Protocol details

1.1 Protocol Title:

ADIE-BC Trial: Managing Anxiety After Completing Treatment For Primary Breast Cancer.

1.2 Protocol Details

Current Version number: V1.1
Date: 26JUN2026

1.3 Names (titles), roles and contact details:

Sponsor
Name of Sponsoring Organisation: King's College London
Name of Sponsor Representative: Bashir Al-Hashimi
Address: Room 8.11, 8th Floor Melbourne House,
44-46 Aldwych, London, SE1 8WA
Telephone: +44 (0)2078487306
Email: vpri@kcl.ac.uk

Chief Investigator
Name: Dr Lauren Heathcote
Address: Health Psychology Section, 5th Floor Bermondsey Wing, Guy's Hospital, Great Maze Pond, SE1 9RT

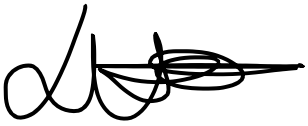
2 CI Signature

The Chief Investigator and the RGO (sponsor office) have discussed this protocol. The investigators agree to perform the investigations and to abide by this protocol.

The investigator agrees to conduct the trial in compliance with the approved protocol, GCP, the Data Protection Act (2018), the UK Policy Framework for Health and Social Care Research, the Sponsor's SOPs, and other regulatory and local requirements as required.

Chief investigator

Lauren Heathcote



Signature

26/06/2026

Date

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3 List of Abbreviations and Definitions

AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
DMEC	Data Monitoring and Ethics Committee
ICF	Informed Consent Form
KCL	King's College London
KCTU	King's Clinical Trials Unit
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
Participant	An individual who takes part in a clinical trial
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RGO	KCL Research Governance Office
SAE	Serious Adverse Event
SOPs	Standard Operating Procedures
SSA	Site Specific Assessment
TMG	Trial Management Group
TSC	Trial Steering Committee

4 Summary/Synopsis

Protocol Full Title	ADIE-BC Trial: Managing Anxiety After Completing Treatment for Primary Breast Cancer
Protocol Short Title/Acronym	ADIE-BC Trial
IRAS Number	369405
REC Reference	26/LO/0459
Trial registration details	Intended registry: ClinicalTrials.gov or ISRCTN
Chief Investigator	Dr Lauren Heathcote
Sponsor name	King's College London
Funder	Wellcome (award identifier: 309734/Z/24/Z)
Medical condition or disease under investigation	Anxiety in breast cancer survivors
Trial Design & Methodology	Randomised controlled, parallel group
Trial Duration	1 July 2026 – 30 December 2028. The main efficacy trial ends 18 weeks post-randomisation, when the final participant completes the 18-week follow-up. After this, participants will be invited to an open-label extension with a 12-month post-randomisation follow-up to assess long-term durability of treatment effects. Data from the extension will not be included in the main trial results. The formal end of trial is when the last participant completes the 12-month follow-up.
Purpose of clinical trial	The purpose of this clinical trial is to evaluate the clinical efficacy and underlying mechanisms of ADIE-BC therapy in individuals who have completed treatment for primary breast cancer, compared with Enhanced Usual Care (EUC)
Primary objective	To evaluate whether ADIE-BC therapy, compared to EUC, leads to lower anxiety at 8 weeks post-randomisation in individuals who have completed treatment for primary breast cancer, as assessed by the State-Trait Anxiety Inventory (STAI-T).
Secondary objective(s)	<u>Secondary Clinical Objectives</u> **Additional anxiety-related outcomes:** To evaluate the effect of ADIE-BC versus EUC on: • Anxiety (STAI-T) at 18-weeks post-randomisation. • Generalised anxiety symptoms (GAD-7) at 8- and 18-week post-randomisation. • Fear of cancer recurrence (FCRI-SF) at 8- and 18-weeks post-randomisation. • Anxiety sensitivity (ASI) at 8- and 18-weeks post-randomisation. **Psychological and quality-of-life outcomes:** To evaluate the effect of ADIE-BC versus EUC on:

	• Depressive symptoms (PHQ-8) at 8- and 18-weeks post-randomisation. • Health-related quality of life (EQ-5D-5L) at 8- and 18- weeks post-randomisation. • Work status (WAS-1 + work status items) at 8-week and 18-weeks post-randomisation **Somatic symptoms:** To evaluate the effect of ADIE-BC versus EUC on: • Fatigue, pain, and hot flush interference (PROMIS Fatigue-7a, Pain-1a, Pain Interference-6a, MENQOL-Vasomotor) at 8- and 18- weeks post-randomisation. <u>Mechanistic Objectives</u> **Interoception:** To determine whether ADIE-BC versus EUC affects: • Interoceptive accuracy (Heartbeat Discrimination and Heartbeat Tracking tasks) at 8 weeks. • Interoceptive sensibility (MAIA-2, BTMS, BMI-2) at 8 and 18 weeks. To explore whether: • Change in interoception (accuracy & sensibility) mediates the effects of ADIE-BC on anxiety. **Biological mechanisms:** To determine whether ADIE-BC versus EUC alters: • Cortisol (saliva) and inflammatory markers (blood) at 8 weeks. • Neural correlates of interoception (task-based fMRI) at 8 weeks. <u>Acceptability & Safety</u> **Acceptability:** To evaluate the acceptability of ADIE-BC using the TAF questionnaire at 8 weeks. **Adherence:** To assess adherence and engagement with ADIE-BC, including session completion and retention rates. **Safety / Serious Adverse Events:** To monitor and describe any serious adverse events related to the intervention. <u>Open-label extension</u> **Durability of effects:** To evaluate long-term maintenance of ADIE-BC effects at 12 months post-randomisation in an open-label extension phase.

Number of Participants	168 participants
Endpoints	The primary endpoint is at 8 weeks post-randomisation. Follow-up endpoints are at 18-weeks and 1-year post-randomisation.
Main Inclusion Criteria	• Aged 18 years or older • Resident in the United Kingdom • Able and willing to attend weekly sessions in London for 8 consecutive weeks • Able to read, write, and follow instructions in English • Have previously received a diagnosis of primary breast cancer (stages 0-III) • Have completed hospital-based cancer treatment between 6 months and 10 years prior to enrolment (long-term adjuvant therapies are permitted) • Meet criteria for at least mild anxiety, defined using a pre-determined cut-off score GAD-2 (≥2) (GAD-2: Kroenke et al., 2007).
Main Exclusion Criteria	• Diagnosis of secondary or metastatic breast cancer or Lobular Carcinoma in Situ (LCIS) only • Previous participation in any ADIE therapy trial • Current severe depression, high risk of suicide, or scheduled to begin Cognitive Behavioural Therapy (CBT) during the intervention period
Study Duration	Approximately 19-25 weeks from informed consent (minimum 18 weeks from randomisation to completion of 18-week follow-up assessment). Participants consenting to the optional long-term follow-up will be contacted at 12 months post-randomisation.
Statistical Methodology and Analysis	All analyses will follow a pre-specified statistical analysis plan and the intention-to-treat principle. Primary and secondary outcomes will be analysed using linear mixed-effects models with repeated measures, adjusting for baseline values and stratification factors, with sensitivity, subgroup, mediation, and exploratory long-term follow-up analyses conducted to assess robustness, mechanisms, and durability of effects.
Human Tissue Samples	• Saliva samples: Participants will provide home saliva samples on two occasions (baseline and endpoint assessment visits), with sampling completed within approximately 3 days prior to each assessment visit. Six samples will be collected per sampling day (waking, +15 min, +30 min, +60 min, midday, and evening). • Blood samples: Venous blood will be collected at baseline and endpoint assessment visits (1 × 5 mL serum tube and 1 × 4 mL plasma tube per visit).

Data to be collected & associated storage arrangements	• Personal Identifiable Data (e.g. contact details) • Self-Report Questionnaires (pseudonymised) • Individual Interview (identifiable) • Heartbeat Biobehavioural Data • Saliva • Blood • Brain fMRI

Amendment History

Amendment number	Protocol version number	Date	Details of changes made
N/A			

5 Roles & Responsibilities

5.1 Role of Sponsor and Funder

The sponsor, King's College London (KCL), takes responsibility for arranging the initiation and management of this research, and for ensuring that appropriate standards, conduct and reporting are adhered to regarding its facilities and staff involved with the project.

5.2 Roles & Responsibilities of Study Management Committees, Groups & Individuals

The TSC will function as an advisory Group for the trial, with the primary function to provide independent oversight and advice on the trial's progress. The committee serves in an advisory capacity only and does not hold decision-making authority regarding trial design, conduct, or analysis. All final decisions remain with the CI and Sponsor.

The TSC will advise on: the trial protocol and amendments, monitoring adherence to the protocol, monitoring patient safety and ensure the rights, safety and well-being of participants, ensuring appropriate ethical and other approvals are obtained in line with the project plan, and provide independent advice on all aspects of the project.

The TSC comprises a chair, who is a senior academic independent of the trial team, independent academic and clinical-academic members with relevant expertise in clinical trials, trial statistics, mental health, and psycho-oncology, plus core members of the trial research team and a Lived Experience Lead. The independent members provide objective oversight while the trial team members ensure the committee is fully informed of operational progress and challenges.

Two independent members of the TSC will be nominated to form a Data Monitoring and Ethics Committee (DMEC) function within the TSC, with responsibility for reviewing safety data in an unblinded capacity.

All members are required to sign and maintain a log of potential conflicts and/or interests. The primary TSC reporting line is via the Chair to the CI.

5.3 Protocol Contributors

Name: Dr Lauren Heathcote
Address: Health Psychology Section, 5th Floor Bermondsey Wing, Guy's Hospital, Great Maze Pond, SE1 9RT
Telephone: 020 7188 2597
Email: lauren.heathcote@kcl.ac.uk

Name: Prof Sam Norton
Address: Health Psychology Section, 5th Floor Bermondsey Wing, Guy's Hospital, Great Maze Pond, SE1 9RT
Telephone: 020 7188 2597
Email: sam.norton@kcl.ac.uk

Name: Dr Cindy Chan
Address: Health Psychology Section, 5th Floor Bermondsey Wing, Guy's Hospital, Great Maze Pond, SE1 9RT
Telephone:
Email: cindy.c.chan@kcl.ac.uk

Name: Dr Faith Borgan
Address: Health Psychology Section, 5th Floor Bermondsey Wing, Guy's Hospital, Great Maze Pond, SE1 9RT
Telephone:
Email: faith.borgan@kcl.ac.uk

Name: Dr Matthew Howard
Address: Centre for Neuroimaging Sciences, King's College London, De Crespigny Park, London, SE5 8AF
Telephone:
Email: matthew.howard@kcl.ac.uk

6 Introduction

Breast cancer is a disease characterised by abnormal cellular growth in breast tissue (Sun et al., 2017). Approximately 2.3 million new cases of breast cancer are diagnosed globally each year, resulting in an estimated 685,000 deaths annually (Arnold et al., 2022). Following

diagnosis and treatment, many individuals experience persistent psychological distress. Anxiety is particularly common, with prevalence estimates of clinically significant anxiety remaining around 18% among survivors in remission (Linden et al., 2012; Mitchell et al., 2013). While existing anxiety interventions such as Cognitive Behavioural Therapy (CBT) are effective for some, they do not benefit all survivors. This is in part because these interventions are not tailored to the unique mechanisms that underlie post-cancer anxiety. Recognising this gap, cancer priority setting groups have designated 'developing a psychological support package to improve mental health during *and after* cancer' a Top 10 Research Priority (James Lind Alliance, 2018a, b). As advances in breast cancer detection and treatment continue to improve survival, the number of breast cancer survivors is increasing, amplifying the scale of unmet psychological needs within this population.

Alterations in interoception, i.e., the sensing, processing, and integration of bodily signals, are observed in individuals experiencing anxiety and can be targeted in anxiety interventions. Likewise, a diagnosis of cancer can shift a person's relationship with their body and bodily sensations – i.e., in interoception. After cancer, individuals can experience bodily sensations as more threatening (Heathcote et al., 2023). The experience of cancer can also change core beliefs about the body, particularly instilling the belief that the body is an adversary (Dowling et al, 2024). These interoceptive changes can compromise the processing of bodily sensations and their link to emotional states, which could diminish the identification (and control) of emotions (Garfinkel et al., 2015). Moreover, aberrant interoception may reinforce core beliefs that the body is untrustworthy and adversarial.

Aligning Dimensions of Interoceptive Experience (ADIE) is a novel intervention approach designed to support more accurate and confident perception of cardiac interoceptive signals alongside adaptive use of bodily signals to regulate emotions (Quadt et al., 2021). The intervention uses real-time heartbeat measurement and provides structured biofeedback-based training in attending to internal cardiac sensations through two established interoceptive paradigms: the Heartbeat Tracking Task and the Heartbeat Discrimination Task. In the Heartbeat Tracking Task, participants are asked to silently count their heartbeats during semi-randomised time-windows. In the Heartbeat Discrimination Task, they judge whether an externally presented auditory tone is synchronised or unsynchronised with their heartbeat. Following each trial, participants provide confidence ratings regarding the perceived accuracy of their responses, encouraging reflection on interoceptive awareness. Through iterative feedback, participants learn to become more accurate and confident in detecting their heartbeat. Interoceptive precision training is delivered once weekly, over six sessions. In addition to the precision training, participants receive supportive materials that encourage an adaptive and non-judgmental engagement with bodily sensations, aiming to promote adaptive interoceptive sensibility and emotion-regulation skills.

