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A multi-centre, pragmatic, randomised controlled trial of comparing enhanced Acceptance and Commitment Therapy (plus) added to usual aftercare, versus usual aftercare only

SUrvivors' Rehabilitation Evaluation after CANcer (SURECAN) Trial

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This protocol has regard for the HRA guidance and order of content

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Signature page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigators agree to conduct the trial in compliance with the approved protocol and will adhere to appropriate research governance framework and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

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

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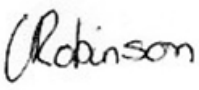
Signature:  Date 02/10/2023

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Glossary of terms and abbreviations

AAQ-II	Acceptance and Action Questionnaire
ACT+	Acceptance and Commitment Therapy enhanced by exercise therapy and vocational rehabilitation, as appropriate
AE	Adverse Event
ASR	Annual Safety Report
CAQ	Committed Action Scale
CI	Chief Investigator
CAF	Consent to Approach Form
CRF	Case Report Form
FACT-G	Functional Assessment of Cancer Therapy – General
GDPR	General Data Protection Regulation
HCP	Health Care Professional
IAPT	Improving Access to Psychological Therapies
ICF	Informed Consent Form
JRMO	Joint Research Management Office (at Queen Mary)
MAAS	Mindfulness Attention Awareness Scale
NHS R&D	National Health Service Research & Development
PCTU	Pragmatic Clinical Trials Unit (Queen Mary)
PI	Principal Investigator
PIS	Participant Information Sheet
PMG	Programme Management Group
PSC	Programme Steering Committee
QMUL	Queen Mary University of London
QoL	Quality of Life
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedure

Summary

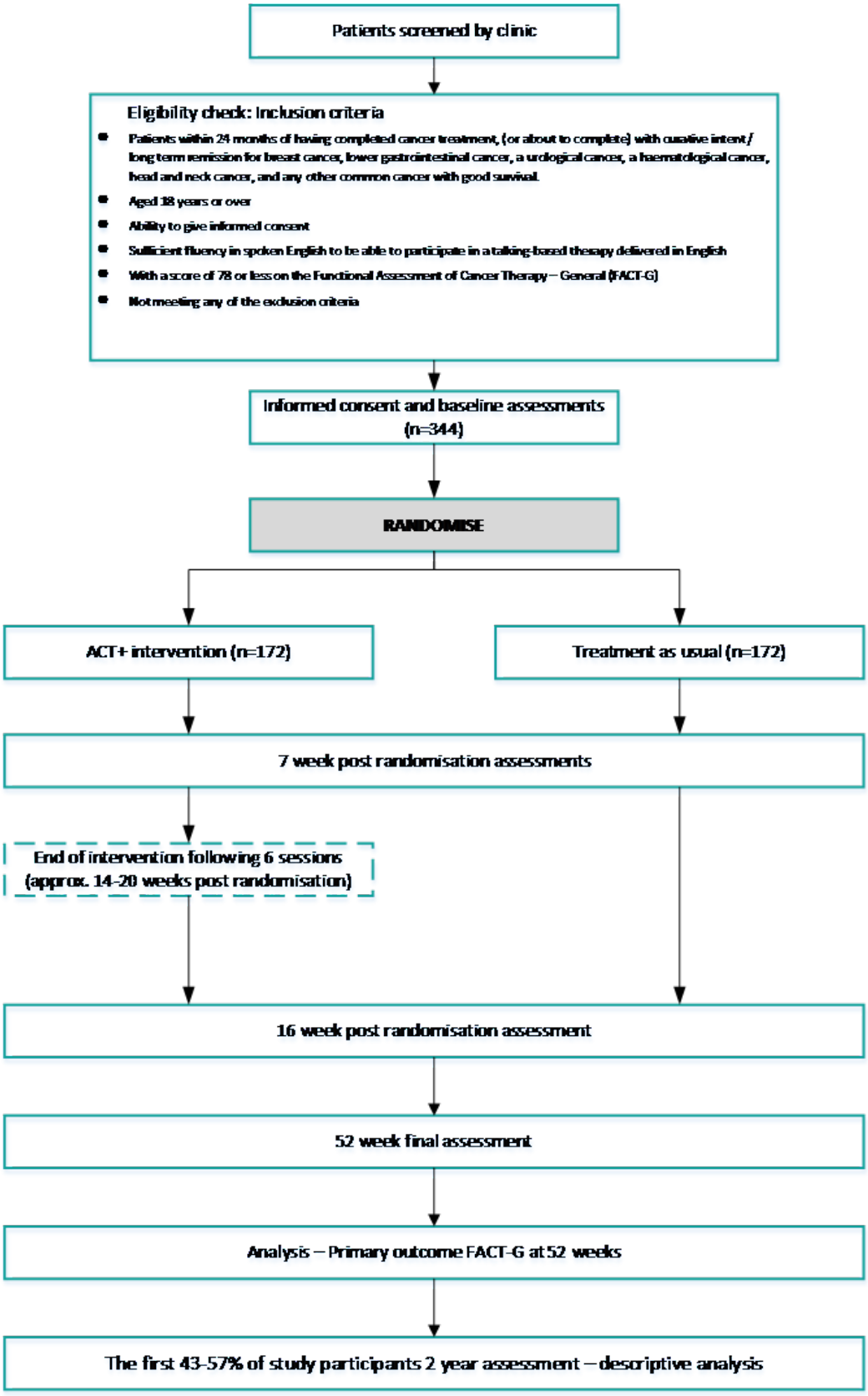
Table 1 Trial summary

Title:	SUrvivors Rehabilitation Evaluation after CANcer (SURECAN) randomised control trial
Short Title/acronym	SURECAN Trial
IRAS number	260823
REC number	19/SW/0214
Sponsor name	Queen Mary University of London
Funder name & reference	National Institute of Health Research (NIHR) Programme Grant for Applied Research (PGfAR): RP-PG-0616-20002
Design	Pragmatic, parallel, two arm randomised controlled trial with an internal pilot, comparing ACT+ in addition to usual aftercare versus usual aftercare only.
Overall aim	To pilot and evaluate whether ACT+ in addition to usual aftercare is more effective and cost-effective than only usual aftercare in improving QoL at one-year follow up in patients living with and beyond cancer
Internal Pilot trial objectives and progression thresholds	Internal pilot trial (threshold for progression to definitive trial) 1. Acceptability of the study and the intervention: a. Ability of clinicians to identify patients that go on to become eligible with FACT-G score of 78 or less once screened by the study team b. If participants randomised to the ACT+ arm took up ACT+ therapy sessions i. 75% receiving one or more sessions ii. 50% receiving three or more sessions 2. Feasibility of future trial: a. Willingness of eligible patients to participate (30%) b. Proportion of trial participants completing the 7 week questionnaire (90%)
Definitive trial outcomes	Primary outcomes: Functional Assessment of Cancer Therapy: General scale (FACT-G) at 12 months Primary health economics outcome: Quality adjusted life years based on EQ-5D-5L and net monetary benefit at 12 months Secondary outcomes: 1. FACT-G sub-scale scores 2. Positive and negative Impact of Cancer scales 3. Fear of cancer recurrence inventory 4. Hospital Anxiety and Depression scale 5. Chalder Fatigue questionnaire 6. Physical activity

	Outcomes for mediation/moderation analysis: 7. Psychological flexibility 8. Values directed behaviour 9. Beliefs about emotions scale 10. Covid-19 related lonliness and worry
Target accrual	• Internal pilot: 45 • Main trial: 299 Combined total = -344
Inclusion criteria	1. Patients within 24 months of having completed cancer treatment of the index cancer, (or about to complete) with curative intent / long term remission for: breast cancer, lower gastrointestinalcancer, a urological cancer, a haematological cancer, head and neck cancer, and any other common cancer with good survival. 2. Aged 18 years or over 3. Ability to give informed consent 4. Sufficient fluency in spoken English to be able to participate in a talking-based therapy delivered in English 5. With a score of 78 or less on the Functional Assessment of Cancer Therapy – General (FACT-G)
Exclusion criteria	1. Will not have not completed their cancer treatment by the commencement of the trial (excepting those receiving long-term, ongoing maintenance treatment e.g. androgen suppression therapy in prostate cancer). 2. Receiving treatment for symptom control alone 3. Currently receiving another psychological intervention (NB participants taking antidepressants or anxiolytic drugs remain eligible) 4. Other serious co-morbid condition which would make it difficult for the participant to receive a talking-based one-to-one intervention 5. Require urgent psychiatric or clinical psychology assessment
Anticipated recruitment duration	25 months including internal pilot
Duration of participant follow up	52 weeks post randomisation Study participants, where possible (before the end of trial), will be followed up at 2 years for descriptive analyses.
Definition of end of trial	Last 52 week post randomisation follow up of last participant recruited

