ISRCTN12027752 https://doi.org/10.1186/ISRCTN12027752

# The Yorkshire Cancer Research ACTION pilot trial of Acceptance and Commitment Therapy for women with breast cancer to support wellbeing and hormone therapy medication decisions

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|---|---|---|
| **Submission date** | **Recruitment status** | [X] Prospectively registered |
| 18/05/2020 | No longer recruiting | [X] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 24/12/2020 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 20/05/2024 | Cancer | |

## Plain English summary of protocol

Background and study aims

Breast cancer is the most commonly diagnosed cancer in women worldwide. In the UK, approximately 55,000 cases occur per year, with 11,000 cancer-related deaths. The majority of breast cancers are oestrogen receptor-positive (ER+) tumours, which means that the hormone oestrogen, can encourage these cancer cells to grow. Hormonal therapies (HTs), in addition to primary treatment (such as surgery), have drastically improved cancer outcomes for women with ER+ tumours and are routine care for this group. However, adherence to these therapies is inadequate. Previous studies have highlighted the proportion of women taking these medications as prescribed ranges from 31% to 73%.

Poor adherence to medication is an issue across all medical conditions. Given that poor adherence is a problem largely occurring at the behavioural level (such as problems in collecting prescriptions, managing regimens, and taking medications), it is unsurprising that a broad range of behavioural and psychological variables– such as mood, illness and treatment beliefs, and motivation- are consistently shown to predict adherence. Despite evidence that psychological /behavioural variables contribute to low adherence to HT, the psychological/behavioural adherence interventions that have been evaluated to date have shown no beneficial effects on medication-taking behaviour. These interventions aimed to improve adherence by providing information about HTs, and problem-solving difficulties with medication-taking. Given the wide range of additional factors that contribute to low adherence, it is perhaps unsurprising that interventions focused largely on giving information about treatments have been unsuccessful. An alternative, and potentially more effective strategy, is to design an intervention to target a range of emotional and physical factors that may affect adherence.

There is a growing evidence base demonstrating that ACT (Acceptance and Commitment Therapy) can improve outcomes (functioning, quality of life, mood) in chronic disease and, in

particular, chronic pain contexts. A systematic review of ACT interventions undertaken by our group returned three trials of ACT for improving outcomes in cancer populations. While these trials suggest that ACT may effectively improve outcomes in cancer contexts, these interventions did not attempt to improve, nor did the trial record, adherence to medication. Indeed, despite several research groups advancing that ACT may be an effective approach to improving medication adherence, to date, there has been just one case study of this approach in any chronic disease. There is therefore interest in developing an ACT-based intervention to improve adherence to HTs (and improve quality of life) in women with breast cancer.

A case study has been conductedby the study team to design the intervention and identify any issues with the training, delivery, and evaluation of the intervention by carrying out a full cycle of the intervention (recruitment, delivery, data collection) at a single NHS site.

The aim of this pilot study is to test the feasibility of undertaking a larger trial of an Acceptance and Commitment Therapy (ACT) based intervention for improving adherence to hormone therapy in women following curative treatment for breast cancer.

Who can participate?
Women aged 18 or over with early-stage (1 to 3a) breast cancer who have been prescribed adjuvant Hormone Therapy and completed curative hospital-based treatment.

What does the study involve?
Eighty women will be randomly allocated to receive treatment as usual (the care they would normally receive at their hospital) or treatment as usual plus the ACTION intervention. The ACTION intervention is an ACT (Acceptance and Commitment Therapy) based therapy developed to improve adherence to hormone therapy in women with breast cancer. The ACTION intervention will be delivered remotely via a video platform by trained NHS therapists and is comprised of one individual (1 h) ACT session followed by three group (90 min each) ACT sessions. Sessions will be recorded to ensure the intervention is delivered as intended. Recordings are encrypted and transferred securely. Any transcriptions are made by persons authorized by the University of Leeds. Participants will also be directed to a website containing supplementary ACT exercises and additional information regarding Hormone Therapy and self-managing side effects, which participants can access before, during and after the individual and group therapy sessions.

Participants will be asked to complete a series of questionnaires before entering the study and after 3 and 6 months of the study. The questionnaires will be looking at issues around health, well-being and medication.

