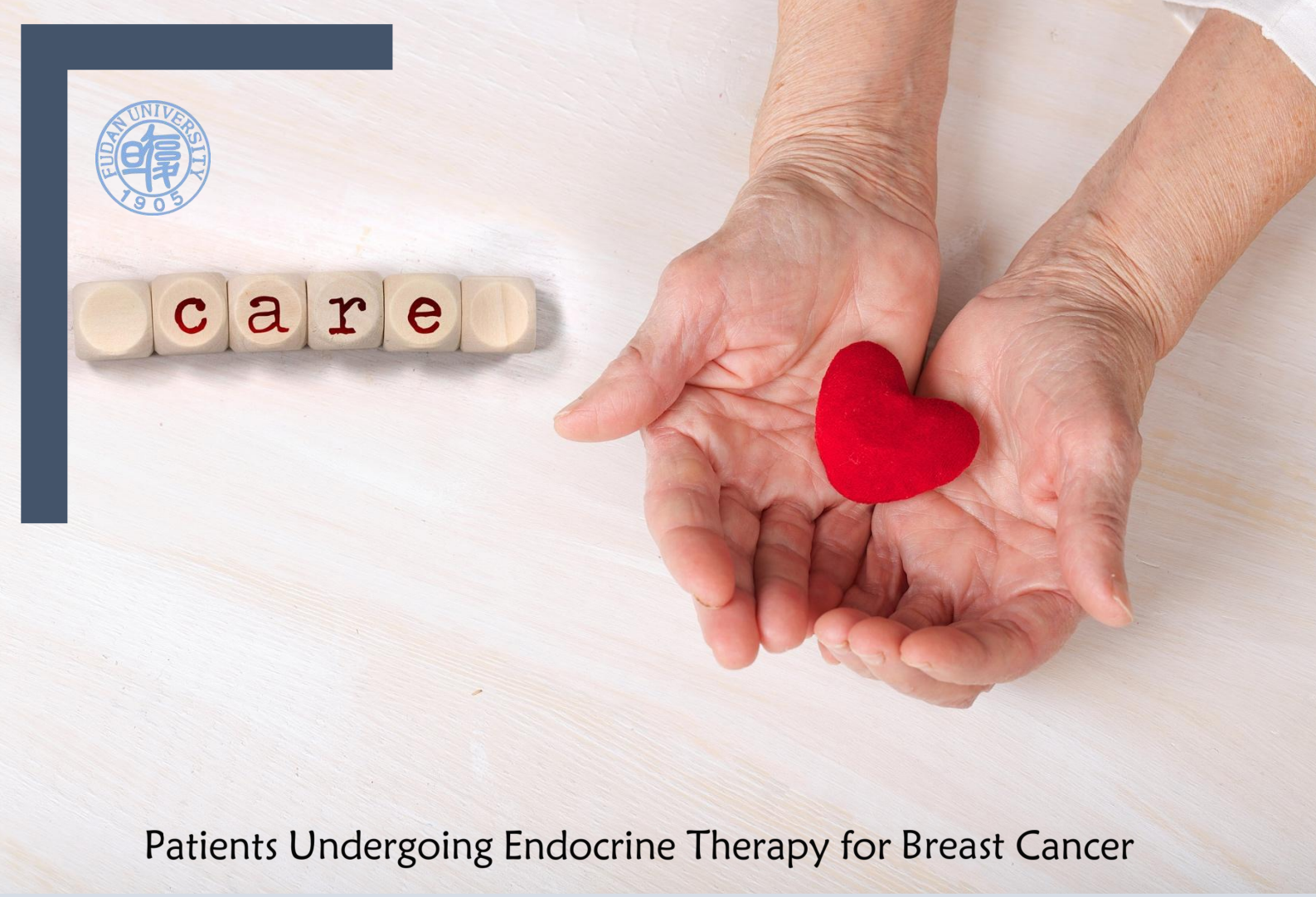
Official Title: Evidence-Based Practice Research on the Management of Musculoskeletal Symptoms in Breast Cancer Patients Undergoing Endocrine Therapy from a Multicultural Perspective

NCT Number: Pending

Document Date: April 17, 2023

Document Type: Study Protocol



Patients Undergoing Endocrine Therapy for Breast Cancer

Musculoskeletal Symptom Management Protocol

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2024.10.31

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1. Research Background

With the continuous rise in global breast cancer incidence, the treatment and management of breast cancer have become major research topics in the medical field. Endocrine therapy is a common treatment for patients with hormone receptor-positive breast cancer; however, this treatment is often accompanied by side effects, such as musculoskeletal symptoms (e.g., pain and stiffness), which significantly impact patients' quality of life. Furthermore, symptom management varies markedly across different cultural backgrounds, influenced by local healthcare resources, nursing practices, and cultural factors. Consequently, effectively addressing musculoskeletal symptoms induced by endocrine therapy within a multicultural context has become an urgent challenge.

To tackle this issue, the Evidence-Based Nursing Center at Fudan University has launched the "Evidence-Based Practice Project for Managing Musculoskeletal Symptoms in Breast Cancer Patients Undergoing Endocrine Therapy from a Multicultural Perspective." This project aims to improve symptom management for breast cancer patients across various cultural backgrounds through the clinical application of scientific evidence, thereby enhancing the quality of nursing care. Based on implementation science, this study explores how to effectively apply and disseminate evidence-based nursing strategies in different regions and cultural environments, fostering cross-cultural healthcare cooperation and advancing the global optimization of breast cancer patient care.

2. Research Objectives (Why)

This study aims to identify best practices for managing musculoskeletal symptoms in breast cancer patients undergoing endocrine therapy within a multicultural context through a multi-center, parallel, randomized controlled implementation study. It also seeks to evaluate the translation and application of scientific evidence across different cultural backgrounds.

The specific objectives are as follows:

2.1 To investigate the current incidence of musculoskeletal symptoms among breast cancer patients undergoing endocrine therapy in Shanghai (China), Dali (Yunnan,

China), and Jakarta (Indonesia), and to assess the knowledge, attitudes, and practices (KAP) of oncology nurses in symptom management in these locations.

2.2 To conduct a multi-center, parallel, randomized controlled study guided by implementation science, evaluating the effectiveness of interventions in managing musculoskeletal symptoms for breast cancer patients undergoing endocrine therapy across different cultural contexts. This study will also validate the translation of scientific evidence in multicultural settings and explore the feasibility and scalability of the interventions across diverse cultural and healthcare systems.

3. Research Design

This study employs a simple randomized controlled trial (RCT) design to assess the effectiveness of musculoskeletal symptom management in breast cancer patients undergoing endocrine therapy from a multicultural perspective.

3.1 Sample Size

The primary measurement tool for this study is the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), used to assess aromatase inhibitor-related musculoskeletal symptoms in breast cancer patients. The sample size estimation is based on effect size and standard deviation data from previous studies, with a significance level of $\alpha=0.05$ and a statistical power of 80%. The calculated effect size is 0.78. Based on these parameters, each group requires 26 patients, with an additional 20% to account for potential attrition, resulting in a total of 33 patients per group.

Each research site will thus recruit 33 patients for both the intervention and control groups.

3.2 Sampling Method

Patients will be screened and recruited on a consecutive enrollment basis, meaning that all patients meeting the inclusion criteria will be enrolled sequentially during the study period until the predetermined sample size is reached.

Upon enrollment, each patient will undergo a comprehensive baseline assessment, and the research team will ensure that patients understand the study's details and voluntarily sign informed consent forms. After enrollment, patients will be assigned

to either the intervention or control group based on a computer-generated random sequence. The intervention group will receive a management program for musculoskeletal symptoms, while the control group will receive standard care.

3.3 Allocation Concealment

To prevent allocation bias, this study uses an allocation concealment technique. The randomization sequence will be managed by an independent third party, ensuring that the clinical research team is unaware of patient group assignments prior to allocation. In practice, the randomization results will be sealed in opaque envelopes, which will be opened by independent personnel after each patient's enrollment to determine group allocation. This blinding method minimizes potential bias and interference during study implementation.

4. Intervention Plan

4.1 Intervention Objectives

4.1.1 Patient Outcomes

- **Target Population**: Patients undergoing endocrine therapy following early-stage breast cancer surgery.
- **Intervention Duration**: The intervention will last for 6 months, with regular follow-up and symptom assessment.
- **Expected Outcomes**: Through intervention, patients' musculoskeletal symptoms (e.g., pain, stiffness) are expected to significantly improve, with a corresponding improvement in quality of life.

