A Pragmatic Randomized Controlled Umbrella Trial of Acupuncture for Ameliorating Multidimensional Psychosomatic Comorbidities in Breast Cancer Patients Under the Shared Decision-Making Model

Study Protocol Design:：Institute of Acupuncture and Moxibustion,The First Affiliated Hospital of Tianjin University of Traditional Chinese Medicine

Protocol No.: 2026006

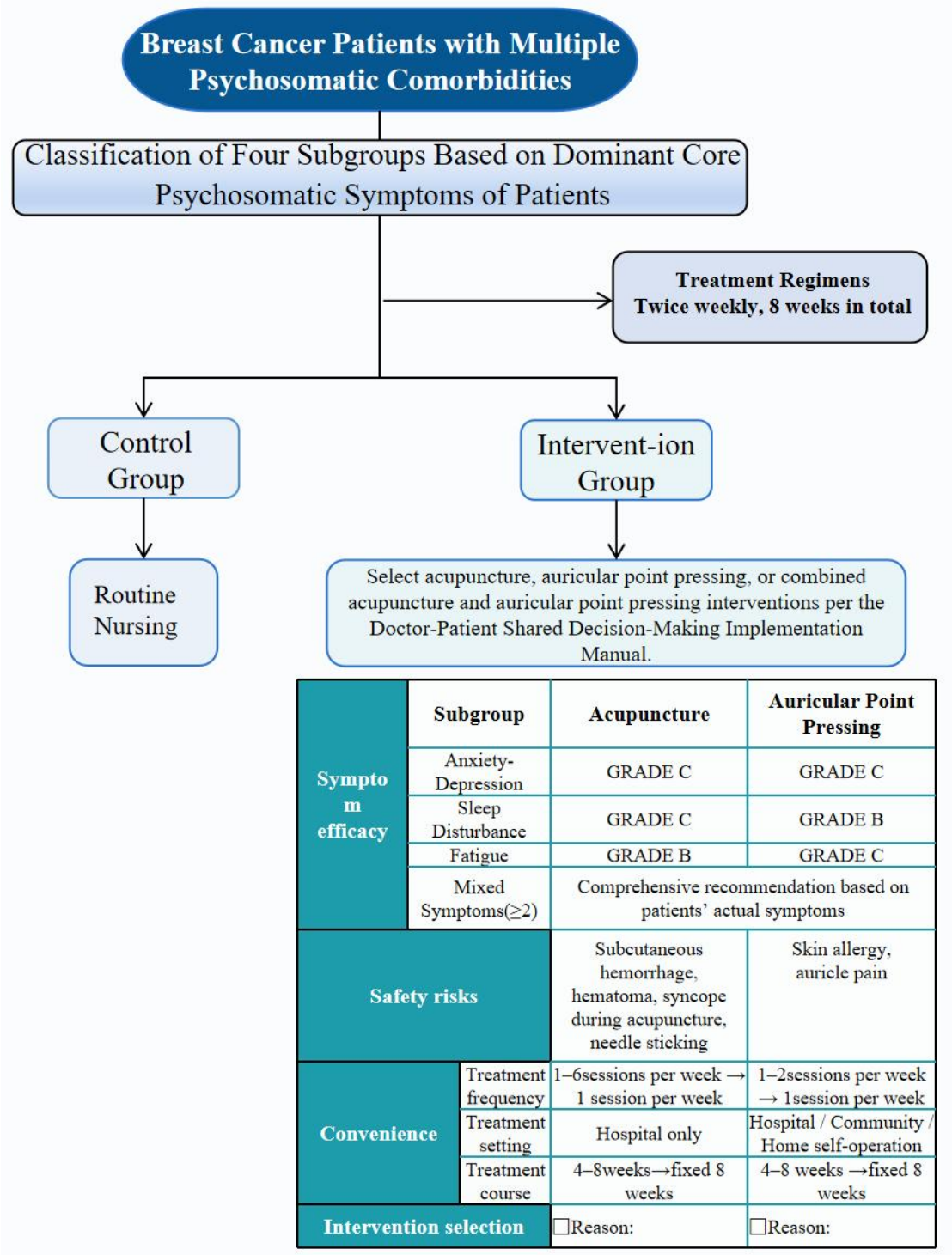
Version: 1.0

Version Date: May 9, 2026

A Pragmatic Randomized Controlled Umbrella Trial of Acupuncture for Ameliorating Multidimensional Psychosomatic Comorbidities in Breast Cancer Patients Under the Shared Decision-Making Model

