# Title: Study protocol of a multicentre randomised controlled trial of self-help cognitive behaviour therapy for working women with menopausal symptoms (MENOS@Work)

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Abstract

Background: Hot flushes and night sweats (HFNS) - the main symptoms of the menopause transition - can impact on quality of life and are particularly difficult to manage at work. A cognitive behaviour therapy (CBT) intervention has been developed specifically for HFNS that is theoretically based and shown to reduce significantly the impact of HFNS in several randomised controlled trials (RCTs). Self-help CBT has been found to be as effective as group CBT for these symptoms, but these interventions are not widely available in the workplace. This paper describes the protocol of an RCT aiming to assess the efficacy of CBT for menopausal symptoms implemented in the workplace, with a nested qualitative study to examine acceptability and feasibility.

Methods/Design: One hundred menopausal working women, aged 45-60 years, experiencing bothersome HFNS for two months will be recruited from several (2-10) large organisations into a multicentre randomised controlled trial. Women will be randomly assigned to either treatment (self-help CBT intervention lasting 4 weeks) or to a no treatment-wait control condition (NTWC), following a screening interview, consent, and completion of a baseline questionnaire. All participants will complete follow-up questionnaires at 6 weeks and 20 weeks post-randomisation. The primary outcome is problem rating of HFNS; secondary measures include HFNS frequency, mood, quality of life, attitudes to menopause, HFNS beliefs and behaviours, work absence and presenteeism, job satisfaction, job stress, job performance, disclosure to managers and turnover intention. Adherence, acceptability and feasibility will be assessed at 20 weeks post-randomisation in questionnaires and qualitative interviews. Upon trial completion, the control group will also be offered the intervention.

Discussion: This is the first randomised controlled trial of a self-management intervention tailored for working women who have troublesome menopausal symptoms.

Trial registration: Clin.Gov [left blank for review]

Key words: menopause, work, menopausal symptoms, hot flushes, cognitive behaviour therapy, vasomotor symptoms, protocol, RCT

## Background

There are over 3.5 million women in employment aged between 50 and 65 in the UK [1] and, as menopause occurs on average between the ages of 50–51 and can last for up to ten years [2] at any one time, a significant proportion of mid-aged and older women workers will be experiencing menopausal symptoms. Hot flushes and night sweats (HFNS) are the main symptoms of the menopause, which for an estimated 20-25% affect quality of life (QOL) largely due to discomfort, embarrassment and the impact of night sweats upon sleep [3,4].

There is a lack of awareness and communication about menopause generally in work settings. There is some evidence that women find that menopausal symptoms are hard to manage at work, and that certain work situations such as formal meetings, working with men and/or younger colleagues, and working in hot or poorly ventilated environments, increase the intensity of menopausal symptoms [5-9]. Hot flushes are often seen as embarrassing and women are concerned about the reactions of others [6]. Women tend to be reluctant to disclose their menopausal status, particularly at work, where embarrassment and fear of ridicule is common, and self-control is highly valued [7,8]. A recent review highlighted the potential impact of menopausal symptoms for working women [10]. Menopause symptoms may affect work capacity for some women, or their self-perceived work ability [11], particularly if depressive symptoms are also reported, but the evidence is mixed [12-18] and more research is needed [10].

Griffiths et al [9] conducted a study of 896 women employed in ten UK-based organisations. Some women found that the menopause transition lead to difficult at work, and the more problematic symptoms reported by women were poor concentration, tiredness, poor memory,

feeling low/depressed and lowered confidence. Hot flushes were described as a major source of discomfort and embarrassment. The majority were unwilling to disclose menopause-related health issues to line managers, most of whom were men or younger than them. Areas suggested for organisational-level support included: (i) greater awareness among managers about menopause as a possible occupational health issue; (ii) flexible working hours; (iii) access to information and sources of support at work; and, (iv) attention to work place temperature and ventilation. This protocol aims to address (iii).

