

Study Protocol: Body-Based Movement, Cranial Nerve and Retained Reflexes Therapy for Menopausal Symptoms — an Open Label Randomised Feasibility Study

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1. Background and Rationale

Menopausal symptoms such as vasomotor disturbances, sleep disruption, mood changes and cognitive difficulties affect a substantial proportion of women and people assigned female at birth (1).

Hormone Replacement Therapy (HRT) remains the most effective treatment for menopause related vasomotor symptoms in women and is recommended as a first-line option in the NICE guidelines. However, not all individuals are able or willing to use HRT due to medical contraindications, personal preferences or concerns about long-term risks. The NICE guidance therefore also contains non-hormonal

pharmacological options (e.g. certain SSRIs/SNRIs, fezolinetant) and psychological approaches such as cognitive behavioural therapy (CBT) for vasomotor symptoms, sleep disturbance and low mood (2). Despite this, many people continue to experience residual symptoms or prefer more “body-based”, integrative approaches (3, 5).

Autonomic nervous system (ANS) dysregulation may contribute to the pathophysiology of menopausal symptoms, particularly vasomotor and sleep symptoms. Menopause has been associated with reduced heart rate variability and a relative shift towards sympathetic dominance, indicating impaired parasympathetic (vagal) tone. Abnormalities in autonomic function have also been linked to the occurrence and severity of hot flushes. These changes may in part reflect altered activity within the hypothalamic–pituitary–ovarian (HPO) and hypothalamic–pituitary–adrenal (HPA) axes with downstream effects on thermoregulation, cardiovascular control, sleep, mood and cognition.

Across multiple fields there is growing interest in body-based interventions that modulate autonomic function and support sensorimotor integration (4,5). Techniques such as breathwork, functional movement, reflex-integration exercises, vagal-modulating practices and related modalities share mechanisms related to improved parasympathetic tone and reduced sympathetic drive. Although evidence varies across individual techniques, studies consistently suggest potential benefits for: autonomic regulation (e.g., increased HRV); stress responsiveness and mood; sleep and perceived symptom burden; overall wellbeing. This collective evidence supports the rationale for exploring body-based approaches as complementary options for menopausal symptom management, particularly among those seeking non-pharmacological strategies.

Given the association between autonomic imbalance and menopausal symptoms, and the emerging evidence across several body-based modalities, an integrated program involving autonomic regulation, cranial nerve engagement, breathwork, functional movement and primitive reflex integration represents a plausible approach. These elements individually show potential to support vagal tone, emotional regulation, sleep and wellbeing. However, these modalities have not been tested together within menopausal populations and little is known about how individuals engage with such a program. A feasibility study is therefore appropriate to evaluate acceptability, participant experience, adherence and preliminary changes in menopausal symptoms and wellbeing. Findings will help determine whether a full-scale randomised controlled trial is warranted and inform its design.

In recent years, consumer-grade wearable devices such as smart rings and watches have become increasingly popular for tracking sleep, heart rate variability (HRV), activity and temperature. The Ultrahuman Ring is marketed as a lifestyle and wellness tracker that provides daily sleep and recovery indices using continuous monitoring of movement, resting heart rate, HRV and peripheral temperature. It is explicitly not classified as a medical device and is not intended for diagnosis or treatment decisions. In this study, the Ultrahuman Ring will be used as an exploratory tool to characterize physiological changes over the intervention period, rather than to guide any clinical management.

1. Nappi RE, Kroll R, Siddiqui E, et al. Global cross-sectional survey of women with vasomotor symptoms associated with menopause: prevalence, impact and treatment patterns. Menopause. 2021.
2. Menopause: identification and management , NICE guidelines, Reference number:NG23, Published: 12 November 2015, Last updated: 07 November 2024
3. Lifestyle and behaviour changes for menopausal symptoms, Australian Menopause Society
4. Thurston RC, Christie IC, Matthews KA. Hot flashes and cardiac vagal control: a link to cardiovascular risk? Menopause. 2010;17(3):456–461. doi: 10.1097/gme.0b013e3181c7dea7. [DOI] [PMC free article] [PubMed] [Google Scholar]
5. Alisa Johnson 1, Lynae Roberts 1, Gary Elkins , Complementary and Alternative Medicine for Menopause, Evid Based Integr Med. 2019 Mar 14;24:2515690X19829380. doi: 10.1177/2515690X19829380

