

12 months post-intervention (Remote collection)

- Patient completed questionnaires:
  - SANE
  - PEM
  - MyMOP
  - EQ-5D-5L
  - NHS Resource use
- Hand assessment:
  - Extension and flexion in study finger
- Interviews with consented individuals (staff and patients)

24 months post-surgery (Remote collection)

- Patient completed questionnaires:
  - SANE
  - PEM
  - MyMOP
  - EQ-5D-5L
  - NHS Resource use
- Hand assessment:
  - Extension and flexion in study finger
- Interviews with consented individuals (staff and patients)

8.2. Treatment of participants

Surgical treatment is routinely performed in the study sites estate/buildings. However, due to long waiting lists, NHS patients in many centres are now having their surgical procedures performed, as NHS patients, in the independent sector. It is thus appropriate for Hand-2 participants to undergo surgical procedures in the independent sector provided the following criteria are met:

a. the participant has already been recruited, consented, completed baseline questionnaires and been randomised and in the normal manner at one of the recruiting NHS centres.
b. the surgery is performed by a surgeon appearing on the delegation log for the relevant host NHS centre.
c. the surgeon is able to complete the pre-surgery "Day of Treatment CRF" including SLiCK measurement, or these measurements have already been performed within the 8 weeks preceding the surgery
d. the participant is able to complete "Day of Treatment: Pre-treatment Delivery questionnaire" on day of surgery or within the 8 weeks prior to the day of surgery.
e. Face to Face follow-up at 6 weeks can be organised so participant can complete "6 weeks post-surgery" questionnaire and research team can complete "6 week post-surgery CRF" back at the recruiting NHS centre.

All surgical procedures will be carried out by either a consultant surgeon, an experienced trainee, or an inexperienced trainee under direct supervision of his/her trainer. Who carried out the treatment and their level of experience will be recorded in the CRF. Participants will receive either needle fasciotomy, or limited fasciectomy.

Following each procedure, the surgeon and/or researcher will record the following details: surgeon(s) who performed the procedure; type of procedure conducted (NF or LF); extent and definition of contracture(s) before treatment; joint contracture release or not; improvement in finger extension; wound closure technique.

8.3. Objective measurements

The extension angular measurement (loss of active extension) will be measured using a goniometer and recorded for the **MCP, PIP and DIP** joints on the **study finger only.** The active loss of extension (flexion deficit) will be measured for all three joints by asking the participant to actively straighten his/her finger as much as possible. While the participant holds the finger as straight as possible the extension loss at each joint of the **study finger only** will be measured. In addition linear measurements of extension and flexion of the study finger will be obtained using the *SLiCK* device (goo.gl/oRxLPz).

Grip Strength. This will be measured in both hands with a standardised grip meter. The same grip meter will be used throughout the study at each recruiting centre to eliminate measurement error due to use of differently calibrated devices.

Two-point discrimination sensation will be measured in the study finger at baseline and at 6 weeks post-treatment. It will be tested at 5mm and 10mm on each of the radial and ulnar aspects of the fingertip (distal pulp space) with the two points in the longitudinal axis of the finger in order to identify digital nerve injuries. The outcome will be classed as normal (5mm), reduced (can identify 2 points at 10 mm but not 5mm, and absent (cannot identify 2 points at 10mm); absent - indicates a severe nerve injury).

8.4. Participants follow up

All methods of delivery and collection of questionnaires and reminders including use of research teams for time points associated with hospitalisation or clinic appointments will be used including postal mail, e-mail, web-based and SMS text, taking into account each participant's stated preferred means of receiving and completing the measures. All questionnaires will ideally be self-completed by the participant but can be completed by a carer/member of staff reading them out aloud to the participant face-to-face or on a phone or video link. Participants will be sent a voucher (of modest value) as a token of appreciation for completion and return of the questionnaires at 12 and 24 months.

Strategies to minimise loss to follow-up will include using postal, text, email and phone reminders. These may be used on the day the questionnaire is due or if questionnaires are not returned. We will make two attempts to collect the data.

Upon completion of all trial visits and questionnaires all participants who consent will receive an end of study letter accompanied by an information sheet thanking them and informing them that their participation in the study is complete.

At the end of the trial follow up period, we will extract information from the hospital medical record system onto a Case Report Form to record any further outpatient appointments, outpatient procedures, emergency department visits or inpatient admissions related to the study hand in the six months after the initial procedure.

8.5. Embedded qualitative research

Patient experiences and acceptability of treatment 2 years post-surgery

Evidence of patient experience and acceptability of treatment for DC is limited. In the Hand-1 feasibility study, qualitative interviews undertaken 1-8 months post treatment demonstrated patient satisfaction with both NF and LF. However, NF has higher risks of recurrence and need for further treatment than LF in the longer term, so that patient views on treatment acceptability may change over time therefore this will be investigated at 2 years.

Up to 30 semi-structured interviews will be conducted with trial participants to explore their experiences and acceptability of treatment around two years after surgery, with the final sample size being determined by data saturation. Some may be interviewed on more than one occasion to assess if views change over time. The majority of interviews are likely to occur by phone, or face to face where feasible. Participants will be purposefully selected to ensure maximum variation in terms of age, sex, type of surgery, study centre, clinical details and timing of surgery. Topic guides will be used to ensure similar topics are covered in each interview but applied in a flexible manner to enable issues of importance to emerge. The guide will focus on their experiences of living with DC pre and post treatment, expectations and experiences of treatment, recovery, recurrence of contractures and any additional treatment received. Interviews will be audio-recorded with consent, transcribed verbatim and analysed thematically. An experienced team member (NM) will independently analyse a proportion of transcripts to assess the dependability of coding, agree further sampling and discuss theoretical development. Findings will be compared with those from the feasibility study.

8.6. Trial Procedures

8.6.1. QuinteT Recruitment Intervention (QRI)

Recruitment and informed consent will be optimised by an embedded QRI - a flexible, tailored intervention to identify and address recruitment difficulties as they arise in study sites(16).The QRI has been applied to over 40 RCTs to date, leading to insights about recruitment issues and the development of targeted strategies that can improve recruitment rates(19, 20). In the Hand-1 feasibility study, the QRI identified site and recruiter specific barriers to recruitment including: less than optimal methods of identifying potential participants and guiding them to recruiting clinics, issues around conveying equipoise with regards to treatment and outcome information, and unease in exploring patients' treatment preferences which is essential to ensure decisions are based on full and accurate information (25) . These insights will enable a 'head start' in the tackling of broad issues around screening methods and consent discussions in the set up/early recruitment phases of Hand-2. In-depth investigation of recruitment within sites is likely to reveal similar and novel challenges, to which the QRI will be well placed to address them.

