ISRCTN18254597 https://doi.org/10.1186/ISRCTN18254597

Dupuytren's interventions surgery vs collagenase

Submission date	Recruitment status	[X] Prospectively registered
04/04/2017	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
11/04/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/11/2024	Musculoskeletal Diseases	

Plain English summary of protocol

Current plain English summary as of 18/11/2020:

Background and study aims
Dupuytren’s contracture is a common problem affecting the hand. The condition is caused by fibrous tissue which forces the finger to bend down into the palm meaning patients cannot straighten their finger. The common treatment is surgery to remove the tissue and straighten the bent finger. A new treatment is a Collagenase injection, which softens the fibrous tissue. This is given in clinic, and is followed up in clinic a few days later where the finger is moved to help to straighten it. Both treatments have been offered on the NHS in England and in the USA and Europe, but it is not known if the injection is as good as surgery at correcting the bent finger, if the correction continues in the long term and if the complication rates are similar. The aim of this study is to find out whether collagenase injections are as good and as safe as surgery for treating this condition and to find out the cost of both treatments to see which is the best value for money. Participants are also asked what they think about the different treatments, to see if they prefer one treatment more than the other.

Who can participate?
Patients aged 18 and over who have Dupytren’s contracture

What does the study involve?
The participant’s hand is assessed and a photograph is taken, and the participant is asked some questions about their condition and their general health. Participants are then randomly allocated to receive either the injection or surgery. Before they receive their treatment, the hand is re-assessed and the participant completes a short questionnaire about their hand health. During the study participants will complete a further 4 visits (face to face in the hospital, via video call or via telephone call) where their hand is assessed, they are asked some questions about their hand function and general health, and a photograph is taken of their hand.

What are the possible benefits and risks of participating?
The information from this study may help doctors to treat people with Dupuytren’s contracture more effectively in the future. However, as with any treatment, there are always potential risks. Common side effects of Collagenase include injection site swelling, bruising and pain. These

often subside within 1 – 2 weeks of the injection. The injection may also cause dizziness, headaches, a tingling sensation or a reduced sense of touch. Very rarely, allergic reactions and tendon rupture may occur. Common side effects of surgery may be experienced such as pain, bruising, swelling or infection, in addition to anaesthetic side effects such as dizziness, headaches and numbness.

Where is the study run from?
York Trials Unit, University of York (UK). The Chief Investigator is Professor Joe Dias (https://www2.le.ac.uk/colleges/medbiopsych/teaching/academic-champions/people/professor-joseph-dias)

When is the study starting and how long is it expected to run for?
May 2017 to July 2022

Who is funding the study?
National Institute for Health Research Health Technology Assessment Programme (UK)

Who is the main contact?
1. Catherine Arundel (public)
catherine.arundel@york.ac.uk
2. Puvan Tharmanathan (scientific)
puvan.nathan@york.ac.uk

_____

Previous plain English summary as of 31/10/2018:

Background and study aims
Dupuytren's contracture is a common problem affecting the hand. The condition is caused by fibrous tissue which forces the finger to bend down into the palm meaning patients cannot straighten their finger. The common treatment is surgery to remove the tissue and straighten the bent finger. A new treatment is a Collagenase injection, which softens the fibrous tissue. This is given in clinic, and is followed up in clinic a few days later where the finger is moved to help to straighten it. Both treatments are offered on the NHS in England and are used in the USA and Europe, but it is not known if the injection is as good as surgery at correcting the bent finger, if the correction continues in the long term and if the complication rates are similar. The aim of this study is to find out whether collagenase injections are as good and as safe as surgery for treating this condition and to find out the cost of both treatments to see which is the best value for money. Participants are also asked what they think about the different treatments, to see if they prefer one treatment more than the other.

