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A randomised controlled trial to assess the impact of a lifestyle intervention (ActWELL) in women invited to NHS breast screening – study protocol

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ABSTRACT

Introduction In Scotland, the incidence of breast cancer is predicted to rise by 27% by 2030 and whilst there are measures to support reductions in morbidity and mortality, the breast cancer community is currently exploring preventative opportunities including supporting weight management programmes in post-menopausal women. This study aims to assess the effectiveness and cost-effectiveness of a theory- based, community delivered, minimal contact, weight management (diet, physical activity and behaviour change techniques) programme (ActWELL) in women with a BMI >25 kg/m2 attending routine breast cancer screening appointments.

Methods and analysis The study will be a 4 centre, 1:1 parallel group RCT of a 12 month weight management intervention initiated in breast cancer screening centres, delivered by trained Breast Cancer Now lifestyle coaches in community settings. The intervention programme involves 2 intervention meetings with coaches plus (up to) nine telephone contacts over 12 months. The programme will focus on personalised diet (including alcoholic and sugary drinks) and physical activity habits. Behaviour change techniques include self-monitoring, goal setting, implementation intentions, action and coping plans. The study has a sample size of 414 women with a BMI>25 kg/m^2 attending routine national **NHS** breast cancer screening appointments. Measures will be taken at baseline, 12 weeks and at 12 month follow up, complemented by qualitative interviews exploring perceived acceptability and impact on habitual behaviours. The two co-primary outcomes are mean change in measured body weight and change in physical activity between groups to 12 months. Secondary outcomes are changes in eating habits, alcohol intake, sedentary time, quality of life, waist circumference, lipid, HbA1c and insulin profiles, blood pressure, and cost-effectiveness of the intervention.

Ethics and dissemination The protocol has been approved by East of Scotland Research Ethics Committee (17/ES/0073). All participants provide written informed consent. Dissemination will be through peer-reviewed publication and conference presentations.

Trial registration number ISRCTN11057518

Keywords Cancer prevention, breast cancer, screening, lifestyle, behaviour modification

Article Summary

Strengths and limitations of this study

- This work has the potential to provide routine support for weight management for women aged over 50 years
- This study has been developed from a well conducted feasibility trial with positive indicative outcomes
- Multi-centre, randomised control design
- Strong study team combining staff from academia, NHS, breast cancer charity and healthy screening attendees
- Novel approach to deliver weight management by trained in community locations
- The study has a large potential reach with around 73% of ALL women of this age group attending appointments including high numbers from disadvantaged backgrounds
- The intervention will not be readily accessible for women who do not accept screening appointments
- Not all women interested in lifestyle change will be able to participate due to capacity issues with lifestyle coaches

Competing interest statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work other than the Scottish Government who funded the award, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, and no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval

Ethical approval for this study was provided by East of Scotland Research Ethics Service (REC reference: (17/ES/0073).

Funding

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Author Contributions

ASA is the principal investigator and has overall responsibility for all aspects of the ActWELL study. She initiated the study, designed the intervention, led on development of the protocol and drafting the manuscript. AC, CMcA and NM were involved in intervention design and training, assessment methodology and finalising the protocol. SG is the trial manager and responsible for co-ordinating all aspects of the ActWELL study and drafting the protocol. EJM has responsibility for clinical issues, inclusion and exclusion criteria, trial design and finalising the protocol. AN is responsible for health economics analysis, assessment methodology and finalising protocol. RO has responsibility for all psychological aspects of intervention design, assessment methodology, fidelity measures and finalising the protocol. NS is responsible for design of blood collection procedures, overseeing analysis or bloods and finalising protocol design. MS is responsible for formative qualitative analysis, intervention design, acceptability measures and finalising protocol. ST is responsible for trial design, recruitment strategies, day to day management decisions (with ASA and SG), and finalising protocol. All authors contributed to writing this paper and approved the final draft.

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Data Sharing Statement

None

INTRODUCTION

Breast cancer accounted for 14.5% of all cancer diagnoses in Scotland in 2014 and accounts for 28% of female cancer cases[1]. Incidence is increasing and current predictions from ISD (Scottish Government) suggest a rise by 27.5% between and 2008-2012 and 2023-2027[2].

Whilst many factors are implicated in aetiology (genetics, reproductive history, hormone use), current estimates suggest that 38% of breast cancers in post-menopausal women in the UK are related to physical inactivity, alcohol consumption and body fatness[3]. There is consistent evidence that being overweight or obese throughout adulthood increases the risk of post-menopausal breast cancer[4].

In addition, gaining weight in adult life is a strong predictor of breast cancer (especially in women who have not taken hormone replacement therapy)[5]. Ahn et al reported that at any BMI, increased weight in adult life is associated with greater risk of breast cancer and a gain of 2-10kg after the age of 50 (e.g. post-menopausal) is associated with a 30% increase in breast cancer risk[6]. Findings from the EPIC study have also demonstrated that high weight gain in middle adulthood increases the risk of breast cancer[7]. In the Women's Health Initiative, Neuhouser et al.[8] reported that post-menopausal women with a BMI<25kg/m^2 at baseline who gained >5kg of body weight during the follow up period (median 13 years) had a 36% increase risk of developing breast cancer.

Lifestyles and weight management are also related to risk reduction. Women meeting at least 5 of the World Cancer Research Fund prevention guidelines for lifestyle show a 60% lower risk for breast cancer compared to women meeting none of the guidelines[9] and a recent systematic review reported that high versus low adherence to cancer prevention guidelines was associated with consistent reductions in breast cancer incidence[10]. Data from audits of bariatric surgery show that large weight losses are associated with large decreases in female cancers[11]. One recent North American study of 22,198 people 3.5 years after bariatric surgery reported reductions in post-menopausal breast cancer of 42%[12]. In addition, moderating weight gain in adult life through caloric adjustment and being physically active is likely to be of benefit for reduction in other cancers related to these behaviours[13] as well as other non-communicable diseases[14,15].

Most (73%) Scottish women aged 50 to 70 years accept invitations to attend the routine NHS Scottish Breast Screening Programme (NHSSBSP) and over 175,000 women attend each year[16]. In addition, women aged over 70 are able to attend through self-referral. The

NHSSBSP therefore provides a unique opportunity to endorse weight management intervention. However, a greater understanding of the benefits, costs, acceptability and impacts are needed to examine whether a NHSSBSP-initiated intervention can be effective and cost efficient.

In 2007, Fisher et al.[17] reported that most women attending breast screening clinics are interested in receiving lifestyle advice, and an updated paper reporting the view of 1,803 women shows overwhelming support for receiving interventions through this setting[18]. However, a review published in 2013[19] reported that whilst the importance of weight management in breast and colorectal cancer prevention is widely recognised, there is little evidence that lifestyle is discussed within cancer screening settings. It was also noted that the lack of advocacy about health behaviour change may endorse poor health behaviours by creating a 'health certificate effect.' This issue may be particularly relevant for body weight, where a lack of guidance to visibly obese patients may imply a lack of medical concern. The cancer research "gap analysis" reviews by Breast Cancer Campaign[20,21] highlighted the role of breast screening programmes as an opportunity for promoting cancer prevention activities, but noted the challenge of finding ways to support and facilitate women to achieve healthy ways of life.

In Scotland, the breast cancer community (government, charities and health professionals) is currently exploring innovative and sustainable preventative opportunities including supporting weight management programmes. The Scottish Health Survey[22] has reported that 72% of women aged 55 to 74 years have a BMI >25kg/m^2 (76% in women living in areas of higher deprivation). Furthermore, 42% of women **do not** achieve the recommendation of 150 minutes of physical activity per week, and this proportion increases with age. The National Institute of Clinical Excellence (NICE)[23] recommend that lifestyle weight management programmes are multi component and aim to reduce a person's energy intake and help them to be more physically active by changing behaviour. However, access to such NHS programmes is limited and commercial programmes have cost implications for low income adults.

It is recognised that partnerships between the NHS and the voluntary sector offer significant value for money and the potential for greater "reach" of interventions into community settings. The recent Lancet series on obesity highlighted that, despite government efforts to reduce the prevalence of obesity, these approaches are insufficient to help adults who are currently overweight or obese[24]. Innovative strategies beyond those currently delivered by health professionals are needed to increase capacity of delivery of weight management programmes.

Community lifestyle interventions initiated in the breast cancer screening setting are a largely unexplored area although repeated triennial appointments offer unique opportunities for initiation and re-enforcement[25]. This setting also provides an opportunity to engage with women from areas of higher deprivation (63%, 71% and 76% of women from Scottish Index of Multiple Deprivation (SIMD 1, 2, 3 quintiles respectively attend for screening)[26].

The ActWELL feasibility study demonstrated that recruitment, retention, indicative results and participant acceptability merited a full randomised control trial to test the long term impact of the intervention. In addition, 31% of participants recruited were from the lowest two quintiles of deprivation[27] indicating significant potential to reach women from higher rates of social deprivation who also tend to be more obese.

Feedback from screening centre users showed whilst many were aware of lifestyle issues in relation to diabetes and cardiovascular disease, information about lifestyle and breast cancer was new and considered "motivating" if the focus was on positive ways to help support behaviour change[28].

The current study is designed to assess the effectiveness of a community based, personalised, minimal contact weight management programme in women with a BMI>25kg/m^2 attending routine breast cancer screening clinics. The intervention programme is a collaboration between the charity Breast Cancer Now (BCN), NHSSBSP, local authority leisure centres and academic partners. This work is the first time that a cancer charity has offered volunteer capacity for cancer prevention action on weight management and offers significant potential to address gaps in public health efforts. The design is pragmatic to increase the relevance of the findings to policymakers, women eligible for breast screening and health professionals (see Appendix 1).

The study aims to assess the effectiveness and cost-effectiveness of a theory based, community delivered, minimal contact, weight management (diet, physical activity and behaviour change techniques) programme (ActWELL) in women with a BMI >25 kg/m^2 attending routine breast cancer screening clinics.

METHODS AND ANALYSIS

Trial design and setting

The study will be a four centre, 1:1 parallel-arm, randomised controlled trial of a 12 month, weight management intervention. The participants will be randomly allocated into two groups (1) standard care with health information leaflet or (2) experimental group who receive the ActWEll intervention. Potential participants will be introduced to the study whilst

attending routine NHS breast cancer screening appointment (static and mobile screening units) in Scotland. The study participant flow is presented in Figure 1.

All trial measurements will be undertaken by trained research nurses at baseline, 12 weeks and 12 months within the NHS Clinical Research Centres (CRC) in the areas served by the breast screening sites.

The intervention is delivered and supported by Breast Cancer Now volunteers who have undergone two days bespoke training on the intervention. The face to face intervention communications are delivered within local authority run leisure centres (or other appropriate community locations).

Participants

All attendees at routine NHS breast screening appointments will be advised about the study by NHSSBSP staff in writing and verbally. On checking in at the clinic women will be given a brief study information leaflet by the receptionist. During their visit the mammographer will briefly (approx. 30 seconds) mention the study verbally. If they are agreeable to a researcher making contact with them, women will be invited to leave their details on a contact card (telephone/email/postcode) which they can place in a study box in the reception area. A pop up banner, or poster, will also be displayed in the breast screening clinic or mobile van to further highlight the study and how to contact the research team. All NHS screening staff will be provided with training which introduces the aims of the study, why the trial is designed the way it is, the importance of their role, how to minimise the time taken to introduce the study and how to answer common questions. Within each site, a team "champion" will be identified from within the NHSSBSP staff to encourage colleagues and co-ordinate recruitment efforts.

Research staff will contact women leaving contact cards within two weeks and assess study eligibility.

Inclusion Criteria

- Attending, or invited to attend, routine breast screening clinics (not recall clinics)
- Measured BMI >25 kg/m^2
- Age 50 to 70 years

Exclusion Criteria

- Currently undergoing treatment for any malignant condition (excluding basal or squamous cell skin cancers)

- Reported contra-indication to physical activity (e.g. recent surgery)
- Reported contra-indication to weight loss (e.g. currently following a recovery programme for weight gain)
- On a specialised diet e.g. gluten free
- Diagnosis of Types 1 diabetes
- Current use of insulin
- No telephone contact
- Unable to consent

Participants who are considered eligible will be invited to attend their local research centre to provide informed consent before commencing baseline measures.

