Study Title: Ecological Momentary Computerised Adaptive Testing to monitor and compare recovery after hand surgery

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No conflicts of interest

Confidentiality Statement
This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

Trial Title: Ecological Momentary Computerised Adaptive Testing to monitor and compare recovery after hand surgery
Protocol Date and Version No: 04/04/2024 Version 1.0

Protocol signature page

The undersigned has read and understood the trial protocol detailed above and agrees to conduct the trial in compliance with the protocol.

Principal Investigator (Please print name)	**Signature**	**Site name or ID number**	**Date**

Following any amendments to the protocol, this page must be updated with the new protocol version number and date and re-signed by the site PI.

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1. KEY CONTACTS

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Funder(s)	The Oxfordshire Health Services Research Committee and the British Society for Surgery of the Hand
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Committees	Not applicable

2. LAY SUMMARY

Patient-reported outcome measures (PROMs) are questionnaires that measure aspects of somebody's health, like hand function. They can monitor a person's health over time. Our team has made a smartphone app that make these questionnaires shorter. Previous research suggests that unlike the full-length questionnaire, people do not mind using the app every day. This could show us how quickly people recover after different types of hand surgery.

We want to see whether our app could be used to compare patients' experiences of recovery after different types of hand surgery. We will look at operations where we expect to see differences in patients' recovery, and check whether the app is detecting these.

We will recruit patients having different types of treatment for:

1) Dupuytren's contracture (when tight fibres cause the finger to bend down towards the palm)
2) Fingers that get stuck in a bent position (trigger finger)
3) Arthritis at the base of the thumb
4) A trapped nerve in the wrist (carpal tunnel syndrome)

Patients will use the app for 3-6 months after surgery. For each condition, we will compare how patients recovered from the different types of treatment.

We also want to know whether the app could be used for remote dynamic/interactive follow up of patients after two common procedures (carpal tunnel decompression and injections to the base of the thumb), instead of having the patient attend a clinic appointment at routine, fixed, time points. We will check whether clinicians could have avoided seeing each patient in clinic, based on the information from the app, or timed the appointment to better meet the patient's needs. To see if people like using the app, we will check how frequently they used it, and interview them about their experience.

3. SYNOPSIS

Study Title	Ecological Momentary Computerised Adaptive Testing to monitor and compare recovery after hand surgery		
Internal ref. no. / short title	EMCAT-2		
Study registration			
Sponsor	University of Oxford RGEA 1st floor, Boundary Brook House Churchill Drive, Headington Oxford OX3 7GB		
Funder	The Oxfordshire Health Services Research Committee and the British Society for Surgery of the Hand		
Study Design	Mixed-methods, observational study		
Study Participants	Adults undergoing treatment for a range of hand conditions (see inclusion criteria)		
Sample Size	Target to meet primary objective: 396 Total required to reach statistical power in all non-essential objectives: 1782		
Planned Study Period	01/06/2024 – 16/12/2026		
Planned Recruitment period	01/06/2024 – 01/06/2026		
	Objectives	Outcome Measures	Timepoint(s)
Primary	Compare the recovery trajectories of patients undergoing percutaneous needle fasciotomy (PNF) to patients undergoing limited fasciectomy (LF), to test whether EMCAT can detect different recovery trajectories over a 12-week period, with less severe post-treatment symptoms in the PNF group within the first 4 weeks.	Patient Evaluation Measure (PEM), administered via the EMCAT platform	Trajectories will be plotted and compared over a 12-week period.

Secondary	Compare the recovery trajectories of other groups that are expected to differ (see Section 6)	Patient Evaluation Measure (PEM), administered via the EMCAT platform	Trajectories will be plotted and compared over a 12-week period.
	Assess the usability of the EMCAT platform	User Engagement Scale, response rates, response times, semi-structured interviews	12-week follow-up
	Assess the criterion validity of EMCAT against the full-length PEM	PEM (linear format) and EMCAT	Baseline, 6 weeks, 12 weeks
Exploratory	Explore whether information provided by the EMCAT platform could have accurately predicted which patients required a change in management during follow up for open carpal tunnel decompression (CTD)	Accuracy of independent clinician assessment of EMCAT trajectory against the recorded consultation outcome	2 weeks and 12 weeks, or whenever follow-up is timed
	Explore whether information provided by the EMCAT platform could help to time follow-up appointments for TBOA injections to coincide with patient need	Plots comparing follow-up appointment dates to EMCAT trajectories	Over 24 weeks
Intervention(s)	Not applicable		
Comparator	Not applicable		

4. ABBREVIATIONS

AWS	Amazon Web Service
CAT	Computerised Adaptive Test
CI	Chief Investigator
CTD	Carpal Tunnel Decompression
EMA	Ecological Momentary Assessment
EMCAT	Ecological Momentary Computerised Adaptive Testing
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HRA	Health Research Authority
ICMJE	International Committee of Medical Journal Editors
LF	Limited Fasciectomy
NDORMS	Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences
NHS	National Health Service
OA	Osteoarthritis
PEM	Patient Evaluation Measure
PI	Principal Investigator
PNF	Percutaneous Needle Fasciotomy
PPI	Patient and Public Involvement
PROM	Patient Reported Outcome Measure
REC	Research Ethics Committee
TBOA	Thumb-Base Osteoarthritis
UES	User Engagement Scale

5. BACKGROUND AND RATIONALE

Patient-reported outcome measures (PROMs) are questionnaires that can quantify symptom severity from the patient's perspective. In research and clinical practice, PROMs are often administered infrequently. This may fail to capture temporal fluctuations in symptom severity, introduce recall bias (if patients are asked to recall how their symptoms have been over a period of time), and contribute to sampling error (for example, if a patient with an inflammatory disease is measured on a particularly 'good' or 'bad' day). Infrequent PROM administration may also fail to detect differences in early recovery trajectories following interventions.

