TreatWELL – a feasibility study to assess the delivery of a lifestyle intervention for colorectal cancer patients undergoing potentially curative treatment

Study Protocol

Study Acronym	TreatWELL
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Chief Investigator	Professor Annie Anderson
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PROTOCOL APPROVAL

This protocol (version 1) has been authorised by:

Chief Investigator

Professor Annie Anderson

Annie S. Anderson.

Signature

Date

LIST OF ABBREVIATIONS

BMI	Body Mass Index
CRF	Case Report Form
CSO	Chief Scientist Office
CNS	Clinical Nurse Specialist
CRC	Colorectal Cancer
ERAS	Enhanced Recovery After Surgery
GCP	Good Clinical Practice
ICF	Informed Consent Form
LCs	Lifestyle counsellors
MUST	Malnutrition Universal Screening Tool
NRT	Nicotine Replacement Therapy
PIS	Participant Information Sheet
PI	Principal Investigator
RCT	Randomised Controlled Trial
RNS	Research Nurse
SOP	Standard Operating Procedure
TMF	Trial Master File

SUMMARY

Colorectal cancer (CRC) survival has improved, but in Scotland, survivors still have notable excess mortality within the first year post diagnosis compared to other European countries. In addition, CRC survivors have high rates of co-morbidities. Evidence suggests that lifestyle improvements have considerable potential to impact on morbidity and recurrence. This study aims to assess the *feasibility* of delivering an intervention programme (TreatWELL) for CRC patients undergoing potentially curative treatments. It is estimated that 30 patients will commence the programme shortly after diagnosis and continue for 31 weeks (to include the period when habits are being re-established). The programme will facilitate stepped changes towards smoking cessation, decreasing alcohol intake, increase in activity to 150 minutes moderate intensity / week and caloric intake appropriate to weight status. Feasibility outcomes include recruitment rates, ease of programme implementation, adherence, patient acceptability or the programme (content, delivery and evaluation measures), factors influencing adherence, retention and delivery costs.

1 INTRODUCTION

1.1 BACKGROUND

Colorectal cancer (CRC) survival has improved in the last decade due to earlier diagnosis and new treatments, but in Scotland, survivors still have notable excess mortality within the first year post diagnosis compared to other European countries[1]. Survivors have a high rate of co-morbidities including treatment related symptoms which are experienced by 15% undergoing colonic surgery, 33% with rectal surgery, 50% of those with chemo-radiation therapy and 66% of patients undergoing short course radiotherapy. Symptoms include fatigue, physical discomfort and bowel function problems and may be present in 72% of cases[2]. There remains a compelling need to improve outcomes in the early months after diagnosis.

1.2 RATIONALE FOR STUDY

It is recognised that smoking cessation, improved physical activity and diet have potential to impact on treatment outcomes and cancer recurrence.

Physical activity

Observational studies have shown that higher levels of physical activity are associated with better physical functioning[3] and reduced fatigue[4]. Follow up studies report better disease free, recurrence free and overall survival[5,6]. Intervention trials have shown that higher levels of physical activity initiated at pre-habilitation (pre-surgery), post-surgery, during and after adjuvant therapies (re-habilitation)[7,8,9] are associated with improved cardiorespiratory fitness, muscular strength, physical functioning, quality of life and reduced psychosocial distress.

Diet

There is growing evidence for the impact of diet on CRC outcomes. A large observational study has reported that a western diet resulted in lower disease free and overall survival[10]. At intervention level, a trial of dietary counselling delivered during treatment[11] showed that nutrition improvements were associated with reduced treatment related co-morbidity at 3 months and after a mean follow up of 6 years. Three post-treatment exploratory trials[12,13,14] of combined diet and lifestyle interventions have reported improved dietary behaviour, reduced fatigue, improved exercise tolerance, functional capacity and quality of life.

The patient journey

There is some evidence to support lifestyle interventions in the pre-surgery and post treatment periods but no trial has yet evaluated an intervention covering the full patient journey. Patients report confusion about appropriate lifestyle behaviours because they have received differing advice at different treatment stages and rarely receive personalised support in the period after treatments end and during return to normal health[15]. It has been noted that only small numbers of CRC patients stop smoking after diagnosis (13.7% pre-diagnosis to 9% 5 months later)[16]. Current data suggest that in CRC patients, activity drops significantly by 6 months post-diagnosis[17]. This may reflect lack of consistent guidance from clinicians and patient confusion over the merits of rest versus activity[15]. Similarly for diet, misconceptions exist over body weight gain (or loss) and understanding appropriate food selection.