3.3.1 Study Design

This study adopts a multicenter, pragmatic, randomized controlled umbrella trial design integrated with the shared decision-making (SDM) model. Participants are stratified into four subgroups based on their core psychosomatic symptom phenotypes (single symptom versus multiple comorbid symptoms). Eligible patients are randomly allocated to the intervention group or control group at a 2:1 ratio. In the intervention group, personalized interventions (manual acupuncture, auricular point pressing, and combined manual acupuncture plus auricular point pressing) are selected through shared decision-making between physicians and patients, whereas the control group receives routine nursing care. This trial evaluates the therapeutic effect on single symptoms and the synergistic alleviation effect of multiple concurrent symptoms across all psychosomatic phenotype subgroups under the SDM framework. The design overcomes the limitation of conventional randomized controlled trials that only target individual symptoms and better fits real-world clinical settings characterized by multimorbidity.



Symptom efficacy	**Subgroup**	**Acupuncture**	**Auricular Point Pressing**
	Anxiety-Depression	GRADE C	GRADE C
	Sleep Disturbance	GRADE C	GRADE B
	Fatigue	GRADE B	GRADE C
	Mixed Symptoms(≥2)	Comprehensive recommendation based on patients' actual symptoms	
Safety risks		Subcutaneous hemorrhage, hematoma, syncope during acupuncture, needle sticking	Skin allergy, auricle pain
Convenience	Treatment frequency	1–6sessions per week → 1 session per week	1–2sessions per week → 1session per week
	Treatment setting	Hospital only	Hospital / Community / Home self-operation
	Treatment course	4–8weeks→fixed 8 weeks	4–8 weeks →fixed 8 weeks
Intervention selection		☐Reason:	☐Reason:

Figure1　Technical Roadmap of Randomized Controlled Trial

3.3.2　Study Subjects

Source of Cases： From June 2026 to April 2028, a total of 216 inpatients and outpatients diagnosed with breast cancer accompanied by psychosomatic symptoms will be recruited from three sub-centers: the First

Affiliated Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin Medical University Cancer Institute and Hospital, and the Affiliated Hospital of Tianjin Academy of Traditional Chinese Medicine.

（1）Inclusion Criteria

①Female patients aged 18–70 years old;

② Confirmed diagnosis of breast cancer via pathological or cytological examination;

③ Meet at least one of the psychosomatic symptom diagnostic criteria:Anxiety or depressive state: HADS anxiety or depression subscale score ≥ 8;Sleep disturbance: Total PSQI score ≥ 8;Cancer-related fatigue: Total BFI score ≥ 4;

④Expected survival time ≥ 1 year;

⑤Clear consciousness, basic communication ability, and capacity to complete scale assessments;

⑥ Voluntary signing of informed consent by the patient or legal representative.

（2）Exclusion Criteria

①Severe mental disorders (e.g., schizophrenia, bipolar disorder) or lack of civil capacity;

② Contraindications to auricular point pressing: auricle skin lesions/infections, or allergic constitution (allergy to Vaccaria seeds or adhesive tape);

③Receiving other acupuncture or acupoint pressing interventions, or unable to discontinue such treatments during the trial;

④Contraindications to manual acupuncture: bleeding tendency (e.g.,

coagulation disorders, purpura) or local acupoint skin lesions;

⑤Complicated with severe dysfunction of vital organs (heart, liver, kidney) or cachexia;

⑥Pregnant or lactating women.

