



# Development and validation of a Tai chi intervention protocol for managing the fatigue-sleep disturbance-depression symptom cluster in female breast cancer patients

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## ABSTRACT

**Objective:** To develop an evidence-based tai chi intervention protocol for managing the fatigue-sleep disturbance-depression symptom cluster (FSDSC) in breast cancer (BC) patients.

**Methods:** The Medical Research Council (MRC) Framework for Developing and Evaluating Complex Interventions (the MRC framework) was utilized to guide the study design. This study focused on Phase I of the MRC framework—the development of the intervention—to develop an evidence-based tai chi intervention protocol for managing the FSDSC in BC patients based on existing research evidence, theories, practice standards/guidelines, and experts' consensus. An extensive literature search was performed to identify current systematic reviews, theories, and practice standards/guidelines that can be utilized to inform the intervention dosage and techniques of tai chi and practice instructions. Content validity assessment was also conducted to assess the content validity of the tai chi protocol through expert panel consensus. The content validity index (CVI) was calculated to identify whether the intervention required further refinement.

**Results:** The components of the tai chi protocol were identified by current research evidence and relevant practice standards/guidelines, including the selection of an appropriate tai chi modality and intensity and the duration of the intervention. The Easy 8 form Yang-style tai chi was selected based on the guidelines of the National Comprehensive Cancer Network, the American College of Sports Medicine, and China's State Commission for Physical Culture and Sports. The intensity and duration of the tai chi intervention were scheduled, respectively, twice per week, with each session lasting about one hour, for eight weeks based on the current systematic review evidence on traditional Chinese exercise for the alleviation of cancer-related symptoms. The practise techniques of tai chi were identified from practise standards released by the State Sport General Administration of China. All the items in the tai chi protocol were determined to be content valid after the first round of rating, with all item-level CVIs at 1.00. The scale-level CVI for the tai chi protocol was also identified as excellent, at 1.00.

**Conclusion:** An evidence-based tai chi program for managing the FSDSC in BC patients was developed by following the MRC framework. The results provided a clear specification of the tai chi intervention protocol for healthcare professionals and researchers in the next phase of the study—pilot testing the tai chi intervention protocol for FSDSC management through a preliminary randomized controlled trial.

## 1. Introduction

Globally, breast cancer (BC) is recognized as the most commonly diagnosed cancer among women.<sup>1</sup> According to the American Cancer Society, the number of BC patients has increased.<sup>2</sup> Although survival rates for BC patients continue to improve, the adverse effects from

cancer and its treatments remain problematic for patients. The most frequent complaints reported by BC patients following the completion of antineoplastic treatments are fatigue, sleep problems, and depression.<sup>3</sup> These distressing symptoms often co-occur in BC patients both during and after treatment, which is commonly referred to as a symptom cluster.<sup>4,5</sup> The concept of cancer symptom cluster was first proposed by

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Dodd et al.,<sup>6</sup> who defined it as “three or more concurrent symptoms that are related to each other” (p. 468). Patients’ outcomes are exacerbated by these concurrent symptoms, such as greater distressing symptoms and decreased physical health status, more financial hardship, and poorer quality of life.<sup>7–9</sup> Additionally, these unpleasant symptoms and their associated physical and psychosocial distress can further interfere with patients’ functional status and quality of life, mainly decreased job performance and the inability to maintain social relationships.<sup>7–10</sup>

Based on current evidence, no specific medications can be recommended to relieve the fatigue-sleep disturbance-depression symptom cluster (FSDSC), and adverse events related to pharmacological approaches are still prominent, such as sleep disturbance, headache, dizziness, and seizures.<sup>11–13</sup> It is necessary to explore the role of non-pharmacological interventions as a combination intervention for symptom cluster management. Existing evidence on numerous non-pharmacological interventions, including behavioural interventions, psychosocial treatments, and complementary and alternative medicine, have demonstrated beneficial effects as adjuncts to pharmacological treatments for cancer symptom management, especially for fatigue, which is the core symptom within the FSDSC.<sup>14–18</sup> However, most of the widely applied non-pharmacological interventions such as acupuncture, relaxation, behavioural interventions, and psychosocial treatments require extensive professional skills and specific equipment, which can impose additional time, energy, and financial burdens on the study investigators, practitioners, patients, and their caregivers. Thus, preferable non-pharmacological interventions for FSDSC management should be relatively risk-free, easy to learn, and less time-consuming.