One solution to this is ecological momentary assessment (EMA)[1]. In EMA, patients complete serial PROM assessments in their natural (ecological) surroundings to report on their health state at the time of the assessment (momentarily). While this is appealing for research and clinical care, the usefulness and uptake of EMA is limited by the response burden caused to patients.

Computerised adaptive testing (CAT) describes the use of algorithms to shorten and personalise PROMs[2]. After the response to an item, CAT algorithms estimate the person's score, and select the next most useful remaining item, based on the score estimate. This is repeated with increasing precision until a prespecified stopping rule is met, for example after reaching a measurement precision threshold. By selecting only the most relevant items for an individual, CAT can produce scores that are very similar to full-length PROM scores from a fraction of items in the PROM. Through CAT, we could deliver higher-frequency and lower-burden EMA with better acceptability to respondents, clinicians and trialists. We have termed this concept ecological momentary computerized adaptive testing (EMCAT).

In simulation studies, our team has shown that CAT can deliver precise measurements from a median of 2 items from the 11-item Patient Evaluation Measure (PEM, a PROM used to measure hand function)[3]. Following this, we built a smartphone application that administers the PEM via EMCAT. We deployed this in a feasibility study involving 40 patients with either thumb base osteoarthritis (TBOA) or recent hand trauma, monitored via EMCAT for 12 weeks. EMCAT significantly reduced the length of the PEM and the time taken to complete it (median 8.8 seconds, vs 1 minute 14 seconds). The median response rate for daily assessments was 93%.

We believe EMCAT could aid the assessment of recovery trajectories in comparative research studies, for example when a new procedure is believed to result in faster recovery times than the current standard of care. This latter point is particularly relevant to the field of hand surgery, where 3 of the top 10 James Lind Alliance research priorities relate to accurate and user-friendly PROM administration, and the assessment of interventions that may improve recovery time, such as arthroplasty for the treatment of TBOA[4].

There is also potential for EMCAT to be used in clinical practice, as a remote monitoring tool. Daily EMCAT assessments might help to detect early issues in postoperative recovery and facilitate early intervention. It may be appropriate to follow-up patients with reassuring EMCAT trajectories virtually, rather than with expensive and burdensome face-to-face appointments. Interval EMCAT assessments could be employed in the longer term, using the principles and lower burden of EMCAT, to improve PROM completion in late clinical follow-up. These principles could be expanded beyond measuring outcomes in the hand.

In conditions that require repeat treatments to manage a patient's symptoms (for example, steroid injections for TBOA), it may be possible to use EMCAT to time treatments to coincide with peaks in a patient's symptom severity. This could potentially improve health outcomes over time. It may also help to mitigate healthcare inequalities that occur when patients who are unable to attend rigid face-to-face clinic appointments go unassessed.

Here, we propose a cohort study (EMCAT-2) that will assess the potential for EMCAT to detect early between-group differences in recovery trajectory, where conventional PROM administration might not. We will also explore the feasibility of EMCAT-based follow-up, through mixed methodology. The goal of EMCAT-2 is to provide preliminary data to support a range of different research avenues, which will all stem from this single study.

6. OBJECTIVES AND OUTCOME MEASURES

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Primary Objective 1. Compare the recovery trajectories of patients undergoing percutaneous needle fasciectomy (PNF) to patients undergoing limited fasciectomy (LF), to test whether EMCAT can detect different recovery trajectories over a 12-week period, with less severe post-treatment symptoms in the PNF group within the first 4 weeks.	The PEM, administered via EMCAT.	Trajectories will be plotted and compared over a 12-week period.
Secondary Objectives 2. Compare the recovery trajectories of other groups that are expected to differ over a 12-week period. Specifically, we will test the following hypotheses, which are based on the researchers' clinical experience: - Steroid injection results in less severe post-treatment symptoms than trapeziectomy, within the first 4 weeks - Trapeziometacarpal arthroplasty results in less severe post-treatment symptoms than trapeziectomy, within the first 4 weeks - Minimally invasive (endoscopic or percutaneous) CTD results in less severe post-treatment symptoms than open CTD, within the first 2 weeks - The difference in the recovery of groups undergoing open release vs steroid injection for trigger finger are not clinically significant over the first 2 weeks *The objective is to test EMCAT's ability to differentiate between recovery trajectories that are expected to differ, rather than to prove or disprove that differences in recovery trajectory exist. The clinical comparisons are a vehicle for testing the measurement properties of EMCAT. Here, the threshold for clinically significant difference is approximated as half a standard deviation of baseline scores of groups being compared. Statistical significance is taken at the 5% level. By symptom severity, we mean PEM EMCAT scores, where a higher (poorer) score reflects more severe symptoms (a poorer level of hand health).*	The PEM, administered via EMCAT.	Trajectories will be plotted and compared over a 12-week period.

3. Assess the usability of the EMCAT platform	UES scores, response rates, response times, and semi-structured interviews	12-week follow-up
4. Assess the criterion validity of EMCAT against the full-length PEM by comparing scores at baseline, 6 weeks, and 12 weeks	Full-length PEM scores and EMCAT PEM scores	Baseline, 6-week and 12-week follow-up
Exploratory Objectives		
5. Explore whether information provided by the EMCAT platform could have accurately predicted which patients required a change in management during open CTD follow up	Accuracy of independent clinician interpretation of EMCAT trajectories against observed patient management	2 weeks and 12 weeks, or whenever follow-up is timed
6. Explore whether information provided by the EMCAT platform could help to time follow-up appointments for TBOA injections to coincide with patient need	Plots comparing follow-up appointment dates to EMCAT trajectories	Over 24 weeks
7. Explore the patient and clinician perceptions of EMCAT-guided follow-up and clinical monitoring	Semi-structured interviews	

7. STUDY DESIGN

We will perform a mixed-methods cohort study to explore the feasibility of EMCAT for measuring between-group differences in postoperative recovery, its potential to guide follow-up type (face-to-face, telemedicine or patient-initiated) in open carpal tunnel decompression, and its potential to guide follow-up timing after steroid injection for TBOA. The study setting will be NHS hospitals in the England, Scotland and Wales.