4.1.2 Practitioner Outcomes

- **Target Population**: Nurses and clinical practitioners involved in managing musculoskeletal symptoms in breast cancer patients.
- **Assessment Tool**: The "Survey on Nurses' Knowledge, Attitude, and Practice (KAP) Regarding Musculoskeletal Symptom Management in Breast Cancer Patients Undergoing Endocrine Therapy in a Multicultural Context." Pre- and post-intervention comparisons will be conducted to assess knowledge, attitudes, and practice skills.

- **Expected Outcomes**: Nursing staff will demonstrate significant improvements in knowledge, beliefs, and practical skills in managing musculoskeletal symptoms, promoting evidence-based nursing practices.

4.1.3 System Outcomes

- **Expected Outcomes**: This study aims to optimize and standardize the management processes for musculoskeletal symptoms related to endocrine therapy in breast cancer patients. By developing a standardized management protocol, we expect to improve the quality and efficiency of clinical nursing, supporting the advancement and optimization of clinical nursing systems.

4.2 Intervention Participants (Who)

4.2.1 Target Population

Patients undergoing endocrine therapy after early-stage breast cancer surgery.

- **Inclusion Criteria**:
    - Pathologically confirmed hormone receptor-positive (HR+) breast cancer patients.
    - Aged 18 years or older.
    - Currently receiving aromatase inhibitor therapy (e.g., anastrozole, letrozole, exemestane) for at least 6 months.
    - Reports musculoskeletal symptoms induced by endocrine therapy before enrollment.
    - Capable of understanding the study and willing to sign informed consent.
- **Exclusion Criteria**:
    - Patients with a history of fracture or surgery within the past 6 months.
    - Patients diagnosed with arthritis (e.g., rheumatoid arthritis).
    - Patients diagnosed with osteoporosis according to WHO criteria (T-score $\leq$ -2.5).
    - Patients with recurrent or metastatic breast cancer.
    - Patients with other primary malignancies.
    - Patients with severe heart, brain, liver, or kidney dysfunction, or infectious diseases.

- Patients with severe mental, cognitive, or behavioral disorders that hinder understanding or participation in the study.

4.2.2 Intervention Team

- **Nursing Manager (1)**: Responsible for human resource management, task allocation, and nursing supervision within the intervention team.
- **Project Coordinator (1)**: Manages project progress, coordinates communication and cooperation among departments, and ensures adherence to the study plan.
- **Recruitment, Intervention, and Follow-Up Staff (2-3)**: Responsible for patient recruitment, intervention implementation, and follow-up management, including patient enrollment, intervention execution, and periodic follow-up to ensure data collection and sustained patient participation.

4.3 Intervention and Follow-Up Duration (When)

This study includes a baseline survey, a 3-month intervention period, and a 3-month follow-up period, for a total duration of 6 months.

4.4 Intervention Location (Where)

4.4.1 Research Centers

- Shanghai, China: Comprehensive Treatment Outpatient Clinic, Fudan University Cancer Hospital
- Dali, China: Breast Oncology Outpatient Clinic, First Affiliated Hospital of Dali University
- Jakarta, Indonesia: Breast Oncology Department, Dharmais Cancer Hospital

4.4.2 Intervention Implementation Sites

(1) Medical Institutions

At each research center, the intervention team implements the following measures:

- **Patient Training**: Nurses provide personalized, face-to-face training to help patients understand musculoskeletal symptoms related to endocrine therapy and their management. Training content includes practical self-management skills, such as pain monitoring, medication side effect management, and guidance on diet and exercise.

- **Regular Assessment**: Nurses guide patients to attend regular hospital assessments of musculoskeletal symptoms during the intervention and follow-up periods. Standardized assessment tools are used to document symptom changes, and treatment plans are adjusted accordingly based on the results.

(2) Home-Based Self-Management

Patients follow the intervention plan for self-management in their daily lives, including the following components:

- **Self-Monitoring**: Regularly record musculoskeletal symptoms, such as pain intensity and stiffness.
- **Health Management**: Follow the intervention guidance provided by nurses for daily exercise, dietary adjustments, and medication management to ensure consistent intervention adherence and continuous monitoring and control of symptoms.
- **Data Feedback**: Patients regularly submit self-management records to the medical team for ongoing evaluation and adjustments.

4.5 Intervention Strategies

In this study, all research centers provide the same symptom management materials, but each center uses different media formats based on local resources and cultural context.

4.5.1 Shanghai and Dali, China

Patients manage their musculoskeletal symptoms through an app platform designed by the research team. The app offers symptom management materials across four main modules: Self-Monitoring and Reporting, Diet and Nutrition Management, Medication Adherence Management, and Exercise and Rehabilitation. Patients can record symptom changes, medication side effects, and daily diet and exercise plans on the platform. The nursing team provides personalized feedback and guidance through the platform, ensuring effective implementation of the intervention and continuous monitoring of patients' symptom management.

4.5.2 Jakarta, Indonesia

In Jakarta, the intervention is conducted offline. The nursing team provides patients

with the same symptom management content as the Chinese research centers, including Self-Monitoring and Reporting, Diet and Nutrition Management, Medication Adherence Management, and Exercise and Rehabilitation. Nurses distribute written and audio materials, offering detailed guidance for home-based self-management. Regular follow-ups and assessments are scheduled to ensure effective intervention implementation and positive outcomes.

5. Intervention Content (What)

Table 1: Evidence Extraction Table

Category	Evidence	Grade
Risk assessment	**1. A thorough risk assessment of MS should be performed on the patient and inform relevant risk factors**	3b
	2. Evaluation records should include age, BMI, hormone replacement therapy history, paclitaxel chemotherapy history, tamoxifen treatment history, cancer stage, date of last menstrual period, existing menopausal symptoms, or joint related diseases (e.g., osteoarthritis, rheumatoid arthritis)	3b
Symptom assessment	**1. Commonly used assessment tools include the BPI-SF, M-SACRAH, PRAI, BCPT-MS, AUSCAN, WOMAC and ect.**	1b
Preventions	**1. Bone mineral density testing is performed before aromatase inhibitor treatment and once a year thereafter, and treatment with bisphosphonate or denosumab is considered based on the evaluation results**	5b
	2. Instruct patients to take calcium and vitamin D supplements	5b
	3. For patients without MS, routine education should be done to strengthen patients' understanding of possible MS. Encourage the patient to participate in exercise and manage weight	5b
	4. Health education on the benefits and side effects of adjuvant endocrine therapy should be strengthened to improve compliance with endocrine therapy	5b
Interventions	**1. Symptomatic treatment with acetaminophen or non-steroidal anti-inflammatory drugs**	5b
	2. Traditional Chinese medicine could be a treatment option	1a

	3. Acupuncture is recommended to treat MS induced by aromatase inhibitors	1a
	4. Night splinting and nonsteroidal anti-inflammatory drugs could be used to relief carpal tunnel syndrome and stenosing tenosynovitis. If symptoms are refractory to nonsurgical intervention, surgical intervention may be warranted	3b
	5. Encourage moderate-intensity physical activity, 30 minutes a day, 5 times a week	1a
	6. A supervised exercise program, including aerobic exercise, resistance training, or a combination of both, is recommended, and the exercise intensity does not exceed 60% to 80% of the maximum heart rate, three times a week for 30 minutes each time	1a
	7. It is recommended to participate in yoga, Tai Chi, Health Qigong-Ba Duan Jin or other activities	2b
Monitoring	**1. Increase the frequency of MS monitoring and follow-up every 3 to 6 months**	5b

Table 2: Audit Criteria Extraction Table

Evidence	Audit criteria
1. A thorough risk assessment of MS should be performed on the patient and inform relevant risk factors	**1. The nurse assesses the patient's risk of MS, informs the relevant risk factors, and records them.**
2. Evaluation records should include age, BMI, hormone replacement therapy history, paclitaxel chemotherapy history, tamoxifen treatment history, cancer stage, date of last menstrual period, existing menopausal symptoms, or joint related diseases (e.g., osteoarthritis, rheumatoid arthritis)	
3. Commonly used assessment tools include the BPI-SF, M-SACRAH, PRAI, BCPT-MS, AUSCAN, WOMAC and ect.	**2. The nurse uses a professional scale to assess the MS.**
4. Bone mineral density testing is performed before aromatase inhibitor treatment and once a year thereafter, and treatment with bisphosphonate or denosumab is considered based on the evaluation results	**3. The doctor tests the patient's bone mineral density once a year and gives treatment when appropriate.**
5. Instruct patients to take calcium and vitamin D supplements	**4. The nurse instructs the patient to take calcium and vitamin D supplements.**

