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Weight loss to support breast cancer survival

Submission date 09/07/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 15/07/2021	**Overall study status** Completed	
Last Edited 10/04/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Women diagnosed with breast cancer who carry excess weight are more likely to be later diagnosed with another breast cancer than women with lower body weight. Excess weight is linked with worse overall health and poorer quality of life. There is some evidence that weight loss could improve the chances of surviving breast cancer, but trials are needed.
We aim to test a Total Diet Replacement (TDR) weight loss programme. 88 women will be randomised to either receive the TDR (provided by an external weight loss company), or enhanced usual care (EUC). Our trial will be the first to test this diet in women with breast cancer. Our long-term aim is to see if weight loss achieved with TDR can improve the chances of surviving breast cancer. The aim of the current trial is to see whether women with breast cancer are willing to take part in a study testing this diet, if they are able to follow the diet as recommended, and if it helps them to lose weight.

Who can participate?
Women aged 18 years or above with a diagnosis of invasive breast cancer within 14 months and a BMI between 27 and 45 kg/m²

What does the study involve?
TDR: Over 3 months, women will receive support from a trained advisor while they use nutritionally balanced meal replacement products, such as shakes and soups, to reduce calorie intake to 810 calories per day. This is followed by 3 months of gradual, supported food reintroduction and 6 months of a weight maintenance programme. This programme has been shown to support greater weight loss than other diets, and has improved the health of people with other diseases, such as diabetes.

EUC: Women will receive the 10 Top Tips leaflet (a leaflet detailing habit-based weight loss advice) plus a 20minute phone call discussing the leaflet.

What are the possible benefits and risks of participating?
The benefits of taking part include: losing weight, which can have benefits for the participants' health and quality of life; free use of a watch and scales for the duration of the study; and helping improve the care of women with breast cancer who have excess weight.

The potential risks of taking part include; the time commitment/burden of taking part, including time to complete questionnaires. For participants allocated to the TDR intervention, additional risks include the time burden of attending support consultations and following a strict diet; potential risks relating to any medication alterations recommended as a result of following this diet (this risk is reduced as it would only be done by participants' GP if required, and in line with tested protocols); possibility of experiencing side-effects as a result of the diet (e.g. constipation), however these are expected to be mild, will be monitored by the advisors, and advice will be given on how to manage these. Patients are only eligible once they have completed their cancer treatment (with the exception of ongoing adjuvant hormone therapy medication), in order to negate any risks associated with undergoing a TDR during active cancer treatment.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
January 2021 to February 2024

Who is funding the study?
Breast Cancer Now (UK)

Who is the main contact?
Dr Rebecca Beeken, r.beeken@Leeds.ac.uk
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
296485

Central Portfolio Management System (CPMS)
49060

Protocol serial number
Grant Codes: 2019DecPR1367

Study information

Scientific Title
WE SURE CAN: WEight loss to SUppoRt brEast CANcer survival

Acronym
WE SURE CAN

Study objectives
Women diagnosed with breast cancer who carry excess weight are more likely to be later diagnosed with another breast cancer than women with lower body weight. Excess weight is linked with worse overall health, and poorer quality of life. There is some evidence that weight loss could improve the chances of surviving breast cancer, but trials are needed.

We aim to test a Total Diet Replacement (TDR) weight loss programme. 88 women will be randomised to either receive the TDR (provided by an external weight loss company), or enhanced usual care (EUC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/04/2021, Wales REC 5 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 230457; Wales.REC5@Wales.nhs.uk), ref: 21/WA/0125

Primary study design
Interventional

Study design
Interventional randomized controlled trial with qualitative follow up and a SWAT

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast Cancer

Interventions
Recruitment route 1: Prospective identification
Women who have completed their hospital-based treatment attend a discharge meeting and / or a holistic needs assessment (either in person or remotely). Research Nurses (RN) will screen patient lists to identify individuals who meet a preliminary set of inclusion / exclusion criteria (e. g. diagnostic stage). RNs will give/email these patients a copy of the invitation letter and participant information sheet, and will be available to answer any questions they have either during this appointment, or by telephone later on. Full eligibility screening will be conducted by the RN over the phone with interested patients, prior to seeking consent.