Our primary objective is to use EMCAT to compare the recovery trajectories of patients undergoing PNF and LF for Dupuytren's disease. We expect to see a difference in recovery trajectory over a 12-week period, with patients undergoing PNF showing less severe symptoms than those undergoing LF over the first 4 weeks. To meet this objective, we will recruit 396 participants (198 undergoing PNF and 198 undergoing LF), who will be followed up for a 12-week period with daily EMCAT assessments.

To address our secondary objectives, we will simultaneously recruit patients undergoing:

- Steroid injection for TBOA
- Steroid injection for trigger finger
- Trapeziectomy for TBOA
- Arthroplasty for TBOA
- Surgical release of trigger finger
- Open CTD
- Minimally invasive (endoscopic or percutaneous) CTD

We will recruit as many participants as we can in these groups, within the limits of the study timing and funding, and up to a maximum of 198 per group. We will use all collected EMCAT data to test the following hypotheses:

- Steroid injection results in less severe post-treatment symptoms than trapeziectomy, within the first 4 weeks

- Trapeziometacarpal arthroplasty results in less severe post-treatment symptoms than trapeziectomy, within the first 4 weeks

- Minimally invasive (endoscopic or percutaneous) CTD results in less severe post-treatment symptoms than open CTD, within the first 2 weeks

- The difference in the recovery of groups undergoing open release vs steroid injection for trigger finger are not clinically significant over the first 2 weeks

The objective is to test EMCAT's ability to differentiate between recovery trajectories that are expected to differ, rather than to prove or disprove that differences in recovery trajectory exist. The clinical comparisons are a vehicle for testing the measurement properties of EMCAT.

Participants undergoing open CTD or steroid injection for TBOA will be automatically entered into a second research stream. Those undergoing steroid injection for TBOA will be followed up with twice weekly EMCAT assessments for a further 12 weeks (24 weeks total). In this stream, participants' medical records will be reviewed by members of the research team at 24 weeks. For patients with TBOA, EMCAT trajectories will be plotted as time series graphs, and follow-up appointment dates will be overlaid onto these plots. They will be inspected to see whether appointments coincide with peaks in symptom severity.

For patients undergoing open CTD, we will record whether the participant underwent any change in management as a result of their follow-up appointment (including but not limited to antibiotic prescription, reoperation, clinical investigation, arrangement of further clinical follow-up and hand therapy referral). We will then ask three independent clinicians to inspect de-identified EMCAT trajectories and predict whether or not the patient required a change in management at their follow up. We will calculate the accuracy of these predictions against what happened to the participant at their follow up.

A subsample of 10 participants recruited from the first and second research streams, and 10 clinicians, will be interviewed about their experiences of the platform. Interviews will follow a schedule that covers the following topics:

- Perceived value of the EMCAT as a data-capture platform
- Acceptability of EMCAT
- Perceived burden of EMCAT
- Facilitators and barriers to using EMCAT
- Areas for improvement within the EMCAT platform
- The potential for EMCAT's to guide follow-up in different scenarios (e.g. open CTD or steroid injections for TBOA)

Participants will be given opportunity to discuss any other aspects of the EMCAT platform they consider important.

8. PARTICIPANT IDENTIFICATION

8.1. Study Participants

Adults undergoing one of the eligible treatments at a participating NHS Trust. Eligible treatments are:

- PNF for Dupuytren's contracture
- LF for Dupuytren's contracture
- Steroid injection for TBOA
- Trapeziectomy for TBOA
- Arthroplasty for TBOA
- Open CTD
- Minimally invasive (e.g. percutaneous or endoscopic CTD)
- Open trigger finger release
- Steroid injection for trigger finger

8.2. Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the study
- Participant is aged 18 years or older
- Participant is going to undergo one of the eligible treatments
- Participant is willing and able to download and engage with the EMCAT application on their own personal device

8.3. Exclusion Criteria

- Participant is undergoing bilateral treatments

- Multiple treatments to the affected hand (for any condition) are planned within the study period
- Participant is unable to engage with the EMCAT application in the English language

8.4. Welsh Language Act

In line with the Welsh Language Act 1993 all clinical appointments in Wales have to be available in Welsh. Neither the PEM questionnaire nor the UES have been item response theory validated in the Welsh language versions. Only the English version of the PEM can be administered in the adaptive manner required by EMCAT. For the purposes of this study, we consider the lack of a validated Welsh language versions to be a reasonable exclusion criteria for potential participants unable to comprehend the English language.

9. PROTOCOL PROCEDURES

9.1. Recruitment

Eligible participants will be identified by clinical members of the research team who have routine access to the data which will be used to identify potentially eligible participants. Prior to the patient's treatment, a member of the research team will discuss the study with them and invite them to partake. Written information will be provided to the potential participant, and they will be offered time alone to read the material and consider taking part. It will be made explicitly clear that participants are free to decline without reason, and this will not affect the care they receive in future. We anticipate that most people will be able to make an informed and considered decision about taking part on the same day as their appointment. If participants are unable to make a decision on the day of their appointment, they will be unable to participate.

If the participant accepts the invitation, written consent will be taken. Participants will be provided with a research team member's email address, and are free to withdraw consent at any time by emailing them as well as by contacting the study team by phone or email, or during the face to face appointments (see section 9.3 for caveats).

