Protocol
V1.0 1st June 2022

1. Full title of study:

Mapping and Identifying Quality and Inequality in Prehabilitation for Cancer Surgery: Evidence for Improvement

1.1 Short title and acronym:

PARITY (**P**rehabilitation for c**a**ncer surge**r**y: quality and inequal**ity**)

1.2 Reference numbers

NIHR HS&DR: NIHR134282

Lancaster University Faculty of Health and Medicine Research Ethics Committee: REAMS 1063

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1.3 Key study contacts

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1.4 Contents

2. Summary of research:

Background: In the setting of cancer surgery, prehabilitation can be described as 'the practice of enhancing a patient's functional capacity before surgery, with the aim of improving postoperative outcomes.' Typically, prehabilitation focuses on physical activity, diet, and psychological support, alone or in combination.

In recent years prehabilitation has become an accepted component of many cancer surgery pathways. However, its evidence base is variable and descriptions of prehabilitation interventions are often imprecise, making it difficult to translate research into practice and compare services. Patients' views on how services are delivered vary, and little is known about what patients want from prehabilitation.

Because many prehabilitation interventions require engagement, time and access to facilities, they may not be acceptable or accessible to all. People from underserved and minority backgrounds often have worse health outcomes and prehabilitation has the potential to worsen these inequalities. This may stem from unequal access to exercise facilities, broadband internet, transport, and employment leave, for example.

Numerous service models for prehabilitation exist. Some are implemented on a regional basis, but many are delivered in a targeted fashion to specific patients. Different services are available to different people in different parts of the UK, and some have no suitable services available at all.

Aims: We aim to make a major contribution towards addressing the problems of variation and inequality in prehabilitation before cancer surgery. This will involve working with patients, carers and healthcare professionals to find ways to describe, measure and assess the quality of services. We will map these criteria on a national scale and identify and share best practice examples of how services are developed, funded, and delivered, as well as ways to address health inequalities.

Research questions: What prehabilitation services are available before cancer surgery? What defines quality in such services, and what values and assumptions underpin successful delivery? What inequities exist in provision, and how might they best be addressed?

Methods: We will use the Promoting Action on Research Implementation in Health Services (PARIHS) framework as an overarching explanatory structure (Rycroft-Malone et al 2002, Kitson et al 2008). Within this are four linked work packages.

WP1. Defining aims, objectives and values: we will work with patients, clinicians and researchers to co-develop criteria that describe what is important about prehabilitation, to characterise and evaluate services. Purposive sampling will be used to recruit participants who are appropriately representative of key stakeholders, and guided discussion will ensure that understanding and engagement is maintained. Consensus on the criteria will be achieved using a modified Delphi method (Taylor 2020).

WP2. Mapping: making use of the co-developed criteria and guided by the Template for Intervention Description and Replication (TIDieR) checklist (Hoffman et al 2014), we will produce a national map of prehabilitation services. This will also capture how services are funded, who delivers them, and how they are delivered. The mapping survey will be developed and piloted with NHS staff to ensure that it is usable and appropriate. In order to avoid disincentivising participation at a time of unprecedented clinical demand, completion of the survey is costed as an NHS research cost in the SOECAT.

WP3. Case studies: using the national map, we will sample services for in-depth analysis using case study methodology (Crowe et al 2011), including documentary analysis, interviews with patients, carers, and staff, and observations of practice. The topic guides for interviews and observations will be developed using the Promoting Action on Research Implementation in Health Services (PARIHS) framework (Rycroft-Malone et al 2002, Kitson et al 2008) and will incorporate the criteria developed in WP1. This will allow us to identify areas of best practice, including how inequalities are addressed, as well as understanding the contextual factors which make services 'work' (Williams and Glaseby 2010, Head 2008).

WP4. Informing policy and practice. We will integrate dissemination throughout the project, using both traditional (e.g., publication) and non-traditional (e.g., social media) techniques to inform and engage stakeholders. We will recruit a multidisciplinary reference group of professionals, system leaders and PPI representatives who will assist with dissemination and knowledge mobilisation, including by participating in the development of best practice principles drawing on the results of the project, using a modified nominal group process (Rycroft-Malone 2001, Masterson-Algar 2018).

Timelines: This study will be conducted over 30 months, comprising: months 1-2 study set-up, months 3-13 WP1, months 5-17 WP2, months 13-23 WP3. Robust preliminary findings will be made available for NHS use as and when they become available, as part of the ongoing dissemination work in WP4, which will run throughout the study, with the best practice principles developed between months 25 and 28, and presented in months 29 and 30.

Anticipated impacts and dissemination: Cancer surgery is common, being part of the treatment received by 45% of patients with a cancer diagnosis (National Cancer Registration and Analysis Service 2017) and there is scope for improvement in longer-term outcomes. This research will answer the call made by the NIHR, Royal College of Anaesthetists and Macmillan to "gather examples of how local areas have had prehabilitation commissioned as part of the cancer pathway". Effective prehabilitation has the potential to cost-effectively transform patients' lives before and after such surgery, and our work will allow this benefit to be extended to all patients, including those who may be otherwise disadvantaged or excluded.

3. Background and Rationale:

Prehabilitation has been defined as 'the practice of enhancing a patient's functional capacity before surgery, with the aim of improving postoperative outcomes' (Banugo and Amoako 2017). Typically, physical, behavioural and psychological interventions are used to enhance the patient's functional capacity prior to starting treatment. Cancer treatment often comprises recurrent major impacts, for example surgery in combination with chemotherapy (Banugo and Amoako 2017, Loughney et al 2016). Whilst prehabilitation has theoretical benefits in this setting, its evidence base in cancer care is variable. A 2016 systematic review in the context of neoadjuvant chemotherapy and surgery concluded that there is insufficient research "to draw reliable conclusions about the efficacy of such an intervention, the optimal characteristics of the intervention, or the impact on clinical or patient reported outcomes" (Loughney et al 2016). More recent reviews in settings of pancreatic cancer surgery and bowel resection are still drawing similar equivocal conclusions (Teo et al 2020, Bundred et al 2020).

Despite uncertain evidence, many healthcare providers offer prehabilitation programmes in the context of cancer care, most of which involve preparation for surgery. Though some are implemented on a regional basis, many are small-scale and limited to a particular service (Wynder-Blyth et al 2017). Whilst these interventions may be welcomed by those who receive them (Ferreira et al 2018), this localised approach creates the conditions for variation between regions, organisations, and diagnoses, thereby creating inequalities. Furthermore, patient preferences on mode of delivery have been found to vary (Durrand et al 2019), and little is known about what patients want from prehabilitation, and how this relates to the aims of those who design, commission and deliver services (Beck et al 2020).

This project aims to provide robust evidence to address the inconsistent and inequitable provision of prehabilitation prior to cancer surgery. This will be achieved by working with patients, carers and healthcare professionals to develop outcome measures against which prehabilitation can be measured, mapping and characterising existing services, and identifying case studies of good practice (e.g., Crowe et al 2011), in order to provide guidance for future service implementation. This is a vital step in moving towards the equitable provision of high-quality prehabilitation, and answers the call made by the NIHR, Royal College of Anaesthetists and Macmillan to "gather examples of how local areas have had prehabilitation commissioned as part of the cancer pathway" (2019). Furthermore, this project aligns with the strategic aims of the Centre for Perioperative Care, and addresses two questions identified in the James Lind Alliance priority setting partnership on anaesthesia and perioperative care: "how can preoperative exercise or fitness training, including physiotherapy, improve outcomes after surgery?", and "what outcomes should we use to measure the 'success' of anaesthesia and perioperative care?" (Boney et al 2015).

The idea for this study was discussed with the National Institute of Academic Anaesthesia Patient, Carer and Public Involvement and Engagement (PCPIE) group, who confirmed that in their experience, the provision for prehabilitation varies markedly between services and healthcare providers. Inequalities, for example based on ethnicity, socioeconomic and geographical factors, result in poorer outcomes following cancer care for people from underserved and minority backgrounds (Wiese et al 2019). Introducing prehabilitation into this landscape has the potential to exacerbate inequalities rather than narrow them, through disparities in access to infrastructures, technologies, and social and financial capital (e.g., Giles and Cummins 2019). An

example of this was shared by a member of the PCPIE group, who noted that though his local hospital provides a gymnasium for prehabilitation, the need for patients to travel to this facility compounds inequalities based on access to transport, funds, and time off work. The PCPIE group considered that addressing inequalities should be a key facet of this study and suggested that those patients who did not participate in prehabilitation must nevertheless be represented.

