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# Review Nonpharmacological interventions for cancer-related fatigue: A literature review

Shufang Zuo<sup>a,b,#</sup>, Hui Cheng<sup>b,#</sup>, Ziyu Wang<sup>b,#</sup>, Tingting Liu<sup>b</sup>, Si Chen<sup>b</sup>, Li Tian<sup>b,\*\*</sup>, Lu Lin<sup>a,b,\*</sup>

<sup>a</sup> The First Affiliated Hospital of Soochow University, Suzhou, China

<sup>b</sup> School of Nursing, Suzhou Medical College of Soochow University, Suzhou, China

ARTICLE INFO ABSTRACT Cancer-related fatigue (CRF) is a prevalent and debilitating side effect of cancer treatment that can persist for Nonpharmacological intervention years posttreatment, significantly impacting patients' quality of life. Given the limited efficacy of pharmacological Cancer-related fatigue treatments, nonpharmacological interventions are gaining attention as effective management strategies for CRF. Oncology nurse This review aims to provide an overview of the most common nonpharmacological interventions for CRF management, including exercise therapies, psychosocial interventions, sensory art therapy, light therapy, nutritional management, traditional Chinese medicine therapies, sleep management, combination therapy, and health education. By synthesizing the findings of high-quality literature, this review presents the definition of each therapy, along with their advantages and disadvantages in treating patients with CRF. Additionally, it addresses the role of oncology nurses in the nonpharmacological management of CRF. In summary, this review aims to inform oncology nurses about the prevalent nonpharmacological interventions for CRF and explore their clinical appli-

cation to facilitate the development of effective CRF management strategies in clinical practice.

# Introduction

Keywords:

Cancer is a significant public health issue globally, with 19.29 million new cases reported worldwide in 2020, according to the 2020 global cancer burden data published by the International Agency for Research on Cancer.<sup>1</sup> China, being the most populous nation, had the highest number of new cancer cases with an estimated 4.82 million cases in 2022.<sup>2</sup> During cancer treatment, patients experience a wide range of symptoms that vary depending on the type and stage of cancer, as well as the specific treatments used. Common symptoms include fatigue, nausea, vomiting, pain, changes in appetite, hair loss, and cognitive dysfunction associated with chemotherapy.<sup>1-3</sup> Cancer-related fatigue (CRF) is the most common concomitant symptom experienced by cancer patients, with an incidence of 40% at diagnosis and 62%-85% during active treatment, and 30%-60% of moderate to severe cases. Severe CRF may occur in 30% of long-term follow-up cancer patients. It is evident that CRF is not limited to the late stages of cancer but can occur throughout the entire disease cycle of cancer patients and persist for several years after treatment completion.<sup>4,5</sup> CRF has physical, mental, psychological, and emotional effects on patients and can take many clinical forms such

as lack of energy, weakness, laziness, apathy, lack of concentration, memory loss, and depression and may be a risk factor for reduced survival rates.<sup>3</sup> Unlike "normal" fatigue, CRF is more intense, develops more quickly, is disproportionate to activity or energy output, lasts longer, and cannot be relieved by rest or sleep.<sup>5</sup> Therefore, early intervention and increased awareness and attention to CRF are of particular significance. Treatable factors in CRF include pain, emotional disturbances, anemia, sleep disturbances, and complications (organ dysfunction or failure, infections, etc.). Depending on the situation, a combination of nonpharmacological and pharmacological interventions is required for these treatable factors. The appropriate medications for CRF can be found in the relevant clinical guidelines. The two most studied classes of drugs for pharmacological interventions in the absence of other treatable factors are psychostimulants and hormones (including cortisol and progesterone).

Considering the limited efficacy of pharmacological treatments, nonpharmacological interventions are gaining attention as effective management strategies for CRF. Mustian et al<sup>7</sup> meta-analyzed the four most commonly recommended treatments for CRF (exercise, psychological intervention, exercise and psychological intervention combined,

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<sup>\*</sup> Corresponding author. The First Affiliated Hospital of Soochow University/School of Nursing, Suzhou Medical College of Soochow University, Suzhou, China \*\* Corresponding author. School of Nursing, Suzhou Medical College of Soochow University, Suzhou, China

E-mail addresses: tianlisz@suda.edu.cn (L. Tian), linlu@suda.edu.cn (L. Lin).

<sup>&</sup>lt;sup>#</sup> Contributed equally.

and pharmacological intervention) for improving CRF during and after primary treatment and found that pharmacological interventions did not improve CRF to the same extent as nonpharmacological interventions. Therefore, it is particularly crucial to provide a comprehensive overview of nonpharmacological interventions for CRF management.

To comprehensively examine nonpharmacological interventions for CRF, this review covers a wide range of interventions such as exercise, psychosocial interventions, sensory art therapy, light therapy, nutritional management, traditional Chinese medicine (TCM) therapies, sleep management, combination therapy, and health education. To ensure the accuracy and reliability of the review, we conducted a thorough search of eight databases, including both English and Chinese literature published in the past five years (2018–2022), limiting our search to clinical guidelines, systematic reviews, meta-analyses, and intervention studies. The search keywords used were "cancer-related fatigue" OR "cancer-induced fatigue" AND "non-pharmacological intervention" OR "non-pharmacological management".

