Systematic development and feasibility testing of a digitally facilitated, remotely supervised, multimodal prehabilitation intervention for patients approaching major surgery

Chief Investigators:

Dr Leah Avery

Associate Professor in Applied Health Psychology and Chartered Health Psychologist, School of Health and Life Sciences, Teesside University.

Email: leah.avery@tees.ac.uk

Professor Gerard Danjoux

Professor of Perioperative Medicine, School of Health and Life Sciences, Teesside University and Hull York Medical School, and Consultant in Anaesthesia and Sleep Medicine at the Department of Anaesthesia and Perioperative Medicine, South Tees Hospitals NHS Foundation Trust.

Email: gerard.danjoux@nhs.net

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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 Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirements.

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 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.

For and on behalf of the Study Sponsor:

Signature: Date:

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Name (please print):

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Position:

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Chief Investigators:

Signature: Date:

Name: (please print):

Signature: Date:

Name: (please print):

Key Study Contacts

Sponsor details:

Research and Development Department, STRIVE centre, South Tees Hospitals NHS Foundation Trust, Marton Road, Middlesbrough, TS4 3BW, UK.

Protocol authors:

Dr James Durrand
PhD Student Northumbria University Department of Sport, Exercise and Rehabilitation.
Specialty Trainee in Anaesthesia and Intensive Care Medicine and Research Fellow South Tees Hospitals Department of Anaesthesia and Perioperative Medicine.

Email: james.durrand@nhs.net

Dr Garry Tew
Associate Professor
Northumbria University, Department of Sport, Exercise and Rehabilitation.

Email: garry.tew@northumbria.ac.uk

Dr Chelsia Gillis
Registered Dietician, Department of Anaesthesia, McGill University

Email: chelsia.gillis@mcgill.ca

Dr David Yates
Consultant in Anaesthesia, Intensive Care and Perioperative Medicine and Clinical Lead for Research, York & Scarborough Teaching Hospitals NHS Foundation Trust.
Academic Alliance of Perioperative Medicine, Hull York Medical School.

Email: david.yates@york.nhs.uk

Dr Joanne Gray
Associate Professor
Northumbria University, School of Nursing Midwifery and Health

Email: joanne3.gray@northumbria.ac.uk

Professor Colin Greaves
Professor of psychology applied to health, School of Sport, exercise and Rehabilitation Sciences, University of Birmingham.

Email: c.j.greaves@bham.ac.uk

Dr John Moore
Consultant in Anaesthesia and Intensive Care and Clinical Director for Adult Critical Care
Manchester University Hospitals NHS Foundation Trust

Email: john.moore@mft.nhs.uk

Dr Alasdair O'Doherty
Senior Lecturer in Exercise Physiology and Health
Northumbria University Department of Sport, Exercise and Rehabilitation

Email: alasdair.odoherty@northumbria.ac.uk

Professor Patrick Doherty
Professor of cardiovascular health, York University Department of Health Sciences

Email: patrick.doherty@york.ac.uk

Contents

1. Study overview

1.1. Aims:

1. Systematically develop a theory and evidence informed, digitally facilitated, remotely supervised, multibehavioural prehabilitation intervention for patients approaching major non-cardiac surgery.

2. Determine the feasibility, acceptability and fidelity of the developed intervention for patients approaching major non-cardiac surgery

1.2. Study design:

This protocol details stage 1 of a planned 2 stage process:

Stage 1: Systematic development of the digital multibehavioural prehabilitation intervention and healthcare professional (HCP) training resource

Planned Stage 2: Feasibility testing of the intervention with patients approaching major surgery at two National Health Service (NHS) centres

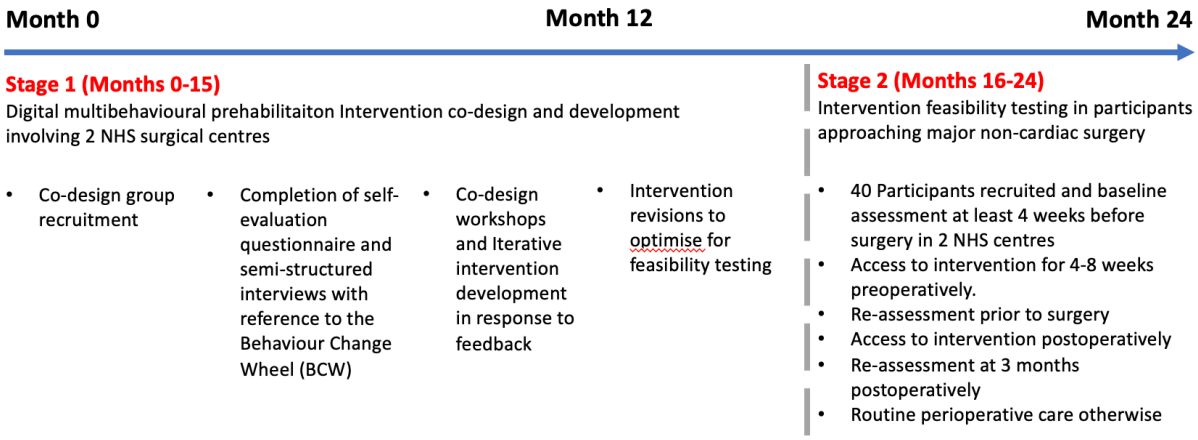
The digital multibehavioural intervention will comprise a web-based programme accessible via desktop, tablet and mobile phone. The programme and an accompanying training resource for HCPs will be co-designed with patients and HCPs to facilitate health behaviour changes toward improved preoperative physical and mental health and wellbeing and reduced perioperative risk.