The QRI will be implemented in two phases:

Phase 1: understanding recruitment

Phase 1 will investigate the recruitment process and how it operates within sites, building up a comprehensive understanding of recruitment challenges that arise during the recruitment. A multi-faceted, flexible approach will be adopted, using one or more of the following methods:

***Mapping patient eligibility and recruitment pathways*:** Detailed eligibility and recruitment pathways will be compiled for clinical sites, noting the point at which potential trial participants receive information about the trial, which members of the clinical/research team they meet, and the timing and frequency of appointments. Recruitment pathways will be compared with details specified in the

trial protocol and pathways from other sites to ensure practices support efficient recruitment. The QRI researcher will also work closely with NCTU to scrutinise detailed logs of potential RCT participants as they proceed through screening and eligibility phases, to help identify points at which they do not continue with recruitment to the RCT and reasons for this. Logs of eligible and recruited individuals will be assembled using simple flow charts and counts to display numbers and percentages of patients at each stage of the eligibility and recruitment processes. These figures will be compared across sites and considered in relation to any estimates that may be specified in the grant application or study protocol.

Audio-recording of recruitment appointments: Clinic appointments in which the study is discussed will be audio-recorded on an encrypted audio-recorder, with consent, to explore study information provision, recruitment techniques, patient concerns and randomisation decisions to identify recruitment difficulties and improve information provision. Recordings will be transferred to the University of Bristol for analysis, via the University of Nottingham, through University-approved secure data transfer facilities, posting the audio-recorder's encrypted SD card or through encrypted flash drives that adhere to NHS Trust policies.

In-depth interviews: To be undertaken with:

I. Members of the Trial Management Group (TMG) including the Chief Investigator (CI) and those closely involved in the design, management, leadership and co-ordination of the trial where relevant
II. Health professionals and researchers who are involved in trial recruitment (trial recruiters)

Interviews with TMG members and trial recruiters will investigate their perspectives on the RCT and experiences of recruitment (where relevant). A topic guide will be used to ensure key areas are covered but with flexibility to let the participants raise issues of importance to them. Key topics to explore will include views about the trial design and protocol; understandings of the evidence on which the trial is based; perceptions of uncertainty/equipoise in relation to treatment for DC; views about how the protocol is delivered in clinical sites; methods for identifying eligible patients; views on eligibility; and examples of recruitment success and difficulties. Interviews are likely to be undertaken over the telephone.

Attendance at TMG and investigator meetings: The QRI researcher will attend TMG and investigator meetings to gain an overview of trial conduct and overarching challenges (e.g. logistical issues etc). Attendance at these meetings can reveal new lines of enquiry and add new dimensions to challenges that have emerged through other data collection methods.

Review of study documentation: The QRI team will work closely with the NCTU and PPI group to ensure that patient-facing study documents are unbiased and clear. As the study progresses, patient information leaflets and consent forms will be compared with interviews and recorded appointments to identify any disparities or improvements that could be made.

Data analysis:

Interviews and recruitment consultations will be audio-recorded, with permission, and transcribed verbatim in full or in parts either by University of Bristol employees or by a University of Bristol approved transcribing service. Transcripts will be labelled with a study-assigned participant number, edited to ensure anonymity of respondents and stored securely adhering to the University's data storage policies. Data will be managed using qualitative data analysis software (such as NVivo). Interviews and recruitment consultations, along with screening logs and study documentation, will be

subject to simple counts, content, thematic and targeted conversation analyses. Preliminary analysis will be used to inform strategies for Phase 2 of the QRI and further data collection.

Phase 2: Development and implementation of recruitment strategies

Findings from Phase 1 will be presented to the CI/TMG, identifying factors that appear to be hindering recruitment. The CI/TMG in discussion with the QRI team will formulate a 'plan of action' grounded in these findings to improve recruitment and information provision, with its format dependent on the nature of the recruitment barriers identified. Supportive and sensitive feedback and training is likely to be a core component of the plan of action. Site-specific feedback may cover institutional barriers such as patient pathways, while multi-site group feedback sessions may address widespread challenges that would benefit from discussion, such as issues around equipoise or patient concerns. All group feedback sessions will be aided by anonymised data extracts from interviews and audio-recorded appointments. Individual confidential feedback may also be offered – particularly where recruiters experience specific difficulties or where there is a need to discuss potentially sensitive issues. Other interventions are likely to include 'tips' documents for recruiters, providing suggestions on how to convey trial information to aid participant understanding, and investigator meetings and/or site visits to discuss technical or clinical challenges (e.g. issues around conveying equipoise).

Phases 1 and 2 will be undertaken in an iterative and cyclical manner, continuing throughout the majority of the recruitment period with close monitoring of changes in screening log data and recruiter practice to optimise recruitment and informed consent, all in close collaboration with the CI and wider study team.

Data protection and patient confidentiality in relation to the QRI and qualitative research data

Recordings of appointments in which the trial is discussed will be held on an encrypted digital recorder and regularly transferred to the University of Bristol (via University of Nottingham) either by uploading onto the study database, posting the recorder's encrypted SD card via an enhanced delivery service, or transferring files onto an encrypted memory stick and posting. Interview data captured on audio-recorder will be transferred to a University of Bristol computer as soon as possible after each interview. All data will be stored in a password protected drive maintained by the University of Bristol.

Recordings will be transcribed in full or part by University of Bristol employees or University approved transcription services as soon as possible after each recording has been received. If an approved external transcription service is used, the transfer of recordings and transcripts will adhere to the secure transfer of recordings/transcripts procedure specified by the University. Transcripts will be labelled with a study-assigned participant number, edited to ensure anonymity of respondents and stored adhering to the University's secure data storage policies. Recordings and anonymised transcripts will be securely retained by the Universities of Bristol and Nottingham for at least five years after study closure. Anonymised quotations and parts of voice modified audio-recordings may be used by the Universities for training, teaching, research and publication purposes for Hand-2and future studies. Anonymised transcripts may be made available to other researchers (including those outside of the Universities) by controlled access if they secure the necessary approvals for purposes not related to this study, subject to individual written informed consent from participants.

8.7. Withdrawal Procedures

Participants are free to withdraw consent to participate at any time. Outcome data derived from medical records will be collected for those that withdraw unless the participant specifically withdraws their consent for this. All data collected up to the point of withdrawal will be retained and used in the analysis. Failure to undergo allocated treatment either because of participant preference or change of circumstance will not result in withdrawal and the participant will continue to participate in trial procedures unless consent to the trial is withdrawn.

9. Adverse Event Reporting

The collection and reporting of Adverse Events (AEs) will be in accordance with the Research Governance Framework for Health and Social Care and the requirements of the National Research Ethics Service (NRES). Definitions of different types of AEs are listed in the table of abbreviations and definitions. The Investigator should assess the seriousness and causality (relatedness) of all AEs experienced by the trial participant, this should be documented in the source data with reference to the protocol.