(3) Discontinuation Criteria

①Severe adverse events occurring during intervention (e.g., severe skin allergy, anaphylactic shock, acute deterioration of disease) requiring trial termination as assessed by researchers;

②Voluntary written request from the patient to withdraw from the trial.

3.3.3 Randomization and Allocation Concealment

(1) Subgroup Stratification

Participants are divided into four subgroups according to the dominant type of core psychosomatic symptoms to cover common clinical phenotypes:

Anxiety-depression phenotype: Only anxiety-depressive state (without the other two categories of symptoms);.

Sleep disturbance phenotype: Only sleep disturbance (without the other two categories of symptoms);

Fatigue phenotype: Only cancer-related fatigue (without the other two categories of symptoms);

Mixed symptom phenotype: Concurrent presence of $\geqslant$ 2 of the above psychosomatic symptoms (e.g., anxiety-depression + sleep disturbance, cancer-related fatigue + sleep disturbance).

(2) Randomization Method

Central stratified dynamic randomization is adopted, with psychosomatic symptom phenotype as the stratification factor. Eligible patients are assigned to the intervention group or control group at a 2:1 ratio via a central randomization system. Dynamic randomization adjusts allocation probability based on baseline characteristics of enrolled patients (e.g., age, tumor stage) to ensure balanced baseline data between groups.

(3) Allocation Concealment and Blinding

Allocation schemes are generated by the randomization system and delivered to therapists on the day of the first intervention. Due to the inherent characteristics of manual acupuncture, auricular point pressing, and interactive physician-patient shared decision-making, blinding of patients and therapists is not feasible. Outcome assessors and data analysts will be blinded throughout the trial.

3.3.4 Intervention and Control Measures

(1) Intervention Protocol Design

Personalized interventions are selected via a three-stage conversational model under shared decision-making between physicians and patients:

① Team discussion: Physicians explain the complexity of multiple concurrent psychosomatic symptoms in breast cancer patients, clarify the potential benefits of adding TCM acupuncture interventions to routine nursing, and invite patients to participate in treatment decision-making.

② Option discussion: A detailed investigator manual is provided to inform patients of viable interventions for their symptom subtype,

including optimal treatment modalities, frequency, treatment locations, and potential adverse reactions.

③Decision discussion: Physicians and patients discuss the risks and benefits of candidate treatments to ensure patients make fully informed decisions based on their symptom profiles and personal preferences.

Intervention cycle: 8 weeks of active treatment + 4 weeks of follow-up, totaling 12 weeks.

Auricular point pressing group: Routine nursing care plus auricular point pressing. Patients may choose treatment locations via shared decision-making:①Hospital/community-based: Patients attend hospitals or community clinics for practitioner-administered auricular point therapy;②Home-based (hospital-community-family linkage model): Physicians perform initial auricular application and deliver standardized training; patients conduct self-administered auricular pressing remotely guided by clinicians or community support staff.

Manual acupuncture group: Routine nursing care plus in-hospital manual acupuncture treatment.

Combined intervention group: Routine nursing care plus in-hospital manual acupuncture and location-flexible auricular point pressing.

Control group: Standard routine nursing only, including dietary guidance, exercise counseling, mood regulation, and/or health education.

(2) Concomitant Basic Treatment

All patients retain their original breast cancer systemic treatment. No new active interventions targeting psychosomatic symptoms (e.g.,

anxiolytics/antidepressants, analgesic dose adjustments, other acupuncture modalities) are initiated during the trial in principle. Any medically necessary additional interventions for psychosomatic complaints will be fully documented, including herbal patent medicines and decoctions. All sub-centers distribute a unified Breast Cancer Psychosomatic Health Education Manual covering diet, exercise, and mood adjustment guidance to ensure consistent baseline nursing across groups.

