ROCSS-EX

5-8 year follow-up of the ROCSS Trial patients

Study Training Presentation

FUNDED BY
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Background

- **ROCSS** Trial
  - Prospective, multi-centre, two-arm, parallel group RCT in 37 hospitals within the UK, Denmark and the Netherlands
  - **AIM:** Compared biological mesh reinforcement of closure against standard closure techniques in patients having an elective stoma closure
  - **RESULTS:** Biological mesh reinforcement reduces the incidence of clinically detectable stoma closure site hernias at two years

    Reinforcement of Closure of Stoma Site (ROCSS) Collaborative and West Midlands Research Collaborative. Prophylactic biological mesh reinforcement versus standard closure of stoma site (ROCSS): a multicentre, randomised controlled trial. Lancet. 2020 Feb 8;395(10222):417-426.

- **ROCSS-EX** is the extended follow-up of **ROCSS** participants
  - Single FU at 5-8 years from trial entry

ROCSS-EX

Aim

1. To investigate if the biological mesh closure group has a significant long-term improvement in their QoL 5-8 years after stoma reversal

2. To determine if the intervention is cost-effective after 5-8 years

ROCSS-EX

Outcomes

- **Primary: Quality of life following closure of stoma site comparing patients who had mesh reinforcement of their abdominal wall with patients that had a standard closure**

  This will be assessed using the HerQLes tool

- **Secondary:**
  - Patient reported incisional hernia rate
  - Number of hospital visits for any hernia related reason
  - Number of interventions related to the stoma closure site or hernia
  - Longitudinal QoL assessed using EQ-5D
  - Cost analysis for all additional hernia related events

ROCSS-EX

Stage 1: Setting up your centre for ROCSS-EX

1. Obtain approval the study locally
2. Identify a collaborator team for data collection and telephone consultation
   - We recommend 1 collaborator per 10 patient.
   - All team members will need up to date GCP and CV

Stage 2: Accessing your local patient cohort

1. Access the local site ROCSS file to get the participant list
2. Look up each participant on the local computer system to prepare mailing list
   - Update contact details for those who are alive
   - Participants who have died: Keep on local database BUT remove from the mailing list
3. Assign participants to the local collaborator team members for follow up

Stage 3: Routinely Collected data

1. Using hospital systems enter 'routinely collected data' on to CRF 1 for all participants (alive or dead)

Stage 4: Contacting Participants

1. Edit 'ROCSS-EX Participant Letter' template from ROCSS-EX local centre pack
2. Post ROCSS-EX Participant Letter + ROCSS-EX Participant Information Sheet to each participant known to be alive

at least 2 weeks…

Stage 5: "Opt Out" Participants

1. Participant contacts centre to Opt Out of telephone consultation
2. Update CRF 1 with electronic data only

Stage 6: Telephone Consultation

1. Phone participants
2. Complete Telephone Consultation - ROCSS-EX Telephone Script provides assistance
3. Enter data on to CRF 2

Stage 7: Data Validation and Completion

Setting up your centre: What do you need to do?

Visit website for downloads and links
www.birmingham.ac.uk/ROCSS-EX

Local R&D Approval Requirements

- Confirmation of C&C for ROCSS substantial amendment #7

Local Research Team Requirements

- Delegation Log: **All staff undertaking research activity should sign delegation log and the duties be authorised by the PI prior to performing any study activities**
  - PI to be listed on the log too
  - Database access granted to PIs and team members assigned “Completion of electronic CRFs/data entry including data query resolution” task

Setting up your centre: What do you need to do?