Participants found to be ineligible to take part, either on telephone screening or at a baseline visit, will be thanked for their time and will be offered, by post or email, lifestyle and cancer prevention information and/or information on local leisure facilities applicable to them. Where possible, this will also apply to women who have expressed an interest (e.g. left a completed card) but who have not been selected to take part in the trial due to the volume of people that can be seen by the research team. In the event of very large numbers of cards being returned it may not be possible to contact all women and this is made clear in the brief information leaflet.

Randomisation

Participants will be randomised centrally at a 1:1 ratio into the intervention or usual care groups using the web-based TRuST system designed by Tayside Clinical Trials Unit (TCTU). Randomisation will be stratified by site and minimised by socio-economic status based on Social index of Multiple Deprivation (SIMD)29 SIMD (two groups: SIMD 1 or 2; SIMD≥3).

In addition, a sub group comprising 146 women (73 from each group) will be randomly allocated by the TRuST system to receive an activPAL™ monitor (accelerometer) as an objective measure of physical activity. This number has been identified to meet statistical power (see below).

Usual care group: Following the end of their baseline measures, participants will receive a cancer prevention leaflet[30]. The study administrator will then notify participants of their

randomisation by letter. On completion of their 12 month follow up visit women will be offered a single personalised coaching session and the ActWELL intervention booklet.

Intervention group: Following the end of their baseline measures participants will receive a cancer prevention leaflet[30]. The study administrator will then notify participants of their randomisation by letter. The Breast Cancer Now volunteer coordinator will allocate a Breast Cancer Now Lifestyle Coach (LC) to the participant. The LC will contact the participant to arrange an appointment for their first face to face visit.

Blinding

The study team will be blind to the participants' group allocation until completion of the primary outcome analysis. Exceptions are the trial manager, study administrator, lifestyle coaches and participants who cannot be blinded owing to the nature of the intervention.

Intervention

Initial work focused on optimising the intervention to scale up the previous prototype for a 12 month follow up period. This was developed from the original feasibility study protocol and using feedback obtained from study participants and lifestyle coaches. Later feedback came from our recent research study offering a weight management lifestyle intervention to women attending family history clinics[31] and our newly formed ActWELL public advisory team. The proposed study builds on existing behaviour change models[32] particularly the COM-B model[33]. Thus, the intervention aims to incorporate **capability** for effective lifestyle change combined with **opportunities** for greater physical activity through an emphasis on walking initiatives and other community facilities (using taxonomy-derived effective behaviour change techniques[34]) and increased **motivation** for weight management (through awareness raising within the teachable moment setting).

In addition, four formative qualitative focus groups with individuals in the target population were held to obtain feedback on the prospective 12 month intervention including refinements on alcohol messaging.

Intervention content: The initial part of the intervention (months 1 to 3) will focus on helping achieve 7% of body weight loss (consistent with the lifestyle intervention in the highly effective Diabetes Prevention Programme[35]) and the remaining months will also combine techniques for weight loss maintenance (WLM) by addressing both caloric intake and energy expenditure.

Behavioural change techniques (BCT) include goal setting, implementation intentions, self-monitoring of body weight and feedback. The latter may be particularly important for WLM.

This part of the intervention will take a habit–formation based approach using the Ten Top Tips shown to be successful for WLM over a 2 year period[36]. Social support will be encouraged throughout the 12 months through regular coach contact and encouragement to share the intervention with a friend/buddy. The initial introduction to the leisure centre will also provide an introduction to locally available exercise facilities and classes.

Tailored personalised advice is a key component of all aspects of the intervention. Motivational interviewing about weight loss will be undertaken to identify participant ambivalence and perceived personal advantages to weight management.

The **caloric prescription** will be based on 600kcals below that required for weight maintenance (calculated using the equations for basal metabolic rate according to gender, age and body weight).

Food and drink choices will be based on information obtained from current eating habits obtained through 24 hour recalls to guide personalised advice on food frequency, portion sizes and foods to limit. Participant agreed goals (and implementation intentions) will be used for one specific food or drinking habit and this will be self-monitored with personalised feedback provided.

Physical activity dose All participants will undertake the Scottish Physical activity screening questionnaire (Scot-PASQ)[37] by the coach as an indicator of current activity levels to help guide the communications about walking plans and signpost other activities (including those offered in the local leisure centres). Participant agreed pedometer goals (and implementation intentions) will be used for habitual walking and this will be self-monitored with personalised feedback provided. Participants will be supported to gradually increase physical activity towards accumulating at least 150 minutes of moderate intensity physical activity per week and then, where appropriate, towards 300 minutes per week (Based on Scottish Intercollegiate Guidelines Network (SIGN)[38] guidance on weight management.

A detailed description of each intervention visit and telephone calls are provided in Appendix 2.

Intervention delivery There will be two face to face intervention meetings (one of 60 minutes and one of 45 minutes). Over a 12 month period there will be up to nine further contacts by telephone. The intervention programme will be delivered by Breast Cancer Now volunteers who have received the training programme to become lifestyle coaches.

Intervention fidelity We will undertake independent analysis of fidelity to the intervention. Fidelity of programme delivery and content will be assessed by audio-recording and transcription from a purposeful sample of approximately 10% of ActWELL lifestyle coaches including face to face interactions and telephone contacts at each site. A researcher independent from the intervention delivery will analyse the transcripts and evaluate the proportion of points covered in each session relative to those described in the intervention protocol. Time for implementation procedures will be recorded by the lifestyle coaches.

Outcome measures

A full list of measurable outcomes is presented in Table 1.

Table 1 Outcome Measures

Primary Outcomes		Baseline	12 week	12 month
Body weight	Measured using digital body weight scales (kg)	X		X
Physical Activity	7 days accelerometry with ActivPAL (steps)	X		X
Secondary outcomes				
Modes of physical activity	Scottish Physical Activity Questionnaire SPAQ[34]	X	X	X
Sedentary behaviour	7 days accelerometry with activPAL™ (subsample only)	X		X
Anthropometric changes	BMI (height and weight) Waist circumference (cm)	X		X
Eating habits	Questionnaire based on Scottish Health Survey[22]	X		X
	• Fruit and vegetable intake[45]		X	
Alcohol intake	Audit C questionnaire[46]	X		X
Psycho-social variables	Modified brief illness questionnaire47	X		X
	Knowledge and beliefs about lifestyle and breast cancer risk (developed in house)	X		X
	Psychosocial health measures resources (perceived motivation, awareness, ability, action, monitoring, and social support around weight management)			X
	Perceived body weight (developed in-house)	x	x	x
Economic outcomes	EQ5D-5L questionnaire42	X	X	X
	Economic health resource usage (Developed by HERU, University of Aberdeen)	X		X
Cardiovascular risk	Blood sampling for lipids	X		X
	Blood pressure	X		X
Diabetes risk	HbA1c	x		x

Data collection will occur at baseline, 12 weeks and 12 months. Data will be collected by the blinded research nurses from the clinical research centres in each location (trained on the study protocol) at baseline and 12 months, and over the telephone at 3 months, and entered directly onto study Case Report Forms and questionnaires. Detailed Standard Operating Procedures (SOPs) will be provided on each aspect of the protocol to ensure consistent methodology is used by all staff.

At baseline, along with the collection of demographic and background (e.g. menopausal and smoking status) data by questionnaire, any contraindications to physical activity will also assessed using the PAR-Q physical activity readiness questionnaire[39,40]. Where required, and in all women aged 70, participants will be asked to seek advice from their GP before becoming more physically active. Height will also be measured to the nearest 1mm using a calibrated stadiometer, with shoes removed, in order to determine BMI and confirm eligibility.

Co-primary outcomes will be change in body weight and change in physical activity by 12 months. Both will be measured as the mean difference between groups at 12 months adjusted for baseline, site and Scottish Index of Multiple Deprivation (SIMD)[29]. Weight will be measured to the closest 100g, in light indoor clothing and without shoes, heavy jewellery or pocket contents, using regularly calibrated electronic scales. Physical activity will be objectively measured using thigh worn activPAL™ (PAL Technologies Ltd., Glasgow, UK) accelerometers. These monitors measure free-living sedentary, upright and ambulatory activity and provide data on step count and time spent sedentary. The devices will be fitted by the research nurses to ensure correct placement, and the participants will be asked to wear them at all times (excluding when swimming or bathing) for 8 nights to ensure a full 7 days of recording. A demonstration and instructions will be provided in case removal is required.

Secondary outcomes will be changes in waist circumference, modes (types) of physical activity, sedentary behaviour, eating habits, alcohol intake, psycho-social variables, economic outcomes, HbA1C, non-fasting lipids and non-fasting insulin, blood pressure, and cardiovascular disease risk (incorporating blood pressure and lipid measures).

Waist circumference will be measured midway between the iliac crest and lower costal margin using a Seca 201 measuring tape. Modes of physical activity will be determined from a 7 day recall questionnaire[41], and sedentary behaviour from analysis of the activPAL™ data. Questionnaire based tools will be used to determine eating habits, alcohol intake, psycho-social variables (e.g. illness perception, knowledge and beliefs about lifestyle and breast

cancer risk, and personal health resources e.g. motivation, awareness and social support around weight management, self-monitoring, and perceived ability to manage weight) (see Table 1). In order to determine the economic outcomes of the trial, data on health-related quality of life was collected using the EQ-5D-5L questionnaire42, along with questions on use of NHS health care resources (number of primary care contacts, inpatient, outpatient and day cases).

Blood pressure will be measured using a Microlife 3BTO digital blood pressure monitor, or other approved BP monitor in the local clinical research facility, with the participant seated and relaxed. One non-fasted blood sample will be taken per person at both the baseline and 12 month follow up visits in order to measure HbA1C, non-fasting lipids and non-fasting insulin. Samples will be processed and stored at local clinical research centres and shipped in batches to Glasgow University laboratories for analysis. All samples will be analysed in a blinded fashion anonymised fashion at the same time to minimise analytical variation, with no individual results being made available to participants.

Delivery Outcomes: In addition to the intervention delivery time recording and fidelity assessments described earlier, delivery will be also be evaluated in terms of engagement (recruitment and retention), using data collected by coaches, exit questionnaires and through interviews with coaches and participants to record their experiences.

Process Evaluation

These measures are aimed at identifying feasibility and acceptability issues pertinent to decisions about roll-out:

a) Breast Screening centres

- Observations from the waiting room by the research team will be conducted on 2 occasions per site before and after recruitment commences. Data on clinic start and end times will be noted and mammography staff asked to provide comments relating to clinic flow.
- In order to estimate the reach of endorsements by mammographers, we will request that clinic numbers are obtained (preferably as appointments attended), and track total ActWELL cards provided to clinics and total cards returned.
- A sample of mammographers will be invited to participate in individual semi-structured qualitative interviews 1 interview per site, total n=4) to explore perceptions and experiences of recruitment, including perceived ease of study introduction, time burden, positive and negative experiences that have arisen,

handling of questions, support from clinic staff and training from research team. Interviews will be conducted shortly after the end of the study recruitment period (e.g. September 2018) to enable mammographers to reflect on experiences over the whole period while recall is still relatively fresh.

b) Breast Cancer Now are collecting information on

- advertising for coaches (where, when and costs),
- responses to advertising (applications and telephone/email queries)
- Time and volunteer/coach experience of joint training programme with ActWELL team
- Volunteer Coach reported problems, queries and reasons for drop out
- Co-ordinators' experience of managing coaches

This data will be used to inform the economic analysis.

c) Breast Cancer Now lifestyle coaches will be asked to collect data on participant contacts

- Number of face to face visits attended
- Number of phone calls achieved
- Time taken for each contact
- Perceived engagement at each contact
- A sample of coaches from each site (2 per site, total n=8) will be invited to participate in individual semi-structured qualitative interviews to explore perceptions and experiences of delivery, including recruitment, training, implementation, participant contact procedures, perception of intervention acceptability, time commitments and exit strategies. The interviews will also explore coaches' perceptions of facilitators and barriers to participant engagement in the programmes. Interviews will be conducted shortly after the end of the delivery period.

d) Leisure centres

- A sample of 4 Leisure Centre co-ordinators will be invited to participate in individual semi-structured qualitative interviews to explore their perceptions and experiences of hosting the coach sessions, including burden, space, time, challenges, and any potential benefits or negative consequences for the Leisure Centre. Interviews will be conducted shortly after the end of the delivery period (e.g. May 2019) to enable co-

ordinators to reflect on experiences over the whole period while recall is still relatively fresh.

e) Participants

Semi-structured qualitative interviews will be conducted with 20 intervention participants (5 per study site) after expression of an interest to participate during the final 12 month visit. Interviews will be conducted via telephone. Interviews will be conducted at the end of each participant's period of engagement in the study to allow participants to reflect over the entire period of their engagement while recall is still relatively fresh. We decided not to interview participants during their engagement in the study so as to avoid introducing any intervention effects which might have arisen from participants being sensitised to the questions and issues under discussion.