It will provide structured support to facilitate simultaneous multibehavioural change. The intervention will include a number of components designed to run over the 4-8 weeks prior to surgery. These may inlcude:

- Structured exercise (aerobic, resistance and inspiratory muscle training)
- Smoking cessation
- Reduction of alcohol intake
- Improved nutrition
- Engagement in self-management behaviours to improve psychological health and wellbeing (reduction of stress, anxiety and depression)
- Sleep duration and quality

Ethical approval to commence stage 2 will be sought via substantial amendment pending progress through stage 1

1.3. Study flowchart



1.4. Timescales

Stage 1: Months 1-15
Stage 2: Months 16-24 (pending ethical approval by substantial amendment and stage 1 outcomes)

1.5. Participants and sample size

Up to **110** participants will take part in the co-design process recruited between the James Cook University Hospital and The York Hospital. This will include up to 55 patient participants and 55 HCP participants. Patient and HCP participants may be recruited to undertake specific components of the development process or to obtain their views on a specific aspect of programme development.

This number represents an absolute maximum. Participant numbers are likely to be far lower as individuals will be invited to take part in multiple aspects of stage 1, the required sample sizes for COM-B quesitonnaires and interviews will be guided by interim analysis after the 1st 20 participants up to a maximum of 40:

- Semi-structured interviews (**20-40** participants)
- COM-B questionnaires for behavioural analysis (**20-40** participants)
- Co-design workshops (up to **25** participants)

Patient participants will include patients approaching or having undergone recent major surgery and HCPs from the wider perioperative teams at both sites. Other stakeholders relevant to later intervention implementation will also be invited to participate.

1.6. Setting

Development of the intervention conceptual overview and co-design workshops will be conducted face-to-face at the James Cook University Hospital and The York Hospital or online via a video-conferencing platform.

1.7. Outcomes

1. A co-designed, theory and evidence informed web-based (digital) multibehavioural prehabilitation intervention to target improvements in health and wellbeing prior to major surgery.

2. A co-designed, theory and evidence informed training resource for HCPs.

3. A framework for future intervention evaluation.

1.8. Funding

This project is funded by grants from Macmillan Cancer Support and Sport England.

2. Background and rationale

Major surgery is frequently a life enhancing or lifesaving health event. However, the 'average' patient undergoing major surgery is aged 67[1], has two chronic health conditions[1] and is unprepared for the physiological demand of their operation[2]. Modifiable health risk behaviours are common in this group including: Inactivity 33-45%[3], smoking 13%[4], excess alcohol consumption 23%[5] and a poor diet causing malnutrition 33%[6]. These factors increase perioperative risk up to 5-fold[3-6]. Our prior research has highlighted the scale of this problem: 90% of preoperative patients have at least one risk behaviour, with clustering of ≥2 in 40%[7].

This leads to sub-optimal outcomes in patients undergoing highest risk 'major' surgical procedures, involving the opening of a main body cavity. UK 30-day mortality following major surgery is 3.5-4%[8] with postoperative complication rates (e.g. cardiopulmonary, kidney and wound problems) of 15-40%[9]. Furthermore, essential preoperative treatments prior to major cancer surgery (e.g. chemoradiotherapy) undermine physical and mental health, compounding risk[10-11].

The NHS performs eight million surgical procedures annually at a cost of £11 billion[12]. Major surgery (1.4 million procedures[12]) accounts for much of this cost, reflecting increased incidence of complications (15-40%[9]) and resulting prolonged hospitalisation[1]. A single organ complication following major surgery increases length of stay from 8 to 21 days[1]. Failing to fully prepare patients for major surgery has substantial costs for the NHS and social care services.

