Centre for Trials Research
Canolfan Ymchwil Treialon

UKCRC Registered Clinical Trials Units

Full Title:

Be Treatment Ready - Colorectal Digital (BeTR-C Digital), the development of a digital based healthcare tool for improved nutritional care of people with colorectal cancer receiving chemotherapy treatment.

VERSION 1.0

DATE: 6TH MAY 2022

Sponsor:	Cardiff University
Sponsor Ref:	SPON 1888-22
Funder:	Cardiff University Innovation for All
Funder Ref:	JA1500IF32
CTR Portfolio UID	1303
REC Ref:	TBA
IRAS number:	303154
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SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the relevant study regulations, GCP guidelines, and CTR's SOPs.

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

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

CTR Cancer Director: **Name: Prof Richard Adams**	Electronic authorisation by email **Signature**	18.05.2022 **Date**
Chief Investigator: **Name: Jane B Hopkinson**	Electronic authorisation by email **Signature**	18.05.2022 **Date:**
Sponsor: **Name: Helen Falconer**	Electronic authorisation by email **Signature**	19.05.2022 **Date:**

General Information This protocol describes the BeTR-C Digital study and provides information about the procedures for entering participants into the study. The protocol should not be used as a guide, or as an aide-memoire for the treatment of other participants. Every care has been taken in drafting this protocol; however, corrections or amendments may be necessary. These will be circulated to the known Investigators in the study. Problems relating to the study should be referred, in the first instance, to CTR.

Contact details

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Study Co-ordination:

The BeTR-C digital study is being coordinated by the Centre for Trials Research (CTR), Cardiff University, a Clinical Research Collaboration (UKCRC) registered study unit.

This protocol has been developed by the BeTR-C digital Study Management Group (SMG) in partnership with the NIHR Cancer and Nutrition Collaborative, Living with and beyond cancer sub-group.

Study Manager:	Dr Joanna Smith	Email: SealJD@cardiff.ac.uk
Director:	Prof Richard Adams	Email: RA3@cardiff.ac.uk

General queries:

General queries should be emailed to the study team at the study email account:

BETRCDIGITAL@cardiff.ac.uk

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Glossary of abbreviations

CI	Chief Investigator
CTR	Centre for Trials Research
GCP	Good Clinical Practice
HCRW	Health Care Research Wales
HRA	Health Research Authority
ICF	Informed Consent Form
ISF	Investigator Site File
NHS	National Health Service
OID	Organisation Information Document
PI	Principal Investigator
PIS	Participant Information Sheet
R&D	Research and Development
REC	Research Ethics Committee
SMF	Study Master File
SMG	Study Management Group

1 Amendment History

The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version.

Amendment No.	Protocol version no.	Date issued	Summary of changes made since previous version
Not applicable	1.0	N/A	First version

2 Synopsis

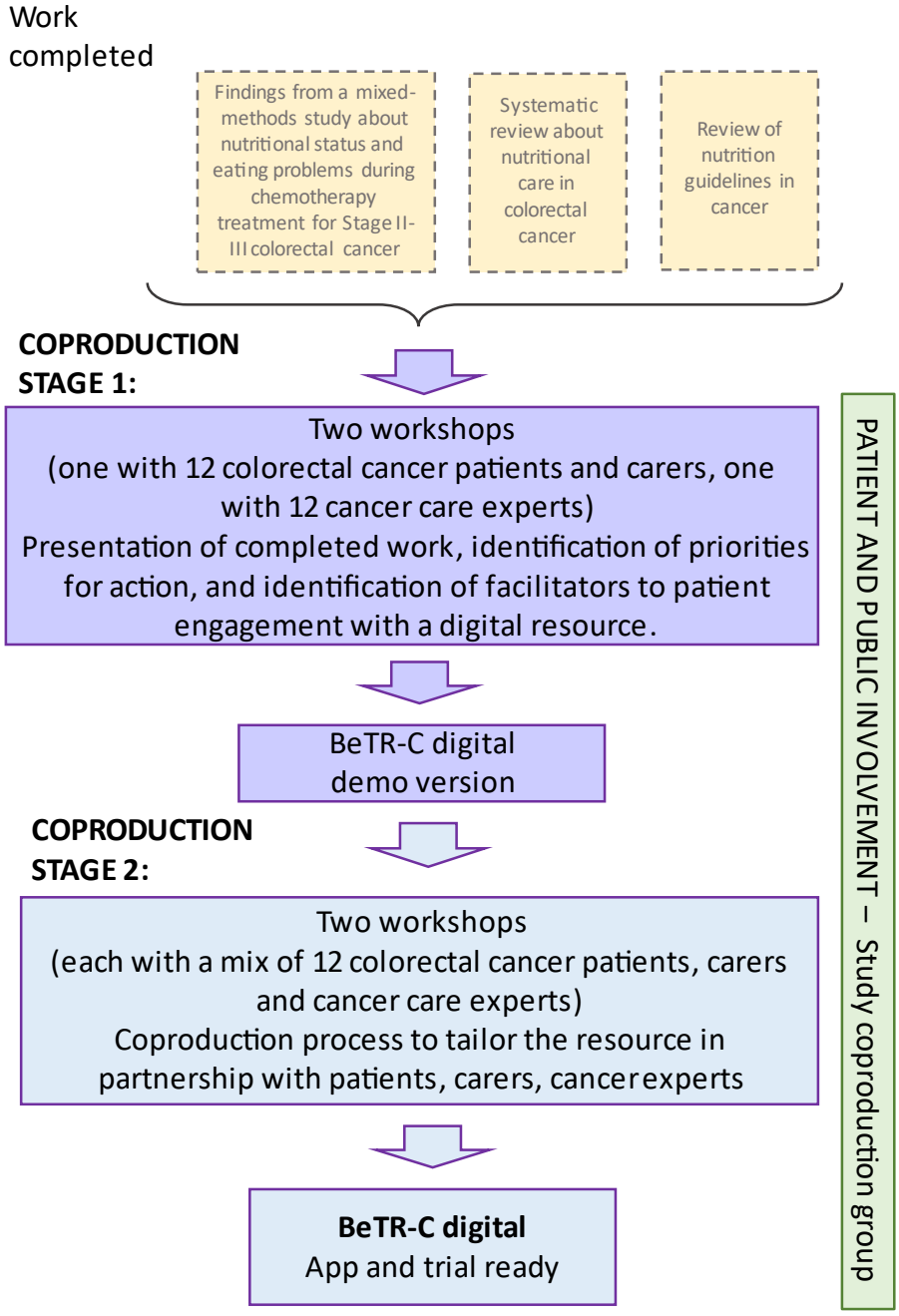
Short title	Be Treatment Ready Colorectal: the development of a digital based healthcare tool
Acronym	BeTR-C digital
CTR UID	1303
Funder and ref.	Cardiff University Innovation for All, JA1500IF32
Study design	Observational
Study participants	Patients receiving systemic anti-cancer treatment for colorectal cancer Stage II-III
Planned sample size	48 total: 12 patients/carers or staff/stakeholders at each of two prioritisation and two refinement workshops
Planned number of sites	1: Velindre Cancer Centre, Cardiff, Wales, UK
Inclusion criteria	**Patient participants** Adult (>18 years old) Colorectal cancer stage II-III Chemotherapy treatment (minimum two cycles) Able to provide informed consent Has internet access **Carer participants** Adult (>18 years old) Identified as a carer by the patient Provides/provided physical or emotional care for the patient during chemotherapy treatment Able to provide informed consent Has internet access **Staff participants** Professional or support staff Experience of the treatment and care of patients with Stage II-III colorectal cancer Has internet access
Exclusion criteria	**Patient participants** More than three months from the end of chemotherapy treatment Unable to give written informed consent (e.g. lacks capacity to consent) **Carer and staff participants** Unable to give written informed consent
Follow-up duration	Not applicable (cross-sectional study)
Planned study period	01/01/2022 to 31/08/ 2022
Primary objective	Our overarching aim is to coproduce a digital based healthcare tool to support good nutrition during chemotherapy treatment for colorectal cancer called, BeTR-C Digital.

