REVIEW

Analysis of Outcome Indicators of Cancer-Related Fatigue Treated with Chinese Herbal Compounding

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Objective: In the direction of evaluating the current status of outcome indicators and control group selection in randomized controlled studies of Chinese herbal compounding (such as Sini plus Renshen Decoction, Jianpifuzhengfang, Bufei Jianzhong Decoction, etc) for cancer-caused fatigue and to provide a reference for clinical studies of Chinese herbal compounding for cancer-caused fatigue.
Methods: Randomized controlled studies of Chinese herbal medicine for cancer-caused fatigue in the midst of 2012 and 2022 were searched in CNKI, PubMed, and EMBASE databases on the China Knowledge Network, and the literature was screened using NoteExpress. Two researchers independently conducted the literature review, and then the studies that met the criteria were grouped and analyzed adopting qualitative analysis of outcome indicators and control groups.
Results: A total of 70 randomized controlled studies that met the requirements were included, and after doing statistical analysis, it can draw to the conclusion that the risk of bias in the included studies was high; at the same time, the TCM evidence score scale, objective indicators, and safety indicators were underutilized; additionally, there were no uniform standards for the fatigue scale, and the selection of control groups lacked balance and consistency.
Conclusion: The outcome indicators of TCM compound treatment of cancer-caused fatigue should be on the basis of the principle of "diagnosis and treatment" in TCM, the proportion of objective indicators should be exaggerated, as well as the interventions in the control group should be unified.
Keywords: Chinese herbal compound, cancer-related fatigue, randomized controlled trial, outcome indicators, control group

Introduction

Cancer-related fatigue (CRF) is defined as a distressing, persistent, subjective feeling of somatic, emotional, or cognitive fatigue or exhaustion that is characterized by rapid onset, duration, severity, and unpredictability.[1] CRF is associated with the tumor itself and treatment, but its specific pathogenesis is still unclear. In recent years, the incidence of cancer-caused fatigue has shown a significant increase, and the current clinical treatment is mainly based on non-pharmacological interventions, supplemented by pharmacological treatments.[2] Chinese medicine compounding is the leading therapeutic tool in traditional Chinese medicine (TCM), and it has achieved a better efficacy in the treatment of CRF.[3] TCM has been applied in the treatment of more than 70% of cancer patients in China. Data have shown that TCM can significantly enhance the sensitivity to chemotherapeutic drugs, enhance tumor-suppressing effects, and significantly improve cancer-related fatigue, bone marrow suppression, and other adverse reactions.[4] Although there exist more clinical studies on the treatment of CRF with herbal compounding, the evaluation of efficacy and outcome indicators alter, and there is no fixed standard for the selection of control groups. Hence, in clinical studies, the selection of outcome indicators and control groups are more critical aspects, and it has been proved that the outcome indicators and control groups adopted in similar clinical studies differed greatly from each other.[5] Therefore, we qualitatively analyzed the current status of the selection of outcome indicators and control groups in randomized controlled studies approaching the treatment of cancer-caused

fatigue with Chinese herbal compound prescriptions over the past few decades to provide more accurate criteria for the assessment of the efficacy of Chinese herbal compound prescriptions in the treatment of cancer-caused fatigue, and to provide an over and above accurate assessment of the effectiveness of Chinese herbal compound prescriptions in the treatment of cancer-caused fatigue. Baseline indicators and control group selection from the randomized controlled study of the Chinese herbal formulation for the treatment of cancer fatigue are provided as references.

Materials and Methods

The data of this study were obtained from the randomized controlled trials (RCTs) papers on Chinese herbal compounds for cancer-caused fatigue in CNKI, PubMed, and EMBASE databases, searched from 2012 to 2022, and the language types included limited in Chinese and English.