Traditional Chinese exercise (TCE) is a promising approach for relieving cancer-related symptoms given that it is relatively risk-free and low-cost nature. Tai chi, a TCE, has been commonly practised in East Asian countries for centuries and is comparatively easy to learn. Meanwhile, increasing evidence supports its positive effects on single-symptom relief in cancer patients, including fatigue, sleep disturbance, and depression.<sup>19–21</sup> Although a number of studies have indicated the benefits of tai chi in managing individual symptom of fatigue, sleep disturbance, and depression in cancer patients,<sup>22,23</sup> an evidence-based tai chi intervention protocol that is tailored to cancer symptom cluster management has not been developed yet. Notwithstanding the high incidence of the FSDSC in BC,<sup>24</sup> no tai chi interventions have been developed to manage the FSDSC. Hence, the aim of this study was to develop and validate an evidence-based tai chi protocol that can be further utilized in a clinical trial to manage the FSDSC in BC patients.

## 2. Methods

The study design was guided by the first phase of the *Medical Research Council (MRC) Framework for Developing and Evaluating Complex Interventions* (the MRC framework),<sup>25</sup> including current evidence identification of cancer symptom management (step 1), theories, practice standards, and/or guidelines identification (step 2), and content validation of the tai chi intervention protocol (step 3). This development and validation study is part of a clinical research project—a preliminary randomized controlled trial (RCT) of tai chi for the FSDSC management in BC patients—which was approved by the Human Research Ethics Committee at Charles Darwin University (H19094) in Australia.

### 2.1. Overview of the MRC framework

The MRC framework has been recommended to assist researchers in recognizing and using appropriate methods for the development and evaluation of complex interventions.<sup>26</sup> The MRC Framework is characterized by the process of development-evaluation-implementation in four different stages, including the systematic development of the intervention (phase I), exploration of the intervention’s feasibility through a pilot study (phase II), evaluation of the intervention (phase

III), and implementation of the intervention (phase IV).<sup>25</sup> The current study focused on Phase I and the study process is presented in Fig. 1.

