Diet, physical activity, and health-related outcomes of endometrial cancer survivors in a behavioral lifestyle program: the Diet and Exercise in Uterine Cancer Survivors (DEUS) parallel randomized controlled pilot trial

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ABSTRACT

Objectives To explore the effectiveness of a theory-based behavioral lifestyle intervention on health behaviors and quality of life in endometrial cancer survivors.

Methods This was a secondary analysis of a randomized controlled pilot trial conducted in two UK hospitals enrolling disease-free stage I-IIA endometrial cancer survivors. Participants were randomized to an 8-week group-based healthy eating and physical activity intervention or usual care using 1:1 minimization. Participants were followed up at 8 and 24 weeks, with the 8-week assessment being blinded. Diet, physical activity, and quality of life were measured with the Alternative Healthy Eating Index 2010, Stanford 7-Day Physical Activity Recall, and the EORTC Quality of life Questionnaire Core 30, respectively. We analyzed all eligible participants using the intention-to-treat approach in complete cases, adjusting for baseline values, body mass index, and age.

Results We enrolled 60 of the 296 potentially eligible endometrial cancer survivors (May - December 2015). Fifty-four eligible participants were randomized to the intervention (n=29) or usual care (n=31), and 49 had complete follow-up data (n=24 in the intervention and n=25 in usual care). Intervention adherence was 77%. At 8 weeks, participants in the intervention improved their diet compared to usual care (difference in Alternative Healthy Eating Index 2010 score 7.5 (95% CI: 0.1 to 14.9), P=0.046) but not their physical activity (0.1 metabolic equivalent-h/day 95% CI: -1.6 to 1.8, P=0.879), or global quality of life score (5.0 (95% CI: -3.4 to 13.3), P=0.236). Global quality of life improved in intervention participants at 24 weeks (difference 8.9 (95% CI: 0.9 to 16.8), P=0.029). No intervention-related adverse events were reported.

Conclusions The potential effectiveness of the intervention appeared promising. A future fully-powered study is needed to confirm these findings.

Trial registration number NCT02433080.

INTRODUCTION

Endometrial cancer affects 9000 UK women annually, most of whom (78%) will live more than 10 years after diagnosis. However, they are the long-term cancer group with the highest comorbidity burden post-treatment who are most likely to die from cardiovascular disease. Moreover, the prevalence of obesity and suboptimal lifestyle behaviors is high, both of which are associated with lower health-related quality of life. Thus, the effect of lifestyle changes on outcomes after endometrial cancer treatment has been identified as one of the ‘top ten’ endometrial cancer research priorities. The early post-treatment period is a key transition time during which women might be more motivated to engage in health behaviors but experience cancer-specific barriers to behavior change. Women also report a desire for in-person advice but that support is lacking post-treatment.

Behavioral lifestyle interventions improve patient-reported outcomes, such as health-related quality of life, in people living with other forms of cancer and are also feasible for people after endometrial cancer treatment. We have previously adapted ‘Shape-Up’, an evidence- and group-based behavioral lifestyle intervention that is already running within the healthcare system, to the particular needs and preferences of this cancer group using patient input and a systematic framework. We piloted the program showing acceptable feasibility and high participant satisfaction.

However, the potential effectiveness of such a program is currently unclear. A recent meta-analysis including two randomized trials of lifestyle interventions and a single arm physical activity intervention showed mixed results for fatigue and global quality of life.
of life in endometrial cancer survivors. Thus, we performed a secondary analysis of our trial to explore its potential effectiveness for improving health behaviors, and health-related quality of life and report standard deviation for these outcomes to allow for sample size calculations for a fully-powered trial.

METHODS

Trial design
The trial protocol has been published. The Diet and Exercise in Uterine Cancer Survivors pilot trial was a parallel, randomized, controlled pilot trial with 1:1 allocation ratio to either the ‘Shape-Up following cancer treatment’ intervention or care as usual. The Consolidated Standards of Reporting Trials (CONSORT) and Template for Intervention Description and Replication (TIDieR) checklists are available as Supporting Information.

Participants and recruitment
Adult endometrial cancer (C54.1) survivors within 3 years of diagnosis were eligible to participate. Stage IVB cancer, active anti-cancer and/or palliative treatment, second primary cancer, lack of mental capacity to take part, severe depression, no availability for longitudinal follow-up, participation in a professionally delivered weight loss or exercise program during the previous 6 months, performance score between 3–4, and inability to understand spoken and written English were the exclusion criteria. At the fifth week of recruitment, the inclusion criterion ‘women willing to attend all sessions’ was removed given the subjective nature of its interpretation and the exclusion criterion ‘women with secondary cancer’ was added to ensure homogeneity. Participants were recruited from two academic hospitals in London, UK between May and December 2015 and followed up until June 2016: full details have been reported previously.