Secondary objectives	Our objectives are: - To hold two stakeholder prioritisation workshops informed by our previous research - To produce a digital prototype of BeTR-C Digital (the I-EAT tool) - To run two coproduction workshops for the refinement of the prototype To seek funding to user test the I-EAT digital tool I-EAT tool and then to measure effect on nutritional status and quality of life during treatment for colorectal cancer
Observations	Qualitative evaluation of the acceptability, usefulness and relevance of the I-EAT tool

3 Study summary & schema

3.1 Study schema

BeTR-C digital_coproduction study schema



3.2 Study lay summary

Be Treatment Ready - Colorectal (BeTR-C Digital), the development of a digital based healthcare tool for improved nutritional care of people with colorectal cancer receiving chemotherapy treatment. Malnutrition is common during chemotherapy treatment for colorectal cancer. It is caused by the disease, its symptoms, and the side effects of treatments. We know that people with good nutritional status during treatment experience less treatment toxicity. They also live longer. In the UK, 16,000 people die from this cancer annually. Three in every five people diagnosed with later Stage III-IV disease will receive chemotherapy. Many of them experience malnutrition and they include people who are underweight or overweight.

We want to know how to support guideline recommended oral nutritional intake during chemotherapy for colorectal cancer patients with a digital resource. Our research question is, What is an acceptable, user friendly and relevant digital resource for colorectal patients receiving chemotherapy and at risk of malnutrition?

This project will be conducted in Southeast Wales, UK. It will use findings from our earlier research and systematic literature review. The purpose will be to coproduce with patients (n=24), carers (n=12) and clinicians (n=12) during four workshops (12 participants per workshop) a digital based healthcare tool (commonly known as an Application or App) which supports good nutrition throughout chemotherapy treatment for colorectal cancer. The tool will be called, I-EAT representative of the mantra **'I Eat to recover from Bowel Cancer'**. Seastorm, a new technical start-up company with focus on healthcare, will build the digital tool. We plan to user test then trial the I-EAT tool for impact on nutritional status in a future project.

The I-EAT tool will be designed to help patients adhere to the European guideline recommended food intake during chemotherapy. These recommendations support nutritional status for good quality of life during treatment and good treatment response with prolonged life.

4 Background

Malnutrition is a treatable condition. Its annual UK healthcare cost is estimated to be £15.2 billion[1. Inappropriate oral food and fluid intake contribute to malnutrition during cancer treatment, in addition to the effects of disease and treatment[2]. Yet, insufficient attention has been paid to

nutritional care in cancer for other than those who need artificial feeding3]. This research seeks to develop a digital resource to raise awareness of nutritional requirements during colorectal cancer chemotherapy and to trigger behaviours for the achievement of guideline recommended oral intake[3,4].

Personalised nutritional counselling is recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) Clinical Guideline on nutrition in cancer for all patients throughout the course of their cancer treatment[11]. Expert consensus is for dietary adaptation using regular foods, fortified foods and oral food supplements to achieve a daily intake of 25-30 kcal/kg and 1.2-1.5g protein/kg[3,4]. The purpose is to prevent malnutrition to improve treatment tolerance, survival and quality of life[5]. Supported self-management of oral intake may help patients adhere to recommendations optimising their nutritional status thereby potentiating cancer treatment[6].

We seek to bring about positive change by working in partnership with the start-up company, Seastorm, local NHS service providers (e.g. Velindre Cancer Centre hosted by Velindre University NHS Trust) and other stakeholders (e.g. Association of UK Dieticians). We have established and continue to strengthen these partnerships and will set up a BeTR-C Digital Advisory Group to facilitate engagement for this project.

The dietitians in the therapies team at the Velindre Cancer Centre have capacity to offer a service to patients with the greatest need with complex problems, for example, those who are severely malnourished thus requiring artificial feeding. Our research programme has arisen from discussions that began in 2015 between academics, Velindre staff, people affected by cancer, and cancer specialists from across the UK, who recognised the potential for improving the nutritional care of people with colorectal cancer receiving chemotherapy, most of whom do not need artificial feeding. The Velindre therapies staff would like to offer a service to every patient with colorectal cancer who is at nutritional risk. They seek a solution that can be embedded within everyday NHS service delivery but makes efficient use of limited clinical time.

Seastorm will work with us on a digital solution. If user testing is successful, then the I-EAT tool has potential to improve the therapies service offered at the Velindre Cancer Centre. It is also an approach that can be replicated in other cancer services and perhaps services for older people at nutritional risk across the UK and beyond contributing to delivery on the values based healthcare agenda.