Following completion of the study, all participants randomised to the intervention group (ACTION) will be invited to participate in telephone interviews with a researcher. The interviews will ask questions that give insight into the acceptability of the intervention and study procedures but also enquire as to which (if any) parts of the intervention/programme were helpful. Similarly, the therapists delivering the intervention will also be invited to participate in semi-structured telephone interviews. These will inquire about therapist’s experiences of delivering the intervention, the practicability of the intervention (within NHS contexts), training, and ways to improve the intervention and training.

What are the possible benefits and risks of participating?
It is hoped that participants will benefit from taking part and that the programme will be helpful, but as the ACTION programme is new, cannot be guaranteed that this will be the case. The main benefits should be stated to be helping the researchers learn more about the

treatment options for women with breast cancer who have been prescribed hormone therapies, the effectiveness and acceptability of ACTION and how it may help in managing treatment side effects and quality of life. It will also help the researchers to find out if they can run a larger study, to find whether a new approach to therapy is an effective approach in supporting women with breast cancer.

Where is the study run from?
Clinical Trials Research Unit, The University of Leeds (UK)

When is the study starting and how long is it expected to run for?
From June 2019 to July 2022

Who is funding the study?
Yorkshire Cancer Research (UK)

Who is the main contact?
1. Ms Rachel Ellison
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2. Dr Sam Smith
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# Contact information

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Scientific

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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number
276424

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
CPMS 44537, IRAS 276424

# Study information

### Scientific Title
The Yorkshire Cancer Research ACTION Pilot Trial: An ACT-based intervention for women with breast cancer to support wellbeing and hormone therapy medication decisions

### Acronym
ACTION Pilot

### Study objectives
1. To test the feasibility of undertaking a definitive phase III Randomised Controlled Trial (RCT) of an Acceptance and Commitment Therapy (ACT) based intervention for improving adherence to hormone therapy in women following curative treatment for breast cancer
2. Establish eligibility, recruitment, retention, and follow-up rates to inform the design of a phase III RCT
3. Assess the acceptability of the intervention and protocol to participants and NHS therapists
4. Assess the extent to which NHS therapists can remotely deliver an ACT intervention with fidelity, following remotely delivered training
5. Demonstrate “proof-of-principle”, via exploration of between-group change in outcome (medication adherence, QoL, mood) and process (psychological flexibility) variables

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 02/12/2020, Yorkshire and the Humber REC- South Yorkshire (Mercure Doncaster Centre Danum, High Street, Doncaster, DN1 1DN, UK; +44 (0)207 1048091; southyorks.rec@hra.nhs.uk), ref: 20/YH/0104

## Study design
Multicenter interventional individually randomized controlled pilot study

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

## Health condition(s) or problem(s) studied
Breast cancer

## Interventions
The format of the intervention being evaluated was co-developed with both potential participants (women with breast cancer) and healthcare professionals involved in their care. It was co-designed through focus groups, interviews, and a half-day workshop during a previous case study phase.

Participants will be randomised on a 1:1 basis to receive either treatment as usual or treatment as usual plus the ACTION intervention and will be allocated a trial number. A computer-generated minimisation programme that incorporates a random element will be used to ensure treatment groups are well-balanced for the following participant characteristics (stratification factors), details of which will be required for randomisation:
1. Recruiting site
2. Recruitment route (recently completed treatment; experiencing medication problems; or retrospective screening)
3. Participant age (≤50 years; 51-69 years; or >70 years)

Participants will be identified and screened from breast cancer services at eligible NHS Trust Hospitals. There will be three recruitment routes for patients to the pilot study:
1.The research nurse (RN) or delegate screens patient records for eligible patients who will be attending their discharge / holistic needs/end of treatment summary meeting in the upcoming week(s). The patient's Breast Care Nurse or member of the patients care team introduces the RN or delegate (trained in taking consent), who attends the relevant meetings to give eligible patients a study pack. Potential participants will have the opportunity to ask the RN or delegate any questions. If the patient feels the study has been adequately explained and has had the opportunity to ask any questions, they may consent to the study at this meeting, however, all potential participants will be given the opportunity to take the study invitation pack home to think about whether they wish to take part and discuss with family and/or friends.
If the patient is happy to take part in the study at the initial meeting, the screening