9.1. Adverse Events

Both interventions being evaluated in this study are minor surgical procedures that are widely available as standard care within the NHS. Adverse events that could be due to the surgical procedures will therefore be probable outcomes that will recorded as safety outcomes for the study on the case report forms rather than reported as adverse events. Complications specific to this trial and attributable to the intervention will be recorded and are listed in Table 2.

Table 2: Hand-2 complications

Small Skin Laceration (less than 1cm)
Medium Skin Laceration (1-2cm)
Large Skin Laceration (> 3cm)
Paraesthesia in study finger in a treated finger
Hypoaesthesia (reduced sensation/feeling of numbness) in a treated finger
Burning sensation in a treated finger
Joint swelling in a treated finger
Delayed wound healing (wound not fully healed by 4 weeks)
Wound infection
Numbness consistent with digital nerve injury
Loss of flexion in operated finger (>2cm AFD)
Loss of flexion in one or more other fingers (>2cm AFD)
Complete division of flexor tendon
ComplexRegional Pain Syndrome (CRPS)
Loss of finger (amputation) due to complications of treatment
Carpal tunnel syndrome starting within 6 weeks of treatment
Tenosynovitis starting within 6 weeks of treatment
Trigger finger starting within 6 weeks of treatment
Evidence of a flexor tendon injury
Finger swelling

Finger stiffness
Surgical scar tenderness/pain
Pain in finger at 6 week follow-up
Nerve injury recoded at time of surgery
Arterial injury recorded at time of treatment
Post-operative bleeding

9.2. Serious Adverse Events

A Serious Adverse Event (SAE) is any adverse event occurring following study mandated procedures, having received the treatment or intervention that results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalisation or prolongation of existing hospitalisation
- A disability / incapacity
- A congenital anomaly or birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalisation may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

For the purposes of this trial, the following are not considered a SAE and need not be reported:

- Hospitalisation for a pre-existing condition that has not worsened
- Hospitalisation for treatment which was elective or pre-planned, for a pre-existing condition not associated with any deterioration in condition

9.2.1.Reporting period

SAEs that occur from time of surgery to 6 weeks follow-up should be reported.

9.3. Reporting Procedure – At Site

9.3.1.Adverse Events

Adverse events will be collected as outcome measures on the CRFs and will not be reportable.

9.3.2.Serious Adverse Events

Participants will be asked to contact the study site immediately in the event of a serious adverse event.

The Medical Monitor/Chief investigator shall be informed within 24 hours of any serious adverse events and shall determine seriousness and causality in conjunction with any treating medical practitioners.

All treatment related serious adverse events will be recorded and reported to the REC as part of the annual reports. Unexpected serious adverse events will be reported within the applicable timeframes to the REC and sponsor as stated below.

Trial Treatment / Intervention Related SAEs
A serious adverse event that is unexpected in its severity and seriousness and deemed directly related to or suspected to be related to the trial treatment or intervention shall be reported to the ethics committee that gave a favourable opinion as stated below.

The event shall be reported immediately of knowledge of its occurrence to the Medical Monitor/Chief investigator.

The Medical Monitor/Chief investigator will:

- Assess the event for seriousness, expectedness and relatedness to the trial treatment or intervention.
- Take appropriate medical action, which may include halting the trial after discussion with Sponsor and other relevant parties.
- If the event is deemed related to the trial treatment or intervention shall inform the REC using the reporting form found on the HRA web page within 7 days of knowledge of the event.
- Shall, within a further eight days send any follow-up information and reports to the REC.
- Make any amendments as required to the study protocol and inform the REC as required

Participant removal due to adverse events
As the interventions in this trial are treatments that are widely available within the NHS and one-off interventions, we do not anticipate a situation where a participant would need to be removed from the study. Follow-up will be conducted for all participants regardless of whether they receive the allocated intervention.

To report an SAE, email the SAE form to: nctu-sae@nottingham.ac.uk

For SAE Forms completed by someone other than the Investigator, the Investigator will be required to countersign the original SAE Form to confirm agreement with the causality and severity assessments. The form should then be returned to the Coordinating Centre and a copy kept in the Site File.
Investigators should also report SAEs to their own Trust in accordance with local practice.

9.3.3.Provision of follow-up information

Participants should be followed up until resolution or stabilisation of the event if the event is deemed related to the trial intervention. Follow-up information should ideally be provided on a new SAE Form.

9.4. Reporting Procedure – Coordinating Centre

On receipt of an SAE the Coordinating Centre will allocate each SAE a unique reference number which will be forwarded to the site as proof of receipt within 1 working day. The SAE reference number will be quoted on all correspondence and follow-up reports regarding the SAE and filed with the actual SAE in the TMF.

On receipt of an SAE Form seriousness and causality will be determined independently by the Chief Investigator or their delegate responsible for determining causality assessments. An SAE judged by the Investigator or Chief Investigator responsible for determining causality assessments to have a reasonable causal relationship with the trial treatment will be regarded as a related SAE. The Chief Investigator responsible for determining causality assessments will also assess all related SAEs for

expectedness. If the event is unexpected (i.e. is not defined in the protocol as an expected event) it will be classified as an unexpected and related SAE.

9.5. Reporting to the Research Ethics Committee

9.5.1. Unexpected and Related Serious Adverse Events

NCTU will report all events categorised as Unexpected and Related SAEs (SUSARs) to the REC within 15 days.

9.5.2. Adverse Events

The REC will be notified immediately if a significant safety issue is identified during the course of the trial.

9.6. Investigators

Details of all Unexpected and Related SAEs and any other safety issue(s) which arises during the course of the trial will be reported to Principal Investigators. A copy of any such correspondence should be filed in the Site File.

9.7. Data Monitoring Committee

The independent Data Monitoring Committee (DMC) will review all SAEs.

10. Data Handling and Record Keeping

10.1. CRF Completion

Data will be reported using an electronic Case Report Form (eCRF). Reported data will be consistent with the source data (see section 10.1) and any discrepancies will be explained. Staff delegated to complete the eCRF will be trained to adhere to ICH-GCP guidelines and trial-specific guidance on the completion of the eCRF, in particular:

- Date format and partial dates
- Time format and unknown times
- Rounding conventions
- Trial-specific interpretation of data fields
- Entry requirements for concomitant medications (generic or brand names)
- Which forms to complete and when
- What to do in certain scenarios, for example if a participant withdraws from the trial
- Missing/incomplete data
- Repeat laboratory tests
- Protocol or GCP non-compliances

In all cases it remains the responsibility of the site's Principal Investigator to ensure that the eCRF has been completed correctly and that the data are accurate, as evidenced by their signature on the eCRF. It is the responsibility of the site's Principal Investigator to ensure there are site staff in place to complete data entry into the eCRF. To assist with data completion, sites will be provided with paper CRF workbooks, data will then be entered onto the eCRF by the investigator "or delegate(s)". Where data is collected first onto a CRF workbook, it should be entered into the eCRF within 7 days.