### 2.2. Step 1: identifying current evidence on tai chi for cancer-related symptom management

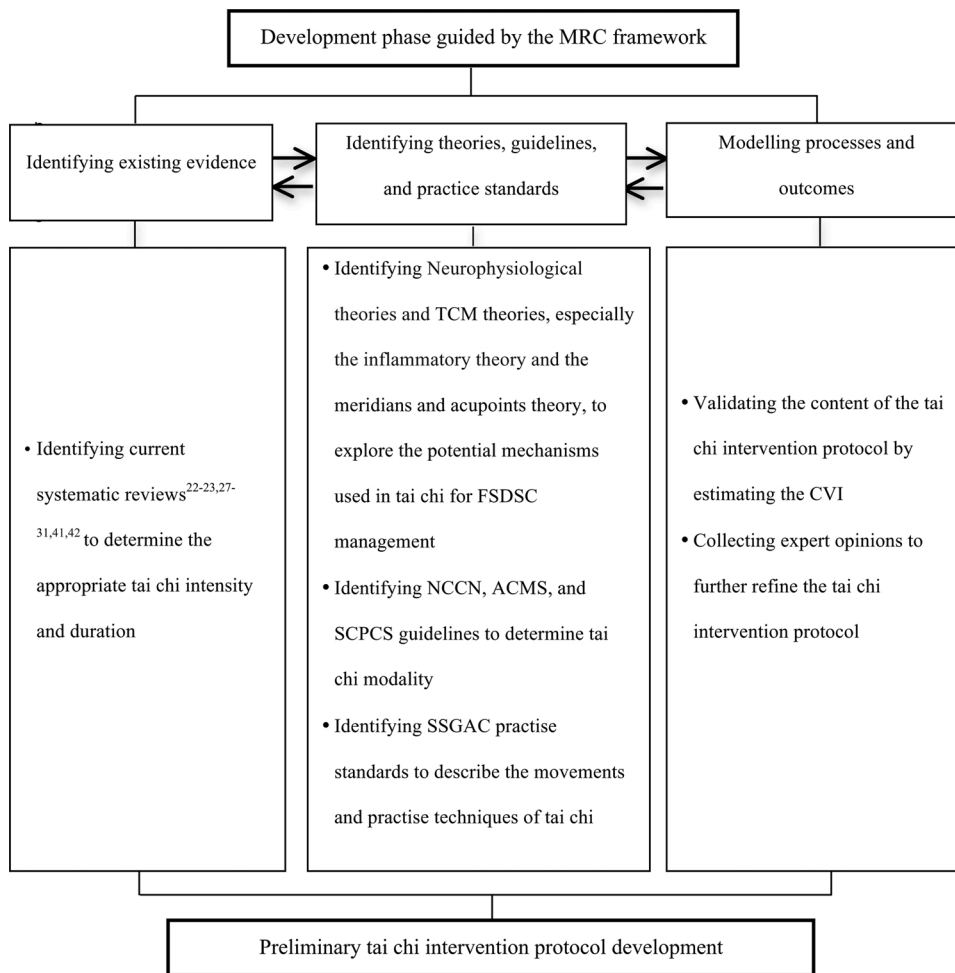
The MRC framework suggests that the optimal approach to developing interventions systematically is by applying the best available evidence and appropriate theories<sup>25</sup>; thus, the first step is to identify existing literature, including systematic reviews and clinical trials on TCE and cancer-related symptom management, to ensure that the optimal approaches are used regarding the intervention and the proposed strategic design issues.<sup>26,32</sup> In this study, an extensive literature search was performed to identify current research evidence associated with tai chi interventions for FSDSC management. These searches were conducted in PubMed, Cochrane Library, Google Scholar, Wan Fang Database, China National Knowledge Infrastructure (CNKI), and Chongqing VIP (CQVIP) to locate original studies and evidence synthesis studies (systematic/integrative/scoping reviews) published from their inception through November 2019. Search terms such as “tai ji”, “tai chi”, “fatigue”, “sleep disturbance”, “sleep disorder”, “symptom cluster”, “neoplasms”, and “cancer” were used for the database search. In general, there was no research regarding practising tai chi to relieve the FSDSC in BC patients. While several relevant systematic reviews describing the effects of TCE on single-symptom relief in cancer patients were found,<sup>23,27–29</sup> and the majority of the evidence was focused on cancer-related fatigue (CRF) as the core and primary symptom within the FSDSC. Additionally, there is no published systematic review on TCE for cancer-related sleep disturbance, the research team therefore conducted a systematic review as part of the study step 1 to identify current evidence for cancer-related sleep disturbance management.<sup>30</sup>

### 2.3. Step 2: identifying theories, practice standards, and guidelines

The MRC framework emphasizes the importance of applying related theories to the intervention design.<sup>33</sup> Moreover, relevant theories should be used to identify the specific mechanisms that will result in an effective intervention.<sup>32</sup> Prior to the development of the intervention in this study, a literature search was performed to identify appropriate theories. Neurophysiological theories and TCM theories could be used to develop a theoretical understanding of the potential mechanisms of the FSDSC in BC patients and guide the intervention selection. After selecting the intervention, a search of guidelines was conducted in the National Center for Complementary and Integrative Health, the National Comprehensive Cancer Network (NCCN), PubMed, Google, CNKI, Wan Fang Database, and CQVIP to identify the appropriate intervention modality. No guidelines were found for FSDSC management and tai chi interventions. Currently, there are several guidelines on exercise for cancer patients, particularly for patients with CRF. Finally, tai chi practise standards were searched in qigong and tai chi organizations, including the State Sport General Administration of China (SSGAC), the National Qigong Association, and the Tai Chi Association of Australia, to identify practise techniques of tai chi. Recommendations for tai chi practise standards were identified in the SSGAC, which described the forms and practise techniques of tai chi in details.<sup>34,35</sup>