By synthesizing the findings of high-quality literature, this review aims to address the following questions: (1) What are the common nonpharmacological interventions for CRF? (2) How effective are these interventions in managing CRF? and (3) What is the role of oncology nurses in non-pharmacological management of CRF? This review presents the definition of each therapy, along with its respective advantages and disadvantages in managing CRF, and provides recommendations for appropriate clinical practice (see Table 1 for details).

# Nonpharmacological interventions for cancer-related fatigue

#### Exercise therapies

The National Comprehensive Cancer Network (NCCN) recommends exercise therapy to manage fatigue symptoms, and the American College of Sports Medicine (ACSM) deems exercise training safe for managing CRF during and after treatment for most cancer survivors.<sup>8,9</sup> Exercise modalities include aerobic exercise, resistance exercise, yoga, qigong, Tai Chi, muscle relaxation training, and combination exercise.<sup>10</sup> Meta-analyses indicate that exercise intervention, especially combined aerobic and resistance exercise, yoga, and regular physical activity, is safe and feasible for relieving CRF<sup>11–13</sup>. Clinical guidelines also recommend exercise therapy to prevent or alleviate CRF during active and posttreatment phases.<sup>8,14</sup> However, exercise intervention for patients with advanced cancer remains controversial, and more targeted research is needed to determine optimal exercise doses for specific cancer diagnoses.<sup>15,16</sup>

As per the ACSM guidelines, moderate-intensity aerobic exercise for at least three times per week for 12 weeks can significantly reduce CRF, and combining aerobic exercise with resistance training sessions, performed 2–3 times per week, or undertaking twice-weekly resistance training, can also be effective in reducing CRF.<sup>17</sup> Multimodal, moderate to high intensity exercise is appropriate for most patients, but those at high risk for disease progression should exercise at low to moderate intensity.<sup>16</sup> There is no set prescription or weekly dosage that would be considered evidence-based for all cancer patients. Supervised exercise interventions are more effective than unsupervised ones, and supervised community/home exercise interventions can be advocated<sup>18–20</sup>. Nurses are a primary driver of exercise among patients receiving cancer treatment, and nurse input is critical to implement exercise into standard care and ensure program feasibility.

# Psychosocial interventions

Psychosocial interventions refer to various psychological and social rehabilitation measures aimed at reducing or eliminating psychocognitive and social impairments in patients.<sup>21</sup> Nurses play a crucial role in planning and educating patients, utilizing professional theories and health knowledge to develop comprehensive and holistic care plans.

They also provide health education and behavioral guidance to promote positive health attitudes and behaviors while listening to and supporting patients to help build their self-confidence in coping with their illness.

#### Cognitive behavioral therapy (CBT)

CBT is a psychosocial intervention that helps improve mental health by changing cognitive distortions and behaviors, improving emotion regulation, and developing coping strategies.<sup>22</sup> It is implemented in three steps: cognitive identification, cognitive reconstruction, and behavioral interventions. CBT involves face-to-face conversations with a trained psychotherapist and lasts for 6-12 weeks with 1-h sessions each week.<sup>23</sup> CBT is effective in reducing CRF scores and improving the overall effectiveness of CRF treatment in cancer patients, as shown in three meta-analyses covering 31 randomized controlled trials (RCTs) with 3599 subjects<sup>24–26</sup>. Several RCT studies have also demonstrated the positive effects of CBT or web-based CBT in improving CRF. The studies included patients with different cancer types, at different stages, and with different treatments, indicating that CBT can improve fatigue symptoms for patients with cancer. In the study by Janse et al, the positive effects of CBT lasted up to 18 months after treatment.<sup>27</sup> However, its long-term efficacy cannot be generalized as the longest follow-up in all other studies was 9 months.

# Mindfulness-based stress reduction (MBSR)

MBSR is a systematic meditation training that aims to relieve stress, negative emotions, and physical symptoms and promote illness adaptation.<sup>28</sup> MBSR consists of techniques such as body scan, meditation, breath observation, walking meditation, and yoga exercises.<sup>29</sup> The recommended MBSR intervention involves group sessions of 2.0-2.5 h, once a week for 8 weeks, with a maximum of 30 participants in each group, plus self-directed training of 45 min per session, six times a week.<sup>30</sup> Most existing studies used interventions lasting between 6 and 9 weeks, and some studies conducted subgroup analyses of CRF according to the length of intervention, the results of which indicated that MBSR improved CRF in patients,<sup>31</sup> and the intervention effect persisted for up to 6 months.<sup>3</sup> However, most studies mainly involved breast cancer patients, limiting its generalization to other tumor types.<sup>33</sup> Additionally, MBSR requires professional guidance, and its longer cycle may pose challenges for patients suffering from inherent fatigue. Thus, more research is needed to evaluate the effectiveness of MBSR in a wider range of cancer patients.<sup>3</sup>

#### Stress management therapy (SMT)

SMT is a psychological intervention that helps patients cope with stress by identifying the source of stress and enhancing coping skills.<sup>34</sup> SMT has been shown to alleviate fatigue, improve quality of life, and self-efficacy among cancer patients.35 SMT for breast cancer patients usually employs a 10-week, structured, manualized intervention to help women cope with stress and optimize social resources.<sup>36</sup> In a study by Vargas et al, 240 breast cancer patients participated in SMT, which consisted of weekly 2-h sessions that included didactic presentations, cognitive behavioral techniques, and relaxation exercises such as progressive muscle relaxation and imagery. While there were no significant differences in changes in fatigue intensity after the intervention, there was a greater reduction in fatigue-related daytime disturbances compared to the control group.<sup>37</sup> SMT provides patients with tools to manage stress and anxiety, modify negative thought patterns contributing to CRF, and is a noninvasive and low-risk intervention. However, SMT may not work for all patients, and there is limited high-quality research on its use to manage CRF in cancer patients. Future large-sample clinical studies are needed to verify the effect of SMT.