6. For patients without MS, routine education should be done to strengthen patients' understanding of possible MS. Encourage the patient to participate in exercise and manage weight	**5. The nurse delivers the patient health education about MS.**
7. Health education on the benefits and side effects of adjuvant endocrine therapy should be strengthened to improve compliance with endocrine therapy	
8. Symptomatic treatment with acetaminophen or non-steroidal anti-inflammatory drugs	**6. The doctor prescribes acetaminophen or non-steroidal anti-inflammatory drugs, traditional Chinese medicine, acupuncture, night splinting other treatments when appropriate.**
9. Traditional Chinese medicine could be a treatment option	
10. Acupuncture is recommended to treat MS induced by aromatase inhibitors	
11. Night splinting and nonsteroidal anti-inflammatory drugs could be used to relief carpal tunnel syndrome and stenosing tenosynovitis. If symptoms are refractory to nonsurgical intervention, surgical intervention may be warranted	
12. Encourage moderate-intensity physical activity, 30 minutes a day, 5 times a week	**7. The nurse instructs the patient to participate in exercise.**
13. A supervised exercise program, including aerobic exercise, resistance training, or a combination of both, is recommended, and the exercise intensity does not exceed 60% to 80% of the maximum heart rate, three times a week for 30 minutes each time	
14. It is recommended to participate in yoga, Tai Chi, Health Qigong-Ba Duan Jin or other activities	
15. Increase the frequency of MS monitoring and follow-up every 3 to 6 months	**8. The nurse regularly monitors patients for MS.**

5. Intervention Content (What)

5.1 Self-Monitoring and Reporting

Nurses guide patients to record their status weekly using the "Patient Self-Monitoring Record Form." The nursing team regularly collects this feedback data.

Table 3: Patient Self-Monitoring Record Form

Date	Type of Musculoskeletal Symptoms	Symptom Location	Start and End Time	Duration	VAS Score	Relief Measures	Remarks

Note: **VAS score** ranges from 0 to 10, where 0 indicates no pain and 10 indicates severe pain.

Instructions for Completion:

- China (Shanghai, Dali): Patients enter self-monitoring data through the app platform. By selecting “Symptom Monitoring” on the app, a musculoskeletal symptom record form will automatically pop up. Patients enter information sequentially to ensure accuracy and completeness. The system automatically saves and submits data to the nursing team for timely evaluation and care plan adjustments.
- Indonesia: Patients use the "Patient Self-Monitoring Record Form" for manual recording. Each week, they fill out the form, documenting symptom type, location, start time, duration, VAS score, and relief measures. Patients submit the completed form to the nursing team on time.

5.2 Diet and Nutrition Management

5.2.1 Daily Vitamin D Supplementation: It is recommended that patients take daily vitamin D supplements.[1]

- For patients aged 18 to 50 with limited sun exposure, a daily intake of 1500-2000 IU of vitamin D is advised.
- For patients over 50, 1600-2000 IU is recommended to maintain serum 25(OH)D levels ≥ 30 ng/mL.[2]

5.2.2 Omega-3 Fatty Acid Intake: Patients are encouraged to consume foods rich in omega-3 fatty acids[3] (e.g., salmon, flaxseed oil, fish oil supplements).

5.2.3 Weight Management for Obese Patients: Patients with obesity (BMI ≥ 30) are advised to engage in weight management.[3]

5.3 Exercise and Rehabilitation

Patients are instructed to follow the standardized exercise and rehabilitation regimen[1, 4-6], with specific movements available in video format.

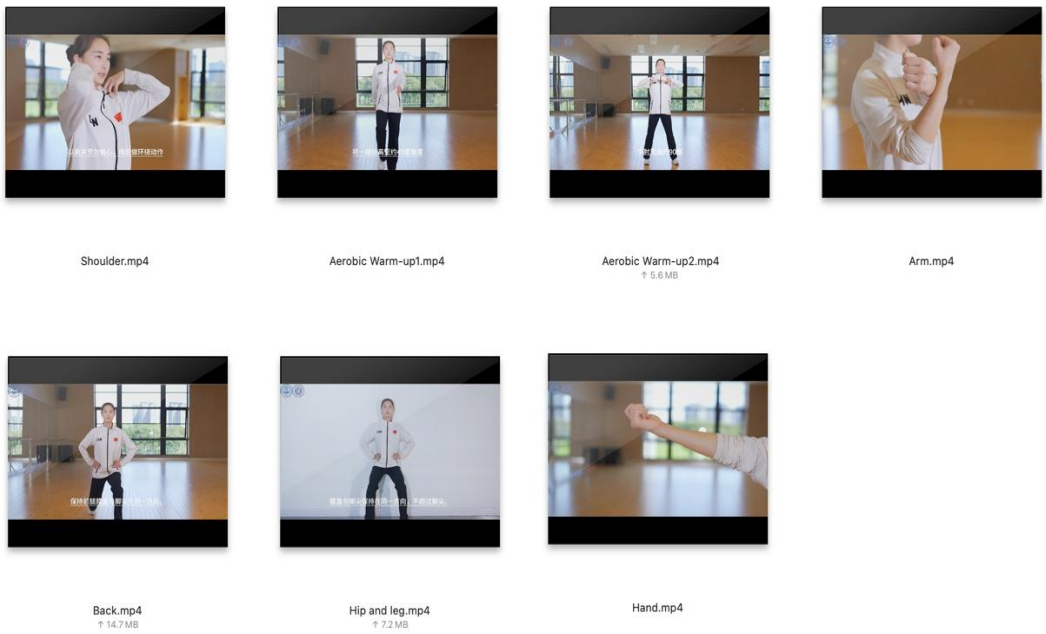

Figure 1: Exercise Demonstration Video Screenshots

Table 4: Standardized Exercise Rehabilitation Program

Aerobic Warm-up
Frequency: 5-7 times per week
Intensity: 60%-70% of maximum heart rate (220-age); RPE 3-4
Duration: 30-45 minutes
Repetitions: 5-10 times per set
Aerobic Warm-up for Young Group
Marching in place
Full-body stretch
Jumping jacks
Side steps with arm circles

Squat with alternating punches
Aerobic warm-up for the elderly group
Marching in place
Full-body stretch
Full-body stretch
Chest expansion exercise
Abduction exercise
Overhead reach
Lateral movement
Hip extension exercise
Calf raises
Functional Training
Frequency: 3-5 times per week
Intensity: RPE 3-4
Duration: 15-30 minutes
Repetitions: 8-12 times per set

Location	Content	Nerves, Muscles, Joints
Hand	Hand functional exercise	Quadriceps, Hamstrings, Gastrocnemius, Soleus, Gluteus Maximus, Hip Flexors
	Wrist rotation	Flexor Carpi Radialis, Flexor Carpi Ulnaris, Extensor Carpi Radialis Longus, Extensor Carpi Radialis Brevis
Arm	Active posterior deltoid stretch	Deltoid (posterior fibers)
	Arm pull down stretch	Triceps Brachii, Latissimus Dorsi
	Active triceps stretch	Triceps Brachii
Shoulder	Arm flexion with shoulder circles	Biceps Brachii, Deltoid, Rotator Cuff muscles
	Shoulder extension with reach	Deltoid, Latissimus Dorsi, Trapezius
	Hands behind head	Trapezius, Deltoid, Rhomboids
	Prone Y extension	Trapezius, Rhomboids, Deltoids
	Wall slides	Deltoids, Trapezius, Rotator Cuff muscles
Hip and leg	Wall sit	Quadriceps, Hamstrings, Gluteus

		Maximus
	Standing left thigh stretch with wall support	Quadriceps
	Bent-over deadlift	Erector Spinae, Gluteus Maximus, Hamstrings
Back	Lunge stretch	Quadriceps, Hamstrings, Gluteus Maximus
	Seated butterfly stretch	Adductor muscles, Sartorius
	Flat back exercise	Erector Spinae, Rectus Abdominis
	Double knee to chest	Rectus Abdominis, Hip Flexors
	Supine knee touch	Rectus Abdominis, Hip Flexors