A Randomised Controlled Trial (RCT) involving 120 individuals with autism found that six sessions of ADIE increased behavioural measures of interoceptive precision for cardiac signals, altered neural markers of brain-body integration, and reduced anxiety compared with an active control intervention (Quadt et al., 2021). Approximately one third of participants receiving ADIE met the study's pre-registered 'recovery' from anxiety, with improvements

maintained at a one-year follow-up. The trial was recognized by the Royal College of Medicine Medical Innovation Summit as one of the notable medical research advances in 2023. Preliminary support for the anxiety-reducing potential of ADIE has also been observed in an unpublished pilot study with non-autistic adults (N=52), suggesting that interoceptive training may have broader applicability beyond autistic populations (Garfinkel, unpublished pilot data).

In light of the substantial unmet clinical need for evidence-based approaches to managing anxiety following breast cancer, and evidence that interoception may be a mechanistic factor associated with anxiety after cancer, this study will assess the efficacy of safety of ADIE therapy as a potential intervention for reducing anxiety in breast cancer survivors.

ADIE-BC: Adaptation of ADIE for survivors of primary breast cancer

To ensure that the Aligning Dimensions of Interoceptive Experience (ADIE) intervention was appropriate and acceptable for individuals who have completed treatment for primary breast cancer, we co-designed an adapted version of ADIE (ADIE-BC) through a series of structured workshops with breast cancer survivors. The purpose of this co-design process was to identify the specific interoceptive challenges experienced in the context of cancer survivorship and to refine the intervention so that it more closely aligned with survivors' needs and lived experiences. Across these workshops, participants highlighted concerns related to heightened vigilance towards physical sensations, fear of misinterpreting bodily cues, and underlying beliefs that their body had become unreliable or threatening following cancer treatment. Guided by these insights, the adaptation process focused primarily on revising and expanding the supportive materials delivered alongside the precision training. These materials were tailored to address common interoceptive concerns in breast cancer survivorship, including difficulties re-establishing a sense of trust in the body. The adapted materials emphasise compassionate and non-judgemental engagement with internal sensations and using their increased interoceptive accuracy to re-establish adaptive beliefs about the body (e.g., "my body is working with me"). The core ADIE precision training tasks and structure (six weekly sessions involving heartbeat tracking and heartbeat discrimination tasks) remain unchanged, while the surrounding psychoeducational and reflective components have been modified to ensure relevance and sensitivity for breast cancer survivors.

7 Trial objectives and purpose

7.1 Research hypothesis

The purpose of this research is to evaluate the clinical efficacy and underlying mechanisms of ADIE-BC therapy in individuals who have completed treatment for primary breast cancer. The primary hypothesis is that ADIE-BC therapy will lead to greater reductions in anxiety at 8 weeks post-randomisation, compared with Enhanced Usual Care (EUC).

7.2 Primary objectives

To evaluate whether ADIE-BC therapy, compared to EUC, leads to lower anxiety at 8 weeks post-randomisation in individuals who have completed treatment for primary breast cancer, as assessed by the State-Trait Anxiety Inventory (STAI-T).

7.3 Secondary objectives

Secondary Clinical Objectives

Additional anxiety-related outcomes:

To evaluate the effect of ADIE-BC versus EUC on:

- Anxiety (STAI-T) at 18-weeks post-randomisation.
- Generalised anxiety symptoms (GAD-7) at 8- and 18-week post-randomisation.
- Fear of cancer recurrence (FCRI-SF) at 8- and 18-weeks post-randomisation.
- Anxiety sensitivity (ASI) at 8- and 18-weeks post-randomisation.

Psychological and quality-of-life outcomes:

To evaluate the effect of ADIE-BC versus EUC on:

- Depressive symptoms (PHQ-8) at 8- and 18-weeks post-randomisation.
- Health-related quality of life (EQ-5D-5L) at 8- and 18- weeks post-randomisation.

Somatic Symptoms:

To evaluate the effect of ADIE-BC versus EUC on:

- Fatigue, pain, and vasomotor symptom interference (PROMIS Fatigue-7a, Pain-1a, Pain Interference-6a, MENQOL-Vasomotor) at 8- and 18- weeks post-randomisation.

Workability:

To evaluate the effect of ADIE-BC versus EUC on:

- Work status (WAS-1 + work status items) at 8- and 18-weeks post-randomisation.

Mechanistic Objectives

Interoception:

To determine whether ADIE-BC versus EUC affects:

- Interoceptive accuracy (Heartbeat Discrimination and Heartbeat Tracking tasks) at 8 weeks.
- Interoceptive sensibility (MAIA-2, BTMS, BMI-2) at 8 and 18 weeks.

To explore whether:

- Change in interoception mediates the effects of ADIE-BC on anxiety.

Biological mechanisms:

To determine whether ADIE-BC versus EUC alters:

- Cortisol (saliva) and inflammatory markers (blood) at 8 weeks.
- Neural correlates of interoception (task-based fMRI) at 8 weeks.

Acceptability & Safety

Acceptability:

To evaluate the acceptability of ADIE-BC using the TAF questionnaire at 8 weeks.

Adherence:
To assess adherence and engagement with ADIE-BC, including session completion and retention rates.
Safety / Serious Adverse Events:
To monitor and describe any adverse serious events related to the intervention.

Open-label extension
Durability of effects:
To determine whether any effects evaluate long-term maintenance of ADIE-BC effects are maintained at 12 months post-randomisation in an open-label extension phase.

8 Trial design & Flowchart

8.1 Trial Design

This study is a two-arm, parallel-group, randomised controlled trial designed to evaluate the clinical efficacy and underlying mechanisms of ADIE-BC, a biobehavioural interoceptive training intervention, compared with Enhanced Usual Care (EUC) in individuals who have completed treatment for primary breast cancer. A parallel design is appropriate because ADIE-BC aims to modify interoceptive processes through structured biobehavioural training; therefore, a crossover design would carry substantial risk of persistent carry-over effects that cannot be washed out.

Type of Trial
This is a main (definitive) trial, intended to determine both the clinical efficacy of ADIE-BC and its mechanisms of action. Participants will be randomised in a 1:1 ratio to receive either ADIE-BC or Enhanced Usual Care (EUC).

ADIE-BC is a biobehavioural intervention that integrates interoceptive precision training with psychological tools designed to support adaptive interoceptive sensibility.

Enhanced Usual Care (EUC) was selected as the comparator because it reflects the standard supportive care typically offered following treatment for primary breast cancer, while providing a minimal control for nonspecific therapeutic factors. EUC includes psychoeducation about anxiety and brief clinical check-ins, offering some therapeutic contact, attention, and supportive dialogue, although the frequency and intensity of contact are not matched to the ADIE-BC intervention. This approach allows EUC to function as a clinically relevant and ethically appropriate comparator while ensuring that any observed effects can be attributed primarily to the specific components of ADIE-BC. A more active control condition was not considered appropriate for this first definitive trial of ADIE-BC, as introducing a structurally similar training or behavioural intervention could obscure estimates of the intervention's specific effects and complicate mechanistic interpretation. In addition, developing and validating an active comparator for interoceptive training would require substantial preliminary work and would increase participant burden without clear scientific

advantage at this stage. A placebo or sham training condition was also deemed infeasible due to the complexity of interoceptive tasks and the high likelihood of unblinding.

Justification for the Design

A parallel-group randomised design:

- enables unbiased comparison of clinical and mechanistic outcomes between groups
- avoids contamination or learning effects that would arise in a crossover design
- supports mechanistic analyses by ensuring that measures of interoceptive accuracy, interoceptive sensibility, physiological biomarkers, and neural activity are not influenced by prior exposure to the intervention
- enhances interpretability of results by controlling for psychoeducation and clinical contact through EUC.

Equality, Diversity and Inclusion (EDI) Considerations

In line with HRA guidance, the trial incorporates strategies to promote equitable, diverse, and inclusive participation:

- Broad eligibility criteria to minimise unnecessary exclusion.
- Multiple recruitment pathways (NHS services, community channels, private health practices, online outreach) to reach individuals from varied socioeconomic, ethnic, and geographical backgrounds.
- Partnership with diversity-focused charity partners, e.g., Black Women Rising, for recruitment and dissemination.
- Flexible scheduling and remote data collection, where feasible, to reduce practical barriers.
- Clear and culturally sensitive participant-facing materials.
- Ongoing monitoring of demographic patterns in recruitment and retention, with adjustments implemented if disparities emerge.

Duration of Treatment

ADIE-BC is designed to be delivered over a 6-week period, consisting of one session per week, mirroring the schedule used in the original ADIE trial by Quadt et al. (2021). This duration is sufficient to provide sufficient interoceptive training sessions while keeping participant burden manageable. Consistency with the established intervention schedule enhances feasibility and fidelity to prior evidence. As in the original ADIE trial by Quadt et al. (20210), flexibility in session delivery (e.g., multiple sessions per week) is built into the study design to support participant needs and competing demands.

Participants allocated to Enhanced Usual Care (EUC) will receive evidence-based psychoeducation on anxiety and anxiety management strategies as well contact opportunities with the clinical team also delivering ADIE-BC. However, the frequency of contact is not matched to the ADIE-BC intervention, reflecting its nature as a supportive care comparator rather than an active training programme.

Timing of Primary Endpoint

The primary endpoint is at 8 weeks post-randomisation. This timing allows for the baseline assessment period following randomisation, completion of all six ADIE-BC sessions, and the post-intervention outcome assessment within a clinically reasonable window.

Participant Participation Duration
Participants remain in the trial from baseline to 18-week follow-up, which marks the formal end of study. This period allows evaluation of immediate post-treatment effects (8 weeks) and short-term maintenance or evolution of effects (18 weeks). This timeframe aligns with similar biobehavioural intervention studies and supports the detection of both acute and early sustained changes in anxiety and interoceptive processes.

Long-Term Follow-up
A 12-month post-randomisation assessment, part of an open-label extension, will explore the durability of intervention effects.

Nested Neuroimaging Sub-Study
A nested neuroimaging sub-study will be conducted with up to 80 participants drawn from the main trial. These participants will undergo functional magnetic resonance imaging (fMRI) at baseline and 8 weeks post-randomisation. The purpose of this sub-study is to characterise treatment-related changes in neural processes underpinning interoception and brain–body integration. Specifically, the neuroimaging component will assess whether ADIE-BC produces alterations in neural activation and connectivity within interoceptive and emotion-regulation networks, and whether such changes correspond to improvements in interoceptive accuracy, interoceptive sensibility, and anxiety. This sub-study will provide mechanistic insight into the neural pathways through which ADIE-BC may exert its therapeutic effects.

8.2 Primary and Secondary Outcomes

Primary Outcome: Anxiety at 8 weeks post-randomisation, measured by the State-Trait Anxiety Inventory-Trait subscale (STAI-T; Spielberger et al., 1983). The STAI-T is a well-validated 20-item self-report measure of anxiety severity, widely used in clinical populations. Scores range from 20-80, with higher scores indicating greater anxiety symptom severity. The trial is powered to detect a 6-point between-group difference, which we defined as a minimally important target difference, corresponding to approximately half a standard deviation of the STAI-T scores observed in the pilot study (see section 17.1 for sample size calculation).