Hormone therapy (HT) is an effective medical treatment for menopausal symptoms [18], but not all women want to take it due to contraindications and personal preference. Cognitive behaviour therapy (CBT) is an effective treatment for anxiety and depression [18], and a CBT intervention has been developed to help women to manage for HFNS [19-22]. CBT examines the relationships and interactions between physical symptoms, thoughts, feelings and behaviours. CBT for HFNS is based on a theoretical model [24] that includes the processes of symptom perception, cognitive appraisal and behavioural reactions, and the model has been supported in recent studies [25-27]. HFNS can be potentiated by stress and are exacerbated by negative beliefs and behavioural reactions [23]. The intervention includes psychoeducation and evidence-based CBT strategies to reduce stress, and to manage hot flushes, night sweats and sleep [24]. For example, women are asked to note down what they are thinking when they are stressed or when they are having a hot flush, and are then helped to generate calmer, supportive thoughts using examples. Beliefs about hot flushes in social contexts, such as ‘everyone is looking at me’, can increase arousal and hot flush intensity; similarly, sleep difficulties are often maintained by worry (e.g. “how will I get through the day tomorrow?”), which impacts further on daytime functioning.

The CBT intervention for HFNS has been found to be effective in reducing the impact of HFNS, i.e. how problematic they are, in several clinical trials [19-22]. Recent UK guidance [18] recommends that doctors offer women information about CBT for menopausal symptoms, and, in a recent Position Statement on non-hormonal interventions for vasomotor symptoms, CBT is strongly

recommended by the North American Menopause Society [23]. CBT appears to work by changing symptom perceptions and cognitive appraisals (women's perceptions, attitudes and beliefs about menopause and symptoms) and well as using helpful behavioural strategies, such as using calm breathing [24,26-27].

Group and self-help CBT for HFNS have been shown to be effective in reducing the impact of HFNS compared to a control group [19]; the self-help booklet (containing the same information with a breathing/relaxation CD) was as effective as the group CBT. Self-help CBT has also been found to produce similar levels of improvement when delivered with miminal guidance [21]. The CBT interventions for HFNS are available in self-help and group formats [28,29], but are not yet widely accessible to women at work.

This paper describes the protocol for a proposed investigation that aims to test whether a modified form of Self-help CBT is effective in meeting the needs of working women who have menopausal symptoms. We hypothesize that CBT will be more effective than no treatment in: (i) reducing the impact of HFNS (problem-rating), and (ii) improving mood and quality of life, attitudes, beliefs and behaviours, and experience of work (work absence, presenteeism, job satisfaction, job stress, job performance, and turnover intention).

## Methods/Design

### Pilot study to develop the intervention

The self-help CBT intervention (SH-CBT) for HFNS will be modified and piloted. We will draw upon previous interviews with working menopausal women [9,30] and modify the existing CBT intervention [19,28] to include specific issues and examples relating to working life. A minimum of ten, working women will be invited to take part in interviews if they have menopausal symptoms, including HFNS. They will be asked about their experience of menopause at work, and their views on the content and particularly on the format of the intervention, e.g. booklet or on-line

version, and questionnaires to be used in the trial. If there is considerable variety in responses then more women will be interviewed in order to reach saturation, whereby similar themes are repeatedly mentioned. The intervention and questionnaires will then be modified accordingly and any necessary changes made before commencement of the main study. An advisory group will oversee the running of the project and include service users and stakeholders who will input to the design and review the study materials.

## Main Study

### Design

The study uses a two parallel groups design to assess the outcomes and feasibility of implementing an evidence-based SH-CBT intervention, adapted to help working women to manage the impact of menopausal symptoms, in a multicentre randomised controlled trial (RCT). We will compare SH-CBT with a no treatment-wait control condition (NTWC), at 6 and 20 week post-randomisation follow-up assessments (Fig 1). Between-group comparisons will be made at 6 and 20 weeks to estimate the effects of SH-CBT versus NTWC using an intention to treat analysis.

### Ethical approval

The study has been approved by [removed for review].