Table 5: Exercise Demonstration Table

Major Category	Sequence Number	Body Position	Exercise Name	Exercise Image	Target Joint
Warm-Up for Young Group	1	Frontal	Marching in place		Shoulder, Hip, Knee
	2	Frontal	Full-body stretch		Elbow, Shoulder, Hip

	3	Frontal	Jumping jacks		Elbow, Shoulder, Hip
	4	Frontal	Side steps with arm circles		Elbow, Shoulder, Hip
	5	Lateral	Squat with alternating punches		Shoulder, Hip, Knee
Warm-Up for Elderly Group	1	Frontal	Chest Expansion Exercise		Wrist, Elbow, Shoulder

	2	Frontal	Chest Stretch Exercise		Elbow, Shoulder, Hip
	3	Frontal	Abduction Exercise		Elbow, Shoulder, Hip
	4	Frontal	Overhead reach		Elbow, Shoulder, Hip
	5	Frontal	Lateral movement		Ankle, Hip, Shoulder

	6	Lateral	Hip extension exercise		Shoulder, Hip, Knee
	7	Lateral	Calf raises		Toe, Ankle, Knee
Shoulder Exercises	1	Frontal	Arm flexion with shoulder circles		Elbow, Shoulder, Hip

	2	Frontal	Shoulder extension with reach		Wrist, Elbow, Shoulder
	3	Frontal	Hands behind head		Elbow, Shoulder, Hip
	4	Frontal	Prone Y extension		Elbow, Shoulder, Hip

	5	Frontal	Wall slides		Elbow, Shoulder, Hip
Arm Exercises	1	Frontal	Active posterior deltoid stretch		Wrist, Elbow, Hip
	2	Lateral	Arm pull down stretch		Elbow, Wrist, Pinky Finger
	3	Frontal	Active triceps stretch		Shoulder, Elbow, Elbow
Hand Exercises	1	Frontal	Hand functional exercise		Elbow, Wrist, Finger

	2	Frontal	Wrist rotation		Elbow, Wrist, Pinky Finger
Body Position	1	Lateral	Lunge stretch		Ankle, Knee, Hip
	2	Lateral	Seated butterfly stretch		Shoulder, Hip, Knee
	3	Lateral	Flat back exercise		Elbow, Shoulder, Hip
	4	Lateral	Double knee to chest		Shoulder, Hip, Knee

	5	Lateral	Supine knee touch		Shoulder, Hip, Knee
Hip Exercises	1	Lateral	Wall sit		Hip, Knee, Ankle
	2	Lateral	Standing left thigh stretch with wall support		Hip, Knee, Ankle
	3	Lateral	Bent-over deadlift		Shoulder, Hip, Knee

5.4 Medication Adherence Management

5.4.1 Guide patients to complete a weekly medication adherence assessment.[1]

Below is a line representing your adherence to prescribed endocrine medication over the past week. A score of 0% indicates no medication taken, while 100% indicates full adherence to the prescribed dose. Please mark "√" at the point on the line that best reflects your medication intake.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%

5.4.2 The nursing team conducts biweekly telephone follow-ups during the intervention period and monthly telephone follow-ups during the follow-up period.[7, 8] The specific follow-up content is as follows:

(1) Self-Monitoring and Reporting

- Do you regularly record changes in musculoskeletal symptoms?
  Never (0) | Occasionally (1) | Often (2) | Always (3)
- Do you encounter any difficulties or uncertainties when recording?
  No (0) | Occasionally (1) | Often (2) | Always (3)
- What was your most recent VAS score (0-10)?
  Specify a score (0-10)
- Has there been any change in symptoms?
  No change (0) | Slight change (1) | Significant change (2) | Severe change (3)
- What relief measures have you used, and how effective were they?
  None (0) | Poor (1) | Moderate (2) | Good (3)
- Have you experienced any new symptoms or worsening of existing symptoms?
  No (0) | Slight worsening (1) | Significant worsening (2) | Severe worsening (3)

(2) Diet and Nutrition Management

- Has there been any change in your recent dietary habits?
  No change (0) | Slight change (1) | Significant change (2) | Severe change (3)
- Is your daily diet balanced?
  Very unbalanced (0) | Unbalanced (1) | Balanced (2) | Very balanced (3)
- Have you been taking supplements?
  None (0) | Occasionally (1) | Often (2) | Daily (3)
  (Follow up with specific types and dosages of supplements)
- Are there any difficulties or questions regarding dietary management?
  None (0) | Slight difficulty (1) | Moderate difficulty (2) | Severe difficulty (3)

(3) Exercise and Rehabilitation

- Do you follow the recommended exercise program?
  Never (0) | Occasionally (1) | Often (2) | Always (3)

- Is the frequency and intensity of your exercise appropriate?
  Not appropriate (0) | Fairly appropriate (1) | Appropriate (2) | Very appropriate (3)
- Do you experience discomfort or worsening of symptoms after exercise?
  No discomfort (0) | Mild discomfort (1) | Moderate discomfort (2) | Severe discomfort (3)
- Do you feel fatigued after exercising?
  Never (0) | Occasionally (1) | Often (2) | Always (3)
- Do you need to adjust your exercise plan?
  No adjustment needed (0) | Slight adjustment (1) | Moderate adjustment (2) | Major adjustment (3)

(4) Medication Adherence Management

- Do you take your medication on time and at the correct dose?
  Never (0) | Occasionally (1) | Often (2) | Always (3)
- Have you missed or incorrectly taken any doses?
  No (0) | Occasionally (1) | Often (2) | Always (3)
- Have you experienced any side effects from the medication, and did they impact your adherence?
  No side effects (0) | Mild side effects (1) | Moderate side effects (2) | Severe side effects (3)
- Have you interrupted endocrine therapy, and if so, what was the reason?
  No interruption (0) | Occasionally (1) | Often (2) | Completely stopped (3)

(5) Referral

- Have any abnormal symptoms or other health issues been detected during monitoring?
  None (0) | Mild abnormality (1) | Moderate abnormality (2) | Severe abnormality (3)
- Do you need to consult a doctor or undergo further testing?
  No need (0) | Possibly needed (1) | Needed (2) | Urgently needed (3)
  (If symptoms worsen or become uncontrollable, a referral to a relevant department is recommended.)

6. Intervention Evaluation

Table 6: Evaluation of Intervention Effectiveness

Assessment	Tools	Baseline T0	Intervention Period			Follow-up Period		
			M1	M2	M3	M4	M5	M6
General Information	Baseline Survey Form							
Biomarker - Bone Density	Dual-Energy X-ray Absorptiometry (DXA) Scanner							
Grip Strength	Digital Hand Grip Dynamometer							
Joint Function	WOMAC, M-SACRAH							
Intervention Implementation Status	Review Indicators							
Practitioner Knowledge, Attitude, and Practice (KAP)	Questionnaire							
System Outcomes	Interview Guide							
Patient Intervention Adherence	Follow-Up Record Form							
Practitioner Compliance Rate	Review Indicator Record Form							

【Biomarker - Bone Density】

At months 0 and 6 of the intervention, bone density will be measured using Dual-Energy X-ray Absorptiometry (DEXA). DEXA is widely recognized as the gold standard for bone density assessment due to its high precision and reliability, making it extensively used in clinical diagnosis and research. The primary measurement sites include the lumbar spine and femoral neck, which reflect bone mineral content and overall bone health.

According to the World Health Organization (WHO) bone density diagnostic criteria[9], the T-score ranges are as follows:

- Normal: T-score ≥ -1
- Low Bone Mass (Osteopenia): T-score between -1 and -2.5
- Osteoporosis: T-score ≤ -2.5

【Grip Strength】

Grip strength will be measured at months 0, 1, 3, and 6 by the exercise team. This measurement primarily evaluates the forearm flexor and hand muscles, representing forearm muscle strength. An electronic handgrip dynamometer will be used. The subject stands with arms relaxed and hanging down, palms facing the thighs, and the dominant arm (non-surgical side) abducted to a 30-degree angle. The participant grips the dynamometer without swinging the arm, squatting, or allowing the dynamometer to touch the body. Each participant will undergo three assessments, with the highest value used for analysis. A 60-second rest interval is provided between each measurement. Reference standards for grip strength are based on normal values from a large-scale national health survey in China.

Normative values for absolute and relative hand grip strength, stratified by sex and age.