The future

If the user testing of the I-EAT tool gives positive results, we will seek funding for a Phase II trial of the tool. This follow-on feasibility and efficacy trial will test the effect of the I-Eat tool on nutritional status of Stage II-IV colorectal cancer patients during chemotherapy. It will also investigate if and why patients adhere to the recommendations of BeTR-C Digital study and I-EAT tool, which will provide a theoretical foundation for translation to other cancer sites, treatments and care contexts.

4.1 Rationale for current study

What we have done so far

In 2018/19, with support from the NIHR Cancer and Nutrition Collaboration, our patient research partners and Tenovus Cancer Care, we conducted mixed-methods research to investigate oral intake in patients with Stage II-III CRC receiving chemotherapy [6]. More than three in five patients were at nutritional risk as measured by the Patient-Generated Subjective Global Assessment (PG-SGA) [7,8], though fewer than one in five were concerned about dietary intake. A majority, 82%, were content with the nutritional information available to them and self-management was inconsistent with achieving the oral intake recommended in clinical guidelines. The sample demographic matched a representative sample of 1071 colorectal patients from 29 centres across the UK [9]. Cognitive and behavioural coping responses are amenable to intervention [10]. There are models for framing interventions, such as the Capability, Opportunity and Motivation leading to Behaviour (COM-B) [11] and a growing evidence base for behavioural change techniques [12]. There is potential for psychoeducation to support self-management of nutritional risk, with implications for better treatment tolerance, quality of life and survival. We have used the findings from our exploratory study [6], systematic literature review [13], and research about eating and advanced cancer underpinning other educational resources 14-17] to devise a paper based prototype complex intervention, Be Treatment Ready - Colorectal (BeTR-C). BeTR-C is a previously tested multicomponent interventions offered to patients with cancer who are at nutritional risk but tailored for those receiving chemotherapy for colorectal cancer and with the addition of embedded behavioural change techniques and family support. We seek to develop a digital version of the BeTR-C prototype complex intervention, namely the I-EAT tool.

5 Study objectives/endpoints and outcome measures

Our research question:

What is an acceptable, user friendly and relevant digital resource for colorectal patients receiving chemotherapy and at risk of malnutrition?

Overarching aim:

Our overarching aim is to coproduce a digital based healthcare tool to support good nutrition during chemotherapy treatment for colorectal cancer called, BeTR-C Digital.

Objectives:

- To hold two stakeholder prioritisation workshops informed by our previous research
- To produce a digital prototype of BeTR-C Digital
- To run two coproduction workshops for the refinement of the prototype
- To seek funding to user test BeTR-C Digital and then to measure effect on nutritional status and quality of life during treatment for colorectal cancer

5.1 Primary outcomes

Expected outcomes:

A professional produced digital Seastorm product (I-EAT tool) with:

- back-end services built using “serverless” technology to be deployed over AWS Lambda (or similar) or “containerised” and deployed using Kubernetes
- back-end services built using security-first principles, likely written in the Python or Go languages
- software product easily translated to app or other digital forms
- portable back-end services (enabling move of services e.g. to NHS providers after the project)
- GDPR/DPA compliance with regards to personal data
- An example of innovation for future use in the NHS with cancer patients
- A Cardiff dissemination event
- Data to inform the design of a feasibility trial (user testing and efficacy study).

6 Study design and setting

The study is a cross-sectional qualitative observational study. It will be conducted in Southeast Wales, UK with patient, carer and staff participants recruited at the Velindre Cancer Centre, Cardiff and

advertisement via public involvement and other stakeholder organisations including Tenovus and Health Care Research Wales Public Involvement teams and the Association of UK Dieticians.
The prototype BeTR-C will be adapted for on-line use. The digital I-EAT resource will initially be hosted by Seastorm with back-end services built using portable "serverless" technology (enabling move of services e.g. to NHS or private software support providers after the project). We will use coproduction methods developed by the team in earlier studies[18, 19] to develop the resources. This will be a consultation process devised with our patient research partners and with stakeholders, which will include four workshops each with 12 patient and/orcarer or relevant staff and/or other stake holders. The purposive sampling method will enable inclusion of people from minority groups and with complex care needs.

6.1 Risk assessment

A Study Risk Assessment has been completed to identify the potential hazards associated with the study and to assess the likelihood of those hazards occurring and resulting in harm. This risk assessment considers;

- The known and potential risks and benefits to human subjects
- How high the risk is compared to normal standard clinical practice
- How the risk will be minimised/managed

This study has been categorised as a low risk study, where the level of risk is comparable to the risk of non-invasive standard medical care. A copy of the study risk assessment may be requested from the Study Manager. The study risk assessment is used to determine the intensity and focus of monitoring activity (see section 22.1).

7 Site and Investigator selection

This study will be carried out at a single participating site within the UK, the Velindre Cancer Centre, Cardiff, Wales, UK. The site will be required to complete a registration form to confirm that they have adequate resources and experience to conduct the study.

Before the Site can begin recruitment a Principal Investigator must be identified. The following documents must be in place and copies sent to the BETRCDIGITAL@cardiff.ac.uk study email account (see contact details on page 4):

- The letter confirming capability and capacity from the site's R&D Department, following sharing of the local information pack
- Favourable opinion of host care organisation/PI from Main Ethics committee
- A signed Study Agreement (Organisation Information Document; OID)
- Current, signed Curriculum Vitae and GCP training certificate of the Principal Investigator (PI)
- Completed Site Delegation Log and Roles and Responsibilities document
- Full contact details for all host care organisation personnel involved, indicating preferred contact
- A copy of the most recent approved version of the Participant Information Sheet(s) and Consent Form(s) on host care organisation headed paper

Upon receipt of all the above documents, the Study Manager will send written confirmation to the Principal Investigator detailing that the centre is now ready to recruit participants into the study. This letter/email must be filed in the site's Study Site File. Along with the written confirmation, the site should receive a study pack holding all the documents required to recruit into the Study.

Should amendments be made to the study documentation listed above. CTR will issue the site with the latest version of the documents as soon as they become available. It is the responsibility of the CTR to ensure that they obtain confirmation of capability and capacity from local R&D organisations to implement the new documents.

8 Participant selection

Participants are eligible for the study if they meet all of the following inclusion criteria and none of the exclusion criteria apply. All queries about participant eligibility should be directed to the Study Manager before registration.

