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Feasibility of an enhanced randomised controlled trial design for treatments of bowel dysfunction after rectal cancer

Submission date
16/11/2022

Recruitment status
No longer recruiting

Registration date
30/12/2022

Overall study status
Completed

Last Edited
07/03/2023

Condition category
Digestive System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Rectal cancer (cancer of the lower part of the bowel) is one of the most prevalent forms of cancer and affects approximately 14,000 people each year in the UK. The treatment for the majority of these patients is the surgical removal of the affected part of the bowel, following which the bowel is joined back together. Some patients may also require chemotherapy and radiotherapy. One consequence of the treatment of bowel cancer is a severe form of bowel dysfunction called major Low Anterior Resection Syndrome (LARS).
LARS is a constellation of symptoms including incontinence to stool, urgency and frequency of bowel movements and incomplete evacuation; it is diagnosed using the LARS scoring tool. Major LARS can have a huge impact on the persons quality of life resulting in social isolation.
Currently, there are no guidelines for the management of LARS. The aim of the POLARiS study is to investigate three different treatments for major LARS; optimised conservative management, a combination of diet, medication, bowel retraining and pelvic floor exercises; transanal irrigation, washing out the back passage of stool with warmed water; and sacral nerve stimulation where an electrical impulse delivered to the sacral nerve to help with bowel function. This feasibility study aims to test the study design ahead of a larger fully powered randomised control trial.

Who can participate?
Patients who have had surgery for rectal cancer (called an anterior resection) and who do not have a stoma are invited to take part in this research.

What does the study involve?
There are two parts to this study. All participants will be enrolled into a cohort, where they will be assessed using a variety of validated questionnaires about their bowel symptoms, general health and quality of life on a 3-monthly basis.
Those who are identified as having the most severe form of LARS based on their questionnaire responses will be invited to the second part of the study. Participants will be randomly assigned

to receive one of three treatments for LARS- TransAnal Irrigation (TAI), Sacral NeuroModulation (SNM) or Optimised Conservative Management (OCM). Randomisation participants will continue to be enrolled and assessed as part of the cohort.

What are the possible benefits and risks of participating?
It's possible that participants will experience improvement in their LARS symptoms by taking part in this research.

Where is the study run from?
Cardiff and Vale University Health Board (UK)

When is the study starting and how long is it expected to run for?
February 2022 to December 2023

Who is funding the study?
Cardiff and Vale University Health Board (UK)

Who is the main contact?
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Contact information

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Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05319054

Integrated Research Application System (IRAS)
307764

Central Portfolio Management System (CPMS)
51890

Protocol serial number
21/JUL/8238

Study information

Scientific Title
A feasibility, multicentre randomised control trial assessing the treatment options for patient with major low anterior resection syndrome to establish a Pathway Of Low Anterior Resection syndrome relief after Surgery

Acronym
POLARiS Feasibility study

Study objectives

This purpose of this study is assess the feasibility of the Trial Within Cohorts (TWiCS) study deigns ahead of a fully-powered trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/02/2022, Wales REC1 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, Cf11 9AB, UK; 02920 785738; Wales.REC1@wales.nhs.uk), ref: 22 /WA/0025

Primary study design
Interventional

Study design
Multi-centre open-label three-arm parallel-group feasibility randomised controlled trial within a cohort

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Treatment of bowel dysfunction symptoms in patients with low anterior resection syndrome

Interventions
All participants in the study will be enrolled into the 'cohort' element. They will be required to complete questionnaire at baseline, which will be repeated at 3-, 6-, 9- and 12-month post recruitment. The assessment will consist of a combination of condition-specific outcome measures, as well as quality of life measures including the LARS score, EORTC CR29&C30, MYMOPII and EuroQol EQ5D-5L.