	Male (n = 16 263)								Female (23 392)							
		Centiles								Centiles						
	n	5th	25th	50th	75th	95th	Mean	SD	n	5th	25th	50th	75th	95th	Mean	SD
HGS (kg)																
Age groups																
8-	170	6	8	10	12	16	10.08	2.94	217	4	6	8	10	13	8.14	2.65
10-	211	8	10	13	15	19	13.03	3.64	236	6	9	11.5	14	18	11.65	3.68
12-	237	10	15	18	23	33	19.5	6.74	201	10	14	17	20	24	16.94	4.53
14-	180	16.5	24	28	33.5	40.5	28.46	7.26	185	13	16	20	22	27	19.75	4.35
16-	183	26	31	36	40	48	35.77	6.71	314	15	18	21	24	29	21.52	4.23
18-	212	27	33.5	38	42	51	38.12	7.57	293	16	20	23	26	31	23.19	4.98
20-	1922	30	37	42	48	55	42.46	7.59	2998	16	21	24	28	33	24.44	5.02
30-	2874	30	37	42	47	55	42.12	7.56	4631	18	22	26	29	34	25.55	5.16
40-	4085	28	36	40	46	53	40.75	7.56	6400	16	22	25	28	34	24.96	5.25
50-	3362	26	32	37	42	51	37.61	7.66	4491	14	19	22	26	30	22.34	4.92
60-	2034	20	28	32.15	38	46	32.91	7.32	2521	12	17	20	23	28	19.95	4.76
70–80	731	16	22	27	32	40	27.07	7.15	820	10	14	17	20	25	17.31	4.75
Overall	16 201	20	32	38	44	52	37.72	9.67	23 307	14	20	23	27	32	23.23	5.80

Figure 2: Reference Standard for Grip Strength

【Audit Record Table】

Table 7: Audit Record Table

Serial Number	Audit criteria	Compliance Status	Remarks
1	**The nurse assesses the patient's risk of MS, informs the relevant risk factors, and records them.**	□ Compliant □ Non-compliant	
2	**The nurse uses a professional scale to assess the MS.**	□ Compliant	

		□ Non-compliant
3	**The doctor tests the patient's bone mineral density once a year and gives treatment when appropriate.**	□ Compliant □ Non-compliant
4	**The nurse instructs the patient to take calcium and vitamin D supplements.**	□ Compliant □ Non-compliant
5	**The nurse delivers the patient health education about MS.**	□ Compliant □ Non-compliant
6	**The doctor prescribes acetaminophen or non-steroidal anti-inflammatory drugs, traditional Chinese medicine, acupuncture, night splinting other treatments when appropriate.**	□ Compliant □ Non-compliant
7	**The nurse instructs the patient to participate in exercise.**	□ Compliant □ Non-compliant
8	**The nurse regularly monitors patients for MS.**	□ Compliant □ Non-compliant

7. Intervention Flowchart

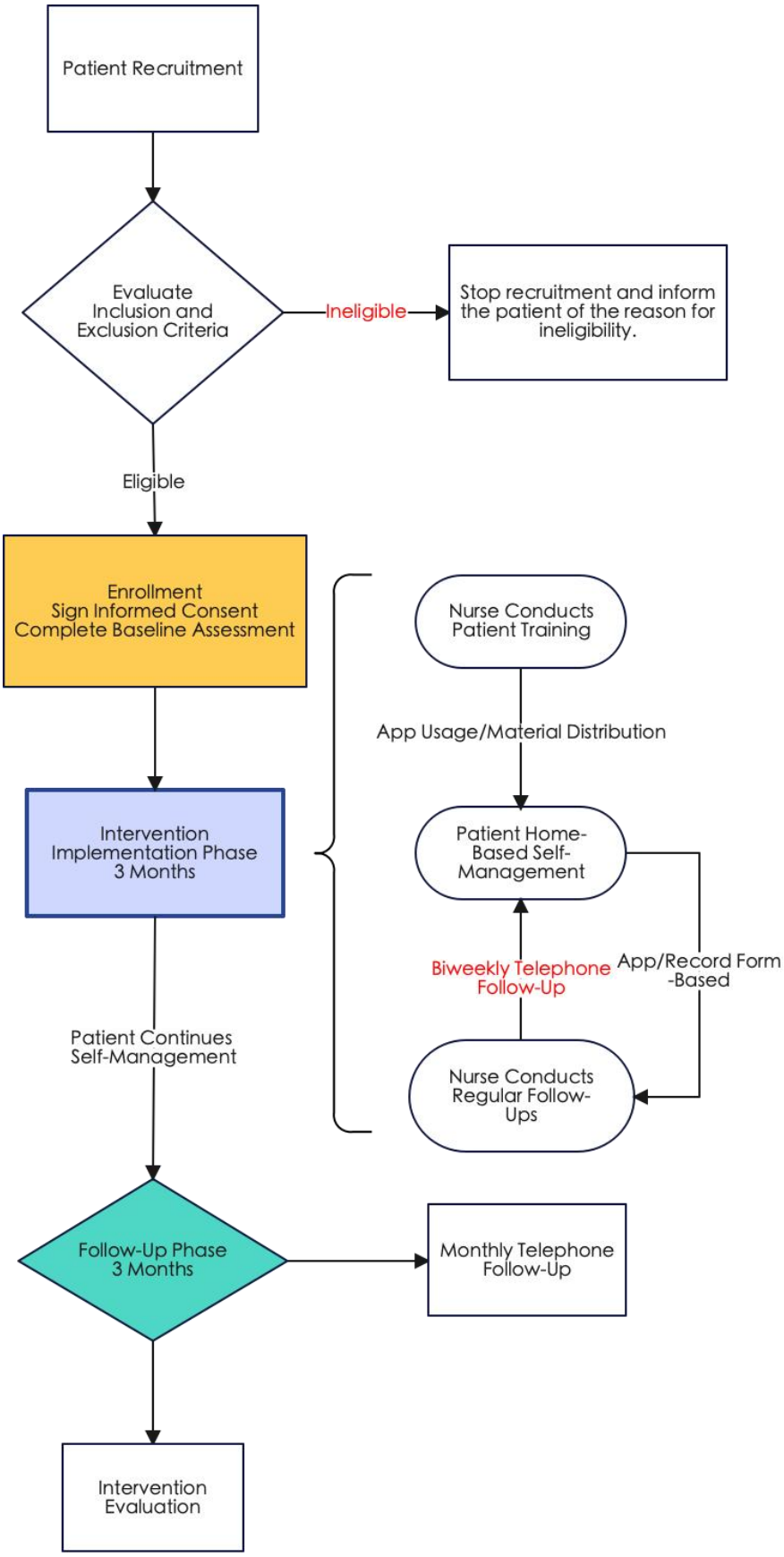

Figure 3: Intervention Flowchart

8. Research Schedule

Table 8: Intervention and Follow-Up Schedule for Managing Musculoskeletal Symptoms in Breast Cancer Patients

	Phase	Duration	Follow-Up Frequency
1	Intervention Initiation	November 2024 - December 2024	/
2	Intervention Period	3 months	Weekly Telephone Follow-Up
3	Follow-Up Period	3 months	Biweekly Telephone Follow-Up

9. Appendix

9.1 Baseline Survey Form - Musculoskeletal Symptom Form

Dear Patients,

In order to better understand your condition during endocrine therapy and to help us provide you with appropriate treatment and care, we have designed the following questionnaire to assess your physical and psychological status. The information you provide will serve as a valuable reference for clinical medical and nursing work. We kindly ask that you fill out the questionnaire thoroughly, reflecting your true situation. Some questions may be completed by medical personnel on your behalf.

We sincerely thank you for your participation, support, and cooperation!

- *There are no right or wrong answers. Please respond based on how you usually feel and act.*
- *Please fill out the form based on your actual situation.*
- *For items with a □, please place a "√" in the appropriate box.*

□ **Outpatient** □ **Inpatient**

Outpatient/Inpatient Number: _____

Enrollment/Follow-up Date: _____

Investigator's Signature: _____

I. General Information

1.Gender:

□ Male □ Female

2.Age: _____ years

3.Height: _____ cm **Weight:** _____ kg

4.Religious Belief:

□ None □ Buddhism □ Christianity □ Islam □ Other

5.Do you regularly participate in religious activities or prayer?

□ Never □ Occasionally □ Sometimes □ Frequently

6.How much does your religious belief influence your lifestyle?