COVID-19 presents numerous challenges to the delivery of prehabilitation and may yet further exacerbate inequalities due to disparities in access to telemedicine and the closure of municipal exercise facilities (Bambra et al 2020, Silver et al 2021). Furthermore, the cessation and recommencement of elective surgery in response to 'surges' of COVID-19 can make scheduling unpredictable (Glasbey et al 2021). The effect of COVID-19 was identified as a key issue by the PCPIE group, who noted that service changes implemented in response to the pandemic may disrupt delivery of care. This project will aim to describe the ways prehabilitation has adapted to the pandemic, including how health inequalities are addressed.

Prehabilitation is based on specific goals, ideals, and medicalised understandings of healthcare behaviours. For example, one purported benefit is that patients may 'better understand' their surgery, implying ignorance with the potential to assign blame. Part of this study will be to examine the values underpinning programmes and the assumptions underpinning design.

3.1 Literature review

In order to summarise the existing research on prehabilitation prior to cancer surgery, MEDLINE, CINAHL, PsychINFO and the Cochrane Database of Systematic Reviews were searched. Titles and abstracts were searched for (prehabilitation or prehab or pre-operative rehabilitation or preconditioning) and (cancer or malign* or carcinoma or neoplas*) and (review of literature or literature review or meta-analysis or systematic review or review). Duplicates, narrative reviews and systematic reviews not concerned with prehabilitation prior to cancer surgery were excluded. This resulted in the retrieval of 21 systematic reviews which are summarised below. Additionally, the text and reference lists of the included reviews were hand-searched to identify relevant individual studies.

In order to identify any previous studies of prehabilitation using similar methodology to our own, we additionally searched MEDLINE, CINAHL and PsychINFO for (prehabilitation or prehab or pre-operative rehabilitation or peri-operative rehabilitation), and (case study or case studies), or (map*), or (survey*). However, this resulted in the retrieval of no relevant papers. We are, however, aware of two recent small surveys of prehabilitation in the UK and Scotland, one of which has been published as an abstract (Carter et al 2019), and the other as part of an NHS Scotland policy document (Transforming Cancer Care Prehabilitation Short Life Working Group 2020).

3.1.1 Exercise-based prehabilitation

Most prehabilitation programmes that have been reported in the literature involve some sort of physical training. These can be broadly divided into programmes that aim to improve cardiorespiratory fitness, and those which aim to target a specific post-operative complication. Of these approaches, targeting specific post-operative complications appears to have a more convincing evidence base, though in limited settings. For example, pelvic floor muscle training has consistently been associated with improved urinary continence in prostate cancer surgery (Treanor et al 2018, Faithfull et al 2019), and respiratory muscle training likewise reduces the risk of postoperative pulmonary complications in surgery involving chest wall incisions, such as lung cancer surgery (Rosera et al 2019, Cavalheri and Granger 2017, Bolger et al 2019). However, not all cancer surgeries are associated with complications that are amenable to targeted pre-operative training, and the evidence for interventions to improve general cardiorespiratory fitness is less consistent.

Most reviews conclude that aerobic exercise results in improved physiological measures of fitness such as six-minute walk distance and cardiopulmonary exercise testing variables (Faithfull et al 2019, Michael et al 2021, Bolshinsky et al 2018, Waterland et al 2021, Hijazi et al 2017), and the 'physical' elements of quality-of-life assessments score higher amongst patients undertaking physical training (Chou et al 2018). However, there is less consistent evidence that this translates into patient benefits. Some reviews have found that length of hospital stay and complications are reduced with aerobic exercise (Waterland et al 2021, Lambert et al 2021), but this is not a consistent finding (Bruns et al 2016, Looijaard et al 2018, Piraux et al 2021,

Thomas et al 2019), which may be due to the wide variety of aerobic exercise interventions offered. Studies describe varying types of supervision (supervised, unsupervised and hybrid), location (home, hospital, gymnasium), duration (between five days and six months) (Brundred et al 2020), exercise intensity, session length (from 30 to 210 minutes) (Michael et al 2021), combination with other modes of prehabilitation, and treatments such as neoadjuvant chemotherapy. This makes studies of exercise-based interventions challenging to synthesise, and therefore translate into practice.

An important finding studies of exercise-based prehabilitation is the variability in recruitment and completion of programmes. Michael et al (2021) noted that between 46 and 100% of patients offered the opportunity to participate in studies agreed to do so, and between 47 and 100% of those recruited completed the studies. The authors reported that commonly-cited reasons for patients declining to participate included low interest, work or time constraints, physical or medical contraindications, and access to transport, and noted that studies in colorectal cancer appeared to recruit a greater proportion of patients than those in oesophagogastric cancer. This suggests that some forms of prehabilitation are more acceptable to patients than others, and that some types of cancer may make prehabilitation more challenging. Lambert et al (2021) noted in their review that compliance and adherence and attendance were poorly-reported, raising the possibility that those patients who were most 'determined' or 'able' to complete prehabilitation may be over-represented in the data. These observations underline the potential of prehabilitation to widen health inequalities and serve some patient groups better than others.

3.1.2. Nutrition-based prehabilitation

Many patients with a cancer diagnosis experience weight loss and have nutritional deficiencies, and there is therefore a clear rationale for nutritional prehabilitation. Approaches include pre-surgery supplementation with carbohydrates, proteins, iron, and substances intended to modulate the immune response to cancer and surgery such as omega-3 fatty acids (Bolshinsky et al 2018, Lau and Chamberlain 2020). When applied in a uniform fashion as in a trial protocol, however, individuals may be provided supplements that they do not require, as noted by Bruns et al in their review of nutritional prehabilitation for colorectal cancer surgery (2018). They contend that whilst most studies in their review provided carbohydrate-based supplements, protein deficiency is more common amongst patients with colorectal cancers and a more individualised approach to nutrition may therefore be warranted. Like exercise-based prehabilitation however, even when targeted nutrition was provided, improvements in physiological measurements did not necessarily translate to patient-centred outcomes. Indeed, Bolshinsky's 2018 review of iron supplementation in abdominal cancer surgery demonstrated a reduction in the incidence of pre-operative anaemia, but no consistent improvement in patient-centred outcomes.

Most reviews of nutrition-based prehabilitation are equivocal, likely hampered by the heterogeneity of interventions (e.g., Treanor et al 2018). For example, the authors of a review of nutritional interventions prior to lung lobectomy concluded that this approach may improve postoperative outcomes but noted that "the length of the interventions ranged from 10 to 35 days with a variety of supplements including an immune-modulating formula, [branched-chain amino acid supplements], herbal remedies, and whey protein." Further, they found that the description and reporting of interventions was limited, with no studies reporting the energy content of the supplements, only one reporting the protein content, and only two reporting the adherence of participants (Ferreira et al 2020).

In contrast to exercise-based prehabilitation, nutritional prehabilitation appears to have consistently high rates of acceptability to patients, with Bruns et al (2018) reporting study compliance rates of between 72-100%.

3.1.3. Psychological prehabilitation

Psychological prehabilitation prior to cancer surgery typically comprises stress management or relaxation techniques, education, counselling or a combination of these approaches. Like other forms of prehabilitation there is marked heterogeneity of interventions, and multiple outcome measures are used, making it difficult to compare or combine findings. Though it is often provided in combination with other forms of prehabilitation, there are several reviews that evaluate purely psychological approaches. Tsimopoulou et al (2015) found benefits in some patient-reported outcomes and immunological function, though no improvement in 'traditional' outcome measures such as length of stay and surgical complications. Chou et al (2021) examined

of the impact of prehabilitation on quality of life, considering psychological prehabilitation as a sub-group. They found that although one study of a stress management programme in the setting of breast cancer surgery indicated improved quality of life (Garssen et al 2013), the others did not. Noting that this study involved more and longer sessions of prehabilitation, they suggested that the number and duration of prehabilitation interventions may be important in achieving improvements in quality of life.

3.1.4. Literature review summary

The systematic reviews and meta-analyses included in our literature review mirror the current uncertainties in the clinical delivery of prehabilitation: different interventions are delivered in various settings, evaluated inconsistently and with little comparison of patient-centred outcomes. Furthermore, it can be seen that some cancer types (e.g., colorectal, lung) have a more comprehensive evidence base than other common cancer types such as gynaecological and head-and-neck cancers. However, the main deficiency of most studies of prehabilitation is that they focus on the clinical elements such as physical activity, nutrition and psychological support. These are all essential, but not in themselves sufficient to create a prehabilitation service that is effective 'in the round' and which reaches everyone it needs to reach. This gap in knowledge about contextual service delivery is what our project will address.