questionnaire will be discussed with the patient to ensure they meet the eligibility criteria. Once eligibility is confirmed they will then be asked to complete the baseline questionnaires either at this visit or asked to take them home for completion. The completed questionnaires will then be given to the RN/delegate or returned in the post using the prepaid envelope provided.
If the patient wishes to take the study invitation pack home before agreeing to consent, patients are instructed to telephone or email their RN/delegate if they decide they would like to take part, have any further questions, or do not wish to take part (in this instance no further contact would be made).
2. Patients discharged following hospital-based treatment but who self-refer to their oncologist to discuss problematic medication side effects and/or adherence problems will be invited to participate. Eligibility will initially be assessed during the appointment by the oncologist. The oncologist will briefly discuss the study with the participant, and if they are potentially interested, the oncologist will email (via secure NHS email) their contact details and name (with the patient's verbal consent) to the RN or delegate. The RN or delegate will telephone potentially eligible patients to discuss the study with them and answer any questions.
Patients who have been screened as eligible and showing an interest in participating will then be posted a study invitation pack, which will include the following:
2.1. Invitation letter
2.2. Participant Information Sheet, including a step by step guide for how to participate and what is involved together with the research nurse's or delegate's contact details
2.3. Baseline questionnaire pack
2.4. Consent form
If on receipt of the information pack the participant is still happy to take part they will be asked to complete the baseline questionnaires and consent form and return it to the RN/delegate in the post using the prepaid envelopes provided. Patients are also instructed to telephone or email their RN/delegate if they have any further questions or do not wish to take part (in this instance no further contact would be made).
3.The Research nurse (RN) or delegate will retrospectively screen patient records for potentially eligible patients who have been discharged in the previous 6 months. The RN or delegate will telephone potentially eligible patients to discuss the study with them and answer any questions. If the patient is happy to be screened for eligibility, the RN/delegate will run through the screening questionnaire with them or rearrange the call for a more suitable date.
Patients who have been screened as eligible and showing interest in participating will then be posted a study invitation pack (as above).
If on receipt of the information pack the participant is still happy to take part they will be asked to complete the baseline questionnaires and consent form and return it to the RN/delegate in the post using the prepaid envelopes provided. Patients are also instructed to telephone or email their RN/delegate if they have any further questions or do not wish to take part (in this instance no further contact would be made).

Regardless of which of the above methods is used to identify a potential participant, if they agree to take part, and eligibility is confirmed through the screening questions, the participant will be asked to sign and return the consent form and complete the baseline questionnaire pack. On receipt of these, the participants will be randomised into the trial by an authorised member of staff at the trial research site via the automated 24 h randomisation system at the Clinical Trials Research Unit in Leeds.

The ACTION intervention will be delivered by practioner psychologists via one individual therapy session (1 h) and three group sessions (each 90 min).

Participants will also be directed to a bespoke website containing supplementary ACT exercises and additional information regarding Hormone Therapies and self-managing side effects, which participants can access before, during, and after the intervention.

Website usage including the number of website visits throughout the trial and pages visited on the website will be summarised by the research team to help answer the secondary endpoint, 'the acceptability of the intervention'. Participants will be asked to provide their consent for this data to be collected.

Following the final group session participants will be invited to take part in an optional semi-structured interview with a member of the research team. This will be to discuss their experiences of the intervention and give feedback on its acceptability. A formal acceptability questionnaire will also be administered, to all the participants in the intervention arm.

Similarly, the therapists delivering the intervention will also be invited to participate in semi-structured telephone interviews. These will inquire about the therapist's experiences of delivering the intervention, the practicability of the intervention (within NHS contexts), training, and ways to improve the intervention and training. Interviews will be digitally recorded, transcribed verbatim, and analysed.

The control group (treatment as usual) will receive the standard care offered to women at this stage of their treatment for cancer and is likely to differ by recruiting site. All women in this population will attend an end of treatment summary meeting with a Breast Care Nurse which lasts up to an hour. This meeting includes a holistic needs assessment and women are provided with a booklet containing information about local services they can access. There may be other care available. For example, at St James University Hospital, women with breast cancer are offered the opportunity to attend a one-off group called "Moving Forwards after cancer", where they are given information about diet, coping, and breast care.

The content of treatment as usual programmes and information on hospital based services accessed will be monitored for women in both arms through hospital records collected at the end of recruitment, as well as patient self report via questionnaire.