Interventions
Shape-Up following cancer treatment
Intervention arm participants received the ‘Shape-Up following cancer treatment’ manual and participated in eight group-based weekly 1.5-hour sessions on healthy eating and physical activity based on social cognitive theory and control theory. In brief, the sessions focused on establishing a regular eating pattern, getting a healthier balance of foods, keeping an eye on portion sizes, reducing sedentary activity, increasing lifestyle and organized activities, and managing triggers to unhealthy behaviors through behavioral self-monitoring and goal-setting, problem-solving, and self-incentives. The sessions took place at University College London Hospitals NHS Foundation Trust. A trained research dietician (DAK) facilitated the face-to-face group discussions following a standardized scripted manual. A second researcher was present in all but the last group for assistance, but did not participate in the discussion. The remaining delivery modifications included splitting the last group into two for convenience purposes, and participation of an additional survivor in one of those groups to enhance the group experience. The sessions were audio-recorded and a researcher (RJB) was present in one group session to assess fidelity based on a predefined checklist.

Care as usual
To match currently offered usual care, participants in this arm were contacted only for the study assessments. They received brief standardized information and a booklet with healthy lifestyle advice after study completion.

Outcomes

Diet
The Automated Self-Administered 24 hours tool was used for dietary assessment with a single weekday recall at each time point. Food records were transferred to the MRC Human Nutrition Unit’s in-house dietary assessment software Diet In Nutrients Out that incorporates the UK food composition database, given the country-specific food nutritional composition. Methodological details are provided in the online supplementary material. An experienced independent data analyst scientist (NZ) guided the process and checked 10% of entries for accuracy.

The Alternative Healthy Eating Index 2010, which scores participants’ diet against the recommended healthy eating patterns, was calculated on a scale of 0–110 with 110 indicating optimal diet. The score is based on 11 dietary components (vegetables, fruits, whole grains, sugar-sweetened beverages, nuts and beans, red and processed meat, polyunsaturated fatty acids, long-chain omega-3 fatty acids, trans fatty acids, alcohol, salt), each contributing equally to the total score.

Physical activity
Physical activity was assessed with a 15-min interview using the reliable, valid, and responsive to change Stanford 7 Day Physical Activity Recall and was calculated using standardized methodology. At the 24-week follow-up, a subsample (n=28) also wore ActivPal (PAL Technologies Ltd, Glasgow, UK) accelerometers for seven consecutive days, including sleep, prior to the study assessment. Using waterproof adhesive dressing, participants attached the device to the middle of their right thigh following standardized guidelines. Data were exported from the ActivPal interface program.

Anthropometry, body composition, hand grip strength, and blood pressure
Weight (to the nearest 0.1 kg) and body composition were measured with a multi-frequency segmental body composition analyzer (MC-980, Tanita Corp., Tokyo, Japan). Body composition is automatically calculated from a proprietary prediction equation. To ensure stable subject conditions, participants were instructed to abstain from large meals or drinks 2 hours before the assessment. They emptied their bladder immediately before the assessment and cleaned their limbs with sanitiser to reduce oil and sweat, which can affect measurement accuracy. Measurements are missing for one participant who refused to remove her socks. Fat-free mass index and fat mass index were calculated based on the body mass index formula (online supplementary material).

Using standardized protocols, height was measured with a stadiometer to the nearest 0.1 cm and handgrip strength using a handgrip dynamometer (T.K.K.5401 grip – D, Takei Scientific Instruments, CO., LTD. Tokyo, Japan). Blood pressure was measured using an automated sphygmomanometer (Omron) with
the participant seated comfortably for 5 min before measurement and their arm supported at the level of the heart. All measurements were taken twice and averaged for analysis.

Health-related quality of life and health care resource use
Participants filled out the widely used, reliable, and validated EORTC QLQ-C3027 and Endometrial Cancer Module (QLQ-EN24). During the final follow-up assessment, participants completed a questionnaire on their healthcare resource use within the past 6 months.29

Sample size, randomization, and blinding
With a significance level of 5%, 64 participants (32 per arm) were needed to assess the feasibility of the study regarding recruitment and adherence rate with 90% power and retention rate with 80% power.17 The trial was not powered to detect differences in diet, physical activity, and health-related outcomes, and these analyzes are therefore exploratory. The procedures for trial arm assignment and blinding have been followed without modification as detailed in the protocol.17 In brief, participants were individually allocated to each arm with minimization, using body mass index and age as stratified variables. The researcher (MM) assessing the 8-week outcomes was blinded to arm allocation.