Trial flow

Figure 1 Overall trial flow diagram



1. Introduction

1.1. Background and rational

The importance of cancer survivorship

Some two million people in the UK have "survived" cancer,[1] and the numbers are increasing,[2] with 50% now surviving cancer by ten or more years.[3] About a third have poor quality of life and more report distress.[4-6] A national survey assessing the quality of life (QoL) of adult cancer survivors reported key issues or concerns, which included: fear of recurrence (57%), fatigue (43%), body image concerns (31%), and complete lack of exercise (30%).[4] Poor QoL is also associated with unemployment in those of working age,[7] with up to a third losing their employment after cancer,[4] There is wide variation in NHS "aftercare",[5, 8] and interventions are only moderately effective, and often unavailable.[8, 9] Two key policy documents highlighted the importance of cancer survivorship[5, 6]. The goals of the National Cancer Survivorship Initiative included reducing the proportion of people with unmet physical and psychological support needs, and increasing the proportion of cancer survivors able to work.[5] The report recommended self-management, after appropriate assessment and treatment, and both physical activity programmes and vocational support.[5] The goals of the Independent Cancer Taskforce, established by NHS England, included every person with cancer having access to a "recovery package" of aftercare with "stratified pathways of follow-up care."[6]

The need for research in this area

The Independent Cancer Taskforce reported the needs for research in this area, particularly highlighting the paucity of the evidence base for interventions and the need for of a good measure of quality of life.[6] Recommendations 68 and 69 of the report focus on the need for more research into survivorship issues and QoL.[6] Recommendation 74 was that "return to work is fully integrated into assessment and care planning."[6] Other recommendations covered the need for rehabilitation services and specific treatment for depression.[6] The need for evidence based interventions to facilitate a return to a normal life is increasingly being recognised by the professions.[10, 11]

We believe that Acceptance and Commitment therapy (ACT) lends itself to addressing these problems in cancer survivors, in helping a patient to accept what cannot be changed (e.g. that the cancer might recur) while committing themselves to the things they can change (i.e. meeting their goals in life, in spite of having had cancer). ACT has shown promise in other chronic conditions,[12] as well as some promise in a small number of trials of patients receiving cancer treatment.[13] An ACT intervention, which is integrated with both an exercise intervention,[14] and work support - when an individual's life goals require them,[15] is person-centred, and applicable to patients with any cancer. We call this integrated approach "ACT Plus (+)". An evaluation of efficacy, safety, and economic outcomes of an intervention, found to be promising in other chronic physical conditions,[12] would be an important contribution to the NHS. This is consistent with our logic model describing the pathway to benefit of the ACT+ intervention and suggesting why ACT+ will be better than other interventions that are currently available.[8, 9]

1.2. Relevant previous and current research

There have been 16 systematic reviews of non-pharmacological interventions aimed at improving QoL in cancer survivors, which we have reviewed in our programme development grant (PDG) work (see below). Only exercise and cognitive behaviour therapy consistently showed efficacy, although the effect sizes were small to moderate, with limited long term follow up.[9] There have been no trials of ACT in cancer survivors,[9] and a few small trials in cancer patients on active treatment.[13] We have

identified one other current study of ACT in cancer patients: the CanACT study of patients receiving palliative care.[16] Our proposed research is complementary to this study, and Sarah Davis, one of the CanACT researchers, is a collaborator on this grant to share learning. Co-applicant Professor Little is the principal investigator of the NIHR funded Cancer Life Affirming Survivorship support in Primary care study (CLASP), which aims to develop and evaluate a guided, internet based, self-help intervention. SURECAN will complement CLASP in providing a more intensive, person centred, face-to-face intervention, in secondary care, for the one third of patients with low quality of life, who may not be suited to web-based delivery and guided self-help in primary care.

Work undertaken previously by the research team leading to the proposed Programme Grant

Programme Development work:
Our rapid evaluation of 16 reviews showed that ACT had not been studied, and vocational rehabilitation, rarely.[9] Exercise interventions showed efficacy, and we have integrated physical activity into ACT+.[14] Cognitive behaviour therapy was found to be moderately effective.[9] Nevertheless, ACT may provide better aftercare for the diverse population of cancer survivors, as it is patient-focused and flexible enough to be helpful for people from different backgrounds and with varied abilities (e.g. range of diseases, problems, levels of distress and cultural backgrounds). We conducted a mixed methods study of 182 cancer survivors to determine the best of the four most commonly used QoL measures in cancer studies, to determine which to use both as a screening instrument and as the primary outcome measure in a subsequent trial (Korszun A, written communication, 23 April 2019). The measures were: FACT-G,[17] EORTC, Warwick Edinburgh well-being measure,[18] and Impact of Cancer Scale.[19] All these measures were closely correlated with each other, with the exception of IOC positive adaptation scale. Our qualitative work supported the use of a generic measure, i.e. FACT-G, rather than measures that attributed all a patient's problems specifically to cancer. We also tested three simple screening questions which demonstrated good receiver operating characteristics when judged against FACT-G. We surveyed NHS oncology healthcare professionals about the aftercare they provided.[8] There were 278 respondents who represented 70% of NHS acute trusts. There was a median of 2 (IQR: 1, 4) aftercare sessions provided. The respondents thought their aftercare did not address important issues, and noted uncertain funding and a lack of evidence-based approaches. ACT+ has been developed into a therapist's manual as well as a patient version. We now know that an RCT would be acceptable to both patients and oncology services, so long as we pay particular attention to training and communication.[20]

Work undertaken as part of the Programme Grant leading up to the trial

Our proposal consists of six interconnected work-streams (WS), aimed at the development of an intervention based on Acceptance and Commitment Therapy (ACT), which is integrated with optional modules of physical activity and work support.

The programme culminates in a definitive, pragmatic randomised controlled trial (RCT) of the SURECAN intervention, ACT+, in addition to usual aftercare compared to usual aftercare provided by the NHS. This document details the protocol for the pilot and definitive trials, however below is a summary of the work undertaken as part of the programme grant leading to this protocol:

SURECAN Development and pre-pilot studies

(April 2019 to September 2019)

Further development of the ACT+ intervention involves:

- Developing and refining the intervention, including therapist and training materials, to ensure it is suitable and acceptable for different cultural diverse groups of patients, through patient focus groups and interviews, as well as interviews with healthcare professionals (HCPs) and other stakeholders who are key to conducting the intervention and/ future trial; and
- Refining further the training to deliver the intervention and to refine the intervention itself through a small "pre-pilot" study where the intervention is delivered to a small number of participants.

The development of the intervention is being conducted as part of Work Stream 2, under protocol number: 012328; IRAS 247223. The study was approved by the by Cornwall & Plymouth Research Ethics Committee. The reference number of the review is 18/SW/0196.

2. **Objectives**

2.1. Overall aims and objectives for this trial

Randomised controlled trial of ACT+ in addition to usual aftercare versus usual aftercare

Aim
Is ACT+ in addition to usual aftercare more effective and cost-effective than usual aftercare in improving QoL at one-year follow up in patients living with and beyond cancer, whilst remaining as safe as usual aftercare?

Secondary aims

- To collect outcome measures at two year post randomisation follow up of study participants, where possible.
- To test potential predictors, moderators and mediators of the intervention.

Internal pilot and feasibility study

Aim
To pilot a randomised controlled trial comparing the ACT+ intervention in addition to usual aftercare against usual aftercare, to test recruitment and retention.

All main trial procedures will be followed. We will aim to recruit 45 participants in total across all participating recruitment sites, within a six month recruitment period. If significant changes to the protocol prove unnecessary, this will be an internal pilot, leading seamlessly into the main RCT, following approval from our trial steering committee and NIHR. Thresholds for progression to the main trial are outlined below:

Objectives and progression criteria to definitive trial

1. Acceptability of the study and the intervention:
    a. Ability of clinicians to identify potentially eligible participants who give their consent to be approached and go on to be eligible with a FACT-G score of 78 or less (target 135 across the participating recruiting sites)

    b. Did participants randomised to the ACT+ arm take up ACT+ therapy sessions
    - 75% receiving one or more sessions
    - 50% receiving three or more sessions

2. Feasibility of future trial:
    a. Willingness of eligible patients to participate (30%)
    b. Proportion of trial participants completing the 7-week questionnaire (90%).

Table 2 Green and amber progression criteria

Objective	**Green**: Proceed to main trial	**Amber**: Some adjustments may be required before proceeding to main trial
Acceptability of the trial		
Ability of clinicians to identify patients that go on to become eligible with FACT-G score of 78 or less once screened by the study team	135 Patients	134-105 Patients
Participants randomised to ACT+ taking the offer up and receiving at least one session	75%	55-74%
Participants randomised to ACT+ receiving 3 or more sessions	50%	30-49%
Feasibility of a future trial		
Proportion of eligible participants recruited into the study	30%	20-29%
Proportion of trial participants completing the 7 week questionnaire	90%	85-89%

3. Trial design and conduct

3.1. Type of design

The SURECAN Trial is a pragmatic, parallel, two arm, individual patient randomised trial, comparing ACT+, added to usual aftercare, versus usual aftercare only.

