



# Group cognitive behavioural therapy of physical and psychological menopausal symptoms of Chinese women, delivered via Internet and mobile phone versus face to face: A protocol for a randomized non-inferiority trial

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## ABSTRACT

**Background:** Menopause syndrome generally includes psychological problems. Group treatment delivered via the Internet and mobile phone (imGT) may improve women's physiological and psychological conditions.

**Objective:** To investigate the efficacy of group cognitive behavioural therapy of menopause-related mood swings and quality of life, delivered face to face or via the Internet and mobile phone.

**Methods:** This protocol is for a randomized controlled clinical trial with a sample of 140 menopausal women divided into 2 groups: imGT and face-to-face group treatment (ffGT). The primary outcome will be the improvement in the menopausal symptoms of the two groups, as assessed by the Greene Climacteric Scale. The secondary outcomes will be: quality of life, assessed by the Short Form 36 Health Survey Questionnaire; insomnia, assessed by the Pittsburgh Sleep Quality Inventory; anxiety, assessed by the Hamilton Anxiety Rating Scale; and therapeutic alliance, assessed by the Working Alliance Inventory-Short Revised and Client Satisfaction Questionnaire-8. imGT will be performed once a week for 1.5 h for 10 weeks with a daily 'Punched-in' on the WeChat app; ffGT will be performed once a week for 1.5 h for 10 weeks. All outcomes will be assessed at baseline, at a post-intervention evaluation (week 10), and at a follow-up evaluation (week 22).

**Discussion:** This study will be the first clinical trial to examine the effects of imGT on menopausal women in China. If imGT is found to be non-inferior to ffGT, it will facilitate access to menopausal health services.

## 1. Introduction

Menopause is accompanied by multidimensional alterations that affect women's quality of life [1]. These changes put women at high risk of health problems, both physical, such as hot flashes, night sweats and sleep disturbance [2–4], and psychological, such as anxiety [4,5]. It is estimated that, by 2030, in China, the number of women over 50 will have increased to more than 280 million [6]. Currently, 51%–55% of women in China experience menopause syndrome [7,8] with hot flashes (62%), fatigue (82%) [9], sleep disturbance (51%) and mood swings (40%) [10]. Mood swings affect not only mental health but also neurocognitive and cardiometabolic function [11]. Medical treatment, such as hormone replacement therapy, is effective in alleviating menopause symptoms; however, several epidemiological studies have confirmed that the side-effects can include increased risk of breast cancer [12,13] and ovarian cancer [14]. Therefore, non-medical

therapy should be investigated for menopausal symptoms.

Group treatment (GT), and in particular cognitive behavioural therapy (CBT), has been shown to have advantages in the treatment of anxiety [15–18], depression [19], posttraumatic stress disorder [20], and chronic pain [21]. A systematic review of 26 randomized controlled trials (RCTs) indicated that CBT can be beneficial for alleviating menopausal vasomotor symptoms [22]. Moreover, CBT was more effective for somatic symptoms when it was delivered as a group treatment ( $-4.43$ , 95% CI:  $-8.47$  to  $-0.39$ ;  $p < 0.05$ ) than as an individual treatment ( $-1.00$ , 95% CI:  $-1.90$  to  $-0.10$ ;  $p < 0.05$ ) [23]. However, there is limited evidence regarding the efficacy of GT for menopausal women [24,25]. Green [26] reported that 8 participants with menopausal symptoms improved on measures of hot flashes ( $t(7) = 3.4$ ,  $p = 0.01$ ), depression ( $t(7) = 3.7$ ,  $p = 0.00$ ), anxiety ( $t(7) = 4.2$ ,  $p = 0.00$ ), and quality of life ( $t(7) = -3.5$ ,  $p = 0.01$ ) after 10 sessions (2 h each) of GT. Ayers [27] reported that compared with a no-

**Abbreviations:** imGT, group treatment delivered via the Internet and mobile phone; ffGT, face-to-face group treatment; GT, group treatment; CBT, cognitive behavioural therapy; QOL, quality of life

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treatment control condition ( $n = 45$ ), GT ( $n = 48$ ) significantly reduced the frequency of night sweats (mean SD, 1.33; 95% CI, 0.54–2.13;  $P = 0.001$ ) after 4 weeks of intervention (2 h once a week), and mood and quality of life also improved.

However, GT typically faces problems such as long waiting times and restricted access [28]. It is also costly for patients to adhere to face-to-face GT [29]. Furthermore, in China, maternal and paediatric hospitals constitute only 0.3% of all medical institutions [30], which means there are limited health resources for menopause syndrome and related mood swings.