Statistical analysis
Following verification of assumptions (linearity, homogeneity of regression slopes, approximate normality of the residuals, homoscedasticity, and homogeneity of variances), analysis of covariance compared outcomes between the trial arms at 8 weeks (end of the active intervention) and at 24 weeks to explore longer-term effects. Two models were run: an unadjusted and an adjusted one for body mass index, age, and baseline values for the outcome of interest. The analysis followed the intention-to-treat strategy. Only eligible participants (n=54) were included in the complete case analysis following the recommendation of the Trial Steering Committee. The majority of missing data were due to non-attendance at follow-up. Group means are presented with standard deviations and between group mean differences with 95% CIs. All analyzes were carried out using the Statistical Package for Social Sciences (SPSS, Chicago, IL) version 23.

RESULTS

Descriptive characteristics
Of the 296 potentially eligible participants, 20.3% (95% CI: 15.7 to 24.9) enrolled in the study. Recruitment was terminated early due to resource constraints. Table 1 presents baseline participants’ characteristics. At enrolment, the mean (± standard deviation) age was 62.1±8.3 years’ old, body mass index 28.0±6.3 kg/m², and time since diagnosis 1.2±1.0 years. More than half of the participants were white (67%) and married (53%). The most common diagnosis was stage IA (49%), type 1 (82%) endometrial cancer. Twenty participants adhered to the intervention based on the pre-defined criteria.17 The CONSORT diagram shows the trial progress (Figure 1).

Diet, physical activity, and self-efficacy
Changes by time and group are presented in Table 2 with analysis of covariance statistics in online supplementary table S1. In the fully adjusted model, there was a significant improvement in the overall AHEI-2010 score in the active intervention group compared with controls at 8 weeks (P=0.046) but not at 24 weeks (P=0.964). The relatively high self-efficacy score at baseline (Cronbach’s alpha=0.77) did not change significantly between arms at follow-up.

Most participants (92.6%) were meeting the recommendations of at least 500 MET-minutes of moderate to vigorous physical activity at baseline. Furthermore, 31.5% were also meeting at least 500 MET-minutes of vigorous physical activity at baseline (online supplementary table S3). There was no evidence of a difference in the total energy expenditure or the energy expenditure from moderate to vigorous physical activities between groups at each time point.

Most participants performed minimal strength and flexibility exercises throughout the study (online supplementary table S4). The self-reported energy expenditure was significantly positively correlated both with estimated energy expenditure from the accelerometer (r=0.42, P=0.03) and with step count (r=0.49, P=0.008). However, the Bland–Altman analysis (n=28) suggested that the questionnaire significantly overestimated total energy expenditure compared with the accelerometer (mean difference=0.8 MET/h, 95% CI: −3.0, 4.7, P=0.03).

Anthropometry, body composition, blood pressure, hand-grip strength
Only 24.1% of participants (19.2% and 28.6% in the active intervention and usual care arm, respectively) were affected by obesity based on body mass index at baseline. There was a statistically significant reduction in weight at 8 weeks for those allocated to the intervention (P=0.007) but not at 24 weeks (P=0.196) in the adjusted model (Table 2). This observation was also evident for body mass index. There was no evidence of significant changes in fat mass index or fat-free mass index. The mean systolic blood pressure was higher than the ideal 120 mmHg value at baseline in each arm. In contrast, the mean diastolic blood pressure and hand-grip strength were normal. No evidence of statistically significant differences between arms was obtained for these physical measurements, apart from handgrip strength at 24 weeks (P=0.04).

Health-related quality of life
Scores for health-related quality of life, function scales, and symptoms are presented in Table 3 for both arms with their changes at each time point. Overall, the baseline scores were high for the functional scales and low for symptoms, except for fatigue, insomnia, and muscular pain. In the adjusted model, there was a statistically significant difference in the global quality of life between groups at 24 weeks (P=0.029) but not at 8 weeks (P=0.52). Those allocated to the intervention reported higher global quality of life at 24 weeks compared with those allocated to usual care. There was no evidence of a between-group difference for the remaining health-related quality of life aspects, or symptoms, except constipation which improved significantly at 8 weeks for those allocated to the intervention arm (P=0.03) in the unadjusted model. Regarding the items specific to endometrial cancer, there was no observed significant change except a significant between-group improvement in the gastrointestinal symptoms at 8 weeks (P=0.02) in the unadjusted model (online supplementary table S5).
Table 1  The Diet and Exercise in Uterine Cancer Survivors pilot trial baseline participant characteristics

