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ORIGINAL ARTICLE

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A pilot randomised controlled trial of acceptance and commitment therapy for medication decision-making and quality of life in women with breast cancer: The ACTION trial

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Abstract

Objective: Non-adherence to adjuvant endocrine therapy (AET) in women with breast cancer is common and associated with medication side-effects and distress. We co-designed an Acceptance and Commitment Therapy intervention (ACTION) to enhance medication decision-making and quality of life (QoL). We undertook a pilot trial of ACTION to inform the feasibility of a phase III trial, and to examine intervention acceptability.

Methods: This was a multi-site, exploratory, two-arm, individually randomised external pilot trial. Women with early breast cancer prescribed AET were randomised (1:1) to receive usual care (UC) or UC + ACTION. The ACTION intervention comprised a remotely delivered one-to-one ACT session followed by three group sessions delivered by clinical psychologists, alongside a website containing ideas for the self-management of side effects.

Results: Of the 480 women screened for eligibility, 260 (54.2%) were approached and 79 (30.4%) randomised. 71 (89.9%) women provided data at 3-month and 70 (88.6%) at 6-month 40 women were randomised to receive UC + ACTION and 32 (80.0%) completed the intervention. Most (75.0%) accessed the website at least once. ACTION was acceptable to participants (Borkovec & Nau Scale: mean = 7.8 [SD = 2.7] out of 10). Signals of effectiveness in favour of the UC + ACTION arm were observed for medication adherence (Adherence Starts with Knowledge questionnaire-12), QoL (work and social adjustment scale), health-related QoL (functional assessment of cancer therapy[FACT] general and FACT-ES-19/23),

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distress (generalised anxiety disorder -7, patient health questionnaire-9) and psychological flexibility (valuing questionnaire).

Conclusions: The ACTION intervention was acceptable to patients. There were promising signals for effectiveness on primary and secondary outcomes. A phase III randomised controlled trial is feasible.

Trial Registration: ISRCTN12027752.

KEYWORDS
acceptance and commitment therapy, breast cancer, group therapy, medication adherence, oncology, pilot, psychological flexibility, quality of life, remote delivery, video conferencing

1 | BACKGROUND

Adjuvant endocrine therapy (AET) medications, such as tamoxifen and aromatase inhibitors, are offered to most women with early breast cancer. Up to three quarters of women struggle with adherence, either discontinuing early or regularly missing doses.[1] This is a significant clinical problem because non-adherence is associated with increased risk of breast cancer recurrence and mortality.[2]

Multiple factors affect medication adherence in women with breast cancer.[3,4] AET can cause side-effects such as hot flushes, joint pain and vulvovaginal symptoms.[5–7] These symptoms reduce quality of life (QoL) and are the primary patient- and clinician-reported reason for non-adherence to AET.[8,9] A range of biopsychosocial factors such as mood, medication beliefs, and relationships with healthcare providers can also contribute to AET decision-making.[4]

Existing interventions for supporting adherence to AET are mostly ineffective.[3,10–12] These interventions often focus on educating women about AET.[13] Education may be essential, but insufficient by itself in helping women navigate the broader emotional and psychological challenges that occur with side-effects which undermine adherence. AET side effects may present tangible and distressing reminders of cancer, at a time when women are expecting to return to the life they experienced before diagnosis. Targeting a broader range of factors associated with adherence, including mood and QoL could more effectively support AET decision-making.[14,15]

We based our approach on Acceptance and Commitment Therapy (ACT).[16] ACT aims to help individuals make choices consistent with their overarching goals and values, especially when challenged by difficult thoughts and feelings.[17] This approach aligns with decision-making regarding AET. Here, most women want to reduce their risk of recurrence by using AET, which may require finding ways to negotiate difficult experiences like side-effects and associated emotions. ACT aims to facilitate decision-making through a range of techniques such as values elicitation, mindfulness and perspective taking that are designed to engender psychological flexibility: '…the capacity to persist or to change behaviour in a way that includes conscious and open contact with thoughts and feelings (openness), appreciates what the situation affords (awareness), and serves one's goals and values (engagement).'[18]

ACT is effective for reducing distress and improving QoL in physical health conditions,[19] with a recent meta-analysis suggesting effectiveness in cancer settings.[20] Evidence supporting ACT for treatment decision-making across physical health conditions has been limited to small case series.[17] In breast cancer, there has been one pilot trial ($N = 88$) of a brief values-elicitation intervention that aimed to engender one aspect of psychological flexibility (engagement) to improve AET adherence. This trial reported a signal of efficacy at 1 month follow-up, but not for longer-term efficacy.[21]

We co-developed an ACT intervention by involving women with breast cancer and clinicians associated with their care in a half-day workshop.[14] Prior to evaluating the intervention in a phase III trial, we sought to address uncertainties relating to the acceptability of the intervention and the feasibility of delivering a larger trial. We therefore undertook a pilot randomised controlled trial (RCT) with a nested qualitative study.[15] We examined: i) participant recruitment, retention, and follow-up rates; ii) the acceptability of the intervention to participants; iii) the extent to which therapists can deliver this ACT intervention with fidelity following training; and iv) proof-of-principle of the intervention on key outcomes and process variables.

2 | METHODS

2.1 | Trial design

We undertook a multi-site, exploratory, two-arm, individually randomised external pilot trial, with a nested qualitative study, with participants randomised (1:1) to receive usual care (UC) or UC plus the ACTION intervention.[15] Criteria corresponding to the objectives of recruitment and follow-up, acceptability, competence and fidelity and proof of principle were used to judge the feasibility of progressing to a phase III trial (Table 1). Levels of the criteria were green (RCT is feasible without changes), amber (RCT is feasible following minor changes) and red (RCT is not feasible without major changes).