To improve access to services, psychotherapeutic interventions delivered via the Internet and mobile phone (IM) have been studied in recent years for conditions such as anxiety [31] and insomnia [32]. The benefits of IM therapies include robust adherence [33,34], cost-effectiveness [35], and an increase in acceptance of a mental health intervention [36]. A meta-analysis of 13 RCTs (participant count 31–201) found that Internet-delivered cognitive behavioural therapy (iCBT) and face-to-face treatment produce equivalent overall effects for psychiatric and somatic disorders, with a pooled effect size (Hedges'  $g$ ) at post-treatment of  $-0.01$  (95% CI:  $-0.13$  to  $0.12$ ) [37]. Further meta-evidence reveals that, compared with the control group at post-intervention among postpartum women, therapist-supported iCBT significantly improves stress ( $d = 0.84$ ,  $n = 5$ ), anxiety ( $d = 0.36$ ,  $n = 6$ ), and depressive symptoms ( $d = 0.63$ ,  $n = 8$ ) [38].

Beyond the academic context, menopausal women may benefit from guided GT or IM therapies due to their feasibility and accessibility. However, no studies have investigated the efficacy of GT with IM for menopause syndrome and its related mood swings. There are also no reports of the effect size of GT with IM.

Therefore, the aim of this study is to compare the efficacy of a group treatment delivered via Internet and mobile phone (imGT) with that of guided face-to-face group treatment (ffGT) for menopausal women with mood swings. We will conduct an RCT comparing the two treatment groups at baseline, at different time points throughout the trial, and at 3-month follow-up. The primary outcome of this study is the status of menopausal symptoms. The secondary outcomes are menopause-related mood swings, including anxiety, insomnia, and menopause-related quality of life (QOL). It is hypothesised that after 10 weeks of intervention, the imGT group will show non-inferiority overall effects on menopause symptoms compared with the ffGT group, especially on hot flushes and mood swings.

The intervention adherence of both groups will be determined by the number participants who complete the entire intervention. This is the first trial in China to evaluate menopause treatment using imGT and ffGT. Adverse events will be evaluated and recorded.

## 2. Method

### 2.1. Trial design

This is a protocol for a single-site, non-blinded RCT with two conditions in a 1:1 allocation: (1) group treatment delivered via the Internet and mobile phone (imGT) and (2) guided face-to-face group treatment (ffGT).

The trial will be reported consistent with the Consolidated Standards of Reporting Trials guidelines for RCTs [39] and the guidelines for Internet intervention trials [40]. This protocol has been approved by the Affiliated Obstetrics and Gynaecology Hospital of Nanjing Medical University in 2018 (NFLZ-2018-106). The results will be published according to the CONSORT statement in peer-reviewed journals. The trial has been registered at ClinicalTrials.gov (NCT03948269), which is a primary registry of the International Clinical Trial Registry Platform of the World Health Organization. The overall study design is illustrated in Fig. 1.

### 2.2. Participants

Participants will be recruited from June 2018 until the targeted sample size has been reached, through lectures (held four times a month), posters and leaflets placed in the Affiliated Obstetrics and Gynaecology Hospital of Nanjing Medical University. Women will opt into the study by scanning the QR code on the posters or leaflets to register their information, including name and mobile phone number.

To be eligible for the study, participants should (a) be women aged 40–60, in menopausal transition or post-menopause, according to the STRAW + 10 definition [41], (b) have Internet access, (c) have mobile phone access, (d) have sufficient knowledge of the Chinese language, (e) have scored in the clinical range for menopause syndrome in a psychiatric interview, and (f) have signed the consent form that will be provided to eligible participants.

The exclusion criteria are as follows: not giving informed consent; presence of hyperthyroidism, coronary atherosclerotic heart disease, hypertension (BP  $\geq 140/90$  mmHg), pheochromocytoma, neuroasthenia, psychosis, or other diseases closely related to the main disease; troublesome drinking; and drug use (hypnotics or hormone therapy) in the past 14 days which might affect mood [3].

The study will be conducted at the Affiliated Obstetrics and Gynaecology Hospital of Nanjing Medical University, which is categorised as tertiary class A and has more than 1000 beds [42]. The therapists are female psychiatrists and psychologists with training in GT. Experienced clinicians will supervise the treatment process. Informed consent will be obtained by psychiatrists during recruitment.