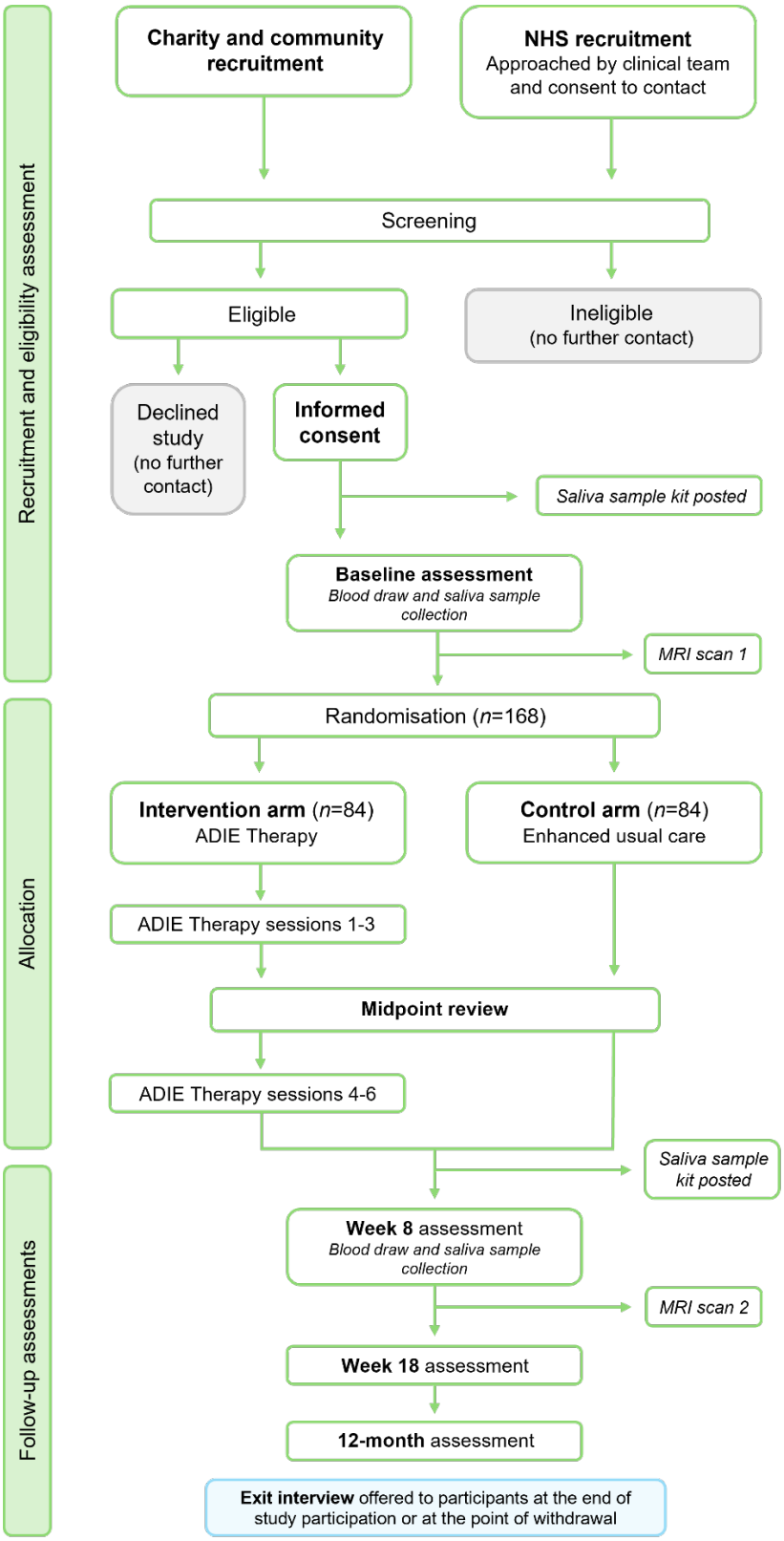
Secondary Outcomes

- Clinical outcomes:
    - Anxiety (STAI-T) at 18 weeks
    - Generalised anxiety (GAD-7) at 8- and 18 weeks
    - Fear of cancer recurrence (FCRI-SF)
    - Anxiety sensitivity (ASI)
    - Depressive symptoms (PHQ-8)
    - Health-related quality of life (EQ-5D-5L)

    - Fatigue (PROMIS Fatigue-7a)
    - Pain intensity and interference (PROMIS Pain-1a, Pain Interference-6a)
    - Menopause-related vasomotor symptoms (MENQOL-Vasomotor)
    - Work status (WAS-1 + work status items)
    - Patient Global Impression of Change (PGIC)
- Mechanistic outcomes:
    - Interoceptive accuracy (Heartbeat Discrimination and Heartbeat Tracking tasks)
    - Interoceptive sensibility (MAIA-2, BTMS-2, BMI-2)
    - Salivary cortisol (diurnal profile)
    - Blood inflammatory markers (e.g., CRP, cytokines)
    - Neural correlates of interoception (task-based fMRI; optional sub-study, n≤80)
- Acceptability, adherence, and safety:
    - Treatment acceptability (TFA)
    - Net Promoter Score (NPS)
    - Intervention adherence (session attendance and completion rates)
    - Serious Adverse Events

Detailed timing of all assessments is provided in Section 7 (Objectives) and Table 1 (Schedule of Assessments). Full descriptions of all measures are provided in Section 10.6. Figure 1 provides an overview of the study flow.

Figure 1. Study flow diagram



8.3 Study Setting

This is a single-centre trial conducted at King's College London, with multisite recruitment taking place across NHS oncology services—specifically Guy's and St Thomas' Hospital (hereafter *Guy's*) and The Royal Marsden Hospital (hereafter *Royal Marsden*)—as well as through charity partners supporting people affected by breast cancer. The choice of these settings is directly aligned with the trial's aim to recruit a diverse and representative sample of individuals who have completed treatment for primary breast cancer, accessed from both clinical and community contexts.

All research activities other than recruitment will occur at King's College London. All in-person research activities other than recruitment will occur on approved research sites on King's College London campuses, including Guy's Campus and Denmark Hill Campus (fMRI only).

Recruitment at NHS sites

We will recruit through NHS oncology services. Guy's and Royal Marsden have been selected because they are major oncology centres with access to large populations of breast cancer survivors who meet the eligibility criteria. Recruitment within the NHS will occur through identification by members of the clinical team during routine follow-up appointments, supportive care contacts, or personal outreach. Site-specific requirements include obtaining NHS R&D approvals and adherence to local governance, data management, and reporting processes.

Recruitment through Charity Partners, Non-NHS Pathways, and Community

We will recruit through charity partners, non-NHS health partners, community settings, and through advertisements that could be shared on social media or the radio. Recruitment is strategically staggered to promote diversity, equity, and inclusion, with particular emphasis on reaching individuals from minoritised or underserved groups who may be less likely to be recruited solely through NHS pathways. Charity and community partners, including but not limited to Black Women Rising, Breast Cancer Now, Future Dreams, and Perci Health will support recruitment by disseminating approved study adverts through their networks, newsletters, online platforms, and community events. With organisational approval, members of the research team may attend open social or support events to raise awareness of the study, share information materials, and answer questions. There will also be posters displayed in the community, including but not limited to London community cafes and shopping centres.

8.4 Trial Schedule

Table 1 Schedule of Assessment

	Screening (including informed consent)	Informed consent	Baseline	Randomisation	ADIE Tx1	ADIE Tx2	ADIE Tx3	Mid-point review	ADIE Tx4	ADIE Tx5	ADIE Tx6	8-week follow-up	18-week follow-up	Open-label 1-year follow-up
Timeframes		*Informed consent up to 14 days post-screening*	*Up to 4 weeks post-consent*	*Up to +14 days post-baseline*	*Up to +14 days post-randomisation*	*Per protocol = 1 session per week. Up to 2 sessions per week allowed. Minimum 4 weeks, maximum 8 weeks to therapy completion. Midpoint for control group – 5-week post randomisation (Up to +/-7 days).*						*Up to +14 days*	*Up to +14 days*	
Mode of assessment	*Over the phone/ Teams or in-person at Guy's*	*Over the phone/ Teams or in-person at Guy's*	*In-person at Guy's*	N/A	*In-person at Guy's*								*Remote (optional over the phone/ Teams or survey link)*	*Remote (optional over the phone/ Teams or survey link)*
Informed consent	*(X)*	*X*												
Screening form	*X*													
Demographics & medical questions			*X*											

STAI-T			X					X			X	X	X
GAD-7			X					X			X	X	X
FCRI-SF			X								X	X	X
PHQ-8			X								X	X	X
MAIA-2			X					X			X	X	X
BTMS			X								X	X	X
ASI			X								X	X	X
BMI-2			X					X			X	X	X
MENQOL-Vasomotor			X								X	X	X
PROMIS-Fatigue-7a			X								X	X	X
PROMIS-Pain-1a			X								X	X	X
PROMIS-Pain Interference-6a			X								X	X	X
Work status (WAS-1 + work status items)			X								X	X	X
EQ-5D-5L			X								X	X	X
TFA											X		
PGIC											X	X	X
NPS											X		
Saliva			X								X		
Blood draw			X								X		
HDT			X					X			X		
HTT			X					X			X		
ADIE Therapy (intervention only)					X	X	X	X	X	X			
Interview	*Offered to participants at the end of study participation or at the point of withdrawal*												

MRI scans (Denmark Hill)

MRI scan 1 will take place up to +14 days post-baseline assessment, with prior fMRI safety screening.

MRI scan 2 will take place up to +10 days post-8-week follow-up, with prior fMRI safety screening.

9 Participant selection

Participants in this trial will be drawn from two primary sources: NHS oncology centres and cancer charity and community partners. Recruitment through Guy's and St Thomas' Hospital and The Royal Marsden Cancer Hospital will enable access to a large and clinically relevant population of individuals who have completed treatment for primary breast cancer. Additional participants will be recruited through breast cancer charities, including but not limited to Black Women Rising, Breast Cancer Now, and Future Dreams. These organisations support broad and diverse communities of breast cancer survivors, including individuals who may no longer be in frequent contact with NHS oncology services. Recruiting through charity partners therefore provides an important complementary route to ensure that the sample includes people from a range of backgrounds, including groups that have been historically underrepresented in research on psychological and biobehavioural interventions for cancer-related anxiety.

9.1 Participant inclusion criteria

Participants will be eligible based on the following criteria:

- Aged 18 years or older
- Resident in the United Kingdom
- Able and willing to attend weekly sessions in London for 8 consecutive weeks
- Able to read, write, and follow instructions in English
- Have previously received a diagnosis of primary breast cancer (stages 0-III)
- Have completed hospital-based cancer treatment between 6 months and 10 years prior to enrolment (long-term adjuvant therapies are permitted)
- Meet criteria for at least mild anxiety, defined using a pre-determined cut-off score GAD-2 (≥2) (GAD-2: Kroenke et al., 2007).

9.2 Participant exclusion criteria

Participants will be excluded if they meet any of the following criteria:

- Unable to provide informed consent

Cancer-related exclusions:

- Diagnosis of Lobular Carcinoma in Situ (LCIS) only
- Diagnosis of secondary or metastatic breast cancer

Other ADIE therapy contraindications:

- Previous participation in any ADIE therapy trial
- Presence of an implantable cardioverter defibrillator and/or pacemaker
- Scheduled to begin Cognitive Behavioural Therapy (CBT) during the intervention period

- Health anxiety specifically related to cardiac symptoms or cardiac events where it is considered to interfere with ADIE therapy
- History of severe cardiac events (e.g., myocardial infarction, sudden cardiac arrest, stroke) within the past 12 months where it is considered to interfere with ADIE therapy

Other physical health exclusions:

- Pregnancy
- Current substance or alcohol dependence where it is considered to interfere with ADIE therapy
- Neurological diagnoses, including epilepsy, dementia, or Parkinson's disease where it is considered to interfere with ADIE therapy

Other mental health exclusions:

- Current medium or high risk of suicide intention and plan, determined by item 9 of the Patient Health Questionnaire (PHQ-9) and accompanying risk assessment questions
- Current severe depression determined by Patient Health Questionnaire (PHQ-8) (≥20)
- Current diagnosis of obsessive-compulsive disorder (OCD), psychosis, or bipolar disorder where is considered to interfere with ADIE

Decisions about interference will be made by the CI in consultation with trial clinicians.

Eligibility criteria for the MRI sub study:

- Participants will be eligible if they are willing to take part in an optional MRI scan.
- Participants will be excluded if they have any contraindications to MRI scanning, as determined by the MRI safety questionnaire.

10 Trial procedures

10.1 Participant recruitment

Method of identification

Charity, non-NHS, and community recruitment

Participants will be identified through charity partners using charity-approved recruitment methods such as email newsletters, display of study posters at charity offices, venues, and public spaces, and via social media (e.g., posts on charity social media platforms, including public posts on Instagram and posts within closed Facebook groups). The charity-initiated communications, including on the study poster, will feature a QR code and/or clickable link that directs potential participants to the screening form, as well as providing the trial email so that interested individuals can directly contact the study team. We will also share approved study flyers with non-NHS partners such as Perci Health and we will post flyers in community settings including but not limited to London cafes and shopping centres, where given permission to do so.

NHS clinic recruitment

Within the NHS recruiting sites, participants will be principally identified and initially approached by a member of the clinical team. This approach could be in-person or remote (e.g., via phone call), which is considered appropriate by the supporting clinical team given the infrequency of hospital appointments during the survivorship period. Members of the clinical team will seek initial consent for the participant to be approached by a member of the research team and will share contact details through a secure NHS email address. The research team will then contact the prospective participant to conduct screening procedures.

In some clinical services, patients completing active treatment are routinely offered the opportunity to indicate whether they would be willing to be contacted about future survivorship research. This process is part of usual clinical practice and is independent of the present study. Where patients have previously provided documented consent to be contacted about research opportunities, and where they are not attending routine hospital visits in person, a member of the clinical team may signpost them to survivorship research opportunities and record their permission for the research team to make contact. The study team will only contact potential participants who have provided prior consent to be contacted about research and where a member of the clinical team has confirmed that contact is appropriate (e.g. no known clinical contraindications or safeguarding concerns). Clinical confirmation of appropriateness is limited to safety and safeguarding considerations and does not constitute eligibility screening or selection. Clinical staff will not undertake recruitment, eligibility assessment, or consent for this study. All eligibility assessment and informed consent procedures will be conducted by the study team.

In line with the role of Participant Identification Centres (PICs), approved study posters may be displayed in waiting rooms or clinic areas to support participant identification and awareness of the study. Display of posters will follow the local site governance process, and internal sign-off will be obtained from the local R&D office or governance team prior to display. Approved study posters may include study team contact details or a link (e.g. email address or QR code) to allow patients to contact the study team directly to request further information. This approach constitutes recruitment advertising only. No eligibility assessment, consent, or research procedures will be undertaken at the PIC site. All screening and consent procedures will be conducted by the study team following initial contact.