Ethical approval was granted by the York and South Yorkshire Health Research Authority Research Ethics Committee (20/YH/0104). The trial was prospectively registered (ISRCTN12027752). We have followed reporting recommendations from the CONSORT extension for pilot and feasibility trials (Appendix). The intervention

TABLE 1 Progression criteria for progression to a phase III RCT.

Meaning	Green RCT is feasible No changes needed	Amber RCT is feasible following minor changes	Red RCT is not feasible without major changes
Objective 1: Recruitment and follow-up			
Eligible patients consent rate	≥30%	>10%	<10%
Randomised participants' adherence to intervention (% attending the individual session and at least one of the three group sessions)	≥75%	>40%	<40%
Loss to follow-up	≤25%	>25%	>35%
Objective 2: Acceptability			
Average score across the three items on the B&N questionnaire	≥6	<6	<4
Objective 3: Competence and fidelity			
Therapists achieving ≥50% on the ACTKQ	100%	≥50%, <100%	<50%
Number of sessions scoring ≥80% on procedural fidelity checklist (procedural fidelity)	≥75%	≥50%, <75%	<50%
Number of sessions scoring ≥39% on ACT-FM (ACT fidelity)	≥75%	≥50%, <75%	<50%
Objective 4: Proof of principle			
Change in adherence measured using ASK-12	Trend towards improvement in the intervention arm	No obvious trend	Worse scores in intervention arm

was described using the TIDieR checklist (Table S1). We previously reported that only a proportion of women would be followed up for 6 months.[15] However, we deviated from the protocol and gave all consenting women the opportunity to provide data at 3- and 6-month.

2.2 | Participants and procedures

Women aged over 18 years prescribed AET (tamoxifen, raloxifene, anastrozole, letrozole, exemestane) as an adjuvant treatment for stage 1 to 3a breast cancer were eligible. We approached women who had completed their hospital-based treatment (e.g. surgery, radiotherapy and/or chemotherapy) within the past 6 months. Key exclusion criteria were: women no longer taking AET due to a clinical contraindication, participation in a similar psychotherapy trial in the last 6 months, current attendance or on a waiting list for psychotherapy services, current diagnosis of active major mental health disorder or known suicide risk. Full eligibility criteria are reported elsewhere.[15]

Potential participants were identified via three routes. In route 1, a research nurse screened upcoming appointments to identify women who had completed their hospital-based treatment. In route 2, women who had self-referred to see a healthcare professional due to problematic side-effects or problems with AET adherence were identified. In route 3, a research nurse screened records of patients who had completed their hospital-based treatment within the past 6 months.

Women were either introduced to a research nurse by a member of their care team (routes 1 and 2) or invited by post (route 3). Women were provided with study documents, and after confirmation of eligibility, consent was recorded. Women were then asked to complete a baseline questionnaire on paper or online.

Participants were randomised by the research site using the University of Leeds Clinical Trials Research Unit (CTRU) automated randomisation system. A computer-generated minimisation programme incorporating a random element was used. Randomisation was stratified by: recruiting site, recruitment route (routes 1 vs. 2 vs. 3), and participant age (≤50 years vs. >50 years and <70 years vs. ≥70 years).

Blinding to allocation was not possible for participants, therapists, research nurses, GPs or staff at CTRU. Participants were informed of their randomised allocation by the research nurse. Trial therapists were informed about participants allocated to receive the ACTION intervention.

2.3 | Study conditions

2.3.1 | Usual Care

Both arms received UC. This was the standard care offered to women at this stage of their treatment. Typically, women approaching the end of their chemotherapy or radiotherapy are offered an end of treatment summary meeting. Patients may receive a holistic needs assessment and local services are signposted. Most NHS sites operate an open discharge, whereby patients can self-refer to a breast cancer nurse if they have concerns.

2.3.2 | Usual Care plus ACTION

The ACTION intervention aimed to enhance psychological flexibility, which we anticipated would have a positive effect on AET decision-making and ultimately adherence, alongside improving QoL and reducing distress.[17] The remotely delivered intervention comprised of a 60 min one-to-one ACT session with a therapist followed by three 90-min group sessions and access to a complementary website[15] (Table S1).

In the one-to-one ACT session, participants received an assessment of psychological flexibility to identify areas where participants could apply psychological flexibility and consider their values. Group session 1 aimed to help participants to see accepting and willing ways of approaching emotions and thoughts, and consider if these strategies enabled choices consistent with their values. Group session 2 aimed to help participants develop a deeper awareness of their personal values and to consider AET decisions in relation to their values. Group session 3 aimed to help participants notice their relationship with themselves, and consider whether more self-compassionate responses could facilitate effective decision-making. Participants remained in the same group throughout the intervention, led by the same therapists. Home practice was suggested at the end of each session. The sessions were digitally recorded. Participants were provided with a participant manual that contained the ACT exercises from the sessions.

The ACTION intervention website included advice about AET medication side-effects, derived from an umbrella review of AET side-effect management reviews and guidelines,[22] and supplementary ACT exercises. Videos of patient stories related to their breast cancer and treatment experiences were embedded within the website. Participants were sent individual login information to access the website.[14,15] The intervention was co-designed prior to the COVID-19 pandemic. To accommodate home-working and social distancing, we adapted the intervention for remote delivery using videoconferencing software.

2.4 | Therapist training

Therapists were trained by two registered clinical psychologists with expertise in ACT (CG and JC) and breast cancer (JC). Training outlined the psychological challenges presented by breast cancer and AET, and discussed how psychological *in*flexibility may limit QoL and adherence to AET. Therapists were taught to assess for and identify psychological inflexibility/flexibility within participant behaviour. They were taught methods for modelling psychological flexibility and for approaching conversations accordingly. ACTION-specific therapy methods were discussed and practiced. Therapists were provided with a training manual and access to the training presentation. Remotely delivered group supervision with CG was scheduled every 2 weeks in addition to local supervision.