Patients with better physical[3], nutritional[6] and mental health[13] are more likely to survive surgery[14], develop fewer, less severe complications, and experience a quicker, more complete recovery[3,6,13-14]. In the short term, complications increase length of stay[1] and risk of readmission[15]. Longer-term, they undermine physical and mental health, threaten functional status[16], postoperative independence[16] and health-related quality of life (HRQOL)[17-18].

We have identified the preoperative period as a psychological 'teachable moment' to facilitate single and multibehavioural change[7]. Patient motivation and volition to change single and multiple behaviours are enhanced by the short-term need to support recovery. However, lower confidence levels indicate structured support is required for patients to achieve change.

Evidence continues to build for structured intervention to capitalise on this and improve physical and mental preparedness for surgery. This is 'Prehabilitation'[19-20]. Interventions including structured exercise training, smoking cessation programmes, reduction in alcohol intake, nutritional support, interventions to improve sleep quality and preoperative psychological wellbeing may form part of a multimodal prehabilitation programme.

Despite several examples of successful face-to-face prehabilitation programmes[21-22], limited support is presently available nationwide. Only 5-6 directly supervised UK services currently exist. Elsewhere, Public Health programmes are insufficient, frequently target single risk behaviours in isolation and are not tailored to the specific requirements and timeframes of the pre-surgical population. A national collaboration between Macmillan Cancer Support, the NIHR and Royal College of Anaesthetists has highlighted an urgent need to address this shortfall and improve outcomes[23].

Past and current prehabilitation research has focussed on face-to-face support. However, our prior work has underlined the demand for remotely supervised alternatives. Barriers to face-to-face support included: Travel difficulties, other weekday commitments and discomfort in a group environment. One-third of patients in our study[7] preferred remotely supervised support, echoed in feedback from our clinical programmes. Of 160 patients approached to participate in one established face-to-face prehabilitation programme, 50% declined due to work commitments/travel difficulties[22].

The Covid-19 pandemic has brought this unmet need into focus. All face-to-face services have been suspended, forcing clinical teams to rapidly provide remote support to hundreds of patients without guidance or evidence-based alternatives. Social restrictions and self-isolation have affected health behaviours in the population (e.g. increased alcohol consumption[24], reduction in physical activity[25] and increased mental health issues[26]) with a disproportionate impact on those awaiting surgery. Preoperative waiting times are extended for at least 12 months following cancellation of approximately 750,000 surgical procedures. Consequently, a 'generation' of unsupported, isolated and anxious patients will approach surgery unprepared and at greater risk[27].

Evidence to support the use of digital technology in older adults is building. National statistics demonstrate that 75% of UK adults aged 65-74 years (cf. 'average' surgical patient) used the internet in the past 3 months and usage amongst adults over 75 increased from 20 to 40% between 2011-2017[28]. The Covid-19 crisis has markedly increased internet usage and highlighted the need to support older adults in utilising digital resources to prevent social isolation[29]. This was strongly supported by our prior PPI work: Participants confirmed widespread device ownership, internet access and increasing technology confidence. Our most recent research, a Discrete Choice Experiment exploring preferences for remotely supervised prehabilitation underlines this. Unpublished findings demonstrate that 50% would prefer a digital alternative.

A digital intervention offers maximum flexibility for patients and staff. The format enables future scalability, can address the lack of prehabilitation provision nationally, and aligns with NHS demands for digital healthcare solutions and patient self-management/empowerment through care closer to home (specifically the NHSE Long-Term Plan[30] and Topol review[31]).

No rigorously developed digitally enabled prehabilitation interventions are currently available.

3. Study objectives

1. To gain consensus on the information content, methods of conveying information, and self-regulation tools incorporated within the digital prehabilitation intervention.
2. To gain consensus on the information content and methods of conveying information utilised in the HCP training resource.
3. To design a framework for intervention evaluation.

4. Study design and methods

In keeping with published guidance on digital intervention development[32] A mixed-method approach will be adopted. The Behaviour Change Wheel (BCW)[33]will be utilised in conjunction with the theoretical domains framework[34] and a Person-Based Approach[35] as the basis for intervention development (stage 1) and future feasibility testing (stage 2), including development of the HCP training resource. These frameworks combined allow identification of the specific behavioural domains that inform intervention development decisions, in turn guiding the selection of specific Behaviour change techniques (BCTs) for inclusion in the intervention.

A conceptual overview of the potential content of the intervention will first be developed drawing together and integrating findings from several sources, including:

- Consulting the evidence base for existing prehabilitation interventions and relevant behavioural interventions in other clinical settings.
- A previously undertaken (unpublished) Discrete Choice Experiment exploring patient preferences for behavioural intervention before surgery.

A co-design group will be recruited to work collaboratively with our multidisciplinary study team to iteratively develop the intervention throughout stage 1. We will aim to ensure balance across the group in terms of age, gender, ethnicity and socioeconomic deprivation.