A semi-structured interview schedule designed to cover key topics whilst also eliciting additional participant perspectives will be used. Interviews will cover participants' views and experiences of engaging with the study, including motives for participation and understanding of the study purpose; possible impact of the study on attendance for screening; perceptions and opinions of the programme content, duration, accessibility intensity, recruitment and exit strategy; views of the coaching process and experience of setting goals; experiences of attempting to make changes over the 12 month intervention period and the facilitators and barriers to making changes. Possible facilitators and barriers to be explored include personal beliefs, motivation, family members, social and coach support. With the consent of participants, all interviews will be audio-recorded.

Statistical considerations

Sample size

Body weight: Using the data from the overweight women (BMI > 25 kg/m^2) in the ActWELL feasibility study (mean body weight 80.9± 17.9kg) a total of 414 women (207 per group) would be needed to detect a 7% weight change at 90% power. Allowing for 25% drop out (based on our findings from the feasibility study) this would mean randomising 552 women. Based on feasibility data we estimate that we would need 849 women to express an interest in the study which allows for 25% who would be ineligible on grounds of BMI<25kg/m^2 and 10% who initially express interest then change their minds. The NHSSBSP screens thousands of women each year so we do not anticipate any problems with 849 women expressing an interest in the study.

Physical activity: Given that the activity data from the ActWELL feasibility study was based on self-report, an objective measurement of steps using pedometers in the predominantly (80%) female participants of the 'Walking for Wellbeing in the West' study[43] was used to inform the sample size calculation. At baseline, a mean of 6,802 ± 3,212 steps were recorded in the intervention group. In order to detect a difference of 2,000 steps between groups at follow-up, at 90% power, 102 women (51 per group) would be required to complete this aspect of the study using ActivPAL accelerometers (shown to be feasible in studies of older adults and enabling accurate estimates of activity and sedentary behaviour[44]). Allowing for 20% drop out plus any equipment malfunction/postal losses we would recruit a further 30% bringing the total enrolment to 146 of the 552 participants for this aspect of the study. In summary a sub-sample of 146 the 552 women recruited above will be asked to wear the accelerometers.

Quantitative analysis

Statistical analysis of outcomes will be undertaken by statisticians at Tayside Clinical Trials Unit (TCTU). In the main analysis we will use an intention to treat analysis with all available data. We will undertake multiple linear regression analyses with mixed effects models adjusted for the corresponding baseline values with group allocation and site as fixed effects. For the primary outcomes we will also undertake a sensitivity analysis using both repeated measures and multiple imputations for missing values.

We do not anticipate that clustering effects will be a substantial issue in ActWELL, which is why we have designed the trial as individually randomised. We anticipate 24 or more Breast Cancer Now lifestyle coaches delivering the intervention, making each cluster small at around 10 participants. It is possible that even more lifestyle coaches will be involved depending on the capacity of BCN. We also anticipate that participants will be evenly distributed across the four breast screening centres rather than having a dominant centre. We will, however, look for evidence of clustering effects as a secondary analysis and present and interpret our results in light of this analysis.

Missing data

The extent of missing data will be examined and, if necessary, methods such as multiple imputation will be implemented to provide robust results, assuming data are missing at random (MAR). We will examine the extent of missing data by considering the differences between those with complete data and those with missing and if they are similar we will assume data is missing completely at random (MCAR). If they do differ we will assume MAR and use multiple imputations and compare with the primary analysis. We will try to obtain

reasons for missing data during the trial and if the probability of missing data is related to the outcome then data may be not missing at random (NMAR). If this looks likely, then mechanisms of missingness and outcomes will be modelled together.

Qualitative analysis

All interview recordings will be transcribed in full for analysis. Transcripts will be coded for thematic analysis, with the coding themes to be agreed among the researchers based on the core questions and topic areas, including any new and emerging themes. The reliability of the themes will then be reassessed by a process of familiarisation with the transcript texts. Discussions between researchers will enable identification of emerging themes and resolution of interpretive difference.

Cost effectiveness analysis

Intervention Costs data will be collected by health economics team including

- Breast Cancer Now costs (co-ordinator salary, training, transport)
- Intervention consumable costs (training packs and participant materials)
- Intervention delivery staff costs (coach training, mentoring and overseeing costs)

The cost-effectiveness analysis of the ActWELL intervention compared with usual care will be based on resource use and outcomes (EQ-5D-5L) data42 (collected from participant's questionnaires and telephone interviews). This will take the format of a within-trial cost-effectiveness analysis and use a cost-utility analysis framework. The effects of the ActWELL intervention will be estimated as gain in quality-adjusted life years (QALYs) at 12 months using EQ-5D-5L data collected at baseline, 3 and 12 months. Estimates of cost-effectiveness will be expressed as the incremental cost per QALY gained (over 12 months).

Public Advisory Group

The public advisory group will be involved in every aspect of the trial. This is particularly important with respect to issues including inequalities, access to intervention, recruitment, perspectives on written, verbal and e-communications, interpretation of qualitative data and dissemination events. The group consists of 3 patient representatives from breast screening attendees recruited by Breast Cancer Now plus a patient advisor on the investigation team (who will chair the public advisory group).

DISCUSSION

This paper describes the protocol for an RCT to determine the effectiveness and cost effectiveness of a weight management intervention targeted at women aged between 50 and 70 years of age who are invited to attend routine breast screening clinics. This is consistent with the concept that "every healthcare contact is a health improvement opportunity" as embodied within NHS Scotland's health promoting health service[48].

Current epidemiological evidence highlights adult weight gain, excess body fat, low levels of physical activity and alcohol intake as modifiable factors associated with an increased risk of developing postmenopausal breast cancer[3]. The NHS Breast Screening setting is one of only a few nationwide opportunities that offers face to face contact by a health professional to over 70% of (healthy) women aged 50 to 70 years including significant numbers of women from deprived areas (>60% of women from SIMD quintile 1 and > than 70% from quintile 2[49]) who may have no other opportunity to access free, personalised lifestyle change support. Few other free, national NHS clinical service provides a routine invitation to reach this number of women in this age group. At present, no support for lifestyle change is provided in this setting although survey and intervention work highlights the potential for engagement and behaviour change[19,28]. Recent work undertaken in Scotland in routine breast screening clinics has reported that a simple women's magazine intervention about breast cancer risk produced by The Scottish Cancer Prevention Network resulted in 60% of respondents claiming an increased knowledge about breast cancer, lifestyle and motivation to find out more about cancer prevention with 40% of respondents expressing intentions to make lifestyle changes[50]. It was notable that there was no difference in results by social position. Whilst concerns have been raised about the potential for increasing health inequalities through individual level interventions, a recent Cochrane review has reported that individual obesity management interventions (in both children and adults) do not increase health inequalities[51].

Whilst the current trial has primary outcomes of increased physical activity and weight loss, the programme will target energy expenditure (caloric usage in physical activity) and dietary intake (caloric intake from foods, soft and alcoholic drinks). The length of the study is designed to embrace the principles of weight loss and weight loss maintenance and therefore has the potential to achieve a long term change in lifestyle habits. The study has been developed from a well conducted feasibility trial with positive indicative outcomes and utilises a gold standard multi-centre, randomised control design methodology. The development of the intervention is a unique combination of staff from academia, NHS, breast cancer charity and healthy screening attendees and employs a novel approach to

deliver weight management by volunteers in community locations. The study is not powered to assess long term risk of breast cancer and indeed the intervention would need to demonstrate effective weight loss prior to investment in a cancer outcomes trial. There have been no trials of primary prevention of breast cancer using a weight management intervention (largely due to length of follow up and study size). However, there are a number of ongoing trials of weight management interventions in women with a breast cancer diagnosis which will report on cancer and all-cause mortality end points (as described by Demark-Wahnefried et al[52]).

It should be noted that the trial is also designed to collect information relevant for clinicians and policy makers responsible for considerations about the potential roll out of the programme throughout the national NHS breast screening programme drawing on feedback from screening staff and participants. This trial is highlighted within the National Cancer Strategy as an investment from Scottish government in cancer prevention[53]. The programme may also have salience internationally where population based breast cancer screening programmes are offered.

Figure Legend

Figure 1 Study Flow Chart

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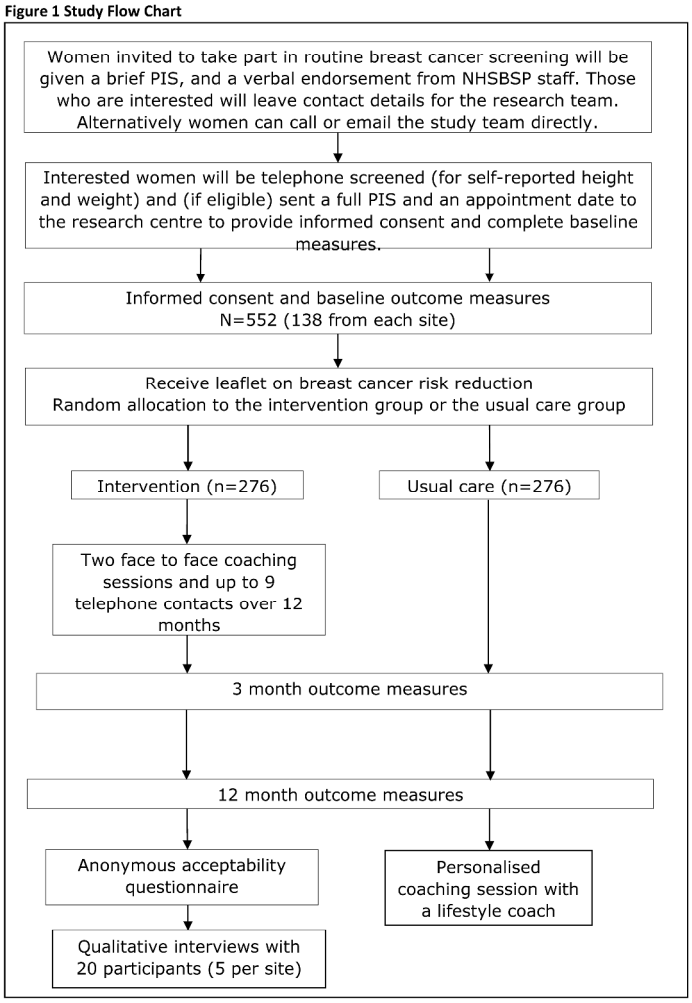
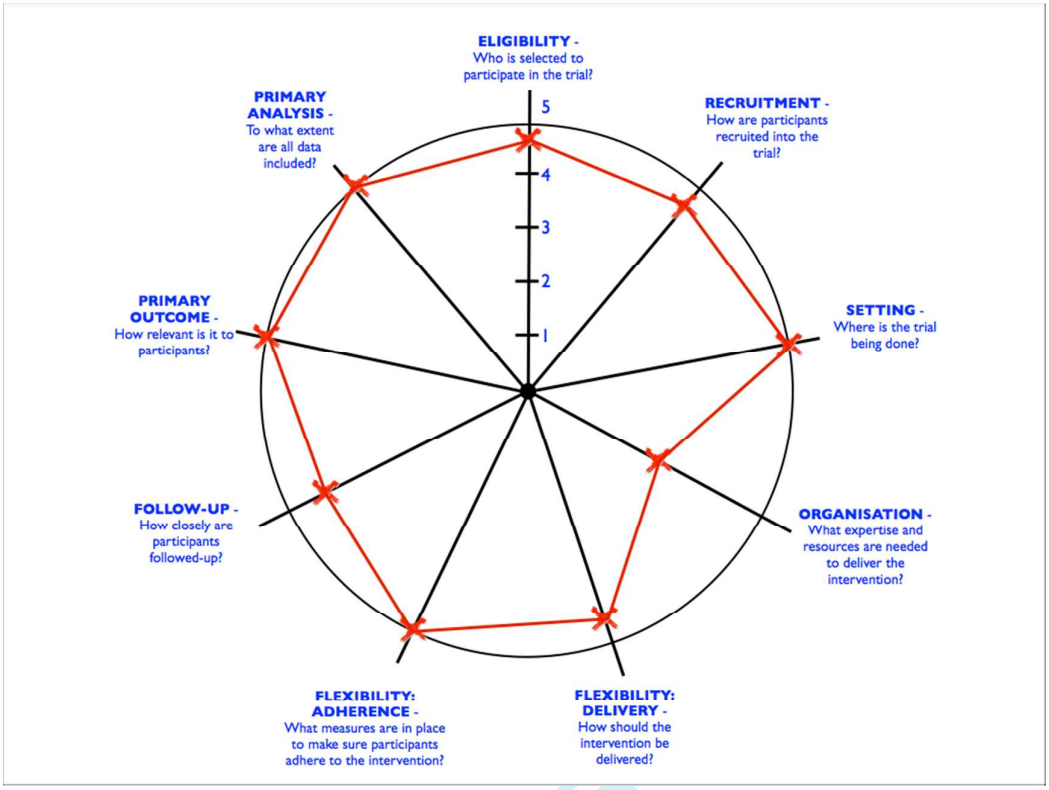
Figure 1 Study Flow Chart



Appendix 1

PRECIS – 2 for ActWELL



PRECIS-2 wheel for the ActWELL trial.