Following identification of potential participants, the study pack can be provided by the clinical care team (where feasible) or the study team. The study pack consists of:

1. Summary Participant Information Sheet, a one-page study overview offering a concise overview of the trial, and
2. The Participant Information Sheet (PIS), which gives detailed explanation of study aims, procedure, risks, and what participation involves, along with the contact details of the ADIE-BC research team.

Consent procedure

Those who meet the eligibility criteria may provide informed consent during the screening contact if they wish. If they prefer more time to decide, the research team will arrange a

follow-up contact to allow sufficient time for questions and consideration. Participants will be encouraged, but not required, to take at least 24 hours to review the information before deciding whether to take part. They may contact the research team via telephone or email to discuss any questions before deciding whether to proceed.

Informed consent will be obtained online using Qualtrics. Participants can either complete the informed consent form (ICF) independently in their own time or with guidance from a Research Assistant in person, over the phone or via Teams. In both cases, the research team will ensure potential participants are fully informed by fully going through the PIS and ICF forms with them over the phone or via Teams beforehand. They will also provide clear instructions on how to contact the team with any additional questions, and by offering opportunity to have any questions answered satisfactorily. A copy of the signed ICF will be emailed to the participant for their records.

Payment of Participants

Participants will be reimbursed for reasonable travel costs incurred when attending in-person assessments, upon submission of receipts to the research team. As a token of appreciation for their time, participants will receive £30 for each survey completed at baseline, 5 weeks, 8 weeks, and 18 weeks, for a total of £120 if all four surveys are completed. An additional £30 will be provided for completing the open-label 1-year follow-up survey, totalling the maximum amount for surveys to £150. Participants who consent to the optional MRI scans will receive £60 per scan, up to a total of £120, as a token of appreciation for their time.

Participants will receive a Love2Shop voucher as the standard reimbursement option, as it is widely accepted across multiple retailers. For those who prefer not to receive a voucher, reimbursement can be provided via BACS bank transfer.

10.2 Screening Procedures

Screening for NHS recruitment

Screening will be conducted by delegated members of the research team using a screening form based on the eligibility criteria outlined in Section 9.1 (Inclusion) and Section 9.2 (Exclusion). Screening may be conducted:

- In person at Guy's Hospital
- Over the phone
- Remotely via Microsoft Teams
- Online screening form

Screening for Charity Partner Recruitment

Due to the nature of self-referral, individuals responding to study adverts will be directed to first complete an online screening form to confirm eligibility. The QR code and clickable link on recruitment materials will direct individuals to this form. Alternatively, the study team can share the screening form with individuals who request it.

- Individuals who do not meet the criteria will receive an onscreen message explaining that they do not meet criteria for this trial, thanking them for their interest, and providing signposting to other available mental health resources and support.
- Individuals who meet the criteria will be asked to provide contact details so that the research team can arrange a call with the potential participant to verify eligibility and discuss participation as per the NHS recruitment process.

The study pack (Summary PIS and full PIS) will be available for download once eligibility is confirmed. This ensures individuals recruited via the charity partner pathway have access to study information prior to the screening call with the researcher.

The Trial Delegation Log will document which members of the research team are authorised to conduct screening.

10.3 Informed Consent

Individuals who meet the eligibility criteria during screening may provide informed consent during the same contact, after screening is complete, if they wish. Alternatively, informed consent may be contained at a separate follow-up contact if the individual prefers additional time to consider participation. The research team will offer the opportunity to ask questions at any point, and participants will be encouraged to take at least 24 hours to review the study information before deciding whether to take part.

Individuals who do not meet the eligibility criteria will be thanked for their time and interest.

Nested neuroimaging study:

During informed consent, participants will be invited to participate in a nested neuroimaging study investigating neural correlates of interoceptive precision following ADIE therapy. Those who are interested will be contacted separately to complete an MRI safety questionnaire, administered by the research team. Eligible individuals who wished to take part in the nested study will provide separate informed consent for the neuroimaging sub-study.

10.4 Randomisation Procedures

Participants will be randomised with equal allocation (1:1 ratio) to either the ADIE-BC intervention arm or the Enhanced Usual Care (EUC) arm. A web-based randomisation system will be designed using the bespoke King's Clinical Trial Unit (KCTU) randomisation system. The randomisation system will be created in collaboration with the trial analyst and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

Randomisation will be at the level of the individual using the method of stratified block randomisation with randomly varying block sizes stratified by:

- Recruitment source: NHS vs charity
- Time since treatment completion: 6 to 23 months, 24-59 months, ≥60 months
- Baseline anxiety severity: STAI-T 20-43 vs STAI-T 44-80

Data Entry
Randomisation will be undertaken centrally by the coordinating study team, by authorised staff onto the randomisation system by going to www.ctu.co.uk and clicking the link to access the randomisation system. A full audit trail of data entry will be automatically date and time stamped, alongside information about the user making the entry within the system.

No data will be entered onto the randomisation system unless a participant has signed a consent form to participate in the trial. Randomisation will be performed only after the participant has provided written informed consent and baseline assessment has been completed.

Security
The CI or delegate will request usernames and passwords from the KCTU. System access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the randomisation system are not shared, and that only those authorized to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested via the CI or delegate (e.g., Trial Manager) from the KCTU team and a request for access to be revoked must be requested when staff members leave the project. Study site staff experiencing issues with system access or functionality should contact the CI or delegate (e.g., Trial Manager) in the first instance.

Data Quality Processes
The CI team will undertake appropriate reviews of the entered data, in consultation with the project analyst, for the purpose of data cleaning. No data can be amended in the system; however, CI or delegate (e.g., Trial Manager) may request King's Clinical Trials Unit to add notes against individual subject entries to clarify data entry errors.

Allocation Communication
Once randomisation is completed, the system will automatically generate a confirmation email to the person who performed the randomisation and to the Trial Manager, indicating the participant's allocated treatment arm. The study team member will then inform the participant of their allocation and schedule the first intervention session (for ADIE-BC arm) or provide the EUC materials (for EUC arm).

Database Lock
Upon request, KCTU will provide a copy of the final exported dataset to the CI in .csv format and the CI will onward distribute as appropriate.

Allocation Concealment
To ensure allocation concealment is maintained, the randomisation sequence is generated and held securely by KCTU, which is independent of the research team responsible for recruitment and screening. The allocation sequence is not accessible to any member of the research team involved in enrolling participants. Randomisation can only occur after a

participant has been deemed eligible and has provided informed consent, ensuring that the allocation is unknown at the time of enrollment decisions.

10.5 Blinding & other measures taken to avoid bias

10.5.1 Blinding

Due to the nature of the ADIE-BC intervention, it is not possible to blind participants or intervention delivery staff to treatment allocation. However, blinding is maintained for key personnel involved in data analysis to minimise the risk of bias in interpreting results.

Unblinded roles:

- The CI will be unblinded at the individual level to enable oversight of intervention delivery, supervision of research staff, safety monitoring, assessment of SAE causality, and management of day-to-day trial operations.
- Participants will be aware of treatment assignment due to the behavioural nature of the intervention.
- Members of the research team delivering ADIE-BC sessions and conducting assessments will be aware of treatment allocation (assessments are self-report, minimising assessor bias).
- The Trial Manager will be unblinded to prepare monitoring reports and conduct data quality checks.
- Specific members of the Trial Steering Committee (TSC) will review unblinded data during the closed portion of TSC meetings to monitor safety, adherence, and any emerging concerns requiring treatment-specific information.
- The Trial Statistician will be unblinded from the point of generating the first TSC report containing treatment arm-specific data. Prior to this, the Junior Statistician will remain blinded during setup of the randomisation system, drafting of the Statistical Analysis Plan, and initial data management activities.

Blinded roles:

- The Senior Statistician will remain blinded to all treatment assignments throughout the trial, including during development, review and finalisation of the Statistical Analysis Plan, and will not have access to the randomisation list, allocation database, or unblinded data until the completion of the primary efficacy analyses. Senior Statistician will provide oversight of all statistical analyses and final sign-off without knowledge of treatment allocation.

- Laboratory personnel processing biomarker samples (saliva and blood) will be blinded to treatment allocation. Samples will be coded with participant study ID only, with no indication of treatment arm.
- Neuroimaging analysts processing fMRI data will remain blinded to treatment allocation during image preprocessing and quality control procedures.

This blinding strategy is appropriate for a behavioural intervention trial where participant and therapist blinding is not feasible.

10.5.2 Other measures taken to minimise/avoid bias

Several additional measures minimise bias beyond randomisation and blinding:

- Standardised procedures: ADIE-BC is delivered according to a manualised protocol with standardised training for all researchers involved in intervention delivery. EUC is standardised through consistent provision of psychoeducation materials.
- Objective measurement: All questionnaire outcomes are self-reported via electronic data capture, eliminating assessor interpretation. Behavioural tasks use automated equipment (XPod sensor), biomarker assays are processed by blinded laboratory personnel, and fMRI data are analysed by blinded neuroimaging staff.
- Pre-specification and transparency: Primary and secondary outcomes are prospectively registered on ClinicalTrials.gov. A detailed Statistical Analysis Plan will be finalised before database lock, preventing selective reporting and post-hoc analytical decisions.
- Intention-to-treat analysis: All randomised participants will be analysed according to allocated treatment arm, regardless of adherence or protocol deviations.
- Retention strategies: Multiple assessment modes (online, phone, in-person), flexible scheduling, regular contact, and financial compensation (£30 per assessment, travel reimbursement) minimise differential attrition.
- Independent oversight: The Trial Steering Committee, including independent experts and patient representatives, provides ongoing monitoring of trial conduct, safety, and scientific integrity.

10.6 Intervention Procedures

<u>Interventional arm (ADIE-BC therapy)</u>

Aligning Dimensions of Interoceptive Experience (ADIE) is an intervention approach designed to support more accurate and confident perception of cardiac interoceptive signals alongside adaptive use of bodily signals to regulate emotions and anxiety in daily life. ADIE-BC is an adapted form of ADIE therapy for individuals who have completed treatment for primary breast cancer, with the additional goal to support individuals in utilising interoceptive skills to

support adaptive body mindsets. The intervention uses real-time heartbeat measurement and provides structured biofeedback-based training in attending to internal cardiac sensations through two established interoceptive paradigms: the Heartbeat Tracking Task and the Heartbeat Discrimination Task. In the Heartbeat Tracking Task (HTT), participants are asked to silently count their heartbeats during semi-randomised time-windows. In the Heartbeat Discrimination Task (HDT), they judge whether an externally presented auditory tone is synchronised or unsynchronised with their heartbeat. Following each trial, participants provide confidence ratings (*ADIE-BC Therapy Training VAS & ADIE Therapy VAS* supporting document) regarding the perceived accuracy of their responses, encouraging reflection on interoceptive awareness. Participants are provided with veridical feedback as to their accuracy on a trial-by-trial basis. Each training session comprises two blocks, between which participants undergo a self-paced, light physical activity that aims to enhance heartbeat perception and lasts 2 to 3 minutes. The time windows in the HTT can be adaptively adjusted to support accuracy training – for example shortening time windows to build confidence with easier trials or lengthening time windows to improve accuracy with increasing task difficulty (*HBC Table* supporting document).

After each ADIE training session, participants will complete the Heartbeat Perception Questions (*ADIE post-training items* supporting document). After the final ADIE session, participants will also complete the Heartbeat Task Preferences Questions (*ADIE post-training items* supporting document). These post-training items form part of the training evaluation. Through iterative feedback, participants learn to become more accurate and confident in detecting their heartbeat. Interoceptive precision training is delivered once weekly, over six sessions, with flexibility to allow up to two sessions per week. Relating to lifestyle and dietary recruitment, participants in the interventional arm are asked to refrain from alcohol consumption prior to attending therapy sessions.

Alongside the precision training, participants receive supportive materials (consisting of the ADIE-BC handbook and reminder card) that encourage an adaptive and non-judgmental engagement with bodily sensations, aiming to promote adaptive interoceptive sensibility, emotion-regulation skills, and helpful body mindsets. Participants are guided through the ADIE-BC, which includes psychoeducation to normalise anxiety after cancer as well as to normalise heartbeat changes throughout the day and to scaffold towards this as a sign that their body is working with them. The handbook also includes strategies and an accompanying Reminder Card to use their interoceptive precision to 'Notice, Normalise, Regulate' emotions in daily life.

<u>Enhanced Usual Care (EUC)</u>

Participants allocated to the EUC arm will also receive a handbook on *Managing Anxiety After Breast Cancer*. The handbook is designed to match the ADIE-BC handbook in style and format,

but without the inclusion of interoceptive elements. The handbook provides psychoeducation to normalise anxiety after cancer and to offer evidence-based, non-interoceptive strategies for managing anxiety in daily life. This includes strategies and an accompanying Reminder Card to 'Notice, Normalise, Regulate' anxiety-related cognitions in daily life. The handbook also signposts participants to sources of help and support, comparative with clinic- and charity-provided resources in usual care (UC). The pack will be provided as a printed booklet and/or PDF via secure email by the research team. Like in the ADIE-BC arm, participants in the EUC arm are provided a clinical check-in at the mid-point assessment with the clinical research team in which they discuss their experience with the handbook and offered personalised support for using the anxiety management strategies to support their anxiety and emotions in daily life.

10.7 Schedule of Treatment/Assessments for each visit

There will be 4 assessments in total, including a mid-point review. They are baseline, mid-point, 8-week follow up, and 18-week follow up assessment. There is a further optional 1-year follow up (see Open-Label Extension).