### 2.4. Step 3: modelling processes and outcomes

The MRC framework recommends that optimal complex intervention should be tailored to local and intended contexts, rather than being completely standardized.<sup>25</sup> Content validation is a useful approach to gain important information about the local contexts of an intervention, which can identify the weaknesses of the intervention, lead to refinements, and improve the applicability of the intervention in clinical practice.<sup>25,36</sup> Content validation was applied in the modelling step in this study, which was comprised of experts’ opinions on and ratings of



**Fig. 1.** Process of the study design guided by the MRC framework.

Note: MRC: Medical Research Council; TCM: traditional Chinese medicine; FSDSC: fatigue-sleep disturbance-depression symptom cluster; NCCN: National Comprehensive Cancer Network; ACSM: American College of Sports Medicine; SCPCS: State Commission for Physical Culture and Sports; SSGAC: State Sport General Administration of China; CVI: content validity index.

all the intervention components to improve the tai chi intervention protocol for BC patients with the FSDSC. After the preliminary version of the tai chi intervention protocol for the FSDSC management was developed, a panel of experts specialized in TCM, TCE, and oncology was invited to assess the content validity of the intervention protocol.

#### 2.4.1. Expert panel

The experts who were invited to participate in the panel had to meet the following criteria: (1) have more than 10 years of clinical or research experience in TCE, TCM, and/or oncology; (2) be willing to participate in the content validity study; and (3) be able to effectively communicate in either Mandarin Chinese or English. The sample size of a content validity study is related to a satisfactory content validation index (CVI) that is applied to assess the content validity of each item of the intervention protocol.<sup>37</sup> In this study, the CVI was adopted to identify the required sample size and level of consensus of the expert panel. As recommended by Lynn,<sup>38</sup> six experts are needed to reach a satisfactory CVI of 0.83 for each item on the content assessment form.

#### 2.4.2. Content validity study procedure

A formal invitation was delivered via telephone or email to solicit eligible experts to participate in the study.<sup>39</sup> Once the experts accepted the invitation, a cover letter and the content validity assessment form were emailed to them. The cover letter consists of the purpose of the study, the selection criteria of the expert panel, detailed information on the assessment form (the tai chi intervention protocol), and instructions for rating each item.<sup>39</sup> The assessment form includes five items associated with the tai chi intervention protocol, namely, the selected tai chi

modality, the scheduled forms of tai chi, the techniques for tai chi practise, the intensity and frequency of the sessions, and the total duration of the tai chi intervention. Lynn suggested rating these items using a 4-point Likert scale (1 = “totally inappropriate”, 2 = “inappropriate”, 3 = “appropriate”, and 4 = “very appropriate”).<sup>38</sup> If the experts scored any of the items below a score of “3” (“inappropriate” or “totally inappropriate”), they were asked to provide comments or suggestions with relevant evidence and references to help the study team further refine the intervention protocol.

#### 2.4.3. Data analysis

The item-level CVI (I-CVI) and the scale-level CVI (S-CVI) were applied to evaluate the content validity of each of the items and the whole tai chi intervention protocol, respectively.<sup>38,39</sup> The I-CVI was calculated by counting the number of experts who rated the item as “appropriate” (a score of 3) or “very appropriate” (a score of 4) and dividing that number by the total number of experts,<sup>39</sup> while the S-CVI was evaluated by calculating the average I-CVI across the items.<sup>39</sup> A CVI of 0.80 or higher and that of 0.83 are considered satisfactory values for the S-CVI and I-CVI, respectively.<sup>40</sup> Any item with a low CVI would be revised based on the experts’ comments or suggestions until the CVI reached the predefined satisfactory value.