10.2. Source Data

In order to allow for the accurate reconstruction of the trial and clinical management of the participant, source data should be made accessible and well maintained. Source data is kept as part of the participant's medical notes generated and maintained at site. Each site will record the location of source data at their site using a source data location log. Data that is not routinely collected elsewhere may be entered directly onto the paper CRF workbooks or the eCRF; in such instances the CRF workbook or eCRF will act as source data, this will be clearly defined in the source data location log.

For this trial, source data refers to, though is not limited to, the participant's medical notes, data recorded directly into the eCRF, source data worksheets (when direct entry to the eCRF is not possible) and follow-up questionnaires.

All data collected directly from participants (via online questionnaires or text messages) will be considered as source data within the eCRF. Where paper questionnaires are issued to participants these will be returned to the NCTU for data entry and will be considered source data. Where questionnaire data is obtained via telephone, this data will be entered directly into the eCRF or collected on paper proforma (where direct eCRF is not possible) by a member of the NCTU and will be considered source data.

10.3. Data Management

All trial data will be entered on a trial specific database through the eCRF with participants identified only by their unique trial number and initials. The database will be developed and maintained by NCTU. Access to the database will be restricted and secure. Any missing or ambiguous data will be queried with the site via the eCRF, sites should respond to the data queries in a timely manner, ideally within 2 weeks of the query being raised.

Data should be entered directly into the eCRF where possible. CRF workbooks will be provided to sites to assist with the collection of data, any completed CRF workbooks should be stored in a secure location separate from any identifiable information to prevent direct data linkage.

Questionnaires returned to NCTU will be entered by staff at NCTU. Data obtained from the patient reported outcomes will not be subject to data queries. The trial management team will follow-up (via telephone, text message, post or email) outstanding questionnaires to achieve maximum adherence. Data may be collected directly via these methods if required.

10.4. Archiving

It is the responsibility of the Principal Investigator to ensure all essential trial documentation and source documents (e.g. signed Informed Consent Forms, Investigator Site Files, participants' hospital notes, copies of CRFs etc.) at their site are securely retained for at least 25 years after the end of trial as defined in section 12. No documents will be destroyed without prior approval from the Sponsor.

11.Quality control and quality assurance

11.1. Site Set-up and Initiation

All participating Principal Investigators will be asked to sign the necessary agreements and supply a current CV to the NCTU. All members of the site research team will also be required to sign a site delegation log. Prior to commencing recruitment all sites will undergo a process of initiation and members of the research team will be asked to provide evidence of GCP training. Key members of the site research team will be required to attend either a meeting or a teleconference covering aspects of the trial design, protocol procedures, Adverse Event reporting, collection and reporting of data and record keeping. Sites will be provided with an Investigator Site File containing essential documentation, instructions, and other documentation required for the conduct of the trial. The NCTU must be informed immediately of any change in the site research team.

11.2. Monitoring

11.2.1. On-site Monitoring

Monitoring will be carried out as required following a risk assessment and as documented in the monitoring plan. Any on-site monitoring activities carried out by NCTU will be detailed in a monitoring report, a copy of which will be provided to the Sponsor upon request. Any issues noted will be followed up to resolution. Additional on-site monitoring visits may be triggered, for example by poor CRF return, poor data quality, lower or higher than expected SAE reporting rates, excessive number of participant withdrawals or deviations. If a monitoring visit is required, NCTU will contact the site to arrange a date for the proposed visit and will provide the site with written confirmation. Investigators will allow the Hand-2 trial staff access to source documents as requested.

11.2.2. Central Monitoring

The NCTU will be in regular contact with the site research team to check on progress and address any queries that they may have. The trial team will check incoming CRFs for compliance with the protocol, data consistency, missing data and timing. Sites will be asked for missing data or clarification of inconsistencies or discrepancies. Sites will be requested to send in copies of signed ICFs for in-house review for all participants. This will be detailed in the monitoring plan and the PIS.

Further central monitoring activities will be carried out in accordance with the monitoring plan.

11.3. Audit and Inspection

The Principal Investigator will permit trial-related monitoring, quality checks, audits, ethical reviews, and regulatory inspection(s) at their site, providing direct access to source data/documents. The Principal Investigator will comply with these visits and any required follow up.

11.4. Notification of Serious Breaches

The Sponsor is responsible for notifying the REC of any serious breach of the conditions and principles of GCP in connection with that trial or the protocol relating to that trial. Sites are therefore requested to notify the Coordinating Centre of any suspected trial-related serious breach of GCP and/or the trial protocol as soon as they become aware of the breach.

Where the Coordinating Centre is investigating whether or not a serious breach has occurred sites are also requested to cooperate with the Coordinating Centre in providing sufficient information to report the breach to the REC where required and in undertaking any corrective and/or preventive action.

Sites may be suspended from further recruitment in the event of serious and persistent non-compliance with the protocol and/or GCP, and/or poor recruitment. Any major problems identified during monitoring may be reported to the Trial Management Group and Trial Steering Committee. This includes reporting serious breaches of GCP and/or the trial protocol to the REC.

12.End of Trial Definition

The end of trial will be at database lock. NCTU will notify the REC that the trial has ended and a summary of the clinical trial report will be provided within 12 months of the end of trial.

13.Statistical Considerations

13.1. Sample size and justification

We were unable to estimate the minimum clinically important difference from the Hand-1 pilot data due to the small number of participants who felt "a little better" after treatment. However, the DISC trial team estimated a six point difference on the PEM at 1 year to represent the threshold at which treatment difference becomes important in this patient population, and which would represent an appropriate non-inferiority margin. We also propose the six point difference in the PEM at 12 months as the non-inferiority margin. This is equivalent to a one point reduction in the scores of six of the 11 questions in the PEM (score range for each = 1-7). From the Hand-1 pilot study, we observed a standard deviation in the PEM of 15.1 at 6 months follow-up. To avoid possible under powering from potential imprecision in the variance estimate from pilot data, we conservatively used the upper 80% confidence limit of 16.6.

The sample size required to achieve 90% power to detect non-inferiority of NF compared to LF within a margin of 6.0 on the PEM at 12 months using SD of 16.6 (an effect size of 0.36), based on 2.5% 1-sided alpha is 324 (162 per arm). Allowing for up to 20% loss to follow-up at 12 months, the target sample size is 406. From the pilot study, we achieved 85% follow-up of participants at the 6 month follow-up appointment without recourse to financial or other incentives. We have not adjusted for surgeon effect as we expect many treating surgeons at each site (≥3), each surgeon treating a small number (≤7) of study participants and at least half of the surgeons able to perform both procedures. We therefore assume any treatment-related clustering to be ignorable. Efforts will be made to maximise adherence with allocated treatment and incentives will be given to maximise follow up.