Baseline assessment
The baseline assessment will take place in person at Guy's. The study team will record participants' concomitant therapies and medications using KCTU-approved logs.

Self-report measures:
The baseline assessment will include self-reported demographics and medical history, validated self-report questionnaires, behavioural tasks, and biomarkers (where consent is provided). The questionnaires will be self-administered by the participant electronically on Medrio.

Demographics & mind-body experience: 1) age, 2) sex, 3) gender identity, 4) ethnicity, 5) education, 6) level of experience with mind-body practice.

Medical characteristics: 1) breast cancer type, 2) month and year of diagnosis, 3) stage at diagnosis, 4) breast cancer treatment history, 5) month and year of active hospital-based treatment completion, 6) endocrine therapy, 7) other adjuvant therapies, 8) pain locations.

- State-Trait Anxiety Inventory, Trait version (STAI-T; Spielberger et al., 1983) is a 20-item self-report measure designed to capturie anxiety that extends beyond transient, momentary states (state anxiety) and reflects broader patterns of anxious thoughts and feelings. Each of the 20 items is scored on a 4-point scale. Anxiety-absent items are reverse scored. Scores range from a minimum of 20 to a maximum of 80. Higher scores indicate greater levels of anxiety.

- The Generalised Anxiety Disorder Assessment (GAD-7; Spitzer et al., 2006) is a 7-item self-reported questionnaire which assesses symptoms of generalized anxiety. Participants

respond by indicating how often in the last two weeks they have experienced each item on a four-point scale.

- Fear of cancer recurrence: The Fear of Cancer Recurrence Inventory – Short Form (FCRI-SF; Simard & Savard, 2009) is a 9-item scale which assesses participants' fears of their cancer returning and how this impacts their lives. Participants respond to the first five items by indicating how much they agree with each statement (five-point scale) and to the following items by responding to each specifically stated question, such as frequency of experience or perceived risk (five-point scales).

- Patient Health Questionnaire (PHQ-8; Kroenke et al., 2009). The 8-item assesses core symptoms and signs of depression. Participants respond by indicating how often they have experienced each item in the last two weeks on a four-point scale. The PHQ-8 does not include the suicidality item.

- Multidimensional Assessment of Interoceptive Awareness Version 2 (MAIA-2; Mehling et al., 2018) assesses multiple dimensions of interoception i.e. awareness of bodily sensations. The MAIA consists of 8 scales addressing 5 dimensions of body awareness).

- The Bodily Threat Monitoring Scale – second version (-2; Heathcote et al., 2023) is a 19-item scale assessing the extent to which participants monitor bodily sensations. Participants respond to each item on a five-point scale.

- The Anxiety Sensitivity Index (ASI; Reiss et al., 1986) is a 16-item scale that assesses different concerns someone could have about their anxiety. Participants respond to each item on a four-point scale.

- Body Mindset Inventory (BMI-2; adapted from Zion et al., 2022) assesses mindsets participants may hold about their body in the context of chronic disease. Participants respond by indicating how much they agree with each statement on a six-point scale.

- Menopause-related vasomotor symptoms (MENQOL-Vasomotor; Hilditch et al., 1996) measures the bothersome-ness of menopause-related vasomotor symptoms, specifically hot flushes, night sweats, and sweating. This is a 3-item domain of the MENQOL, with each domain designed to be scored separately. Participants report whether they are bothered at all by the symptom (no/yes) followed by a 0-6 scale from ‘Not at all bothered’ (0) to ‘Extremely bothered. (6)’

- PROMIS Short Form v1.0 – Fatigue 7a (PROMIS; Cella et al., 2007) is short form of the Patient-Reported Outcomes Measurement Information System (PROMIS). This is a 7-item self-report questionnaire that measures both the experience of fatigue and its impact on daily life over the past seven days. it uses a 5-point Likert scale, and higher scores indicate more fatigue. The 7 items assess fatigue-related symptoms (e.g., tiredness, exhaustion) and how they limit daily activities like self-care, work, and exercise.

- PROMIS-Pain Intensity-1a (PROMIS; Cella et al., 2007) is a single item assessing pain intensity in the past 7 days. Response is rated on a 0 to 10 scale. Responses are rated on an 11-point numerical scale ranging from 0 ("no pain") to 10 ("worst imaginable pain"). Despite its brevity, the item has strong psychometric properties and is widely used when a concise assessment of pain intensity is required.

- PROMIS-Pain Interference-6a (PROMIS; Cella et al., 2007) is a six-item short form that assesses the extent to which pain hinders engagement in social, cognitive, emotional, physical and recreational activities. Respondents rate each item on a 5-point scale, with higher scores indicating greater interference of pain in daily life.

- The Work Ability Score (WAS-1; Ahlstrom, 2010) is a single-item measure derived from the Work Ability Index (Ilmarinen, 2007) and provides a brief assessment of an individual's perceived ability to work. Participants rate their current work ability on a scale from 0 ("0 means that you currently cannot work at all") to 10 ("work ability at its best"). The WAS-1 is widely used in occupational health and survivorship research due to its brevity, sensitivity to change and strong correlation with the full Work Ability Index. In the context of this trial, the WAS-1 will be used to capture perceived work functioning and the potential impact of anxiety and related symptoms on participants' ability to engage in work or usual activities. In addition, an individual item that was designed for this study to capture current work status is used.

- EQ-5D-5L (EQ-5D-5L; Herdman et al., 2011) is a widely used measure of health-related quality of life developed by the EuroQol Group. It assesses functioning across five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, using a five-level response format and includes a visual analogue scale for overall health.

Behavioural tasks:

- Heartbeat Discrimination Task (HDT) (Katkin, 1983). This task intends to measure interoceptive precision. Participants will wear a heartbeat sensor for this task. They will hear 10 tones, that are either at the same time as their heartbeats, or in between their heartbeats. Participants will be asked to judge if the tones were at the same time as their heartbeats or not, and to rate how confident they were in their response. Participants can first practice this task and will then be asked to do this 26 times.

- Heartbeat Tracking Task (HTT) (Schandry, 1981). This task intends to measure interoceptive precision. Participants will wear a heartbeat sensor for this task. They will be asked to count their heartbeats for a specific amount of time without manually feeling for their pulse. They will then be asked how many heartbeats they counted and how confident they are in their response. Participants can first practice this task and will then be asked to do this six times.

Biomarkers:

- Saliva Sampling

  Participants who consent to provide saliva samples will complete a home-based collection to assess biomarkers related to physiological stress. A saliva collection kit will be mailed to participants in advance of the baseline visit, along with written instructions. Participants will be asked to collect six samples over the course of a single day, scheduled to characterise the diurnal cortisol profile: 1. immediately upon waking, 2. 15 minutes post-waking, 3. 30 minutes post-waking, 4. 60 minutes post-waking, 5. midday, and 6. 8pm. Participants will be asked to complete the saliva collection within the three days prior to their baseline assessment and to return the samples by bringing them to their in-person baseline visit. These samples will be used to examine diurnal cortisol patterns, including the cortisol awakening response and diurnal slope, as indicators of stress regulation.

- Blood Sampling

  Participants who consent to provide a blood sample will undergo venepuncture at the baseline assessment. Participants will be instructed to fast for 10 hours (water permitted) prior to each blood draw. Where feasible, samples will be collected in the morning to minimise the impact of fasting. The time of sample collection will be recorded in all cases. Where feasible, samples will be collected between 09:00 and 10:00 to reduce variability associated with overnight fasting and morning physiological fluctuations; the exact time of collection will be recorded for analytic adjustment. A 5 ml serum sample and 4 ml plasma sample will be obtained for the analysis of biomarkers associated with inflammation and stress (e.g., C-reactive protein [CRP], pro- and anti-inflammatory cytokines). Blood collection will take place in a clinical room at the KCL Breakthrough Breast Cancer Research Unit at Guy's, performed by a trained phlebotomist. Participants will be accompanied to the clinical room by a Research Assistant. Following collection, samples will be transported to the KHP Cancer Biobank at Guy's for initial processing and secure storage in accordance with standard operating procedures (SOPs).

Anticipated time required for each activity is as follows:

- Self-report questionnaires: approximately 45–60 minutes
- Behavioural tasks: approximately 30 minutes in total (15 minutes per task)
- Blood sampling: approximately 30 minutes, including movement to the clinical room, consent checks, venepuncture, and post-collection observation

Overall, the baseline assessment is expected to last approximately 1 hour and 15 minutes for participants in the main study, and around 2 hours for participants who also consent to provide a blood sample.

Midpoint review

The mid-point review will take place in person. It will take place at on the same day as Session 4 of the ADIE-BC therapy for participants in the ADIE-BC group, and at 5-week post-

randomisation for the EUC group. The review will include the two behavioural tasks detailed above (i.e., HDT and HTT) and a brief set of questionnaires:

- STAI-T
- GAD-7
- MAIA-2
- BMI-2

Anticipated time required for each activity is as follows,

- Behavioural tasks: approximately 30 minutes in total (15 minutes per task)
- Questionnaires: approximately 15 – 30 minutes

8-week follow-up

The 8-week follow-up is the primary endpoint and will take place eight weeks post-randomisation (with a leeway of up to 14 days). This will be conducted in person at Guy's and will include concomitant therapies and medications logs to denote any chances since baseline, self-report questionnaires, behavioural tasks, and biomarker collection for both the ADIE-BC and EUC groups.

Three additional measures are administered at 8-week follow-up:

- Theoretical Framework of Acceptability (TFA; Sekhon et al., 2022) is a 7-item scale that assesses the acceptability of the intervention. Each item measures a distinct construct, including affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy.
- Patient Global Impression of Change (PGIC; Guy, 1976) is a one-item measure to capture subjective changes related to chronic conditions by quantifying the patient's overall impression of the change.
- Net Promoter Score (NPS; Hamilton et al., 2014) is a one-item measure metric that gauges the likelihood of patients recommending your healthcare services to others.

The anticipated time for the 8-week follow-up will be similar to the baseline assessment: approximately 1 hour and 15 minutes for participants in the main study, and around 2 hours for participants who also consent to provide a blood sample.

18-week follow up

The 18-week follow-up will take place 18 weeks post-randomisation (with a leeway of up to 14 days). This assessment will be conducted remotely for both the ADIE-BC and EUC groups.

Participants will have the option to complete the questionnaires in their own time or arrange a phone call or Teams meeting with a Research Assistant, who will guide them through the process.

The anticipated time for the 18-week follow-up is approximately 45 minutes to 1 hour.

Remote questionnaire completion consideration

Participants completing questionnaires remotely will have the option to save their progress and return later. This is intended to reduce fatigue and allow questionnaires to be completed at a comfortable pace.

To maximise completeness of data, the following strategies will be implemented:

- **Reminders**
  - For remote questionnaire completion, participants will receive reminders (via their preferred contact method) prior to each scheduled assessment and follow-up time point.
  - For in-person assessments, the research team will contact participants to arrange a convenient day and time.
- **Follow-up for incomplete questionnaires**
  Research staff will prompt participants to complete any missing questionnaires within the required timeframe to ensure protocol compliance
- **Reduced measures**
  To minimise participant burden, the option to complete only the primary outcome measure will be offered if completing the full set of questionnaires and research activities is deemed detrimental to participant wellbeing.
- **Support during visits**
  Breaks will be offered during in-person visits to reduce fatigue and improve data quality.
- **Flexible options for assessment completion**
  Multiple modes of completion will be available, including self-completion online, telephone or Teams-assisted completion with a Research Assistant, and in-person completion.
  Note: Remote delivery of ADIE therapy sessions is not possible due to the nature of the intervention; therefore, participants must attend all six sessions in person. MRI scans and blood collection will also need to be carried out in person.

Open-label extension

There will also be a 1-year follow up, which will take place remotely for both the ADIE and EUC groups. Participants will have the option to complete the questionnaires in their own time or arrange a phone call or Teams meeting with a Research Assistant, who will guide them through the process. The anticipated time for this optional 1-year follow up is approximately 45 minutes to an hour.

10.8 Radiology Assessments

Participants who consent to take part in the neuroimaging sub-study will complete two in-person fMRI scans at the Denmark Hill imaging facility (see Schedule of Assessment for fMRI scan timing). These scans are designed to investigate neural correlates of interoceptive processing and brain–body integration associated with ADIE-BC, using functional magnetic resonance imaging (fMRI). On arrival, participants will complete an MRI safety questionnaire to confirm the absence of contraindications to scanning. A brief orientation to the equipment

will be provided, followed by a pre-scan practice session (approximately 30 minutes) conducted in a purpose-built mock scanner.

During each session, participants will complete an interoceptive task paradigm, which involves attending to bodily sensations while undergoing fMRI acquisition. This paradigm allows examination of treatment-related changes in neural activation and connectivity within interoceptive and emotion-regulation networks. Each MRI scan will last approximately 60 minutes. Structural images will be acquired first, followed by functional scans conducted during rest (eyes open) and during simple tasks. For safety reasons, participants will undergo a full MRI safety screening prior to each scan to ensure they remain eligible and safe to enter the MRI environment.