3.2. Evidence explaining why this research is needed now:

This research is needed now because: 1) prehabilitation prior to cancer surgery is not available in all centres, and where it is available its implementation is highly variable; 2) there is a knowledge gap regarding what constitutes quality in prehabilitation; and 3) health inequalities in the UK have widened in recent years, and there is a risk that prehabilitation may further contribute to this problem.

There is clear evidence of a 'postcode lottery' of prehabilitation services prior to cancer surgery in the UK. Some centres do not offer any type of prehabilitation, others offer services only to specific patients, and others make prehabilitation available on a universal basis (Carter et al 2019, Transforming Cancer Care Prehabilitation Short Life Working Group 2020). In centres where prehabilitation is available, it is uncertain whether a targeted or universal approach is more appropriate; where prehabilitation is implemented widely it is likely that it is being employed far beyond its evidence base. Whilst there is little evidence that prehabilitation causes harm (Michael et al 2021), a universal approach may represent a burden for patients without benefit or divert resources away from more effective interventions.

As outlined in the literature review above, although there is a growing understanding of the benefits of some elements of prehabilitation, there is a dearth of understanding regarding service delivery in context. This problem is compounded by the limited capacity of prehabilitation services to audit or evaluate their programmes (Carter et al 2019). As a consequence, the effectiveness and impacts of the approaches currently implemented will continue to be unknown unless research is conducted to establish what services are available and identify best practices.

The UK has experienced rising health inequalities in the last decade (Marmot et al 2020). These have been further exacerbated by the ongoing COVID-19 pandemic (e.g., McKee et al 2021), which has thrown into sharp relief the influence of ethnicity, employment and housing on health. As a complex intervention that requires time, motivation and engagement, prehabilitation has the potential to be more accessible to some patients more than others, even if it is offered to all. During the COVID-19 pandemic, services have been rapidly reorganised, for example moving in-person delivery online (e.g. Raman et al 2021). This creates the potential to further exacerbate inequality based on technological literacy and access to facilities such as broadband internet and a quiet environment in which to engage with online content. As the COVID-19 pandemic has entered an endemic phase, it is likely that prehabilitation services will never return to their prior form. There is therefore a pressing need both to assess how prehabilitation services can best address both new and established health inequalities.

4. Aims and Objectives

4.1 Study Aim

The aim of this study is to understand what constitutes quality, and how healthcare inequalities may be best addressed, in prehabilitation prior to cancer surgery. This will provide a basis for establishing equitable prehabilitation services, regardless of patients' geographical location or circumstances.

4.2 Study Objectives

1. Define the aims, objectives and values of prehabilitation prior to cancer surgery from the perspectives of patients, carers and professionals (WP1)

2. Produce a map and descriptive compendium of the prehabilitation services that are currently available in the UK for patients awaiting cancer surgery, according to geography, funding, commissioning and delivery (WP2)

3. Understand how various models of prehabilitation work in practice, to achieve the aims and objectives and uphold the values deemed important to stakeholders (WP3)

4. Inform the policy and practice of prehabilitation prior to cancer surgery through knowledge mobilisation (WP4)

4.3 Research Questions

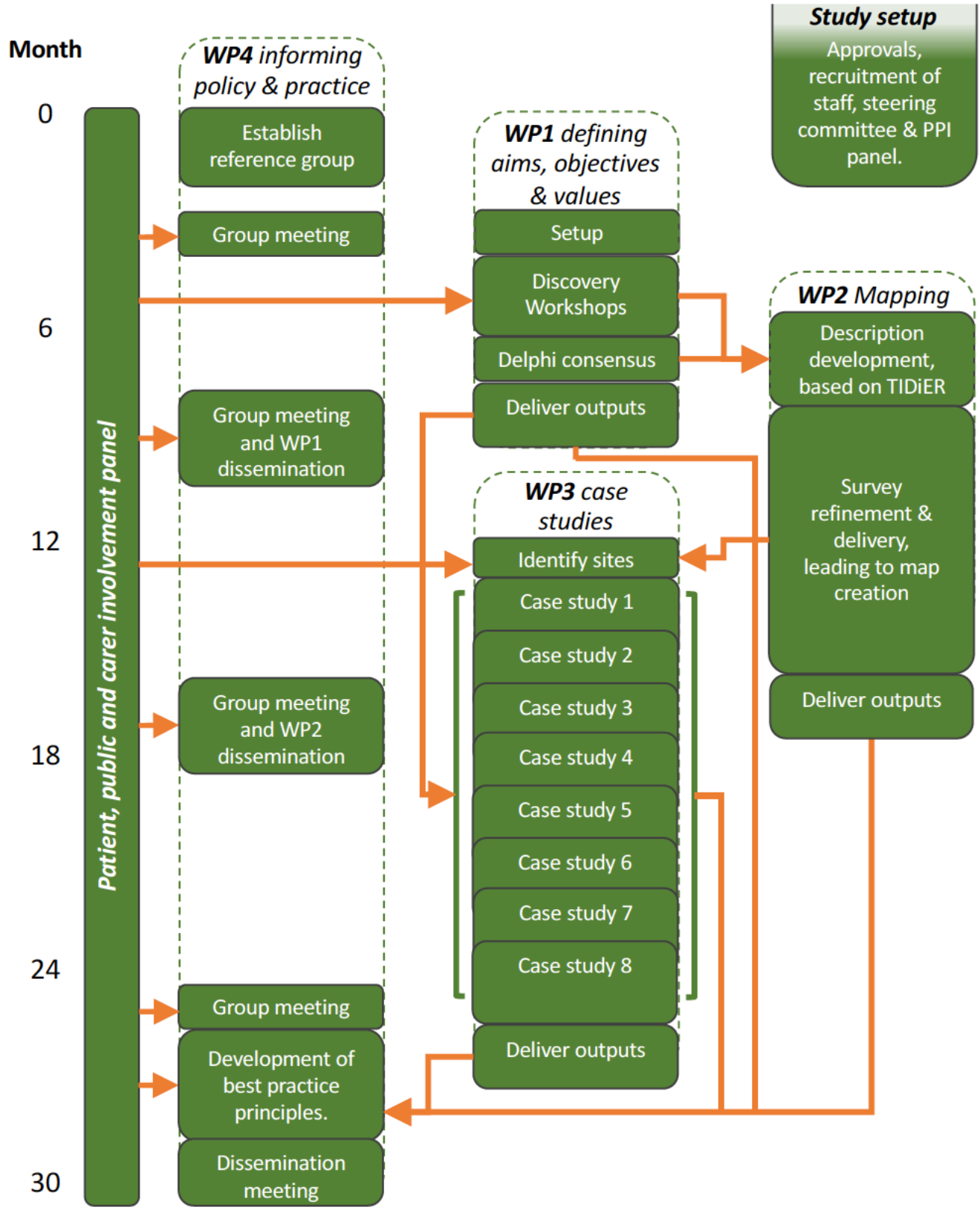
1. What prehabilitation services are available prior to cancer surgery?
    a. What do they consist of?
    b. How are they commissioned and delivered?
    c. Who benefits from them and how?
    d. What values and assumptions underpin their design?
2. What are the best practices in prehabilitation prior to cancer surgery?
    a. How is a quality service delivered?
    b. How are inequalities best addressed?
    c. How have services adapted to the COVID-19 pandemic?
3. How can the delivery of prehabilitation prior to cancer surgery be improved?
    a. What measures should be used to classify and measure services?
    b. What are the important components of best practice principles?

5. Research Plan / Methods

This study will comprise four work packages designed to address the research questions stated above:

- **WP1** is a consensus process that will work with patients, carers and healthcare professionals to develop evaluation criteria for prehabilitation services. It will be based on a series of workshops, conducted in the community.
- **WP2** is a mapping exercise that will obtain data from NHS Trusts and healthcare staff to build a UK-wide map of prehabilitation services. In addition to organisational and descriptive data as per the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al 2014), WP2 will seek data pertaining to the criteria developed in WP1.
- **WP3** will involve eight case studies of prehabilitation services, sampled purposively to represent 'typical' service models of prehabilitation, according to the data obtained in WP2. Analysis will be conducted according to the principles of the Promoting Action on Research Implementation in Health Services (PARIHS) framework ((Rycroft-Malone et al 2002).
- **WP4** will embed stakeholder engagement and knowledge mobilisation throughout the project, though regular meetings with an expert reference panel. It will include dissemination and engagement with groups such as professionals, patients and policymakers.