2. Objectives

Primary Objective	Primary endpoint/variable
To evaluate whether the therapy reduces menopausal symptoms from baseline to end of active treatment sessions at week 8	Change in the Menopause Rating Scale (MRS) score from baseline to week 8
Secondary Objectives	Secondary Endpoints
To evaluate whether the therapy reduces menopausal symptoms at week 6	Change in the Menopause Rating Scale (MRS) score from baseline to week 6

To evaluate whether the therapy reduces menopausal symptoms at week 12 follow up	Change in the Menopause Rating Scale (MRS) score from baseline to week 12 follow-up
To assess effects on sleep	Change in Pittsburgh Sleep Quality Index, (PSQI) score from baseline to week 6, week 8 and week 12
To assess effects on cognitive function	Change in Everyday Memory Questionnaire (EMQ) from baseline to week 6, week 8 and week 12
To assess effects on anxiety symptoms	Change in GAD-7 from baseline to week 6, week 8 and week 12
To assess effects on symptoms of depression	Change in PHQ-9 from baseline to week 6, week 8 and week 12
To evaluate feasibility and acceptability.	Weekly for the 8-week program and follow-up week 12

3. Study Design

3.1 Overall study design

This study is an open-label, two-arm, randomised feasibility and pilot trial evaluating a 6-week group-based program “Autonomic Nervous System Regulation using Body-Based Movement, Cranial Nerve and Retained Reflexes Therapy” compared with treatment as usual (TAU). Participants will be randomised in a 2:1 allocation ratio (intervention:TAU). The intervention will last 8 weeks with 8 weekly sessions and outcomes assessed at baseline, week 6, week 8, and follow-up at week 12.

This feasibility pilot is designed to assess the intervention effectiveness and acceptability in post menopause and peri-menopause women.

Following eligibility screening and informed consent, participants will complete baseline assessments. They will then be randomised to either the intervention group or TAU.

The participant timeline is:

- Screening visit: Week-4.
- Baseline period: Week -2

- Intervention period: Weeks 1–8 (weekly 60-minute sessions for the intervention group)
- Follow-up: Week 12

3.2 Study arms

Intervention arm: Participants will attend eight weekly 60-minute face-to-face group sessions (maximum 14 participants per group) delivered by trained practitioners. Attendance will be recorded at each session. Home practice will be encouraged and monitored using brief self-report adherence checks.

TAU arm: Participants will continue their usual menopause-related care (for example GP visits, HRT and/or other treatment as part of standard of care). No additional sessions will be provided during the 12-week study period. Any changes in the concomitant treatments will be recorded.

3.3 Inclusion and exclusion criteria

Inclusion criteria:

- Women and people assigned female at birth aged 40–65 years.
- Moderate-to-severe menopausal symptoms (MRS $\geq$ 16).

Exclusion criteria:

- Major psychiatric or neurological disorders that could affect participation.
- Recent (<3 months) change in HRT or other menopause treatments.
- Any upcoming plans to change HRT or other menopause treatments (during study timeframe)
- Inability to provide informed consent, complete assessments, or know they will miss more than one session.

3.4 Randomisation and blinding

Eligible, consented participants will be randomised after completion of baseline measures in a 2:1 ratio (intervention:TAU).

Randomisation will use a computer-generated allocation sequence.

Due to the nature of the intervention, participants and facilitators cannot be blinded to group assignment.

3.5. Sample Size and Feasibility

Target sample: 42 participants to estimate effectiveness of the treatment, retention, adherence, and variability in outcomes.

The active treatment group will run consequently.

3.6 Optional WhatsApp group

As part of the active treatment group, participants will have the option to join a WhatsApp group. Joining this group will be voluntary.

The WhatsApp will help the active group participants to stay connected throughout the study. It will be used to:

- Share weekly updates and reminders about the sessions
- Send practice exercises or tasks
- Provide a space for informal peer support
- Allow participants to ask questions or contact the facilitators if something comes up between sessions

3.7 Ultra Human Ring device

Participants in the active and TAU groups will be offered the option to wear an Ultrahuman Ring smart ring for the duration of the study (baseline to final follow-up). The ring is a commercially available lifestyle device that continuously records movement and skin temperature.

The Ultrahuman Ring is marketed as a lifestyle and wellness tracker and is not classified as a medical device; it is not intended for diagnosis, treatment or prevention of disease and is not used for any clinical decision-making in this protocol.

Participants will pair the ring with their own smartphone and personal Ultrahuman account using the standard consumer app. With explicit consent, participants will then authorize a secure data connection (providing dashboard summaries and API) between Ultrahuman and the study database. This connection will allow the automated export of a predefined set of summary variables at daily or weekly intervals for the duration of the participant's involvement in the study. Participants will not be given access to study-specific wearable data exports during the intervention period. This temporary blinding is necessary to minimize behavioural reactivity to sleep or physiological feedback, which could otherwise influence study

outcomes and reduce internal validity. Participants may request a summary of their individual data once their involvement in the study is complete.