# Psychoeducation (PE)

PE interventions consist of a wide range of elements, such as educational program, information, counseling, and supportive interventions and aim to educate and support patients in coping with the side effects of cancer, primarily through face-to-face meetings with healthcare

# Table 1

Advantages and disadvantages of the most common nonpharmacological interventions for CRF and recommendations	; for practice.
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Гуре of intervention	Subtype	Advantages	Disadvantages	Recommendations
Exercise therapies <sup>8–20</sup>		<ul> <li>Various forms available</li> <li>Simple operation, low cost, and easy application</li> <li>Improves physical functioning, quality of life, and psychological well-being</li> <li>May reduce CRF severity and duration</li> </ul>	<ul> <li>Risk of injury during exercise, especially for patients with bone metastasis or advanced cancer</li> <li>Not applicable to all cancer patients, such as those with severe physical limitations or fatigue</li> <li>Requires adherence to an exercise regimen and may require motivation and support</li> <li>Intensity and duration of exercise should be personalized to individual patient needs and may vary throughout treatment</li> </ul>	<ul> <li>For most cancer patients with fatigue, multimodal, medium to high-intensity exercise is appropriate</li> <li>Patients with high risk of disease progression can usually perform low to medium-intensity exercise</li> <li>Exercise needs of patients during palliative treatment vary from person to person</li> <li>Exercise therapy should be provided under the supervision and guidance of trained professionals</li> </ul>
interventions <sup>22–45</sup> therapy ( Mindfuln reduction Stress ma (SMT) <sup>34</sup>	Cognitive behavioral therapy (CBT) <sup>22–27</sup>	<ul> <li>Effective in improving fatigue symptoms in patients with different types, stages, and treatment modalities of cancer</li> <li>Can help patients develop coping strategies to manage stress and anxiety related to cancer treatment</li> <li>Can improve CRF in the short term (up to 18 months after intervention)</li> </ul>	<ul> <li>Limited long-term effects on CRF</li> <li>Requires a trained therapist to deliver the intervention, which may not be widely available in all healthcare settings</li> </ul>	<ul> <li>Ensure that the CBT sessions are conducted by professionally trained psychotherapists</li> <li>Schedule 60-min weekly sessions for 6–12 weeks</li> <li>Use face-to-face conversations to identify and change the patients misconceptions</li> <li>Incorporate behavioral training to alleviate psychological stress and physical symptoms</li> </ul>
	Mindfulness-based stress reduction (MBSR) <sup>28–33</sup>	<ul> <li>Widely recognized positive effect on CRF in cancer patients</li> <li>Intervention effects can last up to 6 months after intervention</li> <li>Helps patients develop mindfulness skills, such as focused breathing and body scanning</li> <li>Can be integrated into daily life for long-term benefits</li> </ul>	<ul> <li>Influenced by subjective factors</li> <li>Requires weekly group sessions for 8 weeks, which may be challenging for cancer patients with inherent fatigue</li> <li>Requires a trained MBSR instructor</li> <li>May not be accessible to all patients due to financial or geographical barriers</li> </ul>	<ul> <li>Group training sessions of 2–2.5 h once a week for 8 consecutive weeks</li> <li>Maximum of 30 people per group</li> <li>Self-directed training of 45 min per time, 6 times a week</li> </ul>
	Stress management therapy (SMT) <sup>34-37</sup>	<ul> <li>Can improve the quality of life and self-efficacy of cancer patients</li> <li>Can help patients identify and modify negative thought patterns contributing to CRF</li> <li>Provides patients with tools to manage stress and anxiety</li> <li>Noninvasive and low risk</li> </ul>	<ul> <li>Few studies on its application to CRF and limited evidence of its effectiveness</li> <li>Long-term and consistent application may be needed to achieve significant results</li> <li>Requires a trained therapist and multiple sessions, which may not be readily available or accessible to all patients</li> <li>May not be effective for all patients, as some may have physical limitations that cannot be addressed through SMT</li> </ul>	<ul> <li>Conduct weekly group sessions, using structured interventions</li> <li>Provide educational and experientiall supported instruction in cognitive-behavioral techniques</li> <li>Teach relaxation exercises such as progressive muscle relaxation and visual imagery to help patients cope more effectively with daily stressors</li> </ul>
	Psychoeducation (PE) <sup>38-40</sup>	<ul> <li>Significantly improves patient symptoms in terms of symptom cluster, fatigue, and sleep disturbances compared to usual care</li> <li>Can be delivered in a group or individual setting, in person or remotely</li> </ul>	<ul> <li>Influenced by subjective factors and less effective than MBSR in improving CRF</li> <li>May require additional resources, such as trained facilitators, materials, and time for preparation and delivery</li> </ul>	<ul> <li>Conduct weekly face-to-face meetings with patients for ≥6 weeks</li> <li>Discuss the impact of CRF on psychological and social functioning</li> <li>Encourage patients to share their experiences related to CRF, while actively listening and providing affirmation</li> <li>Provide education about CRF management techniques and overall health</li> </ul>
	Peer support <sup>41–45</sup>	<ul> <li>Reduces patients' loneliness during the treatment period</li> <li>Enhances self-confidence in treatment</li> <li>Helps patients change bad habits</li> <li>Promotes the recovery of body functions, thus reducing CRF</li> <li>Offers a personalized and flexible approach to support</li> <li>Provides an opportunity for patients to share their experiences and exchange information with peers</li> </ul>	<ul> <li>Requires more time to implement than some other interventions</li> <li>Effectiveness may vary depending on the quality of the relationship between peers, the level of training of peer supporters, and the type of support provided</li> <li>Requires the establishment of organizations to carry out a variety of activities and maintain stability</li> <li>Requires funding and resources to train and support peer supporters, organize support activities and monitor outcomes</li> </ul>	<ul> <li>health</li> <li>Establish a weekly peer support group for patients with CRF</li> <li>Provide lectures and case sharing sessions to educate patients about adverse reactions to cancer treatment</li> <li>Encourage group discussion and interviews to help patients share their experiences and support each other</li> <li>Ensure that the group is moderated by qualified healthcare professional</li> <li>Evaluate the effectiveness of the peer support group on a regular basis</li> </ul>