Visit website for downloads and links
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Local Research Team Requirements

- GCP training: up-to-date certificate – available online (including refresher) through NIHR Learn and see our website for links to training
- CV: up-to-date signed & dated CV – see our website for short research CV template
- Study-specific training: use the online electronic training log record to say you've watched this training video

  - CV & GCP to be within three years (Trust requirements may differ)
  - Completed documents/records to be sent to Trial Office and filed in local Investigator Site File (ISF)
  - Local R&D may require CV ad GCP

Access the local participant list

List location:

1. Participant ID log in original ROCSS Investigator Site File (ISF)
2. ROCSS-EX database
   - Already refined to remove known exclusions
     e.g. non-reversals, withdrawals

- Look up each participant on the local systems to prepare mailing list
  - Are participant still alive?
  - If alive, are contact details present?

Assign participants to team members

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Patient follow-up: Routinely collected data

- No face to face patient contact
- Locally held electronic data

Clinical Follow-up (CRF 1): Locally held electronic data

!!! Data relating to the stoma closure site itself and not unrelated conditions !!!

- Number of readmissions and reasons
- Total in-patient days
- ITU/HDU admissions
- Diagnosis of incisional hernia
  - Date of diagnosis
  - Radiological or clinical
- Out-patient clinic visits for stoma closure site related problems
- Any radiological investigations for stoma closure site related problems
- Operations related to the stoma closure site

ROCSS-EX

Consent

Data entry into eCRFs within the ROCSS-EX REDCap database is disabled by default – it is enabled only where the necessary consent is in place.

Data Entry into CRF1 (Clinical FU)

- For majority of participants, consent was obtained during the original ROCSS Trial for longer term FU using routinely collected data i.e. from local held records
  - Where this consent is already in place, the ROCSS-EX REDCap database will automatically allow you to enter data into the CRF1 (Clinical FU)

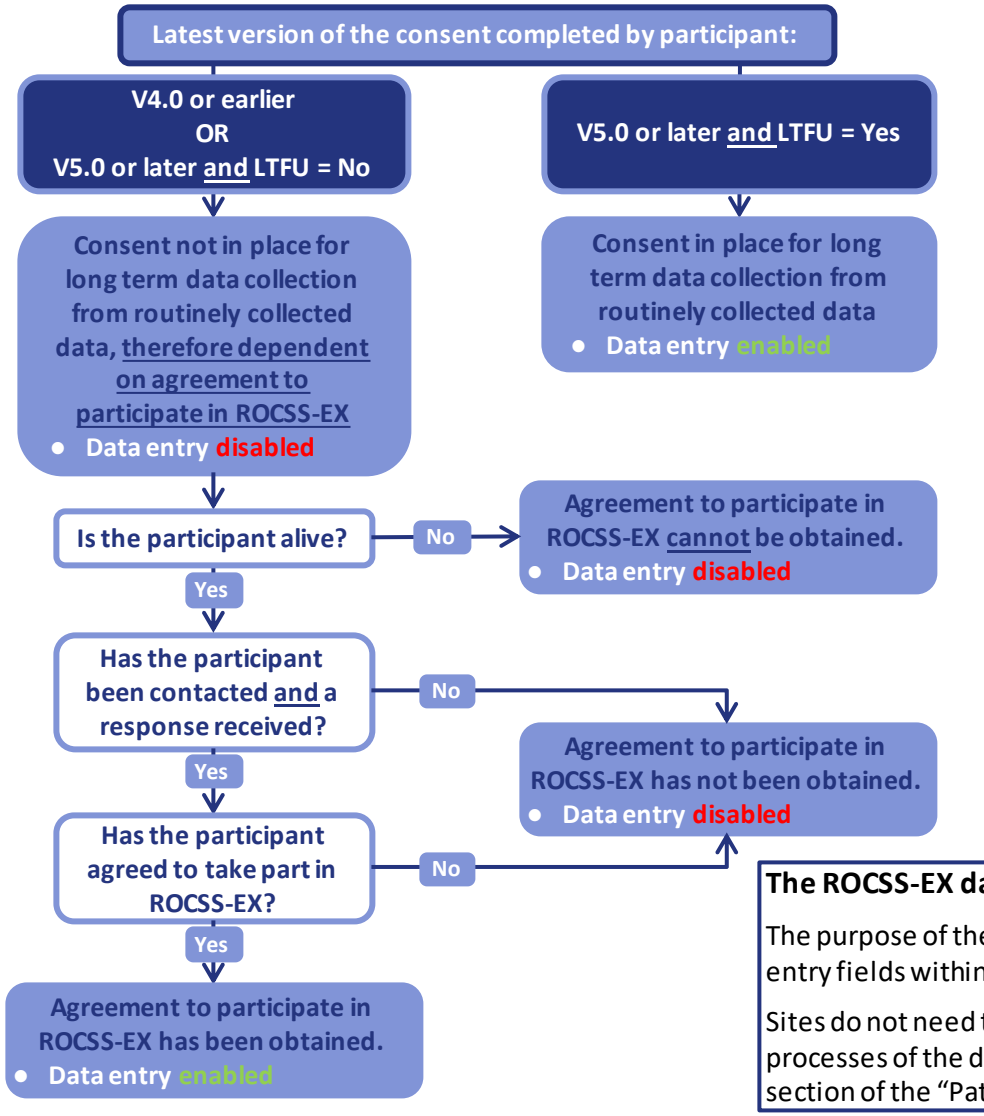
- For minority of participants for whom consent to longer term FU using routinely collected data was not obtained:
  - ROCSS-EX REDCap database WILL NOT allow data entry into CRF1 (Clinical FU) until after VERBAL agreement to ROCSS-EX participation is obtained