Behavioural frameworks and support

There are a number of behavioural frameworks that could support lifestyle change from the start of care, e.g. the concept of the 'teachable moment'[18]. Cancer care clinicians can be powerful advocates to help patients understand the importance of lifestyle, from diagnosis throughout the cancer pathway, and have expressed interest in providing guidance[19]. Patients consider information obtained from cancer specialists to be of the best quality[20]. Despite major concerns over their diagnosis, many patients request advice on what might be done to prepare for surgery and there is a need for clinicians to identify an effective programme with the potential to impact on health in the first year after diagnosis. Increasingly, asymptomatic patients picked up on screening mean that this patient group is less frail than those diagnosed late and have considerable potential to initiate lifestyle change. Opportunities in the 'pre-

habilitation' period have been highlighted recently in *Living with and beyond cancer* (2013) but little is known about likely uptake of interventions.

Pilot studies

We have undertaken two pieces of formative work that demonstrate:

- that CRC survivors would welcome guidance on diet in the immediate post-treatment period to alleviate symptoms and fears about food choices: many patients actively seek lifestyle advice but experience confusion, mixed messages, culturally inappropriate guidance and uncertainty about evidence of benefit[15];
- that lifestyle advice by CRC clinicians is restricted due to patient sensitivity, time available, role constraints and lack of skills and resources in this arena[19]. These findings suggest that patients are interested in lifestyle but these topics are not routinely addressed by CRC staff.

2 AIMS

This study aims to assess the practical aspects of delivering a lifestyle intervention programme (TreatWELL) for CRC patients undergoing potentially curative treatments in order to inform the feasibility of undertaking a randomised controlled trial (RCT) to evaluate the impact of the intervention programme on health outcomes at one year after diagnosis.

2.1.1 Primary Research Questions

(i) What is the uptake of the proposed intervention programme during the period between diagnosis and surgery?

- What are the recruitment levels that can be achieved within the study duration and how do these vary between disease status and socio-demographic factors?
- How soon after diagnosis can patients commence the intervention programme?

(ii) Can all of the intervention components be delivered in the intervention phases?

- Can the programme be successfully implemented within the NHS setting?
- What is the actual length of time in each phase?
- What is the intervention fidelity to the TreatWELL protocol, which areas present delivery challenges and why?

(iii) What are the responses of patients to the intervention programme and evaluation measures?

- To what extent are patients able to achieve smoking, physical activity and dietary change before, during and after treatment (adherence)?
- Can the proposed evaluation measurements on behavioural and health outcomes (relevant for future RCT) be undertaken successfully?
- What is the retention rate at the end of the study period?

(iv) What are the patients' views on the intervention programme?

- How acceptable are the intervention recruitment methods, programme content, delivery, intensity and exit strategy to participants?
- What factors do patients think influence adherence?

(v) What are the intervention programme delivery costs?

2.2 OUTCOME MEASURES BY RESEARCH QUESTION

Data will be collected at baseline (T0), end of phase 1 (T1, 2 days pre-surgery), end of phase 2 (T2, 3 weeks post-surgery) and end of phase 3 (T3).

2.2.1 Recruitment, retention, socio-demographic and clinical data (RQ i, iii)

The research nurse will prospectively collect details on socio-demographic background, clinical information (including tumour stage and site), type of surgery, stoma status, medications and details of adjuvant treatments. Post-surgical morbidity and hospital stay will

also be recorded. Adverse events (including GP visits and hospital admissions) will be reported at each assessment.

2.2.2 Assessment of ability to undertake evaluation measures and procedures (RQ iii)

Note: these measures will be made to assess whether participants can undertake these procedures (pertinent to the outcomes in a full RCT) but *not* to demonstrate the effect of this feasibility study.