# Table 1 (continued)

Type of intervention	Subtype	Advantages	Disadvantages	Recommendations
Sensory art therapies <sup>47–52</sup> Music therapy <sup>47–50</sup> Art therapy <sup>50,51</sup>	Music therapy <sup>47-50</sup>	<ul> <li>Easy to operate and convenient</li> <li>Noninvasive and highly applicable</li> <li>Wide variety of music types and playing forms</li> <li>No special equipment or tools required</li> <li>Can be easily integrated into daily routine</li> <li>Can be customized to fit individual patient preferences</li> <li>Can promote relaxation, improve</li> </ul>	<ul> <li>Most patients require professional guidance to fully benefit from music therapy</li> <li>May not be effective for all patients, depending on individual preferences and musical tastes</li> <li>Requires specialized training to provide professional guidance</li> </ul>	<ul> <li>Recommended for managing CRF in patients with hematological and gastrointestinal cancers during and after treatment</li> <li>Playing music through audio speakers and on-site participation are recommended</li> <li>Selection of music types should consider patient preferences</li> </ul>
	Art therapy <sup>50,51</sup>	<ul> <li>mood, and reduce fatigue</li> <li>Easy to operate, low cost, noninvasive</li> <li>Provides a creative outlet for self- expression and emotional release</li> <li>No restrictions on patient's education, cognitive ability, language, age, location and environment</li> <li>Can be done in a group or individual setting</li> <li>Can be adapted to suit different deiling the set deliving</li> </ul>	<ul> <li>Requires trained and skilled therapists to ensure efficacy</li> <li>Clinical nurses may have limited proficiency in art therapy, thus limiting the quality of the intervention</li> <li>Requires access to art supplies and materials</li> <li>Not suitable for patients who do not enjoy or are not interested in art</li> </ul>	<ul> <li>Can be considered as a potential intervention for managing CRF in children and women groups</li> <li>Due to limited high-quality evidence, specific recommendations for the application of art therapy in CRF management cannot be made</li> </ul>
	Dance movement therapy <sup>52</sup>	<ul> <li>skill levels and abilities</li> <li>Noninvasive and highly applicable, as it can be adapted to suit the physical and emotional needs of individual patients</li> <li>May be delivered in a group or individual setting, depending on patient preference and availability of resources</li> <li>Can be combined with other nonpharmacological interventions</li> </ul>	<ul> <li>High requirements for intervention personnel, with knowledge of psychology, dance, and medicine</li> <li>Safety supervision by surgical or rehabilitation doctors during intervention to prevent injury and ensure patient safety</li> <li>May not be suitable for patients with mobility or balance issues</li> <li>Requires a suitable space for intervention, such as a dance studio or hospital gym, which may not be undebalated in the space of the studies of the studi</li></ul>	<ul> <li>The impact of dance movement therapy on CRF is still controversial and requires further clinical trials for validation</li> <li>A standardized and systematic dance movement program for CRF management is needed</li> <li>A comprehensive follow-up and evaluation system for dance movement therapy in CRF management is lacking</li> </ul>
Light therapy <sup>57_61</sup>	Bright white light therapy (BWL) <sup>57–61</sup>	<ul> <li>An FDA-approved, low-risk intervention that is safe and well- tolerated by cancer patients</li> <li>Simple and easy to implement, and can be self-administered by patients at home</li> <li>Can be used in combination with other nonpharmacological interventions</li> </ul>	<ul> <li>available in all settings</li> <li>May cause discomfort or irritation to the eyes or skin, especially for those who are light-sensitive or have skin sensitivity</li> <li>May not be suitable for patients with certain medical conditions or who are taking certain medications</li> <li>Requires specialized equipment</li> <li>May require adherence to a strict who have negative strict stri</li></ul>	<ul> <li>Use a 4-week light therapy intervention</li> <li>Set the bright white light intensity between 1000 and 5000 lux</li> <li>Administer the therapy for 30 min per day</li> </ul>
Nutritional management <sup>64–66</sup>		<ul> <li>Can be combined with other interventions for a more comprehensive approach</li> <li>Can be integrated into patients' daily routines with minimal disruption</li> <li>Dietary changes can be tailored to the individual patient's preferences and needs</li> </ul>	<ul> <li>schedule or routine</li> <li>The effectiveness of nutritional supplements in cancer patients is controversial and lacks consensus in current research</li> <li>Dietary recommendations may vary depending on the type of cancer and the treatment received, making it difficult to provide specific guidelines</li> <li>Nutritional counseling may require additional resources and expertise, which may not be readily available in all healthcare settings</li> <li>Patients may struggle with adherence to dietary recommendations due to physical and emotional factors related to their</li> </ul>	<ul> <li>Conduct a nutritional assessment for patients to identify potential nutrient deficiencies and personalize interventions</li> <li>Provide individualized nutritional counseling to patients, focusing on maintaining a balanced diet and meeting their specific energy and nutrient needs</li> <li>Encourage patients to consume a diet rich in fruits, vegetables, whole grains, and anti-inflammatory fatty acids, which have been shown to reduce inflammation and improve energy levels</li> </ul>
Traditional Chinese medicine (TCM) therapies <sup>8,67–78</sup>	Acupuncture <sup>67–72</sup>	<ul> <li>Adjusts yin and yang, regulates Qi, and heals the mind</li> <li>Can be integrated with other TCM therapies</li> <li>Can be customized to patient needs</li> </ul>	<ul> <li>cancer diagnosis and treatment</li> <li>Requires professional acupuncturists to operate</li> <li>Possibility of adverse reactions such as needle-stick injury</li> <li>Patients may have fear or discomfort with needles</li> <li>Time-consuming, may require</li> </ul>	<ul> <li>Applicable to breast cancer patients undergoing cancer treatment and lung cancer patients after surgery or chemotherapy</li> <li>ST36 is the most frequently used acupuncture point in treating CRF</li> </ul>