### 3. Results

#### 3.1. Current evidence to identify appropriate tai chi intervention intensity and duration

Nine relevant systematic reviews stated that TCE has statistically significant effects on the cancer-related symptoms of fatigue, sleep disturbance, and depression,<sup>22,23,27–31,41,42</sup> among which, four demonstrated that tai chi has significantly favourable effects on CRF—the core symptom within the FSDSC.<sup>27,29,41,42</sup> These systematic reviews provided evidence to support the finding that tai chi may have beneficial effects on cancer-related FSDSC management. However, the frequency and duration of the tai chi programs varied significantly among the included studies of two systematic reviews.<sup>23,27</sup> As for duration, clinical research has well documented the significant relief of cancer-related symptoms, particularly CRF, achieved by an eight-week tai chi intervention duration.<sup>27</sup> Two systematic reviews demonstrated that the most common frequency of tai chi intervention was twice per week, with each session lasting about one hour.<sup>22,27</sup> Based on the aforementioned systematic review evidence, the appropriate tai chi duration in this study was therefore scheduled for eight weeks, twice per week, with each session lasting about one hour.

#### 3.2. Theories, practise standards, and guidelines for tai chi intervention modality and practise techniques

Neurophysiological theories and TCM theories, especially the inflammatory theory and the meridians and acupoint stimulation theory, were utilized to clarify the potential mechanisms of using tai chi for FSDSC management. Studies have highlighted the important role of cytokines in the development of the FSDSC<sup>43,44</sup> It is commonly believed that the FSDSC results from an inflammatory reaction by the hypothalamic-pituitary-adrenal (HPA) axis and the central nervous system (CNS).<sup>45,46</sup> Evidence is mounting in support of the potential mechanism of tai chi in inflammatory biology, focusing on neuroendocrine-immune mechanisms.<sup>47</sup> Tai chi as one of the most commonly practised mind-body exercise may affect neural regions which play a key role in regulation of downstream stress response pathways (i.e., the HPA axis and the autonomic nervous system [ANS]), and may affect the pro-inflammatory cytokines generation in turn through effects of their ligands on glucocorticoid, cholinergic and adrenergic receptors in immune cells.<sup>47</sup> Furthermore, TCM theories have demonstrated that deficiencies of *qi* and blood, a condition reflecting Yin (inactivity) and Yang (activity) imbalance, are the main pathogenesis of fatigue, sleep disturbance, and depression in cancer patients.<sup>48,49</sup> Tai chi involves a series of physical movements, breathing techniques, and meditation and is based on the theoretical principles of TCM.<sup>50</sup> According to the meridians and acupoints theory, tai chi movements promote *qi* to circulate freely throughout the body via meridians and channels, which are regarded as the energy pathways connecting *zang-fu* organs, serving different parts of the body.<sup>51</sup> The acupoints along the meridians are applied in tai chi as foci to regulate the circulation of *qi* and promote body balanced state through Yin and Yang. Yin and Yang include a dynamical feature of interplay and complementary that require to be “in balance” for optimal functioning. The movement and meditation in tai chi are believed to increase the flow of *qi*, which involves regulating Yin and Yang via redirection of *qi* from excessive accumulation to regions of *qi* deficiency, thus recovering the body to a yin and yang-balance status.<sup>51</sup> All of which clarified an underlying mechanism of tai chi, from the perspectives of the meridians and acupoints theory, for managing the FSDSC in cancer patients.

In practice, the identification of an appropriate modality for a tai chi intervention must consider practical concerns, including the participants' health conditions and the treated disease.<sup>52</sup> According to the NCCN guidelines and the American College of Sports Medicine (ACSM), cancer patients, particularly those experiencing CRF, require physical

activity that is easy to learn and uses less energy consumption to practise.<sup>53–55</sup> These recommendations indicated that an intense intervention with a long duration and frequent TCE should be avoided given that patients have already presented fatigue upon enrolment, which were further adopted to support the identified dosage of tai chi intervention in stage 1 with moderate intensity and duration to fit the physical conditions of cancer patients with CRF. China's State Commission for Physical Culture and Sports (SCPCS) recommends easy 8 form Yang-style tai chi, which greatly reduces the number of movements to be learned.<sup>34</sup> Therefore, our team chose easy 8 form Yang-style tai chi for FSDSC management, since it is simple and repetitive, instead of a complexity and lengthy sequence of tai chi movements that consume participants' much more energy and take much longer to learn.<sup>56</sup> Table 1 provides an overview of the tai chi protocol content and Table 2 presents the forms of the easy 8 form Yang-style tai chi intervention, which were proposed based on the practice standards released by the SSGAC.<sup>34,35</sup>