### Participants' eligibility

Working women, aged 45-60 years, with at least 10 problematic hot flushes per week (score >2) Hot Flush Rating Scale [5], for at least two months will be eligible for the study. They will have a good understanding of English and not currently experiencing major physical or mental health problems that would compromise participation.

## Recruitment

Mid-aged women (aged 45 to 60 years) will be contacted via the Occupational Health or Human Resources Departments (or appointed contact person) of several large organisations (minimum of 2 maximum 10) using various modes of communication (e.g. email, intranet, posters etc.) and invited to contact the researcher if they are experiencing menopausal symptoms. Interested participants will be screened to ensure they meet the eligibility criteria. We aim to have equal numbers of participants from each organisation and it is estimated that a minimum of 100 women will participate.

## Randomisation and blinding

Women who meet the inclusion criteria will be randomised into SH-CBT (n=50) or NTWC (n=50). Randomisation (using the RANDBETWEEN function in Microsoft Excel) will be in the ratio of 1:1, stratifying on the basis of centre, and will occur after the screening and baseline assessment conducted. Women will be informed of their group allocation by post and/or email. Study materials, including post intervention questionnaires, will be sent out by the researcher. The data will be entered by a researcher blind to group allocation and the main statistical analyses carried out by the statistician who is blind to group allocation.

## Sample size

With reference to results from a previous study [19], a total sample size of 80 participants, 40 per arm, are required to detect 2 points difference in HFNS mean score at 6 weeks using regression analysis controlling for baseline level of the outcome, with a 90% power at 2 tailed significance 0.05 level, assuming equal SD (3.0) for both groups and correlation between baseline and follow up

measures at 0.4 for the purpose of being conservative. After taking into account 20% loss to follow up rate, a sample size of 100 is required.

Self-help CBT intervention (SH-CBT)

The intervention is a modified version of an existing evidence-based SH-CBT intervention [19,22]. It will be shortened and adapted during pilot work but it is expected that it will include a booklet with evidence-based information on menopause and coping strategies for work settings and a breathing/relaxation practice that can be downloaded or provided on a CD. The approach is psycho-educational with an active focus upon cognitive and behavioural changes. This intervention lasts for 4 weeks and the materials guide the individual through each chapter and exercise, including the homework set out for each chapter. In total, this intervention is estimated to take approximately 4 hours a week over the 4 weeks, not in work time.

It is anticipated that the booklet will contain the following components:

- Information and advice about menopause and menopausal symptoms with physiological explanation and factors influencing their experience (cognitive behavioural model)
- Monitoring and modifying hot flush precipitants in the work environment
- Paced breathing, relaxation and dealing with stress
- Exercises to challenge unhelpful thoughts and beliefs about menopause and others' reactions
- Encouraging helpful behavioural strategies, e.g. reducing avoidance, pacing activities
- Information and strategies for managing night sweats and sleep
- Information about additional resources

No Treatment-Wait Control (NTWC)

Control participants do not receive CBT treatment but have access to their GP, occupational health

and other healthcare options, as would normally be the case. They will be offered the SH-CBT intervention off-trial following completion of A2.

Measures

These have been used in previous studies by the authors and have good psychometric properties. The measures are completed at assessment points (baseline (A0), 6 weeks (A1) and 20 weeks (A2) post-randomisation), as indicated in Table 1.

Background and demographic measures: Age, ethnicity, family and relationship status, employment status, type of work (i.e. shift work; manual, non-manual work, both; uniform required), work context and environment (i.e. working with others, Health and Safety Executive's (HSE) Management Standards Indicator Tool [31]), job title, menopause status, menopausal symptoms, HRT use and history, treatment for HF/NS, current health conditions, and general health questions (i.e. to measure BMI, physical activity, alcohol and smoking consumption, and a general health item).