    NB. Same requirement for telephone FU data entry

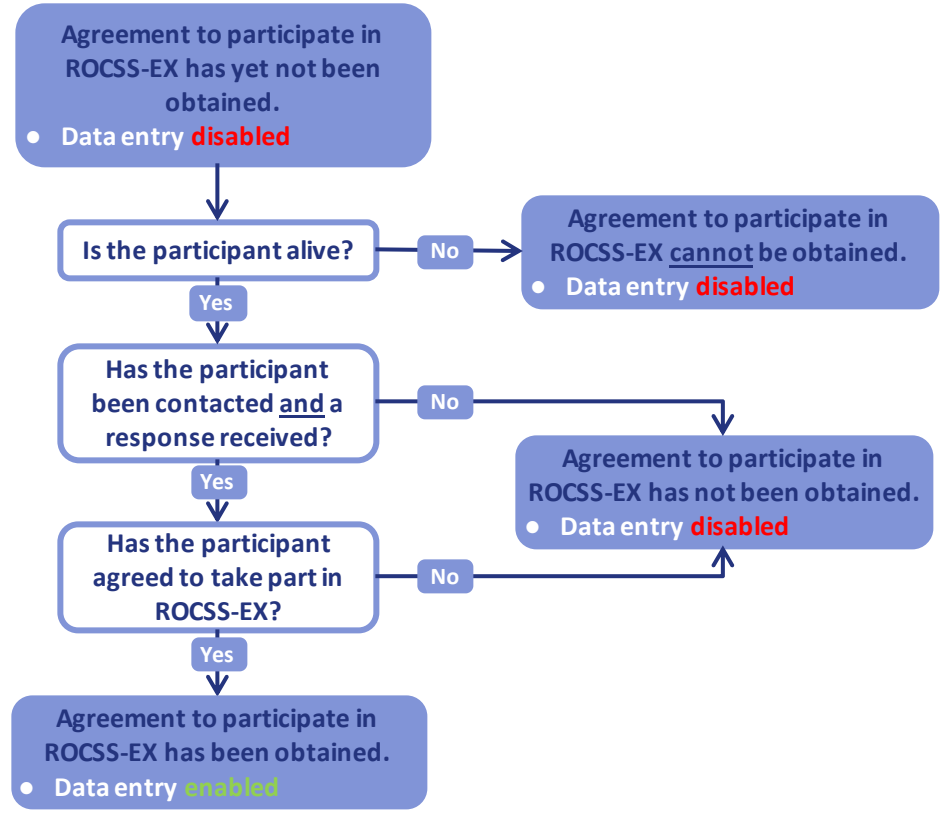
Consent

- **The Telephone Consultation includes obtaining verbal agreement to continued participation**
  - Must be confirmed in the ROCSS-EX REDCap database in **"Patient Record"** to enable data entry into CRF2 (Telephone FU), and where applicable CR1 (Clinical FU)
  - This is to be documented in the participant medical records, either directly in paper based systems, or by writing an electronic note on their health records.
    E.g. ROCSS-EX PIS v2.0 (12-Jan-21) and ROCSS-EX Participant Letter v2.0 (12-Jan-21) sent on 01-Mar-21. Contacted by telephone 15-Mar-21; patient agreed to continued participation in ROCSS and ROCSS-EX telephone consultation undertaken.
  - Outcomes other than agreement to participate should also be documented in their medical records e.g. participant declines to take part, you are unable to contact/lost to FU)

CRF1 (Clinical Follow-up)



CRF2 (Telephone Follow-up)



The ROCSS-EX database does not permit data entry into CRFs until the necessary consent is in place.

The purpose of these flowcharts is to demonstrate how data entry into CRFs is controlled and so allow why data entry fields within a CRF may or may not be accessible to users at site to be appreciated.

Sites do not need to enter information form about the consent forms as it is built in to the background processes of the database – the only input from sites is the response to the questions in the Patient Contact section of the "Patient Record" (indicated above in the unshaded boxes).

Contacting participants

Participants that are still alive…

- **Send ROCSS-EX Participant Letter and Participant Information Sheet**
  - Letters to be personalised with participant details, local contact info and proposed date/time for telephone consultation
    Documents localised with your Trust's header – available form Trial Office
  - Give a date for the consultation at least 2 weeks after letter is sent
  - Monitor "Opt-out" of participants – update "Patient Record" in ROCSS-EX REDCap database

- **Call participant and undertake telephone consultation**
  - Feel free to use the ROCSS-EX Telephone Script
  - Includes obtaining verbal agreement to take part

Patient follow-up: Telephone Consultation

- Single telephone call

ROCSS-EX
Telephone Script

Telephone Follow-up (CRF 2)

!!! Data relating to the stoma closure site itself and not unrelated conditions !!!