# Table 1 (continued)

Type of intervention	Subtype	Advantages	Disadvantages	Recommendations
	Moxibustion <sup>73,74</sup>	<ul> <li>Simple, safe, noninvasive</li> <li>No toxic side effects</li> <li>May be performed at home with proper instruction and incorporated into self-care routine</li> </ul>	<ul> <li>Highly professional and needs to be operated by a professional moxibustion technician</li> <li>May cause adverse reactions such as burns</li> <li>May be difficult to access professional moxibustion services in certain areas</li> </ul>	<ul> <li>Lack of unified standards or consensus on specific moxibustion treatment programs in clinical practice</li> <li>Moxibustion treatment programs should be individualized based on the patient's condition, including cancer stage, fatigue severity, and other symptoms</li> <li>Can be integrated into a comprehensive and individualized treatment plan for CRF, combining with other nonpharmacological interventions, such as exercise therapy and CBT</li> <li>Patients should be closely monitored for adverse reactions and symptoms of foriume</li> </ul>
	Acupressure <sup>8,75,76</sup>	<ul> <li>Noninvasive, safe, and has no side effects</li> <li>Easy to teach and learn, and can be easily integrated into existing nursing care plans and the patient's daily routine</li> <li>Cost-effective and widely available</li> <li>May help improve sleep quality, reduce anxiety, and enhance overall well-being</li> </ul>	<ul> <li>Limited evidence for its effectiveness in managing CRF</li> <li>The optimal frequency, duration, and intensity are unclear</li> <li>May not be suitable for patients with certain medical conditions or those who are experiencing severe fatigue</li> <li>The implementers require professional training and assessment to ensure efficacy of therapy</li> </ul>	<ul> <li>fatigue</li> <li>Acupressure on Hegu (LI4), Zusanli (ST36) and Sanyinjiao (SP6) can be recommended for CRF management</li> <li>One-time acupressure therapy is not sufficient to achieve long-term relief of CRF</li> <li>Regular acupressure sessions are necessary to maintain the effect of acupressure therapy</li> </ul>
Sleep management <sup>79–83</sup>	Relaxation therapy, stimulus control therapy, sleep restriction therapy, sleep hygiene, CBT <sup>77–79,82,83</sup>	<ul> <li>Easy to operate and use</li> <li>Beneficial in relieving fatigue, restoring physical strength, and enhancing immunity</li> </ul>	<ul> <li>Improper sleep management may lead to patient fatigue or increased fatigue</li> <li>Requires proper patient education and training to ensure proper sleep hygiene practices</li> <li>Requires monitoring and follow-up to ensure adherence to sleep management practices and to adjust interventions as needed</li> </ul>	<ul> <li>Establish regular sleep patterns and create a comfortable sleep environment</li> <li>Encourage physical activity during the day and relaxation techniques before bedtime</li> <li>Monitor and manage side effects of cancer treatments that may disrupt sleep</li> <li>Consider referral to a sleep specialist for severe or persistent sleep disorders</li> </ul>
Combination therapy <sup>7,84,85</sup>		<ul> <li>May be superior to a single intervention in reducing CRF</li> <li>Allows for a more comprehensive approach to CRF management by addressing multiple contributing factors simultaneously</li> <li>Offers flexibility in tailoring the treatment plan to each patient's individual needs and preferences</li> </ul>	<ul> <li>Sometimes may be less effective than a single intervention in reducing CRF, as some interventions may not complement each other or may have competing effects</li> <li>The optimal sequencing and timing of interventions is critical for achieving optimal outcomes and may require careful planning and coordination among healthcare professionals</li> <li>Requires more resources and time to implement than a single intervention, which may not be feasible for all patients or healthcare</li> </ul>	<ul> <li>Consider combining nonpharmacological interventions to manage CRF</li> <li>Tailor the combination therapy to the individual needs of the patient</li> <li>Evaluate the effectiveness of the combination therapy in managing CRF through objective measures and patient-reported outcomes</li> <li>Continue to conduct research to identify the optimal combinations of nonpharmacological interventions for managing CRF</li> </ul>
Health education <sup>86</sup>		<ul> <li>No cost and a convenient means of intervention</li> <li>Helps patients and their families to set up correct treatment expectations and generate more positive emotions</li> <li>Can be delivered in a group or individual setting</li> <li>Can be delivered through various channels, such as pamphlets, videos, or online resources</li> </ul>	<ul> <li>settings</li> <li>Educators need to be properly trained and knowledgeable to effectively deliver health education to patients and their families</li> </ul>	<ul> <li>Conduct health education on CRF-related knowledge for cancer patients and their caregivers according to the stage of the disease</li> <li>Provide information on the causes, clinical manifestations, and related relief or treatment measures of fatigue</li> <li>Tailor education to individual needs and preferences</li> <li>Use various educational materials, such as brochures, videos, and interactive tools</li> <li>Encourage patients to participate actively in their care and self-management</li> <li>Monitor and evaluate the effectiveness of the education program</li> </ul>