Group members may be invited to complete a self-evaluation questionnaire informed by the COM-B model to facilitate a behavioural analyses, and a semi-structured interview.

This conceptual overview will inform a series of co-design workshops to develop the protype programme.

A prototype programme is currently in development by our multidisciplinary study design team including: Health psychologists, Perioperative clinicians, researchers with risk behaviour expertise and experience in intervention design and development alongside web developers. The prototype includes early versions of the risk behaviour interventions described above. This prototype will form a starting point for stage 1 of the developmental process.

4.1. Stage 1 eligibility

4.1.1. Inclusion criteria

Patient participants

- Adult patients (≥18 years of age).
- Within 3 months of having undergone major surgery or preparing for major surgery[36]
- Discharged from hospital to their own home.

Healthcare professional participants

- Perioperative team members currently caring for patients approaching major non-cardiac surgical intervention in the preoperative period.
- Employed at South Tees Hospitals NHS Foundation Trust or York & Scarborough Teaching Hospitals NHS Foundation Trust
- A medical, nursing or allied healthcare professional background or a wider stakeholder in perioperative care e.g. an individual with management or commissioning responsibility for perioperative services.

4.1.2. Exclusion criteria

Patient participants:

- Unable to provide informed written consent
- Currently receiving end-of-life care
- Difficulty understanding or communicating in written or spoken English

4.2. Stage 1 recruitment and consent

4.2.1. Patient participants

A list of potential patient participants approaching or having undergone major non-cardiac surgery will be identified by screening of surgical and anaesthetic preassessment clinic lists and electronic health records alongside communication with Macmillan cancer care coordinators. A stage 1 patient participant information sheet (PIS) will be sent by post inviting the patient to join a co-design group. Potential participants will be able to contact the study team directly by telephone or email to express an interest in taking part. Potential participants who do not contact the team will receive a follow-up telephone call 7 days following postage of the PIS to confirm receipt and enquire as to whether they are interested in taking part to allow completion of the screening log.

Those wishing to join the group as participants will complete the stage 1 patient participant consent form prior to any data collection.

Patient participants will be recruited from both hospital sites. The total number of participants will be guided by the developmental process and participants may wish to contribute to all 3 aspects of stage 1 data collection (self-evaluation questionnaire; semi-structured interview and co-design workshops):

- 10 patient participants will initially be invited to complete a COM-B self-evaluation questionnaire, increasing up to 20 participants guided by interim analysis.
- 10 patient participants will initially be invited to undertake a semi-structured, interview, increasing up to 20 participants guided by interim analysis.
- 10-15 patient participants will be invited to contribute to co-design workshops.

We will ask participants to undertake either:

1. Completion of the COM-B questionnaire and a semi-structured interview.
2. Questionnaire, interview and to participate in the co-design workshop series.

We also anticipate that participants may wish to bring a partner, family member or one other person with them to attend co-design workshop sessions or contribute to interviews. We would welcome their contributions to the co-design process, and we will ask individuals attending in support of patients to also complete the stage 1 patient participant consent form in order that their contribution to workshops can be recorded, analysed and used to inform intervention development.

The total number of stage 1 patient participants will not exceed 55 (not including partners/supporting individuals) and is likely to be fewer than this due to individuals participating in multiple components.

4.2.2. Healthcare Professional participants

Potential HCP participants and other stakeholders in perioperative services at both participating sites will be approached by email with a HCP participant information sheet (PIS) inviting them to join the co-design group. Potential participants will be able to contact the study team directly by telephone or email to express an interest in taking part.

Those wishing to join the group as participants will complete the HCP participant consent form prior to data collection.

Anticipated HCP participant numbers mirror patient participants and it anticipated that HCPs will undertake multiple elements of the process:

- 10 HCP participants will initially be invited to complete a COM-B self-evaluation questionnaire, increasing up to 20 participants guided by interim analysis.
- 10 HCP participants will initially be invited to undertake a semi-structured interview, increasing up to 20 participants guided by interim analysis.
- 10-15 HCP participants will be invited contribute to the co-design workshop series.

The total number of HCP participants will therefore also not exceed 55 and is expected to be fewer than this number reflecting individual participation in multiple components.

HCP participants will also be asked to undertake either:

1. Completion of the COM-B questionnaire and a semi-structured interview.
2. Questionnaire, interview and to participate in the co-design workshop series.

4.3. Stage 1 study activities and data collection

Following the consent process, patient participant information will be collected using a paper CRF. These will be stored securely in the study site file on NHS premises and later converted to an electronic pseudo anonymised format for secure storage on NHS and university servers.