8.1 Inclusion criteria

8.1.1 Patient participants

- Adult (>18 years old)
- Colorectal cancer stage II-III
- Chemotherapy treatment (minimum two cycles)
- Able to provide informed consent
- Has internet access

8.1.2 Carer participants

- Adult (>18 years old)
- Identified as a carer by the patient
- Provides/provided physical or emotional care for the patient during chemotherapy treatment
- Able to provide informed consent
- Has internet access

8.1.3 Staff and other stake holder participants

- Professional or support staff
- Experience of the treatment and care of patients with Stage II-III colorectal cancer
- Has internet access

8.2 Exclusion criteria

8.2.1 Patient participants

- More than three months from the end of chemotherapy treatment
- Unable to give written informed consent (e.g. lacks capacity to consent)

8.2.2 Carer participants

- Unable to give written informed consent

8.2.3 Staff and other stakeholder participants

- Unable to give written informed consent

9 Recruitment, Screening and registration

9.1 Participant identification

9.1.1 Patient/carer participants

Patient workshop participants and their carers will be identified by a nominated member of the clinical team at the participating site who will access their record to confirm eligibility. This will be implemented via staff communications, the Velindre University NHS Trust Newsletter, and the Velindre Healthcare Research Group. The PI will approach eligible participants with a written Letter of Invitation, Participant Information Sheet (PIS) and Informed Consent Form (ICF), inviting them to return the enclosed registration form to a researcher at the CTR if they are interested in taking part in the study. We will also ask relevant local patient organisations and charities to advertise the study to potential participants on their websites following these third party's procedures, to include the Health Care Research Wales and Tenovus Cancer Care public involvement teams. Where necessary these sources will arrange Welsh translation and dissemination upon request. Patients who share their contact details with the CTR research team via return of a reply will be approached via the CTR with an offer of a telephone conversation/virtual meeting with a study researcher who will share information about the study, answer any questions about the PIS and/or ICF, check eligibility, take consent, collect participant demographic data, and finally arrange participation in up to two workshops (one prioritisation and one refinement).

9.1.2 Staff participants

Suitable Velindre University Hospital Staff will be identified and approached by the local PI. The PI will give them a written Letter of Invitation, Participant Information Sheet (PIS) and Informed Consent Form (ICF), inviting them to speak with the researcher if they are interested in taking part in the study, check eligibility, collect consent an demographic data, and arrange participation in up to two workshops as descried in Section 9.1.1 for patient participants.

9.1.3 Other stake holder participants

The Association of UK Dieticians will also be approached to identify suitable members willing to be contacted and take part. The Group will be asked to give interested members a written Letter of Invitation, Participant Information Sheet (PIS) and Informed Consent Form (ICF), inviting them to

complete and return the embedded reply slip to a researcher with follow up by the researcher as described in Section 9.1.2 Staff Participants.

9.2 Screening logs

A screening log of all ineligible and eligible but not consented/not approached and/or consented will be kept at the site so that potential participants will receive only one approach. It will also enable assessment of the typicality of the workshop participants of all patients receiving chemotherapy for Stage II-III colorectal cancer during the period of data collection. When at site, logs may contain identifiable information but this **must** be redacted prior to being sent to the CTR at study end.

9.3 Recruitment rates

A total of 48 participants will be recruited as follows:

- 12 patients and carers at prioritisation workshop 1
- 12 staff and other stakeholders at prioritisation workshop 2
- 12 patients and carers at refinement workshop 1
- 12 staff and other stakeholders at refinement workshop 2

9.4 Informed consent

The participant's written, verbal (e.g. over the telephone) or electronic (e.g. via email acknowledgement) informed consent must be obtained using the study Informed Consent Form (ICF).. At the request of the participant the ICF and the PIS will be made available in Welsh language. The participant should be given up to 24 hours after the initial invitation to participate before being asked to sign the ICF. Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study. Participants will be asked to consent to use of data for the purposes of the study. Consent may be taken by the CTR Qualitative Researcher.

Please note, only when fully informed consent has been obtained from the participant and they have been enrolled into the study can they be considered a study participant and additional participant demographic data be collected or the participant attend a workshop.

One copy of the ICF should be given to the participant but the original copy should be kept by the participant. A further copy should be filed in the Study Master File (SMF) held at the CTR. A further copy should be kept with the patient participant's hospital notes (patient participants only).

The right of the participant to refuse to participate in the study without giving reasons must be respected. Similarly, the participant must remain free to withdraw at any time without giving reasons and without prejudicing his/her further treatment.

10 Withdrawal & lost to follow-up

10.1 Withdrawal

Participants have the right to withdraw consent for participation in any aspect of the study at any time. The care of patient participants, or the person a carer participant cares for, will not be affected at any time by the participant declining to participate or withdrawing from the study.

If a participant initially consents, attends a workshop but subsequently withdraws permission to use the data collected the data will not be redacted from the transcript as explained in the PIS.

The withdrawal of participant consent shall not affect the study activities already carried out and the use of data collected prior to participant withdrawal. The use of the data collected prior to withdrawal of consent is based on the informed consent given before its withdrawal.

The CTR will maintain a withdrawal log to document withdrawal.

11 Study procedures

Patient carer and staff participants will take part in up to two workshops (one prioritisation and one refinement) of up to 2 hours in duration. Refinement workshops will be held approximately 4-8 weeks after prioritisation workshops.

Workshops will be held at the Velindre Cancer Centre Cardiff (or virtually, e.g should COVID or other restrictions be in place) and facilitated by the CTR qualitative researcher and the CI, both experienced qualitative researchers with training and track record in running focus groups, and coproduction workshops. Participants written informed consent will be taken prior to attendance and reconfirmed at the start of each workshop.

The workshop schedule will be devised by the cofacilitators using Normalisation Process Theory as the underpinning framework for data generation and methods to include an adapted nominal group technique to identify priorities. Example question topics will be reviewed by a Research Ethics Committee.

Participants will be asked to:

- Give informed consent
- Complete a short questionnaire (demographic data, cancer diagnosis and treatment, digital literacy) to support adequate representation from minority groups (taken by the CTR qualitative researcher by telephone prior to workshop attendance using a study-specific question guide)
- Given a user account (e.g. username and password) for the prototype I-EAT App and instructions on how to use the App and generate dummy data to support I-Eat App testing (refinement workshop attendees only)
- Test the I-Eat App prior to attendance at the workshop (refinement workshop attendees only)at one workshop

The study is a cross-sectional observational study. There will be no follow-up of participants.