Primary outcome:

HFNS Problem-rating is a subscale of the Hot Flush Rating Scale [5] calculated as the mean of three items, each measured on a 10-point scale (low to high). Items include 'To what extent do you regard your flushes/ sweats as a problem?', 'How distressed do you feel about your hot flushes?' and 'How much do your hot flushes interfere with your daily routine? Problem rating—i.e., the extent to which symptoms are bothersome and interfere with life—was chosen, before the trial began, as the primary outcome because problem rating, rather than frequency, is associated with quality of life [4], and it has been recommended as an appropriate patient reported outcome measure in clinical trials of HFNS treatments [32,33]. The scale has good internal consistency (Cronbach $\alpha$=0.9) and test-retest reliability (r=0.8) [5]. Problem rating and severity tend to be associated but

neither are strongly associated with frequency of HFNS [25,32].

Secondary outcomes:

HFNS frequency, is measured by a subscale of the Hot Flush Rating Scale [5] providing a weekly average of HF and NS. The measure gives a retrospective recording of the frequency of HFNS (for example, "How often have you had hot flushes in the past week?") and the average severity of the HFNS for the previous week (1=mild, 2=moderate, 3=severe).

Menopause Representations Questionnaire (MRQ) [34] is designed to assess women's attributions (identity) of symptoms to the menopause (20 items) and beliefs subscales (cognitive representations) about the menopause (17 items). The belief items are scored on 5-point scales from strongly agree (5) to strongly disagree (1), and mean scores are calculated for beliefs subscales. The identity subscale items are scored from 0 to 2 and summed. We also included two belief items from the Menopause Attitude Measure [9] to measure attitude to menopause at work, i.e. whether women feel that their job performance has been affected by menopausal symptoms, and whether they feel that menopause has negatively affected managers' and colleagues' views of competence at work. These are scored on 5-point scales (agree (5) to strongly disagree (1)).

Hot Flush Beliefs and Behaviours are assessed using a combined scale of existing measures. The Hot Flush Beliefs Scale (HFBelS) [35], a 27-item scale comprising three subscales including beliefs about HF in a social context, beliefs about ability to cope/control HFNS, and beliefs about night sweats and sleep. The Hot Flush Behaviour Scale (HFBehS) [36] comprises 11 items to assess behavioural reactions to HFNS, i.e. avoidance, safety behaviours and positive acceptance, using a 6-point scale from strongly disagree (0) to strongly agree (5). Both measures have been found to mediate the treatment effects of CBT [26,27]. A combined Short Form Hot flush Beliefs and Behaviour Scale (HFBelBehScale) is used in this study, which has good reliability and similar

correlations with HFNS Problem rating compared with the longer questionnaires (the Short Form HFNS Beliefs and Behaviour Scale is included in a supplementary file with scoring information).

The Women's Health Questionnaire (WHQ) [37] a measure of physical and emotional symptoms designed for and standardised on women aged 45–65 years, is widely used in studies of menopausal women. The WHQ has 37 items with subscales that assess, for example, depressed mood, anxiety, memory/concentration, somatic symptoms and sleep problems. Participants rate each item on a 4-point scale, according to the extent to which they are experiencing each item; subscale scores are calculated, ranging from 0–1 (higher scores indicate poorer wellbeing). The depressed mood subscale has concurrent validity with the GHQ and the WHQ has good internal reliability for subscales (Cronbach α 0.70–0.84) and test-retest reliability (0.78–0.96). A single item measure of sleep quality was added from the Pittsburgh Sleep Quality Index (PSQI) [38], which is a self-rated questionnaire assessing sleep quality and disturbances over a 1-month time interval using a 4-point Likert scale (1= Very bad to 4 = Very good).

The Work and Social Adjustment Scale [39] measures functional impairment at work, home, and in social situations. It comprises 5 self-report items using an 8-point Likert scale (0=Not at all, 8=Severely) and provides the degree of impact of menopause symptoms on a given activity Responses are summed to provide a score between 0 (no impairment) to 40 (very severe impairment).