| Characteristic                                      | Shape-Up (n=25) | Care as usual (n=24) | Total             |
|-----------------------------------------------------|-----------------|----------------------|-------------------|
| Age, mean (SD)                                      | 62.6 (9.0)      | 61.5 (7.7)           | 62.1 (8.3)        |
| Ethnic background                                   |                 |                      |                   |
| White                                               | 17 (68)         | 16 (67)              | 33 (67)           |
| Asian                                               | 4 (16)          | 5 (21)               | 9 (18)            |
| Black                                               | 3 (12)          | 1 (4)                | 4 (8)             |
| Mixed / other                                       | 1 (4)           | 2 (8)                | 3 (6)             |
| Living arrangement                                  |                 |                      |                   |
| Own outright/mortgage                               | 17 (68)         | 15 (63)              | 32 (65)           |
| Renting                                             | 8 (32)          | 9 (38)               | 17 (35)           |
| Marital status                                      |                 |                      |                   |
| Married / living with partner / civil partnership    | 12 (48)         | 15 (63)              | 27 (55)           |
| Separated/divorced                                  | 7 (28)          | 3 (12)               | 10 (20)           |
| Widowed/single                                      | 6 (24)          | 6 (25)               | 12 (24)           |
| Education                                           |                 |                      |                   |
| Degree / higher degree / higher education below degree level | 11 (44)       | 12 (50)              | 23 (47)           |
| Secondary education                                 | 11 (44)         | 10 (42)              | 21 (42)           |
| No formal qualifications                            | 3 (12)          | 2 (8)                | 5 (10)            |
| Employment                                          |                 |                      |                   |
| Full time / self-employed                           | 9 (36)          | 11 (46)              | 20 (41)           |
| Part time                                           | 3 (12)          | 1 (4)                | 4 (8)             |
| Retired                                             | 10 (40)         | 11 (46)              | 21 (43)           |
| Other                                               | 3 (12)          | 1 (4)                | 4 (8)             |
| Time since diagnosis in months, mean (SD)           | 19.2 (11.2)     | 21.4 (11.3)          | 20.3 (11.2)       |
| Time since completion of primary treatment in months, mean (SD) | 17.1 (11.2)  | 18.5 (11.7)          | 17.8 (11.3)       |
| Treatment                                           |                 |                      |                   |
| Surgery                                             | 25 (100)        | 24 (100)             | 49 (100)          |
| Chemotherapy treatment                              | 3 (12)          | 5 (21)               | 8 (16)            |
| External beam radiotherapy                          | 6 (24)          | 12 (50)              | 18 (37)           |
| Brachytherapy                                       | 11 (44)         | 13 (54)              | 24 (49)           |
| Cancer stage                                        |                 |                      |                   |
| IA                                                  | 11 (44)         | 13 (54)              | 24 (49)           |
| IB                                                  | 11 (44)         | 6 (25)               | 17 (35)           |
| II                                                  | 2 (8)           | 3 (13)               | 5 (10)            |
| IIIA                                                | 1 (4)           | 2 (8)                | 3 (6)             |
| Cancer grade                                        |                 |                      |                   |
| 1                                                   | 6 (24)          | 7 (29)               | 13 (27)           |
| 2                                                   | 13 (52)         | 9 (38)               | 22 (45)           |
| 3                                                   | 6 (24)          | 8 (33)               | 14 (29)           |
| Histology                                           |                 |                      |                   |
| Endometrioid adenocarcinoma                         | 21 (84)         | 19 (79)              | 40 (82)           |
| Serous carcinoma                                    | 1 (4)           | 3 (13)               | 4 (8)             |
| Mixed carcinoma                                     | 1 (4)           | 0 (0)                | 1 (2)             |
| Serous surface papillary carcinoma                  | 0 (0)           | 1 (4)                | 1 (2)             |
| Carcinosarcoma                                      | 2 (8)           | 0 (0)                | 2 (4)             |

Continued
**Table 1** Continued

| Characteristic                | Shape-Up (n=25) | Care as usual (n=24) | Total |
|------------------------------|-----------------|----------------------|-------|
| Adenosquamous carcinoma      | 0 (0)           | 1 (4)                | 1 (2) |
| Histological type            |                 |                      |       |
| Type I                       | 21 (84)         | 19 (79)              | 40 (82)|
| Type II                      | 4 (16)          | 5 (21)               | 9 (18) |
| Charlson Comorbidity Index   |                 |                      |       |
| 2                            | 18 (75)         | 21 (84)              | 39 (80)|
| 3                            | 6 (25)          | 4 (16)               | 10 (20)|
| WHO performance status       |                 |                      |       |
| 0                            | 20 (83)         | 20 (80)              | 40 (82)|
| 1                            | 3 (13)          | 5 (20)               | 8 (16) |
| 2                            | 1 (4)           | 0 (0)                | 1 (2)  |
| Selected comorbidities       |                 |                      |       |
| Diabetes                     | 3 (12)          | 4 (17)               | 7 (14) |
| Hypertension                 | 6 (24)          | 7 (29)               | 13 (27)|
| Dyslipidemia                 | 3 (12)          | 3 (13)               | 6 (12) |
| Asthma                       | 1 (4)           | 2 (8)                | 3 (6)  |
| Osteoporosis                 | 2 (8)           | 4 (17)               | 6 (12) |

Percentages might not add up to 100 due to rounding. Data are presented as n (%) unless otherwise specified. Body composition data for usual care n=23. SD, standard deviation; WHO, World Health Organization.