Adherence to intervention will be assessed by

- Self-reported smoking
- Self-reported alcohol intake
- Physical activity by the Scottish physical activity questionnaire (www.dapa-toolkit.mrc.ac.uk/documents/en/SPA/SPAQ.pdf) and the 6 minute walk test.
- Dietary measures by DINE (www.noo.org.uk/uploads/doc/vid_7237_Review_new.pdf)
- Physiological measures (body weight, height, waist circumference, skin fold)

Health outcomes

- Fatigue will be measured using the multidimensional fatigue inventory (MFI-20).
- Self-reported bowel function by LARS score[21].
- Physical function (and role limitations due to physical health) by the EORTC GLQ C30 Quality of Life questionnaire for bowel cancer patients and the EORTC GLQ C29 Quality of Life questionnaire for colorectal cancer patients.

2.2.3 Time of commencement, NHS implementation and fidelity (RQ i, ii)

The delivery of the intervention programme will be monitored by the lifestyle counsellors who will be asked to complete a structured pro-forma after every patient contact. This will record actual values or scaled ratings on:

- Intervention start time (days after diagnosis)
- Total contact time
- Ease or difficulty of implementing the session
- Perceived fidelity to the intervention programme content and approach
- Extent of patient engagement, receptivity and motivation

Data from pro-formas will be analysed to assess completeness of delivery and areas for improvement, and to provide contextual information (including NHS service issues) on patient engagement.

2.2.4 Acceptability of and engagement in the intervention (RQ iv)

This will be determined by in-depth qualitative interviews (guided by Stirling University) transcribed and analysed using a thematic framework approach. A random sample of 1 in 3 participants (n=10) stratified by degree of engagement with the intervention will be invited for interview at the end of phase 2 and again (another 10 participants) at the end of phase 3. These interviews will explore patient views on recruitment methods and timing, assessment procedures, programme content, activity and body weight goals, delivery, duration, intensity and exit strategy. In addition, participants will be asked to discuss factors influencing adherence including personal beliefs, motivation, family members, social and NHS staff support.

Interviews will also be conducted the two lifestyle coaches and the research nurse, who are members of the research team, for their views and feedback of the intervention delivery.

2.2.5 Cost of intervention delivery (RQ v)

This will be assessed from lifestyle counsellors' time sheets plus any additional consumable costs per person.

3 STUDY DESIGN

This study will be a single arm, single centre feasibility study of the TreatWELL intervention programme.

3.1 STUDY DESCRIPTION

The TreatWELL intervention programme aims to facilitate collaboratively agreed stepped behaviour changes towards achieving and maintaining smoking cessation, increasing physical activity to at least 150 minutes moderate intensity activity per week, caloric intake appropriate to weight status and a nutrient dense diet. It will be initiated shortly after diagnosis (pre-surgery) and continued until 25 weeks after the end of the surgical recovery period (i.e. during adjuvant therapy and when patients are adjusting to normal life and re-establishing eating and activity habits). The programme will be delivered by lifestyle counsellors (LCs) by three face to face contacts and a minimum of 12 phone calls supported by written literature and a range of behavioural techniques. The intervention will be delivered on a one to one basis (due to restricted time frame between diagnosis and treatment commencement which inhibits group sessions). Total intervention period; 3 weeks in phase 1, 3 weeks in phase 2, 25 weeks in phase 3; total intervention period 31 weeks.

Delivery Phases

Participants will receive the TreatWELL personalised intervention programme delivered in three phases. The duration of each phase is based on NHS clinical experience. Decisions about phase completion and progression will be made in conjunction with the clinical nurse specialist (CNS).

Phase 1 Pre-habilitation to start within 3-10 days of diagnosis to surgery
The current target is for treatment to start within 31 days of diagnosis. Pragmatically it is likely that a minimum of three weeks pre-habilitation can be achieved for all participants.

Phase 2 Surgical recovery to start 1 day post-op and aim to complete within 21 days
This phase is estimated at three weeks of post –operative recovery prior to commencing rehabilitation or start of adjuvant therapy. This phase will cover the period when ERAS (Enhanced Recovery After Surgery) procedures are on-going as part of usual care.

Phase 3 Post surgical / adjuvant therapy recovery to start 21 days post-op for 25 weeks
This phase will ensure that all participants are supported during adjuvant therapies (which may be variable in delivery period) and then when re-establishing daily habits. The period is designed to allow a minimum of 10 weeks post treatment for all.