(3) Auricular Point Pressing Protocol

All patients receive a core auricular point prescription, with supplementary auricular points matched to individual psychosomatic symptoms (see Table 1 and Table 2).

Table 1 Core Auricular Point Prescription for Auricular Point Pressing

Auricular Point	Location	Therapeutic Effects
Shenmen	Upper 1/3 of the triangular fossa (Area 4 of triangular fossa)	Improves insomnia, dream-disturbed sleep, neurasthenia; regulates nervous system function
Sympathetic	Junction of the anterior inferior crus of antihelix and inner helix margin (anterior Area 6 of antihelix)	Modulates autonomic nerve function and blood circulation
Endocrine	Inside the intertragic notch, at the base of cavum conchae (Area 18 of cavum conchae)	Regulates endocrine hormone levels
Subcortex	Medial surface of antitragus (Area 4 of antitragus)	Balances excitatory and inhibitory cerebral cortical activity; relieves pain, neurasthenia and insomnia

Table 2 Supplementary Auricular Points for Distinct Symptoms

Symptom Category	Auricular Points	Location
Anxiety-Depression	Liver	Inferoposterior cavum conchae (Area 12 of

		cavum conchae)
	Kidney	Cavum conchae, posterior inferior to inferior crus of antihelix (Area 10 of cavum conchae)
	Heart	Central depression of cavum conchae (Area 15 of cavum conchae)
	Spleen	Below line BD, posterosuperior cavum conchae, inferior margin of the area where helix crus disappears (Area 13 of cavum conchae)
Sleep Disturbance	Heart	Central depression of cavum conchae (Area 15 of cavum conchae)
	Kidney	Cavum conchae, posterior inferior to inferior crus of antihelix (Area 10 of cavum conchae)
	Occiput	Posterior lateral surface of antitragus (Area 3 of antitragus)
Fatigue	Liver	Inferoposterior cavum conchae (Area 12 of cavum conchae)
	Spleen	Below line BD, posterosuperior cavum conchae, inferior margin of the area where helix crus disappears (Area 13 of cavum conchae)
	Kidney	Cavum conchae, posterior inferior to inferior crus of antihelix (Area 10 of cavum conchae)
Mixed Symptoms	Matched to individual symptomatic profiles	

Operational Procedures for Auricular Point Pressing: Treatment is administered bilaterally with patients in sitting position. Auricles are disinfected with iodophor followed by 75% alcohol for deiodination. A spring probe is used to locate the most tender sensitive spots at target auricular points, where Vaccaria seed pressure patches are secured. Patients are instructed to apply pressure until soreness or dull pain is elicited. Self-pressing is required three times daily (morning, noon, evening), 3 minutes per session to maintain soreness.

Product Specification: Zhongyan Taihe Vaccaria seed acupoint pressure stimulation patches (manufactured in Beijing).

Replacement Frequency: Patches are replaced twice weekly for all patients (home or hospital/community setting). Patients return to clinics 2

days after application for patch removal; urgent follow-up is arranged for premature detachment to guarantee continuous intervention over 8 weeks (16 total sessions).

(4) Manual Acupuncture Protocol

All patients receive a core acupuncture prescription, with supplementary acupoints selected according to symptom subgroups; uniform mild reinforcing-mild reducing manipulation is applied.

Needle Specification: Huatuo brand disposable sterile stainless steel acupuncture needles (Suzhou production), diameter 0.25 mm, length 40 mm.

Treatment Frequency: Twice weekly, 30 minutes per session for 8 weeks (16 total sessions).