\*CRF: cancer-related fatigue.

providers, where patients can discuss their experiences with CRF and receive affirmation and support. PE can be delivered in group or individual format and can be done face-to-face or remotely. However, it may require additional resources such as trained facilitators, materials, and preparation time. Studies have shown significant improvements in symptom severity, fatigue burden, and sleep disturbance with PE interventions.<sup>38</sup> One study comparing PE to MBSR found that both interventions produced significant improvements in fatigue outcomes, depression, anxiety, and sleep.<sup>39</sup> A meta-analysis also found that MBSR and PE were the most effective psychosocial therapies for CRF.<sup>40</sup>

# Peer support (PS)

PS is a type of social support that offers emotional, information, and assessment support among people who share similar experiences.<sup>41</sup> PS groups help patients communicate with peers, share experiences, and address questions related to cancer treatment. The effectiveness of PS depends on the quality of relationships between peers, training of supporters, and type of support provided. Studies have shown that PS can reduce patient isolation, enhance self-confidence, and relieve CRF. The positive effects of PS on fatigue relief can be attributed to helping patients develop a positive attitude, gain health information, build confidence, and receive empathetic emotional support<sup>42–44</sup>.

In addition to PS, a meta-analysis of 41 RCTs has shown that cognitive CBT, MBSR, and PE are efficacious in alleviating CRF in cancer patients. MBSR was the most effective intervention, followed by CBT and PE. Future research should focus on investigating the impact of psychosocial interventions in different cancer types to better understand their effectiveness in managing CRF.<sup>45</sup>

# Sensory art therapies

Sensory art therapy encompasses a variety of therapies that use art media to stimulate the senses.<sup>46</sup> Music therapy is easy to apply and effective in relieving CRF in patients with hematological malignancies<sup>47</sup> and gastrointestinal cancers<sup>48</sup> during treatment and rehabilitation.<sup>49</sup> It stimulates the brain's functional processes, providing endorphin, dopamine, and serotonin stimulation, and activating neural pathways to reduce fatigue severity.<sup>50</sup> Art therapy, which involves visual art-making for expression and communication, has positive effects on relieving CRF of breast cancer patients.<sup>49,51</sup> The effect of dance movement therapy on CRF is controversial, with some studies reporting no significant effect<sup>52</sup> and others suggesting that it may help alleviate fatigue.<sup>53</sup> Sensory art therapy is increasingly used in managing CRF in childhood cancer patients, with various recreational and therapeutic games showing improvement in children's emotional and social well-being.<sup>54,55</sup> A one-month study involving professional artists providing painting and manual art therapy to pediatric cancer patients showed a significant improvement in the patients' energy and physical strength.<sup>56</sup> However, implementing sensory art therapy requires medical workers with higher levels of artistic and cultural literacy and systematic training. More research is needed to verify the effects of color therapy, aromatherapy, and play therapy on CRF.