3.2. Trial setting

Trial sites

Recruiting sites

Participants will be recruited from hospital clinics in five or more centres including: Barts Health NHS Trust; Homerton Teaching Hospital NHS Foundation Trust;Kings College Hospital Foundation Trust; University College London Hospital NHS Foundation Trust, and Sheffield Teaching Hospitals NHS Foundation Trust.

Sites must:

- identify and sign-up an appropriate local Principal Investigator (PI);
- identify clinical contacts representing each of the included cancer specialities;
- ensure adherence to the protocol; and
- agree, where possible, to approach all potentially eligible patients and to maintain a screening log

Intervention sites

The ACT+ intervention will be delivered by therapists from Improving Access to Psychological Therapies (IAPT), specialist services or cancer charities who have agreed to participate in the study, and a community interest company (CIC) which provides wellbeing and healthcare services These currently include:

- 10 IAPT services covering the following London boroughs: Camden & Islington, Tower Hamlets, Hackney, Redbridge, Newham, Haringey, Enfield and Barnet;
- an NHS mental health service provider,
- a cancer charity, and;
- a CIC.

The final list can be obtained from the study team.

Sites must:

- indentify and sign-up an appropriate local PI;
- identify therapists to attend compulsory ACT+ training, and deliver the intervention;
- ensure adherence to the protocol and relavant standard operating procedures (SOP); and
- find suitable spaces for intervention delivery where applicable, or the ability to deliver the intervention online/telephone.

Site activation

Once the SURECAN Trial study team have confirmed that all necessary documentation are in place (including signed Clinical Trial Site Agreement (CTSA)/Organisational Information Document (OID) and local NHS permissions), a site activation e-mail will be issued to the PI. Sites will undergo a site

initiation meeting prior to commencing recruitment. All sites' responsibilities are outlined in the CTSA and/or the OID.

3.3. Participant recruitment

Patients attending a participating follow-up cancer clinic and meeting the following criteria are eligible for recruitment into SURECAN.

Inclusion criteria

1. Patients within 24 months of having completed cancer treatment of the index cancer, (or nearing completion) with curative intent / long term remission for: breast cancer, lower gastrointestinal cancer, a urologicial cancer, a haematological cancer, head and neck cancer, or any other common cancer with good survival
2. Aged 18 years or over
3. Ability to give informed consent
4.
5. Sufficient fluency in spoken English to be able to participate in a talking-based therapy delivered in English
6. Score of 78 or less on the Functional Assessment of Cancer Therapy – General (FACT-G) at *both* screening and baseline measurement time points

Exclusion criteria

1. Will not have not completed their cancer treatment by the commencement of the trial (excepting those receiving long-term, ongoing maintenance treatment (e.g androgen suppression treatment for prostate cancer).
2. Receiving care for symptom control alone
3. Currently receiving another psychological intervention (NB participants taking antidepressants or anxiolytic drugs remain eligible)
4. Other serious co-morbid condition which would make it difficult for the participant to receive a talking-based, one-to-one intervention
5. Require urgent psychiatric or clinical psychology assessment

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Trial procedures

Recruitment

The recruitment process involves identification, recruitment and randomisation of eligible participants. Identification and recruitment will be carried out by the site NHS clinical team and study research assistants/fellows, and randomisation by the central study team. The reseach assistants/fellows who will support screening and recruitment of particpants will hold honorary contracts/research passports with the relevant hospital site according local R&D policy.

Eligible participants will tbe identified and recruited via three pathways:

1. Approaching patients in clinic
2. Searching patient medical records/lists to identify patients who are approaching end of treatment with curative (or long term remission) intent, in order to aproach them via telephone
3. Via local cancer support network / infrastructure

1. Direct approach in clinic

Indentified patients i.e. those who have completed cancer treatment with curative intent (or long term remission) within the past two years, visiting the clinic and waiting to be seen/during their appointment can be introduced to the SURECAN study. Patients who are interested can be assesed for possible eligibility using the three quality of life (QoL) questions (outlined below). Should they meet the QoL threshold and other eligibility criteria, they can proceed to formal screening using the FACT-G. If the patient scores 78 or less on the screening FACT-G, the patient is given an Informed Consent Pack – which includes the PIS, Informed Consent Form (ICF), a baseline questionnaire, a return envelope, and a £5 thank you voucher (if the patient has an email address, the baseline questionnaire and the consent can be collected online). If the patient is still interested in joining the study, they can sign the ICF, complete the baseline questionnaire, and return both to the recruiting site clinical staff/researcher (or complete the online forms and submit if applicable).

If there is no time, or it is inappropriate to screen during the clinic, this can be done via telephone at a time convenient for the patient. The site clinical staff/researcher can follow up with the patient. If there is no time to talk about the study, identified patients can be handed a Consent to Approach form and/or a PIS. Patients can read the information and get in touch with the site clinical staff/researcher or the study team if they are interested in participating. The site clinical staff/researcher will also follow-up these patients.

2. Searching patient medical records/lists

Patents who have completed cancer treatment and are recorded on a separate clinical list will be identified by the clinical team/research assistant via their medical records. These patients will be contacted by the clinical team/researcher, however, prior to contacting these patients, they will be sent a PIS with a letter informing them about the study mentioning that a member from the clinic will be in touch to introduce the SURECAN study. Once contacted, the patient will be asked the three QoL screening questions, have their eligibility confirmed, and if identified as potentially eligible, will be screened with the FACT-G. If the patient scores 78 or less on the screening FACT-G, the ICF pack is sent to the patient (or the online version sent via email). If the patient is still interested in joining the study, they can sign the ICF, complete the baseline questionnaire, and return both to the recruiting site clinical staff/researcher (or complete the online forms and submit if applicable).

3. Via local cancer support network / infrastructure

Patients can also approach the named site contact on recruitment posters/advertisements that will be left with/posted by local cancer support network (e.g. Macmillan services at the hospital) to find more information about the study.

If patients contact the study team directly, their name and contact details will be given to the relevant site contact to go through eligibility screening mentioned above in the Trial Procedures section.

The three QoL questions

Among the inclusion criteria is a score of 78 or less on the FACT-G to identify low QoL. To identify low QoL, willing patients will be screened in clinic/via telephone by clinical staff/research assistant with three simple screening questions about their physical health, well-being and quality of life to identify potentially eligible participants who are likely to meet the formal FACT-G inclusion criterion.This is done using a 5-point Likert scale, where a score of 1 is poor, and 5 is excellent. The three questions are:

- How would you rate your physical health?
- How would you rate your feelings of wellbeing?
- How would you rate your quality of life?

Based on work in our earlier Programme Development Grant, a score of <11/15 provides 84% sensitivity and 86% specificity against the FACT-G threshold for the lowest (worst) tertile of QoL.

The participating site can also identify low QoL through their usual practices e.g. Macmillan Holistic Needs Assessment, cancer support centre etc.

Recurence of cancer

Patients identified who have completed cancer treatment within the 24 months, but have a possible or confirmed recurrence, can be recruited depending on any anticipated treatment:

- Patients identified as having completed cancer treatment within 24 months who are currently receiving, or scheduled to receive, treatment for a possible/confirmed recurrence, or a metastasis are “banked”. Once they have finished treatment, they can be approached as long as they have been treated with curative intent or to obtain long term remission, and are within 24 months of their index cancer diagnosis.

- Patients identified as having completed cancer treatment within 24 months who are showing signs of, or being investigated for, a recurrence or a metastasis may be included, as long as they are not receiving treatment, or scheduled to receive treatment, within the next six months (other than long-term, ongoing maintenance treatment).