Theoretical basis

All goals are consistent with the American Cancer Society and World Cancer Research Fund guidance for cancer survivors. The behavioural approaches are informed by two main theoretical frameworks: self-regulatory theory and the health action process approach. At each phase of the programme, personalised, specific goals will be identified with a focus on two health behaviours that are selected as a priority for that individual (e.g. smoking, physical activity). All participants will be asked to engage a support person (e.g. spouse) to assist in their adherence with the programme.

Programme content

Smoking

In phase 1 all participants who smoke will be offered a referral to smoking cessation services in the community. Under the national pharmacy contract, public health element, all community pharmacies are commissioned to offer smoking cessation support. In most pharmacies this consists of a brief intervention, one to one support and the provision of free nicotine replacement therapy (NRT) and assessment to meet the needs of the participant. These services will be promoted again as necessary in phases 2 and 3.

Physical activity
In phase 1, participants will be seen for a one hour session where at least 40 minutes will focus on improving cardiovascular fitness prior to surgery. Each participant will be set personalised, ability appropriate physical activity goals aiming towards achieving and/or maintaining 20-25 minutes moderate intensity activity per day (150 minutes per week) plus exercises designed for cardiovascular fitness and muscular strength. If current physical activity is already at that level, participants will be encouraged to maintain this and a modest increase will be encouraged. Participants will be encouraged to develop personalised action and coping plans. Activities (e.g. brisk walking) will be demonstrated and tried by participants and daily goals set. Two telephone calls will be made to participants in the pre-surgery period to enhance compliance and identify and discuss challenges. Personal activity goals will be based on activity levels at baseline measures. Written support material and an exercise DVD will be loaned.

In phase 2, participants will be encouraged to commence activity in accordance with ability, post-op condition and guidance from collaborating physiotherapist.

In Phase 3, the initial instruction procedure will be repeated and expanded to include emphasis on core strength, mobility and functional ability, with a strict protocol for referral to physiotherapist on any safely issues concerning risk of infection, hernias etc.

Dietary intake and alcohol
In all 3 phases, participants will undergo nutritional screening using the malnutrition universal screening tool (MUST). Participants at risk of malnutrition will be referred to the NHS dietician (as per usual care) for all dietary management. Participants will continue with other aspects of the programme (e.g. smoking cessation and improved physical activity) delivered by the LCs.

In phase 1, advice for participants not at risk of malnutrition (BMI>20kg/m^2) will focus on avoiding weight gain and increasing nutrient quality of diet in line with the department of health eatwell model (www.gov.uk/governmenr/uploads/system/uploads/attachment_data/file/153475/dh_129974.pdf). Participants will also be advised about decreasing alcohol intake, as appropriate. No energy prescription will be set in phase 1.

In phase 2 and initially in phase 3, nutrition advice will focus on symptom management (e.g. anorexia, vomiting and bowel problems) and work towards achieving a nutrient dense diet. All participants (BMI>20kg/m^2) will be given personalised guidance on a nutrient dense diet and avoidance of excess weight gain. Participants with a BMI>25kg/m^2 will be advised on avoidance of weight gain and modest weight reduction (>5% weight loss) using a personalised energy prescription goal.

<u>Behavioural strategies</u>
Informed by the taxonomy of behaviour change techniques used in interventions and the behaviour change wheel[22], a range of evidence-based behavioural techniques will be employed to motivate and support lifestyle change. This will include motivational interviewing, increasing self-efficacy, formation of specific implementation intentions, self-monitoring, personalised action and coping plans, feedback, re-enforcement and social support. To facilitate behaviour change, participants will be offered access to an equipment tool kit (e.g. pedometers, resistance bands and DVDs). Emphasis will be placed on self-monitoring and goal setting, physical activity through pedometers, with weekly feedback in the first week of each phase. In phase 3, the importance of regular self-weighing will be stresses and feedback provided at each telephone consultation.

<u>Programme delivery</u>
The programme design I based on a combination of:

- What might be practically delivered in the NHS by CRC clinical nurse specialists (with relevant training) estimated at a total of 6-8 hours input with each patient over a 31 week period.