2.5 | Measures

Participants completed assessments at baseline, and 3- and 6-month post-randomisation either by post or online. The baseline assessment recorded participant characteristics and participant-reported outcomes, and the 3- and 6-month assessments recorded participant-reported outcomes only. Non-responders were prompted by post, telephone, email and text. We collected data on screening and eligibility for all potentially eligible patients. Among those who consented to participate, we collected information on contact details, randomisation, questionnaire completion, withdrawal, and intervention adherence. Participant characteristics were collected including NHS number, date of birth, marital status, employment status, education, menopausal status, number of children, year of diagnosis, stage of cancer at diagnosis, breast cancer type, breast cancer treatment received, co-morbidities, hormone therapy regimen, supportive therapies used, and previous exposure to psychotherapies. Intervention adherence (number of sessions attended and numbers of participants in group sessions) and UC service-level information, were collected.

2.5.1 | Participant-reported outcomes

Participant-reported outcomes are described in detail elsewhere.[15] They included adherence, assessed with the Adherence Starts with Knowledge questionnaire (ASK)-12).[23] We also collected measures of QoL (McGill-Revised,[24] Work and Social Adjustment Scale [WSAS][25]), health-related QoL (Functional Assessment of Cancer Therapy [FACT-G and Endocrine Symptoms 19 and 23],[26] distress (Generalised Anxiety Disorder [GAD] questionnaire-7,[27] Patient Health Questionnaire [PHQ]-9),[28] psychological flexibility (Valuing Questionnaire [VQ][29]) and service use (UK Cancer Costs Questionnaire [UKCCQ]).[30]

Symptoms and side-effects were assessed using validated questionnaires focussing on the interference they caused in daily life. These included hot flushes (Hot Flash Related Daily Interference Scale [HFRDIS][31]), fatigue (Multidimensional Assessment of Fatigue [MAF][32]), pain (PROMISE Pain interference [6-item][33]), and vaginal symptoms (Day-to-Day Impact of Vaginal Ageing Questionnaire [DIVA], part C[34]).

Acceptability of the intervention was assessed among those allocated to the ACTION intervention using bespoke items designed for the trial, and an adapted version of the Borkovec and Nau Acceptability questionnaire.[35] Use of the ACTION website was monitored using Google Analytics.

2.5.2 | Therapist assessment measures

To assess competency after training, therapists completed the ACT Knowledge Questionnaire (ACTKQ).[36] The first individual session for each therapist was rated by CG for fidelity to ACT principles using

the ACT Fidelity Measure (ACT-FM).[37] After the trial, two independent assessors with expertise in ACT rated 10 randomly selected digital recordings of therapy sessions for fidelity to ACT principles using the ACT-FM. Therapists completed a bespoke procedural fidelity checklist within each intervention session.

2.6 | Safety

We reported serious adverse events that were related to the intervention and were unexpected, known as related and unexpected serious adverse events (RUSAEs). We also recorded deaths, hospitalisations and pregnancies.

2.7 | Sample size

To explore proof of principle of the effect of ACTION on trial outcomes, we used methods developed for phase II screening trials in oncology.[38] We estimated a priori that with 80 patients, allowing for 25% loss to follow-up and using a 1-sided *t*-test with a significance level of 20%, we would have 65% power to detect an effect size of 0.432. This would be sufficient to establish consent and dropout rates, and test trial protocols and acceptability.[39]

2.8 | Data management and access

Study data was held securely at the University of Leeds' CTRU, and operational processes were defined for the transfer, storage, restricted access, and disposal of personal information. Data will be shared for participants who have consented to use of their data for secondary research, and will only be made available in such a way that recipients cannot identify individuals by any reasonable likely means. Data will be shared for projects that are in the public interest and compatible with the original purpose of the data processing. Data access requests should be made to CTRU-DataAccess@leeds.ac.uk.

2.9 | Statistical analyses

Formal hypothesis testing was not conducted. Descriptive analyses and confidence interval estimation were performed on the intention-to-treat population. Summaries and frequencies are provided for the overall trial population and by trial arm and site (where relevant). Proof-of-principle analyses, adjusted for minimisation factors, are reported for the planned primary outcome (ASK-12), and key secondary outcomes. We were unable to estimate the intraclass correlation coefficient due to an insufficient number of therapists being involved in delivering the intervention. All analyses were conducted in SAS, version 9.4.

3 | RESULTS

3.1 | Recruitment, retention and intervention adherence

Recruitment took place at four sites between 27 April 2021 and 15 December 2021. Figure 1 summarises participant flow. 480 patients were screened for eligibility, of whom 260 (54.2%) were eligible for approach. The most common reasons for ineligibility were: not being prescribed AET (37.4%); being outside the approach window (24.7%); and not being treated with curative intent (17.4%). Among eligible patients, 81 (31.2%) were willing to take part and 79 (30.4%) were randomised (UC = 39, UC + ACTION = 40). The two eligible individuals who were not randomised completed the baseline assessments after the study had been closed to recruitment at their site. The eligible patient consent rate (30.4%) met the green progression criterion. The most common reasons patients declined participation were: not wanting the ACTION intervention (20.0%); not having time (13.6%); not liking the idea of a remote intervention (10.4%). Loss to follow-up rates of 10.1% at 3-months and 11.4% at 6-month also met the green progression criterion. Three participants (7.5%) withdrew from the ACTION intervention, of whom two also withdrew from questionnaire completion and the collection of further clinical data collection. No participants withdrew from the UC arm.

The average age of randomised participants was 59.4 years (SD = 10.4), and the majority were White British (96.2%), married (64.6%), and post-menopausal (67.1%) (Table 2). Participants were most likely to have been diagnosed with their first breast cancer (93.7%), with most having a stage 1 (45.6%) or stage 2 (51.9%) cancer. Anastrozole (62.0%) and tamoxifen (34.2%) were the most commonly used AETs at randomisation. The stratification factors of age group, recruitment route and recruiting site were balanced across the trial arms.