Inclusion criteria: (1) The subjects in this study were cancer fatigue patients (race, nationality, cancer type); (2) The study criteria were in accordance with the RCT trial design; (3) The interventions in the study were simple herbal compounds for the treatment group and conventional treatment, chemotherapy, and placebo for the control group; and (4) Outcome indicators were multi-fatigue scales, TCM evidentiary scales, quality of life scales, mood scales, biochemical indicators, safety indicators, etc.

Exclusion criteria: (1) Duplicate literature; (2) Observation group was a combined Chinese herbal medicine protocol, single herbal medicine, or Chinese medicine cream; (3) No complete observation index or single-arm pilot study; (4) Relevant review type, observation type, and incomplete information articles; and (5) Non-Chinese and English literature.

Literature Research Strategy

The search databases included CNKI, PubMed, and EMBASE, and the search dates were between 2012 and 2022. The search was conducted by a combination of subject terms and free words, and the Chinese search terms included: Chinese medicine, cancer-caused fatigue, cancer fatigue, cancer, tumor, fatigue, fatigue, randomized, and control. English search terms included: Chinese medicine, cancer-related fatigue, cancer, fatigue, chance, clinic, etc. Use "or (or)", "and (and)" to connect the disease names of cancer-caused fatigue; use the search in results with "or (or)", "and (and)" to associate with the name of the Chinese herbal compound; use "or (or)" and "and (and)" to connect random and control, and again search in the results. The research methods in Chinese and English were similar, and the specific research strategy was as follows, taking the CNKI research as an example.

CNKI: SU=("Chinese medicine" + "Chinese medicine compound") AND AB=("random" + "control") AND SU= ("fatigue" + "fatigue" + "tiredness" + "exertion" + "fatigue") AND SU=("cancer" + "tumor")

Literature Processing

The titles and abstracts of all literature were independently assessed and screened by two investigators applying NoteExpress software in accordance with the same inclusion and exclusion criteria, and if one of the investigators thought that the title and abstract of a particular article met the inclusion requirements, the full text was read by both of them to make a decision on whether to include it, and any disagreement during the screening process should be arrived at conclusion by discussion or a third party. The main information extracted included the first author of the literature, the year of publication, interventions (observation and monitoring groups), outcome assessment indicators, and risk of bias assessment.

Evaluation of the Risk of Study Bias

The risk of bias in the included studies was assessed by two reviewers using the risk of a bias assessment tool for randomized controlled studies in the Cochrane Handbook.

Statistical Analysis

Qualitative descriptive analysis was used to analyze the classification and frequency of the interventions in the control group in the study of herbal compounding for cancer-caused fatigue; to analyze the classification and frequency of outcome indicators, and to analyze the types of fatigue scales selected in the study.

Results

Literature Screening Results

Seventy randomized controlled studies were ultimately included, and the document selection process is presented in Figure 1.

General Characteristics of the Included Studies

Out of 70 documents included, 65 were in Chinese, and 5 were in English. Among them, 42 were journal papers and 28 were dissertations, published between 2012 and 2022, and the literature in the last 3 years accounted for over 50% of the total literature, indicating that the treatment of cancer-caused fatigue with herbal compounding has received with acceleration attention in recent years. The interventions in the treatment group were limited to simple herbal compounding excluding combined application, and the control group mostly adopted western symptomatic treatment with chemotherapy, as detailed in Table 1.

Results of Risk of Bias Evaluation

The findings of the bias risk assessment of the included studies are presented in Table 2.