The variables requested via the API will be limited to:

- Daily Sleep Index (or equivalent overall sleep score)
- Daily resting heart rate (overnight)
- Daily temperature variations (night and day)
- Daily HRV metric as reported by the app
- Device identifier needed for synchronization (if required), mapped immediately to the study ID within the research database

No raw sensor data, GPS/location data, message content or other app usage information will be imported into the research database. The API will be configured so that only the predefined summary metrics are transferred. Once received, these metrics will be stored in a pseudonymised form, linked only to the study ID. The research team will not have access to participants' Ultrahuman login credentials and will not be able to view or modify data within individual consumer accounts.

The wearable data are collected as exploratory physiological measures to characterise changes over the intervention period. They will not be monitored in real time for safety signals and will not be used to guide clinical management or provide individual feedback beyond what the participant already receives in their personal Ultrahuman app.

3.8 Schedule of assessments

Schedule of study procedures and assessments from screening through week 12.

Active and Treatment-As-Usual (TAU) participants complete the same questionnaire-based outcomes at screening, baseline, week 6, week 8 (post-intervention) and week 12 (follow-up).

The Ultrahuman ring sub study is optional and applies only to those who consent and meet eligibility for ring use.

Assessment / Procedure	Screening	Week ($\leq$ -2 week) Baseline	Weeks 1–8 Intervention	Week 8 Post-intervention	Week 12 Follow-up
Eligibility check (incl. menopause)	X	X			

stage, HRT use, inclusion/exclusion)					
Participant information & informed consent	X				
Demographics	X				
Medical history & concomitant medications	X	Update if needed	Update if needed	Update if needed	Update if needed
Randomisation (2:1 active: TAU)		X			
Therapy session (active group only)		X session1	X	X session 6	
Treatment-as-usual (TAU) group		X		X	X
Session attendance log (active only)		X	X (each week)	X	
Adherence check (home practice, exercises)		X	X (each week)	X	
Menopause Rating Scale (MRS)	X	X	Week 6 only	X	X
Pittsburgh Sleep Quality Index (PSQI)		X	Week 6 only	X	X
Everyday Memory Questionnaire (EMQ)		X	Week 6 only	X	X
GAD-7 (anxiety)		X	Week 6 only	X	X
PHQ-9 (depression)		X	Week 6 only	X	X
Brief acceptability / satisfaction items			X (weekly brief items)	X	X
WhatsApp group participation log (if		X (invite)	X (each week)	X	optional

applicable, active only)					
AEs and SAEs	X	X (from consent onwards)	X (each session)	X	X
Physical safety checks (movement-related issues)		X	X (as needed)	X	X
Mental health risk review (PHQ-9)	X	X		X	X
Eligibility for Ultrahuman ring sub-study (smartphone, sizing)	X				
Ring fitting & app setup (only ring sub-study)		X			
Continuous wear period (sleep, HR, activity – only ring sub-study)		X (start)	X (weeks 1–5)	X (end or continue)	
Ring adherence check (wear time, syncing – only ring sub-study)		X	X (each week)	X	
Ring return					Week 12

4. Ethical Approval and Governance

The study will be reviewed and approved by the Independent Research Ethics Committee UK (IREC-UK). The study will be conducted in accordance with the principles of the Declaration of Helsinki and in line with applicable UK requirements for research governance and data protection (including UK GDPR and the Data Protection Act 2018).

This project is investigator-initiated and independent of any university or NHS institution.

4.1 Sponsor and oversight

The Sponsor is responsible for overall study governance, ensuring the protocol is implemented as approved and that appropriate systems are in place for safety reporting, data protection, and record retention. The Chief Investigator and appropriately delegated study personnel will have day-to-day responsibility for conduct of the study, including participant eligibility, informed consent, delivery of study procedures, and adverse event reporting.

Protocol amendments and reporting: Any substantial amendments will be submitted to the IREC-UK for approval prior to implementation, except where immediate action is required to protect participants. Adverse events and serious adverse events will be recorded and reported in accordance with the protocol and IREC-UK reporting requirements.

Study documentation and archiving: Essential study documentation will be maintained in an Investigator Site File as appropriate, and records will be retained and archived for the period required by the Sponsor and applicable regulations.