Randomisation

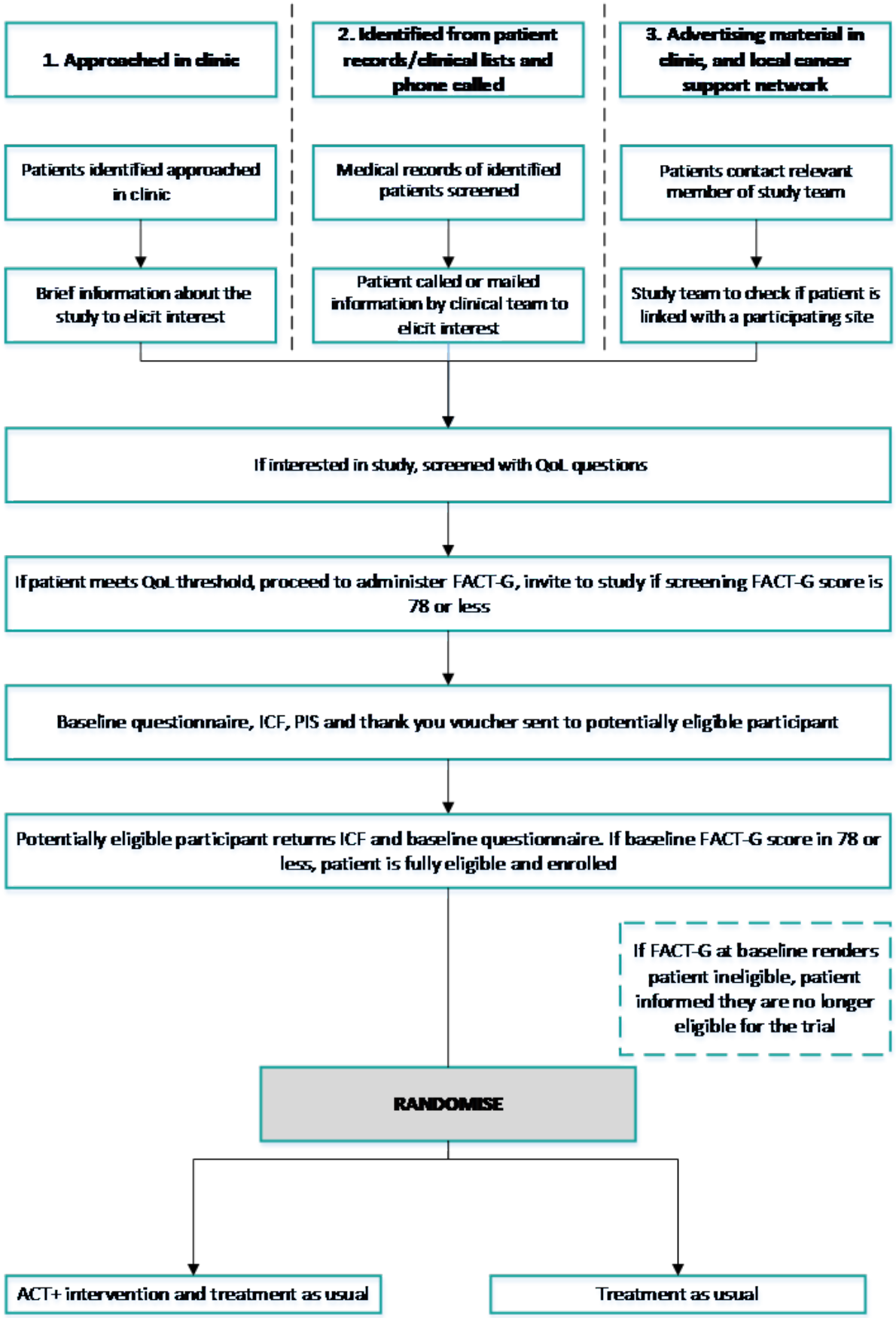
The participant is declared fully eligible if they score 78 or less on the baseline FACT-G (i.e. remain eligible at the point of enrolment/randomisation), in addition to meeting the other eligibility criteria.

If on the baseline FACT-G the participant scores 79 or above, they are no longer eligible and will be notified by letter (improved FACT-G score letter v3.0) and withdrawn from the study. Due consideration is given in the wording of this letter to mitigate any feeling of disappointment. The letter has been approved by our PPI contacts.

Participants returning the ICF and baseline questionnaire, who are remain eligible will be randomised to either receive the intervention or usual aftercare only (1:1 randomisation – see section 7.5). All participants will be informed of the randomisation allocation. The site clinical team/researcher will be blinded to the allocation

Particpants randomised to receive the intervention will be referred to the appropriate therapist to begin the course of therapy with the aim of starting within two weeks from randomisation (see section 4 on Intervention).

Figure 2 Summary of recruitment pathways



3.4. Consent

Consent processes

During contact with the potential participant for screening either face-to-face or over the phone, the researcher will be confirming details about the study with the patients and asking if they have any questions. Before enrolment, participants are sent the ICF along with the PIS to look over the details of the study in their own time. Participants also have the opportunity to ask questions prior to completing and returning the ICF to join the study, and are informed they are free to withdraw from the study at any time. In this way all participants are given ample opportunity to ask further questions or seek more information directly from the research team (on as many occasions as they wish) before completing the ICF to join the study

Some participantswill be asked later during the study if they consent to an interview. This will form part of a separate qualitative study which will have a separate protocol. We have informed partcipants in the PIS for this study of the possibility of being offered for an interview.

The Sponsor requirement is to archive research data for a set period of 20 years (explained in Section 8.1 – *Data storage*). Participants will retain a copy of their signed consent form at the time of their recruitment into the study.

Our funders, NIHR, have recently conducted research on what study participants and the public want from NIHR funded researchers (Johnathan Sheffield, personal communication). They expressed a strong desire to be informed by researchers about the results of research they are invited to participate in, and we believe that NIHR are likely to mandate this in the near future. Accordingly we will seek permission to retain contact details from everyone approached about the study (whether they are interested, in participating and eligible, or not) in order to inform them at a future date about the study progress and results, should they wish this.

Therapist consent
Consent will be also sought from the participating therapists during the ACT+ training or during a site intiation visit. We will seek for their formal consent in delivering the intervention, and consent to be approached about post intervention interviews (which will be part of a separate Process Evaluation of the intervention).

3.5. Usual aftercare

We will partially standardise usual aftercare by providing a Macmillan Cancer Support leaflet about aftercare to all participants, to ensure that appropriate guidance is provided.[21]

However for other elements of support, we have chosen our comparison arm as usual aftercare as currently provided by the NHS and local services.

4. **Intervention**

4.1. Introduction to the ACT approach

The overarching aim of SURECAN is to develop, pilot and evaluate a novel, person-centred, intervention, based on Acceptance and Commitment Therapy (ACT), for people who have completed treatment for cancer with curative intent, but are experiencing poor quality of life. Since we know that exercise is helpful, and work is important to many patients, we will integrate ACT with options for physical activity and work support, if these are deemed important by the participant. We are calling this intervention Acceptance and Commitment Therapy **"ACT Plus (+)"**.

ACT is an empirically based intervention that aims to increase psychological flexibility. Psychological flexibility refers to the ability to adapt to demands, shift perspectives, and balance competing desires and needs. ACT teaches the individual to observe thoughts and feelings without trying to change them, and to behave in ways consistent with individual values irrespective of how they feel.

The core principles of ACT are:

- A = Accept your reactions, thoughts and feelings and be in the present
- C = Choose values-based goals
- T = Take action

ACT is based on a psychological theory of human language called relational frame theory (RFT). RFT argues that the main component of human language and cognition is relating, i.e. the ability to create links between stimuli.[22] As Hayes explained (p16), "when we think, reason, speak with meaning, or listen with understanding, we do so by deriving relations among events – among words and events, words and words, events and events". RFT is a modern behaviour analytic approach to language, which aims to understand the link between human language and behaviour, better. The ACT approach enables people to live a rich, full and meaningful life while effectively handling the difficulties which inevitably comes their way.[23] ACT+ should be seen as a way to equip people with helpful coping strategies to enable them to deal with negative thoughts and feelings that may occur in everyday life. The intervention supports and contributes to psychological wellbeing.

4.2. Format and delivery of ACT+ sessions

Delivery of sessions
Therapy will be delivered by therapists trained in the approach i.e. ACT. They could be situated in Improving Access to Psychological Therapies (IAPT), specialist services or cancer charities. The core profession of the therapists would include clinical psychologists, high intensity therapists (from IAPT), and counsellors. The sessions would be delivered at their respective practices face-to-face, by phone or via online video calling e.g. Skype etc.

Number of sessions
The intervention will take the form of up to eight sessions at weekly or fortnightly intervals using different modalities of delivery to suit individual needs: face-to-face sessions, over the phone or video call. If possible, the first session will be conducted face-to-face with the therapist. The intervention will be introduced and participants will be provided with the ACT+ participant handbook.

Duration of sessions
Each session will take around 1 hour to complete and will include further exercises to be completed at home in time for the next session.

Scheduling of sessions
All sessions should be scheduled and take place within a 14-20 week period starting from when a participant is allocated to the therapist (i.e. from randomisation). Therapists can administer sessions outside of the 14-20 week period if the need arises but we would ask therapists to keep a note of this. Therapists are advised to schedule sessions in advance. However, this is not essential. It may be helpful to hold the sessions on the same day of the week or at the same time of day, should this be possible.