# Light therapy (LT): Bright white light (BWL) therapy

LT is a physical therapy method that uses artificial or natural light to prevent and treat diseases.<sup>57</sup> BWL delivered via a light box for 30 min each morning is effective in reducing CRF compared to dark red light (DRL), and LT lasting 4 weeks is more effective than shorter or longer durations. LT with light intensities of 1000–5000 lux is significantly more effective than controls, while LT with < 1000 lux or > 5000 lux shows no difference.<sup>58,59</sup> A light intensity of 1000–5000 lux is a key factor in LT for CRF relief in cancer patients. Effects of phototherapy for non-Hodgkin's lymphoma typically appear within 2 weeks, and increased fatigue is associated with decreasing light exposure is associated with decreasing fatigue

levels.<sup>60,61</sup> Overall, CRF in cancer patients tended to improve significantly within 2 weeks after a 4-week LT intervention with BWL intensity of 1000–5000 lux for 30 min per day. However, LT may cause discomfort or irritation to the eyes or skin, especially for those with light or skin sensitivities. LT can be used in combination with other nonpharmacological interventions, but is difficult to perform at home due to the specialist equipment and handling required.

# Nutritional management

Nutritional management for CRF is a relatively new area with limited established studies. A comprehensive nutritional assessment, including evaluation of weight changes, nutritional intake disorders, anemia, and imbalances in vitamin intake, fluid, and electrolyte levels, is essential to identify potential nutritional deficiencies and personalized interventions. Nutrition counseling may help manage deficiencies caused by anorexia, diarrhea, nausea, and vomiting. However, it may require additional resources and expertise, which may not be readily available in all healthcare settings. The effectiveness of dietary supplements such as guarana, acetyl-L-carnitine, and coenzyme Q for CRF management remains controversial.<sup>62</sup> Adequate protein intake and a healthy intake of omega-3 fatty acids, omega-6 fatty acids, and high-fiber carbohydrates are recommended to reduce inflammation and obesity. Micronutrient supplementation's benefits in cancer survivors with posttreatment fatigue are not established, and the role of micronutrients in improving CRF needs further study.<sup>63</sup> A dietary pattern rich in fruits, vegetables, whole grains, and anti-inflammatory fatty acids may improve CRF in cancer patients.<sup>64</sup> However, providing specific guidelines for dietary advice can be challenging, given the type of cancer and treatment received. Dietary management can be adjusted to the individual patient preferences and needs, but adherence to dietary recommendations can be difficult due to physical and emotional factors related to cancer diagnosis and treatment. Dietary management can be combined with other interventions and integrated into the daily life of the patients, minimizing interference.

# Traditional Chinese medicine therapies

According to TCM, CRF is caused by an imbalance of qi, blood, yin and yang, resulting in organ function damage. TCM therapies aim to relieve CRF by regulating the viscera and tonifying Qi and blood.<sup>65,66</sup> TCM interventions include acupuncture, acupressure, moxibustion, acupoint massage, Qigong, Tai Chi, Tai Chi sword, Baduanjin (eightsectioned exercise), Wuqinxi (five mimic-animal exercise), and other techniques.

# Acupuncture

Acupuncture, one of the common methods of TCM intervention, has been widely used to manage fatigue. The NCCN guidelines recommend acupuncture for patients with CRF, especially for cancer survivors who have completed cancer treatment.<sup>8</sup> Several systematic reviews and meta-analyses have also confirmed that acupuncture is safe and effective for CRF management,<sup>67,68</sup> particularly for patients with breast and lung cancer, and those undergoing cancer treatment<sup>69–71</sup>. The acupuncture point most commonly used was ST36.<sup>72</sup> However, acupuncture needs to be operated by a professional acupuncturist, with a long course of treatment, and there is the possibility of adverse reactions (acupuncture injury).

# Moxibustion

Moxibustion is a kind of external TCM therapy that is characterized by being simple, safe, effective, and without toxic side effects.<sup>73</sup> It stimulates the body's own endogenous regulatory system through multiple targets and channels, promotes the production of endogenous protective substances, and stimulates relevant acupoints and meridian conduction throughout the body to cure diseases. According to a systematic review by Deng et al,<sup>74</sup> moxibustion is efficacious and safe in CRF treatment. However, currently, there are no unified standards or

consensus on specific acupuncture and moxibustion treatment programs in clinical practice.

# Acupressure

Acupressure has the advantages of being noninvasive, safe and side effect-free, and is one of the nonpharmacological treatments for CRF recommended by NCCN guidelines.<sup>8</sup> Meta-analyses have confirmed that acupressure can effectively relieve CRF.<sup>75,76</sup> A meta-analysis concluded that acupressure may be applied to the body acupoints Hegu (LI4), Zusanli (ST36), and Sanyinjiao (SP6) once daily for 1–3 min each and to the auricular acupoints Shenmen and subcortex once daily for 3 min each to effectively relieve CRF.<sup>75</sup>

## Others

As for other TCM therapies, studies have shown that Tai Chi, Tai Chi Sword, Qigong, Baduanjin (eight-sectioned exercise), and Wuqinxi (five mimic-animal exercise) can also relieve CRF in cancer patients to a certain extent<sup>77,78</sup>. But considering the quality and quantity of the existing literature, trials of higher quality and larger sample sizes are needed to further validate their therapeutic effects in the future.