### 2.3. Group treatment delivered via the Internet and mobile phone

After randomization, participants allocated to the imGT group will have a psychiatric consultation lasting 1 h, which will be carried out by psychiatrists. The consultation will be conducted according to a user manual and will include information about this trial, diagnoses of menopause and mood swings, advice on methods of treatment, health-promoting recommendations and guidance on the completion of questionnaires. The object of this consultation is to increase participants' understanding of imGT and optimize the effects of the interventions.

Based on the previous meta-analysis [23], the therapy consists of 10 modules (15 h in total) in groups of 8 participants over 10 weeks and one follow-up meeting (2 h) 12 weeks after the 10th module (i.e. in week 22). Each module is adapted from the literature on CBT [43,44] and will be conducted online on WeChat, a mobile-phone social networking app with 1 billion users in 2018. First, we will establish a WeChat group containing the imGT group members and psychiatrists, in which everyone can simultaneously participate in real time. The interactive treatments will be conducted every Friday evening for 1.5 h via text, audio or video messaging. Table 1 summarizes the module topics and provides detailed information on the treatment programme. All modules will be saved for repeated viewing after completion.

Second, we will establish another WeChat programme named Punched-in, where participants report on aspects of their everyday life such as diet, sports, readings or mood, according to the plan made by the psychiatrists, via text, audio, photo or video message. This programme will be visible to and able to be commented on only by participants and psychiatrists.

Participants assigned to imGT therapy will have to refuse other psychological treatment for the duration of the study.

### 2.4. Face-to-face group treatment

Participants allocated to the ffGT group will first receive the same psychiatric consultation as the imGT group, though it will aim to improve participants' understanding and patient compliance of the ffGT group. The same 10 modules as the imGT group will be conducted every weekend in the psychological counselling room of the Affiliated