13.2. Definition of Outcome Measures

Primary. The 11 question version of Part 2 of Patient Evaluation Measure (PEM at 12 months). This PROM is regularly used in hand surgery (21), and is the primary outcome in the DISC trial. It takes 6 minutes to complete and in Hand-1 was popular with participants and demonstrated satisfactory responsiveness. A difference of up to 6 points in the PEM was regarded as unimportant in DISC (17), and will be defined as the non-inferiority margin for this study.

Secondary. The MyMOP(22), SANE (23) Overall Assessment section of the PEM and EQ-5D-5L(24) PROMS, loss of finger extension, adverse effects with temporary or permanent impact on hand function (data collection at 6 week clinic visit), NHS resource use, lost productivity and return to usual activities.

Loss of study finger extension. If treatment is planned for only one finger, then this finger is the study finger. If two or more fingers in a hand are bent up by DC and are undergoing NF or LF, then the finger

undergoing treatment which is causing the most difficulties according to the patient will be termed "the study finger". It is never a finger for which treatment with NF or LF is not planned. Loss of finger extension in the "study finger" will be measured at baseline, pre-intervention(within the 8 weeks prior to the intervention or on the day of the intervention, just before the intervention), and 6 weeks in clinic and at home by participants at 6, 12 and 24 months after treatment.The *SLiCK* device (goo.gl/oRxLPz) has been developed to measure this. Participants will be shown how to use the device at baseline and 6 weeks and will be provided with their own device to use at home for the later assessments. An instruction sheet will be provided with every device and an on-line demonstration video will be available to ensure correct measurements are made.

Resource use and return to usual activities. Cost data for the economic analysis will be collected prospectively during the study using a CRF to record key procedure details (duration, staff, equipment, consumables, bed use) as a basis for an activity-based costing of LF and NF procedures. Hospital notes and patient-completed questionnaires (3, 6 weeks + 6, 12, 24 months) will capture NHS costs (secondary, primary care and medications), employment and hours of work lost due to hand problems.

13.3. Analysis of Outcome Measures

The analysis and reporting of the trial will be in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines extension for reporting non-inferiority and equivalence trials. A full statistical analysis plan *(SAP)* will be developed and agreed prior to database lock.

Appropriate descriptive statistics (mean, standard deviation, median, lower and upper quartiles, minimum, maximum or frequencies and percentages) for the demographic and clinical outcome measures at baseline will be used to assess balance between the randomised arms at baseline, but no formal statistical comparisons will be performed. Baseline characteristics will also be descriptively compared between those randomised and those analysed to see if the attrition has introduced any imbalances. Descriptive statistics appropriate for the outcome will also be presented for all outcomes at all collected time points by treatment arm.

Both the intention to treat (ITT), analysing participants in the groups to which they were randomised and a per-protocol analysis, excluding participants who fail to adequately adhere to the assigned treatment, will be performed for the primary outcome between group comparisons as a protection against possible ITT's increased risk of type I error. Primary conclusion will be based on ITT, with per-protocol results used to check the consistency. For the primary outcome a two sides 95% confidence interval (equivalently one sided 97.5 % interval) for the difference in mean PEM score at 12 months between the NF and LF arms will be constructed using a linear mixed model adjusted for baseline PEM and minimisation variables. Non-inferiority of the NF will be inferred if the upper bound of this interval lies within the non-inferiority margin of 6.0 points. The mixed effects model will use all available follow-up outcome data and include a treatment by time interaction to estimate the between group difference at each follow-up time point with 12 months being the primary treatment comparison.

Sensitivity analyses for the primary outcome will include:

- Complete case analysis based on observed outcome data
- Use of multiple imputation with auxiliary variables not included in the primary analysis also included in the imputation model

- Adjustment for the PEM score pre-intervention (in the 8 weeks before the intervention)/ day of intervention rather than the baseline PEM to explore the effect of any significant delays between randomisation and the intervention.
- Adjustment for any other baseline variable (if applicable) with marked imbalance between the two treatment groups.

Between groups comparison of secondary outcomes will be analysed using appropriate mixed effect model for the outcome adjusting for the same variable as the primary analysis. Complications and adverse events will be presented descriptively.

13.4. Procedures for missing, unused and spurious data

Missing baseline data

We anticipate missing baseline data to be very minimal. For questionnaire outcome measures where there are published methods for dealing with missing items, these will be applied. For baseline scores which will be adjusted for as covariates, any missing data will be imputed using the mean score at each centre.

Missing outcome data

Measures will be taken to minimise missing outcome data; however, it is likely that there will be some missing data in outcome measures as participants are lost to follow-up. For the primary outcome, two principled maximum likelihood based methods will be employed to deal with missing data, both assuming that the probability that a response is missing depends on the observed data, but not on the unobserved data i.e. the missing data is missing at random (MAR).

I. Mixed effect model as the primary analysis
II. Multiple imputation as a sensitivity analysis: Multivariate imputation by chained equations (MICE) will be used to generate at least 20 multiply imputed datasets of each missing outcome, with an imputation model including the outcome, all predictors and other auxiliary variables if needed to make the MAR assumption more plausible.

13.5. Definition of populations analysed

For the primary analysis, participants will be analysed according to allocated treatment group regardless of adherence to the allocated intervention. This will be supplemented by analysing only the participants who would comply with their allocated intervention.

Primary analysis will be for participants with outcome data collected at any time point (i.e. using all the available post-intervention data).

For the secondary outcomes, participants will be analysed according to allocated treatment group regardless of adherence to the allocated intervention. Main analysis for each outcome will be for participants with outcome data collected (i.e. without imputation for missing data).

For the safety outcomes, data will be presented according to:

- Participants analysed according to allocated treatment group regardless of adherence to the allocated intervention.
- Participants analysed according to intervention received.

13.5.1. Planned Interim Analysis

There is no planned interim analysis of treatment effectiveness. An internal pilot phase has been built in to the trial and Stop-Go criteria (see section 4.3) will be assessed after the first 10 x months of recruitment.

13.5.2. Planned Final Analyses

Final analyses will be undertaken once the database has been locked, as per the end of trial definition in section 12.

13.5.3. Planned Sub-Group Analyses

There are no pre-specified subgroup analyses for the primary outcome.

14.Health economic analysis

The primary within trial economic analysis will estimate the incremental NHS and personal social services cost per Quality Adjusted Life Year (QALY) gained of NF versus LF at 24 months using an intention to treat approach. This time point is more relevant for policy makers as it includes the costs and consequences of early recurrence and reoperation. The analysis will explore whether the lower initial costs of NF are subsequently offset by high costs of recurrence and poorer patient outcomes.