Recruitment route 2: Retrospective identification
Research Nurses will search hospital records for eligible women who have had a diagnosis in the previous 14 months and meet a preliminary set of inclusion criteria. They will email/post them the study invitation letter and participant information sheet and follow this up with a phone call to assess interest, conduct full eligibility screening in those interested, and where relevant, take consent.

Baseline Measures
Once registered, participants will be emailed a link to the online baseline questionnaires for completion. These will be completed using REDCAP and only authorised individuals in the university study team will have access to this data. These questionnaires consist of a mixture of pre-existing validated questionnaires, and trial specific measures which have been developed by the researchers for this trial. The baseline questionnaires will take approximately 30-45 minutes to complete. Participants will also be posted out a set of scales, a physical activity tracker (watch) and a data hub, along with instruction on set up and use. Participants will be asked to weigh themselves using the scales at baseline, and 4, 7, 10, 13 months. They will also be asked to wear the physical activity tracker for a minimum of 7 consecutive days at these same time-points. They can continue to wear the watch for the duration of the trial if they wish to. Data from the scales and physical activity monitor will automatically sync to the data hub which they will have been asked to set up in their home. The data hub then uploads the (anonymous) data from the scales and physical activity monitor onto the device manufacturers server, where the research team at the University of Leeds can access and download it in order to save it with the rest of the study data. Although technicians at the device manufacturers organisation can access this data, none of it is identifiable data.

Randomisation
Once participants' baseline measures (questionnaires and weight) have been collected, participants will be randomised to the TDR or Enhanced Usual Care on a 1:1 basis via the independent, automated randomisation service at the University of Leeds CTRU. A minimisation algorithm (incorporating a random element) will be used. Randomisation will stratify by BMI status (27-34.9kg/m2 vs. 35-45kg/m2), menopausal status (pre vs. post-menopausal), and Breast cancer hormone receptor status (ER and/or PR positive vs. ER and PR negative). Participants will

be informed of their allocation by the research team at UoL. Participants randomised to the TDR will be informed that they will be contacted by the external weight loss company to arrange their initial appointment. Participants randomised to EUC will be informed they will receive the leaflet via email/post, and will arrange a suitable time in the following month to discuss the leaflet with a researcher over the phone.

TDR intervention
Participants allocated to the TDR intervention will have an initial consultation with their advisor (trained dietitian) over the phone (or video call). They will discuss the programme with them, and request their GPs details. The intervention providers will communicate with their GP to check patient suitability for the diet, and whether they have any conditions or medications that need monitoring as a result of undergoing a low calorie diet.
During the first 12 weeks of the weight loss programme, participants are sent products (soups, shakes) to consume instead of their usual meals. These products reduce energy intake to 810kcal a day. Participants will also have fortnightly consultations with their advisor.
The next 12 weeks involve food reintroduction. Participants reduce the number of products used, and start to eat some usual food again. Fortnightly consultations with their advisors continue.
The final 6 months is the weight maintenance phase, whereby participants should be primarily eating usual meals (rather than reliance on products). They will have monthly consultations with their advisor during this phase.
Participants will also have access to the weight loss programme's app throughout the study, which may help them stick to the diet, and can be used to communicate with their advisor.
During the weight maintenance phase, if weight is regained they will be placed onto a rescue plan. If 2-4kg is gained, they will re-enter the food re-introduction phase. If more than 4kg is gained, they will re-enter the TDR phase, followed by the food re-introduction phase.

Enhanced Usual Care
Participants allocated to the EUC arm will receive the 10 Top Tips intervention. They will be emailed (or posted) the 10 Top Tips leaflet, which details healthy habits for losing weight. They will also receive a one-off phone call from a researcher, discussing the leaflet with them.
Enhanced usual care was suggested instead of usual care by our patient representatives, in order to make participation more acceptable to our sample. The 10 Top Tips leaflet is a pre-existing leaflet that has been tried and tested, and shown to result in a small amount of weight loss. The leaflet is publicly available on the Cancer Research UK website. The final page of the leaflet contains a logbook where participants can choose to record their healthy habits if they wish to, however this is not mandatory.