Participants undergoing open carpal tunnel decompression or steroid injection for TBOA will be included in Streams 1 and 2, with details provided in the participant information material. We will seek consent to contact participants at a later date for recruitment to Stream 3.

Participants who have consented to be contacted about Stream 3 may either be called or emailed with an invitation to take part in the qualitative interviewing (Stream 3). They will be provided with written information and given time to consider their involvement. Separate remote consent will be taken for involvement in the interviews (see section 9.3).

9.2 Screening and Eligibility Assessment

All information required to screen participants will already be known to clinical members of the research team as part of their role in the participant's routine care. On the basis of this information, clinical members of the research team will approach prospective participants and invite them to participate. If the participant accepts the invitation, they will be screened for exclusion criteria.

9.3 Informed Consent

Written and verbal versions of the appropriate participant information and informed consent forms will be presented to the participants detailing no less than: the exact nature of the study; what it will involve for the participant; the implications and constraints of the protocol; and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

The participant will be allowed to consider the information, and the opportunity to question the investigator, their GP or other independent parties to decide whether they will participate in the study, although this is limited by the fact that participants will need to decide whether or not to take part in the study on the day they are approached. For Streams 1 and 2, written informed consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed informed consent form will be given to the participant. The original signed form will be retained at the study site and filed in the site file – this will be kept securely locked in a locked office. A copy of the consent form will be kept in the patient's medical record.

For stream 3 (the qualitative interviews), remote consent will be obtained by a member of the local research team via Microsoft Teams or telephone. Consent forms will be completed by a suitably qualified and experienced member of the local research team on behalf of the participant. The participant will be emailed a copy of their consent form. Consent forms will be retained at the study site – this will be kept securely locked in a locked office. Once consent has been obtained the name and email address of the participant will be passed on to the central study team for the purpose of arranging the interview.

9.4 Enrolment

This study does not involve randomisation. At the point of recruitment, a member of the research team will assist the participant in downloading the EMCAT app and enabling push notifications.

9.5 Blinding and code-breaking

There will be no blinding in this study.

9.6 Description of study intervention(s), comparators and study procedures (clinical)

This is an observational and not an interventional study.

9.6.1 Description of study procedure(s)

EMCAT is a progressive web application maintained by the University of Cambridge Psychometrics Centre. Each day for the first 12 weeks, it will prompt participants to complete an assessment, either by email and/or push notification. Participants undergoing steroid injection for TBOA will receive twice-weekly notifications for a further 12 weeks. When a participant receives a notification, they can choose to engage with the EMCAT app, or dismiss the notification. Those who choose to engage will either click on a hyperlink in an email, or on a push notification button to start the assessment. The application will

pose questions from the PEM questionnaire which the participant will be able to respond to by clicking response options (See Appendix A).

After each response, the application will automatically select the next most useful question to administer. This process is continued until a prespecified stopping rule is met (standard error of measurement < 0.3). We expect that participants will be asked to complete between 1 and 4 questions each time they are notified. EMCAT responses will be collected for a period of 12 weeks (24 weeks for those undergoing steroid injection for TBOA). We may vary the time of day these notifications are scheduled for throughout the study, to reduce server demands.

In addition to the PEM EMCAT, each participant will be asked to complete the full-length PEM part 2 questionnaire (11 questions) at 0, 6 and 12 weeks via the app. At 12 weeks, we will ask participants to complete the User Engagement Scale (UES, 31 questions), also via the app. It is possible that participants who have had a negative experience of the app do not return UES data through it. Therefore, participants who do not respond to the UES via the app will be contacted via email and/or telephone and offered the opportunity to complete the UES either through the app reminder, over email or over the telephone. The method of response to the UES will be recorded, if not through the EMCAT platform.

9.7 Study visit

At the point of recruitment, a member of the research team will assist the participant in downloading the EMCAT app and enabling push notifications. A spreadsheet will be updated with the participants study number, eligibility status, reason for exclusion if applicable, age, sex, ethnicity, employment status, hand dominance, as well as the treatment they are undergoing, the date and the timing of the EMCAT scheduling.

The participant will complete a single full-length PEM assessment and an EMCAT PEM assessment via the application at this appointment.

9.8 Subsequent Visits

Not applicable

9.9 Sample Handling

No samples will be taken from patients.

9.10 Early Discontinuation/Withdrawal of Participants

During the course of the study a participant may choose to withdraw early at any time. This may happen for several reasons, including but not limited to:

- Response fatigue from the EMCAT app
- Inability to comply with study procedures
- Participant decision

Participants can withdraw from the study but permit data obtained up until the point of withdrawal to be retained for use in the study analysis. In this case, no further data would be collected after withdrawal.

Participants can also withdraw completely from the study and withdraw the data collected up until that point. The exception to this is for participants of Stream 3, who will not be able to withdraw qualitative data from semi-structured interviews once the thematic analysis has begun. In that case, the data already collected would not be used in the final study analysis. Patients will be identifiable through a study number that they are assigned at recruitment.

Once thematic analysis has begun, participants will not be able to withdraw interview data – this will be made clear in written participant information. Quantitative data, such as questionnaire responses collected by EMCAT, may be withdrawn at any time prior to the publication of analysis.

In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including, but not limited to:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- Significant protocol deviation
- Significant non-compliance with study requirements

In this case, withdrawal from the study would exclude that participant's data from the analysis if it has not already begun.

Where a participant has withdrawn, or been withdrawn, from the study, we will aim to replace that participant during the recruitment period.

The reason for withdrawal by researcher (and by participant, if this information is volunteered) will be recorded in the study file.

9.11 Definition of End of Study

The end of study date is the date of final EMCAT assessment or final interview, whichever comes later.