The EQ-5D-5L health states will be valued using the interim mapping function developed by van Hout et al. (24) or other NICE-recommended values at the time of analysis and combined with survival data to estimate QALYs. The incremental difference in QALYs between the two arms will be examined through regression methods, consistent with the methods selected in the statistical analysis and controlling for baseline EQ-5D-5L scores. Wherever available, we will use national unit costs (e.g. NHS reference costs, PSSRU unit costs of health and social care) to value resource use. For the activity-based costing of LF and NF procedures we will also utilise hospital procurement costs for equipment, consumables and salaries. Costs and outcomes beyond 12 months will be discounted at standard rates. We will describe the prevalence of missing cost and EQ-5D-5L data and use multiple imputation techniques as appropriate. Uncertainty will be summarised using cost effectiveness acceptability curves and by calculating an incremental net benefit statistic and confidence interval. Although not part of the primary analysis, we will collect information on days lost from work/usual activities due to DC or recovery after DC procedures. This will allow a secondary analysis to explore the impact of care pathways on patient and productivity costs. In sensitivity analyses, we will explore the robustness of our conclusions to plausible differences in key costing assumptions (e.g. the unit costs of NF and LF).

We will develop a simple extrapolation model to assess potential cost-effectiveness of LF, NF and (after pooled analysis of Hand-2 and DISC) CI over longer time horizons (e.g. 5 and 10 years) based on published data on long term recurrence and revision surgery. A health economic analysis plan, reviewed by the TSC, will be developed to pre-specify the within trial and extrapolation model methods in detail.

15.Trial Organisational Structure

15.1. Sponsor

The trial is sponsored by the Nottingham University Hospitals NHS Trust.

15.2. Trials Unit

The trial is co-ordinated by the Nottingham Clinical Trials Unit (NCTU) based at the University of Nottingham.

15.3. Trial Management Group

The TMG will consist of the CI, Professor of Surgery, Professor of Clinical Trials and Medical Statistics, Assistant Professor of Clinical trials, Clinical Associate Professor, Trial Statistician, Trial Manager, Senior Trial Manager and Data Coordinator. They are responsible for the day-to-day management of the trial and will monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of data collected in the trial. Other relevant members of the trial team will be invited to TMG meetings as required.

15.4. Trial Steering Committee

The TSC will provide independent oversight of the trial and will meet at least annually or more often as required, either face-face-face or by teleconference. The TSC will consider and act, as appropriate, upon the recommendations of the Data Monitoring Committee (DMC), and in accordance with the TSC charter, and ultimately carries the responsibility for deciding whether the trial needs to be stopped on grounds of safety or efficacy.

After 10 months of recruitment, the TSC will be presented with the data required to assess the Stop-Go criteria for the internal pilot phase of the trial. The TSC and Data Monitoring Committee (DMC) will review the Stop-Go data and advise whether the trial should continue, outlining any concerns/ required adaptations.

15.5. Data Monitoring Committee

Reports will be supplied in confidence to an independent Data Monitoring Committee (DMC), which will be asked to give advice on whether the accumulated data from the trial, together with the results from other relevant research, justifies the continuing recruitment of further participants. The DMC will operate in accordance with a trial specific charter based upon the template created by the Damocles Group. The DMC will meet initially during the trial set-up period to agree content of the DMC charter. They will then meet 10 months after recruitment of the first participant (to coincide with the assessment of the Stop-Go criteria – see section 13.2.1.1) and annually after unless there is a specific reason.

Additional meetings may be called if recruitment is much faster than anticipated and the DMC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if a safety issue is identified. The DMC will report directly to the Trial Steering Committee (TSC) who will convey the findings of the DMC to the funders, and/or Sponsor as applicable.

After 10 months of recruitment, the DMC will be presented with the data required to assess the Stop-Go criteria for the internal pilot phase of the trial. The DMC and TSC will review the Stop-Go data and advise whether the trial should continue, outlining any concerns/ required adaptations.

15.6. Finance

This trial is funded bythe National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme (funding award number: 127393).

Payments to co-investigator and recruiting sites will be covered in separate contractual agreements, located in the Trial Master File, and are not detailed in this protocol.

16.Ethical Considerations

The trial will be performed in accordance with the recommendations guiding physicians in biomedical research involving human participants, adopted by the 18th World Medical Association General Assembly, Helsinki, Finland, June 1964, amended at the 48th World Medical Association General Assembly, Somerset West, Republic of South Africa, October 1996 (website:https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/).

The trial will be conducted in accordance with the UK Policy Framework for Health and Social Care Research (2018), the Data Protection Act 2018 and the ICH Guideline for Good Clinical Practice E6 (R2).

17.Confidentiality and Data Protection

Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored in accordance with the Data Protection Act 2018.

Participants will always be identified using only their unique trial identification number, date of birth and initials on the Case Report Form and correspondence between the Coordinating Centre and the participating site. Participants will give their explicit consent for the movement of their consent form, giving permission for NCTU to be sent a copy. This will be used to perform in-house monitoring of the consent process.

The Investigator must maintain documents not for submission to the Coordinating Centre (e.g. Participant Identification Logs) in strict confidence. In the case of specific issues and/or queries from the regulatory authorities, it will be necessary to have access to the complete trial records, provided that participant confidentiality is protected.

The Coordinating Centre will maintain the confidentiality of all participant's data and will only disclose information of participants that haven given consent to any third party. Representatives of the Coordinating Centre and Sponsor may be required to have access to participant's notes for quality assurance purposes but participants should be reassured that their confidentiality will be respected at all times.

18.Insurance and Indemnity

The Nottingham University Hospitals NHS Trust will act as sponsor for the trial. Delegated responsibilities will be assigned to the NHS Trusts taking part and NCTU Insurance and indemnity for trial participants and NHS trial staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96) 48. There are no special compensation arrangements, but trial participants may have recourse to the NHS complaints procedure.

The University of Nottingham has appropriate and typical insurance coverage in place (including, but not limited to Clinical Trials, Professional Indemnity, Employer's Liability and Public Liability policies) in relation to the Institution's Legal Liabilities arising from the University's activities and those of its staff, whilst conducting University business and research activity.

The Nottingham University Hospitals NHS Trust is independent of any pharmaceutical company, and as such it is not covered by the Association of the British Pharmaceutical Industry (ABPI) guidelines for participant compensation.

19.Publication Policy

During the period of the trial, press releases may be issued from NCTU. No party will be entitled to submit any publicity material without prior approval from NCTU.

Plans for publication will be outlined in a separate publication plan, which will include details of authorship. Results of this trial will be submitted for publication in a peer reviewed journal(s). The manuscript(s) will be prepared by the Chief Investigator and authorship will be determined by mutual agreement.