5.1 Study flow chart



5.2 Design and theoretical / conceptual framework

This will be a comprehensive study of the prehabilitation services currently available to patients with a cancer diagnosis awaiting surgery. We will focus on defining quality in prehabilitation and investigating the interplay between prehabilitation and health inequalities. This will involve working with patients, carers, and professionals to develop a set of criteria by which prehabilitation services can be evaluated, using these criteria to develop a map of services, and undertaking in-depth case studies to better understand how prehabilitation works in practice. This will lead to the production of best practice principles and an inequalities checklist.

The Promoting Action on Research Implementation in Health Services (PARIHS) will be the overarching study framework, guiding data collection, analysis, and synthesis (Rycroft-Malone et al 2002, Kitson et al 2008, Bergström et al 2020). This framework is relevant to this study because it provides an overarching explanation about how and why innovations, services, and practises are implemented (or not) in practice. Specifically, it focusses on how implementation is facilitated in real world contexts, which is a central concern of this study.

A study steering committee, and patient and public involvement (PPI) panel will be established, contributing to the four linked work packages (see flow diagram, appendix 2), each of which is led by a co-investigator with relevant expertise:

5.3 Work package 1 - defining aims, objectives and values, months 3-11, lead: Lisa Ashmore

We will work with patients and healthcare staff through a five-step process, to develop evaluation criteria for services, based on both the prevailing and desirable aims, objectives and values that underpin prehabilitation. Activities will be responsive to the opinions and views of participants, with regular PPI panel review.

5.3.1 Setup

We will begin by engaging participants, defining levels of involvement, agreeing aims, terms and roles, defining the scope and approach of this phase of the project, and ensuring members are aligned. We will establish areas of common ground and training needs, ***evaluate the group for inclusivity and conduct outreach*** to ensure maximum representation. This phase will also involve review of literatures and presentations from past service users, prehabilitation professionals and academics in the field.

Participants will be ***individuals who represent diverse populations*** in terms of disability, ethnicity, sexual orientation, gender identification, and socioeconomic status. We aim to include participants with lived experience relevant to cancer surgery (including those who have experience of prehabilitation and those who do not) as patients, carers, clinicians, or researchers as well as members of the wider public. A purposive sampling method will be used to ***balance representation*** of demographics, professional background, and lived experience. Recruitment will be facilitated through NHS partners, and by a variety of engagement activities aimed at patients, public and professionals (see section 6.2). To ***ensure that seldom heard people are represented*** we will also use formal and community approaches to recruit patient and public participants, as detailed in the “PPI approach, management, and support” section above. We aim to recruit 30 participants (15 public members and 15 healthcare professionals and researchers) to participate in WP1 activities. This will enable sufficient reliability and accuracy of the modified Delphi process (described below) whilst also allowing manageable group numbers to support tailored participation and high response rates.

In order to ***avoid disincentivising participation*** at a time of unprecedented clinical demand, patient recruitment and NHS staff member participation in WP1 is costed as an NHS research cost in the SOECAT (appendix 1).

5.3.2 Discovery: capture criteria (two multi-access workshops)

Through a range of workshops and creative design practices (building on toolkits established through the work of Lancaster University, The Glasgow School of Art and the Arts and Humanities Research Council), groups will aim to understand what about prehabilitation is important to them and be encouraged to challenge assumptions about prehabilitation services. Through exploring examples of service evaluation criteria

(beyond prehabilitation) and drawing on a wide range of multimedia prompts, (e.g., narratives from patients, presentations, academic and grey literatures, and web-based materials, all ***presented in multiple, accessible forms*** including translated) the discovery stage will help people develop their own understanding of the aims, objectives and values that underpin prehabilitation services.

The multi-access workshop is an open event that allows a broad range of participation including those who may not wish to attend a meeting physically or remotely. Participants will be able to join in person, or via live stream, or listen, participate and share via parallel and ongoing processes encircling the physical events. This will enable ideas, thoughts, and questions to be incorporated, and potential criteria created in open and inclusive environments. Multi-access workshops will ***enable participants to feed in stories or points of view without being physically present if they chose not to***, but their views and opinions will be treated fairly and with equal weight as those attending and will be advocated by our PPI lead Andrea Partridge.

Prior to the events, all participants will have access to the multimedia prompts and responses and input from those not wishing to attend will be captured through multiple feedback modalities, be that one-to-one conversation facilitated by third sector collaborators (i.e., with expertise in working with seldom heard groups) or through completion of written forms, email, or telephone conversation.

We have experience of co-creation of research materials and objectives through several projects including the Northwest Cancer Research funded Gynae Narratives project, involving people with lived experience of cancer, professionals working in oncology in NHS and third sector organisations and academic teams (http://wp.lancs.ac.uk/gynae-cancer-narratives/).

5.3.3 Define & refine criteria (one multi-access workshop)

Following discovery, the definition stage will lead to the collection of a wide range of brainstormed criteria of aims, objectives and values relating to relevance, effectiveness, impact, fit, efficiency, and sustainability of services, as defined by participants.

Once we have generated an extensive list of criteria, a further multi-access workshop will take place to group and explore the criteria in detail, finding patterns and themes amongst key insights to define evaluation criteria, for example goals set within programmes; outcomes and aims; and assessments used to measure the 'success' of prehabilitation.

This process of defining and refining may generate new criteria but will have the aim of crystallising the meaning of criteria put forward. We will also conduct exercises to generate feedback on potential multiple understandings of the criteria and establish if any changes to wording need to be made at this point.

5.3.4 Develop evidence through consensus (modified Delphi method, two – three rounds, including multi-access guided discussions)

To generate evidence to underpin decision making, an initial ranking will be performed by participants, using a modified Delphi technique via a Qualtrics survey (Taylor 2020). Each criterion will be ranked using a 4-point Likert scale (essential, desirable, possible or to be omitted). Completion will be offered ***online, over the phone, face to face or facilitated by a third sector partner***. Items will be deemed to have reached consensus if they are rated consistently by 70% panellists (Sumsion 1998). Items that reach consensus will be removed from subsequent rounds of ranking. A further two or three rounds of prioritisation will take place, stopping after two rounds if convergence of opinion is reached or there is significant diminished return (Fink 1984).

Each round of ranking is to be followed by a guided discussion, with all participants being provided with time and opportunity to provide feedback on the outcome of the previous-round prioritisation. Individual reports will be created for participants outlining the group median, whether an item reached consensus as well as the individual's own ranking. Individual reports will not be shared between participants. There will be the opportunity to add in additional criteria between the first and second round of rankings.

While interaction between the panellists may risk dominance of the discussion by individuals, and remove anonymity of participants, in this modified Delphi technique we will encourage discussion to enable clarification of points and generation of detail underpinning the criteria, including spotting the risks and potential 'black holes' in criteria and thinking of ways to mitigate those (von der Gracht 2012). We aim to use

processes and practices of consensus building as inspirational, generative co-design processes. Qualitative material generated through discussions will be captured to produce descriptions of criteria for subsequent work packages.

5.3.5 Deliverables

WP1 will generate a ***consensus amongst patients, health professionals and researchers*** about the aims, objectives and values that underpin the practices of prehabilitation. This novel work will be communicated to stakeholders through our ***website, social media*** and ***partner organisations*** (see section 6.2), as well as ***accessible formats co-developed with our PPI panel***. It will also be published as an ***open-access scientific paper***. The outputs from WP1 will feed into subsequent work packages, by contributing to the criteria which can be mapped as part of WP2 and will inform the development of the interview and observation topic guides in WP3.

5.4 Work package 2 – mapping study, months 5-17, lead: Andrew Smith

Prehabilitation programmes available to patients awaiting cancer surgery across the United Kingdom will be identified and mapped according to geographical location, organisational and funding arrangements, who provides the service, what is included in the prehabilitation programme, how and when it is delivered, and to whom. This will include an appraisal of the three main elements of prehabilitation (physical activity, nutrition, and psychological support) as outlined above.