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May 2017 to October 2021

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Where is the study run from?
University of York (UK)

When is the study starting and how long is it expected to run for?
May 2017 to October 2021

Who is funding the study?
National Institute for Health Research Health Technology Assessment Programme (UK)

Who is the main contact?
1. Catherine Arundel (scientific)
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Study website
https://www.york.ac.uk/healthsciences/research/trials/research/trials/disc/

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2016-004251-76

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Sponsor ID: 2087230; HTA 15/102/04

Study information

Scientific Title
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

Acronym
DISC

Study objectives

Collagenase injection is not inferior to limited fasciectomy in the correction of Dupuytren’s contracture of the hand.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and Humber Leeds West Research Ethics Committee, 22/05/2017, ref: 17/YH/0120

Study design
Multi-centre randomized controlled non-inferiority pragmatic trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Dupuytren's contracture

Interventions
Current interventions as of 18/11/2020:

The participant's hand is assessed, a photograph is taken and they are asked some questions about their condition and their general health. Participants are randomised to either the intervention or the control group. Before they receive their treatment, their hand is re-assessed and they are asked to complete a short questionnaire about their hand health.

1. Intervention: Collagenase Clostridium histolyticum injections
Depending on the cord affected 0.25ml or 0.20ml of reconstituted solution (0.58mg Collagenase Clostridium histolyticum) is injected as three aliquots: 0.25ml for cord in a metacarpophalangeal (MCP) joint, 0.20ml for cord in a proximal interphalangeal (PIP) joint. The three aliquots are distributed via injection into an affected cord at set anatomical points through a single needle puncture at a single time point. Patients will be scheduled for Collagenase injection within 18 weeks following randomisation (as per referral to treatment time RTT), however where possible sites should complete this procedure within 12 weeks post randomisation. After an interval of one to seven days, the patient then returns to clinic and, under local anaesthetic, the cord is snapped using a four-step process. Two additional visits by the patient may therefore be required for the intervention to be delivered; one for injection and one for manipulation. Separate cords may be injected at the same treatment, in line with the SmPC, following the

injection procedure and using separate vials for each cord. If multiple cords are injected, only the reference cord injection will be deemed to be part of the trial treatment. Given the pragmatic nature of DISC, follow-up Collagenase injections will be at clinician discretion this includes the timing of manipulation and of further injections to the same cord.

2. Control: limited fasciectomy surgery
Limited fasciectomy involves the removal, under anaesthesia and tourniquet control, of the diseased fascia, nodule and cord, or a part of it, to correct the contracture of the joint. As deemed clinically appropriate, the skin may then be left to heal by secondary intention, closed directly, or closed with a Z plasty or closed using a full thickness skin graft. Patients will be scheduled for the limited fasciectomy surgery to be completed within 18 weeks following randomisation (as per referral to treatment time-RTT), however where possible sites should complete this procedure within 12 weeks post randomisation.

During the study participants will complete a further 4 visits (face to face in the hospital, via video call or via telephone call) where their hand is assessed, they are asked some questions about their hand function and general health, and a photograph is taken of their hand.

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Previous interventions:

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During the study participants need to come to the hospital for another 4 visits where their hand is assessed, they are asked some questions about their hand function and general health, and a photograph is taken of their hand.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Collagenase Clostridium histolyticum (CCH)

Primary outcome measure
Hand health and overall hand assessment, measured using the Patient Evaluation Measure at baseline, pre treatment, 3 months, 6 months, 1 year and 2 years post treatment

Secondary outcome measures
Current secondary outcome measures as of 31/10/2018:
1. Disability, measured using the Unité Rhumatologique des Affections de la Main (URAM) Patient Rated Outcome Measure at baseline, 3 months, 6 months, 1 year and 2 years post treatment
2. Hand function, daily activities, work performance, pain, aesthetics and patient satisfaction, measured using the Michigan Hand Questionnaire (MHQ) Measured at baseline, 1 year and 2 years post treatment
3. Extension deficit and total active movement (for stiffness), measured using goniometry and photograph data at baseline, pre-treatment, post-treatment (measurements only) and 3 months, 6 months, 1 year and 2 years post treatment
4. Recurrence, measured using goniometry at 3 months, 6 months, 1 year and 2 years post treatment
5. Further procedures, recorded by clinicians at 3 months, 6 months, 1 year and 2 years post treatment
6. Complications, recorded by clinicians at 3 months, 6 months, 1 year and 2 years post treatment
7. Generic health status, measured using the EQ-5D-5L at baseline, 2 weeks, 6 weeks, 3 months, 6 months, 1 year and 2 years post treatment
8. Resource use, measured using trial specific resource use questionnaire to collect NHS resource use, return to work and out of pocket expenses at 3 months, 6 months, 1 year and 2 years post treatment
9. Time to recovery of function, measured using Single Assessment Numeric Evaluation (SANE) via remote data collection at baseline, 2 weeks, 6 weeks, 3 months, 6 months, 1 year and 2 years post treatment