The Stanford Presenteeism Scale [40] measures an employee's ability to concentrate and accomplish work despite health problems. This measure of workplace presenteeism comprises of 6 items that are summed to produce a total presenteeism score. Each item asks the respondent to indicate their work experience over the last month using a 5-point scale (1=strongly disagree, 5=strongly agree).

Workplace absenteeism is measured by asking participants to provide detail of any time of they have taken off from work over the last 4 weeks because of the menopause (i.e. duration and spells) [9,40], including the duration of absence spells and leaving work early or arriving late.

Menopausal symptom disclosure to managers is measured using a single dichotomous item ('yes' or 'no') [9,30] and whether participants have told their manager about any reduced working hours (i.e. arriving late, leaving early) due to their menopausal symptoms (if appropriate) ('yes', 'no', 'sometimes').

Work turnover intentions [41] are measured with 4 items that assess how likely the individual is to leave their organisation. Each item contains 5 response options indicating low (1) to high (5) intent to remain in their organisation, which are averaged to provide an overall score. Two further items are used to measure the degree to which the individual has considered reducing their working hours or leaving the workforce altogether (response options include: 'yes', 'no', 'sometimes').

Job satisfaction is measured using a single-item 7-point Likert scale (1=extremely dissatisfied, 4=neither dissatisfied or satisfied, 7=extremely satisfied) [9,30] to indicate an individual's level of contentment with their job. Job performance is also measured using a single item; participants are asked to rate their performance compared to others in a similar role or position to themselves using a 5-point Likert scale (1=poor, 5=excellent), and job stress [42] is measured using a single item asking participants to indicate on a 4-point Likert scale how stressful they find their job (1=not stressful, 4=extremely stressful).

The use of medical resources for menopause and treatments for HFNS will also be monitored, by asking, whether or not (and if so how often) they had visited their GP/hospital doctor/nurse about

the menopause (over the past 6 months at baseline and at the final follow-up) (dichotomous response option 'yes' or 'no') and whether they have/are currently taking any treatment (medical or non-medical) for HFNS.

Evaluation of the intervention: adherence, acceptability and feasibility

Adherence to relaxation practice and homework tasks will be monitored. Those who are randomised to SH-CBT will be asked to complete short evaluation questions within the questionnaires (at A1 and A2) to assess adherence to the intervention, i.e. whether (and how much of the booklet) they read, whether they carried out the components of the interventions (listen to breathing/relaxation; used cognitive and/or behavioural strategies), and provide other general feedback information about the intervention.

Data analysis

The analysis will be conducted on an intention-to-treat basis, excluding participants providing no post-intervention follow-up data. Descriptive statistics for variables will be presented by treatment arms across the follow up time points. Mixed-effects (aka multilevel) models will be performed to quantify the treatment effects on the primary outcome (HFNS problem rating) at the 6 and 20 week follow-up assessments [42]. A random-intercept will be estimated to account for the repeated measurement of the outcomes within participants. Predictors entered into the model will be group allocation, time in weeks post-intervention, and a group-by-time interaction term to allow for estimates of the treatment effect at each time point. Additional covariates included will be the baseline level of the outcome variable and centre indicator variables, as this was a stratification factor in the randomisation. Secondary outcomes will be analysed in the same way. Any skewed continuous outcome variables may be transformed for multilevel modelling. A detailed Statistical

Analysis Plan setting out full details of the proposed analyses will be finalised before the trial database is locked for final analysis. Stata 14 will be used for data analysis.

Missing values in all outcomes will be checked and reported across treatment group and following up time. A mixed effect logistic regression will be performed to test the association between group allocation and baseline variables with missing outcome observations at each follow-up assessment. Because mixed-effects models will be used to estimate treatment effects, individuals with at least one post-intervention observation of the outcome will be included in the analysis with the assumption that missing outcome observations are missing at random (MAR) [43]. This implies that treatment effects will be unbiased as long as missingness is either completely at random or influenced only by variables included in the model, and not unobserved variables [43]. Sensitivity analysis will be conducted under a number of plausible missing not at random (MNAR) scenarios to examine the risk of bias introduced where the MAR assumption to be violated [44].