Participants randomised to ACT+ will be provided with information about what they should expect from treatment. This information will explain that participants can choose the mode of delivery that suits their needs. If they choose to have sessions over the phone, they should ensure to be in an appropriate environment where they feel comfortable talking in depth.

Missed sessions
Therapists should outline the procedure for DNAs (i.e. Did Not Attend) in the first session or when they first arrange sessions with participants. This will not be part of therapy time as it is regarded as administration time and therefore should not cut into the time allocated for the session. A session can be re-scheduled to fit in with therapist and participant.Therapists are encouraged to communicate that advanced notice is generally needed in order to be able to reschedule a session. Unreachable participants should be contacted up to six times before they are considered discharged and a letter/text message sent confirming this.

4.3. Supervision

Clinical supervision for discussion of cases will be provided monthly by supervisors employed on the study to ensure quality of therapy and adherence to the study therapy and protocol. Supervision will provide therapists with an opportunity to discuss and tackle any difficulties they may be experiencing, as well as to develop their skills and receive support. The format of supervision will be that of group sessions for shared learning and peer support. Should a therapist wish to have one-to-one supervision, this can be arranged. It may be on the telephone or face to face.

4.4. ACT+ content

Initially sessions concentrate on assessing or getting to know the participant's difficulties and symptoms associated with having had cancer and the ACT+ model is introduced. The subsequent sessions will focus on developing the shared notion that it is perfectly normal to experience symptoms (e.g. fatigue or low mood) or negative thoughts and that trying to stop the unwanted feelings and thoughts does not really work. Conversely trying to control or stop feelings can actually increase the hold that these feelings and thoughts have on us. Instead of fighting thoughts, it is suggested that we should embrace them and in doing so learn that, thoughts and feelings come and go as a normal part of life and that you are not your thoughts.

In addition, we want to promote mindfulness skills such as learning to be present in the moment and to experience thoughts and feelings in a non-judgmental way. In conjunction with promoting these healthy ways to deal with negative thoughts and feelings, we want to help the participant identify their values (i.e. what they really care about; what is important to them). The aspect of the intervention that promotes values should not only increase motivation but also give context to the previous section on

dealing with unhelpful thoughts. If you care about something – a piece of work, a relationship, a hobby – then you will be prepared to endure difficulty to engage with it.

Having introduced helpful ways to deal with negative thoughts and feelings and identified values, the later sessions will involve providing value-based interventions. For example, if becoming more active is an important value for an individual, then sessions will focus on developing realistic and achievable goals around this value.

The exercise component of the ACT+ intervention is designed to be flexible and individually tailored. People can begin at any level: it does not matter if they have little or no experience of exercise. Graded exercise therapy aims to increase regular physical activity, starting with just a little and increasing the amount over time, depending on the participant's current capabilities. The idea is to gradually build up the duration of time when the person is physically active, and then later increase the intensity to recondition the body after periods of inactivity.

4.5. Overview of ACT+

Therapists are provided with session plans, tips and objectives that are meant to be used as a guide and can be adjusted to each person's individual values and goals. This will result in a personalised intervention tailored to each individual's needs.

Session content plans will include the overarching theme for the session, with the objectives and therapeutic skills integrated into the session including between session task suggestions.

Each participant will be given a Participant Handbook which includes materials that supplement the content of the therapy sessions and will help them plan for future sessions. For each session, participants will be asked to do some pre-session reading and complete a reflective exercise. Although the ACT+ sessions follow a structure, each session will have a flexible plan and the participant will be encouraged to add anything important to the session plan. Below is an overview of the ACT+ stages:

Stage 1: Assessment, Engagement and Planning of Treatment (sessions 1 & 2)

Stage 2: Active Treatment (sessions 3 to 6)

Stage 3: Preparation for Discharge (sessions 7 & 8)

4.6. Therapist training and intervention fidelity

Several steps will be taken in order to ensure the fidelity of the ACT+ intervention for the purposes of the SURECAN trial. Throughout this research, our approach to treatment integrity is guided by Perepletchikova et al.'s treatment integrity procedures checklist [24] as shown in Table 3 below.

Table 3 Perepletchikova's treatment integrity checklist

Establishing treatment integrity	Define integrity
	Treatment is operationally defined
	Therapists are trained and supervised
Assessing treatment integrity	Assesses treatment adherence
	Assesses therapist competence
	Includes psychometric properties of integrity measure – where the adherence and competence measures are valid and reliable
Evaluating treatment integrity	Data is representative
	Raters are trained in treatment components and manual & interrater-reliability is assessed
	Adherence and competence measure reactivity is controlled for
Reporting integrity procedures	Reports of procedures for establishing, assessing and evaluating integrity
	Treatment integrity is reported in relation to overall integrity, component integrity and session integrity
Reported output on therapist treatment adherence and competence levels	Data provided in numerical way that is or can be easily converted into a percent integrity

Ensuring treatment fidelity - therapist training

Therapists delivering ACT+ will receive training, which will cover a broad range of practical and theoretical issues relevant to this intervention. We will cover the rationale behind the study and insights into cancer diagnosis, symptoms and impact on quality of life, as well as the theory behind ACT, and the ways in which different cultures experience the NHS and treatment interventions. The therapist manual developed for this trial will be reviewed, as well as details of the study protocol including the role of the therapist, standard operating procedures, recording and storage of the sessions and confidential information, deviations, dropouts and adverse event procedures. The ACT+ training including presentations, exercises and role-plays will last 3 days. Obstacles to participantengagement with ACT+, as well as the challenges of delivering the sessions within a brief period will be discussed. Therapists' knowledge and competence will be assessed before and after the training.

Therapists delivering ACT+ sessions will attend monthly supervision meetings in order to develop their skills and receive support. This will help to ensure therapy integrity and adherence to trial protocol and to maintain the quality of the intervention. Using a manualised approach with structured intervention sessions will also help to promote fidelity.

Measuring treatment fidelity - coding procedure

Selection of sessions to be coded
All sessions between therapists and participants will be routinely audio-recorded on an encrypted digital recorder. At the end of the trial, therapy integrity will be measured by two independent assessors experienced in ACT, adapting a recently developed ACT fidelity measure (i.e. ACT FM) rating 2 sessions in 17 (10%) randomly chosen participants, stratified by therapist and year of trial recruitment. This will enable us to assess the trial therapists' competency/fidelity to the ACT+ intervention within the SURECAN trial.

Interrater reliability
In this study, an interrater agreement between both assessors as to whether the therapy delivered is consistent with ACT+ using Cohen's kappa will be produced. This will establish the degree to which the coders' rating agree. Anything above 80% will be considered good agreement.

Treatment fidelity
This will be assessed by examining the correlation between the ratings on the ACT scale and the global rating of whether therapy was consistent with ACT (Was the therapist delivering therapy which is consistent with ACT?)

Training coders
We will train both assessors prior to the start of coding sessions. Plumb and Vilardaga [25] recommend that the successful training of coders involves regular meetings and multiple shaping opportunities. They also recommend selecting training segments that a lead trainer and trainees can watch and listen to together to discuss the coding choices as they arise. They also recommend that coders are assessed periodically to ensure that ratings have not diverged from the integrity of the coding system which helps clarify any ambiguities that might arise.

5. **Follow-up**

At baseline, seven weeks (approx. mid therapy), 16 weeks (approx. end of therapy) and 52 weeks following randomisation, participants will be asked to complete questionnaires related to the outcome measures (Section 6). Further outcome assessment data will be collected at two years for participants for whom, before the last recruited participant's 52 week follow-up time point, would have had two years elapse from randomisation, and possibly the entire cohort if further funding becomes available and the primary outcome at one year is promising. Participants may also be approached at two years' follow up for a five year follow-up from randomisation (provided consent is given). All outcome measures will be collected by either direct participant input into a secure online study-developed database (developed by the QMUL Pragmatic Clinical Trials Unit) or completed via paper questionnaires and returned for data entry by the study team. The questionnaires will not be available in any languages other than English. Should a participant suffer a recurrance of their cancer during the follow-up period, outcome measures will still be collected as normal, if appropriate.

Participants will be sent the questionnaires (including details on how to access the secure online database where available) by post along with a stamped addressed envelope and a pen, by the SURECAN study team at QMUL. An unconditional gift voucher of £5 will be sent with the questionnaires at all time points. Non-responders at each time point will be sent an email or text reminder, and will be telephoned up to two times (one phone call per week following the response due date) to check whether they have received the questionnaire and offer to complete it over the phone with them or send another if lost. If the participant is unable to complete the entire questionnaire over the phone, the study team will prioritise collection of the FACT-G, the EQ-5D-5L and the CSRI, as they are needed to evaluate the primary outcome. Researchers who complete questionnaires over the phone with participants, will be blinded to the randomisation allocation.