- Current evidence on personalisation and frequency of contact in behavioural change literature (indicating the value of one to one contacts).
- The average age of participants (more familiar with one to one contact rather than electronic counselling).
- The need for different emphasis about lifestyle changes in each treatment phase.

For the purpose of this feasibility study, the intervention will be delivered by two part time dedicated TreatWELL LCs who will work closely with the CRC clinical nurse specialists. The LCs will have a nursing background with bespoke TreatWELL training. A protocol for referral procedures to specialist NHS staff (e.g. dietician, physiotherapist) will be in operation. Each participant will be seen for a minimum of 3 face to face visits (one per intervention phase) plus 6 to 12 support telephone consultations (depending on duration of adjuvant therapy, during which time they will continue to receive telephone support). The main communication format will be verbal (considering poor literacy and numeracy skills and visual difficulties that may be present tin this age group). However, all advice will be supported by written materials (and DVD in the case of exercise) to re-enforce guidance and share with family / NHS staff. The intervention sessions will be delivered in Ninewells Hospital, Dundee.

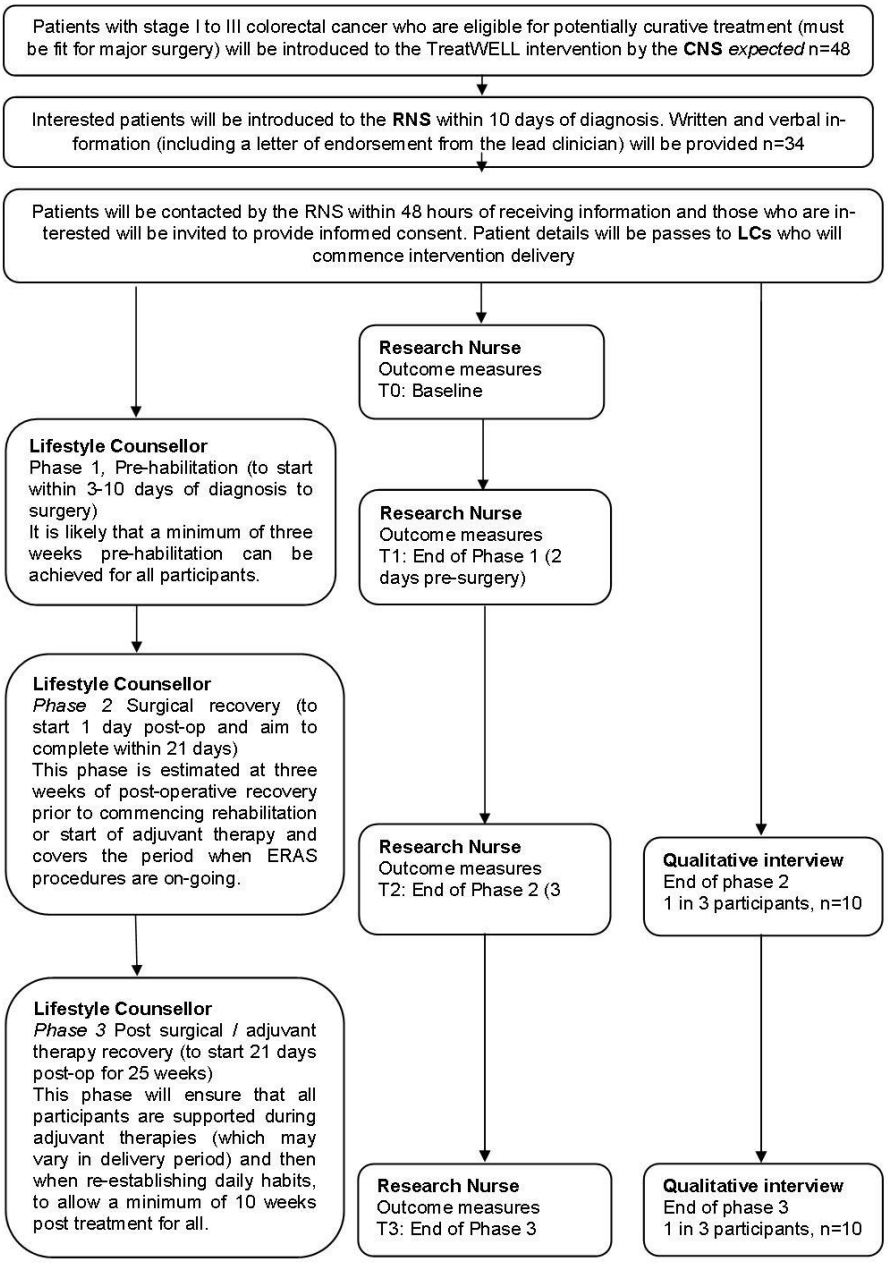
Usual care procedures

Participants will continue to receive usual care procedures (including nutritional screening using the MUST tool and ERAS procedures. In phase 3 all participants will be provided with information on self-management of lifestyle change, e.g. through the ALISS programme (www.aliss.scot.nhs.uk/), to help connect participants with community based and third sector activities (e.g. Move More Dundee).

Exit strategy

Participants with a BMI<20 or >35kg/m^2 will be offered referral to the NHS dietetic service.

3.2 STUDY FLOWCHART



3.3 STUDY MATRIX

Time	T0 Baseline	T1 End of phase 1	T2 End of phase 2	T3 End of phase 3
Collection of socio-demographic, background and clinical information	X			
Medication usage	X	X	X	X
Self-reported smoking	X	X	X	X
Self-reported alcohol intake				
Scottish physical activity questionnaire	X	X	X	X
Six minute walk test	X	X	X	X
DINE (dietary) questionnaire	X	X	X	X
Physiological measures (weight, height, waist circumference, skin fold)	X	X	X	X
Fatigue (MFI-20)	X	X	X	X
Bowel function (LARS)	X	X	X	X
Quality of life (EORTC C29 & C30)	X	X	X	X
Adverse event recording		X	X	X
Acceptability interview (1 in 3, n=10)			X	X

4 STUDY POPULATION

Patients diagnosed with CRC and beginning treatment at Ninewells Hospital, Dundee.