- HerQLes questionnaire
  - 12 abdominal wall function related questions
- EQ-5D
- Number of GP visits with stoma closure site related problems
- Number of planned hospital visits
  - Clinic appointments and hospital procedure/stay
- Number of ED visits
- Prescriptions related to stoma site problems
  - Type, start and duration
  - Hernia truss/support
- Self diagnosis of hernia
  - Date of start

ROCSS-EX

Collecting data

- Data will be entered in to the ROCSS-EX REDCap database directly by the local research team; https://bctu-redcap.bham.ac.uk/
  - A detailed User Guide is available
  - Access is granted to PIs and team members assigned “Completion of electronic CRFs/data entry including data query resolution” on the ROCSS-EX delegation log

- Paper versions of the electronic CRF are available
  - Can be printed off and used as worksheets to collate data before entry into the ROCSS-EX REDCap database
  - Any completed paper CRFs used should be filed in the local Investigator Site File (ISF) but **do not** need to be sent to the Trial Office

Missing data

- All missing, erroneous and/or ambiguous data will be queried via the ‘Data Query Resolution Workflow’ functionality within the ROCSS-EX REDCap database

- The Trial Office will periodically remind sites of things outstanding:
  - Data entry to be completed
  - Data queries to be resolved

Source Data

- Source data is defined as: 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

Data	Source
Participant Reported Outcomes (EQ-5D-5L and HerQLes)	The interview administration EQ-5D-5L and HerQLes is the source, obtained by interview directly with the participant for transcription onto the CRF, in which case the CRF is source data.
Clinical event data	The original clinical annotation is the source document. This may be found on clinical correspondence, or electronic or paper participant records. Clinical events reported by the participant, either in or out of clinic (e.g. phone calls), must be documented in the source documents. Information will be transcribed onto CRFs.
Health Economics data	Obtained by (1) interview directly with the participant for transcription onto the CRF in which case the CRF is source data. (2) To the medical record in which case the original clinical annotation is the source document. Information will be transcribed onto CRFs.
Drop out	Where a participant expresses a wish to withdraw, the conversation must be recorded in the medical records.