13 Statistical considerations

13.1 Sample size

The planned sample size for each workshop is 6-12, the optimal number for group work. The number of workshops is pragmatic based on the limited study resources. We will use purposive sampling to identify and recruit a maximum variation sample. Based on our earlier studies to develop hard copy resources, we anticipate sufficient data will be generated for our planned thematic analysis.

14 Data Collection and Management

Study-specific data management processes will follow standard CTR and Cardiff University data management procedures and be fully documented in the study qualitative data management and analysis plan, including specific details of how participant informed consent and demographic data

will be collected and stored, and I-EAT App development and testing procedures, which will follow standard industry practice and UK GPDR legislation.

Data will be collected on the following source data documents:

- Screening logs (pre-consent and study registration, e.g. held at participating site)
- Informed consent form
- Demographic survey (data will be collected by the CTR researcher post-consent verbally over the telephone using a survey question guide with data entered directly onto a password protected and securely stored Excel spreadsheet)
- Study registration log (including registration number assignment)
- I-EAT App

The CTR will assign workshop participants a unique username and password for App user testing purposes. The CTR will hold the link to the username and password and not share this with third parties. Seastorm will not be able to identify participants via usernames or passwords. Participants will be instructed to only enter dummy data for the purposes of I-EAT App testing. Seastorm will only have access to fully anonymised App testing data.

15 Analysis

15.2 Qualitative analysis

We will adopt the methods and model of coproduction consistent with a participatory partnership approach to research and health service improvement [15], where different people, each with their own knowledge, techniques and experiences, work together in dialectical process [20]. The collaborative participatory framework for the project has the purpose of creating knowledge for action with a focus on education in nutrition and self-management that supports the interests of people affected by colorectal cancer.

The data collection process will involve two cycles of engagement with colorectal cancer patients (firstly prioritisation, secondly refinement), carers and cancer care experts. We will conduct two prioritisation workshops, one each with patients and carers , and cancer care experts, to present the findings of our earlier empirical research and systematic review then seek to prioritise actions to address issues raised in nutritional care during chemotherapy treatment. We will use an adapted

nominal group technique to identify priorities. The prioritisation exercise will inform a mock-up of the I-EAT prototype tool developed with Seastorm.

Feedback will be sought from our BeTR-C Patient Advisory Group and BeTR-C Cancer Staff Dignity Group on software refinement needed, prior to presentation at two refinement workshops, one each with patients and carers, and staff with experience of cancer. The purpose of these final workshops will be to gather data on the acceptability and useability of the I-EAT tool to inform further adjustment for enhanced access by diverse groups with complex care needs.

We will use Normalisation Process Theory to structure our data collection and analysis. We will analyse pre-workshop participant demographic survey data to evaluate representation from minority groups including ethnic minorities, sensory impairment (visual and hearing), and people with comorbidities etc. via to further inform our workshop findings.

16 Protocol/GCP non-compliance

The Principal Investigator should report any non-compliance to the study protocol or the conditions and principles of Good Clinical Practice (GCP) to the CTR in writing as soon as they become aware of it. Non-compliances will be managed and reported to Sponsor, REC and participating sites by the CTR where necessary following the CTR Non-Compliance procedure.

17 End of Study definition

The end of the study is defined as the date of final data capture to meet the study endpoints. In this case end of study is defined as completion of the 2nd round of coproduction workshops.

The Sponsor must notify the main REC of the end of a clinical study within 90 days of its completion or within 15 days if the study is terminated early.

18 Archiving

The SMF and SSF containing essential documents will be archived at an approved external storage facility for a minimum of 15 years. The CTR will archive the SMF and SSFs on behalf of the Sponsor. The Principal Investigator is responsible for archival of the Investigator Site File (ISF) at site on approval from Sponsor. Essential documents pertaining to the study shall not be destroyed without permission from the Sponsor.

19 Regulatory Considerations

19.1 Ethical and governance approval

This protocol has approval from a Research Ethics Committee (REC) that is legally "recognised" by the United Kingdom Ethics Committee Authority for review and approval.

This study protocol will be submitted through the relevant permission system for global governance review Health Care Research Wales (HCRW).

Confirmation of capability and capacity to support the study will be obtained from the host care organisation who will consider local governance requirements and site feasibility. The Research Governance approval of the host care organisation must be obtained before recruitment of participants within that host care organisation.

19.2 Data Protection

The CTR will act to preserve participant confidentiality and will not disclose or reproduce any information by which participants could be identified, except where specific consent is obtained. Data will be stored in a secure manner at the CTR, Cardiff University and will be registered in accordance with the UK General Data Protection Regulation 2018. The data controller for this study is the Sponsor, Cardiff University. The data processors are the CTR and the participating site. Data will be managed as described in Section 14.

19.3 Indemnity

- Non-negligent harm: This study is an academic, investigator-led and designed study, coordinated by the CTR. The Chief Investigator, local Investigator and coordinating centre do not hold insurance against claims for compensation for injury caused by participation in a clinical study and they cannot offer any indemnity.
- Negligent harm: Where studies are carried out in a hospital, the hospital continues to have a duty of care to a participant being treated within the hospital, whether or not the participant is participating in this study. Cardiff University does not accept liability for any breach in the other hospital's duty of care, or any negligence on the part of employees of hospitals. This applies whether the hospital is an NHS Trust or not. The Sponsor shall indemnify the site against claims arising from the negligent acts and/or omissions of the Sponsor or its employees in connection with the Clinical Study (including the design of the Protocol to the extent that the Protocol was

designed solely by the Sponsor and the Site has adhered to the approved version of the Protocol) save to the extent that any such claim is the result of negligence on the part of the Site or its employees.

Patient and/or carer participants recruited at NHS sites NHS indemnity scheme/NHS professional indemnity will apply with respect to claims arising from harm to participants at site management organisations.

19.4 Study sponsorship

Cardiff University will act as Sponsor for study.

19.5 Funding

This study is funded by an Innovation for All, Translational Kickstart grant from Cardiff University: JA1500IF32.