- Demographic details
    - Sex (Participants of any gender will be eligible to take part)
    - age
    - marital status
    - employment status
    - postcode (for calculation of the index of multi-deprivation)
    - prior educational attainment against ONS criteria
- Digital technology utilisation information:
    - Devices owned/accessible at home
    - frequency of device utilisation
    - frequency and duration of internet access and utilisation
    - Prior use of digital health behaviour change interventions
- Clinical details
    - Prior surgical procedure and dates
    - Preoperative and postoperative risk behaviour profile relevant to the intervention e.g. physical activity level, smoking status.
    - Comorbidity profile
    - Details of prehabilitation activity undertaken before surgery

A brief paper CRF will also be completed with HCP participants focussed upon their professional background, role in preparation of patients for major surgery and any prior training or expertise with behavioural and lifestyle change interventions.

4.3.1. Behavioural analysis (COM-B self-evaluation questionnaires)

A behavioural analysis will be conducted with stage 1 participants using COM-B Self-Evaluation Questionnaires[33] aiming to identify behavioural determinants of promoting uptake, and completion of the programme by patient participants and supporting delivery of the programme by HCP participants. 10 patient and 10 HCP participants will complete questionnaires initially which may increase to 20 patients and 20 HCPs as required.

4.3.2. Semi-structured interviews

Participants will be invited to take part in a semi-structured interview lasting up to 60 minutes duration, structured by a topic guide that will be drafted and further informed following responses generated by the COM-B self-evaluation questionnaire.

Interviews will be audio-recorded on an encrypted digital recorder, transcribed verbatim and thematically analysed using the TDF as a starting point thematic framework. In accordance with established principles for data saturation in theory-based interview studies[37] 10 patient and 10 HCP participants will be interviewed initially and an interim analysis conducted. If new ideas/themes emerge by the tenth interview, an additional 3 patients and/or HCPs will be interviewed and the analysis process repeated. This process will be repeated for up to 20 patients and/or 20 HCPs, where it is expected that data saturation will have been reached. Findings from interviews and consultation with relevant literature will inform the prototype programme and a draft training resource, which will be used as a basis for discussion during co-design workshops.

Audio recordings will be stored securely on NHS or university servers and accessible only to study team members. An approved transcription service will convert the audio files to pseudo anonymised transcript files for analysis.

4.3.3. Co-design workshops

A series of structured co-design workshops will be undertaken. Sessions will include patient and HCP participants with facilitation by at least two members of the multidisciplinary study team. To ensure participation of all group members, no more than 25 participants (patients and HCPs) will take part in each workshop.

In recognition of current uncertainty and ongoing risk to participants from Covid-19 over the projected duration of the project, face-to-face and remote participation will be offered. Face-to-face participation will take place at the participating sites in venues able to support required social distancing and Covid-safe measures.

All workshops will be audio recorded electronically with recordings stored securely at NHS or university sites prior to, during and after transcription. Remote sessions will be conducted using a video-conferencing platform supporting local, secure recording and storage of meetings onto secure NHS and University servers (e.g. Zoom/Microsoft teams). Detailed notes will be taken to document the ways in which group members engage with activities in order to understand how and why key decisions were made.

The total number of sessions required will be determined by the requirements of the co-design process. Members are likely to be invited to attend up to 6 workshops each lasting up to 2 hours to inform the iterative development and optimisation of the intervention. Attendees at sessions will usually be a mixture of patient and HCP participants, however patient or HCP specific sessions may be scheduled if required.

Each workshop will begin with a brief introduction and overview of the sessions aims and objectives. The total workshop series will progress through the following key areas in sequence:

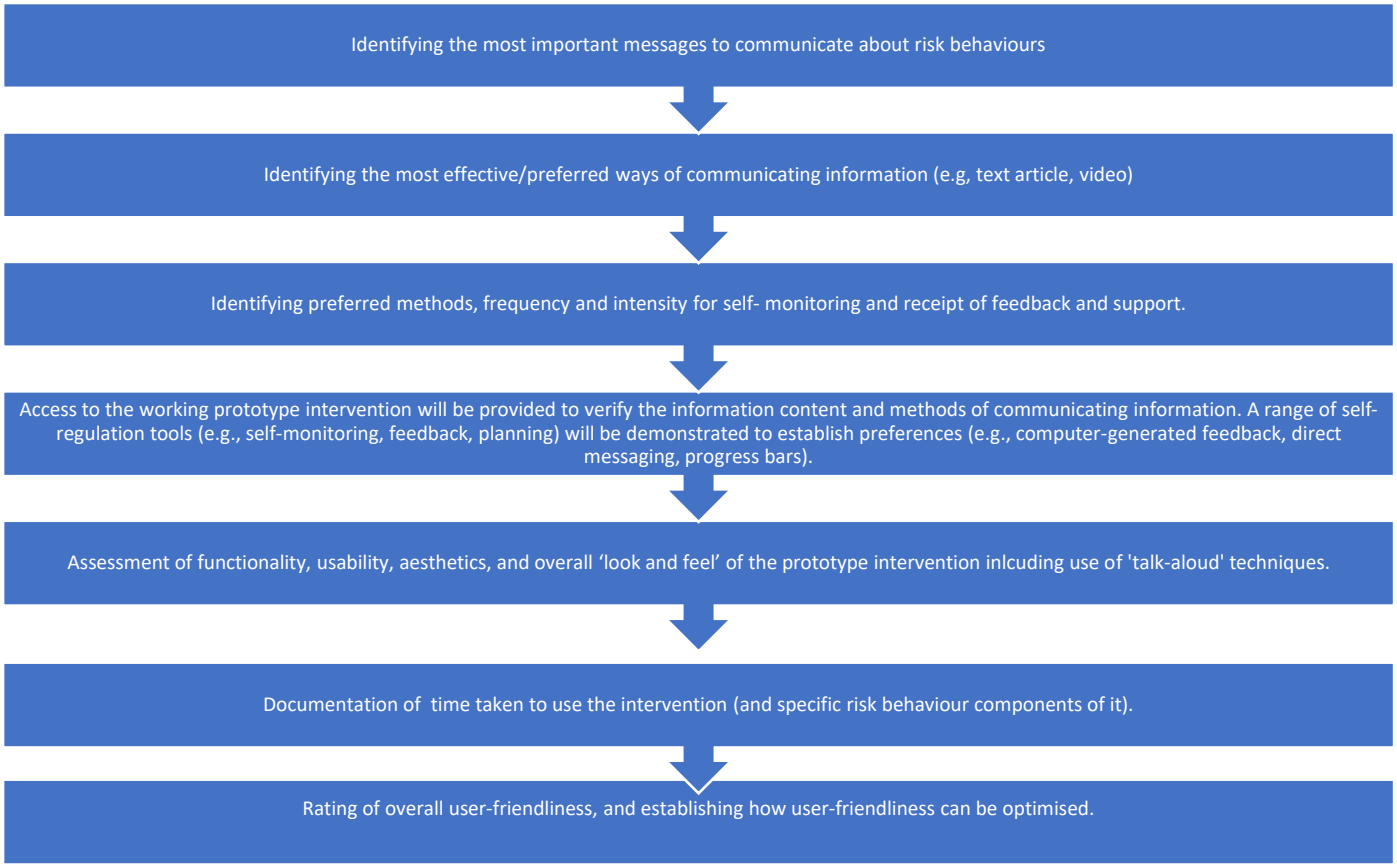


Fig 1: Co-design workshop content

The workshop series will allow review the prototype intervention and draft training resource as they progress, allowing iterative development and optimisation prior to feasibility testing (phase 2).

Audio recordings and transcripts will be stored securely on NHS or university servers and accessible only to study team members

One patient participant from the group will be invited to join the study management group for stage 2 of the project

4.4. Data analysis

4.4.1. Participant semi-structured interviews

All Interviews will be audio recorded and transcribed verbatim. Interview transcripts will be thematically analysed using the Theoretical Domains Framework (TDF)[34]. A two-stage process will be followed. The first interview transcript will be pilot-coded independently by two study team members to agree a coding strategy. Initial findings will be discussed before coding the remaining transcripts. Following this, data from the remaining transcripts will be independently coded by the same two team members. This will involve reading and re-reading transcripts, coding content into themes/subthemes, and mapping these, with supporting direct quotes, to an appropriate theoretical domain of the TDF.

Where data does not fall into a specific domain, additional themes will be generated to reflect the whole data set. One researcher will code/analyse all interview data, 20% coded by a second researcher, with peer review input from the wider team when assigning theme labels. Identification of behavioural determinants of both patients and HCPs, barriers and enablers of behavioural change (using the TDF) will facilitate a 'mapping' process. This will ensure appropriate BCTs are selected for inclusion in the intervention with reference to the Behaviour Change Taxonomy v1[38], and delivery plans will be documented using the Template for Intervention Description and Replication (TIDieR) Framework[39] .

4.4.2. Co-design workshops

In addition to facilitator notes taken during sessions, transcripts will be reviewed with further note taking to ensure all key decision points and drivers were captured and no key details were missed relevant to intervention development.

4.5. Participant discontinuation/withdrawal

Participants will be free to withdraw from the study at any stage without providing a reason.

