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Exercise prehabilitation in colorectal cancer

Submission date
14/02/2023

Recruitment status
Recruiting

Registration date
17/02/2023

Overall study status
Ongoing

Last Edited
09/10/2024

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Colorectal (bowel) cancer is the fourth most common cancer in the UK with over 40,000 cases diagnosed each year. About two in three people who are diagnosed with colorectal cancer have surgery as part of their treatment. Cancer treatment is good at extending the length of a person' s life, but many people are left more limited in their physical function when compared with similar people who have not had cancer or surgery. One way to try and combat this is with 'prehabilitation', which is the improvement of background levels of fitness amongst other things, before surgery. Given this, researchers want to study the effects of exercise on people before surgery for colorectal cancer and to work towards understanding why exercise can affect fitness levels amongst other things.

Who can participate?
Patients aged 18 years or older with colorectal cancer and a plan for curative surgery

What does the study involve?
Participants are randomly allocated to Prehabilitation with High-Intensity Interval Training (HIIT) only or to Prehabilitation with High-Intensity Interval Training (HIIT) and Resistance Exercise Training (RET) (ReHIIT). The study involves exercising for 8-12 sessions before surgery and three assessment sessions where participants will undergo tests of their physical function, blood and urine samples, an x-ray and ultrasound scan, testing of their nerves and muscles (EMG), a thigh biopsy, some questionnaires, and lung tests. In addition, they will also take saliva samples each week, wear a small device to track their function and record what they eat at four points during the study. The study takes about 10 weeks.

What are the possible benefits and risks of participating?
The primary aim of this study is not to directly benefit to participants in its design, but it is likely there may be some advantageous effects for participants. Participants will undergo a supervised exercise training regime, which is likely to increase their levels of physical fitness which may help them in day-to-day activities, and in their return to normal activities after surgery. Participants in the past have expressed feelings of reward for participation in trials and pleasure in the potential to help future patients.

Where is the study run from?
The University of Nottingham Medical School at the Royal Derby Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2022 to August 2026

Who is funding the study?
Medical Research Council (MRC) (UK)

Who is the main contact?
Prof. Bethan Phillips, beth.phillips@nottingham.ac.uk

Contact information

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Principal Investigator

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
321484

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 23005, IRAS 321484

Study information

Scientific Title
A randomised controlled trial of pre-operative high-intensity interval training versus high-intensity interval training plus resistance exercise training in patients with colorectal cancer scheduled for surgery with curative intent: a study to establish mechanisms of adaption to advance optimisation and stratification

Acronym
EPiC

Study objectives
Purpose:
To determine and delineate the underlying biological features of colorectal cancer burden in relation to cardiorespiratory and skeletal muscle adaptation to both High-Intensity Interval Training (HIIT) and High-Intensity Interval Training (HIIT) and Resistance Exercise Training (RET) = ReHIIT.

Primary Objective:
In relation to individuals with colorectal cancer scheduled for treatment with curative intent allocated to either HIIT or ReHIIT study arms:
1. To compare the composite change in anaerobic threshold and whole-body muscle mass

Secondary Objectives:
1. To compare changes in each of cardiorespiratory and skeletal muscle function with HIIT vs ReHIIT
2. To determine the effects of HIIT vs ReHIIT on biological markers of post-operative recovery
3. To determine the relationship between biological features of colorectal cancer and exercise adaptation, and probable prognostic markers of responses to prehabilitation
4. To determine the effects of HIIT vs ReHIIT on clinical outcomes postoperatively

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/04/2023, South Central - Oxford C Research Ethics Committee (Health Research Authority (Bristol), Ground Floor, Temple Quay House, 2 The Square, BS1 6PN, UK; +44 (0)207 104 8241; oxfordc.rec@hra.nhs.uk), ref: 23/SC/0115

Study design
Single-centre interventional randomized controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home, Hospital, Laboratory, University/medical school/dental school

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Prehabilitation in patients with colorectal cancer scheduled for surgery with curative intent

Interventions
Patients attend a testing session to assess their physical function and measure muscle mass and structure using whole-body x-ray and ultrasound. Patients will be asked to complete simple questionnaires about their physical activity, diet and quality of life (QoL).

Participants will be randomized using https://www.sealedenvelope.com. Participants will be stratified by sex and age group (5-year divisions). No blinding given the nature of the intervention.