Any secondary publications and presentations prepared by Investigators must be reviewed by the Chief Investigator and members of the Trial Management Group as required. Manuscripts must be submitted to the Chief Investigator and Trial Manager in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues. Authors must acknowledge that the trial was performed with the support of the Nottingham University Hospitals NHS Trust.

Trial publications and conference abstracts will be submitted to the National Institute for Health Research (NIHR) for approval prior to submission to the event organisers or the editors. All publications will acknowledge the support of the NIHR in funding this trial. Neutral or negative results will not constitute a reasonable justification to delay publication. A lay summary of the results will be sent to all participants at the end of the trial.

20. Reference List

1. Geoghegan JM, Forbes J, Clark DI, Smith C, Hubbard R. Dupuytren's disease risk factors. J Hand Surg Br. 2004;29(5):423-6.
2. Roush TF, Stern PJ. Results following surgery for recurrent Dupuytren's disease. J Hand Surg Am. 2000;25(2):291-6.
3. Engstrand C, Boren L, Liedberg GM. Evaluation of activity limitation and digital extension in Dupuytren's contracture three months after fasciectomy and hand therapy interventions. J Hand Ther. 2009;22(1):21-6; quiz 7.
4. Hospital Episode Statistics database on the internet. http://www.hscic.gov.uk/searchcatalogue?q=title%3A%22Hospital+Episode+Statistics%2C+Admitted+patient+care+-+England%22&area=&size=10&sort=Relevance. 2013 [
5. Bebbington E, Furniss D. Linear regression analysis of Hospital Episode Statistics predicts a large increase in demand for elective hand surgery in England. J Plast Reconstr Aesthet Surg. 2015;68(2):243-51.
6. van Rijssen AL, Gerbrandy FS, Ter Linden H, Klip H, Werker PM. A comparison of the direct outcomes of percutaneous needle fasciotomy and limited fasciectomy for Dupuytren's disease: a 6-week follow-up study. The Journal of hand surgery. 2006;31(5):717-25.
7. van Rijssen AL, ter Linden H, Werker PM. Five-year results of a randomized clinical trial on treatment in Dupuytren's disease: percutaneous needle fasciotomy versus limited fasciectomy. Plast Reconstr Surg. 2012;129(2):469-77.

8. Rodrigues JN, Becker GW, Ball C, Zhang W, Giele H, Hobby J, et al. Surgery for Dupuytren's contracture of the fingers. Cochrane Database of Systematic Reviews. 2015(12).
9. van Rijssen AL, Gerbrandy FSJ, Linden HT, Klip H, Werker PMN. A Comparison of the Direct Outcomes of Percutaneous Needle Fasciotomy and Limited Fasciectomy for Dupuytren's Disease: A 6-Week Follow-Up Study. Journal of Hand Surgery. 2006;31(5):717-25.
10. Davis TR. Surgical treatment of primary Dupuytren's contractures of the fingers in the UK: surgeons' preferences and research priorities. J Hand Surg Eur Vol. 2013;38(1):83-5.
11. Rodrigues JN SB, Davis TRC, editor The true indications for Dupuytren's disease surgery: A study of patient-determined goals. Briitsh Society for Surgery of the Hand, Autumn scientific meeting; 2012; York.
12. Rodrigues JN, Zhang W, Scammell BE, Davis TR. What patients want from the treatment of Dupuytren's disease--is the Unite Rhumatologique des Affections de la Main (URAM) scale relevant? J Hand Surg Eur Vol. 2015;40(2):150-4.
13. (England) N. Evidence-Based Interventions: Guidance for CCGs 2018. Available from: https://www.england.nhs.uk/wp-content/uploads/2018/11/ebi-statutory-guidance.pdf.
14. NICE. Dupuytren's disease 2015 [Available from: https://cks.nice.org.uk/dupuytrens-disease#!topicsummary.
15. James Lind Alliance. Common Conditions Affecting the Hand and Wrist PSP final report. 2017 [Available from: http://www.jla.nihr.ac.uk/priority-setting-partnerships/common-conditons-affecting-the-hand-and-wrist/downloads/JLA-Final-Summary.pdf.
16. Donovan JL, Rooshenas L, Jepson M, Elliott D, Wade J, Avery K, et al. Optimising recruitment and informed consent in randomised controlled trials: the development and implementation of the Quintet Recruitment Intervention (QRI). Trials. 2016;17(1):283.
17. Dias J, Tharmanathan P, Arundel C, Watson M, Bainbridge L, Craigen M, et al. DISC: Dupuytren's Interventions Surgery vs. Collagenase. A pragmatic multi-centre randomised controlled non-inferiority, cost effectiveness trial comparing injections of collagenase into the cord to surgical correction in the treatment of moderate Dupuytren's contracture in adult patients 2017 [updated 07.07.17. Available from: https://www.journalslibrary.nihr.ac.uk/programmes/hta/1510204/#/.
18. Davis TRC, Hollingworth W, Blazeby J, Mills N, Duley L, Montgomery A. Needle fasciotomy versus limited fasciectomy for the treatment of Dupuytren's contractures of the fingers: a study which investigates the feasibility, acceptability and design of a multicentre randomised trial. Research for Patient Benefit Report: PB-PG-0613-31083. 2017: https://www.nottingham.ac.uk/research/groups/cebhs/documents/research-documents/rfpb-dupuytrens-report.pdf.
19. Donovan JL, Lane JA, Peters TJ, Brindle L, Salter E, Gillatt D, et al. Development of a complex intervention improved randomization and informed consent in a randomized controlled trial. J Clin Epidemiol. 2009;62(1):29-36.
20. Rooshenas L, Scott LJ, Blazeby JM, Rogers CA, Tiling KM, S H, et al. The QuinteT Recruitment Intervention supported five randomised trials to recruit to target: a mixed methods evaluation. J Clin Epidemiol. 2018;106:108-20.
21. Macey AC, Burke FD, Abbott K, Barton NJ, Bradbury E, Bradley A, et al. Outcomes of hand surgery. British Society for Surgery of the Hand. J Hand Surg Br. 1995;20(6):841-55.
22. Welcome to MyMOP: Centre for Academic Primary Care, University of Bristol; [Available from: http://www.bris.ac.uk/primaryhealthcare/resources/mymop/.
23. Williams GN, Gangel TJ, Arciero RA, Uhorchak JM, Taylor DC. Comparison of the Single Assessment Numeric Evaluation method and two shoulder rating scales. Outcomes measures after shoulder surgery. Am J Sports Med. 1999;27(2):214-21.
24. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value Health. 2012;15(5):708-15.

25. Husbands S, Elliott D, Davis TR, Blazeby JM, Harrison EF, Montgomery AA, et al. Optimising recruitment to the HAND-1 RCT feasibility study: integration of the QuinteT Recruitment Intervention (QRI). Pilot and feasibility studies. 2020;6(1):1-11.