9.12 Study sequence

1. Potential participants will be identified by clinical members of the research team during routine care.

2. The clinical team members will invite potential participants to participate on the day of their treatment.

3. Potential participants will be provided with a written information pack, and given time to read this and discuss it.

4. The investigator will take informed consent from the participant at that point, if the participant feels they have had sufficient time to consider taking part.

5. At the point of recruitment, a member of the research team will assist the participant in downloading the EMCAT app and enabling push notifications.

6. At the point of recruitment, prior to the treatment, the participant will complete the full-length (11-item) PEM part 2 via the EMCAT app, and a single EMCAT assessment.

7. Over the next 12 weeks, participants will complete daily PEM EMCAT questionnaires (if they choose to) when prompted by email or push notification.

8. In addition, at 6 and 12 weeks, participants will be asked to complete the full-length PEM part 2 via the app, separately.

9. At 12 weeks, participants will also be asked to complete the UES via the app. Participants who do not respond with 7 days will be contacted via email or telephone and asked if they would like to return UES responses either via email or over the telephone. The method of UES response (app/email/telephone) will be recorded, if not via the ECMAT platform.

10. At 12 weeks, notifications will stop for all participants except those who underwent steroid injection for TBOA – these participants will continue to receive EMCAT notifications twice weekly for a further 12 weeks.

11. For participants undergoing steroid injection for TBOA or open CTD, at the 24-week timepoint, a clinical member of the research team will review the participant's medical record and record follow-up appointment dates and (for those who underwent open CTD) whether the follow up resulted in a change of management.

12. Three independent clinicians will review de-identified EMCAT trajectories and appointment dates for patients who underwent open CTD, and predict whether each participant required a change in management.

13. We will identify and approach 10 patients and 10 clinicians with invitations to take part in semi-structured interviews – interviews will take place no later than 14 days after finishing use of the EMCAT platform.

14. Interview participants will be provided with additional written information and time to consider their involvement in the interviews, a member of the research team will then take informed consent for participation in the interviews remotely.

15. We will conduct interviews with the participants using the Microsoft Teams videoconferencing platform. The audio of these interviews will be recorded, transcribed and then de-identified (all identifiable text redacted and the transcript assigned a study number). Recordings will then be deleted. Interviews are expected to last approximately 20 minutes.

16. Participants will not be followed up after interview.

17. We will notify all participants when the results of this study have been made available in the public domain.

18. Personal data will be held securely for a maximum three-year period, and then destroyed, with the exception of email addresses which will be deleted as soon as participants have been notified that the results are in the public domain. De-identified interview transcripts will be held

for 7 years and then destroyed. Anonymised research data from Stream 1 and 2 will be made publicly available to support future methodological work.

10 SAFETY REPORTING

This study is not likely to result in any adverse events.

11 STATISTICS AND ANALYSIS

11.3 Statistical Analysis Plan (SAP)

The plan for the statistical analysis of the study are outlined below. There is not a separate SAP document in use for the trial.

11.4 Description of the Statistical Methods

The hypotheses outlined in the primary and secondary objectives will be tested with mixed-effects linear modelling. These models will comprise: EMCAT score (continuous dependent variable on a logit scale, derived from a graded response model); participant number (random intercept); age, sex, and baseline score (fixed effects); and an interaction term between time (number of days following the intervention) and treatment allocation. Marginal means will be derived from these models and between-group differences calculated at daily timepoints after Tukey adjustment for multiplicity. This will be performed with the *emmeans* R package, or equivalent software. For each comparison, marginal means will be plotted, and differences compared to a minimal important difference (MID) estimate of half a standard deviation of baseline scores. Clinically and statistically significant (at the 5% level) differences will be compared to those predicted (see section 6).

EMCAT completion rates (number of completed response sets divided by number of invitations), response times, and UES scores will be analysed through descriptive statistics. The UES was originally intended to measure 6 user engagement constructs, but subsequent studies have suggested that it follows a 4-factor structure. Items of the UES will be grouped into the 4 subscales described by O'Brein et al, to measure: focused attention, aesthetic appeal, perceived usability and reward[5].

The criterion validity of the EMCAT scores against the full-length PEM scores will be assessed by comparing pairs of EMCAT scores and full-length PEM scores that were obtained from the same participant on the same day. Comparison will be made by calculating Pearson's correlation coefficient, mean absolute error, root mean squared error and the Bland-Altman method[6].

In Stream 2, three independent clinicians will review EMCAT trajectories (presented as time series plots) and follow-up appointment dates for participants that underwent open CTD. They will be asked to predict whether a change in management was required at the follow-up appointment. We will calculate inter-rater reliability of these assessments (Fleiss' kappa) and, for each clinician, the accuracy, sensitivity, specificity, positive predictive value and negative predictive value of their predictions against the reference standard (whether or not the patient received a change in management).

The 24-week EMCAT trajectory for patients undergoing steroid injection for TBOA will be plotted as a time series, with follow-up appointment dates overlain. These plots will be inspected and presented to

give an impression as to whether follow-up appointments coincide with peaks in symptom severity. This will not be formally tested with quantitative methods.

11.5 Sample Size Determination

Our primary objective is to use EMCAT to compare the recovery trajectories of patients undergoing PNF and LF for Dupuytren's disease. To have a 90% chance of detecting a moderate effect size of 0.35 between groups on a z-score scale (with a standard deviation of 1), at the 5% significance level, 344 patients are required for each comparison (172 per group). Assuming a 15% attrition, this leaves a target sample size of 396 for the primary objective (198 per group).