Table 3 Core Acupuncture Prescription

Acupoint (Meridian Code, Bilateral Unless Specified)	**Location**	**Needling Manipulation**
Hégǔ (LI4)	Dorsum of hand, between the 1st and 2nd metacarpals, midpoint of the radial side of the 2nd metacarpal	Perpendicular insertion 0.5 – 1 cun
Nèiguān (PC6)	Anterior forearm, 2 cun proximal to distal wrist crease, between palmaris longus and flexor carpi radialis tendons	

Zúsānlǐ (ST36)	Lateral shank, 3 cun inferior to Dubi (ST35), 1 finger-breadth lateral to anterior tibial crest, on the line connecting Dubi and Jiexi (ST41)	Perpendicular insertion1 – 1.5 cun
Yánglíngquán (GB34)	Lateral shank, depression anteroinferior to fibular head	
Dànzhōng (RN17)	Anterior midline, level with the 4th intercostal space, midpoint of the bilateral nipple connecting line	Transverse insertion 0.3 – 0.5 cun
Tàichōng (LR3)	Dorsum of foot, between the 1st and 2nd metatarsals, depression anterior to metatarsal base junction, or palpable arterial pulsation	Perpendicular insertion1 – 1.5 cun

Table 4 Supplementary Acupoint Prescriptions by Symptom Subgroup

Subgroup	Supplementary Acupoint	Location	Needling Manipulation
Anxiety-Depression Phenotype	Shénmén (HT7)	On the palmar aspect of the wrist, at the ulnar end of the transverse wrist crease, in the depression on the radial side of the flexor carpi ulnaris tendon	Perpendicular insertion0.5 – 0.8 cun
	Yìntáng (EX-HN3)	On the forehead, at the midpoint between the two eyebrows	Transverse insertion 0.5 – 0.8cun
	Bǎihuì (DU20)	On the head, 5 cun directly above the midpoint of the anterior hairline	Transverse insertion 0.5 – 0.8cun
	Gānshū	On the back, below the spinous process	Oblique insertion

	(BL18)	of the 9th thoracic vertebra, 1.5 cun lateral to the posterior midline	0.5 – 0.8 cun
	Píshū (BL20)	On the back, below the spinous process of the 11th thoracic vertebra, 1.5 cun lateral to the posterior midline	Oblique insertion 0.5 – 0.8 cun
Sleep Disturbance	Zhàohǎi (KI6)	In the ankle region, 1 cun below the tip of the medial malleolus, in the depression along the lower margin of the medial malleolus	Perpendicular insertion0.5 – 0.8 cun
	Shēnmài (BL62)	On the lateral aspect of the foot, in the depression directly below the lateral malleolus	Perpendicular insertion0.3 – 0.5 cun
	Ānmián (EX-HN22)	Posterior to the ear, at the midpoint of the line connecting Yìfēng (TE17) and Fēngchí (GB20)	Perpendicular insertion1 – 1.5 cun
	Xīnshū (BL15)	On the back, below the spinous process of the 5th thoracic vertebra, 1.5 cun lateral to the posterior midline	Oblique insertion 0.5 – 0.8 cun
	Shènshū (BL23)	On the back, below the spinous process of the 2nd lumbar vertebra, 1.5 cun lateral to the posterior midline	Perpendicular insertion0.5 – 1 cun
Fatigue	Qìhǎi (RN6)	On the anterior midline, 1.5 cun below the umbilicus	Perpendicular insertion1 – 1.5 cun
	Guānyuán (RN4)	On the anterior midline, 3 cun below the umbilicus	Perpendicular insertion1 – 1.5 cun

	Yīnlíngquán (SP9)	On the medial aspect of the lower leg, in the depression between the lower border of the medial condyle of the tibia and the medial margin of the tibia	Perpendicular insertion1 – 2cun
	Píshū (BL20)	On the back, below the spinous process of the 11th thoracic vertebra, 1.5 cun lateral to the posterior midline	Oblique insertion 0.5 – 0.8 cun
	Shènshū (BL23)	On the back, below the spinous process of the 2nd lumbar vertebra, 1.5 cun lateral to the posterior midline	Perpendicular insertion0.5 – 1 cun
Mixed Symptoms	根据症状选用不同的配穴		

3.3.5 Outcome Indicators and Assessment Timepoints

(1) Primary Outcome Indicator

Functional Assessment of Cancer Therapy-Breast (FACT-B)

Dimensions: 36 items covering physical well-being, social/family well-being, emotional well-being, functional well-being, and breast cancer-specific subscale; total score range 0 – 144, with higher scores indicating superior quality of life.