The trial aims to be highly pragmatic in design approach, which is reflected in the wheel with the exception of the *Organisation* domain. The ActWELL intervention involves a new way of delivering lifestyle counselling (Breast Cancer Now volunteers) so the trial is more explanatory on this domain. Evaluating this mode of delivery is, however, the aim of the trial and should the intervention prove effective, the trial would provide support for involving the voluntary sector in routine delivery of the ActWELL intervention.

More information on PRECIS-2 is available at https://www.precis-2.org and in Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ 2015; 350: h2147–7.

Appendix 2

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

1. Brief Name

ActWELL

2. WHY

Following the COM-B model the intervention aims to incorporate increased **M**otivation for weight management (through awareness raising within the teachable moment setting) combined with increased **C**apability for effective lifestyle change combined with **O**pportunities for greater physical activity through an emphasis on walking initiatives and other community facilities using taxonomy-derived effective behaviour change techniques.

3. WHAT

a) Materials

Visit 1

- Touch, Look Check leaflet (http://breastcancernow.org/sites/default/files/public/tlc_breast_awareness_guide.pdf)
- Breast cancer and lifestyle FAQ and links to science base (WCRF) (in house developed)
- BMI chart to identify BMI number and weight status (NHS)
- Assessing baseline step count (in house developed)
- Physical activity recommendations from UK Department of Health
- Kettlecise ways to reduce sedentary behaviour (http://www.cancerpreventionscotland.org.uk/resources/kettlecise/)
- Warm up exercises (in house developed)
- Walking Plan and Diary (in house developed)
- Implementation intention sheets (in house developed)
- Information sheet on calories and alcohol infographic https://www.behance.net/gallery/5830267/Calories-Alcohol-infographic
- Sugar savvy quiz https://www.wcrf-uk.org/sites/default/files/are-you-sugar-savvy-game.pdf
- Weight awareness plan (weekly weight logbook) (in house developed)
- Five day food and drink diary (in house developed)

Visit 2

- Eatwell Guide (NHS Tayside)
- Personalised weight loss plan (British heart Foundation)

- Implementation Intentions sheet (in house developed)
- Portion distortion quiz
- Food Labelling Guidance – credit card size (NHS Tayside)
- British Heart Foundation Booklet 'Your simple guide to weight loss' https://www.bhf.org.uk/publications/healthy-eating-and-drinking/facts-not-fads---your-simple-guide-to-healthy-weight-loss

b) Procedures

Overall: Two face to face visits plus nine monthly phone calls

Visit 1 (60 minutes)

- Check well-being
- Self-identification of BMI

- Instruct participant on pedometer use and proposed walking programme
- Walk and talk 10 min
  (interactive walking session and discussion about increasing physical activity)
- Physical activity goal setting
  (implementation intention setting and personalised walking programme)
- Discuss how to reduce sedentary behaviour

- Caloric value of (hot and cold) alcohol and sugary drinks discussed
  "Sugar Savvy" quiz undertaken (https://www.wcrf-uk.org/sites/default/files/are-you-sugar-savvy-game.pdf)
  (advice given on alternatives, portion size, frequency)
  (Possibility of implementation intention setting on drinks)

- Weight loss goal
  (emphasis on modest up to 7% in 12 months)
- Motivational interviewing questions on weight loss
- Guidance on weekly self-weighing, reporting and feedback–
  (implementation intention setting for weighing– scales available for home use)

- Initial dietary challenges – snacking and "weakness foods"
  (based on a verbal 24 hour intake)

- Summarise meeting – goals set, times of relapse

- All participants invited to undertake a 24 hour written diet recall for 5 days for review at visit 2

Visit 2 (45 minutes)

- Check well being
- Praise success (however modest)
- Evaluate and appraise PA goals
  (Discuss how they feel physically and mentally about success of walking, or problems and possible solutions, review goals)
- Check body weight recorded

- Reminder about body weight and breast cancer risk reduction (even after 50)

- Highlight weight loss principles
  (revising snacking, importance of meal patterns and 5 a day)
- Remind about goal set for weight loss and how this converts to personal eating plan

- Review 24 hour diet recall sheets (handed out last visit)
  (or take a 24 hour recall if sheets not completed)
- Discuss calories – focus on -600kcal deficit diet
  (Identify personalised eating plan using British Heart Foundation (BHF) materials)
- Discuss Portion sizes and frequencies
  (use images from BHF materials and portion distortion information)

- Food labelling
  (Identify energy values for low and high, advise avoiding red TL, advise using at home)
- Identify Implementation intentions on one food/drinking habit
  (set one only- if suggestions needed base on 24 hour recordings)

- Summarise goals and key challenges, check all materials provided
- Arrange first two telephone appointments
- Discuss leisure centre activity to meet staff (if interested)

Phone Calls
For all calls:

- Check well being
- Check goal progress, self-reported weight, re-enforce the importance of self-monitoring
- Identify success and challenges
- Discuss possible problems ahead (e.g. holidays)
- Coping strategies and starting again if intentions failed
- Start discussion on the importance of habits in eating behaviours using Ten Top Tips.

Weight Loss and Weight Loss Maintenance (using Ten Top Tips)

- Stress the importance of physical activity and socials support Refer to *Tips Walk off the weight (TC1)*
- Highlight the role of lower calorie and lower fat foods Refer to *Go Reduced Fat and Look at the Labels (TC2)*
- Highlight the importance of regular food intake (including breakfast) and portion size Refer to *Keep to your meal routine and Focus on Food (TC3)*
- Stress the importance of physical activity and social support Refer to *Tips Walk off the weight (TC4)*
- Re-enforce information on snacking Refer to *Pack a Healthy snack* and *Five a Day (TC5)*
- Re-enforce information on drinks sweet and alcohol and value of water Refer to *Think about your drinks* (TC6)

- Re-evaluate portions size (as per BHF booklet) Refer to *Caution with your portions*(TC7)
- (TC 8) return to discussing physical activity and reducing sedentary behaviour Refer to *Up on your feet*
- Re-evaluation of goals, where next , summarise success (TC9)

4. WHO PROVIDED

The intervention will be delivered by Breast Cancer Now Volunteer coaches. These will have a background and experience of counselling and receive a bespoke training programme by the research team including

- Evidence base for reducing risks of breast cancer by lifestyle
- Key principles and application of healthy food and drinks choices, appropriate portions and coping with social consumption challenges
- Key principles and application of increased physical activity and reduced sedentary behaviour
- Key principles and application of weight management
- Personalisation of advice
- Motivational interviewing techniques (key questions only)
- Use of evidence-based behavioural change techniques (BCTs)
- Handling confidential data
- The intervention protocol and importance of its delivery. Confidentiality.
- Role play and assessments (face to face and telephone contact)
-

The programme is likely to be delivered over 4 bespoke sessions training programme. An exit certificate will be provided for those who successfully achieve the assessments and role play.

Role play and observations will be undertaken prior to commencing the actual intervention.

5. HOW

Two individual 1:1 coach to participant face to face visits are planned (approx. 6 weeks apart) with monthly telephone contacts thereafter.

6. WHERE

The face to face visits are scheduled to take part in office space in local leisure centres. Each town has identified more than one possible venue and these will be noted. No home visits are scheduled and other locations are discouraged.

7. WHEN and HOW MUCH

The coaches will collect data for each participant on; date of contact, duration of contact and perceived engagement for both face to face and 9 telephone contacts. Other contacts e.g. SMS/email will also be noted. These data will allow dose and duration and outcomes to be assessed by individual coaches as well as overall.

8. TAILORING

Personalised advice is a key component of all aspects of the intervention. Motivational interviewing about weight loss will be undertaken to identify participant ambivalence and perceived personal advantages to weight management.

Caloric prescription: this will be based on -600kcals required for weight maintenance (calculated using the equations from Miflin St Jeor according to gender, age and body weight). Participant agreed goals (and implementation intentions) will be used for weighing and recording body weight (self-monitoring) and personalised feedback will be provided.

Food and drink choices will be based on information obtained from current eating habits obtained through 24 hour recalls to guide personalised advice on food frequency, portion sizes and foods to limit. Participant agreed goals (and implementation intentions) will be used for one specific food or drinking habit and this will be self monitored with personalised feedback provided.

Physical activity dose and duration will be based on the brief Scottish Physical Activity questionnaire to guide walking plans and signpost other activities (including those offered in the local leisure centres). Participant agreed goals (and implementation intentions) will be used for one specific aspect of habitual walking and this will be self- monitored with personalised feedback provided

9. MODIFICATIONS

Recommendations for modifications may arise from

a) Feedback from coaches (individual issues or during regular round table meetings)
b) Changes in evidence base for guidance
c) Adverse events

10. HOW WELL

Fidelity Procedures: We will undertake qualitative process measures to assess fidelity to the intervention. Time for implementation procedures will be recorded by intervention staff. Fidelity of programme delivery and content will be assessed by audio-recording and transcription of a random sample of LC face to face interactions and telephone contacts at each site. These will be compared to the protocol specified number of points to be covered in each session by a researcher at University of Stirling independent from the intervention.

BMJ Open

A randomised controlled trial to assess the impact of a lifestyle intervention (ActWELL) in women invited to NHS breast screening – study protocol

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A randomised controlled trial to assess the impact of a lifestyle intervention (ActWELL) in women invited to NHS breast screening – study protocol

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ABSTRACT

Introduction In Scotland, the incidence of breast cancer is predicted to rise significantly in the next few decades and whilst there are measures to support reductions in morbidity and mortality, the breast cancer community is currently exploring preventative opportunities including supporting weight management programmes in post-menopausal women. This study aims to assess the effectiveness and cost-effectiveness of a theory- based, community delivered, minimal contact, weight management (diet, physical activity and behaviour change techniques) programme (ActWELL) in women with a BMI >25 kg/m2 attending routine breast cancer screening appointments.

Methods and analysis The study will be a 4 centre, 1:1 parallel group RCT of a 12 month weight management intervention initiated in breast cancer screening centres, delivered by trained Breast Cancer Now lifestyle coaches in community settings. The intervention programme involves 2 intervention meetings with coaches plus (up to) nine telephone contacts over 12 months. The programme will focus on personalised diet (including alcoholic and sugary drinks) and physical activity habits. Behaviour change techniques include self-monitoring, goal setting, implementation intentions, action and coping plans. The study has a sample size of 414 women with a BMI>25 kg/m^2 attending routine national **NHS** breast cancer screening appointments. Measures will be taken at baseline, 12 weeks and at 12 month follow up, complemented by qualitative interviews exploring perceived acceptability and impact on habitual behaviours. The two co-primary outcomes are mean change in measured body weight and change in physical activity between groups to 12 months. Secondary outcomes are changes in eating habits, alcohol intake, sedentary time, quality of life, waist circumference, lipid, HbA1c and insulin profiles, blood pressure, and cost-effectiveness of the intervention.