Objective 2 (see section 6) sets out 4 more comparisons, involving 7 other groups of patients:

- Steroid injection for TBOA
- Steroid injection for trigger finger
- Trapeziectomy for TBOA
- Arthroplasty for TBOA
- Surgical release of trigger finger
- Open carpal tunnel decompression
- Minimally invasive (endoscopic or percutaneous) carpal tunnel decompression

At 198 participants per group, and 9 groups total, a further 1386 participants (1782 total) would be required to reach statistical significance in all of our secondary (non-essential) objectives. We will recruit as many participants as we can in these groups, within the limits of the study timing and funding, and up to a maximum of 198 per group.

In summary, our recruitment target is 396 (172 participants undergoing LF and 172 participants undergoing PNF), but we will recruit up to a maximum of 1782 participants (198 in each of the groups described above).

11.6 Analysis populations

All participants as enrolled will be included in the analysis unless withdrawn.

11.7 Decision points

No interim analyses are planned.

11.8 Stopping rules

No stopping rules are planned.

11.9 The Level of Statistical Significance

Statistical significance will be defined at the 5% level.

11.10 Procedure for Accounting for Missing, Unused, and Spurious Data.

Data which are clearly spurious will be excluded. Missing data will be described. For each variable, the association of missingness and the values of other variables will be analysed through descriptive statistics. All available data will be used to fit the models used for the primary analysis. We will not impute missing data and do not plan to undertaken any sensitivity analyses.

11.11 Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Deviations from the statistical plan will be described and justified in the final report.

11.12 Health Economics Analysis

Not applicable.

11.13 Qualitative Interviews and Analysis

In Stream 3, semi-structured interviews will be conducted using the Microsoft Teams videoconferencing platform. The audio (but not video) of the interviews will be recorded and transcribed verbatim. Transcripts will be de-identified (all identifiable text redacted and the transcript assigned the same study number that the participant had previously), and then identifiable recordings will be erased.

Interviews will follow a schedule that covers the following topics:

- Perceived value of the EMCAT as a data-capture platform
- Acceptability of EMCAT
- Perceived burden of EMCAT
- Facilitators and barriers to using EMCAT
- Areas for improvement within the EMCAT platform
- The potential for EMCAT's to guide follow-up in different scenarios (e.g. open CTD or steroid injections for TBOA)

Participants will be given the opportunity to discuss any other aspects of the EMCAT platform they consider important.

We will perform an inductive thematic analysis with the de-identified interview transcripts. We have chosen an inductive (data-driven) approach as there is relatively little evidence to support an *a priori* theoretical framework with which to classify themes relating to the use of EMCAT in patient follow-up. This will involve reading and re-reading transcripts, using the NVivo platform to generate codes for elements of the transcript, and grouping these into themes. Each time a theme is generated, previous transcripts will be reviewed to identify data that could be categorised into the new theme. Themes will be named and structured (if appropriate) into a framework that aids their interpretation.

A purposively diverse sub-sample of 10 participants from Stream 1 and 2, and 10 healthcare professionals who have experience of the EMCAT platform, will undergo qualitative interviewing. This

sample size is expected to achieve thematic saturation based on previous research and published guidance[7].

12 DATA MANAGEMENT

The plan for the data management of the study is outlined below. There is not a separate Data Management document in use for the study.

12.3 Source Data

Source documents are where data are first recorded, and from which participants' CRF data are obtained. These include, but are not limited to, hospital records (from which medical history and previous and concurrent medication may be summarised into the CRF).

CRF entries will be considered source data if the CRF is the site of the original recording (e.g. there is no other written or electronic record of data). All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name.

12.4 Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

12.5 Data Recording and Record Keeping

Informed consent forms will be kept in the site file, which will be securely stored in a locked office, or electronically, at the recruitment site, in line with local policy. These will be stored for 3 years following the study end date. A copy of the informed consent form will be kept in the participant's medical notes for as long as those notes are retained.

Participants will be identified by a unique study specific number and/or code. For each participant, pseudonymised study data (study number, eligibility status, reason for exclusion if applicable, age, sex, ethnicity, employment status, hand dominance, as well as the treatment they are undergoing, the date and the timing of the EMCAT scheduling) will be directly entered onto a password-protected Excel spreadsheet, which will be stored securely at each site, in line with local policy.

For participants recruited at a given site, study numbers will be linked to participants names, hospital numbers and email addresses with a password-protected excel spreadsheet, securely stored at the site, with access limited to research team members at that site. This is a different spreadsheet to the one that will collect pseudonymised study data. This will allow the research team to identify study participants when required for the purpose of the study, and allow clinical members of the team to access patient records to record data collected in Stream 2. It is necessary to include the email addresses in this document as they will be used to inform participants once the results of the study have appeared in the public domain, enable the research team to contact participants to troubleshoot with any issues that arise with the EMCAT application, and allow the research team to recruit participants to the qualitative research stream. As soon as participants have been notified that the results of the study are in the public

domain, these spreadsheets including the email addresses will be deleted. This information will only be stored locally, and not transferred to the central research team.

The EMCAT platform will collect pseudonymised responses to the PEM EMCAT questionnaire which will be stored on an Amazon Web Service (AWS) server, based in the EU. Email addresses will also be uploaded to the EMCAT web-platform by the researcher that recruits the participant. The EMCAT application will securely store these on the AWS server. Members of the app development team at the Psychometrics Centre, University of Cambridge, may have access to participants' email addresses and questionnaire responses for app administration purposes (e.g. to troubleshoot issues with app administration). They will not use the data for any other purpose, and will destroy the data at the end of the study. This will be detailed in participant information sheets and in the service agreement between the University of Oxford and the team at the Psychometrics Centre. De-identified data will be transferred from the AWS server to the study team at the University of Oxford at the end of the study. All data will then be deleted from the AWS server. Deidentified questionnaire responses will be made publicly available when the results of the study are published.