□ No influence □ Slight influence □ Some influence □ Significant influence

7.Educational Level:

□ Primary school or below

□ Middle school

□ Technical school/High school

□ College/University

□ Graduate degree or higher

8.Employment Status:

□ Unemployed □ Part-time job □ Full-time job □ Retired □ Homemaker

9.Marital Status:

□ Single □ Married □ Divorced □ Widowed

10.Living Situation:

□ Stable □ Unstable □ Homeless

11.Medical Expenses:

□ Fully self-paid

□ Mostly self-paid

□ Partially self-paid

□ No self-payment

12.Economic Pressure:

□ None □ Slight □ Some □ Significant

13.Understanding of your disease:

□ Not at all □ Slightly □ Somewhat □ Very well

II. Medical History

1. Diagnosis Date: _____ Year _____ Month

2. Surgical Approach: _____

3. Pathological Type: _____ (e.g., ductal carcinoma, lobular carcinoma, ductal carcinoma in situ, lobular carcinoma in situ, inflammatory breast cancer, mucinous carcinoma, medullary carcinoma) (may consult healthcare professionals for completion)

4. Comprehensive Treatment Plan:

□ Chemotherapy: _____ □ Radiotherapy: _____

□ Targeted Therapy: _____ □ Other: _____

5. Tumor Stage:

□ Stage 0 □ Stage I □ Stage II □ Stage III □ Stage IV □ Unclear

6. Endocrine Therapy Medication Currently Administered (please specify the detailed regimen on the line below): _____

Start Date of Endocrine Therapy: _____

□ Anastrozole □ Letrozole

□ Exemestane □ Ovarian function suppression medication

□ Other: _____

7. Do you have any other chronic diseases? (select all that apply):

□ Hypertension □ Diabetes □ Coronary heart disease

□ Other: _____ □ None

III. Menstrual and Fertility Status

1.Time Since Last Menstruation: _____ years (If within one year, fill in 0.5 years)

IV. Dietary Habits and Nutrition

(1) Dietary Habits and Nutrition

1.Do you take dietary supplements (e.g., fish oil, calcium tablets, vitamin D, etc.)?

□ Yes, type and dosage: _____ □ No

(2) Behavioral Habits

1.Do you smoke?

□ Yes □ Used to, but quit □ No

2.Do you drink alcohol?

□ Yes □ Used to, but quit □ No

3.Exercise frequency:

□ Daily □ 3-4 times per week □ 1-2 times per week □ Rarely exercise

4.Exercise intensity:

□ Light activity □ Moderate activity □ Intense activity

(3) Sleep Situation

1.Sleep quality in the past month:

□ Very good □ Fairly good □ Fairly poor □ Very poor

V. Medication Adherence

The following line represents **how closely you followed your prescribed medication regimen in the past week.** 0% means you did not take any medication, and 100% means you took the full amount as prescribed. Please place a "√" on the line at the point that best reflects your adherence.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%

VI. Symptom Assessment

Type of Musculoskeletal Symptoms: _____

Please rate the musculoskeletal symptoms you are experiencing using the VAS score. Mark "√" at the point on the line that best reflects your symptom score. (Note: VAS score ranges from 0 to 10, where 0 indicates no pain and 10 indicates severe pain.)

0	1	2	3	4	5	6	7	8	9	10

Hand Symptoms and Function Assessment

Please select your answers based on your actual situation in the past 48 hours (with scores increasing from 0 to 100):

1. Pain experienced while inactive:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

2. Pain experienced during intense work:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

3. Severity of stiffness upon waking in the morning:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

4. Severity of stiffness after sitting, lying down, or resting:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

5. Difficulty in opening/closing doors:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

6. Difficulty in buttoning/unbuttoning clothes:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

7. Difficulty in turning a faucet on/off:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

8. Difficulty in pulling up/down a zipper:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

9. Difficulty in tying shoelaces:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

10. Difficulty in opening a jar:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

11. Difficulty in turning pages of a newspaper:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

12. Difficulty in writing:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

Knee and Hip Joint Symptoms and Function Assessment

Please select your answers based on your actual situation in the past 48 hours (with scores increasing from 0 to 100):

1. Intensity of knee or hip pain while ambulating on a flat surface:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

2. Intensity of knee or hip pain during stair ascent or descent:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

3. Intensity of knee or hip pain during nocturnal rest:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

4. Intensity of knee or hip pain while seated or in a supine position:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

5. Intensity of knee or hip pain while in an upright position:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

6. Severity of stiffness in the knee or hip upon waking in the morning:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

7. Severity of stiffness in the knee or hip following periods of sitting or rest during the day:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

8. Difficulty experienced during stair ascent:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

9. Difficulty experienced during stair descent:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

10. Difficulty in transitioning from a seated to a standing position:

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

11. Difficulty while maintaining an upright position

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

12. Difficulty in bending forward to reach the ground

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

13. Difficulty while ambulating on a flat surface

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

14. Difficulty in entering and exiting a vehicle or boarding a bus

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

15. Difficulty experienced during shopping activities

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

16. Difficulty in donning socks

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

17. Difficulty in doffing socks

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

18. Difficulty in rising from a supine position in bed

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

19. Difficulty while lying in bed

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

20. Difficulty in exiting a bathtub or bathroom

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

21. Difficulty in transitions between sitting and standing

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100
22. Difficulty in rising from a toilet seat

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100
23. Difficulty in performing heavy household chores

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100
24. Difficulty in performing light household chores

☐0 ☐10 ☐20 ☐30 ☐40 ☐50 ☐60 ☐70 ☐80 ☐90 ☐100

9.2 The WOMAC (Western Ontario and McMaster Universities) Index of Osteoarthritis

Overview:

The WOMAC (Westren Ontario and McMaster Universities) index is used to assess patients with

osteoarthritis of the hip or knee using 24 parameters. It can be used to monitor the course of the disease or to determine the effectiveness of anti-rheumatic medications.

Pain:

(1) walking

(2) stair climbing

(3) nocturnal

(4) rest

(5) weight bearing

Stiffness:

(1) morning stiffness

(2) stiffness occurring later in the day Physical function:

(1) descending stairs

(2) ascending stairs

(3) rising from sitting

(4) standing

(5) bending to floor

(6) walking on flat

(7) getting in or out of car

(8) going shopping

(9) putting on socks

(10) rising from bed

(11) taking off socks
(12) lying in bed
(13) sitting
(14) sitting
(15) getting on or off toilet
(16) heavy domestic duties
(17) light domestic duties

While the index was being developed performance of social functions and the status of emotional function were also included. These were not included in the final instrument.

Social function:

(1) leisure activities
(2) community events
(3) church attendance
(4) with spouse
(5) with family
(6) with friends
(7) with others

Emotional function:

(1) anxiety
(2) irritability
(3) frustration
(4) depression
(5) relaxation
(6) insomnia
(7) boredom
(8) loneliness
(9) stress
(10) well-being

Scoring and Interpretation

Response	**Points**
none	0
slight	1
moderate	2
severe	3
extreme	4

Alternatively a visual analogue scale (VAS) may be used ranging from 0 to 10. score

=

= SUM(points for relevant items) average score =

= (total score) / (number of items) Interpretation:

• minimum total score: 0

• maximum total score: 96

• minimum pain subscore: 0

• maximum pain subscore: 20

• minimum stiffness subscore: 0

• maximum stiffness subscore: 8

• minimum physical function subscore: 0

• maximum physical function subscore: 68

9.3 Modified Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (M-SACRAH)

PART 1: DIFFICULTIES PERFORMING DAILY ACTIVITIES

Think about the **difficulties** you have had in the past 48 hours doing the following physical daily activities **because of your finger joint problems**. This means your ability to **move easily and do things yourself**. (Please mark each answer with an "X" on the line.)

QUESTION: How difficult was it for you...

1. To unlock the front door with a key?

No difficulty _____ Impossible

2. To button or unbutton buttons?

No difficulty _____ Impossible

3. To turn on the faucet?

No difficulty _____ Impossible

4. To zip or unzip a zipper?

No difficulty _____ Impossible

5. To tie shoelaces?

No difficulty _____ Impossible

6. To unscrew and screw on the toothpaste cap?

No difficulty _____ Impossible

7. To turn the pages of the newspaper?

No difficulty _____ Impossible

8. To write by hand?

No difficulty _____ Impossible

PART 2: STIFFNESS

Think about the **stiffness** (not pain) you have had in the past 48 hours because of your **finger joint problems**. Joint

stiffness is normally experienced as a **limitation or reduction in the mobility of your joints**.