Ethics and dissemination The protocol has been approved by East of Scotland Research Ethics Committee (17/ES/0073). All participants provide written informed consent. Dissemination will be through peer-reviewed publication and conference presentations.

Trial registration number ISRCTN11057518

Keywords Cancer prevention, breast cancer, screening, lifestyle, behaviour modification

Article Summary

Strengths and limitations of this study

- This work has the potential to provide routine support for weight management for women aged over 50 years
- This study has been developed from a well conducted feasibility trial with positive indicative outcomes
- Multi-centre, randomised control design
- Strong study team combining staff from academia, NHS, breast cancer charity and healthy screening attendees
- Novel approach to deliver weight management by trained in community locations
- The study has a large potential reach with around 73% of ALL women of this age group attending appointments including high numbers from disadvantaged backgrounds
- The intervention will not be readily accessible for women who do not accept screening appointments
- Not all women interested in lifestyle change will be able to participate due to capacity issues with lifestyle coaches

Competing interest statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work other than the Scottish Government who funded the award, no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, and no other relationships or activities that could appear to have influenced the submitted work.

Clinical trials registration

Ethical approval for this study was provided by East of Scotland Research Ethics Service (REC reference: (17/ES/0073). Our initial submission to ethics in January 2017 was withdrawn as we were advised to submit the formative work to the University of Dundee ethics committee (approved 05/04/17, Ref 020/17) and the remainder to NHS ethics once the formative work was completed. This process took several months (to complete the

formative work) and delayed both the NHS ethics submission (and approval provided on 22/06/17) and the recruitment start date. This resulted in a delay in registering the study with ISCRTN until the final protocol was completed and the submission details updated. This was assigned prospectively on 21/07/2017. Recruitment for the study commenced on 01/08/17 (after the registration date) with first participant randomised on 05/09/2017 due to the aforementioned project delay.

Funding

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Author Contributions

ASA is the principal investigator and has overall responsibility for all aspects of the ActWELL study. She initiated the study, designed the intervention, led on development of the protocol and drafting the manuscript. AC, CMcA and NM were involved in intervention design and training, assessment methodology, finalising the protocol, reading, editing and approving the manuscript. SG is the trial manager and responsible for co-ordinating all aspects of the ActWELL study, drafting the protocol and reading, editing and approving the manuscript. EJM has responsibility for clinical issues, inclusion and exclusion criteria, trial design, finalising the protocol and reading, editing and approving the manuscript. ARN is responsible for health economics analysis, assessment methodology, finalising protocol and reading, editing and approving the manuscript. REO'C has responsibility for all psychological aspects of intervention design, assessment methodology, fidelity measures, finalising the protocol and reading, editing and approving the manuscript. PR is responsible for statistical design, analysis plan drafting protocol and reading, editing and approving the manuscript. NS is responsible for design of blood collection procedures, overseeing analysis of bloods, finalising protocol design and reading, editing and approving the manuscript. MS is responsible for formative qualitative analysis, intervention design, acceptability measures, finalising protocol and reading, editing and approving the manuscript. ST is responsible for trial design, recruitment strategies, day to day management decisions (with ASA and SG), finalising protocol reading, editing and approving the manuscript.

Provenance and Peer Review Externally peer reviewed.

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Data Sharing Statement

None

INTRODUCTION

Breast cancer accounted for 14.5% of all cancer diagnoses in Scotland in 2014 and accounts for 28% of female cancer cases[1]. Incidence is increasing and current predictions from ISD (Scottish Government) suggest a rise by 27.5% between and 2008-2012 and 2023-2027[2].

Whilst many factors are implicated in aetiology (genetics, reproductive history, hormone use), current estimates suggest that 38% of breast cancers in post-menopausal women in the UK are related to physical inactivity, alcohol consumption and body fatness[3]. There is consistent evidence that being overweight or obese throughout adulthood increases the risk of post-menopausal breast cancer[4].

In addition, gaining weight in adult life is a strong predictor of breast cancer (especially in women who have not taken hormone replacement therapy)[5]. Ahn et al reported that at any BMI, increased weight in adult life is associated with greater risk of breast cancer and a gain of 2-10kg after the age of 50 (e.g. post-menopausal) is associated with a 30% increase in breast cancer risk[6]. Findings from the EPIC study have also demonstrated that high weight gain in middle adulthood increases the risk of breast cancer[7]. In the Women's Health Initiative, Neuhouser et al.[8] reported that post-menopausal women with a BMI<25kg/m^2 at baseline who gained >5kg of body weight during the follow up period (median 13 years) had a 36% increase risk of developing breast cancer.

Lifestyles and weight management are also related to risk reduction. Women meeting at least 5 of the World Cancer Research Fund prevention guidelines for lifestyle show a 60% lower risk for breast cancer compared to women meeting none of the guidelines[9] and a recent systematic review reported that high versus low adherence to cancer prevention guidelines was associated with consistent reductions in breast cancer incidence[10]. Data from audits of bariatric surgery show that large weight losses are associated with large decreases in female cancers[11]. One recent North American study of 22,198 people 3.5 years after bariatric surgery reported reductions in post-menopausal breast cancer of 42%[12]. In addition, moderating weight gain in adult life through caloric adjustment and being physically active is likely to be of benefit for reduction in other cancers related to these behaviours[13] as well as other non-communicable diseases[14,15].

Most (73%) Scottish women aged 50 to 70 years accept invitations to attend the routine NHS Scottish Breast Screening Programme (NHSSBSP) and over 175,000 women attend each year[16]. In addition, women aged over 70 are able to attend through self-referral. The

NHSSBSP therefore provides a unique opportunity to endorse weight management intervention. However, a greater understanding of the benefits, costs, acceptability and impacts are needed to examine whether a NHSSBSP-initiated intervention can be effective and cost efficient.

In 2007, Fisher et al.[17] reported that most women attending breast screening clinics are interested in receiving lifestyle advice, and an updated paper reporting the view of 1,803 women shows overwhelming support for receiving interventions through this setting[18]. However, a review published in 2013[19] reported that whilst the importance of weight management in breast and colorectal cancer prevention is widely recognised, there is little evidence that lifestyle is discussed within cancer screening settings. It was also noted that the lack of advocacy about health behaviour change may endorse poor health behaviours by creating a 'health certificate effect.' This issue may be particularly relevant for body weight, where a lack of guidance to visibly obese patients may imply a lack of medical concern. The cancer research "gap analysis" reviews by Breast Cancer Campaign[20,21] highlighted the role of breast screening programmes as an opportunity for promoting cancer prevention activities, but noted the challenge of finding ways to support and facilitate women to achieve healthy ways of life.

In Scotland, the breast cancer community (government, charities and health professionals) is currently exploring innovative and sustainable preventative opportunities including supporting weight management programmes. The Scottish Health Survey[22] has reported that 72% of women aged 55 to 74 years have a BMI >25kg/m^2 (76% in women living in areas of higher deprivation). Furthermore, 42% of women **do not** achieve the recommendation of 150 minutes of physical activity per week, and this proportion increases with age. The National Institute of Clinical Excellence (NICE)[23] recommend that lifestyle weight management programmes are multi component and aim to reduce a person's energy intake and help them to be more physically active by changing behaviour. However, access to such NHS programmes is limited and commercial programmes have cost implications for low income adults.

It is recognised that partnerships between the NHS and the voluntary sector offer significant value for money and the potential for greater "reach" of interventions into community settings. The recent Lancet series on obesity highlighted that, despite government efforts to reduce the prevalence of obesity, these approaches are insufficient to help adults who are currently overweight or obese[24]. Innovative strategies beyond those currently delivered by health professionals are needed to increase capacity of delivery of weight management programmes.

Community lifestyle interventions initiated in the breast cancer screening setting are a largely unexplored area although repeated triennial appointments offer unique opportunities for initiation and re-enforcement[25]. This setting also provides an opportunity to engage with women from areas of higher deprivation (63%, 71% and 76% of women from Scottish Index of Multiple Deprivation (SIMD 1, 2, 3 quintiles respectively attend for screening)[26].

The ActWELL feasibility study demonstrated that recruitment, retention, indicative results and participant acceptability merited a full randomised control trial to test the long term impact of the intervention. In addition, 31% of participants recruited were from the lowest two quintiles of deprivation[27] indicating significant potential to reach women from higher rates of social deprivation who also tend to be more obese.

Feedback from screening centre users showed whilst many were aware of lifestyle issues in relation to diabetes and cardiovascular disease, information about lifestyle and breast cancer was new and considered "motivating" if the focus was on positive ways to help support behaviour change[28].

The current study is designed to assess the effectiveness of a community based, personalised, minimal contact weight management programme in women with a BMI>25kg/m^2 attending routine breast cancer screening clinics. The intervention programme is a collaboration between the charity Breast Cancer Now (BCN), NHSSBSP, local authority leisure centres and academic partners. This work is the first time that a cancer charity has offered volunteer capacity for cancer prevention action on weight management and offers significant potential to address gaps in public health efforts. The design is pragmatic to increase the relevance of the findings to policymakers, women eligible for breast screening and health professionals (see Appendix 1).

The study aims to assess the effectiveness and cost-effectiveness of a theory based, community delivered, minimal contact, weight management (diet, physical activity and behaviour change techniques) programme (ActWELL) in women with a BMI >25 kg/m^2 attending routine breast cancer screening clinics.

METHODS AND ANALYSIS

Trial design and setting

The study will be a four centre, 1:1 parallel-arm, randomised controlled trial of a 12 month, weight management intervention. The participants will be randomly allocated into two groups (1) standard care with health information leaflet or (2) experimental group who receive the ActWEll intervention. Potential participants will be introduced to the study whilst

attending routine NHS breast cancer screening appointment (static and mobile screening units) in Scotland. The study participant flow is presented in Figure 1.

All trial measurements will be undertaken by trained research nurses at baseline, 12 weeks and 12 months within the NHS Clinical Research Centres (CRC) in the areas served by the breast screening sites.

The intervention is delivered and supported by Breast Cancer Now volunteers who have undergone two days bespoke training on the intervention. The face to face intervention communications are delivered within local authority run leisure centres (or other appropriate community locations).

Participants

All attendees at routine NHS breast screening appointments will be advised about the study by NHSSBSP staff in writing and verbally. On checking in at the clinic women will be given a brief study information leaflet by the receptionist. During their visit the mammographer will briefly (approx. 30 seconds) mention the study verbally. If they are agreeable to a researcher making contact with them, women will be invited to leave their details on a contact card (telephone/email/postcode) which they can place in a study box in the reception area. A pop up banner, or poster, will also be displayed in the breast screening clinic or mobile van to further highlight the study and how to contact the research team. All NHS screening staff will be provided with training which introduces the aims of the study, why the trial is designed the way it is, the importance of their role, how to minimise the time taken to introduce the study and how to answer common questions. Within each site, a team "champion" will be identified from within the NHSSBSP staff to encourage colleagues and co-ordinate recruitment efforts.

Research staff will contact women leaving contact cards within two weeks and assess study eligibility.

Inclusion Criteria

- Attending, or invited to attend, routine breast screening clinics (not recall clinics)
- Measured BMI >25 kg/m^2
- Age 50 to 70 years

Exclusion Criteria

- Currently undergoing treatment for any malignant condition (excluding basal or squamous cell skin cancers)
- Reported contra-indication to physical activity (e.g. recent surgery)
- Reported contra-indication to weight loss (e.g. currently following a recovery programme for weight gain)
- On a specialised diet e.g. gluten free
- Diagnosis of Types 1 diabetes
- Current use of insulin
- No telephone contact
- Unable to consent

Participants who are considered eligible will be invited to attend their local research centre to provide informed consent before commencing baseline measures.

Participants found to be ineligible to take part, either on telephone screening or at a baseline visit, will be thanked for their time and will be offered, by post or email, lifestyle and cancer prevention information and/or information on local leisure facilities applicable to them. Where possible, this will also apply to women who have expressed an interest (e.g. left a completed card) but who have not been selected to take part in the trial due to the volume of people that can be seen by the research team. In the event of very large numbers of cards being returned it may not be possible to contact all women and this is made clear in the brief information leaflet.

Randomisation

Participants will be randomised centrally at a 1:1 ratio into the intervention or usual care groups using the web-based TRuST system designed by Tayside Clinical Trials Unit (TCTU). Randomisation will be stratified by site and minimised by socio-economic status based on Social index of Multiple Deprivation (SIMD)[29] SIMD (two groups: SIMD 1 or 2; SIMD≥3).