Email addresses are sent from the EMCAT platform automatically via an application programming interface request to a third party (Mailgun) in order to send email notifications to participants. Mailgun stores the metadata of the emails (including email address) for 30 days. Suppressions (as a result of a hard bounce, complaint or unsubscribe) are stored on the Mailgun server until they are deleted by the CI. The CI will check their Mailgun account monthly, and at the end of the study, to identify any suppressions and delete them. This means the CI might see participants' email addresses, in the case of a suppression. The EU has been chosen as the region for data processing for region-bound data and Mailgun acts as a data processor in line with General Data Protection Regulation (GDPR). Any remaining data on the Mailgun server will be deleted at the end of the study. This will be detailed on the participant information sheet (PIS).

In Stream 2, for patients who have undergone steroid injection for TBOA or open CTD, a clinical member of the team will access the participants medical record after the 24-week timepoint to record data relating to the exploratory objectives in the site's study data spreadsheet. This includes the timing of follow-up appointments and (for open CTD), whether the patient underwent a change in clinical management (e.g. antibiotic prescription, reoperation or hand therapy referral) during their follow-up. Deidentified study spreadsheets will be securely transferred from the sites to the central research team in line with local policies. These will be stored up on the CI's University of Oxford SharePoint. De-identified data will be analysed using a password protected personal device that meets NDORMS Mobile Devices policy and accessed via the University VPN to ensure a high level of security. The deidentified study data spreadsheets will be stored for three years on SharePoint. This will be detailed on the PIS.

In Stream 3, semi-structured interviews will be conducted using the Microsoft Teams videoconferencing platform. The audio (but not the video) of these interviews will be recorded onto a password protected personal device that meets NDORMS Mobile Devices policy and accessed via the University VPN to ensure a high level of security, and transcribed verbatim by one of the central researchers. This will be achieved by turning off the video in the meeting prior to recording. Transcripts will be de-identified immediately and then identifiable recordings will be deleted. Deidentified transcripts will be stored on the CI's University of Oxford SharePoint. They will be stored for three years on the personal device and SharePoint. In order to arrange the timing of these meetings, the names and email addresses of participants recruited to Stream 3 will be securely transferred to the central research team. This will be detailed on the Stream 3 consent forms.

Appendix B contains a flowchart illustrating the flow of participant data.

13 QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

13.3 Risk assessment

No formal risk assessment will be undertaken due to the low-risk nature of this study.

13.4 Study monitoring

Due to funding constraints, no GCP monitoring activities are planned for this study.

13.5 Study Committees

Due to the safe and simple nature of this study, there will be no study committees.

14 PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file.

15 SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the trial subjects; or

(b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the C.I., the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

16 ETHICAL AND REGULATORY CONSIDERATIONS

16.3 Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

16.4 Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

16.5 Approvals

Following Sponsor approval the protocol, informed consent form and participant information sheet will be submitted to an appropriate Research Ethics Committee (REC), HRA (where required) and a host institution (Trust).
The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

16.6 Other Ethical Considerations

Participants may have limited time to consider taking part in Stream 1 as they are required to consent on the day of their procedure. This is mitigated by the low-risk and low-burden nature of the study. We will ensure the study is carefully explained to potential participants, in line with GCP.

It is possible that participants may have difficulty using the EMCAT app due to their hand condition, but based on clinical experience and the findings of the first EMCAT study, this is unlikely. This will be explained in the PIS.

In stream 2, participants' medical records will be accessed by members of the research team and as a result, researchers may see sensitive data. Only clinical members of the research team (doctors, nurses, hand therapists or other appropriate allied health professionals, approved by the local PI), who are bound by a duty of confidentiality, will access these records and only for the purpose of completing the study data capture spreadsheets. This will be explicit in both the PIS and consent form.

The interviews will focus on the usability of the EMCAT app and the potential for its use in clinical monitoring. There is a chance that these interviews remind participants of health concerns addressed by the app, such as pain and disability. In the unlikely event that they arise, we will recommend any medical or psychiatric red flags are discussed with a medical professional in an appropriate context.

16.7 Reports

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation, Sponsor and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties.

16.8 Transparency in Research

Not applicable the research is non-interventional.

16.9 Participant Confidentiality

The study will comply with the UK GDPR and Data Protection Act 2018, which require data to be de-identified as soon as it is practical to do so. The processing of the personal data of participants will be minimised by making use of a unique participant study number only on all study documents and any electronic database(s), with the exception of the EMCAT and Mailgun servers, which require participant email addresses for the conduct of the study. All documents will be stored securely and only accessible by study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data.

16.10 Expenses and Benefits

Funding for this study does not permit the payment of expenses or benefits. This will be made explicit on written participant information sheets.

17 FINANCE AND INSURANCE

17.3 Funding

This study will be funded by a grant from the Oxfordshire Health Services Research Committee and the British Society for Surgery of the Hand.

17.4 Insurance

The University has a specialist insurance policy in place which would operate in the event of any participant suffering harm as a result of their involvement in the research (Newline Underwriting Management Ltd, at Lloyd's of London).

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17.5 Contractual arrangements

Appropriate contractual arrangements will be put in place with all third parties.

18 PUBLICATION POLICY

The investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by the Oxfordshire Health Services Research Committee and the British Society for Surgery of the Hand. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. Study participants will be notified by email once the results of this study appear in the public domain.

19. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by employees of the University vests in the University. The University will ensure appropriate arrangements are in place as regards any new IP arising from the study.

19 ARCHIVING

Identifiable data will be held securely at the research sites, and then destroyed after the study is published and participants have been made aware of this. Research data (including the consent forms) will be kept at sites for 3 years and then destroyed. Research data including de-identified interview transcripts will be held securely (centrally) for a three-year period following publication of this research, and then destroyed. Anonymised EMCAT response data will be made publicly available.