4.1 NUMBER OF PARTICIPANTS

Over a 5 month recruitment period, it is estimated that 60 patients will be diagnosed with CRC and begin treatment. Based on our previous lifestyle trial in CRC patients[13] it is estimated that 48 of 60 patients will meet the inclusion criteria and 34 (71%) will agree to participate.

4.2 INCLUSION CRITERIA

Adults (i.e. aged 18 years and over), who are capable of giving informed consent, with stage I to III colorectal cancer, who are eligible for potentially curative treatment (must be fit for major surgery) will be included in the study

4.3 EXCLUSION CRITERIA

Patients who:

- have been diagnosed with severe cognitive impairment,
- have emergency surgery,
- are receiving pre-operative neo-adjuvant therapy.

5 PARTICIPANT SELECTION AND ENROLMENT

5.1 IDENTIFYING PARTICIPANTS

When patients receive their cancer diagnosis they are routinely referred to the clinical nurse specialist (CNS) to discuss treatment and care plans. At present, the CNS provides brief (2-3 minutes) lifestyle advice. During the study, the CNS will inform eligible patients about the study and endorse the importance of the study for helping achieve lifestyle change in the pre

surgery period. Pateints will be asked if they would be interested in taking part, or in hearing more about the study, and those interested will be introduced to the TreatWELL research nurse (RNS) (up to 10 days of diagnosis) who will be present at the clinic.

If patients indicate to the CNS that they are happy to be introduced to the research nurse, the RNS will provide face to face verbal and written information about the study and request permission to re-contact patients within 48 hours, allowing at least 24 hours to consider taking part in the study. Patients details will be collected by the RNS on a response form. Information will include a participant information sheet and an invitation and endorsement letter from the lead CRC clinician for Tayside..

5.2 CONSENTING PARTICIPANTS

On re-contact, participants who wish to participate will be given a unique identifier and will be invited to complete informed consent and an appointment will be made for baseline measures (at Ninewells Hospital). Informed consent will be taken by the research nurse, one copy will be filed securely in the trial master file and one copy will be given to the participant. As part of the informed consent process the patient will be asked for their permission to inform their GP that they are taking part in the study, once given, the participant's GP will be informed that they are taking part and will be given a copy of the participant information sheet.