Primary analytical endpoint: Change in total FACT-B score at Week 8 relative to baseline (Δ FACT-B = Week 8 score − baseline score).

(2) Secondary Outcome Indicators

Core symptom scores per phenotype: ① Anxiety-depression

phenotype: HADS anxiety and depression subscale scores; ② Sleep disturbance phenotype: Total PSQI score plus sleep latency and sleep efficiency subdomain scores; ③ Fatigue phenotype: Total BFI score; ④ Mixed symptom phenotype: Composite response rate (≥30% reduction in both anxiety and sleep scores, or equivalent dual-symptom improvement).

Brief Pain Inventory (BPI): Evaluates the impact of pain on all psychosomatic comorbidity subgroups.

Synergistic relief effect: Pearson correlation coefficients of score changes across individual symptoms in the mixed phenotype subgroup, to assess multi-target synergistic effects of acupoint therapy.

Long-term sustained efficacy: All indicator scores and score changes at Week 8 (end of intervention) and Week 12 (end of follow-up).

(3) Safety Indicators

Adverse event documentation: All adverse reactions (e.g., skin allergy, auricular pain, dizziness) recorded with onset time, severity, intervention measures, and clinical outcomes.

Vital signs: Resting body temperature, heart rate, respiratory rate, blood pressure.

Safety evaluation: Calculation of adverse event incidence to assess the safety of manual acupuncture and auricular point pressing.

(4) Adherence Indicators

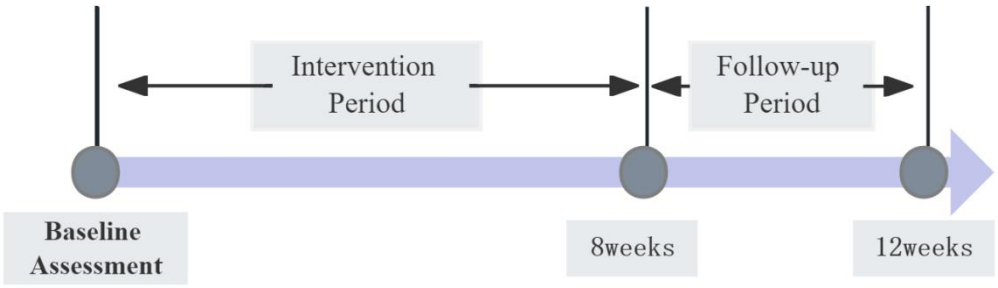
Treatment adherence rate = (actual completed auricular point pressing sessions / required total sessions) × 100%; adherence defined as ≥80% completion.

Self-pressing adherence rate: Recorded via patient daily logs and

cross-verified at follow-up visits; good adherence defined as ⩾ 90% compliance with daily self-pressing requirements.

(5) Assessment Timepoints

Evaluations are conducted at three time points: baseline, Week 8 (end of active intervention), and Week 12 (end of follow-up).



3.3.6 Data Management

All assessment and treatment data are recorded in electronic Case Report Forms (eCRFs) to ensure timely, complete, accurate, and authentic documentation of primary trial data. Original source documents are preserved for subsequent source data verification.

3.3.7 Quality Control

All researchers must complete standardized protocol training covering trial procedures, acupoint selection, communication frameworks, and operational details, and pass formal assessments before delivering trial interventions. Screening staff and data collectors receive unified SOP training prior to trial participation. The research team conducts source data audits in compliance with GCP standards. A third-party CRO performs on-site monitoring at three stages: after enrollment of the first 10 patients, mid-trial, and post-completion of all enrollment and follow-up. Source data and

trial records are reviewed, process evaluations are conducted, and formal monitoring reports are submitted to the research team for corrective action.