Forty participants were randomised to receive UC + ACTION of which 32 (80.0%) attended the individual session and at least one group session. Intervention adherence therefore meets the green progression criterion. Of those randomised to UC + ACTION, nearly all (95.0%) received the individual session, with attendance declining over the three group sessions (77.5%, 72.5%, 65.0%). Most participants reported completing at least some (39.5%) or all (44.7%) home practice set in the ACT sessions. Tables S2 and S3 report the UC services available and accessed.

Most (75%) participants allocated to receive UC + ACTION logged into the website at least once. The average number of logins per participant was 3.9 (SD = 4.0), with each session lasting an average of 10 min (SD = 9.7). Website pages related to the management of side-effects were more frequently visited than pages related to ACT skills (Table S4).

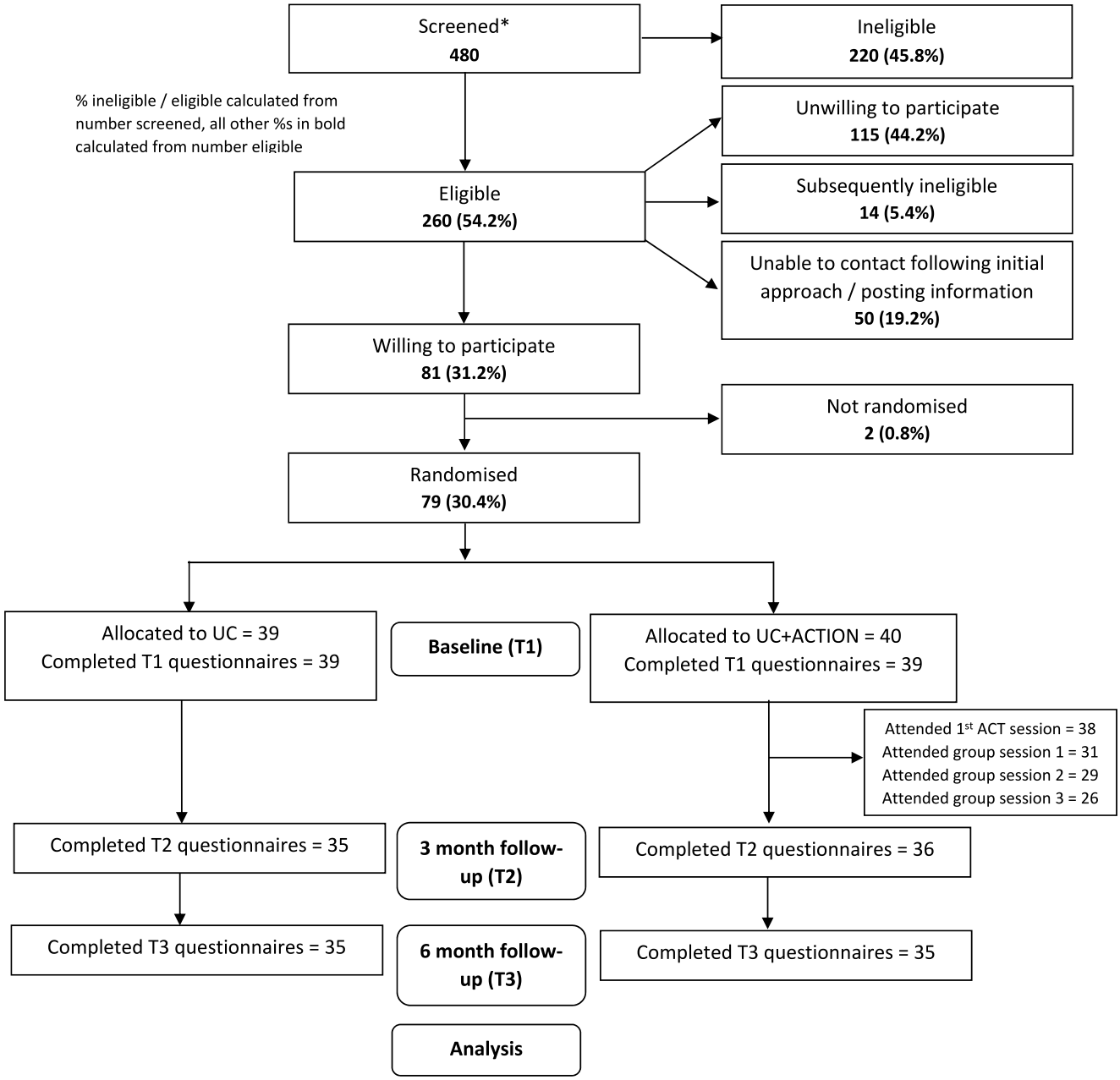

FIGURE 1 Participant flow through Screening, Recruitment and Follow-up. * Sites conducted screening of hospital records to assess for patient eligibility. Three sites provided data on the number of records screened but one did not. The total screened is therefore the number screened for the three sites who returned this data plus the number of patients eligible for approach from the fourth site.

3.2 | Acceptability of the intervention

Among the 31 (77.5%) UC + ACTON participants who completed the acceptability questions, the mean score across all three items was 7.8 (SD = 2.7) out of 10, which met the green progression criterion. The mean score for each item was: 'How confident would you be in recommending the ACTION programme to a friend?' (7.8, SD = 2.8), 'How interesting and engaging was the ACTION programme overall?' (7.6, SD = 2.6), and 'How satisfied were you with the overall quality of the ACTION programme?' (7.9, SD = 2.7).