5.3 SCREENING FOR ELIGIBILITY

The CNS will screen all participants diagnosed with CRC over a 5 month recruitment period for eligibility.

5.4 INELIGIBLE AND NON-RECRUITED PARTICIPANTS

During the informed consent process, individuals will be informed that they can decline to consent to take part and their care will not be affected. Information on reasons why patients choose not to participate and demographic characteristics will be recorded if patients wish to provide that information.

5.5 INTERVENTION ALLOCATION

Consented patients' contact details will be passed to LCs who will then commence the TreatWELL personalised intervention delivered in three phases. The duration of each phase is based on individual treatment regimens (e.g. those receiving adjuvant therapy will be on the programme for a longer period). Decisions about phase completion (e.g. defining the end of post-surgical recovery) and progression will be agreed in conjunction with the CNS.

5.5.1 Withdrawal procedures

Individuals have the right to withdraw consent for participation in any aspect of this study at any time. Care from other services will not be affected at any time by declining to participate or withdrawing from the trial.

6 STUDY & SAFETY ASSESSMENTS

Adverse events including GP visits and hospital admissions will be recorded at each assessment (with the RNS and the LCs). The RNS / LCs will follow the guidelines for reporting adverse events (including serious adverse events) as written in a standard operating procedure.

In all phases participants will undergo nutritional screening using the malnutrition universal screening tool (MUST). Participants at risk of malnutrition will be referred to the NHS dietician (as per usual care) for all dietary management (but will continue with other aspects of the intervention delivered by the LCs).

7 DATA COLLECTION & MANAGEMENT

7.1 DATA COLLECTION

At each contact with the RNS (T0, T1, T2, T3) data will be collected and recorded directly onto a paper case report form (CRF) which will be comprised of a number of questionnaires:

- Physiological measures (body weight, height, waist circumference, skin fold)
- Medication usage data
- Self-reported smoking
- Self-reported alcohol intake
- The scottish physical activity questionnaire
- Six minute walk test
- The DINE questionnaire
- The multidimensional fatigue inventory (MFI-20)
- Self-reported bowel function by LARS score
- The EORTC Quality of Life questionnaires for bowel cancer patients and colorectal cancer patients

The LCs will complete a structured pro-forma after every patient contact. This will record actual values or scaled ratings on:

- Intervention start time (days after diagnosis)
- Total contact time
- Ease or difficulty of implementing the session
- Perceived fidelity to the intervention content and approach
- Extent of patient engagement, receptivity and motivation

7.2 DATA MANAGEMENT SYSTEM

Data from the CRFs and pro-formas will be entered into SPSS for analysis.

8 STATISTICS AND DATA ANALYSIS

Feasibility measures that will be assessed are programme implementation, fidelity to protocol, achieved measurements, recruitment, response, retention and adherence to programme.

Outcome measures (changes between baseline and follow up time points) will be analysed but it should be noted that these are indicative results only as this trial is not powered to show definitive results.

Data from pro-formas completed by LCs will be analysed to assess completeness of delivery and areas for improvement, and to provide contextual information (including NHS service issues) on patient engagement.

All participant interviews that take place at the end of stages 2 and 3 will be recorded, transcribed and analysed using a thematic framework approach to identify what might be considered practical and acceptable for intervention recruitment and delivery. Analysis of interview data will identify likely facilitators and barriers to conducting a full RCT.

Cost of intervention delivery will be analysed from LCs costs and other consumables.

8.1 SAMPLE SIZE CALCULATION

This is a feasibility study to test practical aspects of study design which will help inform the calculation of effect sizes required for a subsequent RCT. It is estimated that within the 5 month recruitment period that 60 patients will be diagnosed with CRC and begin treatment. Based on our previous lifestyle trial in CRC patients[13] it is estimated that 48 of 60 patients will meet the inclusion criteria and 34 (71%) will agree to participate. These numbers should

provide sufficient data on feasibility measures. Feasibility studies are not designed to test hypotheses but to provide data to inform sample size required to show significant differences in health outcome variables in a fully powered RCT.