5.4.1 Mapping study inclusion criteria

Prehabilitation programmes meeting the following criteria will be eligible for inclusion in the mapping study:

- Intervention designed to enhance a patient's functional and / or psychological capacity
- Delivered following a cancer diagnosis and prior to cancer surgery.
- Part of the funded usual care pathway for patients in the trust / health board and offered, referred to, or signposted by the NHS cancer care team.
- May be for all cancer types and operations or specific cancers or operations
- May be offered universally (all patients), targeted (high risk patients) or specialist (for those with complex needs).
- May be delivered in hospital, community, or online settings, including by a commissioned non-NHS provider (including third sector, commercial and local authorities)

5.4.2 Development of intervention description template and survey

Description development: based on our experience in weight management service intervention description (Heggie et al 2020), we will develop an intervention description template based on the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al 2014), including specific items on funding, commissioning, setting, leadership, scale, scope and aims. ***We will also include items that may affect equity of access***, such as timing of sessions, travel, out of pocket expenses, digital literacy assessment, training and provision of equipment or non-digital equivalents, and tailoring based on gender or ethnicity (e.g., women-only exercise sessions).

Survey refinement and delivery: the intervention description template will be refined through semi-structured interviews with five sites (via telephone or video call), an online version of the template (using Qualtrics) will then be piloted in 10 further sites, focussing on the ability to ***capture details across a diverse range of services*** and also on time and ease of completion. Then the final version will be shared across all acute trusts / health boards in the UK. Recruitment to the pilot/survey refinement stage will be from trusts / health boards directly identified by the research team (as described in section 5.3.3), ensuring a mix of geographical areas, service type and size.

In order to ***avoid disincentivising participation*** at a time of unprecedented clinical demand, completion of the survey (at refinement, pilot and full study stages) is costed as an NHS research cost in the SOECAT (appendix 1).

Map creation: by analysing the characteristics assessed in WP2, we will generate a classification system for prehabilitation services and record this data for services across the UK.

We have successfully used this approach to map and describe the components of complex multidisciplinary prevention programmes in both the NIHR funded BE:COME (NIHR 129523) and REMISSION (NIHR 132075) studies.

5.4.3 Recruitment to mapping study

The research team will search trust and health board websites, recent policy documents on prehabilitation (e.g., Transforming Cancer Care Prehabilitation Short Life Working Group 2020), and the compendium of preoperative services complied during Andrew Smith's recent project 'Fit for surgery? Or fit for life?' (NIHR 127879), and specifically target those services we can identify directly for both the initial pilot/ survey refinement stage, as well as the full mapping exercise. In addition, to ***ensure all trusts and health boards are approached***, we will use the Clinical Research Network and equivalent systems across the devolved nations, to ask R&D departments to work with surgery and oncology clinicians, and clinical managers, to identify the services that fit the above criteria available to their population. In addition to this, early dissemination and engagement with clinicians about this project (detailed in section 6.2) will ensure that the study is recognised and anticipated by clinicians working in these services, with the ability for them to contact the research team directly to get involved through our website. Finally, ***trainee research collaboratives*** (general surgery and anaesthetics), which run across the majority of regions in the UK, will be invited to support the study by coordinating survey completion. This is a proven way to maximise return of such surveys and we will incentivise and acknowledge their contribution by listing the names of all local investigators in publications as well as registering the study for inclusion in the NIHR associate PI scheme (if this type of study is eligible by that time).

As not all NHS Trusts offer access to prehabilitation (Carter et al 2019), we anticipate survey returns from 50-60% of the ~150 acute hospital trusts in England, ~5 health boards in Scotland, 4 in Wales and 3 in Northern Ireland. In total, we anticipate responses from 100 organisations and believe that the ***multiple recruitment methods, incentivisation and reimbursement of time*** described above will ensure that this is achievable.

5.4.4 Deliverables

WP2 will produce a detailed ***map and descriptive compendium of UK prehabilitation*** services available to patients awaiting cancer surgery. We will publish this as a ***standalone report***, ***available online to patients, professionals and researchers***, and disseminated as outlined in section 6.3. The results of WP2 will also form the basis for case study site sampling in WP3.

5.5 Work package 3 - case studies, months 12-25, lead: Cliff Shelton

Eight services from across the United Kingdom will be selected for in-depth analysis as case studies. These will be instrumental in nature (Crowe et al 2010), aiming to represent 'typical' examples of the various service models identified in WP2. By undertaking multiple case studies, ***different models for prehabilitation will be compared and contrasted***. We have opted to include eight services because we anticipate this to be both practical and able to provide sufficient opportunity for capturing variation whilst not compromising depth of analysis.

5.5.1 Case study site sampling

Case study sites will be sampled using a purposive approach aiming to target 'maximum variation', based on the service models identified in the classification system and map developed in WP2. We will situate ***at least one case study each in Wales, Scotland, and Northern Ireland***. Because it is likely that the COVID-19 pandemic will still be a concern at the time of the study, we will identify alternative sites for each service type, to mitigate the disruption that may be caused by local surges of COVID-19 interfering with planned cancer surgery, or restrictions in access for visiting researchers.

5.5.2 Case study methods

Case studies will involve interviews and extensive in-person visits to the participating services, according to the following methods:

Orientation: initial data collection will aim primarily to orient the researchers to the service. This will involve integrating the findings of WP2 with sources such as literature (e.g., guidelines, patient leaflets and service level agreements), demographic and statistical information, and interviews with those responsible for service coordination and management. This will help to guide the data collection phase of the case studies by ascertaining the local funding, management and governance arrangements, how and where prehabilitation is provided, to whom, and what decision-making processes are involved in enrolling patients in a particular service.

Individual sampling: participants will be purposively sampled on the basis of their role within the service. Recruitment of patients and carers will take place prior to prehabilitation (identified by their usual clinical team on referral to prehabilitation), and also prior to surgery (identified by their usual clinical team on referral to pre-operative assessment clinic), so that ***those who do not receive prehabilitation*** may nevertheless have the opportunity to participate. By ensuring that these individuals are represented, we will account for the possibility that ***prehabilitation programmes may broaden inequalities,*** investigate the reasons why this may occur, and how it may be mitigated. To ensure that potential participants have time to consider whether to participate, discussions would take place prior to a clinic appointment (at either prehabilitation or pre-operative clinic). This will likely take place in-person in the hospital setting, but an online / telephone alternative may be required depending on how prehabilitation services are delivered.

Based on our previous work (e.g., Shelton et al 2018, Shelton 2019) we expect to recruit 10 staff members, 10 patients, and five carers per site. Our sampling approach will incorporate ***outreach and support*** measures to ***ensure that seldom heard people are supported*** to participate, for example by working with translators to explain the research. Furthermore, we will draw on our prior experience of ***including people without mental capacity*** in studies of practice to ensure that the experiences of people with cognitive impairment and learning disability (who have a higher risk of perioperative complications) and their carers are represented in the data (Shelton 2019). Participant information will be designed in collaboration with our PPI panel, and made available in ***various accessible formats*** (e.g., large type, audio, translated) to suit the needs of potential participants.

Individual inclusion criteria

Healthcare Staff:

- Involvement with the prehabilitation services available to patients awaiting cancer surgery at a case study institution.
- Involved in the commissioning, funding, coordination, management and / or delivery of prehabilitation prior to cancer surgery.
- Willing to participate in interviews and / or observations.

Patients:

- Age over 18
- Under the care of a case study institution.
- Awaiting surgery for treatment of any cancer diagnosis
- EITHER - Referred to a prehabilitation programme prior to cancer surgery as part of their NHS care
- OR – Referred to pre-operative clinic prior to cancer surgery as part of their NHS care
- Willing to participate in interviews and / or observations.

Carers:

- Age over 18

- Nominated by a patient involved in the study.
- The primary carer (paid or unpaid) of any patient involved in the study.
- Close family members (spouse, parent or child) of any patient involved in the study.
- Willing to participate in interviews and / or observations.

The mode and location of interviews (e.g., telephone, teleconference or in-person), and the time at which they are conducted will be ***flexible to suit participants***, and ***translation costs are included*** in our budget. Any participant expenses (e.g., travel) incurred to attend interviews will be covered in order to ensure that there is ***no financial disincentive to participation***. Observation of practice will not increase the time spent in hospital, so should not be burdensome for participants.

Data collection: interview sampling will be purposive, aiming to follow the prehabilitation process, both from a clinical (i.e., from patient enrolment to discharge) and strategic (i.e., from service planning and commissioning to delivery) perspective. Both staff and patients will be invited to participate in semi-structured interviews, conducted by a member of the research team, trained in conducting interviews. These will include peri-operative interviews (i.e., shortly before or after surgery), which will allow us to ***involve patients who have not experienced prehabilitation***. We anticipate that this will provide particularly useful data, which will help us to understand why some patients may not engage with, or access, prehabilitation services. As in WP1 and 2, NHS staff participation in interviews is costed as an NHS research cost in the SOECAT (appendix 1) to avoid disincentivising participation.