3.3.8 Ethics, Trial Registration and Filing

Prior to trial initiation, the protocol will obtain ethical committee approval, be registered on ClinicalTrials.gov, and filed in the National Medical Research Registration System.

3.3.9 Sample Size Calculation

Sample size estimation is based on the primary endpoint: change in total FACT-B score at Week 8 relative to baseline. A two independent samples t-test is used for calculation, with a 2:1 allocation ratio between the SDM intervention group and routine nursing control group. Calculation parameters are derived from a prior published clinical trial（Wang Y, Li X, Ji X, Wu J, Li J, Zheng W, Wu C, Huang L, Geng Z, Zhou J. Adaptive Auricular Point Acupressure for Sleep Disturbance in Women with Breast Cancer: A Randomized Controlled Trial. Evid Based Complement Alternat Med. 2022 Oct 31;2022:8637386. doi: 10.1155/2022/8637386.).A minimal clinically important between-group difference of 1.03 FACT-B points and standard deviation of 2.0 are assumed, with $\alpha=0.05$ and statistical power $(1-\beta)=0.9$. Sample size calculation is performed via PASS 15.0 software, with a 15% anticipated dropout rate incorporated. The final target sample size is 216 participants: 144 in the SDM intervention group and 72 in the routine nursing control group.

3.3.10 Statistical Analysis

All data processing and statistical analyses will be performed using SPSS 24.0 and R 4.2.2. Two-tailed statistical tests are applied for all analyses; $P < 0.05$ is defined as statistically significant. Bonferroni

correction is applied for multiple comparisons for primary endpoint analyses, with adjusted $\alpha = 0.025$ for pairwise comparisons between the intervention and control groups, and between single-symptom and mixed-symptom subgroups. Secondary and post-hoc analyses are exploratory without multiple comparison adjustment.

Analyses follow the modified Intention-To-Treat (mITT) principle, including all randomized participants who received at least one trial intervention. The Last Observation Carried Forward (LOCF) method is applied to handle missing data. Baseline data include demographic characteristics, medical history, FACT-B scores, and all secondary outcome measures.

Baseline Data Analysis:Descriptive statistics are generated for all baseline variables: continuous variables are reported as mean ± standard deviation (Mean ± SD) or median (interquartile range) [M (IQR)]; between-group comparisons use independent samples rank-sum tests. Categorical variables are summarized as frequency (proportion) [n (%)], with intergroup comparisons via chi-square test or Fisher's exact test as appropriate.

（1）Primary outcome analysis: Independent samples t-test to compare the mean change in FACT-B total score from baseline to Week 8 between the SDM intervention group and control group.

（2）Longitudinal follow-up analysis (secondary outcome): Linear mixed-effects models to evaluate between-group differences in FACT-B score changes across repeated timepoints (Week 4, Week 12). Fixed effects include treatment group, time, and group-by-time interaction, adjusted for time-invariant demographic confounders and time-varying covariates.

Random intercepts (baseline FACT-B score) and random time slopes are incorporated.

（3）Stratified exploratory subgroup analysis: Linear mixed-effects models to assess intergroup differences in FACT-B, HADS, PSQI, and BFI score trajectories across Week 4, Week 8, and Week 12 for single-symptom and mixed-symptom subgroups, with identical fixed and random effect specifications as the longitudinal model above.

Sensitivity Analysis

To evaluate result robustness, analyses are repeated on the Per-Protocol Set (PPS), consisting of participants who completed all scheduled interventions and follow-up visits. Multiple imputation (MI) is applied as an alternative missing data handling strategy.

Safety Analysis

All adverse events are categorized as adverse events, serious adverse events, acupuncture-related adverse events, serious acupuncture-related adverse events, adverse events leading to trial withdrawal, and fatal adverse events. Case counts, number of affected participants, and incidence rates are summarized for each category.

Adherence Evaluation

Frequencies and constituent ratios are used to describe compliance with scheduled treatment sessions and avoidance of prohibited concurrent therapies across study groups.