Very few participants reported a 'not at all useful' rating for the individual (0.0%) and group sessions (7.5%), the website (12.5%) and the participant manual (5.0%) (Table S5). The ACT skills were considered similarly useful to each other. A large proportion of the sample felt the ACTION intervention would be 'very' or 'somewhat' useful for improving their QoL (52.5%), supporting their AET decision-making (40%), and helping them manage side-effects (37.5%) (Table S6).

3.3 | Therapist fidelity and ACT knowledge

Four clinical psychologists were trained to deliver ACTION. The mean post-training score on the ACTKQ was 10.3 (SD = 1.0) out of 16, with all scoring ≥50% correct responses. The green progression criterion was therefore met.

TABLE 2 Summary of participant characteristics overall and by study arm.

	UC (n = 39), N%	UC + ACTION (n = 40), N%	Total (n = 79), N%
Age (mean, SD)	60.2 (10.2)	58.5 (10.6)	59.4 (10.4)
Age group			
=< 50 years	8 (20.5%)	9 (22.5%)	17 (21.5%)
>50 and < 70 years	23 (59.0%)	24 (60.0%)	47 (59.5%)
≥ 70 years	8 (20.5%)	7 (17.5%)	15 (19.0%)
Recruitment route			
1. Recently completed treatment	17 (43.6%)	15 (37.5%)	32 (40.5%)
2. Medication problems	1 (2.6%)	0 (0.0%)	1 (1.3%)
3. Retrospective screening	21 (53.8%)	25 (62.5%)	46 (58.2%)
Research site			
St James's University Hospital	8 (20.5%)	12 (30.0%)	20 (25.3%)
York Hospital	9 (23.1%)	7 (17.5%)	16 (20.3%)
Harrogate District Hospital	7 (17.9%)	6 (15.0%)	13 (16.5%)
Mid Yorkshire Hospitals NHS Trust	15 (38.5%)	15 (37.5%)	30 (38.0%)
Ethnicity			
White British	38 (97.4%)	38 (95.0%)	76 (96.2%)
Any other White background	1 (2.6%)	1 (2.5%)	2 (2.5%)
Mixed White and Black Caribbean	0 (0.0%)	1 (2.5%)	1 (1.3%)
Marital status			
Married	24 (61.5%)	27 (67.5%)	51 (64.6%)
Single	3 (7.7%)	1 (2.5%)	4 (5.1%)
Living with partner	5 (12.8%)	1 (2.5%)	6 (7.6%)
Divorced or separated	3 (7.7%)	6 (15.0%)	9 (11.4%)
Widowed	3 (7.7%)	3 (7.5%)	6 (7.6%)
Missing	1 (2.6%)	2 (5.0%)	3 (3.8%)
Employment status			
Full time	11 (28.2%)	10 (25.0%)	21 (26.6%)
Part time	8 (20.5%)	9 (22.5%)	17 (21.5%)
Not currently working	5 (12.8%)	4 (10.0%)	9 (11.4%)
Retired	14 (35.9%)	11 (27.5%)	25 (31.6%)
Other	1 (2.6%)	4 (10.0%)	5 (6.3%)
Missing	0 (0.0%)	2 (5.0%)	2 (2.5%)
Education			
Postgraduate qualification	6 (15.4%)	3 (7.5%)	9 (11.4%)
Degree level education	12 (30.8%)	9 (22.5%)	21 (26.6%)
Higher educational qualifications	5 (12.8%)	9 (22.5%)	14 (17.7%)
Vocational qualifications (NVQ1+2)	5 (12.8%)	4 (10.0%)	9 (11.4%)
A-level or equivalent	3 (7.7%)	5 (12.5%)	8 (10.1%)
GCSE/O-level/CSE	7 (17.9%)	7 (17.5%)	14 (17.7%)
No formal qualifications	1 (2.6%)	0 (0.0%)	1 (1.3%)
Missing	0 (0.0%)	3 (7.5%)	3 (3.8%)

(Continues)

TABLE 2 (Continued)

	UC (n = 39), N%	UC + ACTION (n = 40), N%	Total (n = 79), N%
Do you have children?			
Yes	30 (76.9%)	37 (92.5%)	67 (84.8%)
No	9 (23.1%)	2 (5.0%)	11 (13.9%)
Missing	0 (0.0%)	1 (2.5%)	1 (1.3%)
Cancer incidence at randomisation			
First primary	37 (94.9%)	37 (92.5%)	74 (93.7%)
Second primary	1 (2.6%)	1 (2.5%)	2 (2.5%)
Recurrence of previous primary	1 (2.6%)	0 (0.0%)	1 (1.3%)
Missing	0 (0.0%)	2 (5.0%)	2 (2.5%)
Current stage of cancer			
Stage IA	16 (41.0%)	16 (40.0%)	32 (40.5%)
Stage IB	2 (5.1%)	2 (5.0%)	4 (5.1%)
Stage IIA	15 (38.5%)	16 (40.0%)	31 (39.2%)
Stage IIB	6 (15.4%)	4 (10.0%)	10 (12.7%)
Stage IIIA	0 (0.0%)	2 (5.0%)	2 (2.5%)
Breast cancer treatment received[a]			
Surgery: Lumpectomy	30 (76.9%)	25 (62.5%)	55 (69.6%)
Surgery: Unilateral mastectomy	10 (25.6%)	14 (35.0%)	24 (30.4%)
Surgery: Double mastectomy	0 (0.0%)	0 (0.0%)	0 (0.0%)
Radiotherapy	19 (48.7%)	22 (55.0%)	41 (51.9%)
Chemotherapy	6 (15.4%)	9 (22.5%)	15 (19.0%)
Other treatment	0 (0.0%)	3 (7.5%)	3 (3.8%)
Hormone therapy regimen[a]			
Tamoxifen	15 (38.5%)	12 (30.0%)	27 (34.2%)
Anastrozole	22 (56.4%)	27 (67.5%)	49 (62.0%)
Raloxifene	0 (0.0%)	0 (0.0%)	0 (0.0%)
Exemestane	2 (5.1%)	2 (5.0%)	4 (5.1%)
Letrozole	0 (0.0%)	1 (2.5%)	1 (1.3%)
Menopausal status			
Pre-menopausal	5 (12.8%)	6 (15.0%)	11 (13.9%)
Peri-menopausal	5 (12.8%)	4 (10.0%)	9 (11.4%)
Post-menopausal	27 (69.2%)	26 (65.0%)	53 (67.1%)
Unsure	2 (5.1%)	4 (10.0%)	6 (7.6%)

Abbreviations: CSE, Certificate of Education; GCSE, General Certificate of Secondary Education; NVQ, National Vocational Qualification; O-Level, Ordinary level; C, Usual Care.