(Please mark each answer with an "X" on the line.)

QUESTION:

9. How **severe** was your joint stiffness **after you first woke up** in the morning?

No stiffness _____ Unbearable stiffness

10. How **severe** was your joint stiffness later in the day after your hands had been at rest for a while?

No stiffness _____ Unbearable stiffness

PART 3: PAIN

Think about the pain you have had in the past 48 hours because of your finger joint problems.

(Please mark each answer with an "X" on the line.)

QUESTION: How severe was your pain…

11. During your work activities or difficult house chores?

No pain _____ Unbearable pain

12. When your hands were at rest in the evening?

No pain _____ Unbearable pain

9.4 Informed Consent Form

Study Title:

Evidence-Based Practice Research on the Management of Musculoskeletal Symptoms in Breast Cancer Patients Undergoing Endocrine Therapy from a Multicultural Perspective

Lead Institution:

School of Nursing, Fudan University

Collaborating Institutions:

Fudan University Shanghai Cancer Center; Dali University Affiliated Hospital; Dharmais Cancer Hospital (Indonesia)

You are being invited to participate in a clinical research study. This informed consent form provides information to help you decide whether to participate in this clinical study. Please read it carefully, and if you have any questions, do not hesitate to ask the researchers responsible for the study.

Your participation in this study is entirely voluntary.

This study has been reviewed and approved by the Ethics Committee of the institution conducting the research.

Background and Purpose of the Study:

The purpose of this study is to help breast cancer patients undergoing endocrine therapy better manage musculoskeletal symptoms related to their treatment. By analyzing the current symptom management practices of patients from tertiary hospitals in Shanghai (China), Dali (China), and Jakarta (Indonesia), we aim to develop and evaluate a series of personalized management plans. These plans include strategies for self-monitoring and reporting, medication adherence, diet and nutrition,

exercise and rehabilitation, and health education, with the goal of improving patients' symptoms and quality of life. Through evidence-based practice research, we hope to implement these management plans in different regions and enhance the overall quality of breast cancer care through cross-cultural collaboration. This study seeks to provide targeted nursing support for patients and promote international nursing cooperation along the Belt and Road Initiative.

Study Procedures:

If you agree to participate in this study, you will be asked to:

1. If technically feasible, download and use the intelligent symptom management app provided by the research team.
2. Regularly record your musculoskeletal symptoms, including data such as pain levels and quality of life.
3. If you are unable to use the app due to technical issues or other reasons, the research team will provide paper records or telephone follow-ups as an alternative.
4. This study will last for six months, with three months of intervention and three months of follow-up. During the intervention phase, you will participate in the symptom management plan, and during the follow-up phase, you will be contacted for follow-up once a month.
5. Your participation is voluntary, and you may withdraw at any time without impacting the medical care you are currently receiving.
6. Additional information: During the course of the study, new information related to the research methods may emerge. If this occurs, your study physician or nurse will inform you promptly and discuss whether you wish to continue participating. If you decide to continue, you may be required to sign a new informed consent form. During the follow-up phase, your physician or nurse may contact you via text messages, phone calls, or clinic visits to check

on your condition.

Potential Benefits:

While we cannot guarantee direct health benefits from participating in this study, we hope that the intelligent symptom management plan will help improve your ability to manage musculoskeletal symptoms. Furthermore, your participation will contribute to the development of better symptom management tools for other breast cancer patients undergoing endocrine therapy.

Costs and Compensation:

There will be no additional medical costs incurred by participating in this study. The research team will reimburse you for any transportation costs associated with participating in the study. All expenses related to data collection and analysis will be covered by the research team.

The research team will make every effort to prevent and address any harm caused by the study. If adverse events occur, a medical expert committee will assess whether they are related to the study. If deemed study-related, the sponsor will provide compensation and cover any necessary medical treatment in accordance with relevant regulations.

Information and Consultation:

You are free to ask questions about the study at any time, and these questions will be addressed promptly. If new information arises during the study that might affect your decision to continue participating, your doctor or nurse will notify you immediately.

Privacy and Data Confidentiality:

We will maintain strict confidentiality regarding all of your personal information. All health data provided, including symptoms recorded through the app or other means,

will be stored anonymously on encrypted servers, accessible only to the research team. Upon completion of the study, all data will be destroyed in accordance with legal and ethical guidelines, and will not be used for other studies. Your privacy will be protected to the fullest extent possible.

Right to Withdraw:

You have the right to withdraw from the study at any time, without it affecting the breast cancer treatment you are currently receiving. Upon withdrawal, your data will no longer be used and will be destroyed as per legal and ethical requirements. If you wish to withdraw, please contact the research team at any time.

Contact Information:

If you have any questions or require further information regarding this study, you may contact the lead researcher:

Cao Yuling (Phone:+86 13961102420; Email: caoyulingedu@163.com).

Consent Statement:

I have read and understood the information provided above, and the research team has answered my questions.

I understand that participation in this study is voluntary, and I can withdraw at any time without affecting my medical care.

I agree to participate in this study.

Participant's Name: _____

Participant's Signature: _____

Date: _____ Month _____ Day _____ Year

I have accurately explained this document to the participant, who has read the informed consent form thoroughly and has been given the opportunity to ask questions.

Researcher's Name：_____

Researcher's Signature：_____

Date：_____ Month _____ Day _____ Year

(Note: If the participant is legally incapacitated, a legal representative must sign.)

9.5 Questionnaire on Nurses' Knowledge, Beliefs, and Practices Regarding the Management of Musculoskeletal Symptoms in Breast Cancer Patients Undergoing Endocrine Therapy in a Multicultural Context

We are conducting a study on the differences in nurses' knowledge, attitudes, and practices regarding the management of musculoskeletal symptoms in breast cancer patients undergoing endocrine therapy in a multicultural context. We sincerely invite you to participate in this research. If you agree to take part, you will be asked to complete a four-part questionnaire, which is expected to take approximately 15-20 minutes. Your participation will greatly contribute to our understanding and improvement of the quality of care for breast cancer patients.

There are no known risks associated with this study. All data collected will be anonymized and kept strictly confidential. You are free to withdraw from the study at any time without providing any reason. We greatly appreciate your support and participation.

Part I: Basic Information

1. Name of your workplace: _____

2. Your gender [Single choice question]

A. Male

B. Female

3. Your age: _____

4. Years of nursing experience: _____ years

5. Your current professional title [Single choice question]

A. Nurse

B. Registered Nurse

C. Charge Nurse

D. Deputy Head Nurse

E. Head Nurse

F. Other: _____

6. Your highest academic degree [Single choice question]

A. Junior college and below

B. Bachelor's degree

C. Master's degree or Postgraduate diploma

D. Doctoral degree and above

7. The number of beds in your department is: _____

8. Your working city [Single choice question]

A. Shanghai

B. Dali

C. Indonesia

D. Other: _____

9. Are you familiar with the clinical guidelines for the management of musculoskeletal symptoms among breast cancer patients with endocrine therapy? [Single choice question]

A. Yes

B. No

10. Does your institution have an internal implementation plan or process for the management of musculoskeletal symptoms among breast cancer patients with endocrine therapy? [Single choice question]

A. Yes

B. No

11. Have you participated in training related to the management of musculoskeletal symptoms among breast cancer patients with endocrine therapy? [Single choice question]

A. Yes

B. No

12. If you have **not** received the relevant training, what are the reasons? [Multiple choice question]

A. Heavy workload in the department, no time or energy

B. Lack of interest, training is not a concern

C. Unaware of such training notifications and information

D. Low seniority, no opportunity or quota to participate in training

13. If you have received the relevant training, what type of training have you received? [Multiple choice question]

A. Training organized by the department

B. Training organized by the hospital

C. Training organized by external organizations

D. Other: _____

14. What are your main sources for acquiring knowledge about endocrine therapy for breast cancer patients? [Multiple choice question]

A. Institutional education

B. Relevant books and literature

C. Academic conferences or lectures

D. Departmental business learning

E. Self-study due to personal interest or work requirements

F. Training courses

G. Have not yet paid attention to this knowledge area

15. Do you think it is necessary to learn and master more knowledge about the management of musculoskeletal symptoms among breast cancer patients with endocrine therapy? [Single choice question]