Observations of prehabilitation practice will target all stages of decision-making and patient contact. This may include, for example, multidisciplinary team meetings where decisions are made about whether to offer prehabilitation to patients, physical activity sessions, and 'surgery schools'. Depending on the proportion of patients recruited into prehabilitation services, we anticipate observing between five and eight patient journeys (out of 10 patients recruited) per site. Observations will be 'overt', where the researcher clearly identifies themselves and their role to all who are being observed; patients, carers, and all staff involved in any healthcare process observed will be invited to consent to the observation in advance of the observation period.

Interview and observation guides will be developed drawing on the PARIHS framework (Rycroft-Malone et al 2002, Rycroft Malone et al 2004, Kitson et al 2008), based on the criteria developed in WP1 and the features of prehabilitation identified in WP2. Although the precise content of observations and interviews will depend on the results of WPs 1 and 2, these will incorporate data collection on the relationship between prehabilitation and healthcare inequalities and will include the core components of the PARIHS framework:

- The level and nature of any evidence used in the design or delivery of prehabilitation practice (e.g., studies, service evaluations, and the experiences and opinions of individuals involved).
- The context and environment in which prehabilitation occurs (e.g., organisational structure and funding arrangements, and social factors such as cultural norms and organisational ethos)
- The method or way in which the process is facilitated (e.g., mode of delivery, schedule and content of prehabilitation).

Analysis: an inductive thematic analysis of the data from all eight case studies will draw together best practices (Braun and Clarke 2006), with a particular focus on the features of a high-quality service, from the perspectives of patients, carers and professionals, and how services and clinicians address (or do not address) inequalities. We will adopt an interpretative approach, aiming to understand contexts and processes as perceived from different perspectives in order to identify and understand both individual and shared meanings. Because ***patient and carer perspectives and the factors that influence inequality*** in prehabilitation are central to this project, Andrea Partridge will participate in this analysis as a co-investigator, in liaison with the PPI panel.

5.5.3 Deliverables

WP3 will generate ***rich descriptions and explanations of the ways in which prehabilitation services are designed, managed and delivered***, unpacking the tacit knowledge and 'practical wisdom' of those involved in prehabilitation (Williams and Glasby 2010, Head 2008). These will include examples of ***best practice and***

practices that could be improved. Findings will be integrated with those from the other work packages using the PARIHS framework. This synthesis will be used to develop ***actionable outputs*** including feeding into a set of best practice principles (WP4). Findings will be shared with stakeholders as outlined in section 6.3.

6. Work package 4 – knowledge mobilisation, outputs, dissemination, and anticipated impact. Months 1-30. Lead: Jo Rycroft-Malone

Stakeholder engagement and knowledge mobilisation will be integrated throughout the project rather than end of grant activity. To recognise the importance of this activity it will be managed in an embedded work-package with a co-applicant lead and full engagement of all team members.

A reference group will be formed, with ***clinicians,*** representatives from ***professional associations, system leaders*** including from the ***devolved nations, commissioning, third sector organisations,*** and at least two members of the ***PPI panel***; this group will meet in months 3, 12, 16 and 24. The group will provide advice to the team across the project to facilitate engagement and the potential for impact – this will be a different role to the study steering committee whose terms of reference will focus more specifically on matters related to conducting the research (although that will not preclude their input and advice on matters of relevance to WP4). The reference group will also help with ensuring we appropriately tailor and target our knowledge mobilisation activities and products to relevant evidence users, including non-academic.

6.1 What we intend to produce from our research

We will use the findings from the work-packages to develop a set of ***best practice principles*** with the reference group using a modified nominal group process (Rycroft-Malone 2001), which we have successfully used in previous research for a similar purpose (e.g. Masterson-Algar et al 2018). The best practice principles will be aimed at promoting high-quality prehabilitation services that ***address the needs of all patients and carers***. Involving the reference group as an evidence user nominal group in the development of these principles should increase relevance, enhance dissemination and potential for uptake in future service provision.

Phase 1 of the nominal group process, which will begin in month 25 will involve drawing together the findings from work-packages 1, 2 and 3 to develop a set of best practice principle statements, which will be led by Jo Rycroft-Malone with input from team members. Reference/nominal group participants will be asked to rate each of the statements on '*how important is it for this principle to be included'* to help make a difference to future service provision. A 1-9 scale will be used, where a median of between 7-9 on each best practice statement will be viewed as agreement.

In Phase 2, the group will be presented with a revised set of best practice principle statements based on the results of phase 1. Each participant will be able to see the spread of agreement and how their results related to the results of the group. The reference group will meet (in person if possible, but this could also be managed via Teams/Zoom if needed or if more convenient for participants) to discuss statements where agreement had not been reached. Consensus will be reached on a final set of best practice principles through discussion.

The best practice principles will be made openly accessible and will also be disseminated in a targeted way through engagement with relevant stakeholders and organisations identified in the following sections. We will seek to ensure that access to these principles is sustained through their adoption by relevant professional bodies (e.g., Royal Colleges, the Centre for Perioperative Care, the Perioperative Exercise Testing and Training Society). A linked ***inequalities checklist***, underpinned by the principles, will be produced to help services identify the risk of broadening inequalities, and the best practice principles will highlight approaches by which they can address and/or improve them.

A further output from this project will be ***a report*** that includes the presentation of existing and possible models of prehabilitation services. The report will be supplemented by ***summary infographics***.

There will also be ***presentations*** at national (e.g., National Cancer Research Institute Festival) and international conferences (e.g., European Association for Cancer Research). Academic and clinically focussed ***publications*** will also be produced as the study progresses.

A number of other outputs are identified in section 6.2.

6.2 How we will inform and engage patients, NHS and the wider population about our work

Prior to starting the research, we will engage patients, the public, clinicians, researchers and cancer organisations throughout the UK using a combination of publishing the study protocol in an appropriate surgery journal, newsletter emails, disseminating a short video "trailer" (via YouTube) and an infographic of our research project to trusts and other relevant organisations. The protocol will be showcased at national conferences (e.g., National Cancer Research Institute Festival) and alongside this we will raise the profile of the study for the general public via for example, The Conversation, which makes the work of the academic and research community more accessible to the general media.

Throughout the research project, we will develop and deploy a multi-faceted and targeted knowledge mobilisation strategy with our reference group, which is likely to include:

Media: We will use a purpose-built project website, institutional websites, plus appropriate professional and organisational Twitter accounts to publicise the project before, during and after the funded period. We will also ensure that the research programme, resources, and practice principles are made available in a range of accessible media including audio and video. In particular, we will make use of podcasts, both to be posted on our own sites, but also in connection with articles published in journals, when they have the ability to do so. We will also make use of mainstream news media as much as possible, as we are aware that we are dealing with a topic of interest to the public at large. The research team have considerable expertise in the use of social media in research engagement. Cliff Shelton was formerly the Twitter and podcast editor for the journal *BJA Education,* and the team have published numerous papers with wide social media engagement, as evidenced by Altmetric attention scores in the top 5% of outputs (e.g., Mackenzie et al 2019, Shelton et al 2021, Gaffney et al 2017, Lewis et al 2018, Rycroft-Malone et al 2012).

Patients' and carers' organisations: Engaging with our PPI panel's expertise and national networks, we will develop suitable materials for a lay readership and make them available to relevant patients' and carers' organisations. We will also seek to involve relevant voluntary and third sector organisations e.g., Macmillan, Maggie's Centres, Live Through This.

Healthcare policy and guidance: We anticipate that the results of this study will be highly relevant in the commissioning of prehabilitation programmes. We will engage commissioners in the study steering group and in WP4's reference group. We also plan to organise an online workshop event for clinical and public health policymakers (month 29/30). This will not only enable cost-efficient preliminary dissemination of our emerging findings and share best practices, it will also give us the opportunity to ask participants to highlight critical findings and help with further policy implementation. We also plan to link into the NHS commissioning process (see below) and would make our reviews available for guideline production by forwarding the links to our work to NICE and specialty-specific professional bodies (e.g., the Association of Anaesthetists, The Chartered Society of Physiotherapy)

Professional groups: As well as engaging representatives in the steering group and reference group, we will distribute our briefing sheets to relevant national organisations such as the Royal College of General Practitioners, Royal Colleges of Anaesthetists, Physicians, Surgeons and Nursing, the Pre-operative Association and the Centre for Perioperative Care. We will also present our work to healthcare professionals at national meetings. As well as the peer-reviewed journals of these organisations, we will write more accessible pieces for their members' newsletters and similar publications.