Classification of the Control Group

The interventions in the 70 RCT treatment groups included in this research were limited to herbal compounding alone, and the interventions in the control group included studies with symptomatic treatment at most as the control
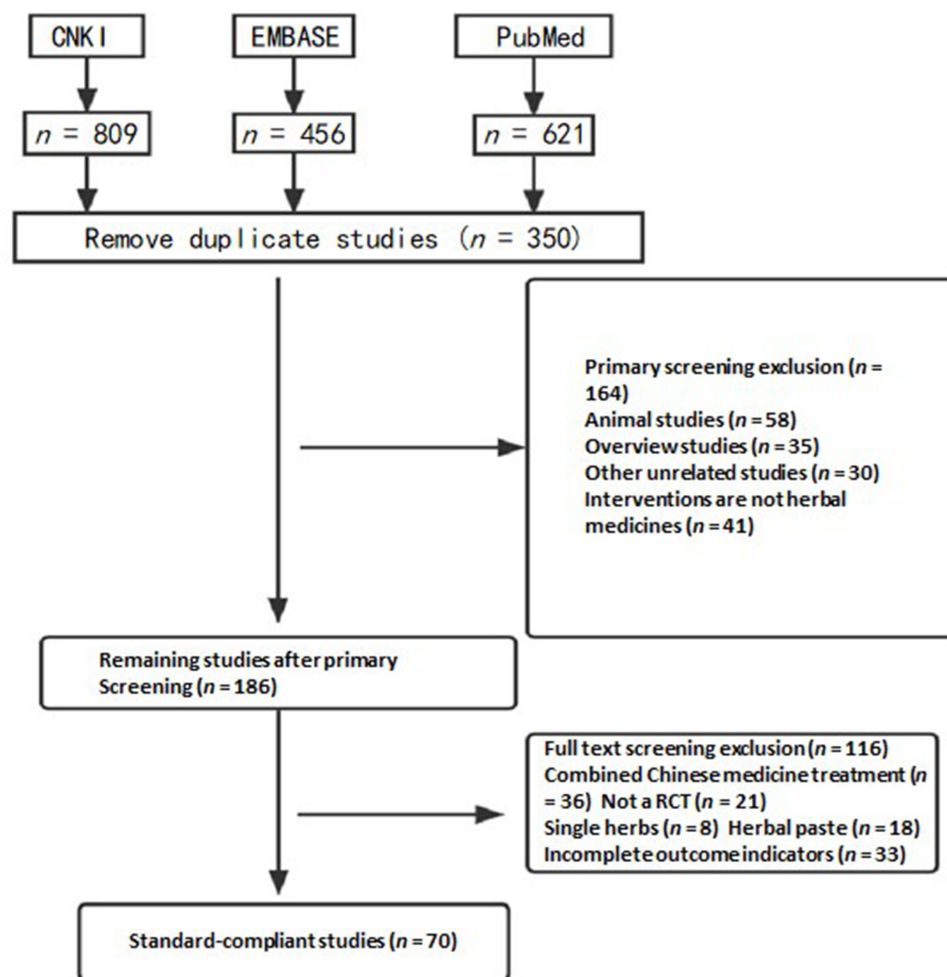

Figure 1 Study search flow chart.