#### Sleep management

CRF is a prevalent symptom among cancer patients due to multiple factors, and sleep disturbance has been identified as both an influencing and treatable factor. To alleviate CRF in cancer patients, sleep management is recommended.<sup>4</sup> Nonpharmacological sleep management strategies include relaxation therapy, stimulus control therapy, sleep restriction therapy, sleep hygiene, and cognitive behavioral therapy. Stimulus control therapy, which has five major steps, is a key component of cognitive behavioral therapy for insomnia and is recommended as a Level I method in the NCCN guidelines for sleep disorder treatment. Sleep restriction therapy requires avoiding long naps and limiting the total time spent in bed.<sup>79</sup> Sleep hygiene involves establishing a regular sleep schedule, avoiding physical or mental exercise close to bedtime, and improving the bedroom environment. Both CBT and BWL therapy mentioned earlier can improve CRF and are effective in treating sleep disorders<sup>80–83</sup>. However, further research is needed to determine the optimal timing and duration of BWL therapy. Proper education and training, as well as monitoring and follow-up, are necessary to ensure appropriate sleep hygiene practices and compliance with sleep management interventions, with referral for severe sleep disorders. Sleep management can relieve fatigue, restore physical strength, and enhance immunity, but inappropriate management can worsen fatigue.

# Combination therapy (CT)

CT is defined as including two or more nonpharmacological interventions, such as exercise therapy combined with sleep management<sup>84</sup> or exercise therapy combined with CBT.<sup>85</sup> According to a meta-analysis,<sup>7</sup> pharmacological interventions, as they have been studied so far, are ineffective for improving CRF during and after primary treatment. In contrast, exercise, psychological interventions, and a combination of both have been found to be significantly more effective for CRF relief. However, it should be noted that the effect of exercise plus psychological interventions as combination therapy is not always better than that of exercise or psychological interventions alone. This may be due to the fact that the combination of different therapies may increase the complexity and duration of the intervention, leading to a reduction in patient adherence, which is counterproductive. Thus, the optimal order and timing of interventions are essential to achieving optimal outcomes and may require careful planning and coordination among healthcare professionals.

Furthermore, it is important to consider that a combination therapy requires more resources and time to implement than a single intervention, which may not be feasible for all patients or healthcare settings. None-theless, a combination therapy can also be synergistic, achieving a "1 +

1>2" effect and better alleviating CRF. This provides an opportunity to customize the treatment options according to the patient's individual needs and preferences. Future studies are needed to evaluate the effectiveness of combination therapy in managing CRF through objective measures and patient-reported outcomes, as well as to identify the optimal combination of nonpharmacological interventions for CRF management.

## Health education

Health education aims to enhance health knowledge, attitudes, skills, and behavior by developing individual, group, institutional, community, and systemic strategies. It is cost-free and convenient and not only improves the health behavior of individuals and communities but also the living and working environments that affect their health.<sup>86</sup> In the context of cancer, scientific health education for patients and their families can help raise their awareness of the disease and set the right expectations for treatment. This can result in more positive emotions and better treatment outcomes. Oncology nurses can provide health education about CRF and its clinical manifestations, causes, and related relief or therapeutic measures through brochures, videos, or online resources. However, the degree of CRF and other cancer-related symptoms can vary at different stages of the disease, such as the active treatment phase, posttreatment phase, and terminal phase. Therefore, when providing health education, it is important to consider the patient's disease stage and inform them about what they may experience. For instance, patients should be informed that they may experience moderate to severe CRF during radiotherapy, chemotherapy, or immunotherapy. They should also be aware that they may still experience varying degrees of fatigue even after the completion of treatment, but this does not mean that the treatment was ineffective or that it will exacerbate the disease. A good attitude from the nurse can help make the health education better received by patients and their caregivers. It is important to note that customized education programs should incorporate individual needs and preferences. Patients should be encouraged to actively participate in their care and self-management and monitor and evaluate the effectiveness of the educational program. Educators must have appropriate training and knowledge, as well as good attitudes, to ensure that patients and their caregivers receive effective health education.

# Conclusions

The etiology and pathogenesis of CRF are still being explored, and pathogenesis-led interventions are not yet available. However, nonpharmacological interventions such as exercise therapies, psychosocial interventions, sensory art therapy, light therapy, and TCM therapies can be used to relieve CRF in patients. To improve patient outcomes and their quality of life, oncology nurses can apply evidence from established evidence-based studies in clinical practice for CRF management. They can also collaborate with researchers to conduct clinical intervention studies and validate the effectiveness of the intervention measures. Additionally, oncology nurses can participate as clinical nursing experts in the development of expert consensus or guidelines on CRF management. Future research could explore the implementation of dynamic CRF management in clinical practice, which involves precise interventions based on the stage of the disease and the symptoms and needs of the patient.

# Credit author statement

Shufang Zuo: Data collection, Writing – Original draft. Hui Cheng: Data collection, Writing – Original draft. Ziyu Wang: Data collection, Writing – Original draft. Tingting Liu: Data curation, Software. Si Chen: Software, Validation. Li Tian: Conceptualization, Supervision. Lu Lin: Conceptualization, Methodology, Supervision, Writing – Reviewing and editing. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

# Declaration of competing interest

All authors have none to declare. The corresponding author, Dr. Lu Lin, is an assitant editor of *Asia-Pacific Journal of Oncology Nursing*. The article was subject to the journal's standard procedures, with peer review handled independently of Dr. Lu and their research groups.

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## Ethics statement

Not required.

# Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

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