Participant discontinuation will occur with any of the following:

- Completion of the study protocol
- Illness requiring hospital readmission
- Death of a participant or commencement of end-of-life care
- Loss of capacity to consent to continue participation
- Participant decision to withdraw
- Investigator decision
- Study management group or chief investigator decision

If a patient wishes to withdraw or is discontinued from the study, the following procedures will be observed:

- Withdrawal of consent/ discontinuation of the study will be clearly documented in study documentation and the participant's medical record.
- No further data will be collected from the participant. However, existing data held will be retained and used for the study.

5. Data handling

Study data will be securely collected, stored and analysed as described below and in accordance with data protection laws. Informed consent will be obtained to cover this activity. This is described in the study Participant Information Sheet. Participants will also consent to inspection of their data and/or medical records by regulators.

Data will be checked for accuracy, consistency and completeness by manual or electronic checks. Discrepancies in the data will be brought to the attention of the study team as necessary. Resolutions to these issues will be reflected in the dataset.

If the results of the study are published, the subject's identity will remain confidential. The investigator will maintain a list based on screening logs to enable subjects' records to be identified.

5.1. Data collection, storage, access and transfer

Participant paper CRFs, completed COM-B questionnaires and workshop facilitator notes will be stored securely in the site files in locked offices on NHS premises. Paper data will converted to a password protected electronic formats (e.g. Microsoft excel/Microsoft word)

Interview and workshop audio recordings will be transferred from their encrypted recorders and stored securely on NHS servers with password protection. Audio files will be converted to a pseudo anonymised password protected transcript file by an approved transcription service for subsequent transfer and analysis. A data management agreement will be in place between the transcription service and sponsor. Once transcribed, original audio files will be deleted.

Direct access to data will be granted to authorised representatives from the Sponsor, academic institutions and the regulatory authorities to permit study-related monitoring, audit and inspections.

Whilst data will be pseudo-anonymised prior to transfer to study team members at partner academic institutions for storage and analysis, specific informed consent will be sought from participants allow

Transfer of pseudo anonymised data will be between secure institutional email accounts e.g. nhs.net to ac.uk.

5.2. Confidentiality

All study team members must comply with the requirements of The Data Protection Act 2018 and General Data Protection Regulations 2018 regarding the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. Any personal data recorded will be regarded as confidential, and any information which

would allow individual participants to be identified will not be released into the public domain.

5.3. Archiving

The study data will remain the property of South Tees Hospitals as per the data agreement. A complete copy of the study data will be kept on the trust secure IT service at the end of the study. At the end of the study, all documents and data relating to this project will be stored securely at the trust for 5 years following project completion.

Sites must retain source data and documents associated with this clinical trial until the Sponsor provides written permission to destroy the documents. The Chief Investigator must notify the Sponsor if he/she wishes to assign the essential documents to someone else, remove them to another location or is unable to retain them for a specified period.

6. Administrative, Ethical and regulatory compliance

6.1. Study Sponsor

South Tees Hospitals NHS Foundation Trust, James Cook University Hospital, Marton Road, Middlesbrough, TS4 3BW will be the study sponsor. Study management responsibilities will be delegated to the chief Investigators and study team.

6.2. Peer review

This project has been peer reviewed as part of a competitive application for funding. In addition, the protocol is planned for submission for publication in a peer-reviewed journal.

6.3. Funding body

This study is funded Jointly by Macmillan Cancer Care and Sport England.

6.4. Ethical approval

No study activity will be undertaken until ethical approval has been confirmed. The study protocol and associated documentation have undergone assessment by a HRA Ethics Committee (North West- Preston Research Ethics Committee 21/NW/0219). Progression to stage 2 of this study will be by substantial amendment.

6.5 Participating sites

Participating sites have been pre-selected and will confirm capacity and capability prior to commencement. All investigators and key study personnel will have undertaken Good Clinical Practice (GCP) training appropriate to their role.

The study will be conducted in accordance with, but not limited to, ICH/GCP, the Human Rights Act 1998, The Data Protection Act 2018/General Data Protection Regulations 2018, Freedom of Information Act 2000 and the UK Policy framework for Health and Social Care research.

Participants will be informed of how data are recorded, collected, stored and processed, in accordance with The General Data Protection Regulation (GDPR) (EU) 2016/679.

6.6. Participant and public involvement

This study protocol and the prototype digital platform are the direct result of a prior body of PPI activity conducted by the study team with patients approaching major surgical intervention and participants in an existing face-to-face prehabilitation service. Patients are central to the stage 1 co-design process and at least one patient representative from the stage 1 participant development group will be invited to sit on the study management group prior to commencement of stage 2.

6.7. Study monitoring and interim reporting

A study management group (SMG) will be established by the chief investigators prior to the commencement of stage 2 with representation from the sponsor, participating sites and institutions and research partners. The group will oversee conduct of the feasibility study and meet on a regular basis as required.

remote monitoring of data will be performed. Triggered monitoring, or audit, may be performed if required. Routine monitoring of stage 2 will occur in accordance with the sponsors protocols.