All participants will be evaluated using questionnaire data, measuring medication adherence, quality of life, mood, and psychological flexibility. These will be assessed before a participant is randomised (baseline), and at 3 and 6 months (6 month follow up will be collected from all participants randomised 3 months prior to the end of the recruitment phase). Participants can complete the 3 and 6 month questionnaires on paper or online.

## Intervention Type
Behavioural

## Primary outcome measure
1. Eligibility, recruitment, retention and follow up rates to inform the design of a phase III RCT will be measured using the following patient data collected from study sites for the duration of the recruitment and the intervention periods and at 3, and 6 months:
1.1. Number of patients screened for eligibility
1.2. Number and proportion of patients eligible out of those screened and reasons for ineligibility
1.3. Number and proportion of patients who consent out of those eligible and reasons for non-consent
1.4. Number and proportion of patients consenting to randomisation out of those eligible and

reasons for non-randomisation
1.5. Number of participants randomised per site per month
1.6. Questionnaire completion rates at each time-point
1.7. Number of items of missing data per questionnaire at each time-point
1.8. Number and proportion of randomised participants lost-to-follow-up
1.9 Number, proportion, type, and timing of participant withdrawals out of those randomised and reasons for withdrawal

## Secondary outcome measures

1. Acceptability of the intervention and protocol to participants and NHS therapists assessed using the following:
1.1. Intervention adherence for patients in the intervention arm (number of sessions attended, number of participants in the group sessions, whether homework was completed, and reasons for non-attendance / non-compliance) measured using patient data collected from study sites for the duration of the recruitment and the intervention periods and at 3, and 6 months
1.2. Website use including the number of website visits throughout the trial, pages visited, materials downloaded, videos watched, and clicked links measured from data collected by the website server during the intervention period
1.3. Number of patients deemed as having completed the intervention (minimum exposure is defined as attending the individual session and at least one of the three group sessions) measured using patient data collected from study sites during the intervention period
1.4. Treatment as usual content in both arms from participants (number of sessions attended and content of sessions) and sites (initiatives implemented during trial) measured using patient data collected from study sites during the intervention period
1.5. Safety (deaths and hospitalisations related to the trial intervention recorded until the end of the study) measured using patient data collected from study sites for the duration of the intervention period and at 3, and 6 months
1.6. Acceptability of the ACTION intervention to participants measured using the Acceptability Questionnaire at 6 months
1.7. Acceptability of the ACTION intervention to participants measured using the B&N questionnaire (used for the acceptability progression criteria) at 6 months
1.8. Number, proportion, and timing of therapist withdrawals and reasons for withdrawal measured using data provided at the time of withdrawal
1.9. Acceptability of the intervention and RCT procedures and which (if any) intervention components were helpful to participants assigned to the intervention group measured using telephone interviews with a researcher at the end of the intervention
1.10. Therapist experience of delivering the intervention, the practicability of the intervention (within NHS contexts), training, and ways to improve the intervention and training measured using semi-structured telephone interviews with therapists at the end of the intervention
2. Competency and fidelity of delivery of an ACT intervention by NHS therapists following training measured using: the ACT Knowledge Questionnaire (ACTKQ), administered pre- and post-training by therapists; the Acceptance and Commitment Therapy Fidelity Measure (ACT-FM) completed by an external rater at the end of the study through reviewing audiotapes recorded at the first individual session; and using the Procedural Fidelity Checklist by therapist self-rating by the lead clinical psychologist after each ACT session
3. Between-group change in outcome and process variables to demonstrate “proof-of-principle” using the following measures:
3.1. Adherence measured using the Adherence Barrier Survey (ASK-12) at baseline, 3, and 6 months
3.2. QoL/Mood measured using the Generalised Anxiety Disorder Scale (GAD-7), the McGill QoL - revised, and the Patient Health Questionnaire (PHQ-9) at baseline, 3, and 6 months

Symptom Interference measured using the Work & Social Adjustment Scale, the Hot Flash Related Daily Interference Scale (HFRDIS), the Multidimensional Assessment of Fatigue (MAF), the • PROMIS Pain Interference, and the Day-to-Day Impact of Vaginal Aging (DIVA, part C) at baseline, 3, and 6 months
3.3. Symptom Frequency measured using the Functional Assessment of Cancer Therapy - Endocrine Symptoms (FACT-ES) at baseline, 3, and 6 months
3.1. Process variables measured using the Valuing Questionnaire (VQ) at baseline, 3, and 6 months