6.3 How our outputs will enter our health and care system or society as a whole

We have close links with those currently delivering prehabilitation services. As noted in the proposal, we have brought many relevant clinicians into the project as members of our study steering committee, and we will ensure representation in WP4 reference group. We will also gather a large number of contacts during WP2, as we catalogue existing prehabilitation services nationally.

We plan for our outputs to enter the health system at multiple, mutually complementary levels, this knowledge mobilisation being facilitated by our study steering committee and WP4 reference group:

- By influencing or strengthening existing health policy.

- Drawing on our mapping and case study visits, we will develop best practice principles towards the end of the project to guide the development and effective deployment of prehabilitation services, with a menu of options and strategies for implementation. We will circulate this to all the services who participated in the mapping and case studies, and also make it freely available to any and all healthcare professionals, voluntary organisations, patients and carers, using the following approaches:
    - **Partner organisations:** We will promote the best practice principles to the relevant governance, professional, voluntary, and third sector organisations as noted above. We have representatives of many professional groups within our study steering committee, and established links to community and voluntary organisations, through which we will be able to access national contacts for promoting our findings.
    - **Massive open online course:** We will develop a publicly available massive open online course (MOOC) hosted through Lancaster University. This virtual online resource will include both public- and staff-facing elements, to help to inform and educate about the benefits of prehabilitation and provide a blueprint for best practice. This resource has several key benefits including: 1) it can be delivered at scale with unlimited participation; 1) it can be delivered during the COVID-19 pandemic where face-to-face activities may be limited; 3) the MOOC can be made accessible to different audiences including by using multimedia and translation into different languages; 4) it can help reduce inequalities because it can be delivered asynchronously; 5) it is a carbon-efficient method for dissemination, consistent with the 'net zero' commitments of the NHS. Lancaster University has significant expertise in this domain, having created several online MOOCs, including a successful programme in our faculty as part of the International Observatory on End-of-Life Care (https://www.futurelearn.com/courses/palliative).
    - **Engaging case study sites:** We will present interim findings at the case study sites. This will facilitate dissemination of the developing findings of our work across the UK, foster engagement, and build on the relationships established during the case studies, without adding substantially to the cost or environmental impacts of our work. These dissemination activities present an excellent opportunity to engage those who helped deliver our research with its findings. Exemplars of best practice will be presented at multi-disciplinary team (MDT) meetings of all case study sites. These meetings are an ideal opportunity for dissemination as they involve a broad spectrum of healthcare staff involved in the treatment of patients with cancer, thus maximising the colleagues we can share best practice with.
- Local and regional healthcare practice: through our local study steering committee and reference group members and local healthcare commissioners. As we gather our research and practical intelligence, we expect that professionals involved with the study will incorporate aspects of what we find into their practice. We will keep a 'transferability log' of such measures.

We will engage with the NHS Innovation Agency North West Coast as we develop the practice principles, with a view to seeking follow-on funding for a multi-site validation once our project is complete.

6.4 What further funding or support will be required if this research is successful?

We anticipate two main types of follow-on activity:

- Service development: we are aware of two NHS Trusts in our region who are currently in the process of planning prehabilitation services. Specific unanswered questions notwithstanding, we will capitalise on our links with these organisations to feed the findings of our work into the design and development of these services, thereby ensuring that they incorporate best practice principles and mitigate the risks of inequalities by design,
- Further research: we intend to use our findings to design an implementation study of the most promising interventions; this would need further research funding in due course.

6.5 Impacts of project, and possible barriers for further research, development, adoption and implementation.

The impact we would be most pleased with would be demonstrably consistent, high-quality, patient-focused prehabilitation services nationally.

At this stage, barriers to adoption are speculative, but from a professional point of view, may include: lack of time during existing consultations; clinicians simply not considering the possibility of prehabilitation before treatment; and organisational divisions which may mean that, although staff may be aware of the benefits of prehabilitation, funding and accountability issues prevent them from offering the service. From a patient/carer's standpoint, lack of consistent messaging about how to engage, especially with increasing physical activity levels; specific difficulties relating to medical conditions/ disabilities etc; the possibility that prehabilitation may be less accessible to less privileged patients; and the topic of prehabilitation simply not being broached in consultations, may all play their part.

However, as the promotion of physical activity and sound nutrition are key health policy imperatives, the barriers may be weaker than previously, and the broadening understanding of the importance of pre-treatment condition as a determinant of outcome will also facilitate the adoption of prehabilitation. Effective engagement with relevant stakeholders throughout the project will mitigate some of these barriers.

6.6 Sharing the progress and findings of our research with study participants

We will establish a project website and invite interested parties and prehabilitation services to sign up to email progress reports throughout the project. As noted above, we will maintain a list of contacts gathered during the national mapping exercise and make our findings available as they emerge – including with patients and the public. We have included costs for translation and dissemination in accessible formats (e.g., podcasts, infographics) to ensure that all study participants can be kept up to date about the progress of our work.

7. Project / research timetable

Prior to the start of the funding, we will work with the NIHR to appoint of the study steering committee and work with them to finalise the study protocol. We will obtain ethical and governance approvals from Lancaster University Faculty of Health and Medicine and the Health Research Authority, as appropriate. We will also recruit the study research staff.

We anticipate starting the project on 1st March 2022, although we are prepared to flex the timetable to accommodate any issues with NHS staff capacity or researcher safety imposed because of developments in the COVID-19 pandemic. A week-by-week summary of activities and key outputs is included in the Gantt chart (below, section 12).

8. Project management

The overall project will be managed and led by Cliff Shelton (lead applicant and chief investigator), supported by Andrew Smith (joint lead applicant). The study sponsor will be Lancaster University and the study will be based at Lancaster Medical School. The lead NHS research and development office will be at University Hospital of Morecambe Bay NHS Trust, with other NHS trusts being enrolled as study sites for WP3 as needed. Lancaster Medical School and University Hospital of Morecambe Bay have a long history of effective partnership, and both institutions have a track record of supporting NIHR grants. Two applicants (Andrew Smith and Jennifer Logue) have posts in both organisations, facilitating collaboration and communication between institutions.

The study investigators have a breadth of academic and clinical expertise relevant to the project and includes three academic clinicians with roles relevant to prehabilitation including anaesthesia and perioperative medicine (Andrew Smith and Cliff Shelton) and metabolic medicine (Jennifer Logue), which will facilitate access to professional networks and engagement with healthcare professionals. The investigators will be supported by a study steering committee with complementary clinical and health services expertise, who will assist with the development of the study protocol, advise on study conduct, and contribute specific knowledge (e.g., of healthcare systems in the 4 nations of the UK). We already have expressions of interest from a geographically and professionally diverse range of healthcare and prehabilitation professionals to join this group should the study be funded, including Dr Andy Knox (general practitioner and NHS commissioner, Morecambe Bay CCG and Ash Trees Surgery, Carnforth, England), Jo Norris (gynae-oncology specialist physiotherapist, Swansea Bay University Health Board, Swansea, Wales), Ciara O'Donnell (consultant anaesthetist, Royal Victoria Hospital, Belfast, Northern Ireland), and Julia Clarke (dietitian, Clan Cancer Support, Inverurie, Scotland). It will also include representation from two members of our PPI panel. As per

NIHR research governance guidelines, at least 75% of this study steering committee will be independent of Lancaster University, University Hospital of Morecambe Bay NHS Trust, or any of the study sites.

The PPI panel will be chaired by Andrea Partridge, our PPI co-applicant. The role of the PPI panel will be to represent the interests and views of patients in study design and conduct and advise on patient-facing materials. Andrea has pre-existing links with numerous patient and public groups, as evidenced in the attached letters of support (appendix 3). This will facilitate engagement with a diverse range of patient and public representatives, an important element of our approach to avoiding inequalities in this research project.

The reference group in WP4 is distinct from the study steering group and the PPI panel, though it will include practitioners, professional leaders, members of the public and patients as reference group members. Its function is to help translate the project findings into actionable best practice principles, that can be used by system leaders, practitioners and patients, and, potentially, integrated into national guidelines. To date, we have received expressions of interest from Kirsty Rowlinson-Groves (exercise trainer, Prehab4Cancer / GMActive, Manchester) and John Saxton (professor of clinical exercise physiology, Hull University) to join this group should the study be funded.