Table 1 Characteristics of Included Studies

Ref.	Number (T/C)	Intervention Measures		Treatment Cycle	Outcome Indicators
		T	**C**		
Cao et al,[6] 2022	34/34	Symptomatic treatment + sini plus renshen decoction	Symptomatic treatment	21 d	1, 2, 3, 5
Gao et al,[7] 2022	30/30	Symptomatic treatment + xiaqi decoction	Symptomatic treatment	21 d	1, 2, 3, 4, 6
Zuo et al, 2022[8]	29/30	Symptomatic treatment + jianpifuzhengfang	Symptomatic treatment + guipiwan	56 d	1, 2, 5
Dao, 2021[9]	36/36	Self-made bufei jianzhong decoction	Buzhongyiqiwan	14 d	1, 2, 3, 6
Gao et al, 2021[10]	34/34	Symptomatic treatment + buzhongyiqiguben decoction	Symptomatic treatment	30 d	1, 2, 3, 4
Du et al, 2021[11]	30/30	Chemotherapy + feifukangfang	Chemotherapy	84 d	1, 2, 4, 6
Zhao et al, 2021[12]	50/50	Chemotherapy + feiliu xiaoji fang	Chemotherapy	84 d	1, 2, 3
Xu, 2021[13]	26/26	Chemotherapy + fuzheng jiedu decoction	Chemotherapy + jiedu decoction	56 d	1, 2, 3, 4, 5
Huang, 2021[14]	35/35	Symptomatic treatment + guiluerxianjiao tang	Symptomatic treatment	28 d	1, 2, 3, 5, 6
Zheng et al, 2021[15]	120/120	Modafinil + huoxue fuxing decoction	Modafinil	21 d	1, 3, 5, 6
Du, 2021[16]	25/25	Symptomatic treatment + jianpi bushen fang	Symptomatic treatment	28 d	1, 2, 3
Xin, 2021[17]	40/40	Symptomatic treatment + jianpixiaoji tang	Symptomatic treatment	30 d	1, 3
Li et al, 2021[18]	62/61	Symptomatic treatment + jianpiyiqi tang	Symptomatic treatment	28 d	1, 2, 3, 5
Guo, 2021[19]	40/40	Non drug treatment + neibu huangqi decoction	Non drug treatment	28 d	1, 2, 3, 5, 6
Cao, 2021[20]	30/30	Symptomatic treatment + qiyuliujun tang	Symptomatic treatment	28 d	1, 2, 3, 5, 6
Gao, 2021[21]	30/30	Symptomatic treatment + shengyangyiweisanxian tang	Symptomatic treatment	14 d	1, 2, 3, 4, 6
Cao et al, 2021[22]	30/30	Symptomatic treatment + sini decoction	Symptomatic treatment	56 d	1, 2, 5
Xu, 2021[23]	32/32	Chemotherapy + weining fang	Chemotherapy	48 d	1, 2, 3, 5, 6
Chen et al, 2021[24]	40/40	Symptomatic treatment + yangzhengjiefa tang	Symptomatic treatment	28 d	1, 2, 6
Hu et al, 2021[25]	60/60	Buzhongyiqi tang	Placebo	21 d	1, 4, 5
Lee et al, 2021[26]	24/24	Sini tang	Placebo	21 d	1, 4
Li et al, 2021[27]	55/55	Fuzhengjiedu fang	Zhenqi fuzheng capsule	28 d	1, 5
Jiang, 2020[28]	45/45	Chemotherapy + yiqiyangyin fang	Chemotherapy	56 d	1, 4, 5
Qin, 2020[29]	30/30	Symptomatic treatment + bazhen decoction	Symptomatic treatment	30 d	1, 2, 3, 4, 5, 6
Zhang et al, 2020[30]	32/32	Symptomatic treatment + shenling baizhu powder	Symptomatic treatment	30 d	1, 2
Zhang, 2020[31]	30/30	Symptomatic treatment + shengqidihuang tang	Symptomatic treatment	14 d	1, 2, 3, 5
Jiang et al, 2020[32]	30/30	Symptomatic treatment + chaihu pingwei powder	Symptomatic treatment	7 d	1, 3, 4, 5, 6
Sun, 2020[33]	30/30	Bufeihuaji tang + aidi injection	Aidi injection	34 d	1, 2
Wang, 2020[34]	35/35	Symptomatic treatment + tiaogan yangxue fang	Symptomatic treatment	28 d	1, 2, 3, 5, 6

(*Continued*)

Table 1 (Continued).