20 Study management

The Sponsor has delegated the management of the study to the Centre for Trial Research (CTR) as documented in the study delegation of duties document.

The Sponsor has subcontracted the I-EAT Digital App software metadata development and management of fully anonymised end user dummy test data to a local company, Seastorm.

The National Institute for Health Research (NIHR), Cancer and Nutrition Collaborative, Living With and Beyond Cancer subgroup is in support of the project and will offer guidance on project delivery, follow-on bid writing, and dissemination. This group includes consultant dietitians, medical consultants, scientists and members of the public affected by cancer.

As BETR-C Digital is an observational, non-CTIMP study with low data and safety risks a formal Independent Data Monitoring Committee (IDMC) or Trial Steering Committee (TSC) is not planned. Instead the Sponsor will appoint a Study Management Group (SMG) and Project Management Group (PMG) as described below.

20.1 SMG (Study Management Group)

The SMG will be chaired by the CI and SMG members will be required to sign up to the remit and conditions set out in the combined SMG/PMG Charter. The SMG will meet at least twice during the course of the study; once prior to opening the study to participant recruitment and again during the

study closure phase. The SMG will be responsible for reviewing study progress against project milestones and data, steering and compliance oversight.

20.2 PMG (Project Management Group)

A sub-group of the SMG will act as the PMG responsible for day-to-day management of the study and chaired by the CI. PMG members will be required to sign up to the remit and conditions set out in the combined SMG/PMG Charter. The PMG will meet at least once a month. PMG members will be required to sign up to the remit and conditions set out in the study SMG Charter.

21 Quality Control and Assurance

21.1 Monitoring

The clinical study risk assessment has been used to determine the intensity and focus of central and on-site monitoring activity in the BeTR-C digital study. Due to the low risk of this observational study, there is no planned monitoring above and beyond SMG, PMG and Sponsor oversight and low central monitoring (e.g. participant consent and withdrawal and GDPR compliance) as documented in the SMG/PMG charter and qualitative data and management plan respectively. There is no planned site monitoring is formal monitoring plan. However, PIs should agree to allow study related triggered monitoring, including audits and regulatory inspections, by providing direct access to source data/documents as required. Participant consent for this will be obtained.

Findings generated from monitoring, audit or inspection activities will be shared with the Sponsor, CI, PI & local R&D.

21.2 Audits & inspections

The study is participant to inspection by Health Care Research Wales (HCRW) and REC regulatory bodies. The study may also be participant to inspection and audit by Cardiff University under their remit as Sponsor.

22 Publication and dissemination

All publications and presentations relating to the study will be authorised by the SMG. A Publication Plan will be drafted during study set up to document planned and actual publications. The results of

the study will be presented at the end of the study at a study dissemination event with attendance by invite only.

23 References

1. Stratton R, Smith T, Gaby S (2018) Managing malnutrition to improve lives and save money. BAPEN, Worcestershire, UK
2. Arends J et al. (2017) ESPEN expert group recommendations for action against cancer-related malnutrition. Clin Nutr. 36(5),1187-1196.
3. Arends J et al. (2017) ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 36,1–48.
4. Neuzillet C et al. (In press) Nutrition and physical activity: French intergroup clinical practice guidelines. BMJ Supportive & Palliative Care.
5. Aapro M et al. (2014) Early recognition of malnutrition: a position paper of a European School of Oncology Task Force. Ann. Oncol. 25(8),1492-9.
6. Hopkinson J et al. (2020) Diet and weight management by people with non-metastatic colorectal cancer during chemotherapy: mixed methods research. Colorectal Cancer. 9(2), article number: CRC16. (10.2217/crc-2019-0017).
7. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur. J. Clin. Nutr. 56(8),779-85 (2002).
8. Abbott J, McKavanagh LTD, Watson J, McCarthy AL, Isenring E. Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) is a vaild screening tool in chemotherapy outpatients. Support Care Cancer. 24(9),3883-3887 (2016).
9. Wheelwright S et al. (2020) Does quality of life return to pre-treatment levels five years after curative intent surgery for colorectal cancer? Evidence from the ColoREctal Wellbeing (CREW) study. PloS one. 15(4):e0231332.
10. Health Foundation (2016) Supporting self-management A guide to enabling behaviour change for health and wellbeing using person- and community centred approaches. Available at: http://www.health.org.uk/sites/health/files/RtVSupportingSelfManagement.pdf
11. Michie S, Atkins L, West R (2014) The Behaviour Change Wheel: A guide to designing interventions. Silverback Publishing. UK. See pp 59-86.
12. Behavioural Change Project (2020) Available at, https://theoryandtechniquetool.humanbehaviourchange.org/tool
13. Hopkinson J et al. (2020) What is known about oral nutritional care of patients receiving radiotherapy, chemotherapy or chemoradiotherapy for colorectal cancer: a systematic review and narrative synthesis. PROSPERO CRD42020178160
14. Hopkinson JB (2007) How people with advanced cancer manage change in eating habits. JAN, 59(5) 454-462.
15. 8. Hopkinson JB et al. (2010) The deliverability, acceptability and perceived effect of the Macmillan Approach to Weight loss and Eating difficulties (MAWE): Phase II cluster

randomised exploratory trial of a psychosocial intervention for weight- and eating-related distress. JPSM. 40(5), 684-695.

16. 9. Hopkinson J, Richardson A. (2015) A mixed-methods qualitative research study to develop a complex intervention for weight loss and anorexia in advanced cancer: The Family Approach to Weight and Eating (FAWE). Pall Med. 29, 164-176.
17. 10. Hopkinson JB (2016) Food connections: weight- and eating-related distress in families affected by advanced cancer. EJON. 20: 87-96.
18. Wright D et al. (2006) Listening to the views of people affected by cancer about cancer research. Health Expectations. 9,3-12.
19. 42. Latter S et al. (2018) Supporting family caregivers to manage pain medication in cancer patients at end of life. Pall Med. 32(1) 246-256.
20. Arnstein, Sherry R. "A Ladder of Citizen Participation," JAIP, Vol. 35, No. 4, July 1969, pp. 216-224.
21. Cornwall J, Jewkes R (1995) What is participatory research? Social Science and Medicine. 41(12); 1667-1676.