5. Insurance and Indemnity

The Sponsor holds professional and research indemnity insurance that covers the study team and participants for any harm that may arise as a direct result of study participation.

Insurance is in place to start following a favorable decision from the ethics board and will be in place prior to any data collection or commencement of any intervention programs. Proof of insurance will be provided as part of the IREC submission package.

6. Data Protection and Confidentiality

The Sponsor will act as Data Controller under UK GDPR.

All study data will be anonymized, stored securely on encrypted servers located in the UK/EU and retained for 10 years following study closure before destruction.

A Data Protection Impact Assessment (DPIA) will be completed. Access will be restricted to authorised personnel only.

6.1 Roles and responsibilities related to the use of the Ultra Human Ring

For the purposes of this study, the sponsor (The Open Practice) is the data controller for all research data held in the study database, including wearable-derived metrics imported via the API.

Ultrahuman Healthcare Pvt Ltd, as the provider of the Ultrahuman app and related cloud services, processes participants' wearable data in two capacities:

- as an **independent controller** for its own direct-to-consumer service under its public Terms of Use and Privacy Policy; and
- as a **data processor** on behalf of the sponsor for the restricted subset of summary metrics transmitted via the study API connection, in line with a written data processing agreement (DPA).

The lawful basis for processing wearable-derived data for research purposes is:

- Article 6(1)(e) UK GDPR – task carried out in the public interest / exercise of official authority (or 6(1)(f) legitimate interests, if more appropriate for your setup); and
- Article 9(2)(j) – processing necessary for scientific research purposes, subject to appropriate safeguards, with explicit informed consent obtained from each participant.

In line with the principles of data minimisation and purpose limitation, the API will be configured to transfer only the small set of prespecified summary variables listed in Section 2. No direct identification information (such as name, email address, phone number or full date of birth) will be imported via the API. On receipt, all wearable data will be stored against the participants' study ID in the research database. A separate, access-restricted linkage file connecting study IDs to personal identifiers will be held by the sponsor and not shared with Ultrahuman.

6.2 Data flows and security related to the optional Ultra Human ring use as part of the study

Data transmitted from Ultrahuman Healthcare Pvt Ltd to the study database via the API will be encrypted in transit. The research database will be hosted on secure, access-controlled infrastructure within the UK (The Open Practice Clinic). Only authorised members of the research team will have access to pseudonymised wearable data.

Ultrahuman Healthcare Pvt Ltd may store and process participants' full wearable datasets on servers located outside the UK/EEA as part of its global consumer service, subject to its own technical and organisational security measures and international transfer mechanisms. This independent consumer-level processing is outside the control of the sponsor and will be clearly explained in the Participant Information Sheet (PIS), which will direct participants to review Ultrahuman's current privacy policy before deciding to connect their account for research purposes.

6.3 Participant choice and withdrawal

Participation in the wearable sub-study (Ultrahuman Ring and API connection) is optional. Individuals may take part in the main study without consenting to the wearable component, without any impact on their access to the intervention or other study procedures. Participants who initially consent to the API connection may later revoke this permission by notifying the research team; in that event, no further data will be imported from the time of revocation. Data already collected up to the point of withdrawal may continue to be used in analyses in line with UK GDPR provisions for research, as described in the PIS.

6.4 Retention

Wearable-derived research data will be retained in pseudonymised form for the same duration as other study data after which they will be securely destroyed or anonymised for long-term secondary analysis, in accordance with the sponsor's retention policy and applicable regulatory requirements.

7. Intervention (TIDieR Description)

- **Name:** Autonomic Nervous System Regulation using Body-Based Movement, Cranial Nerve and Retained Reflexes Therapy
- **Why:** Targets neurological and autonomic mechanisms thought to underlie symptom regulation, especially based on overactivity in the sympathetic nervous system.
- **Who provides:** practitioners trained in somatic and neuro-developmental movement methods.
- **What:** Psychoeducation combined with guided exercises targeting cranial/vagus nerve activation, primitive reflex integration, and gentle somatic movements.
- **How:** Delivered face-to-face, small group max 12 per class.
- **When/how much:** Weekly 60-minute sessions for 6 weeks.
- **Tailoring:** Adjusted for mobility or health limitations.
- **Adherence monitoring:** Attendance logs and self-reported home practice of daily exercises.

8. Comparator

Treatment-As-Usual (TAU): Participants continue their existing menopausal care (e.g., GP follow-up, HRT, lifestyle management) with no added intervention. Aimed to match for menopause stage, and HRT status

In order to enhance TAU participant retention, participants allocated to the TAU group will be offered access to a menopause and perimenopause educational workshop and one Body-Based Movement group session following completion of the study participation. Participation in these sessions will be voluntary and will not affect study involvement.