Ref.	Number (T/C)	Intervention Measures		Treatment Cycle	Outcome Indicators
		T	**C**		
Lin, 2020[35]	30/30	Symptomatic treatment + fuzhengkangai tang	Symptomatic treatment	30 d	1, 2, 3, 4, 5, 6
Gan et al, 2020[36]	48/48	Symptomatic treatment + fuzhengxiaoliu tang	Symptomatic treatment	56 d	1, 4, 5
Zhao, 2020[37]	38/37	Symptomatic treatment + fuzhengyangrong fang	Symptomatic treatment	56 d	1, 2, 3, 4, 5, 6
Liu, 2020[38]	30/30	Symptomatic treatment + gancaoxiexin tang	Symptomatic treatment	56 d	1, 2, 3, 4, 6
Dai, 2020[39]	30/30	Chemotherapy + jianpiyangwei fang	Chemotherapy	14 d	1, 2, 3, 4, 5, 6
Ning, 2020[40]	40/40	Symptomatic treatment + buzhongyiqi tang	Symptomatic treatment	21 d	1, 2, 3, 4 6
Xu, 2020[41]	40/38	Chemotherapy + buyixusun fang	Chemotherapy	42 d	1, 4, 5
He et al, 2020[42]	34/34	Symptomatic treatment + jianpibushen fang	Symptomatic treatment	14 d	1, 3, 6
Xie et al, 2020[43]	46/46	Chemotherapy + buzhongyiqi tang	Chemotherapy	42 d	1, 4, 6
Han, 2020[44]	36/36	Symptomatic treatment + shuyuwan	Symptomatic treatment	21 d	1, 2, 3, 6
Yich et al, 2020[45]	42/41	Renshenyangrong tang	Huangqi	42 d	4
Xiao et al, 2020[46]	30/30	Jianpishengsui fang	Placebo	42 d	1, 2, 4
Liu et al, 2019[47]	66/66	Feiyanning fang + kangliuzengxiao fang	Kangliuzengxiao fang	90 d	1, 5
Lu et al, 2019[48]	45/45	Symptomatic treatment + compound shougong powder	Symptomatic treatment + compound cantharidin capsule	90 d	1, 5
Bao, 2019[49]	25/25	Symptomatic treatment + zhenqifuzheng fang	Symptomatic treatment	56 d	1, 2, 4
Zhan et al, 2019[50]	42/38	Chemotherapy + jianpishengsui fang	Chemotherapy	21 d	1, 5
Li, 2019[51]	44/43	Chemotherapy+jianpiyishenbuqi tang	Chemotherapy + buzhongyiqi mixture	90 d	1, 5, 6
Tao, 2019[52]	30/30	Symptomatic treatment + jianpiyishenyangxue fang	Symptomatic treatment	42 d	1, 2, 3, 5, 6
Cai, 2019[53]	41/41	Chemotherapy + jusan decoction	Chemotherapy	84 d	1, 5, 6
Li, 2019[54]	30/30	Symptomatic treatment + shashenmaidong tang	Symptomatic treatment	14 d	1, 2, 3
Han et al, 2019[55]	30/30	Symptomatic treatment + shiquandabu tang	Symptomatic treatment	14 d	1, 2, 3, 5
He, 2019[56]	25/25	Chemotherapy + wenbupishen fang	Chemotherapy	42 d	1, 2, 3, 5, 6
Lin et al, 2018[57]	32/32	Symptomatic treatment + buzhongyiqi tang	Symptomatic treatment	14 d	1, 2, 3
Shi et al, 2018[58]	55/55	Chemotherapy + changyi decoction	Chemotherapy	84 d	1, 4, 5
Ning et al, 2018[59]	68/68	Chemotherapy + fuzhengsanjiejiedu tang	Chemotherapy	168 d	1, 3, 4, 5
Liu, 2018[60]	35/35	Health education + guipi decoction	Health education	56 d	1, 2, 4, 6
Liu, 2018[62]	32/32	Symptomatic treatment + guipi decoction	Symptomatic treatment	21 d	1, 3
Li et al, 2018[63]	42/42	Symptomatic treatment + shiquandabu tang	Symptomatic treatment	14 d	1, 4, 5
Jia et al, 2018[64]	54/54	Bozhi glycopeptide + jianpiyishenjiedu tang	Bozhi glycopeptide	84 d	1, 5
Jee et al, 2018[65]	15/15	Guipi decoction	Placebo	14 d	1, 4

(*Continued*)

Table 1 (Continued).