20 REFERENCES

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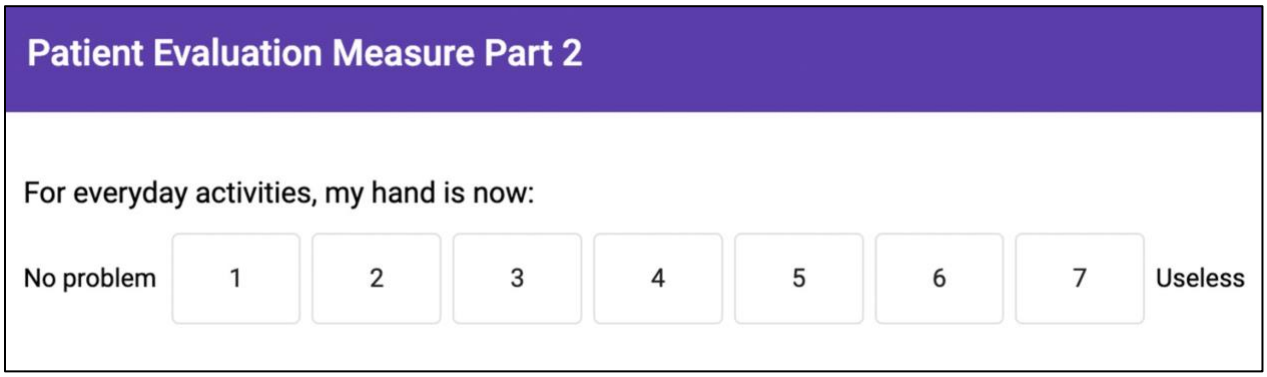
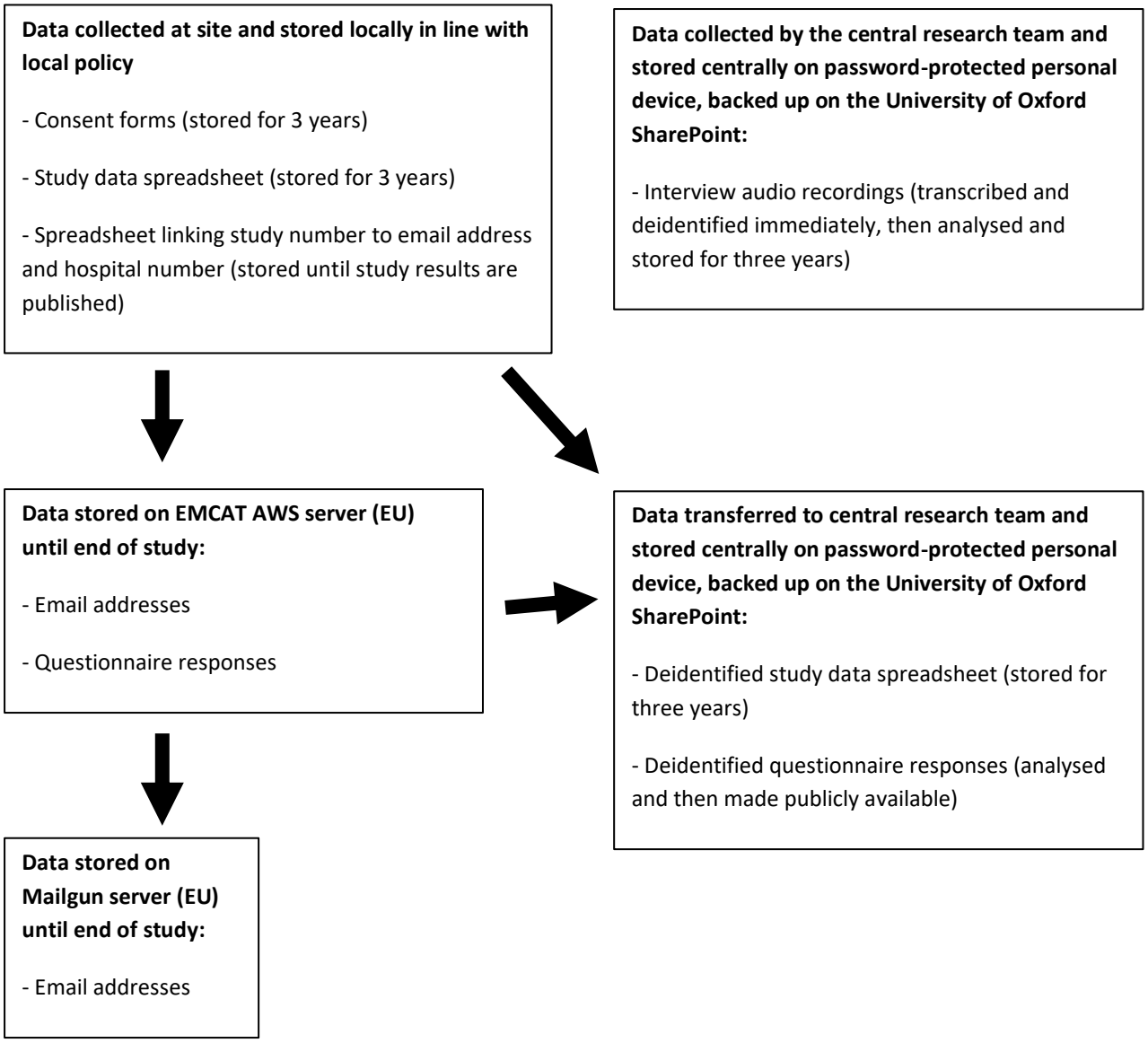
21 APPENDIX A: Screenshot from the EMCAT platform



22 APPENDIX B: Flowchart Demonstrating Transfer of Participant Data



23 APPENDIX C: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made