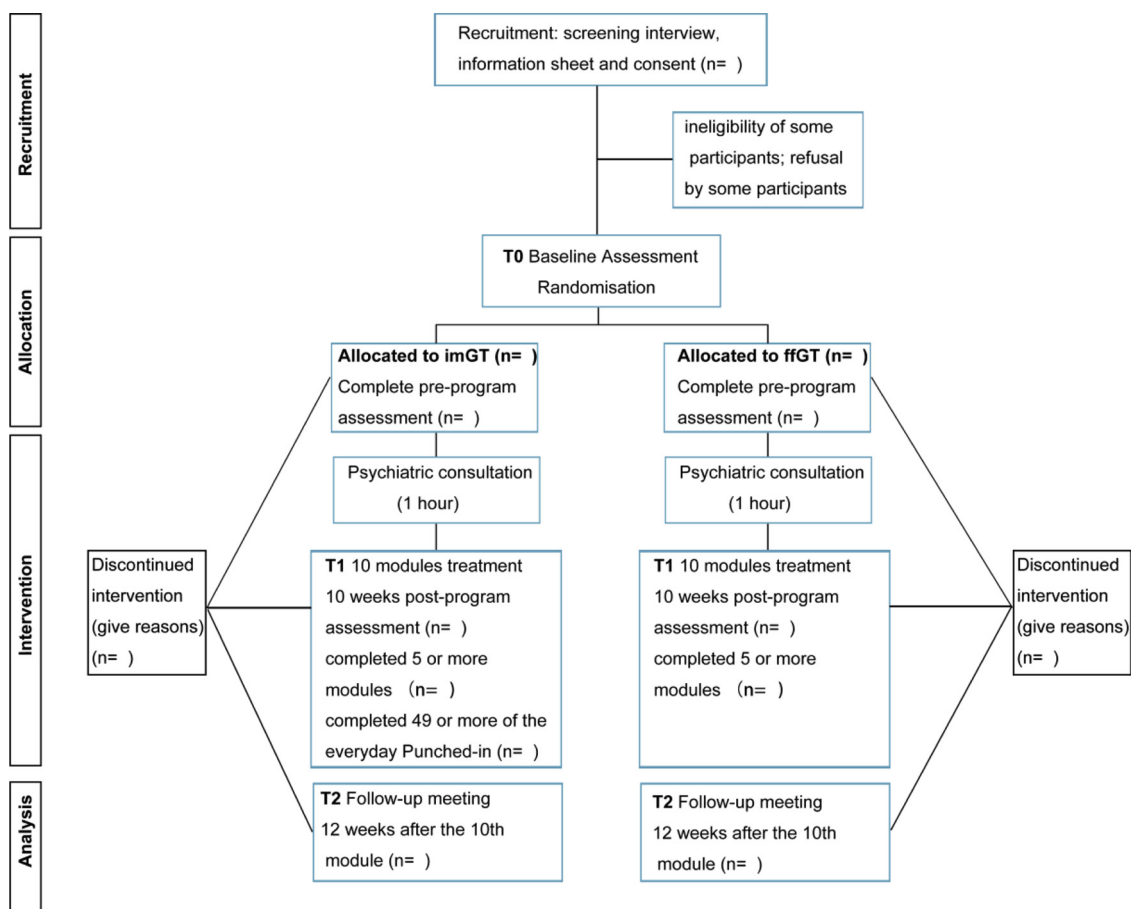


Fig. 1. Flow diagram of this study imGT, group treatment delivered via Internet and mobile phone; ffGT, face-to-face group treatment.

Obstetrics and Gynaecology Hospital of Nanjing Medical University. Participants assigned to ffGT therapy have to refuse other psychological treatment for the duration of the study.

2.5. Compliance and attrition

Therapy compliance will be assessed by the number of participants who complete the treatment modules. To enhance compliance, we will offer instant consultation about participants' menopausal symptoms through the WeChat app for the imGT group or by telephone for the ffGT group. The imGT intervention will be recorded both online and offline by video, audio or pictures, while the ffGT intervention will be

recorded by video. Both treatments can be accessed by an external panel to ensure adherence to the treatment protocol. Interventions will be discontinued upon participant request. When there is poor compliance or dropout, the reason will be sought and recorded if possible.

2.6. Assessment and outcome measures

For both imGT and ffGT, assessment will be conducted at baseline (T<sub>0</sub>), at completion of the intervention (10 weeks, T<sub>1</sub>), and at 12-week follow-up after the 10<sup>th</sup> intervention (T<sub>2</sub>). The trial will collect patient-reported outcome (PRO) data. T<sub>1</sub> is set to be the principal time point, to avoid the risk of multiple statistical testing. Table 2 presents a list of

Table 1  
Content of group therapy sessions [43,44].

Module	Psychotherapeutic technique	Content
1 Goal setting	Psychological support therapy	Introduction, psychometric assessments, goal setting, treatment agenda
2 Menopause education	Psychological support therapy; Cognitive behavioural therapy	Discussion of homework assignments, menopause introduction, psycho-education
3 Sleep and relax	Mind-body relaxation therapy	Discussion of homework assignments, discussion of reasons for insomnia
4 Healthy attitudes	Psychological support therapy; Cognitive behavioural therapy	Discussion of homework assignments, identification of personal values and barriers
5 Stress tolerance	Music therapy; Breathing therapy	Discussion of homework assignments, discussion of reason for stress, problem-solving, diary writing
6 Lifestyle education	Psychological support therapy; Cognitive behavioural therapy	Discussion of homework assignments, lifestyle education, planning diet and physical exercise
7 Relationship management	Cognitive behavioural therapy; Role play	Discussion of homework assignments, communication training, sharing life experiences
8 Mood management	Breathing therapy; Psychological support therapy	Discussion of homework assignments, emotion control, write out feelings
9 Review and summary		Discussion of homework assignments, repeat of psychometrics
10 Share and future		Talking about successful experiences, future planning, future directions

**Table 2**  
Outcome measures.

Instrument	items	Weeks			
		0	10	22	
Menopause symptoms	GCS <sup>1</sup>	21	×	×	×
Quality of life	SF-36 <sup>2</sup>	36	×	×	×
Insomnia	PSQI <sup>3</sup>	19	×	×	×
Anxiety	HAM-A <sup>4</sup>	14	×	×	×
Therapeutic alliance	WAI-SR <sup>5</sup>	12		×	
	CSQ-8 <sup>6</sup>	8		×	

<sup>1</sup> Greene Climacteric Scale.

<sup>2</sup> The Short Form 36 Health Survey Questionnaire.

<sup>3</sup> Pittsburgh Sleep Quality Index.

<sup>4</sup> The Hamilton Anxiety Rating Scale.

<sup>5</sup> The Working Alliance Inventory-Short Revised.

<sup>6</sup> Client Satisfaction Questionnaire-8.

outcomes and measurements.

### 2.7. Primary outcome

The Greene Climacteric Scale (GCS) [45] is used for evaluating menopausal symptoms. It contains 21 questions covering 5 domains: anxiety, depression, somatic symptoms, vasomotor symptoms, and sexual function. Each question is answered on a 4-point Likert scale. The answers to all 21 questions are summed to give a total quality-of-life measure; a higher score indicates a worse quality of life. According to the hypothesis and the PRO-specific domains of this trial, vasomotor symptoms, anxiety and depression will be analysed specifically. The Chinese version of this questionnaire [46] has high validity (0.90), and the Cronbach's alpha coefficient is 0.95, while its test-retest reliability is 0.94 ( $P < 0.01$ ).