Ref.	Number (T/C)	Intervention Measures		Treatment Cycle	Outcome Indicators
		T	**C**		
Zhang et al, 2017[66]	80/80	Symptomatic treatment + bazhen tang	Symptomatic treatment + buzhongyiqi mixture	90 d	1, 2, 4, 5
Nian, 2017[67]	19/19	Symptomatic treatment + shuganjianpi granule	Symptomatic treatment	56 d	1, 2, 3, 4, 5, 6
Li et al, 2016[68]	45/45	Chemotherapy + jianpixiaoji tang	Chemotherapy	40 d	1, 3
Liu et al, 2016[69]	41/41	Chemotherapy + buzhongyiqi tang	Chemotherapy	21 d	1, 6
Li 2016[70]	75/75	Symptomatic treatment + jianpiyishen fang	Symptomatic treatment	63 d	1, 2, 3, 5, 6
Xu, 2016[71]	30/30	Symptomatic treatment + yiqijianpibushen fang	Symptomatic treatment	28 d	1, 2, 4
Zhao, 2016[72]	33/33	Symptomatic treatment + jinshuifuyuan fang	Symptomatic treatment	14 d	1, 2, 3, 6
Li, 2015[73]	30/30	Chemotherapy + jianpiyishen fang	Chemotherapy	42 d	1, 2, 3
Ji, 2015[74]	30/30	Symptomatic treatment + shiquandabu tang	Symptomatic treatment	14 d	1, 3, 4, 5, 6
Ma et al, 2015[75]	23/22	Chemotherapy + xingjian tang	Chemotherapy	60 d	1, 2, 3
Tan et al, 2012[76]	32/31	Chemotherapy + jianpiyishenhuatan fang	Chemotherapy	14 d	1

Notes: T, treatment; C, control; 1, fatigue scale; 2, traditional Chinese medical syndrome scale; 3, quality of life scale; 4, other scales; 5, biochemical indicators; 6, safety indicators.

Table 2 Results of Risk of Bias Evaluation of Included Studies [Articles (%)]

Projects	High Bias Risk	Low Bias Risk	Risk of Bias Unknown
Random sequence generation	4 (5.71)	48 (68.6)	18 (25.7)
Using blind method	0	10 (14.3)	60 (85.7)
Integrity of result data	0	51 (72.9)	19 (27.1)
Assign Hide	0	21 (30.00)	49 (70.00)
Selective Ending Report	0	11 (15.7)	59 (84.3)
Other sources of bias	0	0	70 (100.00)

group[6,8,12,14–16,18–20,22,27,29,30,32–36,38,40,42,47,50,52,53,55,59,60,64,67–69,71,74] in 35 studies, chemotherapy alone as a control group[9,10,21,26,37,39,41,48,51,54,56,57,65,66,70,72,73] in 17 studies, placebo as a control group[23,24,44,62] in 4 studies, and the rest adopting symptomatic treatment + buzhongyiqi compound,[63] symptomatic treatment + compound zebrano capsules,[46] symptomatic treatment + guipiwan,[6] chemotherapy + detox tang,[11] chemotherapy + buzhongyiqi compound,[49] addy injection,[31] buzhongyiqi wan,[7] anti-tumor and potent formula,[45] modafinil capsule,[13] zhenqifuzheng capsule,[25] bozhi glycopeptide,[61] huangqi,[61] health education[58] as the control group, and the results are shown in Table 3.

Classification of Outcome Indicators

The outcome indicators used ranged significantly across the 70 included studies. The largest number of studies used the fatigue scale (68) among the outcome indicators, followed that the TCM symptom rating scale (44), quality of life scale (40), biochemical indicators (39), safety indicators (29), other functional evaluation scales (29), with the quality of life measurement scale for cancer patients (QLQ-C30) being adopted more frequently (17), mood-based scales (7), the Pittsburgh sleep quality index scale (3), and the rest of the scales were handled only in individual studies, and the results are demonstrated in Table 4.