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Overall study start date
01/05/2017

Completion date
31/07/2022

Eligibility

Key inclusion criteria
1. Male or female and aged 18 years or over
2. Presence of discrete, palpable, contracted cord involving the metacarpophalangeal joint and /or proximal interphalangeal joint of a finger
3. Degree of contracture ≥30 degrees in either joint i.e. patient cannot put the palm of the hand flat on a table (Hueston's Table top test)
4. Able to identify a predominant cord for treatment which would not require more than one Collagenase injection as treatment
5. Appropriate for limited fasciectomy surgery and Collagenase injection for Dupuytren's contracture (i.e. cords suitable for CCH and limited fasciectomy and not requiring skin grafting or PNF (e.g. discrete MCP cords in elderly))
6. Patient is willing and able to give informed consent for participation in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

710

Total final enrolment
673

Key exclusion criteria
Current exclusion criteria as of 31/10/2018:
1. Severe contractures of both metacarpophalangeal joint and/or proximal interphalangeal joints (Tubiana Grade 4)
2. History of previous intervention for Dupuytren's contracture (e.g. surgery, Collagenase injection or needle fasciectomy) to the study reference digit
3. History of any other pre-existing disorder of the hand causing significant restriction of movement and/or pain and affecting hand function e.g. post traumatic stiffness, stiffness due to other causes, infection, arthritis
4. Non-English speaking because of the need to complete multiple questionnaires which have not been validated in multiple languages
5. Resident in a location where attendance for follow up at one of the study recruiting centres will not be possible
6. Contraindicated for use of Collagenase including hypersensitivity to: Collagenase, Sucrose, Ketorolac Trometamol, hydrochloric acid, calcium chloride dehydrate, sodium chloride
7. Diagnosis of a coagulation disorder
8. Any other significant disease or disorder (including autoimmune disorders) which, in the opinion of the Investigator, may put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
9. Participation in another research study involving an investigational product in the past 12 weeks
10. Female participants who report to be pregnant or breastfeeding

Previous exclusion criteria:
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2. History of previous intervention for Dupuytren's contracture (e.g. surgery, Collagenase injection or needle fasciectomy) on the same hand
3. History of any other pre-existing disorder of the hand causing significant restriction of movement and/or pain and affecting hand function e.g. post traumatic stiffness, stiffness due to other causes, infection, arthritis
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Date of first enrolment

01/05/2017

Date of final enrolment
31/03/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals of Leicester
United Kingdom
LE5 4QF

Study participating centre
Derby Teaching Hospitals NHS Foundation Trust
United Kingdom
DE22 3NE

Study participating centre
The Royal Orthopaedic Hospital NHS Foundation Trust
United Kingdom
B31 2AP

Study participating centre
University Hospital Southampton NHS Foundation Trust
United Kingdom
SO16 6YD

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
United Kingdom
L7 8XP

Study participating centre

The Newcastle Upon Tyne Hospitals NHS Foundation Trust
United Kingdom
NE7 7DN

Sponsor information

Organisation
University Hospitals of Leicester NHS Trust

Sponsor details
Trust HQ
Level 3
Balmoral Building
Leicester Royal Infirmary
Infirmary Square
Leicester
England
United Kingdom
LE1 5WW

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan
Results will be published in peer reviewed journals. Summaries of the findings will be sent to NICE and other relevant bodies so that findings can inform clinical practice. The trialists will also work with the relevant National Clinical Director in the Department of Health to ensure findings are considered when implementing policy. The trialists will also work with relevant Speciality Advisory Committees to incorporate findings into training curriculum's for clinicians.

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		30/09/2021	19/10/2021	Yes	No
Other files	Health economics analysis plan version 1.0	29/09/2021	03/02/2023	No	No
Statistical Analysis Plan	version 1.0	29/09/2021	03/02/2023	No	No
HRA research summary			28/06/2023	No	No
Results article		09/10/2024	10/10/2024	Yes	No
Other files	Results Infographic version 1.0	19/06/2023	06/11/2024	No	No
Other unpublished results	End of Study Report version 1.0	15/06/2023	06/11/2024	No	No