6. **Outcome measures**

6.1. Primary Outcome

Clinical evaluation
The primary outcome will be Functional Assessment of Cancer Therapy: General scale (FACT-G) [26] and primary end-point at 52 weeks follow up, but we will compare the pattern of response over time between arms. FACT-G is a generic measure of physical, social, emotional, and functional quality of life (QoL), matched to ACT+ targets.

Health Economic evaluation
The number of therapy contacts will be recorded on a proforma by therapists centrally. Other measures of health and social care utilisation, informal care, and lost employment, will be measured recorded using an adapted version of the Client Service Receipt Inventory [27]. This will cover the three months before randomisation, and the periods up to 16-week and 52-week follow-up. The CSRI will be self-completed by participants. We will also request Hospital Episode Statistics (HES) data from NHS Digital to supplement the CSRI. HES data will include inpatient care, outpatient contacts and visits to A&E. The EQ-5D-5L will be used to generate Quality-Adjusted Life Years (QALYs) for use in the economic evaluation. We will also examine the association between costs and outcomes that are of most clinical importance and hence we will also use the FACT-G.

6.2. Secondary Outcomes

Secondary outcomes will include: the FACT-G sub-scale scores, [26] fear of cancer recurrence, [28] the positive and negative Impact of Cancer scales which address both aspects of impact of cancer on QOL, [19] the Hospital Anxiety and Depression scale, [29] the Euroqol (EQ-5D-5L),[30] the Chalder Fatigue Scale,[31] and a measure of physical activity. These are validated and extensively used instruments that measure variables which either contribute to poor QoL, or provide additional aspects, such as the Impact of Cancer scales. [19] We will also collect data related to the affects of Covid-19 such as lonliness and worry about contracting the virus.

Meditators and Moderators
Mediation analysis will explore predictors and moderators of the therapy on the primary outcome FACT-G and cost effectiveness as the dependent variables, and will explore mediators of any therapy effects.

Several mediators will be tested, their measures being commensurate with the theory of ACT+ and consistent with assumptions in our logic model (Appendix 3). The measures to be used are:

Acceptance and Action Questionnaire (AAQ-II): The AAQ measures psychological flexibility using a 7 item scale [32].

Values Questionnaire (VQ): 10-item self-report measure assessing the extent to which one lives consistently with their values[33].

Committed Action Questionnaire (CAQ): The CAQ 8-item measure is derived from an original scale of 24 items [34]. Committed action is goal-directed, flexible persistence.

Beliefs about emotions scale (BAE)[35]: This 12 item scale represent types of beliefs about the unacceptability of experiencing and expressing emotions that have been specified in cognitive models.

These measures will be collected at all follow-up time points (see Section 8).

Moderators are likely to include factors such as age, gender, type of cancer and severity of depression. A separate moderation analysis plan will be developed.

7. **Analysis**

7.1. Trial analyses

Detailed statistical analysis plans will be written by the blinded Trial and Senior statistician with input from blinded members of the Trial team and independently approved before the database is frozen for analyses. The statistician will be blinded to treatment group. Analysis will use intention to treat principles, with secondary missing data sensitivity analyses implemented through multiple imputation if appropriate. The main analysis will be a mixed effects linear regression model, adjusting for baseline scores, stratification factors, and allowing for cluster effects of therapists. The FACT-G primary end-point will be at follow-up at 52 weeks after randomisation. Secondary outcomes will be analysed similarly, with the exception of the global impression scale, which will be analysed by mixed effects logistic regression.

7.2. Health Economics

The cost-effectiveness analysis will be conducted from health and social care perspectives, with secondary analyses including informal care and lost employment costs. Costs of ACT+ and usual aftercare will be calculated based on therapist time, overheads, training and supervision. Other costs will be derived from additional service use,[27] informal care time and days lost from work will be valued using average wage rates. Costs will be compared between the two arms using regression models with baseline costs controlled for. Confidence intervals around the cost differences will be produced, based on boot strapped resamples. Cost-effectiveness will be assessed by incremental cost-effectiveness ratios. Sensitivity analyses will be conducted by varying key cost parameters, in particular the cost of the intervention and the unit costs attached to informal care and lost employment.

To assess the long-term cost-effectiveness of ACT+ we will develop a decision model using Markov processes. This will entail defining health states over time to which costs and QALYs will be attached. Epidemiological data on cancer recurrence and survival will be of used in the modelling. We will aim to adapt a 5-year, 10-year, and lifetime time horizon in different versions of the model. We are aware of existing quality of life data from other cancer studies relating to cancer stage and we will seek further estimates. The structure of the model will be developed within the early stages of the programme and will consist of states defined both by clinical severity and quality of life. We will initially conduct a systematic review of previous modelling studies in order to derive parameters for our model. If this review does not produce estimates then we will conduct a review of relevant studies that have collected primary data, supplemented if necessary by expert opinion. The model will be subjected to extensive deterministic and probabilistic sensitivity analyses.

7.3. Mediation and Moderation

Mediation analysis will test single, multiple and sequential mediator models for the AAQ-II, VQ, CAQ and BAE scales. Analysis will control for potential confounders and stratification factors used in the trial. Mediator and outcome variables and amount of missing data will be summarised using mean and standard deviation, or frequency and percentage, as appropriate. Variables will be summarised using unadjusted mean profile. For modelling, baseline and follow-up mediator and outcome variables will be standardised to baseline by subtracting the mean at baseline and dividing by the standard deviation (SD) at baseline. Effect estimates will be in baseline SD units, with the indirect/mediated effects in outcome baseline SD units.

The distributions of the putative moderators will be described by relevant summary statistics within trial arms as well as across the trial sample. Moderation modelling will be carried out for the primary

outcome at 12 months after randomisation. The moderation of treatment effects will be investigated by expanding the models employed in the primary analysis of the trial to include interactions between trial arm differences and the baseline moderator variable in question.

Predictors of costs and cost-effectiveness will also be identified, the latter being calculated as the monetary value of QALYs minus therapy costs. Generalised or standard linear models will be used as appropriate.

7.4. Sample size

Assuming alpha = 0.05 and power = 0.9, we would need 133 participants per arm (266 total) for an effect size (ES) between treatment arms of 0.4; this ES was chosen as a minimally clinically important difference based on existing literature, determined previously as 0.42 and 0.46 for FACT-G.[36, 37] This ES represents a difference of 6 points on FACT-G in a cancer population.[38] Allowing for drop-out by 52 weeks of 15% and inflating the sample sizes for a cluster effect in both arms (5 therapists and 5 cancer clinical nurse specialists nurses (involved in participant identification and recruitment) per arm, per centre, with an ICC = 0.01), the estimated total sample size required is 344 (172 per arm) patients to be recruited over 25 months. This represents an average of 13.8 participants per month in total across participating sites. N.B. This assumes that the pilot will be an internal pilot. Based on the numbers of patients seen in three sites (845 per annum) this sample size can be achieved assuming a recruitment rate of at least 20% of eligible participants.

7.5. Randomisation

After confirmation of eligibility and collection of informed consent and baseline measures, participants will be randomised to either the intervention or usual aftercare. The allocation ratio will be a 1:1 ratio, intervention: control. Allocation will be by stratified randomisation, overseen by the Pragmatic Clinical Trials Unit at Queen Mary, remote to researchers, to preserve strict allocation concealment. Allocations will be stratified by cancer type and centre, in block sizes unknown to researchers.

7.6. Blinding

In pragmatic trials of complex behavioural interventions, such as this, it is not possible to mask fully informed study participants to their treatment group. However research assistants collecting any outcome data by phone will be blinded to participants' allocated arm and Trial Statisticians will be blinded to allocation until data lock. The Trial Manager and the Research Administrator are the only members of the study team who will be unblinded, we have found in other similar studies that this is invaluable for the efficient running of the study (e.g. for being able to ensure that participants randomised to the intervention receive the intervention in a timely fashion). Data extraction from primary care records will be done by masked study personnel as will data entry.

8. **Data collection and management**

8.1. Data collection – participants

Data collected for all participants recruited:

Cancer and treatment data

To be collected by clinical site staff/research assistant includes the following:

- Data confirming eligibility including:
    - Approximate date of completion of last cancer treatment with curative intent
- Type of cancer (i.e. breast, colorectal, leukaemia, lymphoma, a urological cancer, head and neck)
- Curative treatment
- Recurrances

Healthcare resource data

Healthcare resource use including: medicine and equipment prescribed, outpatient appointments, primary care visits, accident and emergency and walk in clinic visits, hospital stays and all other NHS treatments and services e.g. physiotherapy, speech therapy in the three months prior to randomisation and in the 12 months following randomisation.