All participants: Follow-up measures
All participants will be requested to complete follow-up measures at 4, 7, 10, and 13months post randomisation. These measures include: online questionnaires, weighing themselves using the scales provided to them, and wearing the physical activity tracker watch for 7 consecutive days.
Email, telephone, and SMS prompts and reminders will be used to improve completion rates.
If a participant is struggling to complete the online questionnaires, a researcher may assist them over the phone.
The questionnaires include questions on participants' health and wellbeing, side-effects, health services use, physical activity levels, sleep, weight management behaviours, COVID-19 experiences.

Embedded Process Evaluation
A random selection of participants (n=20) at each time point, stratified by study arm, will be invited to participate in telephone or video interviews with a researcher at 4, 7 and 13 months

post randomisation. Interviews will ask questions that give insight into the acceptability of trial procedures (including use of scales and physical activity monitor), and their experiences and acceptability of the interventions, as well as their views on other, established, weight loss interventions. Participants in the intervention arm will be asked additional questions on the barriers and facilitators to adherence to the weight loss programme.

All 'actors' involved in the delivery or management of the interventions will be invited to participate in telephone interviews with a researcher, at the following time points:

Research Nurses: 3 months post-randomisation
Advisors: 15 months post first patient randomised (assuming that by this point, around half of participants will have completed the CW intervention).

We will aim to interview a minimum of 1 couterweight advisor (maximum of 2), and 2 research nurses (maximum of 4).

Interviews will ask questions that give insight into their acceptability of trial procedures, of the intervention itself, and their experiences regarding any interactions they have had with trial participants. Interview schedules will be tailored for each group (CW advisors, RNs)

Interviews will be digitally recorded, transcribed verbatim, and analysed using Thematic Analysis. Participants can request that their quotes from the interviews will not be used publicly (e.g. in any subsequent reports or publications).

A SWAT (Study Within A Trial) will also be conducted within this trial. This will evaluate the effects of sending SMS pre-notifications (prompt notification vs. no notification) and SMS reminders (prompt vs. a specific prompt based on behaviour change techniques) on questionnaire response rates (retention) at 4, 7 and 10-month post-randomisation follow-up assessments. This will have a 2by2 factorial design with participants being randomised to one of four experimental conditions. All participants recruited into the We Sure Can trial, and who remain as fully participating (i.e., have not fully withdrawn or have died at each time-point where questionnaires are administered (4, 7 and 10-months post host trial randomisation) will be eligible for the SWAT. There are no additional inclusion or exclusion criteria. Participants in the main trial will receive SMS reminders regardless of the SWAT, therefore explicit consent into the SWAT will not be obtained.

Intervention Type
Behavioural

Primary outcome(s)
1. Number of patients screened for eligibility assessed at the screening stage
2. Number and proportion of patients eligible out of those screened and reasons for ineligibility assessed at the screening stage
3. Number and proportion of patients who consent out of those eligible and reasons for non-consent assessed at the recruitment stage
4. Number and proportion of patients consenting to randomisation out of those eligible and reasons for non-randomisation assessed at the recruitment stage
5. Number of participants randomised per site per month assessed at the end of the trial
6. Number and proportion of randomised participants lost-to-follow-up assessed at the end of trial
7. Number, proportion, type, and timing of participant withdrawals out of those randomised and reasons for withdrawal assessed at the end of trial

8. Questionnaire completion rates and method of completion at each time-point assessed at baseline, 4, 7, 10 and 13 months
9. Number of items of missing data per participant-reported outcome measure at each time-point (baseline, 4, 7, 10 and 13 months)
10. Number and proportion of participants with weight measurements at each time-point (baseline, 4, 7, 10 and 13 months)
11. Number and proportion of participants with physical activity monitor data at each time-point (baseline, 4, 7, 10 and 13 months)
12. Estimation of Intracluster Correlation Coefficient (ICC) assessed at the end of trial

Key secondary outcome(s)