10.9 Modifications or discontinuation of intervention

The trial may be prematurely discontinued by the Sponsor, Chief Investigator, or Funder on the basis of new safety information. In the event of premature trial discontinuation, all active participants will be informed, and no further participant data will be collected.

Modifications to the intervention
Where participants experience fatigue during study activities (either reported by the participant or observed by the study team), including during ADIE-BC therapy sessions and/or assessments, appropriate adjustments will be made. These may include offering rest breaks or splitting a session across two separate days.

If necessary, a change of research assistant delivering study activities may also be implemented to ensure continuity of participation and participant comfort.

10.10 End of Study Definition

The end of study is 18 weeks post-randomisation, when the last participant completes the 18-week follow-up assessment. This timepoint defines the completion of the main efficacy trial. Following completion of the main trial, participants will be invited to continue in an open-label extension phase with a follow-up assessment at 12-months post-randomisation. This extension phase evaluates the long-term durability of treatment effects but does not form part of the primary efficacy analysis.

The trial may be prematurely discontinued by the Sponsor, Chief Investigator, or Funder if new safety information or other circumstances arise that, in their opinion, make continuation of the trial unjustifiable. In the event of early termination, all actively participating individuals will be informed, and no further data collection will take place.

11 Laboratories

11.1 Central/Local Laboratories

Biological samples collected during the study will be processed and stored within the KHP Cancer Biobank at Guy's Hospital. Blood samples will be stored at –80°C, and saliva samples will be stored at –20°C or below until analysis. All samples will be handled in accordance with established laboratory protocols for secure storage, traceability, and biosafety.

Following initial processing, samples will be transferred to a collaborating research laboratory within King's College London or to an external laboratory vendor approved by King's College London for the analysis of biological samples. Samples will be transported under conditions that maintain sample integrity, and upon receipt will be logged and stored according to SOP. All materials will be labelled with pseudo-anonymised unique codes, ensuring that the identity of the participant cannot be determined from the samples.

At all processing and analysis sites, any remaining biological material will be destroyed once analyses are complete or when samples are no longer required. Analytical results will be linked only to pseudo-anonymised identifiers and stored securely in compliance with data protection regulations and institutional policy.

Comprehensive sample tracking logs will be maintained throughout the lifecycle of each sample, documenting collection, storage, transport, processing, and analysis. These logs will be retained until all samples have been analysed, destroyed or reach the end of their retention period, providing full traceability and adherence to good clinical and laboratory practice.

11.2 Sample Collection/Labelling/Logging

Biological samples (blood and saliva) will be collected only from participants who have provided prior written informed consent.

Blood sampling:

Blood samples will be collected at the in-person baseline and endpoint assessment visits by a trained phlebotomist at the King's College London Breakthrough Breast Cancer Research Unit, Guy's Hospital. Immediately following venipuncture, the serum tube will be transported at ambient room temperature, and the plasma tube will be transported on ice to maintain sample cooling prior to receipt at the KHP Cancer Biobank laboratory. Where feasible, sampling will take place between 09:00–10:00 to minimise the impact of overnight fasting. A total of one 5 mL serum tube and one 4 mL plasma tube will be collected per visit. Samples will then be transferred immediately to the KHP Cancer Biobank at Guy's Hospital for initial processing and storage.

Saliva sampling:

Participants will self-collect saliva samples at home within the 3 days prior to in-person baseline and endpoint assessment visits. Six samples per day will be obtained using Sarstedt Salivettes (waking, +15 min, +30 min, +60 min, midday, and evening). Participants will store samples in a domestic refrigerator until return during their in-person visit, transporting them in insulated packaging with instant cool packs to ensure samples remain chilled and do not reach room temperature. Samples will be transferred immediately to the KHP Cancer Biobank at Guy's Hospital for storage.

Labelling and pseudo-anonymisaton:
All samples will be labelled with:

- Unique pseudo-anonymised participant study ID
- Study acronym
- Sample type (serum / plasma / saliva)
- Timepoint (baseline / endpoint)
- Date and time of collection

No personal identifiers will appear on any primary or secondary tubes, packaging or shipping manifests.

Logging and documentation:
Collection and processing information will be recorded on study-specific proformas for blood and saliva and subsequently transferred into secure sample tracking spreadsheets (audit logs). For blood samples, the collection proforma will document participant pseudo-ID, study visit, date and exact time of venepuncture, time since the participant last ate, collector initials and date. For saliva samples, participant pseudo-ID, study visit, sampling date, and collection timepoints will be recorded.

Upon receipt at the KHP Cancer Biobank laboratory, processing and storage information will be captured on dedicated laboratory sample record forms, including: participant pseudo-ID, study visit, date collected, date and time delivered to the laboratory, receiving staff initials, condition on arrival, total number of aliquots prepared, number stored, date and time stored, and freezer location (unit, shelf, rack and box position).

Tracking logs will therefore document the full chain of custody from participant collection to clinic receipt, processing, storage and subsequent shipment and analysis.

11.3 Sample Analysis Procedures

Blood (serum and plasma) and saliva samples will be analysed for exploratory inflammatory and stress-related biomarkers (e.g., cytokines, CRP, cortisol). These assays are research-use only and are not used for clinical diagnosis. SOPs for centrifugation, aliquoting, storage, assay preparation and QC will be followed. All resulting data will be stored using pseudo-anonymous identifiers.

11.4 Sample Storage Procedures

Blood samples will be stored at –80°C, and saliva samples at –20°C or below, within the KHP Cancer Biobank at Guy's Hospital. Freezers are temperature monitored with alarm systems, and access is restricted to delegated study personnel. Samples not immediately required for analysis will remain under these conditions until batch shipment where the same controlled storage procedures will be followed until analysis or destruction.

11.5 Results Recording/Reporting

Laboratory results will:

- be linked only to pseudo-anonymous study codes
- be recorded in secure electronic data files
- be stored on restricted-access KCL servers in non-clinical formats

Results will not be added to NHS medical records and incidental findings with potential clinical relevance are not anticipated or applicable due to the exploratory nature of the biomarker assays.

11.6 Sample Receipt/Chain of Custody/Accountability

On arrival at the processing or analytical laboratory:

1. Samples will be inspected for physical integrity and correct temperature.
2. Received sample labels will be checked against the manifest.
3. Tube count will be verified.
4. Samples will be booked into an accountability log with freezer location recorded.

Any deviations, including loss, breakage, temperature excursion or manifest discrepancy, will be recorded and reported to the trial team and Sponsor. Chain of custody will be maintained until destruction.

11.7 Sample transfer to sites outside the organisation

Following initial processing, samples will be transferred from the KHP Cancer Biobank at Guy's Hospital to collaborating laboratories within King's College London (Denmark Hill campus) and/or to external laboratory vendors approved by King's College London for analysis. Transfers will use temperature-controlled transport and packaging prepared in accordance with institutional SOPs. Shipments will be accompanied by a manifest and tracking documentation, including date of dispatch, courier details and storage conditions.

Transfers to collaborating laboratories within King's College London will be conducted under the same institutional governance framework and will not require external vendor agreements. Where samples are transferred to external KCL-approved laboratory vendors, all transfers and analyses will be conducted in accordance with King's College London governance requirements, biobanking policies, and material handling procedures.

11.8 Sample storage for ancillary use

Surplus material will not be used for ancillary studies. At the end of the retention period, all remaining samples will be destroyed in accordance with KCL or approved vendor laboratory waste procedures.

12 Regulatory Approvals

The study protocol and other documentation will be submitted to *[Name of REC to be inserted after submission] [and HRA]* for review and approval before the start of the study. All correspondence with the REC and HRA will be retained.

12.1 Modifications

Modifications will be submitted to the relevant regulatory bodies (REC, HRA, Sponsor, NHS R&D) for review following sponsorship approval. Modifications will not be implemented without the required regulatory and site approvals in place, as determined by the HRA.

12.2 End of Study Reporting

12.2.1 End of Study Declaration

The end of the study will be declared to the REC within 90 days of the study ending. The end of study declaration will be sent to the HRA once all participants have completed the study assessment points and the biological samples have been analysed.

12.2.2 End of Study Reporting

The end of the study report will be submitted to the REC within 12 months of the study ending.

13 Ethical considerations

Peer Review Process

As part of the larger programme funding application, this trial has been extensively reviewed, including internally by the wider team of co-applicants, our lived experience advisory board, and through formal peer-review processes as part of the Wellcome funding application

Patient and Public Involvement

Patient and public involvement (PPI) is central to the ADIE-BC trial. Wherever possible, we strive to co-produce the research. Our Lived Experience Partnership Board of people with a lived experience of cancer have been involved since the inception of the programme and will continue to play a crucial role across the trial, from design to dissemination. The Board is made up of a diverse group of individuals in terms of cancer stage, ethnicity and age; ensuring that we are representing and considering the needs of people with different experiences. Below is a summary of their involvement and plans for their involvement in the trial:

The Board has so far provided input on the grant application and members are named co-applicants and collaborators on the grant. The lived experience partners will also participate in the programme steering committee meetings to ensure the research aligns with the needs, preferences, and priorities of people with a lived experience of cancer.

The ADIE-BC trial was co-designed with lived experience partners. To adapt ADIE therapy for breast cancer survivors, two co-design workshops were held in 2023 and 2024 with six women aged 30–60 from diverse ethnic backgrounds (Black British, South Asian, and White British), all with lived experiences of breast cancer. Participants were recruited through UK breast cancer charities and included individuals with both primary and secondary diagnoses, all at least one-year post-active treatment. Workshop 1 (held in-person in 2023) explored how anxiety manifests in the body post-cancer and the acceptability of ADIE therapy in individuals with breast cancer. Feedback highlighted how the training could help de-threaten anxiety by taking an embodied approach and re-establish a sense of mind-body connection. Workshop 2 (held online in 2024) focused on co-designing the psychoeducational materials for ADIE Therapy, with input on the content, language, tone, imagery, and delivery. Group members reflected on what makes materials feel validating, engaging, and empowering for people living with and beyond breast cancer. Insights from both workshops directly informed the design and delivery of the ADIE-BC intervention and supporting materials.

We also hold monthly Lived Experience Partnership board meetings which aim to support the co-design of the clinical trial. These meetings are used to gather perspectives on the acceptability of measures included in the trial to ensure they are aligned with the needs and priorities of breast cancer survivors. The meetings are also used to provide project updates and tailored training and support to lived experience partners to support the meaningful co-design and co-development of the trial.

For this study, the Lived Experience Partnership board, as well as academic and clinical collaborators have been involved in reviewing research materials such as questionnaires, participant information sheets to ensure they are acceptable and culturally appropriate for a range of audiences. We also work closely with the Lived Experience representative collaborators and co-investigators to constantly reflect on lived experience partner involvement and to discuss future opportunities for involvement and influence.

We continue to work closely with multiple breast cancer organisations, including Black Women Rising, Breast Cancer Now, and Future Dreams. We will work with the lived experience partners and provide training, where necessary, to those who would like to present the findings charity events, meetings and community groups. With the Lived Experience Partnership board, we will develop a user-friendly, lay summary of the RCT results for sharing the findings with relevant charity and community groups.

Allowances for special groups
Due to the nature of the intervention, participation by non-English speakers is not permissible. Participation of this study requires the ability to follow and respond to instructions and provide feedback in English. Similarly, completion of study questionnaires necessitates comprehension of English.

Equality diversity and inclusion
To address the under-representation of minoritised and traditionally underserved groups in prior trials of psychological interventions for cancer-related anxiety, recruitment strategies will intentionally include outreach and invitation processes designed to enhance diversity within the sample. This may include collaboration with community organisations, targeted communication materials, and engagement with networks supporting individuals from minoritised and socioeconomically underserved backgrounds, and with official partners such as Black Women Rising.

14 Safety & Adverse Events Reporting

14.1 Assessment of Safety

This is a low-risk, non-CTIMP study involving questionnaires, behavioural tasks, and the use of a commercially available heart rate monitor (finger pulse oximeter) to support interoceptive training. The heart rate monitor is used only as an adjunct to the behavioural intervention and is not itself the object of evaluation. Appropriate procedures are in place to identify, record, and respond to any serious adverse events, as described below.

An Adverse Event (AE) is any untoward medical occurrence in a participant to whom an intervention has been administered.

A Serious Adverse Event (SAE) is an AE that results in one or more of the following:

- death
- a life-threatening state or condition

- hospitalisation or prolonged hospitalisation (must include an overnight stay; excluding planned hospitalisation)
- persistent or significant disability or incapacity
- congenital abnormality or birth defect

All AEs and SAEs will be monitored throughout the study period, and participants will be encouraged to report any concerns at any time. Adverse events will be recorded from the time of randomisation until the end of the participant's involvement in the study.

1. **Participant-Initiated Reporting**

Participants will be informed during the consent process, and reminded throughout the trial, that they may report any adverse events or safety concerns directly to the research team either in-person during study visits or via phone, text or email. It will be made explicit that these communication channels are monitored during working hours only (Monday-Friday, 9am-5pm, excluding Bank Holidays). If there is a concern of urgent risk to the self or others, the research team aims to respond within one working day.

Participants contacting the research team by phone will reach a voicemail outside of monitored hours. The voicemail will advise:

- the expected response timeframe
- to consult the resources listed in the PIS or to contact their GP for clinical advice, and
- to attend A&E or call emergency services if immediate help is required.