Data will be linked to Hospital Episode Statistics (HES) via NHS digital

Baseline and follow-up data

The following data is to be collected by questionnaires/eCRFs for all participants. The detailed process for collection for outcome measures is outlined in Section 5

Table 4 Screening and data collection schedule

	Screening	Baseline	7 weeks	16 weeks	52 weeks	2 years (where possible, for partcipants still in the study)
Collected by clinics						
Cancer and Treatment details		x			x	
Eligibility	x					
Follow-up questionnaires sent to participants						
FACT-G	x	x	x	x	x	x
Client Service Receipt Inventory (adapted)		x		x	x	
(FACT-G) – Subscale scores		x	x	x	x	x
EQ-5D-5L		x	x	x	x	x
Demographics		x				
New recreational activities				x	x	
Self-Administered Comorbidity Measure		x				
Fear of cancer Recurrence		x	x	x	x	x
Positive and negative Impact of Cancer scales		x	x	x	x	x
Hospital Anxiety and Depression scale		x	x	x	x	x
Chalder Fatigue Scale		x	x	x	x	x
Psychological flexibility		x	x	x	x	x
Goal directed behaviour		x	x	x	x	x
Values		x	x	x	x	x
Beliefs about emotions		x	x	x	x	X
Lonliness and Covid-19 impact		x	x	x	x	x
Exercise		x	x	x	x	x

x: as collected

Process data collected by therapists:

Intervention data which includes:

- Therapist details
- Therapy session log i.e.sessions completed/missed, duration.End of sessions summary i.e. if participant dropped out, engagement etc…

8.2. Data management

The SURECAN study team will work closely with staff at participating sites to ensure accurate (complete, valid and reliable) collection of data. Extensive completeness, range and consistency checks will further enhance the quality of the data. Two levels of data validation will be incorporated into the eCRF. The first prevents obviously erroneous data from being entered, e.g. entering a date of birth that occurred after the date of consent. The second level checks for data completeness and any unusual data entered, i.e. a variable that was outside of the pre-defined range. The site PI is responsible for ensuring that all data queries are resolved. Ongoing data entry, validation at adherence to the trial protocol at sites will be closely monitored by the study team and any concerns will be raised to the participating sites.

All PCTU SOPs with regard to data management will be adhered to by the study team. A data management plan will be written to cover all aspects of managing the data such as, the CRF design, the data management system for data collected, data entry, data handling processes including data checking, query management and cleaning, data transfer, quality control procedures, processes for interim and final data extractions, the procedures for freezing and locking the databases.

CRF design
The PCTU SOPs including the associated documents on CRF design have been used to design the relevant CRFs for the trial. The CRF documents contain the Participant ID, study name, site number/ID, researcher name, (where appropriate), CRF document name and other relevant information on each page and space to record appropriate signatures. All questionnaires, to be captured in CRFs, will receive all necessary research governance and ethics approval.

Data management system and data storage
All study data will be uploaded onto a dedicated folder on the secure virtualised environment at the Barts Cancer Centre (BCC). This is where all data analysis of the PCTU trial data is carried out. Within the BCC, an identifiable spreadsheet developed by the study team comprising participant full name, contact details will be kept in a separate secure folder to the trial data. The BCC environment requires dual factor authentication to access the portal and the folders where the data are stored are only accessible to the appropriate members of the PCTU and the SURECAN study team.

9. **Ethics**

9.1. Research ethics approval

This Protocol, Patient Information Sheets, Consent to Approach and Informed Consent Forms, and other trial-related documents will be reviewed and approved by the Sponsor and Research Ethics Committee (REC) with respect to scientific content and compliance with applicable research regulations involving human subjects. Details of the informed consent procedure are reported in Section 3.4.

9.2. Protocol amendments

Any modification to the protocol and/or trial-related documents which may impact on the conduct of the trial, potential benefit to participants or participant safety will require a formal amendment to the protocol. Such amendments will be agreed by the Sponsor, PMG and approved by the REC. Administrative changes of the protocol, which have no impact on the conduct of the trial or participant safety, will be agreed by the Sponsor. The REC will be notified but formal approval will not be required.

9.3. Safety

We consider that the trial carries a very low risk of adverse events. These will be reported using the QMUL PCTU Adverse Events Log.

We will be aware of the risk of psychological distress for participants and will seek to minimise them. ACT is a tried and tested evidence-based intervention though it has not previously been used in combination with options for work and exercise support. All adverse events and serious adverse events will be recorded and reported in line with the ethics committees and sponsors requirements.

The therapists delivering the intervention to participants are either high intensity therapists, counsellors, or clinical psychologist employed by the Increasing Access to Psychological Therapies (IAPT) services, cancer psychological services, or by other psychological support centres. Should the participant become distressed about their situation and their condition; or more seriously, expresses suicidal intent or is at risk of harm to themselves or others, the therapists are fully trained and experienced to deal with such circumstances. Should any participant become distressed at any point whilst interacting with the study team for data collection, we will always encourage the participant to contact their GP or other relevant health care professionals themselves. When this is the case we will seek permission from the participant to contact them later to confirm they were able to speak to their health care professional. However, it is possible that information contained in a participant's response to a form, or communicated during follow-up calls, may indicate an issue which may jeopardise the safety of the participant e.g. expressing suicidal intent. If there is any indication in a trial participant's response of a serious problem, or any issue in relation to their personal safety, this will be reported to the Co-CI Professor Trudie Chalder (lead clinical psychologist) who will decide on the appropriate action. This may on very rare occasions necessitate a breach of participant confidentiality in order to maintain their safety. Disclosure of such information may be necessary in situations where failure to disclose appropriate information would expose the participant, or someone else, to a risk of serious harm or death.

If necessary, with participant consent, we will contact the health care professional or social services on their behalf, and set up relevant appointments. Professor Trudie Chalder will be contactable to discuss with therapists or researchers appropriate actions in response to adverse events.

Adverse events (AEs): AE are any clinical change, disease or disorder experienced by the participant during their participation in the trial, whether or not considered related to the use of treatments being studied in the trial.

Serious adverse events: An AE is defined as serious (an SAE) if it results in one of the following outcomes:

- A life-threatening AE
- In-patient hospitalisation or prolonged hospitalisation not related to their cancer diagnosis, which are expected events
- Persistent or significant disability/incapacity
- A congenital anomaly/birth defect in the offspring of a subject
- Is otherwise considered medically significant by the investigator
- Other medical events requiring intervention to prevent one of the above outcomes.

Follow-up after SAEs: An SAE occurring to a research participant should be reported to the main REC where in the opinion of the Co-Chief Investigator (Co-CI) the event was:

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

The Co-CI or Sponsor will complete and send a SAE report for non-ctimps (clinical trial of investigational medical products) to the REC within 15 days of becoming aware of the event.

After a SAE (except for death), a decision will be made by the study team, after advice from the relevant authorities and the participant's clinical team, as to whether the participant should be withdrawn from either their randomised treatment or from the trial. However, we do not envisage such a situation.

Arrangements will be made by the study team for further assessment and management as agreed with the relevant authorities, GP and participant.

The investigator will provide the study team with a 1-month follow-up report on all SAEs. Further monthly reports should be provided in the absence of resolution. These reports will be communicated to the Programme Steering Committee, REC, and to the local R&D office. Blank Adverse Event Forms will be distributed to sites that are delivering the intervention.

AEs that do not require reporting: Expected AEs include planned/elective hospitalisations, or unplanned but expected hospitalisation due to cancer reoccurrence: these are expected during the course of the trial and will not be collected as SAEs. AEs related to injury due to exercise encourage as part of the course of therepy, or suicidal ideation should be recorded.

Stopping the trial

Due to the low risk nature of the study, there will be no data monitoring and ethics committee (DMEC). The trial may be prematurely discontinued by the Sponsor or Chief Investigators on the basis of new safety information or for other reasons given by the Programme Steering Committee (PSC) or REC concerned. The trial may also be prematurely discontinued due to lack of recruitment or on advice from the PSC (if applicable), who will advise on whether to continue or discontinue the study and make a recommendation to the Sponsor. There will be no formal stopping rules based on the intervention outcomes. In the unlikely event that the study is prematurely discontinued, active participants will be informed and no further participant data will be collected. For participants who are receiving the intervention, their therapist will determine whether further psychological support is needed outside the scope of the study.

9.4. Confidentiality

Information related to participants will be kept confidential and managed in accordance with General Data Protection Regulation (GDPR), NHS Caldecott Principles, The Research Governance Framework for Health and Social Care, and the conditions of Research Ethics Committee Approval.