**Health care resource use**

Over the study period, participants reported a mean (standard deviation) 1.4 (1.9) visits to their general practitioner and 1.7 (1.6) visits to hospital outpatients, mainly in the oncology department. There were no hospital admissions or use of other healthcare services. They also reported taking on average (SD) 1.4 (1.9) medications at the last follow-up visit. No intervention-related adverse events were reported.

**DISCUSSION**

This is the first study of a health behavior change intervention in UK endometrial cancer survivors indicating potential effectiveness for behavior change and patient-reported outcomes. In this exploratory analysis, overall diet improved at 8 weeks, while physical activity remained unchanged, and weight was statistically but not clinically significantly reduced. Despite the wide CI, global quality of life improved significantly at 24 weeks, approaching clinical significance.30

Strengths of the study include the systematic development of the theory-based intervention with patient input,13 use of a randomized design, validated outcome measures, masking of the 8-week assessor to intervention allocation, and medium-term follow-up. The intervention fits within the top 10 research priorities for endometrial cancer research5 and with the National Cancer Survivorship Initiative aim of delivering sustainable personalized lifestyle support to people with cancer.31 Thus, a fully-powered trial should assess the potential impact of the intervention on the second NHS Outcome framework domain (‘enhancing QoL for people with long term conditions’).32 We had an excellent retention rate (91%) compared with the 15%–20% drop-out typically seen in lifestyle trials at 6 months.13

Limitations of the study include the small sample size, lack of power, and the presence of multiple testing that render the interpretation of all secondary outcomes as preliminary. However, the study provides a rich dataset for the estimation of outcome measures for an efficacy trial. For example, a trial of 108 participants randomized 1:1 to the intervention or usual care would provide definitive evidence of a 12-point clinically significant improvement of global quality of life assuming a standard deviation of 19, 90% power, and 5% alpha error. The definitive trial should also be powered for sustained behavior change. Using the same assumptions, a total sample size of 98 participants would be needed to detect a clinically significant 10-point increase in the Alternative Healthy Eating Index 2010 index (standard deviation=15) and a sample of 120 to detect an increase of 30 min in weekly moderate to vigorous physical activity using accelerometry (standard deviation=50).

The 24-week assessment was unblinded and contamination of the control group has been reported.14 Both physical activity and dietary data were self-reported. Using objective physical activity measurements in future trials would avoid the substantial overestimation of self-reported physical activity. The single weekday 24-hours recall could not account for day-to-day variations in dietary intake but was sufficient to determine between group differences.34 Diet was comprehensively assessed with the Alternative Healthy Eating Index 2010, which strongly predicts survival24 and its components were targeted with the intervention. Although bioelectrical impedance falls behind other techniques in accuracy, it still provides a practical, non-invasive, and reliable method for body composition estimation. Furthermore, relatively high levels...
of health behaviors, health-related quality of life, and functioning were reported at baseline, which limits the generalizability of the findings and could hinder future studies with similar samples from observing differences due to ceiling effects. Hence, future studies should consider the implementation of potential entry cut-offs for health-related quality of life, functioning, and behavioral measures. Limited evidence suggests these ceiling effects might be less common in the Functional Assessment of Cancer Therapy General (FACT-G) questionnaire, which may also have stronger reliability and validity compared with the EORTC-QLQ-C30. Thus, future trials should consider using multiple instruments to assess HRQoL.

Baseline AHEI-2010 scores were comparable to those of a UK population-based study using the early Alternative Healthy Eating Index version that indicated a negative association between Alternative Healthy Eating Index adherence and mortality. Previous studies in endometrial cancer survivors have mainly assessed fruit and vegetable intake as a dietary quality proxy, with similar or higher scores for fruit and vegetables. However, this approach fails to comprehensively assess various dietary constituents that can affect disease risk. Therefore, future dietary assessment should consider an overall dietary approach.
Table 2  Arm means (standard deviation) and differences between arm means for dietary, self-efficacy, and physical activity, anthropometric, blood pressure, and grip strength outcomes