1. Intervention adherence for patients in the intervention arm (number of intervention support consultations attended during the total diet replacement phase, amount of days covered by intervention product, measured by the intervention provider at the end of the total diet replacement phase)
2. Acceptability of the intervention products, explored in the qualitative process evaluation by interviews conducted at 4, 7 and 13 months
3. Acceptability of the intervention support consultations, explored in the qualitative process evaluation by interviews conducted at 4, 7 and 13 months.
4. Number and proportion of participants in the intervention arm deemed as having completed the intervention assessed at the end of trial from data during the total diet replacement phase
5. Number and proportion of participants in the enhanced usual care arm participating in a discussion of the healthy habits leaflet assessed at end of trial
6. Acceptability of the leaflet and discussion in the EUC arm, explored in the qualitative process evaluation by interviews conducted at 4, 7 and 13 months.
7. Treatment as usual content in both arms from participants (number of sessions attended and content of sessions) and sites (initiatives implemented during trial) assessed at the end of trial
8. Barriers, facilitators and reasons for non-attendance / non-compliance in both arms, explored in the qualitative process evaluation assessed by interviews conducted at 4, 7 and 13 months.
9. Site research team, and intervention providers' advisors' acceptability of intervention and trial procedures, explored in the qualitative process evaluation by interviews conducted at 3months (with research nurses) and 15months post first patient randomised to the intervention arm (for the intervention provider interviews)
10. Number of participants who indicate they would consent to bloods collection in a future trial assessed at baseline by online questionnaire
11. Number of and details of SAEs (deaths, case of deaths, and hospitalisations related to the trial intervention recorded until the end of the study) and number of and details of RUSAEs assessed at the end of trial from patient records and eCRFs
12. Exploration of the impact of the intervention on participant-reported outcomes. Summary and scale scores (where relevant) for each measure. Assessed at the end of the trial.
13. Generate evidence of proof-of-principle, via exploration of between-group change in overall weight, and proportions achieving 5% and 10% weight loss. Assessed at the end of the trial
14. Frequency of wearing the physical activity monitor and reasons of not wearing it all the time, assessed at 13month by online questionnaire
15. Exploration of the impact of the intervention on average physical activity (type of activity, duration of activity, daily steps and daily travelled distance) and sleep (number of hours sleep per night and sleep quality) across seven continuous days, assessed at 4, 7, 10, and 13 months using a physical activity monitor

Completion date

24/02/2024

Eligibility

Key inclusion criteria

1. Diagnosis of invasive breast cancer within 14 months prior to trial registration
1.1. Neoadjuvant subjects should have no evidence of clinical T4 disease prior to chemotherapy and surgery; eligibility for neoadjuvant patients can be defined by either clinical (cTNM) stage prior to therapy or pathologic (pTNM) stage at surgery; if patient is eligible based on either, they are eligible for the study as long as they do not have T4 disease prior to therapy
1.2. Bilateral breast carcinoma is allowed provided diagnoses are within 3 months of one another and at least one of the two breast carcinomas meet the eligibility criteria, and neither are Her-2 positive or inflammatory
2. HER-2 Negative as defined for the purpose of treatment.
3. Eligible tumour-node-metastasis (TNM) Stages include:
3.1. Oestrogen receptor (ER) and Progesterone receptor (PR) negative: T2 or T3 N0, T0-3N1-3
3.2. ER and/or PR positive: T0-3N1-3 or T3N0
ER and PR status is as defined for the purpose of treatment
4. Patients must have had a bilateral mammogram within 14 months prior to registration, unless the initial surgery was a total mastectomy, in which case only a mammogram of the remaining breast is required. (Patients with bilateral total mastectomies do not require imaging).
5. All triple negative patients must receive chemotherapy of the treating clinician's recommendation.
6. ER/PR positive patients must receive chemotherapy (of the treating physician's choice) unless Oncotype Dx or another genomic predictor score indicates that they are at low or intermediate risk of disease recurrence with endocrine therapy alone.
7. All adjuvant or neoadjuvant chemotherapy and radiation completed at least 21 days prior to registration. Concomitant biologic therapy, hormonal therapy, and bisphosphonates are acceptable.
8. Surgical margins should be clear, with no tumour at ink for invasive, ductal in situ disease, and pleomorphic lobular carcinoma. Grossly positive margins should be re excised. Focally positive margins (<4mm) should ideally be re excised if technically possible but if not, consideration of radiotherapy boost should be given. Classical LCIS at the margin does not warrant re excision.
9. All surgery completed at least 3 months prior to registration. (Patients may have breast reconstruction during protocol participation, if scheduled for more than 6 months after registration into the trial).
10. Participants must be women
11. Capacity to provide informed consent
12. Aged ≥18 years at time of trial screening
13. Have a self-reported Body Mass Index of 27.0 – 45.0 kg/m² at time of trial screening
14. Have a BMI of 27.0 – 45.0 kg/m² at time of randomisation, using data from e-scales
15. Have sufficient proficiency in English to contribute to the intervention supporting consultations/ten top tips discussion, and complete the data collection required
16. Treated with curative intent
17. The participant is willing to complete the study assessments (questionnaires and anthropometric measures)
18. Participant reports they are able to stand without support to use the weighing scales provided, or has access to scales suitable for people who cannot stand without support