#### 3.3. Content validity assessment

Invitations to participate in the content validation were sent to nine experts in China, Australia and the US; seven experts responded within five working days, of which, six experts accepted the invitation. Six experts with extensive practice and research experience in the fields of TCE, TCM, and oncology participated in this study to determine the content validity of the proposed intervention protocol. The experts' response rates to each item was 100 %. Table 3 shows the characteristics of the expert panel.

Since the I-CVI and the S-CVI in this study both achieved adequate consensus after completing the first round of panel rating, it was unnecessary to include them in another round for reassessment. The content validity results are presented in Table 4. All the items of the tai chi protocol were determined to be content valid, with all I-CVIs at 1.00. The S-CVI for the whole tai chi protocol was also identified as excellent, at 1.00. Although the tai chi protocol was graded by all the experts with excellent agreement, some suggestions were provided. Three experts

**Table 1**  
Contents of the tai chi intervention protocol for FSDSC management.

Process	Contents	Justification
Selection of appropriate tai chi method	Easy 8 form Yang-style tai chi	<ul style="list-style-type: none"> <li>■The most frequently applied tai chi style in practice<sup>52</sup></li> <li>■Consumes much less energy and takes a shorter time to learn for participants<sup>54,56</sup></li> </ul>
Duration of the tai chi program	Eight weeks	<ul style="list-style-type: none"> <li>■The most common duration is between eight and 12 weeks<sup>23</sup></li> <li>■Cancer patients with CRF require physical activity that is easy to learn and uses less energy consumption to practise<sup>53–55</sup></li> <li>■An eight-week intervention duration can benefit CRF<sup>27</sup></li> <li>■Significant relief of cancer-related symptoms was achieved with an eight-week tai chi intervention duration<sup>20,57,58</sup></li> </ul>
Intensity (frequency) and techniques of tai chi exercise	Twice per week, with each session lasting about one hour	<ul style="list-style-type: none"> <li>■An intense intervention with a long duration and frequent exercise should be avoided given that patients have already presented fatigue upon enrolment<sup>53,54,59</sup></li> <li>■Current systematic review evidence indicated that the most common tai chi intervention intensity was twice per week, with each session lasting about one hour<sup>22,27</sup></li> </ul>

**Note:** NCCN: National Comprehensive Cancer Network; ACSM: American College of Sports Medicine; TCE: traditional Chinese exercise.

**Table 2**  
The easy 8 form Yang-style tai chi.

	Forms of the Easy 8 Form Yang-style Tai Chi
Form 1	Commencing Form, <i>Qishi</i>
Form 2	Repulse Monkey, <i>Juangongshi</i>
Form 3	Grasp Peacock's Tail (Ward off, Rollback, Press, Push), <i>Lanquewei</i>
Form 4	Wave Hands Like Clouds, <i>Yunshou</i>
Form 5	Fair Lady Works at Shuttles (Left and Right), <i>Zuoyouchuansuo</i>
Form 6	Golden Cock Stands on One Leg, <i>Jinjiduli</i>
Form 7	Brush Knees and Twist Steps, <i>Louxiaobu</i>
Form 8	Closing Form, <i>Shoushi</i>

Note: Based on Committee of Chinese Sports College Textbook,<sup>34</sup>; also cited in Li, Fisher, Harmer, & Shirai,<sup>35</sup>.