24 Appendices

24.1 Appendix 1 – PG-SGA Metric Non-Tool V4.3.20

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History: Boxes 1 - 4 are designed to be completed by the patient.
[Boxes 1-4 are referred to as the PG-SGA Short Form (SF)]

Patient Identification Information

1. Weight *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____ pounds
I am about _____ feet _____ inches tall

One month ago I weighed about _____ pounds
Six months ago I weighed about _____ pounds

During the past two weeks my weight has:
☐ decreased (1) ☐ not changed (0) ☐ increased (0)

Box 1 ☐

2. Food intake: As compared to my normal intake, I would rate my food intake during the past month as
☐ unchanged (0)
☐ more than usual (0)
☐ less than usual (1)

I am now taking
☐ *normal food* but less than normal amount (1)
☐ little solid food (2)
☐ only liquids (3)
☐ only nutritional supplements (3)
☐ very little of anything (4)
☐ only tube feedings or only nutrition by vein (0) **Box 2** ☐

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)
☐ no problems eating (0)
☐ no appetite, just did not feel like eating (3)
☐ nausea (1)
☐ constipation (1)
☐ mouth sores (2)
☐ things taste funny or have no taste (1)
☐ problems swallowing (2)
☐ pain; where? (3) _____
☐ other (1)** _____
☐ vomiting (3)
☐ diarrhea (3)
☐ dry mouth (1)
☐ smells bother me (1)
☐ feel full quickly (1)
☐ fatigue (1)
**Examples: depression, money, or dental problems
Box 3 ☐

4. Activities and Function:
Over the past month, I would generally rate my activity as:
☐ normal with no limitations (0)
☐ not my normal self, but able to be up and about with fairly normal activities (1)
☐ not feeling up to most things, but in bed or chair less than half the day (2)
☐ able to do little activity and spend most of the day in bed or chair (3)
☐ pretty much bed ridden, rarely out of bed (3)

Box 4 ☐

The remainder of this form is to be completed by your doctor, nurse, dietitian, or therapist. Thank you.

Additive Score of Boxes 1-4 ☐ **A**

email: faithotterymdphd@gmail.com or info@pt-global.org

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History: Boxes 1 - 4 are designed to be completed by the patient.
[Boxes 1-4 are referred to as the PG-SGA Short Form (SF)]

Patient Identification Information

1. Weight *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____ pounds
I am about _____ feet _____ inches tall

One month ago I weighed about _____ pounds
Six months ago I weighed about _____ pounds

During the past two weeks my weight has:
☐ decreased (1) ☐ not changed (0) ☐ increased (0)

Box 1 ☐

2. Food intake: As compared to my normal intake, I would rate my food intake during the past month as
☐ unchanged (0)
☐ more than usual (0)
☐ less than usual (1)

I am now taking
☐ *normal food* but less than normal amount (1)
☐ little solid food (2)
☐ only liquids (3)
☐ only nutritional supplements (3)
☐ very little of anything (4)
☐ only tube feedings or only nutrition by vein (0) **Box 2** ☐

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)
☐ no problems eating (0)
☐ no appetite, just did not feel like eating (3)
☐ nausea (1)
☐ constipation (1)
☐ mouth sores (2)
☐ things taste funny or have no taste (1)
☐ problems swallowing (2)
☐ pain; where? (3) _____
☐ other (1)** _____
☐ vomiting (3)
☐ diarrhea (3)
☐ dry mouth (1)
☐ smells bother me (1)
☐ feel full quickly (1)
☐ fatigue (1)
**Examples: depression, money, or dental problems
Box 3 ☐

4. Activities and Function:
Over the past month, I would generally rate my activity as:
☐ normal with no limitations (0)
☐ not my normal self, but able to be up and about with fairly normal activities (1)
☐ not feeling up to most things, but in bed or chair less than half the day (2)
☐ able to do little activity and spend most of the day in bed or chair (3)
☐ pretty much bed ridden, rarely out of bed (3)

Box 4 ☐

The remainder of this form is to be completed by your doctor, nurse, dietitian, or therapist. Thank you.

Additive Score of Boxes 1-4 ☐ **A**

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24.2 Appendix 2 – PG-SGA Metric Tool V4.3.20

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History: Boxes 1 - 4 are designed to be completed by the patient.
[Boxes 1-4 are referred to as the PG-SGA Short Form (SF)]

Patient Identification Information

1. Weight *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____kg
I am about _____ cm tall

One month ago I weighed about _____ kg
Six months ago I weighed about _____ kg

During the past two weeks my weight has:
☐ decreased (1) ☐ not changed (0) ☐ increased (0)

Box 1 ☐

2. Food intake: As compared to my normal intake, I would rate my food intake during the past month as
☐ unchanged (0)
☐ more than usual (0)
☐ less than usual (1)

I am now taking
☐ *normal food* but less than normal amount (1)
☐ little solid food (2)
☐ only liquids (3)
☐ only nutritional supplements (3)
☐ very little of anything (4)
☐ only tube feedings or only nutrition by vein (0) **Box 2** ☐

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply)
☐ no problems eating (0)
☐ no appetite, just did not feel like eating (3)
☐ nausea (1)
☐ constipation (1)
☐ mouth sores (2)
☐ things taste funny or have no taste (1)
☐ problems swallowing (2)
☐ pain; where? (3) _____
☐ other (1)** _____
☐ vomiting (3)
☐ diarrhea (3)
☐ dry mouth (1)
☐ smells bother me (1)
☐ feel full quickly (1)
☐ fatigue (1)
Examples: depression, money, or dental problems **Box 3 ☐

4. Activities and Function:
Over the past month, I would generally rate my activity as:
☐ normal with no limitations (0)
☐ not my normal self, but able to be up and about with fairly normal activities (1)
☐ not feeling up to most things, but in bed or chair less than half the day (2)
☐ able to do little activity and spend most of the day in bed or chair (3)
☐ pretty much bed ridden, rarely out of bed (3)

Box 4 ☐

The remainder of this form is to be completed by your doctor, nurse, dietitian, or therapist. Thank you.

Additive Score of Boxes 1-4 ☐ **A**

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Scored Patient-Generated Subjective Global Assessment (PG-SGA)

Worksheet 1 – Scoring Weight Loss
To determine score, use 1-month weight data if available. Use 6-month data only if there is no 1-month weight data. Use points below to score weight change and add one extra point if patient has lost weight during the past 2 weeks. Enter total point score in Box 1 of PG-SGA.