SWAT INCLUSION CRITERIA
All participants recruited into the We Sure Can trial, and who remain as fully participating (i.e.,

have not fully withdrawn or have died at each time-point where questionnaires are administered (4, 7 and 10-months post host trial randomisation) will be eligible for the SWAT. There are no additional inclusion or exclusion criteria.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Total final enrolment
52

Key exclusion criteria
1. Currently participating, or have consented to participate in another weight loss or dietary clinical trial. Co-enrolment in some trials involving pharmacologic therapy is allowed if there is no expected impact of the therapy on weight.
2. Unable to participate in a video or telephone call.
3. History of invasive breast cancer in 5 years prior to study registration other than the current diagnosis (prior ductal carcinoma in situ [DCIS] is permitted)
4. Patients cannot have metastatic breast cancer or inflammatory breast cancer
4.1. If there is a concern for metastatic disease, all investigations (e.g. chest x-ray, staging CT scan, bone scans), have been performed between first histologic diagnosis and registration
5. Patients with triple negative breast cancer are not eligible if they have T1N1mi disease
6. Patients with ER and / or PR positive breast cancer are not eligible if they have T0N0, T1N0, T2N0 or T1N1mi and T2N1mi disease
7. History of other malignancy within the past 4 years, except for malignancies with a >95% likelihood of cure (e.g. non-melanoma skin cancer, papillary thyroid cancer, in situ cervical cancer). Patients cannot have metastatic cancer at any site.
8. Refusal of breast cancer treatment that has been recommended by the treating clinician. However, where it has been a shared decision not to follow treatment (i.e. due to borderline risk), women are eligible.
9. Current or historic diagnosis of an eating disorder
10. Taking antipsychotic medication
11. Patients who have required hospitalization for depression, have unstable/untreated major depression, active severe depression or bipolar disorder or personality disorder, and any other mental illness at a severity which would prevent participation in an organised weight loss programme and for giving informed consent.
12. Heart failure
13. Type I or Type II diabetes if prescribed any anti-diabetic medication other than metformin
14. Diabetes Insipidus
15. Taking Warfarin

16. Hypertension if prescribed more than one anti-hypertensive drug
17. Lactose intolerance
18. Vegan
19. Alcohol dependence
20. Dependence on substances other than tobacco
21. Taking any anti-obesity medication
22. Had bariatric surgery or scheduled bariatric surgery
23. Experienced a heart attack or stroke in the past 3 months
24. Taking monoamine oxidase inhibitor (MAOI) medication
25. History of malabsorption and/or serious digestive problems, including inflammatory bowel disease and chronic diarrhoea
26. Angina, atrial fibrillation, arrhythmia, or prolonged QT syndrome
27. Renal failure
28. Epilepsy
29. Active liver disease (except non-alcoholic fatty liver disease (NAFLD)), a history of hepatoma or within 6 months of onset of acute hepatitis
30. Active treatment or investigation for possible or confirmed gastric or duodenal ulcer; maintenance treatment with acid suppression is not a contraindication
31. Porphyria
32. Scheduled for any surgery (including breast reconstruction) within 6 months from registration
33. Oxygen-dependent pulmonary disease
34. Sleep apnoea requiring CPAP
35. Pregnant, breastfeeding, or within 4 months post-partum and not breastfeeding
36. Undergoing fertility treatment
37. Under investigation for any of the conditions that have been excluded
38. Comorbid conditions that would cause life expectancy of less than 5 years

Date of first enrolment
21/09/2021

Date of final enrolment
14/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Luton & Dunstable University Hospital
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Lewsey Rd
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Study participating centre
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Study participating centre
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Study participating centre
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ME7 5NY

Study participating centre

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Study participating centre
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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Charity

Funder Name
Breast Cancer Now

Alternative Name(s)
BCN

Funding Body Type
Government organisation

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

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version V3.1	04/05/2021	15/07/2021	No	Yes