9. Outcomes

Primary Outcome:

- Change in total MRS score from baseline to Week 8

Secondary Outcomes:

- Change in total MRS score from baseline to Week 6
- Change in total MRS score from baseline to Week 12 follow up
- PSQI (sleep quality)
- EMQ (cognitive functioning)
- GAD-7 (anxiety)
- PHQ-9 (depression)
- Qualitative interviews on feasibility and acceptability.

10. Data Collection Schedule

Timepoint	Screening	Baseline	6 Weeks	8 weeks	12 Weeks
MRS	X	X	X	X	X
PSQI		X	X	X	X
EMQ		X	X	X	X
GAD-7		X	X	X	X
PHQ-9	X	X	X	X	X
Adverse Events	X	X	X	X	X

11. Statistical Analysis Plan

11.1. Sample size justification

Consistent with methodological recommendations for pilot and feasibility RCTs, which typically suggest 12 participants per arm to obtain stable variance estimates and to evaluate trial procedures, we will recruit a total of 42 participants, with 28 allocated to the active intervention (14 per group) and 14 to treatment-as-usual (TAU), using a 2:1 randomisation ratio. This sample size is considered sufficient to assess feasibility parameters (recruitment and retention rates, adherence across the 6-week program and completion of outcome measures at weeks 6, 8 and 12) and to generate preliminary effect size estimates on the MRS, PSQI, EMQ, GAD-7 and PHQ-9. Allowing for some attrition, the proposed numbers will still meet commonly accepted minimum per-group thresholds for feasibility RCTs.

11.2 Statistical Analysis Plan

- Feasibility metrics will be described with summary statistics.
- Initial Analysis will use simple paired samples t-tests to assess the effectiveness of intervention in the active condition.
- Further to this, if the active condition holds then a mixed effects ANOVA per outcome variable on the time x condition outcome variable.
- Exploratory ANCOVA's will be used with baseline covariates (e.g., HRT use, menopause stage, or baseline severity score)
- If we have full and complete data for 3+ time points, then primary and secondary outcomes will be analysed using linear mixed-effects models with baseline covariates (e.g., HRT use).
- Analyses will follow an intention-to-treat principle, controlling for adherence where appropriate.
- Missing data will be handled by multiple imputation when appropriate (Provided this is no more than 10% of entries).

12. Safety Monitoring

Adverse events (AEs) and serious adverse events (SAEs) will be recorded from baseline till the end of the study (w12). A designated Safety Monitor will review all events monthly.

Given the non-invasive, behavioural nature of the study, a formal Data Monitoring Committee is not required.

13. Informed Consent

Written informed consent will be obtained before participation during the screening visit. Participants will be provided with a detailed Participant Information Sheet (PIS) outlining study purpose, procedures, potential risks, confidentiality, and the right to withdraw.

14. Dissemination

Results will be shared through peer-reviewed journals, conferences, and a lay summary to participants. The protocol and final dataset (de-identified) will be made openly available where feasible.

Included in the Pack

- A. Study Protocol
- B. Insurance Certificate (confirmation email, later replaced with certificate after gaining ethical favour)
- C. Investigator CVs
- D. Participant Information Sheet
- E. Participant Consent Form
- F. Demographic document
- G. Outcome Measure Instruments and Permissions
- H. WhatsApp protocol
- I. Weekly adherence document
- J. Recruitment Materials

Note: *There are two instances of the length of the intervention indicated to be 6-weeks instead of 8-weeks as intended. This is a typo, as is reflected in all other descriptors of the length of intervention. As well as in all communication with participants to indicate 8 weeks/ 8 sessions. In order to reflect the state of the study protocol prior to ethical approval this has not been changed. The locations of these errors are in section 3.1 Overall Study Design (first sentence); and in section 7. Intervention (How).*

Abbreviations

AE/SAE Adverse Event / Serious Adverse Event
HPO Hypothalamic–Pituitary–Ovarian axis
HPA Hypothalamic–Pituitary–Adrenal axis
HRT Hormone Replacement Therapy (HRT)
MRS Menopause Rating Scale
PSQI Pittsburgh Sleep Quality Index
EMQ Everyday Memory Questionnaire
GAD-7 Generalized Anxiety Disorder-7
PHQ-9 Patient Health Questionnaire-9
PIS Participant Information Sheet
TAU Treatment as Usual
PI/CI Principal Investigator / Chief Investigator
GDPR General Data Protection Regulation