Study arms:
1. Prehabilitation with High-Intensity Interval Training (HIIT) only
2. Prehabilitation with High-Intensity Interval Training (HIIT) and Resistance Exercise Training (RET) = ReHIIT

Patients will then complete 8-12 supervised sessions of exercise before surgery. The researchers will repeat the tests in the days before surgery, and again 6 weeks later.

Intervention Type
Behavioural

Primary outcome measure
A composite primary endpoint of change in anaerobic threshold determined via cardiopulmonary exercise testing (CPET) (Hedges g effect size: 1.32) and whole-body muscle mass measured by dual-energy X-ray absorptiometry (DXA) (Hedges g effect size: 1.1) measured at baseline, pre-op (approx. 4 weeks after baseline) and 6 weeks post-op (approx. 10 weeks after baseline)

Secondary outcome measures
All outcome measures except those detailed otherwise will be measured at baseline, pre-op (approx. 4 weeks after baseline) and 6 weeks post-op (approx. 10 weeks after baseline):
1. Muscle protein synthesis determined via laboratory analysis of vastus lateralis muscle and saliva collection in conjunction with consumption of D2O
2. Muscle protein breakdown determined via blood sample analysis and 3-methylhistidine tracer consumption
3. Whole-body contractile mass determined via urine sample analysis and D3-creatine tracer consumption
4. VO_2 peak determined via CPET
5. VL muscle architecture determined via muscle ultrasound
6. Neuromuscular function determined via electromyography
7. Mitochondrial respiration determined via Oroboros analysis of vastus lateralis biopsies
8. Anabolic cell signalling determined via Western blotting analysis of vastus lateralis biopsies
9. Clinical outcomes determined via hospital data at the end of the study (approx. 10 weeks), or earlier if information becomes available
10. Dietary intake determined by analysis of a 4-day diet diary undertaken at four timepoints: prior to the first assessment (baseline assessment), during the intervention period (week 0-4), immediately post-operation (approx. week 4-5), and 3 weeks after the operation (approx. week 7-8)
11. Functionality (including physical activity) determined via a 6-minute walk test, handgrip strength, a short performance physical battery test (measuring balance, chair-rise ability and natural gait speed), a vertical jump test (using a G-Walk [Gait and Motion Technology Ltd, Bury St Edmunds] device), exercise assessments, Duke Activity Status Questionnaire, and leg-extensions measured via dynamometery
12. Habitual activity determined using a wearable device (ActivPAL™ monitor) at four timepoints: prior to the first assessment (baseline assessment), during the intervention period (week 0-4), immediately post-operation (approx. week 4-5), and 3 weeks after the operation (approx. week 7-8)
13. Self-reported QoL determined using the EORTC-QLQ-C30 questionnaire

Overall study start date
01/10/2022

Completion date
01/08/2026

Eligibility

Key inclusion criteria
1. Age ≥18 years at the time of discussion at the multidisciplinary team
2. No maximum age range so long as the participant is deemed fit for surgery by the clinical team
3. MDT outcome of a tissue-proven, or radiologically and clinically suspected colorectal neoplasia or dysplasia with the intention to treat with curative surgery

4. Due to undergo elective operative resection (by any route) with curative intent
5. Ability to and willingness to participate in exercise regimes and assessments
6. Able to travel to the Royal Derby Hospital for the duration of the study to facilitate exercise sessions
7. Availability for the study period to attend a minimum of eight exercise sessions and three assessment sessions

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
56

Key exclusion criteria
1. Age <18 years at the time of discussion at the multidisciplinary team
2. No maximum age range so long as the participant is deemed fit for surgery by the clinical team
3. MDT outcome of a tissue-proven, or radiologically and clinically suspected colorectal neoplasia or dysplasia with the intention to treat with curative surgery
4. Due to undergo elective operative resection (by any route) with curative intent
5. Ability to and willingness to participate in exercise regimes and assessments
6. Able to travel to the Royal Derby Hospital for the duration of the study to facilitate exercise sessions
7. Availability for the study period to attend a minimum of eight exercise sessions and three assessment sessions

Date of first enrolment
28/07/2023

Date of final enrolment
30/04/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

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Study participating centre
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Sponsor type
University/education

Website
http://www.nottingham.ac.uk/

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type

Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Doctoral thesis
4. Conference presentation
5. Publication on website

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The 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?
HRA research summary			20/09/2023	No	No