Participants will be invited to participate in the RCT within the cohort, with the eligibility based on their 'cohort' questionnaires responses and assessment scores. They may be randomised to one of three treatments (depending on eligibility and availability at the local organisation). All RCT participants will continue to followed-up as per 'cohort' schedule. No additional research follow-ups will be conducted.
1. Optimised conservative management- Patients randomised to OCM will undergo training and receive a bespoke treatment package of the conservative treatment including medication, lifestyle & dietary advice and physiotherapy (were possible and appropriate). Treatment package will be assessed and revised after 30-days.
2. Trans-Anal-Irrigation- TAI group will receive an irrigation system as agreed with the patient and host organisation. Patients will attend a troubleshooting appointment 2 weeks after commencing intervention and followed-up as per standard care.
3. Sacral Neuromodulation- SNM group will receive a device as agreed by the host organisation. All patients will undergo a 2-week training phase with a temporary device to determine effectiveness of the device. Participants that have positive outcomes using the temporary device will have a permanent device fitted and followed-up as per standard of care.

Randomisation will be according to a block stratified design based on variable block length. Due to the nature of the interventions this is a non-blinded study. The randomisation programme

being used is GEN24.
The treatments being investigated are all approved for use within the National Health Service (NHS) and will follow usual local administration practices.

Intervention Type
Mixed

Primary outcome(s)
The recruitment rate to the RCT measured in terms of relative number of cohort participants measured at 3-, 6- and 9- months.

Key secondary outcome(s)
1.Change in LARS severity measured using the LARS score over 12 months.
2. Quality of Life measured using the EuroQoL EQ5D-5L over 12 months
3. Quality of life measured using the European Organisation for Research and Treatment of Cancer Colorectal Quality of Life Questionnaire (EORTC QLQ-CR29) over 12 months
4.Quality of life measured using the European Organisation for Research and Treatment of Cancer Cancer Quality of Life Questionnaire (EORTC QLQ-C30) over 12 months.
5. Medical outcome profile measured using the Measure Yourself Medical Outcome Profile (MYMOP) over 12 months.

Completion date
01/12/2023

Eligibility

Key inclusion criteria
Inclusion for Cohort:
1. Diagnosis of rectal or sigmoid cancer
2. Low or high anterior resection (with anastamosis to the rectum)
3. Functioning anatamosis
4. Aged 18 years and older
5. Primary surgery/reversal of ileostomy less than 10 years before recruitment
6. Reversal of ileostomy at least 12 weeks prior to recruitment with at least a further 12 weeks of standard care to manage symptoms following reversal
7. Willing and able to provide valid informed consent

Inclusion for Randomisation:
1. Recruited to cohort study
2. Willing and able to provide valid informed consent for randomisation
3. Major LARS symptoms (Defined as score of 30+ on LARS scoring tool)
4. Previous unsuccessful conservative treatment determined by treating clinician and patient

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Exclusion from cohort:
1. Inability to understand and complete study questionnaires independently (Due to cognitive or intellectual impairment; Due to insufficient English language skills)

Exclusion from randomised control trial:
1. Pregnancy
2. No previous conservative treatment plan for the management of LARS
3. Does not meet any treatment-specific criteria

Exclusion from TAI randomisation:
1. Unable to perform TAI
2. History of anastomotic leak with evidence of ongoing leak/sinus
3. Previous use of TAI for LARS
4. Site unable to offer TAI as a treatment
5 Any other contraindications advised by the care team, product manufacturer or distributor

Exclusion from SNM randomisation:
1. <12months since primary cancer surgery
2. Palliative disease
3. Site unable to offer SNM as a treatment
4. Previous SNM
5. Specific contraindications to implantation
6. Any other contraindications advised by the care team, product manufacturer or distributor.

Date of first enrolment
25/05/2022

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre

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Study participating centre
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
Cardiff and Vale University Health Board

ROR
https://ror.org/0489f6q08

Funder(s)

Funder type
Charity

Funder Name
Bowel Research UK

Alternative Name(s)
Bowel Research United Kingdom, BRUK

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Cardiff and Vale University Health Board

Results and Publications

Individual participant data (IPD) sharing plan
Individual Participant Data will not be shared as part of this study. Dataset will be held by the sponsor, Cardiff and Vale University Health Board.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		10/01/2023	07/03/2023	Yes	No
HRA research summary			26/07/2023	No	No