- In order to allow for the accurate reconstruction of the trial and clinical management of the participant, source data will be accessible and maintained

PI Oversight

- PI is ultimately responsible for conduct of ROCSS/ROCSS-EX at their site
  - Article 73 of the Clinical Trial Regulation: PI must ensure compliance
  - Shall assign tasks among members in a way in which does not compromising reliability and robustness of data generated in trial, nor safety of subject – e.g.
    - Being able to provide evidence that all team members have received appropriate training prior to duties being delegated to them – *e.g. training log/records, GCP*
    - Ensuring the integrity of the data being submitted for use in the trial – *e.g. sign-off of data*
- Each Principal Investigator must:
  - Read the approved protocol and sign protocol signature page
  - Adhere to the approved protocol
  - Ensure current protocol is in ISF

PI Signature Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Principal Investigator agrees to conduct the trial in compliance with the approved protocol.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

This protocol has been approved by:

Trial Name:	
Protocol Version Number:	Version: 8.0
Protocol Version Date:	12 / Jan / 2021
PI Name:	
Name of Site:	
Signature and date:	_____ __ __/__ __/__ __ __ __

PI Sign-off of Data

- Sign-off of the data provided from the PI is required
  - Required before the database is locked prior to the final analysis
  - To be done once all data entry is complete – this included resolution of queries
- Undertaken following request from Trial Office or can be done pro-actively
- Documentation of sign-off
  - Within the ROCSS-EX REDCap database – for each participant there is a PI data sign-off form
  - Alternative methods are available e.g. where sites have a higher number of participants

Trial Management

Investigator Site File (ISF)

- Contains essential documents necessary for the PI & research team to conduct a trial
  - Sites are expected to keep the site file up to date e.g. following amendments to the trial or changes to the processes within the study
  - Includes version control document for key documents (protocol, PIS, ICF, CRF etc.)
  - Must be kept up to date and current approved documents used
- To be stored securely but accessible to members of local research team
- If any documents that should be stored in the site file are kept elsewhere, a Note to File should be filed in the relevant section referencing the true location

Confidentiality

- All information collected during course of trial will be kept strictly confidential
- Trial Office and sites will comply with all aspects of Data Protection Act 2018 (and subsequence regulations)

Trial Management

Audit and Inspection

- Your site is subject to audit/inspection by Sponsor
  - Can occur at any time during recruitment and follow-up
  - Investigators are obliged to cooperate in any audits/inspections
- Investigators must tell the Trial Manager immediately if they are being inspected/ audited E.g. local audits by R&D

Deviations and Breaches

- Protocol deviations must be reported to the Trial Office as soon as possible
  - Advise on documentation required, corrective and preventive measures

Serious breaches in GCP or trial protocol

- Likely effect to significant degree:
- Serious breaches are reported to REC
  - All trial investigators must promptly notify CI or Sponsor of a serious breach

Trial Management

Monitoring (central) – Trial Office will:

- Be in regular contact with the site research team to check on progress and address queries
- Check completed eCRFs for compliance with the protocol, data consistency and missing data
- Ask sites for missing data or clarification of inconsistencies or discrepancies
- Protocol compliance via checks on data
- Ask sites to complete document checklists (e.g. Investigator Site File Checklist)

Monitoring (on-site) - requires access to medical records/notes

- May occur if triggered (e.g. poor data return/quality, excessive non-compliances)
- If required, the Trial Office will contact the site to arrange a date for the proposed visit and will provide the site with written confirmation.