Participants contacting the team by email will receive an automated reply containing the same information.

While the study does not include any questions relating to safeguarding, abuse, or unsafe care, we recognise that there is a remote possibility that a participant could voluntarily disclose information suggesting a safeguarding concern. In the unlikely event that this occurs, our research team will follow King's College London safeguarding procedures. Any disclosure raising immediate risk of harm would be escalated to the IoPPN safeguarding lead following the King's College London Safeguarding Reporting Process. Participants are informed at consent that confidentiality may be breached if there is concern about risk of serious harm.

2. **Direct Assessment by the Research Team**

Given that the 18-week and 12-month follow-up assessments will be completed remotely and thus there is no opportunity to report adverse events in-person, the self-report assessments will include a structured set of safety questions to determine whether any adverse events occurred since the previous contact. These checks will explicitly ask about negative changes in physical and mental health symptoms. The participants will be informed at this assessment that the study team may contact them by phone call to further discuss anything that they have reported (e.g., to determine seriousness).

3. **Mitigation and participant support**

Participants will be informed that temporary fluctuations in mood or emotional discomfort may occur when completing behavioural tasks, questionnaires, or interviews, and such changes are not uncommon. If a participant expresses distress or appears in need of additional support, the study team will:

- direct them to relevant support services provided by the breast cancer charity partners,
- remind them of all support resources included in the PIS, and
- advise them to contact their clinical care team or GP if they require clinical guidance or further psychological support.

Clinical cover procedures are in place to ensure that research staff have access to a clinically qualified senior member of the team – specifically, an experienced Clinical Psychologist – who can provide individualised advice on risk management and appropriate actions following disclosure that may indicate participant risk.

Where a participant presents with extended or worsening anxiety, depressive symptoms, or other psychological difficulties, they will be signposted to their GP for further assessment and support. Participants will also be reminded or additional support options, including organisations listed in the PIS that offer mental health support and crises resources

Serious Adverse Events

Adverse Events (AEs) and Serious Adverse Events (SAEs) will be assessed by the research team and CI according to the criteria below (ICH, 1994)

- **Severity:** AEs will be classified as 'Mild', 'Moderate', or 'Severe'. This ranges from events that cause slight discomfort, but warrant no further investigation, to events that are causing significant interference in the participants routine and/or health.
- **Expectedness:** SAEs will be classified as 'Expected' or 'Unexpected', dependent on whether the event is consistent with the information provided about the study procedure outlined in this protocol.
- **Relatedness (causality):** SAEs will be rated on the following scale:
    - Related: there is some or clear evidence suggesting a causal relationship between the event and the device/trial. Other potential contributing factors have been ruled out.
    - Not related: There is no evidence linking the event to the device/trial.

  All SAEs judged as having a reasonable suspected causal relationship (possibly, probably, definitely) to the trial or device will be considered as related.
- **Outcome:** This will be classified as 'Resolved', 'Resolved with sequelae', 'Continuing', 'Fatal', or 'Unknown'. Date of resolution or death will be recorded.

Reporting procedures

SAEs may be considered related to the study if they resulted from administration of any of the research procedures. Reports of related and unexpected SAEs will be submitted to the Sponsor within 24 hours of the CI becoming aware of the event. The REC will be informed within 15 days.

15 Compliance and withdrawal

15.1 Participant compliance

Participant compliance with the study intervention and follow-up assessments will be monitored by the research team throughout the study.

For participants allocated to the intervention arm, attendance will be recorded to describe intervention uptake and fidelity. Non-attendance or partial attendance will not constitute protocol deviation or withdrawal from the study.

Participants who miss or fall behind on scheduled sessions will be contacted by the research team (via phone, text message, or email) to support re-scheduling and session completion wherever possible. The number and timing of reminders will be tailored to the participant's remaining sessions and the time available before follow-up assessments. Efforts to support continued engagement will be proportionate prioritise participant preference and wellbeing.

Compliance with follow-up assessments will be monitored at each scheduled time point. Participants who do not complete assessments as planned may be contacted to encourage completion, where appropriate. Unless a participant explicitly withdraws from follow-up, all randomised participants will remain in the trial until completion of their final scheduled follow-up visit, irrespective or treatment attendance of engagement. Participants may decline specific follow-up measures without withdrawing fully from the study.

15.2 Withdrawal / dropout of participants

Participants will be informed that participation is voluntary, and they may withdraw at any time, without giving a reason.

Discontinuation of the intervention refers to when participants no longer wish to complete their remaining intervention sessions. This does not automatically constitute withdrawal from study follow-up or data collection. Unless a participant explicitly withdraws consent for further contact or data collection, participants will not be contacted to complete the remaining sessions, but they will be contacted about follow-up assessments. This is also voluntary, and they are free to decline. The study team will record the date of and reason for the discontinuation of sessions if known.

Withdrawal from the trial refers to when participants state that they no longer want to complete their sessions and follow-up assessments. In such cases, the research team will record the date of and reason for the withdrawal if known. Data collected up to the point of withdrawal will be retained and analysed in accordance with the consent provided and applicable regulations, unless the participant requests otherwise.

All participants who withdraw from the trial will be asked on one occasion if they would be willing to complete an interview about why they decided to withdraw, which is voluntary, and

they are able to decline. After this, they will no longer be contacted by the study team. The study team will record the date of and reason for the withdrawal if known.

15.3 Protocol Compliance

A Protocol deviation is usually an unintended departure from the expected conduct of the study protocol, which does not need to be reported to the Sponsor. All protocol deviations will be logged in the protocol deviation log, which will be stored in the Internal Site File (ISF) and will be monitored by the CI.

Any significant deviations or those that frequently recur will be assessed by the CI to see if an amendment to the Protocol is required. Any deviations that are considered significant enough to be a full protocol breach will be reported to the REC Committee with the Sponsor in copy within 7 calendar days of the breach being confirmed as serious and action taken through Corrective and Preventative Actions (CAPAs), information for which will be retained in the Site File. A 'serious breach' is defined as a breach likely to affect to a significant degree:

- the safety or physical or mental integrity of the participants of the trial;
- The scientific value of the trial.

16 Data

16.1 Data to be collected

Seven types of data will be collected as part of this trial:

1. Personal identifiable data (PID) including name, contact details for both 1) individuals who expressed interest in the study but were screened and deemed ineligible, 2) individuals who consented to the trial.
2. Questionnaires data – responses to study-related questionnaires completed by participants.
3. Biobehavioural data – heartbeat.
4. Biomarkers including saliva and blood sample.
5. MRI scan – imaging data from participants who consent to this procedure.
6. Interview – audio and video recordings of interviews conducted with consenting participants.

An overview of the data types and collection details can be found in separate document, Data Specification.

16.2 Data handling and record keeping

Data handling and record keeping

King's College London (KCL) is the sole Sponsor and Data Controller for this study. All study data will be handled in accordance with UK General Data Protection Regulation (UK GDPR), the Data Protection Act 2018, Good Clinical Practice (GCP), the Caldicott Principles, the NHS Code of Confidentiality, and relevant institutional policies.

All reasonable precautions will be taken to protect participant confidentiality. Participants will be identified using unique study identification numbers, and personally identifiable information will be stored separately from research data. Access to identifiable data will be restricted to authorised members of the research team only.

Study data will be collected and managed using a secure, web-based electronic data capture system hosted within King's College London, with role-based access controls and a full audit trail. Only data from participants who have provided informed consent will be entered into the study database. Data will be monitored and reviewed by the Chief Investigator or delegate to ensure completeness and accuracy prior to database lock and analysis.

Hard copy study documents will be stored in locked cabinets in secure KCL premises, and electronic data will be stored on encrypted, access-restricted KCL servers. Interview data will be pseudonymised, and any identifiable information will be removed from transcripts.

16.3 Access to the dataset

During the study, access to data will be restricted to authorised members of the research team, the study statistician, and relevant sponsor representatives for monitoring and oversight purposes.

Access to the final coded dataset will be controlled by the Chief Investigator. Requests for secondary analysis or data sharing will be considered on a case-by-case basis, subject to appropriate governance approvals and data sharing agreements. Any shared datasets will be fully anonymised.

For a detailed description of this section, please refer to the Data Flow Diagram provided as a separate attachment.

17 Statistical considerations

17.1 Sample size calculation

The target sample of N=168 (84 per arm) was determined on the basis of an initial power calculation for the GAD-7, which was specified as a primary outcome in the funding

application. This provides adequate power to detect a clinically meaningful difference on the revised primary outcome (STAI-T), as described below.

The funding application specified a total sample of N=168 (84 per arm) to provide 90% power (two-sided α=0.05) to detect a 2-point difference in mean GAD-7 scores between arms at the primary endpoint (8 weeks post-randomisation). This 2-point difference represents the minimum clinically important difference (MCID) for the GAD-7 in clinical populations. The calculation assumed a standard deviation of 4.1 based on GAD-7 data from a breast cancer population (Esser et al., 2018), a pre-post correlation of r=0.5, and 20% attrition over the trial period. The pre-post correlation adjustment reflects the efficiency gain from baseline covariate adjustment, reducing the required sample from 106 to 84 per arm after accounting for attrition. Single-arm pilot data (N=20) supported these assumptions, with an observed mean reduction of 2.2 points, SD=3.7, and 15% attrition.

Following the completion of recruitment to the pilot study and prior to submission of the trial protocol for ethical review, the primary outcome was revised from the GAD-7 to the STAI-T. This decision was informed by two sources of emerging evidence. First, patient engagement work conducted during trial development indicated a preference for the STAI-T as a measure of anxiety, due to perceived better content validity. Second, pilot data indicated that the STAI-T may be more sensitive to detecting change in this population given that no participants scored at the floor of the STAI-T at baseline, compared with 10% who scored at the floor of the GAD-7.

No established MCID exists for the STAI-T in breast cancer populations where levels of psychological distress are typically anticipated to be in the mild-moderate range. Following distributional methods, we defined a minimally important target difference of 6 points, corresponding to approximately half a standard deviation of the STAI-T scores observed in the pilot (SD=12.1). Applying the same operating characteristics as the funder-approved calculation (two-sided α=0.05, pre-post correlation r=0.5, 20% attrition), the pre-specified sample of N=168 (84 per arm) provides 91.6% power to detect this 6-point difference, which marginally exceeds the 90% specified in the funder application. Therefore, no increase in sample size is necessary due to the change in primary outcome.

17.2 Statistical analysis

Analysis Responsibility and Principles

All statistical analyses will be conducted by the trial statistician in accordance with a pre-specified analysis plan. Analyses will follow the intention-to-treat (ITT) principle, whereby all randomised participants will be included in the analysis according to their allocated treatment arm, regardless of treatment received or adherence to the intervention protocol. The statistical analysis will be conducted in accordance with the ICH E9(R1) addendum on estimated and sensitivity analyses, with the estimated framework guiding the definition of the treatment effect of interest, the population to which it applies, and how intercurrent events (such as treatment discontinuation or use of alternative treatments) will be handled.

The primary estimated targets the treatment policy strategy, estimating the effect of being assigned to ADIE-BC versus Enhanced Usual Care (EUC), regardless of adherence to the assigned intervention. This approach reflects the pragmatic nature of the trial and provides an estimate of effectiveness relevant to clinical decision-making and implementation.

Descriptive Analyses

Baseline characteristics will be summarised by treatment arm using appropriate descriptive statistics: means and standard deviations (or medians and interquartile ranges for skewed distributions) for continuous variables, and frequencies and percentages for categorical variables. Summaries will include demographic characteristics, clinical characteristics (cancer stage, time since treatment completion, current adjuvant therapy), and baseline outcome measures. No formal statistical testing of baseline differences will be conducted.

Participant flow through the trial will be documented using a CONSORT flow diagram. Adherence to the ADIE-BC intervention will be summarised as the number and percentage of participants completing each of the six treatment sessions.

Primary Outcome Analysis

The primary outcome is STAI-T score at 8 weeks post-randomisation. The primary analysis will use a linear mixed-effects model (LMM) with repeated measures from mid-point (5 weeks), primary endpoint (8 weeks), and maintenance follow-up 18-weeks. The model will include fixed effects for treatment arm, time point, and the treatment-by-time interaction, with baseline STAI-T and any stratification factors used in the randomisation procedure included as covariates. Participant will be included as a random effect to account for within-person correlation across time points. The treatment effect at 8 weeks will be estimated from the treatment-by-time interaction term, representing the difference in mean change from baseline between arms at the primary endpoint.

The primary analysis will be conducted on all available data under the missing-at-random (MAR) assumption. The treatment effect will be reported as the adjusted mean difference with 95% confidence interval and two-sided p-value. Effect size will be calculated as standardised mean difference using Hedge's g with small sample adjustment. Statistical significance will be concluded where $p<0.05$.

Secondary Outcome Analyses

Secondary outcomes will be analysed using the same LMM framework as the primary outcome, incorporating data from 5-week, 8-week, and 18-week assessments. For continuous outcomes (GAD-7, FCRI-SF, PHQ-8, MAIA-2, BTMS, ASI, BMI-2, PROMIS measures, EQ-5D-5L), linear mixed-effects models will be fitted with treatment arm, time, and treatment-by-time interaction as fixed effects, baseline values and stratification factors as covariates, and participant as a random effect. Treatment effects will be estimated at each time point from the interaction terms.