### Overall study start date
01/06/2019

### Completion date
20/07/2022

## Eligibility

### Key inclusion criteria
1. Written (signed and dated) informed consent
2. Capacity to provide informed consent
3. Women with early stage (1 to 3a) breast cancer
4. Aged > = 18 years at the time of screening for ACTION
5. Have sufficient proficiency in English to contribute to the therapy sessions and data collection required.
6. Treated with curative intent
7. Completed their hospital-based treatment (e.g. surgery, radiotherapy and/or chemotherapy)
8. Currently prescribed oral adjuvant Hormone Therapy (tamoxifen, anastrozole, letrozole, exemestane)
9. The participant is willing to be audio recorded during the therapy sessions
10. The participant is willing to complete the study questionnaires
11. The participant is willing and able to attend all intervention sessions and/or complete therapy workbook

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Female

### Target number of participants
Planned Sample Size: 80; UK Sample Size: 80

### Total final enrolment
79

### Key exclusion criteria
1. Stopped taking adjuvant hormone therapy if it is clinically contraindicated according to clinical recommendation
2. Currently or recently (last 6 months) involved in another psychotherapy (e.g. using CBT/ACT, mindfulness etc.) research study where medication adherence is a primary outcome
3. Currently attending, or on a waiting list for psychotherapy/psycho-oncology/psychology /counselling services, for any reason (related to medication or not)
4. Known element of risk (e.g. clinical team are aware that patient has made a recent attempt to end their life, or has recently disclosed plans to do so). Three questions from the C-SSRS will be used at the point of screening to rule out risk:
4.1. Recently (in the last month), have you had any thoughts about harming yourself or ending your life? (If a patient responds 'yes' to question 1 and 'no' to question 2 & 3 they will still be eligible)
4.2. Have you thought about how you might go about it?
4.3. Do you intend to carry out this plan?

### Date of first enrolment
27/04/2021

### Date of final enrolment
31/12/2021

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Mid Yorkshire Hospitals NHS Trust**
Rowan House
Aberford Road
Wakefield
United Kingdom
WF1 4EE

### Study participating centre
**York Teaching Hospital NHS Foundation Trust**
York Hospital
Wigginton Road
York
United Kingdom
YO31 8H

### Study participating centre
**Harrogate and District NHS Foundation Trust**
Harrogate District Hospital
Lancaster Park Road
Harrogate
United Kingdom
HG2 7SX

### Study participating centre
**Leeds Teaching Hospitals NHS Trust**
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

## Sponsor information

### Organisation
University of Leeds

### Sponsor details
Faculty of Medicine and Health Research Office
Level 9, room 9.29, Worsley Building
Leeds
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United Kingdom
LS2 9JT
+44 (0)1133434897
governance-ethics@leeds.ac.uk

### Sponsor type
University/education

### Website
http://www.leeds.ac.uk/

### ROR
https://ror.org/024mrxd33

## Funder(s)

### Funder type

Charity

### Funder Name
Yorkshire Cancer Research; Grant Codes: L417

### Alternative Name(s)
YCR

### Funding Body Type
Government organisation

### Funding Body Subtype
Trusts, charities, foundations (both public and private)

### Location
United Kingdom

## Results and Publications

### Publication and dissemination plan
Planned publication of results in a peer-reviewed scientific journal, internal report, and conference presentation. The results will inform the design of the definitive randomised controlled trial.

### Intention to publish date
31/05/2024

### Individual participant data (IPD) sharing plan
Current individual participant data (IPD) sharing statement as of 01/07/2022:
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.
CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.
The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets.

Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.
The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

Previous individual participant data (IPD) sharing statement:
The datasets generated during and/or analysed during the current study are/will be available upon reasonable request from CTRU-DataAccess@leeds.ac.uk. Data will be shared according to a controlled access approach. Data will only be shared for participants who have given consent to use of their data for secondary research. Requests will be reviewed by relevant stakeholders. No data will be released before an appropriate agreement is in place setting out the conditions of release.

## IPD sharing plan summary
Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | | 08/02/2022 | 10/02/2022 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Basic results | version 1.0 | 11/03/2024 | 11/03/2024 | No | No |
| Results article | | 16/05/2024 | 20/05/2024 | Yes | No |