The investigators will permit study related monitoring, audits, HRA/ REC review, providing direct access to all data and documents as required. South Tees Hospitals NHS Foundation Trust has accepted the role of sponsor of the study and will put in place appropriate governance and oversight arrangements

6.8. Protocol Compliance

Intentional protocol deviations are not permitted under any circumstances. The study team will record technical/minor deviations. Deviations will include isolated issues that do not put participants at risk of harm nor risk data credibility. The sponsor will be notified of other deviations significantly impacting the risk profile of the study or significantly interrupting study services or supplies. Identified or suspected serious breaches of the study protocol or principles of GCP will be notified to the Sponsor.

6.9. Protocol Amendments

Planned research activity changes will require an amendment initiated by the chief investigators. Proposed changes will be submitted in writing to the sponsor. Amendments will be categorised as substantial or non-substantial.

Required changes in documentation following original ethical approval will also be submitted as an amendment to the Health Research Authority (HRA) by the study team. Substantial amendments will not be implemented until REC and HRA approval are provided if required.

An amendment history log will be maintained by the study team ensuring the most recent versions of the protocol and related documents are in use.

6.10. Liability and indemnity

The sponsor is an NHS organisation. The NHS indemnity scheme will apply in the event of harm to participants arising from the study management.

6.11. Study summary report

The study team and chief investigator are responsible for compiling and submitting the final study report to the sponsor and REC within one year of study closure.

6.12. Early dissemination of important safety findings

Any findings likely to impact patient care in a positive or negative manner will be fed back via research site governance structures

6.13. Publication policy

The study data will belong to South Tees Hospitals NHS Foundation Trust as sponsor. The chief investigator will act as the data custodian. The study results will be offered for publication in a peer reviewed journal, on behalf of all collaborators.

Participants will be given the option to request a summary of the study results if requested.

7. Adverse event reporting

7.1. Terms and Definitions

7.1.1. Adverse Events

An Adverse Event (AE) is defined as any untoward medical occurrence in a participant who has undergone a research procedure, including occurrences which are not necessarily caused by or related to that procedure.

7.1.2. Serious Adverse Events

A Serious Adverse Event (SAE) is defined as an untoward occurrence that:

- Results in death
- Is life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect
- Is otherwise considered medically significant by the investigator

7.1.3. Notes on Adverse Event Inclusions and Exclusions

The risk of AEs/SAEs relating to stage 1 of this project is felt to be low. We will ensure clear channels for participants to raise non-emergency concerns with the study team and how to access help.

Common Terminology Criteria for Adverse Events (CTCAE Version 5.0) grading will be used to assess adverse events and adverse device effects.

The safety reporting window includes AEs that occur from the time of participant consent to the end of their involvement in the study. AE and ADEs will be followed up until event resolution (for ADEs) or stabilisation.

Any adverse event included in the criteria outlined above will be documented in the study notes. The AE will be assessed for seriousness, causality and expectedness by a designated clinician.

Any adverse events identified which meet the criteria to be reported as an SAE will be recorded using the sponsor approved SAE form and submitted to the Chief Investigator within 24 hours of the study team becoming aware of the event. Upon receipt, the Chief Investigator will review the event and the following will be considered:

- Whether there is a causal link with study participation.
- Whether the event is, or is not expected.

The outcome of the assessment will be documented and filed in the trial master file and the sponsor informed.

7.2. Adverse events of Special Interest

There are no adverse events of special interest.

7.3. Reporting of Serious Adverse Events

An SAE occurring to a research participant will be reported to the REC where in the opinion of the Chief Investigator the event was:

- "Related" that is, it resulted from administration of any of the research procedures, and
- "Unexpected" that is, the type of event is not listed in the protocol as an expected occurrence

Related here refers only to SAEs resulting from the application of the biosensor.
Reports of related and unexpected SAEs will be submitted to the REC within 15 days of the Chief Investigator becoming aware of the event, using the 'Non-CTIMP safety report to REC form'. https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

A copy of the complete report and the REC acknowledgement will be forwarded to the sponsor.

8. Dissemination policy

It is expected that study data will be submitted as a whole or in part for presentation at national and international conferences and publication in peer reviewed journals.

Participants will be offered copies of any publications or presentations on request.

In addition the developed intervention and study outcomes will be publicised via Macmillan and Sport England channels.

9. Educational Projects

Dr Durrand is contributing to this project as a component of a Doctor of Philosophy (PhD) studentship at Northumbria University. Dr Durrand is expected to write up appropriate study activity and present appropriate study data as part of his thesis submission.

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