Though they have distinct roles, the study steering group, PPI panel and reference group will maintain links through each group being attended by a nominated member of the others, and by sharing minutes of meetings via Microsoft Teams.

Each WP will be led by an experienced academic, with methodological and content expertise tailored to the WP objectives. The WP leads will maintain communication with Cliff Shelton and Andrew Smith through email, remote team working with Microsoft Teams, and monthly investigators meetings (in-person or by Teams as appropriate). WP leads will manage the research staff assigned to the WPs, with the assistance of a project administrator. Both of our research staff will work across WPs, with clear reporting lines and their time commitment to each WP specified in advance. This will allow parallel working where required (e.g., the overlap between WPs 1 and 2 in months 5-11, and WPs 2 and 3 in months 12-17), enable cross-covering in the event of staff absence, and will ensure that all research staff maintain an overview of the project; this is beneficial because of the interlinked nature of the WPs.

9. Ethics / regulatory approvals

Research sites will be based in England, Wales, Scotland, and Northern Ireland, and therefore, we will apply for ethical approval from the National Research Ethics Service (NRES). We will seek support from the Clinical Research Network or National equivalents as this is a multi-centre trial and will designate a local principal investigator at each site. The study will be sponsored by Lancaster University. To maximise time for data collection, we will seek ethics and governance approvals for WP1 via the Lancaster University Faculty of Health and Medicine Research Ethics Committee as soon as we are notified that our application has been successful. The approvals for WP2 and 3 will be sought as soon as possible (once sufficient data from WP1 are available) via the Integrated Research Application System, The trial and protocol will be preregistered on researchregistry.com.

In order to maximise inclusivity and maintain our focus on reducing health inequalities, the study will be open to all including those who lack the capacity to give informed consent. In these instances, a capacity assessment will be made by the lead investigator or a trained representative. Patients without capacity will be included in the study only if their consultee deems that they would wish to participate and the patient does not object to participation, as per the Mental Capacity Act (2005).

If inappropriate clinical practice or potential error that may lead to patient harm is identified, researchers will be permitted to challenge or highlight this during observations of clinical practice (with an appropriate documentation made in the observation fieldnotes). This may also be reported using local guidelines and those outlined in the NHS Code of Practice for Confidentiality, if appropriate for the safeguarding of patient safety and following discussion with the site principal investigator and / or chief investigator and appropriate documentation. Likewise, inappropriate clinical practice identified in interviews or documentary sources may be reported according to legal and governance requirements and guidelines. If good practice is identified that has the capacity to save lives and / or improve outcomes, we will seek to publish this quickly as a rapid report to make the information widely available.

In-person research is required for some of this project (e.g., observations of practice), and may be preferable for others (e.g., interviews). In the context of the ongoing COVID-19 pandemic, we will ensure that in person contact is limited to when it is appropriate for methodological or data collection reasons, and we will ensure that all researchers are appropriately trained in the use of personal protective equipment available at the study sites and briefed to avoid in-person contact if there is any evidence that they, or research participants, may have SARS-CoV-2 infection. We will only undertake observations and interviews in areas which are suitable to accommodate a researcher under room occupancy / social distancing guidelines if these remain in place at the time of the study.

10. Project / research expertise

Cliff Shelton is a Senior Clinical Lecturer and Consultant in Anaesthesia. His research focuses on frailty and healthcare quality in perioperative care, including ethnographic research to understand quality in anaesthesia for hip fracture surgery. He is the lead applicant and Chief Investigator and will be responsible for management of the project overall as well as leading the case studies (WP3). He will also contribute to data analysis and interpretation, and apply his expertise in social media and podcasting to support dissemination and knowledge mobilisation (WP4).

Andrew Smith, Professor of Anaesthesia and Perioperative Medicine and Consultant Anaesthetist, leads the Lancaster Patient Safety Research Unit, a thriving NHS-based health services research unit, was CI of the NIHR project evidence synthesis 'Fit for surgery' or 'fit for life'? (NIHR 127879), and wil use this expertise in his leadership of WP2. He is the Co-ordinating Editor of the Cochrane Anaesthesia Research Group. He is joint lead applicant and will act as mentor to Cliff Shelton. He will also apply his expertise in consensus methods and case studies to contribute to WPs 1 and 3, and will use his access to professional groups and networks to support dissemination and knowledge mobilisation (WP4).

Lisa Ashmore is a Senior Lecturer in Social Sciences and trained as a Therapeutic Radiographer. Her recent research has focussed on the co-production and evaluation of digitally delivered supportive care for patients with gynaecological cancer. Lisa will lead on WP1 and support Andrea Partridge in her role as PPI lead. She will assist with the design and analysis of WP3, which links to the outputs of WP1, and will also contribute to project management, particularly regarding project finances.

Chris Gaffney is a Lecturer in Integrative Physiology whose research investigates physiological stress associated with ageing and surgery, including work on prehabilitation before hepatobiliary and pancreatic cancer resection. This project will harness Chris' expertise in the dissemination of research findings to healthcare professionals, academics, and the general public as part of WP4. The impact and dissemination work he has led as part of the Molecular Muscle Experiment has been featured as an exemplar case by the Biotechnology and Biological Sciences Research Council (UKRI) (bbsrc.ukri.org/news/features/worms-in-space-the-molecular-muscle-experiment/). He will also contribute to the design and data analysis of WP3 and in project management.

Jo Rycroft-Malone is a Professor of Implementation and an internationally recognised expert in mixed methods applied health research and implementation science. She will lead on dissemination and knowledge mobilisation (WP4), and contribute to project management, data analysis and interpretation.

Andrea Partridge is the service user involvement coordinator for the Corporate Cancer Team at Lancashire Teaching Hospitals NHS Foundation Trust. Andrea also has lived experience of cancer care. She will lead the PPI aspects of this study, supported by Lisa Wood. She will also contribute to data analysis and interpretation.

The project will be supported by a full-time Research Fellow (grade 8) and Research Associate (grade 7), and an Administrator (grade 5) at 25% FTE. As described in section 8, they will work across WPs, and will be supervised in the context of this work by the WP lead as appropriate. Overall supervision / management will be provided by Cliff Shelton as CI.

11. Success criteria and barriers to proposed work

The criteria for success are the production of the deliverables as specified in sections 5.2.5 (WP1), 5.3.4 (WP2) and 5.4.3 (WP3), as well as the production and dissemination of the best practice guide and inequalities checklist as detailed in section 6 (WP4). Potential risks and mitigations are detailed below:

Risks	**Mitigations**
Difficulties in recruiting representative and diverse groups of patients / carers / public in WPs 1 and 3, and for PPI	We have designed a comprehensive and inclusive approach to promoting diversity in PPI and WP1, including formal and community approaches. In WP3 we will recruit patients and carers both during prehabilitation and in the peri-operative period. Translation costs are included, and the team have expertise in involving patients without mental capacity in research.
Difficulties engaging NHS staff and institutions at a time of unprecedented clinical demand	We have costed the additional time that NHS staff may spend on this project (e.g., for survey completion and as interview participants) as an NHS research cost in SOECAT, thereby allowing time to be back-filled. We will also work with professional networks and trainee research collaboratives and use social media and newsletters to engage NHS colleagues. We have begun to recruit our steering committee and reference group and have had an enthusiastic response from NHS staff.
Delays in gaining ethical approval	Whilst the NRES approval timescales have returned to near pre-pandemic, further COVID-related delays are possible. Whilst NRES approval for the whole project is preferrable, we have designed the project so that WPs 1 and 2 will be eligible for Lancaster University ethical approval if there are delays with NHS ethics approval.
Health risks of in-person research during COVID-19	We will ensure that all investigators and research staff are trained in the use of PPE and infection control measures, arrange for them to attend a local induction at case study sites, and provide risk assessment and occupational health advice as necessary. All local and national infection prevention regulations will be observed. As SARS-CoV-2 vaccination is now available to all adults, researchers will have the opportunity to be vaccinated.
Delays or limitations in research access due to COVID-19	We have outlined a realistic timetable for our work but can flex this to accommodate the needs of the NHS in the event of further national ‘waves’ of the pandemic. We will identify alternative sites for each case study to mitigate against local outbreaks.
Staff absence, including due to COVID-19 / track and trace.	We will make use of remote working in this project where possible and have also opted to deploy all research staff across all WPs to allow them to cross-cover.

12. Gantt Chart