If the treatment effect on the primary outcome (HFNS problem rating) is observed to be statistically significant, exploratory analysis will be conducted to explore the efficacy mechanism in relation to several putative mediators (such as HFNS beliefs, mood, HFNS frequency) using mediation analysis performed by the product-of coefficients approach [45]. If there is not effect on the primary outcome and the estimated effect size is less than .4, explanatory analysis will be conducted in order to determine whether poor adherence to the intervention or centre level variation were potentially related to the null finding.

Nested qualitative study

After the final assessment questionnaire is completed, all women in the intervention arm will be invited to take part in a 20-30 minute semi-structured interview to explore their perceptions of the feasibility, acceptability, and their experience of having the intervention. This will include their

perceived impact on themselves, their quality of life at work and in general their feedback on the intervention and its delivery. The interviews will be carried out by a research psychologist (telephone or face to face at the university or agreed location) and audio recorded with consent. The interviews will be analysed using framework analysis [46]. Fifty per cent (or 25) will be randomly selected before being coded and analysed by the research psychologist; 50% will be coded in parallel by an independent researcher to ensure reliability. Qualitative responses from the evaluation questionnaires will also be coded by the researcher on the project and analysed in the same way. Content categories will be independent checked by an additional independent researcher.

## Discussion

This study will investigate the feasibility and outcome of offering a brief self-help intervention to help women to manage menopausal symptoms at work. To our knowledge this is the first study to do so and if effective the intervention could have benefits to working women, and possibly also to their employers. Moreover, because the majority of mid-aged women in the UK are working and are likely to continue to do so for 10-15 years after the menopause [1], the outcomes of the study could have far reaching impacts through increased availability of CBT for menopausal symptoms [47]. If the intervention is feasible and successful, we plan to offer it to other organizations.

No negative impact on the study participants is expected. Some women consider the menopause a taboo subject and may be embarrassed about the topic of the questionnaires and some content within the SH-CBT intervention (menopause, hot flushes, night sweats, etc). However, we plan to ensure that all potential participants are fully informed about study materials prior to obtaining consent and are given the opportunity to withdraw from the study, should they feel too uncomfortable. As women will also be randomised into two groups, one active treatment group and one no-treatment group, some participants may be disappointed that they are not receiving a potentially helpful treatment immediately. However, we offer all no-treatment participants the

intervention at the end of the trial and ensure that are fully aware of the randomisation procedure prior to obtaining informed consent.

The results of the study will be disseminated by publication of journal articles and conference attendance. We aim to reach a variety of relevant groups, such as occupational health professionals, human resource managers, employers and managers, trade unions, health and occupational psychologists, menopause researchers, clinicians and organisational stake holders (e.g. at British Menopause Society Conference, International Menopause Society Congress, Society of Occupational Medicine Continued Professional Development events and annual scientific meetings, Trade Union events for health and safety representatives, Chartered Institute of Personnel and Development annual conference, Health and Wellbeing at Work conference). In addition to academic papers, outlets will be sought in professional and practitioner magazines.

Future research might include development and evaluation of on-line versions of the intervention and translations into additional languages. We are also planning to develop and evaluate a brief intervention for managers and employers to increase knowledge and awareness of the menopause and the needs of menopausal women.

Supplementary file (attached)

Abbreviations

CBT (cognitive behaviour therapy); SH-CBT (self-help cognitive behaviour therapy); HFNS (hot flushes and night sweats); NTWC (No Treatment-Wait Control); Quality of life (QOL); WHQ (Women's Health Questionnaire); WASAS (Work and Social Adjustment scale); MRQ (Menopause Representations Scale); HFBelS (Hot Flush Beliefs Scale); HFBeS (Hot Flush Behaviour Scale); HFBelBehScale (Hot Flush Beliefs and Behaviour Scale); MAR (missing at random).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' contributions

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Authors' information

[Left blank for review]

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