Table 3 Selection Classification of Chinese Medicine Compound for Cancer-Caused Fatigue Control Group

Control Group Classification	Control Group Interventions	Number of Studies
Symptomatic treatment	Symptomatic treatment alone[4,5,8,12,14–16,18–20,22,27,29,30,32–36,38,40,42,47,50,52,53,55,59,60,64,67–69,71,74]	35
	Symptomatic treatment + guipiwan[6]	1
	Symptomatic treatment + compound zebrano capsules[6]	1
	Symptomatic treatment + buzhongyiqi compound[63]	1
Chemotherapy	Chemotherapy alone[63]	17
	Chemotherapy + detox tang[11]	1
	Chemotherapy +buzhongyiqi compound[49]	1
Other drugs	Buzhongyiqi wan[7]	1
	Modafinil capsule[13]	1
	Zhenqifuzheng capsule[25]	1
	Addy injection[31]	1
	Huangqi[31]	1
	Anti-tumor and potent formula[45]	1
	Bozhi glycopeptide[45]	1
	Placebo[23,24,44,62]	4
Non-drug	Health education[58]	1

Classification of Fatigue Scales

From the 70 included studies, six fatigue scales were used in the herbal preparation for cancer fatigue of which 25 studies[6,14,16,18,20,26,29,32–34,37–40,44,46,50,51,54,55,57,64,65,71,72] used the piper fatigue scale (PFS) and 18 studies[6,14,16,18,20,26,29,32–34,37–40,44,46,50,51,54,55,57,64,65,71,72] took advantage of the PFS revised (PFS-R), 11 studies[4,9,13,17,23,31,42,45,49,61,73] using the cancer fatigue scale, and 8 studies[5,10,24,25,45,60,62,68] using the brief fatigue inventory, 3 studies[47,48,66] using the fatigue symptom inventory, and 2 studies[8,47] using the multidimensional fatigue inventory.

Discussion

A statistical review of 70 studies revealed that approximately 97% of the studies applied the fatigue scale as an outcome indicator, about 63% used the Chinese medicine evidence rating scale as an outcome indicator, about 57% used the quality of life scale as an outcome indicator, and around 56% used biochemical indicators as an outcome indicator, followed by the functional assessment scale (41%), safety indicators (41%), and others. For the selection of the control group, all over 50% used symptomatic treatment as an intervention in the control group and about 24% used chemotherapy as an intervention in the control group. After compiling the 70 studies, the following issues were identified in the selection of outcome indicators and control groups in the plant-based composition studies for cancer fatigue.

There is still not enough use of the TCM syndrome scale. Chinese medicine treatment for CRF is mostly guided by the "holistic concept" of Chinese medicine and is administered according to the patient's condition, hence, the Chinese medicine symptoms are the premise and basis of prescription. In modern Chinese medicine, it is considered part of the category of "insufficient work" in Chinese medicine. Deficiency labor also acknowledged as deficiency loss is a general term for a variety of chronic debilitating symptoms on the basis of deficiency of internal organs and deficiency of qi, blood, yin, and yang as the basic pathology. Cancer-caused fatigue originates from cancer itself, and different cancer types invade different internal organs, and different patients have a different physical constitution, so a clear standard TCM symptom score is of vital importance. Although most researchers have recognized the importance of TCM symptoms, there is a need to further increase the application of this index and standardize the TCM symptoms scale to improve the clinical effectiveness of evidence-based treatment.

No uniform standard exists for fatigue ladders. The fatigue scale is the primary indicator of the results of the cancer fatigue assessment, and six fatigue scales were used in the study. Even if the same treatment measures were applied,

Table 4 Six Categories of Outcome Indicators for Cancer-Caused Fatigue Treated with Chinese Herbal Compounding