In addition, a sub group comprising 146 women (73 from each group) will be randomly allocated by the TRuST system to receive an activPAL™ monitor (accelerometer) as an

objective measure of physical activity. This number has been identified to meet statistical power (see below).

Usual care group: Following the end of their baseline measures, participants will receive a cancer prevention leaflet[30]. The study administrator will then notify participants of their randomisation by letter. On completion of their 12 month follow up visit women will be offered a single personalised coaching session and the ActWELL intervention booklet.

Intervention group: Following the end of their baseline measures participants will receive a cancer prevention leaflet[30]. The study administrator will then notify participants of their randomisation by letter. The Breast Cancer Now volunteer coordinator will allocate a Breast Cancer Now Lifestyle Coach (LC) to the participant. The LC will contact the participant to arrange an appointment for their first face to face visit.

Blinding

The study team will be blind to the participants' group allocation until completion of the primary outcome analysis. Exceptions are the trial manager, study administrator, lifestyle coaches and participants who cannot be blinded owing to the nature of the intervention.

Intervention

Initial work focused on optimising the intervention to scale up the previous prototype for a 12 month follow up period. This was developed from the original feasibility study protocol and using feedback obtained from study participants and lifestyle coaches. Later feedback came from our recent research study offering a weight management lifestyle intervention to women attending family history clinics[31] and our newly formed ActWELL public advisory team. The proposed study builds on existing behaviour change models[32] particularly the COM-B model[33]. Thus, the intervention aims to incorporate **capability** for effective lifestyle change combined with **opportunities** for greater physical activity through an emphasis on walking initiatives and other community facilities (using taxonomy-derived effective behaviour change techniques[34]) and increased **motivation** for weight management (through awareness raising within the teachable moment setting).

In addition, four formative qualitative focus groups with individuals in the target population were held to obtain feedback on the prospective 12 month intervention including refinements on alcohol messaging.

Intervention content: The initial part of the intervention (months 1 to 3) will focus on helping achieve 7% of body weight loss (consistent with the lifestyle intervention in the

highly effective Diabetes Prevention Programme[35]) and the remaining months will also combine techniques for weight loss maintenance (WLM) by addressing both caloric intake and energy expenditure.

Behavioural change techniques (BCT) include goal setting, implementation intentions, self-monitoring of body weight and feedback. The latter may be particularly important for WLM. This part of the intervention will take a habit–formation based approach using the Ten Top Tips shown to be successful for WLM over a 2 year period[36]. Social support will be encouraged throughout the 12 months through regular coach contact and encouragement to share the intervention with a friend/buddy. The initial introduction to the leisure centre will also provide an introduction to locally available exercise facilities and classes.

Tailored personalised advice is a key component of all aspects of the intervention. Motivational interviewing about weight loss will be undertaken to identify participant ambivalence and perceived personal advantages to weight management.

The **caloric prescription** will be based on 600kcals below that required for weight maintenance (calculated using the equations for basal metabolic rate according to gender, age and body weight).

Food and drink choices will be based on information obtained from current eating habits obtained through 24 hour recalls to guide personalised advice on food frequency, portion sizes and foods to limit. Participant agreed goals (and implementation intentions) will be used for one specific food or drinking habit and this will be self-monitored with personalised feedback provided.

Physical activity dose All participants will undertake the Scottish Physical activity screening questionnaire (Scot-PASQ)[37] by the coach as an indicator of current activity levels to help guide the communications about walking plans and signpost other activities (including those offered in the local leisure centres). Participant agreed pedometer goals (and implementation intentions) will be used for habitual walking and this will be self-monitored with personalised feedback provided. Participants will be supported to gradually increase physical activity towards accumulating at least 150 minutes of moderate intensity physical activity per week and then, where appropriate, towards 300 minutes per week (Based on Scottish Intercollegiate Guidelines Network (SIGN)[38] guidance on weight management.

A detailed description of each intervention visit and telephone calls are provided in Appendix 2.

Intervention delivery There will be two face to face intervention meetings (one of 60 minutes and one of 45 minutes). Over a 12 month period there will be up to nine further contacts by telephone. The intervention programme will be delivered by Breast Cancer Now volunteers who have received the training programme to become lifestyle coaches.

Intervention fidelity We will undertake independent analysis of fidelity to the intervention. Fidelity of programme delivery and content will be assessed by audio-recording and transcription from a purposeful sample of approximately 10% of ActWELL lifestyle coaches including face to face interactions and telephone contacts at each site. A researcher independent from the intervention delivery will analyse the transcripts and evaluate the proportion of points covered in each session relative to those described in the intervention protocol. Time for implementation procedures will be recorded by the lifestyle coaches.

Outcome measures

A full list of measurable outcomes and sources ([39,40,41,42]) is presented in Table 1.

Table 1 Outcome Measures

Primary Outcomes		Baseline	12 week	12 month
Body weight	Measured using digital body weight scales (kg)	X		X
Physical Activity	7 days accelerometry with ActivPAL (steps)	X		X
Secondary outcomes				
Modes of physical activity	Scottish Physical Activity Questionnaire SPAQ[34]	X	X	X
Sedentary behaviour	7 days accelerometry with activPAL™ (subsample only)	X		X
Anthropometric changes	BMI (height and weight) Waist circumference (cm)	X		X
Eating habits	Questionnaire based on Scottish Health Survey[22]	X		X
	• Fruit and vegetable intake[39]		X	
Alcohol intake	Audit C questionnaire[40]	X		X
Psycho-social variables	Modified brief illness questionnaire[41]	X		X
	Knowledge and beliefs about lifestyle and breast cancer risk (developed in house)	X		X
	Psychosocial health measures resources (perceived motivation, awareness, ability, action, monitoring, and social support around weight management)			X
	Perceived body weight (developed in-house)	x	x	x
Economic outcomes	EQ5D-5L questionnaire[42]	X	X	X
	Economic health resource usage (Developed by HERU, University of Aberdeen)	X		X
Cardiovascular risk	Blood sampling for lipids	X		X
	Blood pressure	X		X
Diabetes risk	HbA1c	x		x

Data collection will occur at baseline, 12 weeks and 12 months. Data will be collected by the blinded research nurses from the clinical research centres in each location (trained on the study protocol) at baseline and 12 months, and over the telephone at 3 months, and entered directly onto study Case Report Forms and questionnaires. Detailed Standard Operating Procedures (SOPs) will be provided on each aspect of the protocol to ensure consistent methodology is used by all staff.

At baseline, along with the collection of demographic and background (e.g. menopausal and smoking status) data by questionnaire, any contraindications to physical activity will also assessed using the PAR-Q physical activity readiness questionnaire[43,44]. Where required, and in all women aged 70, participants will be asked to seek advice from their GP before becoming more physically active. Height will also be measured to the nearest 1mm using a calibrated stadiometer, with shoes removed, in order to determine BMI and confirm eligibility.

Co-primary outcomes will be change in body weight and change in physical activity by 12 months. Both will be measured as the mean difference between groups at 12 months adjusted for baseline, site and Scottish Index of Multiple Deprivation (SIMD)[29]. Weight will be measured to the closest 100g, in light indoor clothing and without shoes, heavy jewellery or pocket contents, using regularly calibrated electronic scales. Physical activity will be objectively measured using thigh worn activPAL™ (PAL Technologies Ltd., Glasgow, UK) accelerometers. These monitors measure free-living sedentary, upright and ambulatory activity and provide data on step count and time spent sedentary. The devices will be fitted by the research nurses to ensure correct placement, and the participants will be asked to wear them at all times (excluding when swimming or bathing) for 8 nights to ensure a full 7 days of recording. A demonstration and instructions will be provided in case removal is required.

Secondary outcomes will be changes in waist circumference, modes (types) of physical activity, sedentary behaviour, eating habits, alcohol intake, psycho-social variables, economic outcomes, HbA1C, non-fasting lipids and non-fasting insulin, blood pressure, and cardiovascular disease risk (incorporating blood pressure and lipid measures).

Waist circumference will be measured midway between the iliac crest and lower costal margin using a Seca 201 measuring tape. Modes of physical activity will be determined from a 7 day recall questionnaire[45], and sedentary behaviour from analysis of the activPAL™ data. Questionnaire based tools will be used to determine eating habits, alcohol intake, psycho-social variables (e.g. illness perception, knowledge and beliefs about lifestyle and breast

cancer risk, and personal health resources e.g. motivation, awareness and social support around weight management, self-monitoring, and perceived ability to manage weight) (see Table 1). In order to determine the economic outcomes of the trial, data on health-related quality of life was collected using the EQ-5D-5L questionnaire[42], along with questions on use of NHS health care resources (number of primary care contacts, inpatient, outpatient and day cases).

Blood pressure will be measured using a Microlife 3BTO digital blood pressure monitor, or other approved BP monitor in the local clinical research facility, with the participant seated and relaxed. One non-fasted blood sample will be taken per person at both the baseline and 12 month follow up visits in order to measure HbA1C, non-fasting lipids and non-fasting insulin. Samples will be processed and stored at local clinical research centres and shipped in batches to Glasgow University laboratories for analysis. All samples will be analysed in a blinded fashion anonymised fashion at the same time to minimise analytical variation, with no individual results being made available to participants.

Delivery Outcomes: In addition to the intervention delivery time recording and fidelity assessments described earlier, delivery will be also be evaluated in terms of engagement (recruitment and retention), using data collected by coaches, exit questionnaires and through interviews with coaches and participants to record their experiences.

Process Evaluation

These measures are aimed at identifying feasibility and acceptability issues pertinent to decisions about roll-out:

a) Breast Screening centres

- Observations from the waiting room by the research team will be conducted on 2 occasions per site before and after recruitment commences. Data on clinic start and end times will be noted and mammography staff asked to provide comments relating to clinic flow.
- In order to estimate the reach of endorsements by mammographers, we will request that clinic numbers are obtained (preferably as appointments attended), and track total ActWELL cards provided to clinics and total cards returned.
- A sample of mammographers will be invited to participate in individual semi-structured qualitative interviews 1 interview per site, total n=4) to explore perceptions and experiences of recruitment, including perceived ease of study introduction, time burden, positive and negative experiences that have arisen,

handling of questions, support from clinic staff and training from research team. Interviews will be conducted shortly after the end of the study recruitment period (e.g. September 2018) to enable mammographers to reflect on experiences over the whole period while recall is still relatively fresh.

b) Breast Cancer Now are collecting information on

- advertising for coaches (where, when and costs),
- responses to advertising (applications and telephone/email queries)
- Time and volunteer/coach experience of joint training programme with ActWELL team
- Volunteer Coach reported problems, queries and reasons for drop out
- Co-ordinators' experience of managing coaches

This data will be used to inform the economic analysis.

c) Breast Cancer Now lifestyle coaches will be asked to collect data on participant contacts

- Number of face to face visits attended
- Number of phone calls achieved
- Time taken for each contact
- Perceived engagement at each contact
- A sample of coaches from each site (2 per site, total n=8) will be invited to participate in individual semi-structured qualitative interviews to explore perceptions and experiences of delivery, including recruitment, training, implementation, participant contact procedures, perception of intervention acceptability, time commitments and exit strategies. The interviews will also explore coaches' perceptions of facilitators and barriers to participant engagement in the programmes. Interviews will be conducted shortly after the end of the delivery period.

d) Leisure centres

- A sample of 4 Leisure Centre co-ordinators will be invited to participate in individual semi-structured qualitative interviews to explore their perceptions and experiences of hosting the coach sessions, including burden, space, time, challenges, and any potential benefits or negative consequences for the Leisure Centre. Interviews will be conducted shortly after the end of the delivery period (e.g. May 2019) to enable co-

ordinators to reflect on experiences over the whole period while recall is still relatively fresh.

e) Participants

Semi-structured qualitative interviews will be conducted with 20 intervention participants (5 per study site) after expression of an interest to participate during the final 12 month visit. Interviews will be conducted via telephone. Interviews will be conducted at the end of each participant's period of engagement in the study to allow participants to reflect over the entire period of their engagement while recall is still relatively fresh. We decided not to interview participants during their engagement in the study so as to avoid introducing any intervention effects which might have arisen from participants being sensitised to the questions and issues under discussion.