### 2.8. Secondary outcomes

The Short Form 36 Health Survey Questionnaire (SF36) [47] is widely used to evaluate the potential benefits of healthcare interventions. It comprises eight dimensions (physical functioning, social functioning, physical and emotional role limitations, mental health, energy/vitality, pain, and general health perceptions), and the score ranges from 0 to 100, where better health achieves higher scores [48]. This questionnaire was chosen because of the validation of the Chinese version [49] with a sensitivity of 0.72–0.88 and specificity of 87.5%–100%.

The Pittsburgh Sleep Quality Index (PSQI) [50] is a self-rated inventory that evaluates sleep quality and disturbances over a 4-week period. It comprises 19 individual items giving a global score that ranges from 0 to 21. The Cronbach's alpha coefficient is 0.80, and the correlation coefficient of the PSQI for test-retest reliability is 0.82 [51]. A Chinese PSQI score  $> 7$  yielded a sensitivity of 98.3% and specificity of 90.2% in distinguishing between good and poor sleepers ( $\kappa = 0.89$ ,  $p < 0.01$ ) [52].

The Hamilton Anxiety Rating Scale (HAM-A) [53] is a rating scale developed to measure symptoms of anxiety. It is a semi-structured clinician-rated interview consisting of 14 items that measure both psychological and somatic symptoms [54]. For each item a 5-point scale ranging from 0 (not present) to 4 (severe) is used, giving a total severity score of 0–56;  $< 17$  indicates mild anxiety and 25–30 is considered moderate–severe. The Chinese version of the HAM-A will be used in this study [55].

### 2.9. Therapeutic alliance and treatment satisfaction

The Working Alliance Inventory-Short Revised (WAI-SR) provides an assessment of the therapeutic alliance [56] and contains 12 items

with three dimensions of working alliance: agreement on the tasks of therapy, agreement on the goals of therapy, and development of an affective bond between client and therapist. Items are rated on a 5-point scale (from 1 = “never” to 5 = “always”).

Treatment satisfaction will be measured by the Client Satisfaction Questionnaire-8 (CSQ-8) [57], which evaluates service utilization and psychotherapy outcome. It has high internal consistency ( $\alpha = .91$ ).

### 2.10. Sample size estimation

Power estimation is based on the primary hypothesis regarding changes in menopausal symptoms measured with the Greene Climacteric Scale. According to previous research, iCBT group showed an effect size of 0.63 for hot flush, and 0.33 for overall menopausal symptoms. The standard deviation is estimated to be 9 units [58]. We assume the non-inferiority margin of  $d = 0.6$  effect sizes. For a mixed-linear model, there is no available software to calculate the sample size for analysis, and so an  $f$  index of 0.3 is used as a substitute for an effect size of 0.6 (Cohen's  $d$ ). Thus, with a statistical power of 0.80 and an alpha level of 0.05, the minimum sample size should be approximately 116 (58 for each group). Considering the attrition rates of previous trials, a 20% dropout rate [59] can be expected for this study, so the required sample size is 140 (70 per group).

### 2.11. Randomization procedure

Eligible participants will be randomized to either the imGT or the ffGT group after baseline data collection. Randomization and allocation will be conducted by a statistician not involved in the trial. For randomization, a computer algorithm with permuted block sizes (ranging from 2 to 8) will be used to ensure balanced group sizes of 1:1 and allocation concealment. The procedure will be conducted at <http://www.randomization.com>. The randomization will not have any stratification factors. After the baseline measurement, the participants who consent to be involved in the trial will receive an opaque envelope containing a randomized code for group allocation. Due to the nature of the intervention, blinding of the therapist and participants is not possible within the course of the study. Data will be recorded on separate data sheets by someone not involved in the study; hence, the data will be analysed without information regarding group allocation.

### 2.12. Data collection and management

Outcome data will be assessed via self-report using a secure online survey platform ([www.wjx.cn](http://www.wjx.cn)). Participants will be recommended to finish the questionnaires in hospital or at home, and they will be reminded by instant message, email and phone call, to avoid missing data. Only the study team can access the information from this study; information will be saved in local, password-protected data files. We will back up the primary database weekly. The data will be monitored by physicians across the trial so that they can respond if a participant's clinical symptoms worsen. A unique identification number will be given to each participant so that no individual subjects can be identified.