[a]More than one response could be provided.

Two independent assessors reviewed and rated 10 randomly selected therapy sessions (five individual and five group) using the ACT-FM. All four therapists were represented within the sessions. Of these 20 ratings, all scored ≥39%, which met the green progression criterion for ACT fidelity.

Fifty therapy sessions (38 individual and 12 group) were delivered and of these, 49 (98.0%) scored ≥80% on the procedural fidelity checklist, which met the green progression criterion. The mean procedural fidelity score was 6.8 (SD = 0.5) out of seven for the individual sessions, and maximum scores were recorded for all group sessions.

TABLE 3 Exploration of trial outcomes.

	3 months						6 months					
	UC		UC + ACTION		Difference		UC		UC + ACTION		Difference	
	Mean (95% CI)	*N*	Mean (95% CI)	*N*	95% CI	*N*	Mean (95% CI)	*N*	Mean (95% CI)	*N*	95% CI	*N*
Adherence												
ASK-12 (total)	21.9 (20.3, 23.4)	35	21.7 (20.2, 23.3)	33	−0.2 (−2.3, 2.0)	68	22.4 (21.1, 23.7)	35	21.4 (20.0, 22.8)	31	−1.0 (−2.9, 0.9)	66
Inconvenience	5.7 (5.0, 6.4)	34	5.8 (5.1, 6.5)	29	0.1 (−0.9, 1.1)	63	6.2 (5.5, 6.8)	35	5.4 (4.7, 6.2)	27	−0.7 (−1.7, 0.3)	62
Beliefs	9.0 (8.3, 9.7)	35	8.6 (7.9, 9.3)	34	−0.4 (−1.4, 0.6)	69	8.7 (7.9, 9.6)	35	8.7 (7.8, 9.6)	32	0.0 (−1.3, 1.2)	67
Behaviour	7.0 (6.2, 7.8)	35	7.1 (6.2, 7.9)	32	0.0 (−1.1, 1.2)	67	7.5 (6.7, 8.2)	35	7.0 (6.2, 7.7)	31	−0.5 (−1.6, 0.6)	66
Quality of life												
McGill-R (total)	7.2 (6.9, 7.6)	35	7.5 (7.1, 7.8)	35	0.3 (−0.2, 0.8)	70	7.4 (7.0, 7.8)	34	7.6 (7.2, 8.0)	34	0.2 (−0.4, 0.7)	68
Physical	7.1 (6.5, 7.8)	35	6.8 (6.2, 7.4)	35	−0.4 (−1.2, 0.5)	70	7.1 (6.5, 7.7)	35	7.1 (6.5, 7.8)	34	0.0 (−0.9, 1.0)	69
Psychological	7.1 (6.5, 7.7)	35	7.9 (7.3, 8.6)	35	0.8 (0.0, 1.7)	70	7.2 (6.5, 7.8)	34	7.7 (7.1, 8.4)	34	0.5 (−0.4, 1.5)	68
Existential	6.8 (6.5, 7.2)	35	7.2 (6.9, 7.5)	35	0.3 (−0.1, 0.8)	70	7.0 (6.5, 7.5)	34	6.9 (6.4, 7.4)	34	−0.1 (−0.8, 0.6)	68
Social	7.7 (7.2, 8.2)	35	8.1 (7.7, 8.6)	35	0.5 (−0.2, 1.2)	70	8.3 (7.8, 8.7)	34	8.6 (8.1, 9.1)	34	0.3 (−0.4, 1.0)	68
WSAS	10.0 (7.4, 12.7)	33	9.4 (6.6, 12.1)	31	−0.7 (−4.5, 3.2)	64	9.6 (7.2, 12.1)	30	5.7 (3.4, 8.1)	33	−3.9 (−7.3, −0.5)	63
Health-related quality of life												
FACT-G	80.9 (77.3, 84.4)	35	84.1 (80.6, 87.6)	35	3.3 (−1.8, 8.3)	70	81.4 (77.2, 85.6)	34	88.1 (83.8, 92.4)	33	6.7 (0.6, 12.8)	67
FACT ES-19	137.2 (132.5, 141.9)	35	141.7 (137.0, 146.4)	35	4.5 (−2.2, 11.2)	70	138.8 (133.6, 144.0)	34	147.5 (142.3152.8)	33	8.7 (1.3, 16.2)	67
FACT ES-23	148.2 (143.0, 153.5)	35	152.7 (147.5, 158.0)	35	4.5 (−3.0, 12.0)	70	150.3 (144.7, 156.0)	34	159.5 (153.8165.2)	33	9.2 (1.1, 17.3)	67
Distress												
GAD-7	4.8 (3.6, 6.0)	35	4.3 (3.0, 5.5)	32	−0.5 (−2.3, 1.2)	67	4.7 (3.5, 5.9)	35	3.1 (1.8, 4.3)	31	−1.6 (−3.4, 0.1)	66
PHQ-9	5.6 (4.4, 6.8)	35	4.9 (3.7, 6.1)	35	−0.7 (−2.4, 0.1)	70	5.0 (4.0, 6.1)	35	3.9 (2.8, 5.0)	34	−1.1 (−2.7, 0.4)	69
Symptoms												
HFRDIS	2.7 (1.9, 3.4)	34	2.3 (1.6, 3.1)	35	−0.3 (−1.4, 0.7)	69	2.5 (1.8, 3.1)	34	2.2 (1.5, 2.9)	34	−0.3 (−1.2, 0.7)	68
MAF	21.1 (17.9, 24.3)	35	20.4 (17.2, 23.7)	34	−0.7 (−5.4, 4.0)	69	19.5 (16.1, 22.9)	35	18.7 (15.2, 22.3)	32	−0.8 (−5.8, 4.3)	67
PROMIS-pain	51.3 (49.1, 53.6)	35	50.8 (48.5, 53.0)	34	−0.5 (−3.8, 2.7)	69	49.8 (47.4, 52.2)	35	49.7 (47.2, 52.2)	32	−0.1 (−3.6, 3.5)	67
DIVA	1.4 (1.0, 1.7)	34	1.2 (0.8, 1.5)	31	−0.2 (−0.7, 0.3)	65	1.5 (1.1, 1.8)	34	1.0 (0.6, 1.3)	32	−0.5 (−1.0. 0.0)	66