21.Appendix

21.1. Needle Aponeurotomy/Needle Fasciotomy Protocol

Component/Step of intervention	Specifics of step	Type of Standardisation	Description	Conditions	Limits
Before incision	Setting	Mandatory	Setting in which procedure is performed: outpatient clinic room, minor operating room, or operating theatre	All cases	Boundaries: must be one of the three options
	Perioperative skin preparation	Mandatory	Skin preparation with surgeon's routine antimicrobial preparation – alcoholic or aqueous chlorhexidine or povidone-iodine	All cases Full flexibility with choice of antimicrobial agent	Boundaries: must use antimicrobial agent
	Local anaesthetic use	Optional	Local anaesthetic infiltration to area being treated.	No boundaries regarding agent used	Boundaries: choice and use at surgeon's discretion
	Regional anaesthetic or general anaesthetic	Prohibited	Anaesthetic blocks to named nerves not contiguous with site to be needled, i.e. median + ulnar nerve block at wrist or plexus block, or general anaesthetic	All cases	Exactly
Incision and access	Instrument used	Mandatory	19G – 23G hypodermic needle used only (no other needles, no scalpel)	All cases	Boundaries: must use a needle from 19G – 23G inclusive.
	Formal incision	Prohibited	Skin incision beyond percutaneous passage of	All cases	Exactly

			needle,No incision to allow direct visualisation of structures permitted		
Dissection	Sharp or blunt dissection of subcutaneous tissues and deeper structures under vision	Prohibited	Dissection of subcutaneous tissues and deeper structures except freeing up of cord from skin using percutaneous with percutaneous needle/scalpel tip	All cases	Exactly
Resection	Removal of tissue implicated in Dupuytren's disease	Prohibited	Resection of skin and/or subcutaneous tissue or Dupuytren's cord	All cases	Exactly
Haemostasis	Intra-operative haemostasis	Optional	Use of adrenaline-soaked swabs or other haemostasis techniques to control bleeding from a skin tear	All cases	Boundaries: choice and use at surgeon's discretion
Reconstruction	Reconstructive surgical procedure	Prohibited	Use of reconstructive surgery techniques to close a skin tear	All cases	Exactly
Closure	Closure of skin tear by using sutures or other closure devices to appose wounds edges.	Prohibited	Sutures (absorbable or non-absorbable), staples, or other closure device e.g. glue	All cases	Exactly
After skin closure	Application of conventional dressings to a wound/graft/flap	Optional	Application of conventional dressings to wound	All cases	Boundaries: choice and use at surgeon's discretion
Insertion of adjunct	Insertion of drain in the wound	Prohibited	Placement of a surgical drain into the wound	All cases	Exactly
Intraoperative diagnosis	Not applicable				
Other	Not applicable				

21.2. Fasciectomy Protocol

Component/Step of intervention	Specifics of step	Type of Standardisation	Description	Conditions	Limits
Before incision	Setting	Mandatory	Setting in which procedure is performed: minor operating room or operating theatre	All cases	Boundaries: must be in standard setting (usually operating room or theatre) for hospital. Not a Covid compromise.
	Perioperative skin preparation	Mandatory	Skin preparation with surgeon's routine antimicrobial preparation – alcoholic or aqueous chlorhexidine or povidone-iodine	All cases Full flexibility with choice of antimicrobial agent	Boundaries: must use antimicrobial agent
	Local anaesthetic use	Optional	Local anaesthetic infiltration to area being treated. May be used for WALANT technique, or in conjunction with general or regional anaesthesia	No boundaries regarding agent used	Boundaries: choice and use at surgeon's discretion according to her/his usual practice. Not a Covid compromise
	Regional anaesthetic or general anaesthetic	Optional	Anaesthetic blocks to named nerves not contiguous with site to be treated, e.g, median/ulnar nerve block at wrist or	No boundaries regarding agent used	Boundaries: choice and use at anaesthetist and surgeon's discretion. Not a

			plexus block, or general anaesthetic		Covid compromise
Incision and access	Instrument used	Optional	May include different scalpel blades, scissors or diathermy for different parts of incision and dissection	No boundaries regarding instruments used	Boundaries: choice and use at surgeon's discretion
	Formal incision	Mandatory	Skin incision to allow direct visualisation of one/more deeper structure(s) (i.e. neurovascular bundles and Dupuytren's cords)	All cases	Exactly
Dissection	Sharp or blunt dissection of subcutaneous tissues and deeper structures under vision	Optional	Dissection of subcutaneous tissues and deeper structures, including joint releases	All cases	Boundaries: extent of dissection at surgeon's discretion. Use of joint release techniques at surgeon's discretion
Resection	Removal of tissue implicated in Dupuytren's disease	Mandatory	For contractures involving the MCP joint, the cord will be excised proximally at least to the proximal margin of the transverse fibres of the palmar aponeurosis. Digital cords will be excised completely from their origin. In all cases the distal margin of the cord excision will be the insertion of the cord onto the flexor sheath (or other structure).	All cases	Boundaries: extent of excision of tissue at surgeon's discretion
Haemostasis	Intra-operative haemostasis	Optional	Use of diathermy (monopolar or bipolar), or	All cases	Boundaries: choice and use

			alternative techniques such as adrenaline-soaked swabs		at surgeon's discretion
Reconstruction	Reconstructive surgical procedure	Optional	Use of reconstructive surgery techniques to close the surgical wound, such as local flaps (e.g. z-plasties). Not a pre-planned skin graft.	All cases	Boundaries: local flap-based techniques permitted at surgeon's discretion. No pre-planned full or split thickness skin grafting allowed.
Closure	Closure of wound by using sutures or other closure devices to appose wounds edges.	Optional	Sutures (absorbable or non-absorbable), staples, or other closure device e.g. glue. May leave wound open (e.g.McCash technique)	All cases	Boundaries: choice and use at surgeon's discretion
After skin closure	Application of conventional dressings to a wound/graft/flap	Optional	Application of conventional dressings to wound	All cases	Boundaries: choice and use at surgeon's discretion
Insertion of adjunct	Insertion of drain in the wound	Optional	Placement of a surgical drain into the wound	All cases	At surgeon's discretion
	Insertion of Kirschner wires across joint(s)	Optional	Transarticular k-wires (buried or left proud), but removed after a period.	All cases	Boundaries: temporary use only, at surgeon's discretion. Permanent placement and

					arthrodesis prohibited
Intraoperative diagnosis	Not applicable				
Other	Planned arthrodesis, amputation or skin graft to the study finger	Prohibited	Strategic aim to arthrodese joint, amputate the study finger or perform a dermofasciectomy from the outset of the procedure, rather than for unanticipated per-operative complications	All cases	Boundaries: May be performed if becomes required during the procedure