### 2.13. Statistical analysis

No interim data will be analysed during the trial. Intention-to-treat (ITT) samples will be analysed to evaluate the efficacy of the imGT and ffGT interventions. Mixed-effects models (random intercept) [60] with interaction effects of group and time will be conducted on primary and secondary outcomes. Time, imGT group, baseline Greene Climacteric Scale score, and age will be included as covariates at randomization. Such a model can take account of the multiple time points for data collection and is reasonably robust to missing data, especially with a restricted maximum likelihood approach for a small sample size [61]. Multiple regression models will be used to test potential mediating or

moderating effects. The therapeutic alliance and treatment satisfaction questionnaires will be analysed using t-tests. According to the pattern of missing data, strategies will be evaluated to judge possible bias [62].

Complier average casual effect (CACE) analysis will be conducted to estimate the degree of protocol compliance within the intervention arms [63]. CACE analysis can also be used to compare the treatment effect between those who complied with treatment and those who would have complied if given the opportunity [64]. In this analysis, “full” participation is defined as going to at least five of the ten sessions for both imGT and ffGT groups, which is the minimum number of attendances to benefit from the programme [65]. For the ffGT group, completing 49 of the 70 everyday Punched-in is defined as full participation [66].

Sensitivity analysis will be conducted under the missing-at-random scenarios to examine bias. All analyses will be conducted with a two-sided level of significance ( $\alpha = 0.05$ ). Stata SE 15.0 software (Stata Corp LLC) will be used for data analysis. If there is no significant effect on the primary outcome and the estimated effect size is less than 0.6, explanatory analysis will be conducted to determine potential reasons for the null findings, such as poor adherence or heterogeneity effects.

### 3. Discussion

The aim of this study is to verify the feasibility and effects of imGT on menopausal syndrome, mood swings, and quality of life in menopausal women. There have been few studies on imGT [67–70], and none has focused on menopausal imGT. If imGT is found to be non-inferior to ffGT, it could help menopausal women and possibly also their families. Moreover, because of the wide use of the WeChat app, imGT is a feasible and cost-effective way to conduct group therapy without regard to participants’ travel time.

Systematic reviews and meta-analyses have verified the ability of CBT to improve the physical and mood symptoms of menopausal women [27,71–73]. However, in the field of menopause, GT has not been well studied, especially in relation to effect size, interventional contents, adherence, and limitations. Thus, this RCT is designed to investigate the effect size of imGT and ffGT.

The limitations of our study design are as follows. First, for imGT, there are two components of the intervention: a group treatment once a week and everyday daily Punched-in. It is difficult to determine which component is more important or if the two components complement each other. Second, blinding is not possible for the clinical assessment. This is a general problem in CBT. Third, the assessment and treatment of imGT are conducted via mobile phone, and they may therefore be affected by the phone or network environment. Finally, self-report scales are used to assess menopause and its related mood swings, which may cause participant recall bias as a systematic error.

The results of this study will be published in journals and presented at conferences. Future research could focus on the cost-effectiveness of imGT and ffGT. We are also planning to develop a brief questionnaire to evaluate imGT to increase knowledge and awareness of menopausal group therapy.

### 4. Trial status

This study is currently in the recruitment stage, and pre-intervention assessments are being made.

### Contributors

Jianqian Chao revised the paper.

Dan Li drafted the manuscript and contributed to specific aspects of the patient-reported outcome of the trial protocol.

Jing Kong contributed to specific aspects of the patient-reported outcome of the trial protocol, sourcing funding, and quality control.

Ying Yang is responsible for the psychological intervention.

Suli Wang is responsible for the psychological intervention  
Jiangping Wu is the director of department of maternal health who manages the program.

All the authors conceived and designed the study.

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### Ethical approval

This protocol was approved by the Affiliated Obstetrics and Gynaecology Hospital of Nanjing Medical University in 2018 (NFLZ-2018-106).

### Provenance and peer review

This article has undergone peer review.

### Research data (data sharing and collaboration)

According to the data sharing statement policy of International Committee of Medical Journal Editors, individual participant data will be available including data dictionaries. All of the individual participant data collected during the trial will be shared after deidentification. Research documents will be available following publication (no end data) to anyone who wishes to access the data. These include Study protocol, Statistical Analysis Plan and Analytic Code. Requests should be directed to 230179269@seu.edu.cn.

### Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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