| Scores                          | Mean (SD) Active intervention minus usual care | Adjusted mean group difference at 24 w (95% CI) | Unadjusted mean group difference at 24 w (95% CI) | Adjusted mean group difference at 8 w (95% CI) | Unadjusted mean group difference at 8 w (95% CI) |
|--------------------------------|-----------------------------------------------|-----------------------------------------------|-------------------------------------------------|-----------------------------------------------|-------------------------------------------------|
|                                | Shape-Up FCT (n=25)                           | Care as usual (n=24)                           |                                                 |                                               |                                                 |
|                                | Baseline                                     | Change at 8w                                   | Change at 24w                                   | Baseline                                      | Change at 8w                                   | Change at 8w                                   |
| AHEI-2010                      | 58.7 (12.6)                                  | 4.4 (15.3)                                     | 3.0 (14.0)                                     | 59.3 (15.4)                                  | -2.9 (14.1)                                    | 2.2 (17.8)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 7.4 (-0.7 to 15.5)                             | 7.5 (0.1 to 14.9)                             |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 1.0 (-8.3 to 10.2)                             | 0.2 (-7.7 to 8.0)                             |
| Total EE (MET-h/day)           | 35.1 (2.1)                                    | -1.4 (2.2)                                     | 0.2 (2.1)                                      | 35.7 (2.9)                                    | -1.8 (3.6)                                     | 0.4 (2.7)                                      |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -0.3 (-2.1 to 1.6)                             | 0.1 (-1.6 to 1.8)†                             |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -0.2 (-2.1 to 1.6)                             | 0.1 (-1.1 to 1.3)††                            |
| Shape-Up self-efficacy score§  | 3.6 (0.4)                                     | 0.2 (0.5)                                      | 0.1 (0.5)                                      | 3.6 (0.6)                                     | -0.2 (0.7)                                     | -0.1 (0.3)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.3 (-0.1 to 0.7)                              | 0.3 (-0.1 to 0.7)††                            |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.2 (-0.2 to 0.5)                              | -                          |
| Weight (kg)                    | 69.8 (14.8)                                   | -0.9 (1.4)                                     | -1.1 (2.6)                                     | 71.9 (15.2)                                   | 0.3 (1.5)                                      | -0.2 (2.5)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -3.3 (-12.0 to 5.3)                            | -1.2 (-2.0 to 0.3)†                             |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -3.0 (-11.3 to 5.3)                            | -0.9 (-2.4 to 0.5)                             |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.0 (-8.3 to 10.2)                            | -1.2 (-11.3 to 1.1)††                          |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.2 (-0.2 to 0.5)                              | -                          |
| BMI (kg/m²)                    | 27.3 (6.5)                                    | -0.4 (0.5)                                     | -0.4 (1.0)                                     | 28.8 (6.1)                                    | 0.1 (0.6)                                      | -0.1 (1.0)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.9 (-5.5 to 1.7)                             | -0.5 (-0.8 to 0.1)††                          |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.8 (-3.3, 1.7)                               | -0.4 (-0.9, 0.2)††                            |
| FMI (kg/m²)                    | 10.0 (4.3)                                    | -0.1 (0.8)                                     | -0.4 (0.8)                                     | 10.9 (4.2)                                    | 0.1 (0.5)                                      | -0.2 (0.8)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.1 (-3.5 to 1.3)                             | -0.2 (-0.6 to 0.1)††                          |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.1 (-3.5 to 1.2)                             | -0.3 (-0.7, 0.2)††                            |
| FFMI (kg/m²)                   | 17.3 (2.6)                                    | -0.2 (0.6)                                     | 0.0 (0.5)                                      | 17.8 (2.2)                                    | 0.0 (0.5)                                      | 0.1 (0.5)                                      |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -0.7 (-2.2 to 0.7)                             | -0.2 (-0.5 to 0.1)††                          |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -0.6 (-2.0 to 0.8)                             | -0.1 (-0.4 to 0.2)††                            |
| Systolic BP (mmHg)             | 142.9 (27.8)                                  | -7.9 (16.6)                                    | -11.1 (14.9)                                   | 139.7 (15.5)                                  | 0.7 (20.4)                                     | -8.0 (10.7)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -5.5 (-21.0 to 10.1)                           | -6.3 (-16.1 to 3.6)                           |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.1 (-10.9 to 11.0)                            | -1.9 (-8.3 to 4.5)                            |
| Diastolic BP (mmHg)            | 80.2 (7.4)                                    | -1.9 (6.1)                                     | -5.4 (5.6)                                     | 79.3 (9.0)                                    | 3.3 (9.8)                                      | -3.3 (6.5)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -4.3 (-10.2 to 1.7)                            | -                          |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | -1.2 (-6.3 to 3.8)                             | -2.1 (-5.3 to 1.1)                            |
| Hand grip strength (kg)        | 22.5 (4.4)                                    | -0.3 (2.4)                                     | 0.0 (2.4)                                      | 23.1 (4.0)                                    | -1.7 (3.1)                                     | -1.3 (1.9)                                     |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.8 (-2.1 to 3.8)                              | 1.5 (-0.1 to 3.1)††                           |
|                                |                                               |                                               |                                                 |                                               |                                                 |                                                   | 0.7 (-1.8 to 3.1)                              | 1.3 (0.1 to 2.5)††                            |

Analyses shown with (-) were not performed, as the statistical assumptions were not met. Optimal potential Alternative Healthy Eating Index 2010 (AHEI-2010) score=110. Optimal potential scores for AHEI-2010 and self-efficacy were 110 and 5, respectively.