(Continues)

TABLE 3 (Continued)

	3 months						6 months					
	UC		UC + ACTION		Difference		UC		UC + ACTION		Difference	
	Mean (95% CI)	N	Mean (95% CI)	N	95% CI	N	Mean (95% CI)	N	Mean (95% CI)	N	95% CI	N
Psych flexibility VQ												
Progress	20.3 (18.9, 21.8)	35	21.9 (20.4, 23.3)	35	1.5 (−0.5, 3.5)	70	21.3 (19.8, 22.8)	35	23.0 (21.5, 24.6)	33	1.8 (−0.4, 3.9)	68
Obstruction	8.7 (6.9, 10.4)	35	6.5 (4.7, 8.2)	35	−2.2 (−4.7, 0.3)	70	7.8 (6.3, 9.3)	35	6.3 (4.8, 7.9)	33	−1.5 (−3.7, 0.6)	68

Note: Baseline adjusted means and 95% confidence intervals by arm and time point. Analysis is adjusted for baseline scores for the measure and the stratification factors (Recruiting site, recruitment route and participate age). ASK-12: higher scores indicate more barriers to adherence or greater problems with adherence behaviour; McGill-revised: higher scores indicate better quality of life; WSAS: lower scores indicate better quality of life; FACT: higher scores indicate better quality of life; GAD-7: higher scores indicate more severe anxiety; PHQ-9: higher scores indicate more severe depression; HFRDIS: higher scores indicate greater interference with daily life and overall quality of life; MAF: higher scores indicate more severe fatigue; PROMIS-pain: higher scores indicate greater consequences of pain; DIVA: higher scores indicate greater impact of vaginal symptoms; Valuing questionnaire: higher scores represent better progress scores and worse obstruction.

Abbreviations: ASK-12, Adherence Starts with Knowledge questionnaire; DIVA, Day-to-Day Impact of Vaginal Ageing Questionnaire; FACT-ES, Functional Assessment of Cancer Therapy Endocrine subscale; FACT-G, Functional Assessment of Cancer Therapy General; GAD, Generalised Anxiety Disorder; HFRDIS= Hot Flash Related Daily Interference Scale; MAF, Multidimensional Assessment of Fatigue; PHQ, Patient Health Questionnaire; PROMIS-Pain, Patient-Reported Outcomes Measurement Information System-Pain; VQ, Valuing Questionnaire; WSAS, Work and Social Adjustment Scale.

3.4 | Exploration of trial outcomes

Table 3 presents a summary of the non-powered proof of principle analyses.

3.4.1 | Adherence

Changes from baseline to three-months showed a small improvement in the treatment belief subscale of the ASK-12 for UC + ACTION over UC, but this was not maintained over 6-month. Changes from baseline to 6-month showed small improvements across the inconvenience/forgetfulness and behaviour subscales and ASK-12 total score for UC + ACTION over UC. This trend provides evidence to support meeting of the green progression criterion for proof of principle.

3.4.2 | Quality of life and symptom interference

Differences in total and subscale scores on the McGill-revised were generally in favour of the UC + ACTION arm. There were differences on the WSAS scale at 6-month, with participants in the UC + ACTION arm reporting better QoL (adj. mean difference = −3.9, 95% CI = −7.3, −0.5).

3.4.3 | Breast cancer-specific health-related quality of life

There were between-arm differences in favour of the UC + ACTION arm at 6-month for the FACT-G (adj. mean difference = 6.7, 95% CI = 0.6, 12.8), FACT-ES-19 (adj. mean difference = 8.7, 95%CI = 1.3, 16.2), and FACT-ES-23 (adj. mean difference = 9.2, 95%CI = 1.1, 17.3). A similar trend was observed at 3-month.

3.4.4 | Psychological distress

Total scores on the GAD-7 and PHQ-9 generally indicated lower levels of anxiety and depression in the UC + ACTION arm. The magnitude of differences increased at each time point.

3.4.5 | Symptoms and side effects

There were small trends in favour of the UC + ACTION arm for the HFRDIS, MAF, PROMIS-pain and DIVA.

3.4.6 | Psychological flexibility

Participants in the UC + ACTION arm reported higher levels of progress and less obstruction at both 3-month and 6-month.

3.5 | Safety

Seventeen (21.5%) participants were admitted to hospital, attended accident and emergency or were referred to hospital during the trial; 7 UC (17.9% participants), 10 UC + ACTION (25.0% participants). The mean number of events experienced per participant was similar between the arms; 1.4 (SD = 0.7) for UC and 1.1 (SD = 0.3) for UC + ACTION. No RUSAEs, mental health crisis referrals, pregnancies or deaths were reported.