**Table 3**  
Characteristics of the six invited experts.

Characteristics of the Experts (N = 6)	Number (%)
<b>Types of working institutions</b>	
University	4 (66.7 %)
Hospital	2 (33.3 %)
<b>Age</b>	
40 - 50 years old	2 (33.3 %)
50 - 60 years old	3 (50.0 %)
<60 years old	1 (16.7 %)
<b>Highest academic degree</b>	
Doctorate degree	3 (50.0 %)
Master's degree	2 (33.3 %)
Bachelor's degree	1 (16.7 %)
<b>Academic/professional rank</b>	
Full professor and chief physician	1 (16.7 %)
Full professor	3 (50.0 %)
Chief physician	1 (16.7 %)
Associate professor	1 (16.7 %)
<b>Years of working experience</b>	
16–20 years	2 (33.3 %)
<20 years	4 (66.7 %)
<b>Practice and/or research experience with traditional Chinese exercise</b>	
Yes	6 (100 %)
No	0 (0%)
<b>Practice and/or research experience with cancer care</b>	
Yes	6 (100 %)
No	0 (0%)

suggested that the frequency of the tai chi intervention should be increased from twice per week to three times per week. Two experts suggested increasing the total duration of the tai chi intervention from eight weeks to 12 weeks.

#### 4. Discussion

This study presented a systematic and structured development and validation process of an evidence-based tai chi intervention protocol that aims to improve FSDSC management in BC patients. The development process was guided by the MRC framework, and the intervention protocol was developed using an evidence-based approach that included the following: the best available research evidence; neurophysiological theories and TCM theories; the NCCN, ACSM, and SCPCS guidelines; and practise standards released by the SSGAC. To our knowledge, this is the first tai chi intervention directed at the management of the FSDSC in BC patients that was developed by following the MRC framework. In this study, a detailed description of the development and validation process of the tai chi intervention protocol was provided, which is absent in most of studies on complex interventions in clinical trials.<sup>26</sup>

The MRC framework was utilized as a theoretical guide for the development and validation of the tai chi intervention protocol. Generally, the MRC framework is a useful tool for guiding the development, evaluation, and reshaping of a complex intervention. The

**Table 4**  
Results of the content validity assessment of the tai chi intervention protocol.

Item	Description of the Item	Content Validity Assessment (total number of experts = 6)			
		Number of Experts Rating "Very appropriate" (4)	Number of Experts Rating "Appropriate" (3)	Number of Experts Rating Content Valid (3 or 4)	CVI
Tai Chi Intervention Protocol					
1	Selected tai chi modality	5	1	6	[Item-level] 1.00
2	Scheduled forms of tai chi	5	1	6	[Item-level] 1.00
3	Techniques for tai chi practise	4	2	6	[Item-level] 1.00
4	Duration and frequency of tai chi intervention sessions	2	4	6	[Item-level] 1.00
5	Total duration of tai chi intervention	3	3	6	[Item-level] 1.00
S-CVI for the whole tai chi protocol					[Scale-level] 1.00

Note: S-CVI: scale content validity index.

utilization of the MRC framework removes the risk of assessing unfeasible interventions and utilizing designs that do not fit, as well as increases the chance of developing a successful intervention and assessment.<sup>60</sup> In this way, research waste is reduced and the likelihood of success is enhanced.<sup>36</sup> This study stated how the framework might be utilized to develop a tai chi intervention for FSDSC management in BC patients. Based on existing research, an evidence-based tai chi intervention following the elements of the MRC development phase was proposed to improve the future intervention design. Including the elements of the systematic identification of research evidence, identification of theories and practice standards/guidelines, and modelling processes through content validity assessment will result in a tai chi intervention protocol that provides researchers a better chance of developing an intervention that is evidence-based, fits its context, and is feasible and ready for further piloting and trialling in the future.