*P<0.05, **P<0.01
†Age was not included in this model as covariate because the linearity assumption was not met.
‡Body mass index (BMI) was log transformed for this model.
§n=23 for active intervention.
¶Only baseline FFMI was included as covariate in this model because the linearity assumption was not met for age.
**BMI was not included in this model as covariate because the linearity assumption was not met. BMI was not included as covariate in the models for weight, FMI, and FFMI.
BP, Blood pressure; EE, Energy expenditure; FCT, following cancer treatment; FFMI, Fat free mass index; FMI, Fat mass index; MET, Metabolic equivalents.
### Table 3  Arm means (standard deviation) and differences between arm means for general health-related quality of life outcomes

| Scores                      | Mean (SD) | Active intervention minus usual care |
|-----------------------------|-----------|--------------------------------------|
|                             | Shape-Up FCT (n=25) | Care as usual (n=24) | Adjusted mean group difference at 24 w (95% CI) | Unadjusted mean group difference at 24 w (95% CI) | Adjusted mean group difference at 8 w (95% CI) | Unadjusted mean group difference at 8 w (95% CI) |
|                             | Baseline  | Change at 8w | Change at 24w | Baseline  | Change at 8w | Change at 24w | 
| Physical functioning        | 89.6 (12.0) | 2.4 (9.4) | 1.6 (9.3) | 91.1 (15.1) | -2.3 (7.4) | 0.3 (6.4) | 3.3 (-4.7 to 11.3) | 4.5 (-0.3 to 9.4) | -0.2 (-7.4 to 7.0) | 1.1 (-3.0 to 5.1) |
| Role functioning            | 88.7 (15.0) | -1.3 (24.5) | 2.7 (19.6) | 93.1 (12.9) | -7.6 (26.0) | -6.3 (20.2) | 1.9 (-10.5 to 14.4) | 4.5 (-6.1 to 15.2) | - | - |
| Emotional functioning       | 78.3 (22.4) | 4.0 (20.3) | 9.0 (18.9) | 82.2 (20.0) | -2.8 (14.5) | 0.4 (9.6) | 1.7 (-9.2 to 12.5) | 5.0 (-4.4 to 14.5) | - | - |
| Cognitive functioning       | 83.3 (12.7) | 3.3 (16.7) | 7.3 (16.0) | 86.8 (13.9) | -2.8 (16.8) | 1.4 (9.9) | 2.6 (-7.9 to 13.2) | 2.3 (-5.2 to 9.7) | - | - |
| Social functioning          | 88.7 (17.8) | 2.7 (15.0) | 6.7 (18.0) | 86.1 (20.1) | 3.5 (18.4) | 6.3 (15.4) | 1.8 (-6.9 to 10.4) | 3.0 (-4.8 to 10.8) | - | - |
| Fatigue§                    | 19.6 (13.3) | -0.9 (19.2) | -5.1 (16.7) | 18.8 (16.9) | 8.2 (20.4) | 2.9 (15.4) | -8.2 (-20.3 to 3.9) | -6.8 (-17.8 to 4.1) | -6.0 (-15.5 to 3.5) | -6.2 (-14.8 to 2.3) |
| Pain                        | 20.7 (26.9) | -4.7 (15.6) | -6.7 (21.5) | 10.4 (15.4) | 6.3 (21.3) | 6.3 (21.9) | -0.7 (-12.8 to 11.4) | -2.7 (-15.3 to 9.9) | - | - |
| Nausea and vomiting         | 3.3 (8.3) | 8.7 (30.5) | -1.3 (4.6) | 2.1 (5.6) | 1.4 (10.9) | -1.4 (4.7) | 8.5 (-3.9 to 21.0) | 1.3 (-2.0 to 4.6) | - | - |
| Dyspnoea                    | 6.7 (13.6) | 0.0 (13.6) | -4.0 (17.5) | 15.3 (21.9) | 0.0 (17.0) | -2.8 (16.8) | -8.6 (-20.7 to 3.5) | -9.8 (-20.4 to 0.7) | - | - |
| Insomnia                    | 32.0 (28.0) | -5.3 (26.7) | -12.0 (27.0) | 40.3 (35.4) | -1.4 (30.3) | -12.5 (35.2) | -12.2 (-28.8 to 4.4) | -6.6 (-20.3 to 7.1) | -7.8 (-24.4 to 8.8) | -2.5 (-17.1 to 12.1) |
| Appetite loss               | 5.3 (20.8) | -1.3 (26.3) | 0.0 (27.2) | 4.2 (11.3) | 0.0 (9.8) | -1.4 (12.0) | -0.2 (-7.7 to 7.4) | 2.6 (-4.9 to 10.1) | - | - |
| Constipation                | 2.7 (8.2) | 0.0 (9.6) | 0.0 (13.6) | 12.5 (25.7) | 5.6 (25.4) | -1.4 (23.0) | -15.4 (-29.6 to 1.2) | -8.4 (-19.7 to 2.8) | - | - |
| Diarrhea                    | 1.3 (6.7) | 2.7 (13.3) | -1.3 (6.7) | 4.2 (11.3) | -2.8 (9.4) | 0.0 (17.0) | 2.6 (-2.7 to 7.9) | -4.2 (-10.5 to 2.1) | - | - |
| Financial difficulties      | 6.7 (16.7) | -2.7 (9.2) | -4.0 (17.5) | 2.8 (9.4) | 0.0 (9.8) | -1.4 (6.8) | 1.2 (-4.7 to 7.1) | 1.3 (-3.4 to 6.0) | - | - |