9 STUDY MANAGEMENT AND OVERSIGHT ARRANGEMENTS

9.1 STUDY MANAGEMENT GROUP

All investigators and the study manager will be invited to participate in study management group (SMG) meetings (face to face or by teleconference) and will be responsible for the day to day running of the study

9.2 STUDY MANAGEMENT

The study will be led by the PIs. A study manager, will oversee the day to day running of the study, will be responsible for checking the CRFs for completeness, plausibility and consistency and will be accountable to the PIs and the SMG. Any queries will be resolved by the PIs or other member of the study team.

A study-specific delegation log will be prepared, detailing the responsibilities of each member of staff working on the study.

Budgeting control will be overseen by the divisional research manager.

9.3 INSPECTION OF RECORDS

The institutions involved in the study will permit study related monitoring, audits, and REC review. The PIs agree to allow the sponsor or, representatives of the sponsor, direct access to all study records and source documentation.

10 GOOD CLINICAL PRACTICE

10.1 ETHICAL CONDUCT OF THE STUDY

The study will be conducted in accordance with the principles of good clinical practice (GCP). No investigational medicinal products are being tested in this study and therefore it is not regulated by the UK's Medicines and Healthcare products Regulatory Agency.

In addition to sponsorship approval, a favorable ethical opinion will be obtained from the East of Scotland Research Ethics Service and appropriate NHS R&D approval will be obtained prior to commencement of the study.

Advice and support on governance and GCP will be provided by the Tayside Clinical Trials Unit. TreatWELL will make use of the University of Dundee's Standard Operating Procedures for tasks such as obtaining informed consent, managing and archiving data, training and how to handle breaches of GCP.

All staff involved with patient care during the study will undergo GCP training (CNS, RNS and LCs).

10.1.1 Confidentiality

All evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in a secure storage area with limited access to study staff only. Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the sponsor or its designee. The PIs and study staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior

written agreement from the sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

10.1.2 Data Protection

The PIs and study staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. The PIs and study staff will also adhere, if appropriate, to the current version of the NHS Scotland Code of Practice on Protecting Patient Confidentiality. Access to collated participant data will be restricted to the PIs and appropriate study staff.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants.

10.1.3 Insurance and Indemnity

The University of Dundee is sponsoring the study.

Insurance The University of Dundee will obtain and hold a policy of Public Liability Insurance for legal liabilities arising from the study.

Where the study involves University of Dundee staff undertaking clinical research on NHS patients, such staff will hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Indemnity The sponsor does not provide study participants with indemnity in relation to participation in the study but has insurance for legal liability as described above.

11 STUDY CONDUCT RESPONSIBILITIES

11.1 PROTOCOL AMENDMENTS, DEVIATIONS AND BREACHES

The PIs will seek approval for any amendments to the protocol or other study documents from the sponsor, REC and NHS R&D office. Amendments to the protocol or other study documents will not be implemented without these approvals.

In the event that the PIs need to deviate from the protocol, the nature of and reasons for the deviation will be recorded in the CRF, documented and submitted to the sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the sponsor for approval and then to the REC and NHS R&D office for review and approval.

In the event that a serious breach of GCP is suspected, this will be reported to the sponsor immediately using the form "Notification to Sponsor of Serious Breach or Serious Deviation".

11.2 STUDY RECORD RETENTION

Data will be held according to GCP requirements. All data will be held for a minimum of five years from completion of the study.

11.3 END OF STUDY

The study will be considered closed when the last piece of follow up information has been collected for the last participant. The sponsor and / or the PIs have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the sponsor and REC within 90 days, or 15 days if the study is terminated prematurely. The PIs will ensure that any appropriate follow up is arranged for all participants.

A summary report of the study will be provided to the sponsor and REC within 1 year of the end of the study.

12 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

12.1 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team and their respective employers. On completion of the study, the study data will be analysed and tabulated, and a clinical study report will be prepared.

12.2 PUBLICATION

The publication policy will be drafted by the SMG and will state the principles for publication, describe a process for developing output and contain a map of intended outputs with a timeline for delivery. The publication policy will respect the rights or all contributors to be adequately represented in outputs (e.g. authorship and acknowledgements) and the study to be appropriately acknowledged. Authorship of parallel studies initiated outside the SMG will be according to individuals involved in the study but must acknowledge the contribution of the SMG.

13 REFERENCES

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