A. Yes

B. No

Part II: Knowledge (K)

1. Which of the following adverse reactions are most common in endocrine therapy for breast cancer patients? [Multiple choice question]

A. Hot flashes and sweating

B. Musculoskeletal pain

C. Decreased bone density, increasing the risk of fractures

D. Vaginal dryness and decreased libido

E. Endometrial thickening, potentially increasing the risk of endometrial cancer

F. Liver function abnormalities, such as elevated transaminases

G. Cardiovascular events, such as thrombosis

2. Which factors may exacerbate musculoskeletal symptoms during endocrine therapy for breast cancer patients? [Multiple choice question]

A. Weight gain

B. Prolonged sedentary behavior

C. Insufficient intake of calcium and vitamin D

D. Lack of regular exercise

3. What is the recommended daily calcium intake during endocrine therapy for breast cancer patients? [Single choice question]

A.1000mg

B.1200mg

C.1500mg

D.2000mg

4. What is the recommended daily vitamin D intake during endocrine therapy for breast cancer patients? [Single choice question]

A.400IU

B.800IU

C.1000IU

D.2000IU

5. Vitamin D is crucial for the skeletal health of breast cancer patients with endocrine therapy. Which of the following is the primary function of vitamin D? [Single choice question]
A. Promotes calcium absorption and maintains bone health
B. Enhances muscle function
C. Regulates the immune system
D. Improves cardiovascular health

6. Which of the following foods helps prevent osteoporosis? [Single choice question]
A. Milk and dairy products
B. Green leafy vegetables
C. Nuts and seeds
D. Fish (such as salmon)

7. Which mineral helps maintain bone health? [Single choice question]
A. Magnesium
B. Iron
C. Zinc
D. Calcium

8. Which of the following behaviors is most beneficial to bone health? [Single choice question]
A. Vitamin D and calcium supplementation
B. Prolonged bed rest
C. Restricting fat intake
D. High-fiber diet

9. What is the recommended frequency for bone density tests in breast cancer patients with endocrine therapy? [Single choice question]
A. Every 6 months
B. Annually
C. Every 2 years

D. Every 5 years

10. What is the purpose of regular bone density testing during endocrine therapy for breast cancer patients? [Single choice question]
A. Monitoring blood sugar levels
B. Assessing bone health status
C. Measuring blood pressure
D. Checking vision

11. Which medication is commonly used to alleviate joint pain caused by endocrine therapy for breast cancer? [Single choice question]
A. Nonsteroidal anti-inflammatory drugs (NSAIDs)
B. Calcium and vitamin D supplements
C. Bisphosphonates
D. Opioids

12. Which type of physical therapy can help breast cancer patients with endocrine therapy to alleviate musculoskeletal symptoms? [Single choice question]
A. Yoga
B. Swimming
C. Specific exercises under the guidance of physical therapy
D. Heat therapy

13. How many minutes of moderate-intensity aerobic exercise should adults engage in per week during endocrine therapy for breast cancer? [Single choice question]
A. 75 minutes
B. 150 minutes
C. 225 minutes
D. 300 minutes

14. Which of the following behaviors helps maintain bone health during endocrine therapy for breast cancer? [Single choice question]
A. Engaging in regular moderate-intensity exercise
B. High-sugar diet

C. Prolonged bed rest

D. Restricting calcium intake

------**Part III: Attitude (A)**

1. Do you think managing the musculoskeletal symptoms of breast cancer patients is important? [Single choice question]

A. Extremely important

B. Important

C. Moderately important

D. Unimportant

E. Extremely unimportant

2. Do you think nurses play a crucial role in managing the musculoskeletal symptoms of breast cancer patients? [Single choice question]

A. Strongly agree

B. Agree

C. Uncertain

D. Disagree

E. Strongly disagree

3. What kind of knowledge do you think nurses need to have to manage musculoskeletal symptoms caused by endocrine therapy for breast cancer? [Multiple choice question]

A. Symptom recognition

B. Medication management

C. Physical therapy

D. Nutritional guidance

E. Exercise advice

F. Other: _____

4. Are you willing to receive training on the management of musculoskeletal symptoms related to endocrine therapy for breast cancer? [Single choice question]

A. Very willing

B. Willing

C. Uncertain

D. Unwilling

E. Very unwilling

5. Do you think the current training is sufficient to meet the needs of patients with endocrine therapy for breast cancer? [Single choice question]

A. Strongly agree

B. Agree

C. Uncertain

D. Disagree

E. Strongly disagree

6. What do you think are the main challenges in managing musculoskeletal symptoms in actual work? [Multiple choice question]

A. Low patient compliance

B. Lack of professional knowledge

C. Lack of practical experience

D. Insufficient hospital support

E. Other: _____

7. Do you think it is necessary to establish a specialized management plan for musculoskeletal symptoms? [Single choice question]

A. Strongly agree

B. Agree

C. Uncertain

D. Disagree

E. Strongly disagree

8. How much do you think musculoskeletal symptoms affect the quality of life of breast cancer patients? [Single choice question]

A. Very significant

B. Significant

C. Moderate

D. Slight

E. Very slight

9. What do you think are the main responsibilities of nurses in managing musculoskeletal symptoms? [Multiple choice question]
A. Assessing and monitoring symptoms
B. Providing education and guidance
C. Developing and implementing management plans
D. Collaborating with physicians and other healthcare team members
E. Other: _____

10. Do you believe that health education can effectively improve patient compliance with musculoskeletal symptom management? [Single choice question]
A. Strongly agree
B. Agree
C. Uncertain
D. Disagree
E. Strongly disagree

Part IV: Practice (P)

1. Do you actively assess the musculoskeletal symptoms of breast cancer patients in your daily nursing practice? [Single choice question]
A. Never
B. Occasionally
C. Sometimes
D. Often
E. Always

2. Do you provide health education on musculoskeletal symptom management to breast cancer patients and their families? [Single choice question]
A. Never
B. Occasionally
C. Sometimes
D. Often
E. Always

3. Do you tailor musculoskeletal symptom management plans to the individual patient's situation in your actual work? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

4. Do you regularly review and adjust the musculoskeletal symptom management plans for patients? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

5. Do you collaborate with other healthcare team members to jointly manage the musculoskeletal symptoms of breast cancer patients? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

6. Do you regularly participate in relevant training or learning to improve your knowledge and skills in musculoskeletal symptom management? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

7. Do you proactively learn and apply new technologies and methods in musculoskeletal symptom management in your work? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

8. Do you record the patient's compliance in managing musculoskeletal symptoms? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

9. Do you participate in the establishment and (or) strict implementation of the unit's processes and standards for managing musculoskeletal symptoms in breast cancer patients? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

10. Do you regularly assess and improve your nursing practice to enhance the quality of care for breast cancer patients? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

11. Do you share your experience and skills in managing musculoskeletal symptoms with new nurses or interns? [Single choice question]

A. Never

B. Occasionally

C. Sometimes

D. Often

E. Always

------Thank you very much for your participation! Your answers will provide valuable insights for our study!

9.6 Interview Guide

1. **Intervention Implementation Process**
    - Could you briefly describe the specific process of implementing the intervention at your site?
    - Were there any aspects of the implementation that differed from your initial expectations? Please explain in detail.
2. **Facilitators of Intervention Implementation**
    - In implementing the intervention, what specific factors (e.g., team collaboration, resource support, patient engagement) do you believe contributed positively to the smooth execution of the plan?
    - Have you observed any management processes or system support that effectively enhanced the intervention outcomes?
3. **Barriers to Intervention Implementation**
    - What major difficulties or challenges did you encounter during implementation? How did these challenges specifically affect the execution of the intervention plan?
    - Do you believe there were any resource or condition limitations that created obstacles in carrying out the plan? Additionally, were there cultural or policy factors that acted as barriers?
4. **Feedback from Patients and Team**

- How did the nursing team respond to the intervention during implementation? Were there any factors that affected team participation or execution?
- What is your perception of patient acceptance of the intervention? Were there any specific factors that influenced patient engagement?

5. Improvement and Sustainability of the Intervention

- Based on your experience, what aspects of the intervention could be further optimized or improved?
- Do you believe this intervention has the potential for long-term application in clinical practice? What factors might influence its sustainability in the future?

10. Attachments

(1) Patient Health Education Handbook

(2) Expert Review Scoring Form

11. References

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