Trial Management

Record Retention & Archiving - at end of trial:

- It is the responsibility of the PI to ensure all essential trial documentation and source documents (e.g. signed ICFs, ISF, eCRFs, worksheets etc.) at their site are securely retained for at least 10 years

No documents will be destroyed without prior approval from the SUNRRISE Trial Office on behalf of the Sponsor

- Once permission is given by the Sponsor, documents can be archived in accordance with the sites processes and procedures in an appropriate archive facility
- If the PI leaves after the end of the study, all responsibility for archiving should be transferred to a designated person acceptable to the Sponsor
- Following written authorisation from Sponsor, arrangements for confidential destruction will then be made

Authorship

- Corporate authorship policy - all collaborators with be PubMed citable.

- ROCSS-EX Collaborative
  - Local PIs
  - Trainee Investigators, Research Nurses etc. completing follow-up for 10 participants

    However, individual circumstances for a given sites will be taken into consideration, such as number of participants recruitment, number of participants included in ROCSS-EX and participants decisions, favouring inclusion in the Collaborative.

Timelines

ROCSS-EX GANTT CHART	2020		2021											
	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Month number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CRF Development														
Protocol development														
Ethics approval														
TMG meeting														
Recruitment of PIs and local collaborators in centres														
Main study data collection														
Data collation and cleaning														
Data analysis														
Preparing reports for publication and presentation														
Study closes														

ROCSS-EX Regional Trainee Leads

Each ROCSS site has been assigned to ROCSS-EX Trainee Lead who are part of the central ROCSS-EX Trial team and will:

- Keep regular contact with designated sites
- Be point of contact for PI/Trainee Investigators/Research Nurses for questions related to ROCSS-EX
- Communicate developments between Sites and ROCSS-EX Trial Team

Region & Lead	Sites
NORTH Zoe Gates zgates83@gmail.com	Chesterfield Royal Hospital
	Doncaster Royal Infirmary
	Macclesfield District General Hospital
	Queen's Medical Centre
	Raigmore Hospital
	Royal Albert Edward Infirmary
	Royal Stoke University Hospital
	Tameside General Hospital
	University Hospital Of North Tees
	Wythenshawe Hospital
	York Hospital

Region & Lead	Sites
CENTRAL Alasdair Ball alasdair.ball@googlemail.com	Birmingham Heartlands Hospital
	King's Mill Hospital
	Leicester General Hospital
	James Paget University Hospital
	Manor Hospital
	New Cross Hospital
	Norfolk & Norwich University Hospital
	Pilgrim Hospital
	Queen Elizabeth Hospital Birmingham
	Sandwell General Hospital
	University Hospital Coventry
	Worcestershire Royal Hospital

Region & Lead	Sites
SOUTH Ellen Jerome ellen.jerome1@nhs.net	Bristol Royal Infirmary
	Broomfield Hospital
	Dorset County Hospital
	Queen Elizabeth The Queen Mother Hospital
	Royal United Hospital Bath
	Salisbury District Hospital
	St Mark's Hospital
	St Peter's Hospital
	St Richard's Hospital
	Yeovil District Hospital

- Alistair Ball: alasdair.ball@googlemail.com
- Zoe Gates: Zoe.gates3@nhs.net
- Ellen Jerome: ellen.jerome1@nhs.net
- "ROCSS-EX Help Forum" WhatsApp group – join using the QR code shown or by using this link; https://chat.whatsapp.com/LyOn1lbffaTDx3iuNyiir6
- Trial Office: rocss@trials.bham.ac.uk

Thank you

Please remember to document your training using electronic ROCSS-EX Training Record;
https://bctu-redcap.bham.ac.uk/surveys/?s=7CWDX78E8X

Please contact us if you have any questions…
rocss@trials.bham.ac.uk