A semi-structured interview schedule designed to cover key topics whilst also eliciting additional participant perspectives will be used. Interviews will cover participants' views and experiences of engaging with the study, including motives for participation and understanding of the study purpose; possible impact of the study on attendance for screening; perceptions and opinions of the programme content, duration, accessibility intensity, recruitment and exit strategy; views of the coaching process and experience of setting goals; experiences of attempting to make changes over the 12 month intervention period and the facilitators and barriers to making changes. Possible facilitators and barriers to be explored include personal beliefs, motivation, family members, social and coach support. With the consent of participants, all interviews will be audio-recorded.

Statistical considerations

Sample size

Body weight: Using the data from the overweight women (BMI > 25 kg/m^2) in the ActWELL feasibility study (mean body weight 80.9± 17.9kg) a total of 414 women (207 per group) would be needed to detect a 7% weight change at 90% power. Allowing for 25% drop out (based on our findings from the feasibility study) this would mean randomising 552 women. Based on feasibility data we estimate that we would need 849 women to express an interest in the study which allows for 25% who would be ineligible on grounds of BMI<25kg/m^2 and 10% who initially express interest then change their minds. The NHSSBSP screens thousands of women each year so we do not anticipate any problems with 849 women expressing an interest in the study.

Physical activity: Given that the activity data from the ActWELL feasibility study was based on self-report, an objective measurement of steps using pedometers in the predominantly (80%) female participants of the 'Walking for Wellbeing in the West' study[45] was used to inform the sample size calculation. At baseline, a mean of 6,802 ± 3,212 steps were recorded in the intervention group. In order to detect a difference of 2,000 steps between groups at follow-up, at 90% power, 102 women (51 per group) would be required to complete this aspect of the study using ActivPAL accelerometers (shown to be feasible in studies of older adults and enabling accurate estimates of activity and sedentary behaviour[46,47]). Allowing for 20% drop out plus any equipment malfunction/postal losses we would recruit a further 30% bringing the total enrolment to 146 of the 552 participants for this aspect of the study. In summary a sub-sample of 146 the 552 women recruited above will be asked to wear the accelerometers.

Quantitative analysis

Statistical analysis of outcomes will be undertaken by statisticians at Tayside Clinical Trials Unit (TCTU). In the main analysis we will use an intention to treat analysis with all available data. We will undertake multiple linear regression analyses with mixed effects models adjusted for the corresponding baseline values with group allocation and site as fixed effects. For the primary outcomes we will also undertake a sensitivity analysis using both repeated measures and multiple imputations for missing values.

We do not anticipate that clustering effects will be a substantial issue in ActWELL, which is why we have designed the trial as individually randomised. We anticipate 24 or more Breast Cancer Now lifestyle coaches delivering the intervention, making each cluster small at around 10 participants. It is possible that even more lifestyle coaches will be involved depending on the capacity of BCN. We also anticipate that participants will be evenly distributed across the four breast screening centres rather than having a dominant centre. We will, however, look for evidence of clustering effects as a secondary analysis and present and interpret our results in light of this analysis.

Missing data

The extent of missing data will be examined and, if necessary, methods such as multiple imputation will be implemented to provide robust results, assuming data are missing at random (MAR). We will examine the extent of missing data by considering the differences between those with complete data and those with missing and if they are similar we will assume data is missing completely at random (MCAR). If they do differ we will assume MAR

and use multiple imputations and compare with the primary analysis. We will try to obtain reasons for missing data during the trial and if the probability of missing data is related to the outcome then data may be not missing at random (NMAR). If this looks likely, then mechanisms of missingness and outcomes will be modelled together.

Qualitative analysis

All interview recordings will be transcribed in full for analysis. Transcripts will be coded for thematic analysis, with the coding themes to be agreed among the researchers based on the core questions and topic areas, including any new and emerging themes. The reliability of the themes will then be reassessed by a process of familiarisation with the transcript texts. Discussions between researchers will enable identification of emerging themes and resolution of interpretive difference.

Cost effectiveness analysis

Intervention Costs data will be collected by health economics team including

- Breast Cancer Now costs (co-ordinator salary, training, transport)
- Intervention consumable costs (training packs and participant materials)
- Intervention delivery staff costs (coach training, mentoring and overseeing costs)

The cost-effectiveness analysis of the ActWELL intervention compared with usual care will be based on resource use and outcomes (EQ-5D-5L) data[42] (collected from participant's questionnaires and telephone interviews). This will take the format of a within-trial cost-effectiveness analysis and use a cost-utility analysis framework. The effects of the ActWELL intervention will be estimated as gain in quality-adjusted life years (QALYs) at 12 months using EQ-5D-5L data collected at baseline, 3 and 12 months. Estimates of cost-effectiveness will be expressed as the incremental cost per QALY gained (over 12 months).

Patient and Public involvement

The development of research questions and outcome measures arose from pilot work[27] which included feedback from participants. A public advisory group was established comprising 3 patient representatives from breast screening attendees recruited by Breast Cancer Now, plus a patient advisor on the investigation team (who will chair the public advisory group). The public advisory group will be involved in every aspect of the trial. This is particularly important with respect to trial design and feedback, issues including

inequalities, access to intervention, recruitment, perspectives on written, verbal and e-communications, burden of study procedures (including questionnaires), interpretation of qualitative data, conduct of the study and dissemination events. In addition, information attained from formative research with screening participants will be used to assist in the design of the intervention content and delivery. After the study is complete participants will be interviewed to gain insight to the study burden and procedures. A summary of results will be available for all participants.

Ethics and dissemination

The ActWELL trial follows all procedures set out by the Tayside clinical trials unit including reporting adverse and serious adverse events. All reports will be reviewed by the senior clinician and appropriate actions taken. The intervention is considered low risk and all coaches are trained on supporting modest changes in physical activity to decrease risks associated with vigorous or intense activity.

The study dissemination plan includes reports to the funder to assist in decision making about potential roll out. Reports of the findings will also be shared with Breast Cancer Now, Scottish Screening Committee, Scottish Cancer Task Force, participating screening centres, participating leisure centres and our public advisory group. A summary of findings will be available for all participants.

Academic dissemination through papers in peer reviewed journals and conference presentations will be focussed on reporting the main impact of the intervention on primary and secondary outcomes, health economic evaluation and qualitative findings that will assist decisions about roll out. Findings related to recruitment challenges, the experience of volunteer coaches and psyco-social findings which may have impacted on process and outcomes will also reported.

Public dissemination will utilise social media channels including those of the Scottish Cancer Prevention Network, academic institutions involved and public events such as ‘café science’.

DISCUSSION

This paper describes the protocol for an RCT to determine the effectiveness and cost effectiveness of a weight management intervention targeted at women aged between 50 and 70 years of age who are invited to attend routine breast screening clinics. This is

consistent with the concept that "every healthcare contact is a health improvement opportunity" as embodied within NHS Scotland's health promoting health service[48].

Current epidemiological evidence highlights adult weight gain, excess body fat, low levels of physical activity and alcohol intake as modifiable factors associated with an increased risk of developing postmenopausal breast cancer[3]. The NHS Breast Screening setting is one of only a few nationwide opportunities that offers face to face contact by a health professional to over 70% of (healthy) women aged 50 to 70 years including significant numbers of women from deprived areas (>60% of women from SIMD quintile 1 and > than 70% from quintile 2[49]) who may have no other opportunity to access free, personalised lifestyle change support. Few other free, national NHS clinical service provides a routine invitation to reach this number of women in this age group. At present, no support for lifestyle change is provided in this setting although survey and intervention work highlights the potential for engagement and behaviour change[19,28]. Recent work undertaken in Scotland in routine breast screening clinics has reported that a simple women's magazine intervention about breast cancer risk produced by The Scottish Cancer Prevention Network resulted in 60% of respondents claiming an increased knowledge about breast cancer, lifestyle and motivation to find out more about cancer prevention with 40% of respondents expressing intentions to make lifestyle changes[50]. It was notable that there was no difference in results by social position. Whilst concerns have been raised about the potential for increasing health inequalities through individual level interventions, a recent Cochrane review has reported that individual obesity management interventions (in both children and adults) do not increase health inequalities[51].

Whilst the current trial has primary outcomes of increased physical activity and weight loss, the programme will target energy expenditure (caloric usage in physical activity) and dietary intake (caloric intake from foods, soft and alcoholic drinks). The length of the study is designed to embrace the principles of weight loss and weight loss maintenance and therefore has the potential to achieve a long term change in lifestyle habits. The study has been developed from a well conducted feasibility trial with positive indicative outcomes and utilises a gold standard multi-centre, randomised control design methodology. The development of the intervention is a unique combination of staff from academia, NHS, breast cancer charity and healthy screening attendees and employs a novel approach to deliver weight management by volunteers in community locations. The study is not powered to assess long term risk of breast cancer and indeed the intervention would need to demonstrate effective weight loss prior to investment in a cancer outcomes trial. There have been no trials of primary prevention of breast cancer using a weight management

intervention (largely due to length of follow up and study size). However, there are a number of ongoing trials of weight management interventions in women with a breast cancer diagnosis which will report on cancer and all-cause mortality end points (as described by Demark-Wahnefried et al[52]).

It should be noted that the trial is also designed to collect information relevant for clinicians and policy makers responsible for considerations about the potential roll out of the programme throughout the national NHS breast screening programme drawing on feedback from screening staff and participants. This trial is highlighted within the National Cancer Strategy as an investment from Scottish government in cancer prevention[53]. The programme may also have salience internationally where population based breast cancer screening programmes are offered.

Figure Legend

Figure 1 Study Flow Chart

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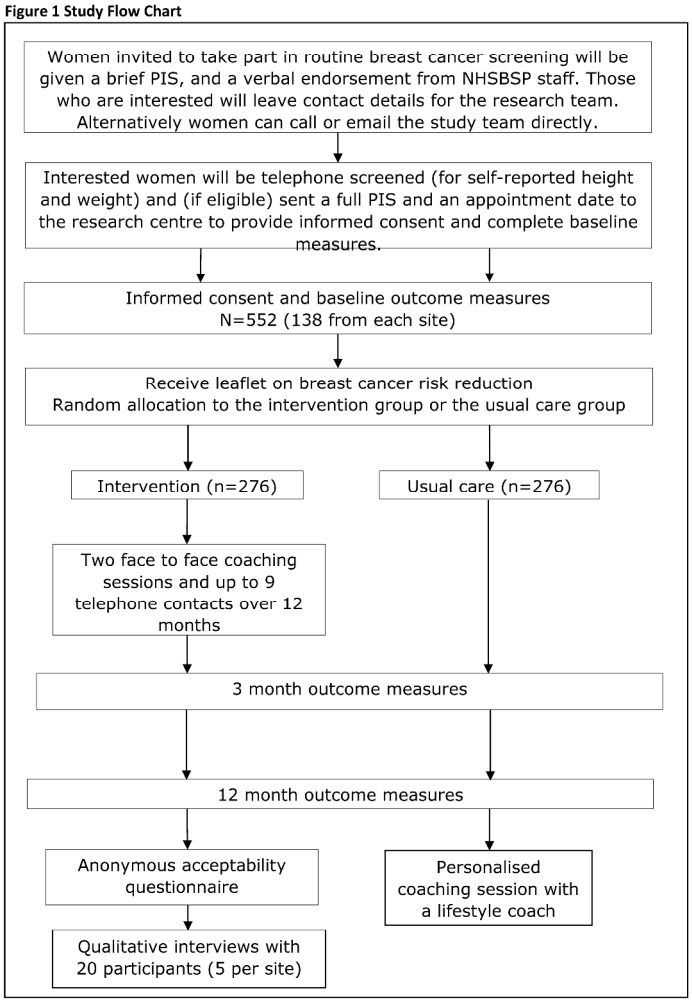
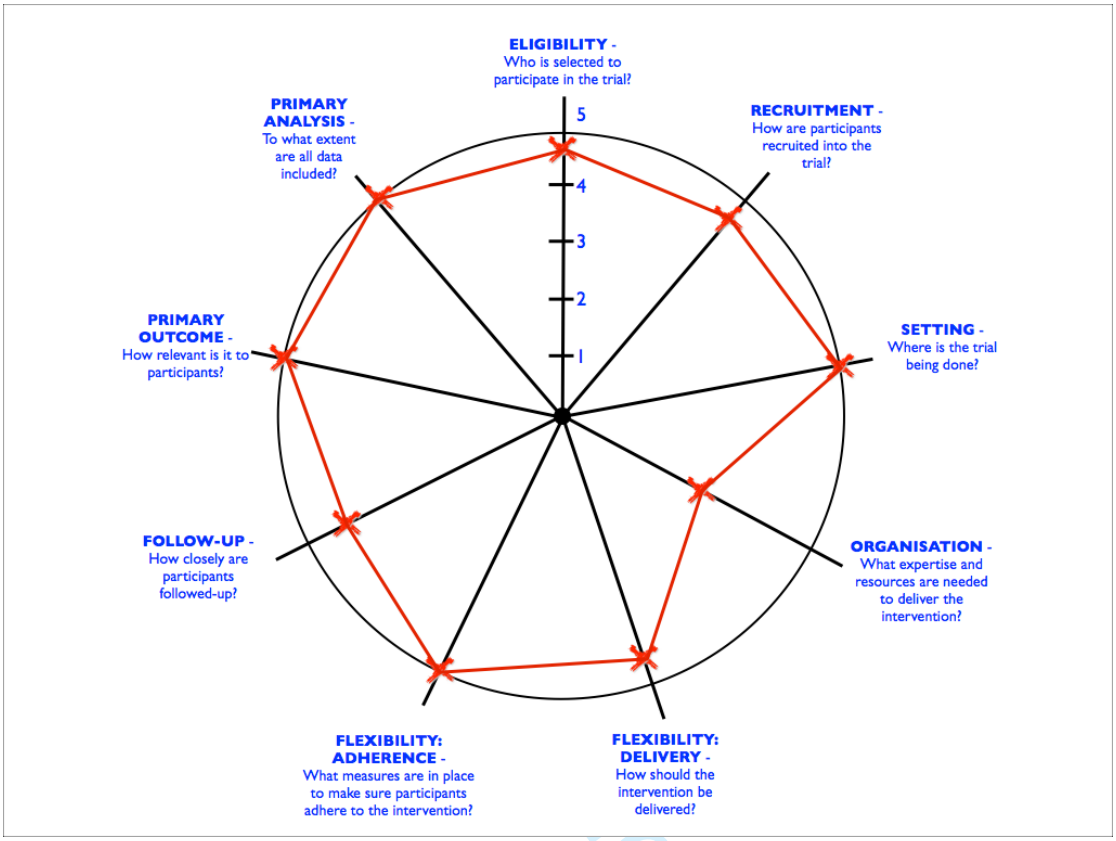
Figure 1 Study Flow Chart