The main finding of the content validation of the tai chi intervention protocol was that all five items exhibited excellent agreement among the expert panel members. The proposed evidence-based tai chi protocol achieved excellent content validity that was applicable to the FSDSC management in BC patients. Although satisfactory agreement regarding the tai chi protocol was generally gained from the expert panel, three experts suggested changing the tai chi intervention from twice per week to three times per week. Additionally, two experts suggested changing the total duration of the tai chi intervention from eight weeks to 12 weeks. Reviewing current research evidence<sup>23,27</sup> and discussing among the senior researchers in the study team who have clinical and research expertise in TCE, TCM, and cancer symptom management, no further modification was made to the frequency and duration of the tai chi intervention. Theoretically, a longer intervention duration with more frequent intensity of tai chi may generally contribute to a better symptom outcome; however, the duration and the intensity of tai chi should also consider the patients' health conditions<sup>52,61</sup> given that our targeted study population in the future RCT will be BC patients who have been experiencing persistent fatigue, which is the core symptom within the FSDSC. In addition, it has been demonstrated that fatigue and weakness have often been found to be associated with a low adherence rate to a

longer duration of and more frequent exercise, which can negatively affect the credibility of study findings.<sup>62</sup> In other words, an intense tai chi intervention with a long duration and frequency should be avoided given that patients have already presented fatigue upon enrolment.<sup>59</sup> Furthermore, clinical research has well documented the significant relief of cancer-related symptoms, particularly CRF, can be achieved by utilizing an eight-week tai chi intervention duration.<sup>20,57,58</sup>

The major strength of the study is that it followed the MRC framework by utilizing systematic methods to identify the best available research evidence, appropriate theories, and relevant guidelines and practise standards to develop a research-informed and evidence-based healthcare intervention. In detail, the tai chi intervention was properly defined based on neurophysiological theories and TCM theories, existing systematic reviews, the NCCN, ACSM, and CSPCS guidelines, and the SSGAC practise standards. Furthermore, experts in TCE, TCM, and oncology were involved in the content validation of the intervention. Previous studies have demonstrated that expert panels provide valid representations of the views of the fields that they represent.<sup>63</sup> Moreover, involving experts and clinicians in the process of confirming the content validity of an intervention will indicate the intervention that has clinical integrity and is tend to be more acceptable to those implementing it.<sup>64</sup>

This study also has some limitations. The content validation did not include interviews with the target patients. However, it was not feasible to interview the BC patients before practising the tai chi given that they may not have the experience of practising tai chi before and might not be able to do a proper assessment of the tai chi intervention protocol. Nevertheless, the intervention protocol development was only the phase one study of a clinical research project. Patients' view towards the intervention and the intervention feasibility and clinical utility will be explored in a pilot RCT and semi-structured interviews as the phase two study to further evaluate the feasibility and clinical utility of the tai chi protocol among BC patients. Additionally, the use of a panel of experts only may be another limitation. Although the experts were identified based on their knowledge of and experience with tai chi and they provided a broad range of perspectives, each expert was only able to draw on their own experiences, and a limited understanding of the symptom cluster could be a potential limitation given that this topic has not been frequently researched in clinical settings yet, particularly in complementary medicine-related health intervention studies.

The current study is the study phase one of a multiple-phase research project that aims to develop and evaluate an evidence-based tai chi intervention for managing the FSDSC in BC patients. Following the completion of the study phase one, a pilot RCT will be conducted afterwards to preliminarily explore the effects of the tai chi intervention on the FSDSC among BC patients. The standardized evidence-based tai chi intervention protocol utilized in our research project can be further modified in clinical practice to develop personalized intervention that is tailored to the health conditions of individual cancer patient.

## 5. Conclusion

This study developed an evidence-based tai chi program for the FSDSC management in BC patients based on the first phase of the MRC framework, which included a systematic approach of "identifying existing evidence for cancer-related symptom management", "identifying relevant theories, practice standards and guidelines for tai chi", and "validating the content of the tai chi intervention protocol". The results provided a clear specification of the tai chi intervention protocol for healthcare professionals and researchers in the next phase of the study—pilot testing the tai chi intervention protocol for FSDSC management through a preliminary clinical trial.

## Authors' contributions

Yao LQ designed the study, conducted data analysis and drafted and

revised the manuscript. Tan JY contributed to the study conception and design, and revised the manuscript; Turner C contributed to the study design and manuscript revision; Wang T contributed to data collection and manuscript drafting and revision. All authors approved the final version of the article, including the authorship.

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## Declaration of Competing Interest

All authors declare that they have no competing interests.

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