4 | DISCUSSION

This pilot trial demonstrated the acceptability of the ACTION intervention to women with early breast cancer and the feasibility of undertaking a definitive trial of an ACT-based complex intervention to support medication decision-making and QoL in this population. A priori progression criteria for recruitment, follow-up, acceptability, and competence and fidelity were met. Exploratory proof of principle analyses demonstrated trends in favour of UC + ACTION for medication adherence, QoL, health-related QoL, psychological distress, and psychological flexibility.

The ACTION intervention was co-designed by patients and healthcare professionals during a workshop.[14] This study constitutes the first quantitative examination of the acceptability of ACTION. Most participants found the intervention components to be useful and felt the intervention as a whole was interesting, engaging and of satisfactory quality. This pilot included a detailed evaluation of the effectiveness of the training offered to therapists, by evaluating ACT knowledge, ACT fidelity and procedural fidelity. The four therapists were qualified clinical psychologists, and all reached a pre-specified level of ACT knowledge following training. Within sessions, nearly all study procedures were delivered as expected. External assessments demonstrated sessions were delivered with excellent fidelity to ACT principles. Given the high levels of fidelity achieved, training psychological practitioners with less experience (e.g. assistant psychologists), could increase intervention cost-effectiveness.

ACT has become a dominant therapy model for treating distress in conditions that involve objective stressors (fatigue, physical impairment), such as chronic pain or chronic illness.[19] Commensurate with the challenge of adhering to AET, the model provides methods for making effective decisions, while acknowledging the situation is challenging and the resultant emotions, thoughts and urges are understandable.[17] Given relevance to the problem of AET adherence it is surprising ACTION represents the only trial using the full ACT model in this context. The recent pilot RCT of a brief intervention informed by part of the ACT model (engagement) reported a short-term impact on adherence at 1-month follow-up.[21] This intervention included pragmatic methods for keeping women aware that taking AET is consistent with their own values.[21] In comparison, the ACTION intervention had a focus on effective decision making in the presence of side effects. ACTION was a higher intensity intervention and included a wider range of treatment targets, aiming to engender all aspects of psychological flexibility and including pragmatic methods for managing side-effects.[17]

4.1 | Limitations

The intervention was adapted for remote delivery following the COVID-19 pandemic.[14] While we focussed on retaining the core components of ACTION, the change in delivery modality may have altered the intervention. The trial was originally designed such that therapists from multiple sites would deliver the intervention. This was changed to a single site being responsible for intervention delivery due to restrictions in the use of specific video conferencing software within the NHS. The high fidelity and competency reported should be replicated in multiple centres. Finally, future evaluations of ACTION and other comparable interventions should prioritise the inclusion of women from a diverse range of ethnic and educational backgrounds.

4.2 | Clinical implications

Adherence to AET is a clinically and economically valued behaviour.[2] Our co-design approach, considered cost and feasibility of delivery within NHS services.[14] It is therefore encouraging that this lower intensity, largely group-based, intervention appears to be acceptable to patients, with promising signals for change in outcomes. Furthermore, we have shown clinicians already working in psycho-oncology services can deliver the intervention with excellent fidelity after brief training. Such interventions could therefore be rapidly implemented into NHS services if effectiveness is shown in future evaluations. ACT is also one of the most common psychological therapies offered to people with cancer,[40] with growing evidence for distress and anxiety within this context.[20] While the configuration of the present intervention is specific, the techniques, metaphors and exercises used to engender psychological flexibility are common across ACT interventions.[17] If ACT-based interventions are shown to be effective for improving adherence, it raises the possibility that common approaches to distress and anxiety management used in standard practice could be expanded to target medication adherence.

5 | CONCLUSION

In this pilot trial of an individual and group-based ACT intervention in women with early breast cancer, progression criteria were met, demonstrating the likely feasibility of a phase III trial. The trial recruited to target and successfully retained a high proportion of patients. Participants found ACTION acceptable and useful, and there was preliminary evidence of effectiveness for medication adherence, QoL, health-related QoL, distress and psychological flexibility. Further evaluations of ACT-based interventions to support medication adherence are warranted.

AUTHOR CONTRIBUTIONS

Graham, Ellison, Hall, Clark, McNaught, Green, Wilkes, Robson, Lorentz, Holmes, Bould, Hartley, Naik, Proctor, Buckley, Hirst, Hartup, Foy, Neal, Velikova, Farrin, Collinson and Smith have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; Graham, Ellison, Hall, Clark, McNaught, Green, Wilkes, Robson, Lorentz, Holmes, Bould, Hartley, Naik, Proctor, Buckley, Hirst, Hartup, Foy, Neal, Velikova, Farrin, Collinson and Smith have been involved in draughting the manuscript or revising it critically for important intellectual content; Graham, Ellison, Hall, Clark, McNaught, Green, Wilkes, Robson, Lorentz, Holmes, Bould, Hartley, Naik, Proctor, Buckley, Hirst, Hartup, Foy, Neal, Velikova, Farrin, Collinson and Smith have given final approval of the version to be published. Graham, Ellison, Hall, Clark, McNaught, Green, Wilkes, Robson, Lorentz, Holmes, Bould, Hartley, Naik, Proctor, Buckley, Hirst, Hartup, Foy, Neal, Velikova, Farrin, Collinson and Smith have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST STATEMENT

Naik declares that he has received honoraria for delivering non-promotional educational workshops from Astra Zeneca and Daiichi Sankyo. Foy is a member of the UK National Institute for Health and Care Excellence Implementation Strategy Group. All other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from CTRU-DataAccess@leeds.ac.uk upon reasonable request.

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SUPPORTING INFORMATION

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