Appendix 1

PRECIS – 2 for ActWELL



PRECIS-2 wheel for the ActWELL trial.

The trial aims to be highly pragmatic in design approach, which is reflected in the wheel with the exception of the *Organisation* domain. The ActWELL intervention involves a new way of delivering lifestyle counselling (Breast Cancer Now volunteers) so the trial is more explanatory on this domain. Evaluating this mode of delivery is, however, the aim of the trial and should the intervention prove effective, the trial would provide support for involving the voluntary sector in routine delivery of the ActWELL intervention.

More information on PRECIS-2 is available at https://www.precis-2.org and in Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ 2015; 350: h2147–7.

Appendix 2

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

1. Brief Name

ActWELL

2. WHY

Following the COM-B model the intervention aims to incorporate increased **M**otivation for weight management (through awareness raising within the teachable moment setting) combined with increased **C**apability for effective lifestyle change combined with **O**pportunities for greater physical activity through an emphasis on walking initiatives and other community facilities using taxonomy-derived effective behaviour change techniques.

3. WHAT

a) Materials

Visit 1

- Touch, Look Check leaflet (http://breastcancernow.org/sites/default/files/public/tlc_breast_awareness_guide.pdf)
- Breast cancer and lifestyle FAQ and links to science base (WCRF) (in house developed)
- BMI chart to identify BMI number and weight status (NHS)
- Assessing baseline step count (in house developed)
- Physical activity recommendations from UK Department of Health
- Kettlecise ways to reduce sedentary behaviour (http://www.cancerpreventionscotland.org.uk/resources/kettlecise/)
- Warm up exercises (in house developed)
- Walking Plan and Diary (in house developed)
- Implementation intention sheets (in house developed)
- Information sheet on calories and alcohol infographic https://www.behance.net/gallery/5830267/Calories-Alcohol-infographic
- Sugar savvy quiz https://www.wcrf-uk.org/sites/default/files/are-you-sugar-savvy-game.pdf
- Weight awareness plan (weekly weight logbook) (in house developed)
- Five day food and drink diary (in house developed)

Visit 2

- Eatwell Guide (NHS Tayside)
- Personalised weight loss plan (British heart Foundation)

- Implementation Intentions sheet (in house developed)
- Portion distortion quiz
- Food Labelling Guidance – credit card size (NHS Tayside)
- British Heart Foundation Booklet 'Your simple guide to weight loss' https://www.bhf.org.uk/publications/healthy-eating-and-drinking/facts-not-fads---your-simple-guide-to-healthy-weight-loss

b) Procedures

Overall: Two face to face visits plus nine monthly phone calls

Visit 1 (60 minutes)

- Check well-being
- Self-identification of BMI

- Instruct participant on pedometer use and proposed walking programme
- Walk and talk 10 min
  (interactive walking session and discussion about increasing physical activity)
- Physical activity goal setting
  (implementation intention setting and personalised walking programme)
- Discuss how to reduce sedentary behaviour

- Caloric value of (hot and cold) alcohol and sugary drinks discussed
  "Sugar Savvy" quiz undertaken (https://www.wcrf-uk.org/sites/default/files/are-you-sugar-savvy-game.pdf)
  (advice given on alternatives, portion size, frequency)
  (Possibility of implementation intention setting on drinks)

- Weight loss goal
  (emphasis on modest up to 7% in 12 months)
- Motivational interviewing questions on weight loss
- Guidance on weekly self-weighing, reporting and feedback–
  (implementation intention setting for weighing– scales available for home use)

- Initial dietary challenges – snacking and "weakness foods"
  (based on a verbal 24 hour intake)

- Summarise meeting – goals set, times of relapse

- All participants invited to undertake a 24 hour written diet recall for 5 days for review at visit 2

Visit 2 (45 minutes)

- Check well being
- Praise success (however modest)
- Evaluate and appraise PA goals
  (Discuss how they feel physically and mentally about success of walking, or problems and possible solutions, review goals)
- Check body weight recorded

- Reminder about body weight and breast cancer risk reduction (even after 50)

- Highlight weight loss principles
  (revising snacking, importance of meal patterns and 5 a day)
- Remind about goal set for weight loss and how this converts to personal eating plan

- Review 24 hour diet recall sheets (handed out last visit)
  (or take a 24 hour recall if sheets not completed)
- Discuss calories – focus on -600kcal deficit diet
  (Identify personalised eating plan using British Heart Foundation (BHF) materials)
- Discuss Portion sizes and frequencies
  (use images from BHF materials and portion distortion information)

- Food labelling
  (Identify energy values for low and high, advise avoiding red TL, advise using at home)
- Identify Implementation intentions on one food/drinking habit
  (set one only- if suggestions needed base on 24 hour recordings)

- Summarise goals and key challenges, check all materials provided
- Arrange first two telephone appointments
- Discuss leisure centre activity to meet staff (if interested)

Phone Calls
For all calls:

- Check well being
- Check goal progress, self-reported weight, re-enforce the importance of self-monitoring
- Identify success and challenges
- Discuss possible problems ahead (e.g. holidays)
- Coping strategies and starting again if intentions failed
- Start discussion on the importance of habits in eating behaviours using Ten Top Tips.

Weight Loss and Weight Loss Maintenance (using Ten Top Tips)

- Stress the importance of physical activity and socials support Refer to *Tips Walk off the weight (TC1)*
- Highlight the role of lower calorie and lower fat foods Refer to *Go Reduced Fat and Look at the Labels (TC2)*
- Highlight the importance of regular food intake (including breakfast) and portion size Refer to *Keep to your meal routine and Focus on Food (TC3)*
- Stress the importance of physical activity and social support Refer to *Tips Walk off the weight (TC4)*
- Re-enforce information on snacking Refer to *Pack a Healthy snack* and *Five a Day (TC5)*
- Re-enforce information on drinks sweet and alcohol and value of water Refer to *Think about your drinks* (TC6)
- Re-evaluate portions size (as per BHF booklet) Refer to *Caution with your portions*(TC7)

- (TC 8) return to discussing physical activity and reducing sedentary behaviour Refer to *Up on your feet*
- Re-evaluation of goals, where next , summarise success (TC9)

4. WHO PROVIDED

The intervention will be delivered by Breast Cancer Now Volunteer coaches. These will have a background and experience of counselling and receive a bespoke training programme by the research team including

- Evidence base for reducing risks of breast cancer by lifestyle
- Key principles and application of healthy food and drinks choices, appropriate portions and coping with social consumption challenges
- Key principles and application of increased physical activity and reduced sedentary behaviour
- Key principles and application of weight management
- Personalisation of advice
- Motivational interviewing techniques (key questions only)
- Use of evidence-based behavioural change techniques (BCTs)
- Handling confidential data
- The intervention protocol and importance of its delivery. Confidentiality.
- Role play and assessments (face to face and telephone contact)
-

The programme is likely to be delivered over 4 bespoke sessions training programme. An exit certificate will be provided for those who successfully achieve the assessments and role play.

Role play and observations will be undertaken prior to commencing the actual intervention.

5. HOW

Two individual 1:1 coach to participant face to face visits are planned (approx. 6 weeks apart) with monthly telephone contacts thereafter.

6. WHERE

The face to face visits are scheduled to take part in office space in local leisure centres. Each town has identified more than one possible venue and these will be noted. No home visits are scheduled and other locations are discouraged.

7. WHEN and HOW MUCH

The coaches will collect data for each participant on; date of contact, duration of contact and perceived engagement for both face to face and 9 telephone contacts. Other contacts

e.g. SMS/email will also be noted. These data will allow dose and duration and outcomes to be assessed by individual coaches as well as overall.

8. TAILORING

Personalised advice is a key component of all aspects of the intervention. Motivational interviewing about weight loss will be undertaken to identify participant ambivalence and perceived personal advantages to weight management.

Caloric prescription: this will be based on -600kcals required for weight maintenance (calculated using the equations from Miflin St Jeor according to gender, age and body weight). Participant agreed goals (and implementation intentions) will be used for weighing and recording body weight (self-monitoring) and personalised feedback will be provided.

Food and drink choices will be based on information obtained from current eating habits obtained through 24 hour recalls to guide personalised advice on food frequency, portion sizes and foods to limit. Participant agreed goals (and implementation intentions) will be used for one specific food or drinking habit and this will be self monitored with personalised feedback provided.

Physical activity dose and duration will be based on the brief Scottish Physical Activity questionnaire to guide walking plans and signpost other activities (including those offered in the local leisure centres). Participant agreed goals (and implementation intentions) will be used for one specific aspect of habitual walking and this will be self- monitored with personalised feedback provided

9. MODIFICATIONS

Recommendations for modifications may arise from

a) Feedback from coaches (individual issues or during regular round table meetings)
b) Changes in evidence base for guidance
c) Adverse events

10. HOW WELL

Fidelity Procedures: We will undertake qualitative process measures to assess fidelity to the intervention. Time for implementation procedures will be recorded by intervention staff. Fidelity of programme delivery and content will be assessed by audio-recording and transcription of a random sample of LC face to face interactions and telephone contacts at each site. These will be compared to the protocol specified number of points to be covered in each session by a researcher at University of Stirling independent from the intervention.

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	
Protocol version	3	Date and version identifier	NR
Funding	4	Sources and types of financial, material, and other support	4
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 5
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6, 7
	6b	Explanation for choice of comparators	6, 7
Objectives	7	Specific objectives or hypotheses	

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8, 9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9, 10
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11, 12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	16-18
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-16
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	12 (See Figure 1)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	18, 19
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	
Methods: Assignment of interventions (for controlled trials)			
Allocation:			

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10, 11
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10, 11
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	11
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	15-18
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NR
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19, 20
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	22
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	4
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NR
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	10
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NR
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	4
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	NR
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	22
	31b	Authorship eligibility guidelines and any intended use of professional writers	NR
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NR

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.