Analyses of interoceptive accuracy measures (Heartbeat Discrimination Task and Heartbeat Tracking Task) will follow the same LMM approach, using data from 5-week and 8-week assessments, as these behavioural tasks are only administered at in-person visits.

Extension Analysis: 12-Month Follow-Up

The 12-month follow-up assessment will be analysed separately following completion of data collection at this time point. This extended follow-up aims to evaluate the durability of intervention effects beyond the primary trial period. Given the optional nature of this assessment and anticipated variability in completion rates, the 12-month analysis will be clearly identified as exploratory. LMMs will be extended to incorporate the 12-month time point, enabling estimation of treatment effects at this extended follow-up while accounting for the within-person correlation structure across all available time points. The 12-month analysis will be conducted and reported after the main trial results have been analysed and disseminated, as specified in the trial timeline.

Mediation Analyses

Mediation analyses will evaluate whether changes in hypothesised mechanistic variables mediate the effect of ADIE-BC on anxiety outcomes. The primary mediation pathway of interest examines whether changes in interoceptive measures (both accuracy and sensibility) at 8 weeks mediate the effect of treatment on STAI-T at 8 and 18 weeks.

Mediation analyses will use a causal mediation analysis approach using the potential outcomes framework. The indirect effect of the treatment on the outcome via the mediator will be estimated, along with the proportion of the total effect mediated. Mediators to be examined include interoceptive accuracy (from behavioural tasks), interoceptive sensibility (MAIA-2, BTMS, BMI-2), and anxiety sensitivity (ASI). Additional exploratory mediation analyses may examine whether changes in secondary outcomes (e.g., depression, quality of life) are mediated through changes in interoceptive processes.

Subgroup and Sensitivity Analyses

Pre-specified exploratory subgroup analyses will explore whether treatment effects differ according to baseline characteristics including anxiety severity, time since treatment completion, and current adjuvant therapy status. Subgroup effects will be evaluated by including treatment-by-subgroup interaction terms in the primary analysis model. Given the exploratory nature of these analyses and the risk of Type I error inflation, results will be interpreted cautiously and reported with appropriate caveats regarding multiple testing.

Sensitivity analyses will assess the robustness of the primary analysis to key assumptions, including: (1) per-protocol analysis restricted to participants who completed at least four of six ADIE-BC sessions in the intervention group and excluding participants who commence alternative psychological interventions (e.g., CBT) during the trial period from either group; (2) complier-average causal effect (CACE) analysis to estimate effects in participants who would comply with either treatment assignment; (3) pattern-mixture models under alternative missing data assumptions to assess sensitivity to the MAR assumption.

Statistical Software and Reporting
All analyses will be conducted using Stata (version 19 or later) and/or R (version 4.0 or later). Results will be reported in accordance with CONSORT guidelines for reporting randomised trials, including appropriate measures of effect size, precision (95% confidence intervals), and statistical significance. Full details of all planned analyses, including model specifications, handling of missing data, and sensitivity analyses, will be documented in a SAP to be finalised prior to database lock.

17.3 Interim analysis and data monitoring

17.3.1 Stopping/ discontinuation rules and breaking of randomisation code

Interim Efficacy Analyses
No formal interim analyses for efficacy are planned. The primary analysis will be conducted once all participants have completed the 18-week follow-up assessment and the database has been locked. This decision reflects the relatively short duration of the trial, the established safety profile of the ADIE intervention from previous trials, and the moderate sample size

Safety Monitoring
While no interim efficacy analyses will be conducted, ongoing safety monitoring will occur throughout the trial. Two independent members of the Trial Steering Committee (TSC) will serve in a Data Monitoring and Ethics Committee (DMEC) capacity, with responsibility for reviewing safety data in an unblinded fashion. The DMEC members will review summaries of AEs and SAEs by treatment arm at regular TSC meetings (approximately every 6 months), or more frequently if safety concerns arise.

Safety data will be reviewed in aggregate form during the open (non-confidential) portion of TSC meetings, with individual-level safety data reviewed during closed sessions attended only by the independent DMEC members and the trial statistician.

Trial Discontinuation
The trial may be prematurely discontinued if:

- New safety information emerges suggesting that continuation would pose unacceptable risk to participants
- External evidence becomes available that definitively answers the research question, rendering continuation of the trial unnecessary or unethical
- Recruitment or retention rates are substantially lower than anticipated, such that the trial cannot achieve adequate power within a reasonable extended timeframe
- Regulatory or ethical approval is withdrawn

Any decision to discontinue the trial will be made in consultation with the TSC and DMEC members and will be reported to the Research Ethics Committee and Sponsor within the required timeframes. In the event of early termination, all actively participating individuals will be informed and offered appropriate signposting to alternative sources of support.

Breaking the Randomisation Code

The randomisation code will be maintained securely by King's Clinical Trials Unit (KCTU). Emergency unblinding of individual participant allocation may be requested in exceptional circumstances where knowledge of treatment allocation is deemed essential for participant safety or clinical management. Such circumstances are anticipated to be extremely rare given the behavioural nature of the intervention, where participants and the research team are not blinded. Any request for emergency unblinding must be made by the Chief Investigator to KCTU, with full documentation of the reason for the request, the date and time, and the personnel to whom the allocation is disclosed.

All instances of unblinding will be recorded in a dedicated unblinding log, which will be reviewed by the TSC. Emergency unblinding of an individual participant will not automatically result in their withdrawal from the trial. They may continue to provide outcome data if willing and able to do so and will be included in the intention-to-treat analysis.

17.3.2 Monitoring, quality control and assurance

Study Monitoring

The trial will be monitored in accordance with the Sponsor's requirements and proportionate to the risk profile of the study. As a low-risk behavioural intervention trial, central monitoring will be the primary approach, supplemented by targeted site monitoring as needed.

Central monitoring will be conducted by the research team and will include:

- Regular review of recruitment and retention rates against targets
- Monitoring of protocol deviations and corrective actions
- Review of data completeness and quality, including identification of missing data patterns, outliers, and inconsistencies
- Monitoring of adverse event reporting and follow-up
- Review of informed consent processes and documentation
- Assessment of adherence to intervention delivery protocols

Data quality will be maintained through several mechanisms:

- Use of validated, standardised outcome measures with established psychometric properties
- Electronic data capture with built-in range and logic checks to minimise data entry errors
- Regular data monitoring reports generated by the trial statistician to identify patterns of missing data or inconsistencies
- Training of research staff in data collection procedures and Good Clinical Practice (GCP) principles
- Standard operating procedures (SOPs) for all key trial processes

Quality Assurance

All research staff involved in the trial will complete GCP training appropriate to their role and will adhere to the trial protocol and relevant SOPs. Research staff delivering the ADIE-BC intervention will receive specific training in the intervention protocol and will be supervised by experienced members of the team to ensure fidelity to the intervention manual.

The Sponsor's Quality Assurance team may conduct audits of trial conduct at any time. Any such audits will be facilitated by the Chief Investigator and Trial Manager, and findings will be reported to the TSC and addressed through appropriate corrective and preventative actions (CAPAs).

Trial Steering Committee Oversight
The TSC will provide independent oversight of trial conduct, reviewing progress against milestones, recruitment and retention data, data quality metrics, and safety data. The TSC will meet approximately every 6 months, or more frequently if required. The TSC Terms of Reference document the committee's composition, responsibilities, and operating procedures, including procedures for decision-making and escalation of concerns to the Sponsor.

18 Risk Management & Safeguarding

18.1 Risk Management

This trial involves a low-risk behavioural intervention with established safety data from previous trials. However, several potential risks have been identified and mitigation strategies are in place.

Psychological distress
As part of risk assessment management, individuals meeting exclusion thresholds for severe depression on the PHQ8 (≥20) at eligibility screening will not be invited to take part in the study. Nevertheless, participants may experience emotional discomfort when reflecting on their cancer experience, symptoms, or general wellbeing during assessments or intervention activities.

Mitigation strategies:

- Delegated research staff will be trained to recognise signs of distress and to respond appropriately in line with training delivered by the trial's Clinical Psychologist.
- Participants will be reminded that they may pause or stop any session or assessment at any time without consequence.
- If significant distress is reported to the study team, they may seek clinical oversight from the trial's Clinical Psychologist.
- Any adverse events related to distress will be documented and reported according to the study's AE procedures.

Suicide risk

As part of risk assessment management, a suicide risk question is asked during eligibility screening. Individuals meeting exclusion thresholds for current suicidal intent or plan (medium or high risk, as determined by PHQ9 Item 9 and associated risk assessment questions) will not be invited to participate and will be signposted to support.

Although the study population is not expected to be at elevated suicide risk, participants may disclose suicidal thoughts or concerns during study activities.

Mitigation strategies:

- Staff conducting screening will be trained to manage disclosures of suicidal intent and to document actions taken appropriately.
- Individuals screened as unsafe to participate will not be enrolled and will be supported with appropriate signposting.
- Any disclosure of suicide risk during study activities will be managed following the Wileman et al (2024) procedure, including immediate risk assessment and escalation (e.g., GP, A&E) as appropriate.
- Any adverse events related to suicide risk will be documented and reported in accordance with the study's AE procedures.

No routine or repeated suicide risk assessment will be conducted during the trial.

Physical safety (venepuncture, MRI)
Venepuncture and MRI components may involve minor physical risks such as transient discomfort, bruising, dizziness (venepuncture), or claustrophobia (MRI).

Mitigation strategies:

- Venepuncture will be performed only by trained and delegated staff.
- MRI procedures will follow standard KCL screening and safety procedures.
- Participants may discontinue at any time without affecting trial participation.

Staff safety
Staff may encounter emotionally distressed individuals or lone-working situations.

Mitigation:

- To ensure staff safety, screening and research activities will be conducted within office hours. In-person patient visits will be scheduled to end by 16:30. This is to ensure there is sufficient time for the research team to respond appropriately should any adverse events occur.
- Where possible, another member of the research team will be present in the office vicinity as backup when participant-facing activities are taking place. Staff will also have access to a work phone switched on during research activity for emergency use.
- Regular supervision and support will be provided, including clinical supervision from the trial Clinical Psychologist.
- Any concerns will be documented and escalated through standard governance routes.

18.2 Safeguarding

Safeguarding context
The participant demographic (adult cancer survivors who experience anxiety) may be considered vulnerable adults; however, they are competent adults capable of providing informed consent. Safeguarding incidents as a direct result of trial participation are not anticipated.

All research team members will be familiar and adhere to KCL safeguarding policy (*https://www.kcl.ac.uk/assets/policyzone/governancelegal/safeguarding-policy.pdf*), including the designated point of contact for raising concerns. The research team also hold DBS check and undertake training relevant to the safeguarding of the demographic involved in the study.

The research aims, benefits, potential risks, data use, and participant rights, including the right to withdraw, are clearly explained to all participants prior to obtaining informed consent. Capacity to provide informed consent is assessed by the participant's ability to retain information about the trial, including its purpose and implications. This process is continuous, and participants will be reminded of their rights at each contact.

Disclosure management
Questionnaires and interviews do not ask about historic or current abuse, exploitation, or other safeguarding concerns. However, spontaneous disclosures of past or current abuse may occur during conversations with research staff.

If such information is disclosed, either with respect to the participant or other individual, the researcher will respond calmly without judgement, explain the duty of care and limits of confidentiality, and record the disclosure in writing. Where appropriate, accuracy will be confirmed with the participant and signed by both parties. Where there is imminent risk, emergency services will be contacted immediately. All disclosures will be reported to the safeguarding lead in accordance with KCL's policy.

Confidentiality and Information Sharing
Participant confidentiality is maintained in accordance with data protection legislation and NHS Caldicott principles. Personal information will only be shared beyond the research team without consent in exceptional circumstances where:

- There is a safeguarding concern requiring escalation
- There is imminent risk of serious harm to the participant or others
- There is a legal obligation to share information

In such cases, only the minimum necessary information will be shared, and participants will be informed of this where safe and appropriate to do so.

19 Financing

This trial is part the ENTRUST programme of research, funded by a 5-year Wellcome Mental Health Award which began in February 2025 and aims to conduct several studies to understand interoceptive mechanisms of anxiety reduction in people living beyond cancer (award identifier: 309734/Z/24/Z).

20 Insurance

The study is sponsored by King's College London (KCL). The sponsor will, at all times, maintain adequate insurance in relation to the trial: KCL through its own professional indemnity (Clinical Trials) & no-fault compensation, in respect of any claims arising as a result of negligence by its employees, brought by or on behalf of a trial participant.

NHS staff (including honorary contract holders) undertaking research as part of their job role are covered by NHS Resolution indemnity schemes if working for a member of those schemes, subject to the usual scheme terms and conditions: https://www.hra.nhs.uk/about-us/news-updates/indemnity-cover-nhs-staff-delivering-research/

21 Publication and Dissemination

21.1 Publication

The results of the study will be published in peer-reviewed journals and presented at relevant national and international conferences. The findings will also contribute to research assignments of BSc, MSc, or DClin students at King's College London and reflective reports for training purposes. The results will also be published in an internal report and will be used to inform the upcoming programme aims.

21.2 Informing participants and other relevant groups

After the study is finished, participants who provided consent to receiving study findings will receive a summary via email or post according to their preferences.

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