Higher scores in quality of life and functioning scales indicate higher quality of life and higher level of functioning, respectively. Higher scores in symptom scales indicate higher symptomatology. Analyses shown with (-) were not performed, as the statistical assumptions were not met.

*Only baseline global quality of life score was included as covariate in this model, because the linearity assumption was not met for age and body mass index.

†Usual care n=23 for both follow-ups and active intervention n=24 for 24 weeks. FCT, following cancer treatment.
The significant improvement in overall diet at 8-week follow-up within the intervention arm, indicates the potential effectiveness of ‘Shape-Up following cancer treatment’. However, diet quality seemed to decline at 24 weeks, indicating that a behavioral maintenance program may be required. Such a program could include similar behavior change techniques to those included within the current intervention. The lack of change in physical activity, while potentially attributable to ceiling effects, could also indicate that this aspect of the program would benefit from greater input. In line with this, we have previously reported that participants in the program suggested additions to the program focusing on physical activity would be beneficial.

As the intervention promoted healthy eating and physical activity for overall health but not for weight loss, the combined lack of calorie restriction advice and the high prevalence of participants with normal weight probably accounted for the lack of clinically significant weight loss. However, the demonstrated weight change provides confidence that the program could promote avoidance of weight gain and acts as a surrogate marker of program adherence. Furthermore, clinically significant weight loss might not be necessary for health benefits provided there is sustained practice of health behaviors.

While mostly not significant, mean differences for various health-related quality of life outcomes between the active intervention and control arms generally trended toward the expected direction, and those allocated to the intervention reported higher global quality of life at 24 weeks compared to those allocated to usual care. Our data are in line with a previous lifestyle weight loss trial showing significant improvements in fatigue and physical function between groups and in total QoL score within the lifestyle intervention.

In the mission of survivorship advancement through lifestyle, healthcare professionals can play an integral role. Provision of brief lifestyle advice to endometrial cancer survivors after treatment and directing them to relevant resources may help facilitate lifestyle changes, as survivors report being more likely to engage in behavior change following counseling from their oncologist. Given the time constraints during clinical appointments, interventions training healthcare professionals to deliver very brief lifestyle advice to endometrial cancer survivors after treatment, and those allocated to the intervention reported higher global quality of life at 24 weeks compared to those allocated to usual care. Our data are in line with a previous lifestyle weight loss trial showing significant improvements in fatigue and physical function between groups and in total QoL score within the lifestyle intervention. Furthermore, clinically significant weight loss might not be necessary for health benefits provided there is sustained practice of health behaviors.

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CONCLUSION

In conclusion, the self-help group intervention showed promising effectiveness. Further consideration should be given to improving the physical activity component and behavior maintenance aspects of the intervention. A large-scale evaluation of the intervention could inform whether it will help endometrial cancer survivors improve their health behaviors and, subsequently, well-being, and whether it has the potential to minimize healthcare costs.

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Contributors The authors’ contributions were as follows. AL and MTK conceived the study and were the grant holders. AL and RM were the site investigators for University College London Hospitals and Barts Health, respectively. DAK, AL, RJF, and MTK initiated the study design, and RM helped with protocol development and implementation. DAK and MM recruited the study participants. RJF was responsible for randomization and auditing. DAK was the trial manager, ran the group sessions, and conducted the baseline and 24-week follow-up assessments. MM conducted the 8-week follow-up assessments. NZ guided the dietary data analysis and checked entries for accuracy. MB provided the statistical support, and DAK conducted the statistical analyses. DAK drafted the manuscript, which was amended following comments from all other authors. All authors read and approved the submitted manuscript. All listed authors meet the criteria for authorship and no individual meeting these criteria has been omitted.

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Competing interests DAK and RJF are volunteers for the charity Weight Concern, which developed the ‘Shape-Up’ program for the general population.

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