The participant information sheets will set out arrangements relating to confidentiality, security, storage of data and accessibility of data only to the study team. They will also be informed about transfer of any hard copy data about them to the host centre/s for secure and confidential storage. All documentation containing identifiable participant data such as in informed consent forms and contact details logs, will be filed separately from case report forms (CRFs), adverse event logs, in a secure electronic folder, or cabinet, in a locked room with key code access at the host centre/s. The researcher will add to the informed consent form, the SURECAN study unique ID. All participants will be assigned a unique SURECAN participant ID. The CRFs will be pseudo-anonymised with the SURECAN study participant ID. For details of data transfer, data management and data access, see Section 8, also the SURECAN Trial Data Management Plan.

9.5. Withdrawal

All participants are free to withdraw from the study at any time before main trial analysis without giving reasons and without prejudicing further treatment. Once analysis has started, it will not be possible to exclude a participant's data from the analysis. Their right and access to their usual NHS treatment will not be compromised in any way if they do not agree to participate in, or subsequently withdraw from, the study. All research team members have received appropriate training including good clinical practice training and are experienced in the process of taking consent.

In line with GDPR guidelines, study participant rights to access, change or remove their information will be limited, as we will need to manage information in specific ways in order for the research to be reliable and accurate. If a participant chooses to withdraw from the study, we will keep the information that we have already obtained (in accordance with the GDPR regulations) unless the participant explicitly requests data collected to be withdrawn, in which case a minimum dataset including randomisation date/time, date of withdrawal and reason of withdrawal will be used. To safeguard participant rights, we will use the minimum personally-identifiable information possible at all stages of the study. Study participants can withdraw at any time and contact the research team based at Queen Mary, University of London or their clinic if they wish to withdraw, using the contact details provided in participant information leaflets for the study and on the website. Or they can inform the therapists to discontinue their therapy session for partcipants randomised to the intervention arm. Participants who withdraw from the intervention will still be followed-up by the study team unless the participant informs the study team they want to withdraw from follow-up in addition to the intervention.

10. Monitoring and study oversight

10.1. SURECAN Study Team

All day-to-day management of SURECAN will be the responsibility of Professors Stephanie Taylor (Co-CI) and Trudie Chalder (Co-CI). Staff who work on SURECAN (including the Programme Manager, Mr Imran Khan; Researchers Dr Sheila Donovan and Dr Elisavet Moschopoulou), will also be involved in the day-to-day operations of the study. The SURECAN study team will meet regularly to discuss, the progress of the trial and findings from other related research.

10.2. Programme Management Group (PMG)

The wider PMG comprising of the co-applicants will also convene on a regular basis to discuss the progress of the trial.

10.3. Programme Steering Committee (PSC)

The progress of the trial will be monitored and supervised by the PSC. The PSC will liaise with the study funders, the NIHR. In the case of study deviations or serious breaches of protocol, study deviation forms will be completed and forwarded to the PSC and the study sponsor. The PSC will also be informed of any adverse events. The PSC has already been formed and include the following members:

Chair (Independent)

- Prof Janet Dunn, Professor of Clinical Trials and Head of Cancer Trials, Warwick Medical School

Independent members

- Dr Jo Armes, Reader in Cancer Care, University of Surrey
- Dr Toral Gathani, Consultant oncoplastic breast surgeon and clinical epidemiologist, Nuffield Department of Population Health, University of Oxford
- Ms Lesley Turner, Independent Cancer Patients Voice (ICPV)

Non-Independent members

- Prof Stephanie Taylor, Professor in Public Health and Primary Care, Queen Mary University of London (Co-Chief investigator)
- Prof Trudie Chalder, Professor of Cognitive Behavioural Psychotherapy, King's College London (Co-Cheif investigator)

Due to the low-risk nature of the study, there will be no data monitoring ethics committee (DMEC).

11. **Trial closure**

The end of the trial will be when the final participant has completed their 52 week follow-up, and data checked and cleaned. At which point the Declaration of End of Trial Form will be submitted to the funder, as required.

12. **Finance and funding**

The study is funded by the NIHR Programme Grants for Applied Research funding stream (REF: RP-PG-0616-20002)

13. **Indemnity**

Queen Mary University of London will be the study sponsor. The sponsorship will be given on the basis of meeting the 'Conditions of sponsorship' which means that the research should be conducted and managed as per the UK Policy Framework for Health and Social Care research 2017and/or the Medicines for Human Use (Clinical Trials) Regulations 2004.

Queen Mary University of London has a no fault indemnity insurance policy for research participants. These compensation arrangements apply where harm is caused to a participant that would not have occurred if they had not taken part in the study. These arrangements do not affect participants' rights to pursue a claim through legal action.

14. **Dissemination policy**

It is a good use of properly anonymised data for it to be responsibly shared with other scientists. We will explicitly ask consent from participants to be able to share appropriate, anonymised data with other scientists, so long as there is no risk of personal identification. Appropriate study data will be anonymised and stored within the PCTU data processing safe haven, and made available for sharing within two years of the final report.

Approaches to share data will be handled by the PCTU's Data Sharing Committee which includes a Senior Statistician and a Senior Data Manager. All requests for data sharing will follow the PCTU data sharing procedures, regarding assessing access requests with guarantees of confidentiality and pre-specified analysis plans.

The funding body (NIHR) will be acknowledged in all outputs. Participants can request to be informed about the progress and results of the study by indicating that they want this, and giving permission to store contact details for this purpose on the consent form.

Projected publications

On publication of our study we will disseminate our findings to all study participants and all cancer services and trusts involved in the study, all CCGs in the UK and all cancer services in the UK, via an electronic or paper newsletter, according to participant preference, or participant letters. Pilot and main trial participants will also be sent an electronic or paper newsletter once or twice during the trial to give them news of the programme as well as news that might be of interest to them (e.g. resumes of published papers of interest regarding QoL and its improvement in cancer survivors).

We will use social media, e.g. a dedicated twitter account, to raise awareness of, and interest in, the project.[40] The study will have a dedicated, up to date web site. With material targeted at both participants, the general public and health professionals

Peer reviewed scientific publications and presentations

We will submit abstracts for the main findings to be presented at scientific and health service related conferences. The conference presentations will also aid the dissemination of our findings to clinicians, patients and charities. Conferences we will target will include: National Cancer Research Institute, UK Oncology Nursing Society, and Breast Cancer Care.

Papers will be prepared and submitted in peer reviewed scientific journals with open access arrangements. We plan to publish our protocol and we will approach a widely read, high impact journal for the main trial paper.

Other papers will be submitted to relevant journals such as the Journal of Cancer Survivorship. Appropriate publicity, such as press releases and press conferences will be arranged for the main publications, taking into consideration advice from the journals concerned, University public relations departments, and the Science Media Centre (http://www.sciencemediacentre.org/). In the application, we have submitted requests for funds to ensure that all papers are published with open access. We will prepare a separate publication for the Health Services Journal.

We will work closely with our collaborator Macmillan Cancer Support to disseminate our results as widely as possible to patients and the public.

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16. **Appendices**

16.1. Appendix 1 - protocol amendments

Protocol:		**Amendments:**		
Version no.	**Date**	**Amendment no.**	**Protocol Section (no./title)**	**Summary of main changes from previous version.**
v1.0	24 Sept 19	N/A	N/A	N/A
V1.1	5 Dec 19	1	7.1 Trial data	Detailed statistical analysis plans for internal pilot, main trial and mediation analysis
V1.1	5 Dec 19	1	7.5 Randomisation	Randomisation overseen by PCTU
V1.1	5 Dec 19	1	5 Follow-up	Consent to approach for 5 year follow-up
V.2	10 Sept 20	2	All	Various administrative updates including specifying the length of the pilot trial
V.2	10 Sept 20	2	3, 5	Section 3: Adding further detail around the recruitment process Section 5: Follow-up procedure
V.3.0	6 Feb 21	3	6, 7 and 8	Addition of questions understanding the contextual factors of Covid-19 Addition of questions related to monitor physical exercise change Removal of Process Evaluation section Minor administrative changes

V.4.0	16 June 22	4		Widening eligibility with inclusion of other cancers Defining what is meant by curative Other wording changes to eligibility criteria Simplfying the screening and enrolment process to better represent the recruitment process used/currently being used Removing monitoring plan
V.5.0	2 October 22	5	3.2 Intervention sites	Include the non-profit Community Interest Company (CIC), Mind-Growth Mastery CIC Registration No: 12069614 (2019), to support delivery of the intervention in addition to our existing providers

16.2. Appendix 2 - trial timeline

Study month	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30	31-33	34-36	37-39	40-42
Internal Pilot														
Recruit & randomise 45 participants	45													
Deliver ACT+ to 22 participants														
7 week assessment														
16 week assessment														
52 week assessment														
Main trial														
Recruit 299 participants				60	60	60	60	59						
Deliver ACT+ to 150 participants														
7 week assessment														
16 week assessment														
52 week assessment														
24 month follow-up first patients where possible														

Likely that the main trial will continue from pilot without a large gap

16.3. Appendix 3 - logic model