Weight loss in 1 month	Points	Weight loss in 6 months
10% or greater	4	20% or greater
5-9.9%	3	10- 19.9%
3-4.9%	2	6- 9.9%
2-2.9%	1	2- 5.9%
0-1.9%	0	0- 1.9%

Numerical score from Worksheet 1 ☐

Additive Score of Boxes 1-4 (See Side 1) ☐ **A**

5. Worksheet 2 – Disease and its relation to nutritional requirements:
Score is derived by adding 1 point for each of the following conditions:
☐ Cancer
☐ AIDS
☐ Pulmonary or cardiac cachexia
☐ Chronic renal insufficiency
☐ Presence of decubitus, open wound or fistula
☐ Presence of trauma
☐ Age greater than 65
Other relevant diagnoses (specify) _____
Primary disease staging (circle if known or appropriate) I II III IV Other _____
Numerical score from Worksheet 2 ☐ **B**

6. Worksheet 3 – Metabolic Demand
Score for metabolic stress is determined by a number of variables known to increase protein & caloric needs. **Note:** Score fever intensity or duration, whichever is greater. The score is additive so that a patient who has a fever of 38.8 °C (3 points) for < 72 hrs (1 point) and who is on 10 mg of prednisone chronically (2 points) would have an additive score for this section of 5 points.

Stress	none (0)	low (1)	moderate (2)	high (3)
Fever	no fever	> 37.2 and < 38.3	≥ 38.3 and < 38.8	≥ 38.8 °C
Fever duration	no fever	< 72 hours	72 hours	> 72 hours
Corticosteroids	no corticosteroids	low dose (< 10 mg prednisone equivalents/day)	moderate dose (≥ 10 and < 30 mg prednisone equivalents/day)	high dose (≥ 30 mg prednisone equivalents/day)

Numerical score from Worksheet 3 ☐ **C**

7. Worksheet 4 – Physical Exam
Exam includes a subjective evaluation of 3 aspects of body composition: fat, muscle, & fluid. Since this is subjective, each aspect of the exam is rated for degree. Muscle deficit/loss impacts point score more than fat deficit/loss. Definition of categories: 0 = no abnormality, 1+ = mild, 2+ = moderate, 3+ = severe. Rating in these categories is *not* additive but are used to clinically assess the degree of deficit (or presence of excess fluid).

Muscle Status		Fat Stores	
temples (temporalis muscle)	0 1+ 2+ 3+	orbital fat pads	0 1+ 2+ 3+
clavicles (pectoralis & deltoids)	0 1+ 2+ 3+	triceps skin fold	0 1+ 2+ 3+
shoulders (deltoids)	0 1+ 2+ 3+	fat overlying lower ribs	0 1+ 2+ 3+
interosseous muscles	0 1+ 2+ 3+	**Global fat deficit rating**	**0 1+ 2+ 3+**
scapula (latissimus dorsi, trapezius, deltoids)	0 1+ 2+ 3+	**Fluid status**	
thigh (quadriceps)	0 1+ 2+ 3+	ankle edema	0 1+ 2+ 3+
calf (gastrocnemius)	0 1+ 2+ 3+	sacral edema	0 1+ 2+ 3+
Global muscle status rating	**0 1+ 2+ 3+**	ascites	0 1+ 2+ 3+
		Global fluid status rating	**0 1+ 2+ 3+**

Point score for the physical exam is determined by the overall subjective rating of the total body deficit.
No deficit score = 0 points
Mild deficit score = 1 point
Moderate deficit score = 2 points
Severe deficit score = 3 points
Again, muscle deficit/loss takes precedence over fat loss or fluid excess.

Numerical Score for Worksheet 4 ☐ **D**

Total PG-SGA Score (Total numerical score of A+B+C+D) ☐

Clinician Signature _____ RD RN PA MD DO Other _____ Date _____

Global PG-SGA Category Rating (Stage A, Stage B or Stage C) ☐

Worksheet 5 – PG-SGA Global Assessment Categories

Category	Stage A Well-nourished	Stage B Moderate/suspected malnutrition	Stage C Severely malnourished
Weight	No weight loss OR recent non-fluid wt gain	≤ 5% loss in 1 month (≤10% in 6 months) OR Progressive weight loss	> 5% loss in 1 month (>10% in 6 months) OR Progressive weight loss
Nutrient intake	No deficit OR Significant recent improvement	Definite decrease in intake	Severe deficit in intake
Nutrition Impact Symptoms (NIS)	None OR significant recent improvement allowing adequate intake	Presence of NIS (Box 3 of PG-SGA)	Presence of NIS (Box 3 of PG-SGA)
Functioning	No deficit OR Significant recent improvement	Moderate functional deficit OR Recent deterioration	Severe functional deficit OR Recent significant deterioration
Physical Exam	No deficit OR chronic deficit but with recent clinical improvement	Evidence of mild to moderate loss of muscle mass &/or muscle tone on palpation &/or loss of SQ fat	Obvious signs of malnutrition (e.g., severe loss muscle, fat, possible edema)

Nutritional Triage Recommendations: Additive score is used to define specific nutritional interventions including patient & family education, symptom management including pharmacologic intervention, and appropriate nutrient intervention (food, nutritional supplements, enteral, or parenteral triage).
First line nutrition intervention includes optimal symptom management.
Triage based on PG-SGA point score
0-1 No intervention required at this time. Re-assessment on routine and regular basis during treatment.
2-3 Patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey (Box 3) and lab values as appropriate.
4-8 Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms (Box 3).
≥ 9 Indicates a critical need for improved symptom management and/or nutrient intervention options.

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24.2 Appendix 3 –List of Key Study Documents

- Protocol
- Combined Participant Invite/Participant Information Sheet (PIS)/Informed Consent Form (ICF) x 3 (1 each for patient, carer, staff and/or other stakeholder)
- Risk Assessment Form
- Demographic survey question guide
- Demographic survey Excel data spreadsheet
- Prioritisation and refinement workshop question topics
- HCRW and Tenovus participant adverts
- App Specification
- Publication and Dissemination Plan
- SMG/PMG Charter
- Qualitative Data Management Plan
- Public Involvment Plan
- Screening Log
- Study Opening Checklist
- Site Opening Checklist
- Study Closure Checklist
- Site Closure Checklist
- Site agreement (Organisation Information Document)