Classification of Outcome Indicators	Name	Number of Studies
Fatigue scale	Cancer fatigue scale[4,9,13,17,23,31,42,45,49,61,73]	11
	Piper fatigue revised scale[7,11,12,21,22,27,30,36,41,53,56,58,59,63,67–70]	18
	Piper fatigue scale[6,14,16,18,20,26,29,32–34,37–40,44,46,50,51,54,55,57,64,65,71,72]	25
	Brief fatigue inventory[5,10,24,25,45,60,62,68]	8
	Multidimensional fatigue inventory[8,47]	2
	Fatigue symptom inventory[8,47]	3
Quality of life scale	Karnofsky[4,5,7,8,10–14,16,18,19,21,27,29,30,32,33,35–38,40,42,50,52,55,57,59,67,69–72,74]	35
	Comprehensive quality of life assessment inventory[15]	1
	Eastern cooperative oncology group[64]	1
	Quality of life inventory: European Organization for Research and Treatment of Cancer-quality of life questionnaire-short form 36[65]	1
Emotion scale	Hospital anxiety and depression scale[24,27,58,64]	4
	Depression inventory[60]	1
	Self-rated anxiety and depression scales[60]	1
	Beck depression inventory[62]	1
Other functional scales	Chinese medicine evidence scoring scale[4–12,14,16–22,27,29,31–33,35–38,42,44,47,50,52–55,58,63,64,67–70,72,74]	43
	European Organization for Research and Treatment of Cancer[9,11,19,24,26,33,34,36,37,39,41,44,47,56,57,63,68]	17
	Functional assessment of cancer therapy[8]	1
	Insomniaseverityindex[62]	1
	Scored patient-generated subjective global assessment[62]	1
	Functional assessment of breast cancer treatment scale[35]	1
	Pittsburgh sleep quality index[35]	3
	Numerical rating scale[71]	1
	Sleep quality point scale[71]	1
	Weight score[71]	1
	Lung cancer specificity scale[60]	1
	Adult dispositional hope scale[60]	1
	Montreal cognitive assessment[62]	1
	Appetite loss score[5]	1
	MD Anderson symptom inventory[43]	1
Biochemical indicators	T lymphocyte subpopulation[4,11,12,16–18,23,25,26,30,33–35,37,45,46,49,51,53,54,56,57,60,61,63,71]	26
	Natural killer cell[12,16,26,34,56,63]	6
	Albumin[6,27,39]	3
	Hemoglobin[6,11,16,26,27,29,32,39,48,53,71,73]	12
	Platelet[16,29,32]	3
	White blood cell[11,16,26,29,32,53,71,73]	8
	Lymphocyte[29]	1
	Neutrophil[32,48,53,71,73]	5
	C-reactive protein[13,27,34,50,54,64]	6
	Tumor necrosis factor-α[16,34,63]	3
	Interleukin-1β,[63] interleukin-2,[26,64,67] interleukin-4,[64,67] interleukin-5,[67] interleukin-6,[13,16,34,54,64] interleukin-8,[54] interferon-γ,[63,64,67] interleukin-10,[64] interleukin-17a[64]	8
	Immunoglobulin G, immunoglobulin A, immunoglobulin M[21,51,56,57]	4
	CD56+, CD19+[45]	1
	Cortisol level[45]	2
	Adrenocorticotrop(h)ic hormone[13]	1
	CEA,[13] Cyfra21-1,[20] CA125,[20] CA199,[25,37] CA724[25]	3
	Thyroid stimulating hormone, free triiodothyronine[25]	1

(Continued)

Table 4 (Continued).

Classification of Outcome Indicators	Name	Number of Studies
Safety indicators	Hypertension, body temperature, pulse, breathing[7,27,36,50,58,67]	6
	Hematology,[5,7,9,12,13,17,18,21,27,33,35–38,42,50,54,58,64,67,69] urine routine,[7,12,21,35–37,50,64,67] convenient routine[7,12,36,37,50,64,67]	20
	Liver and kidney function[9,12,13,17–19,27,32,33,35–38,40,42,50,54,58,64,67,69]	20
	Electrocardiogram[7,12,17,18,21,27,35–37,42,50,64,67,69]	14
	Gastrointestinal reactions[7,12,17,18,21,27,35–37,42,50,64,67,69]	5
	Myelosuppression[30,49,66]	3
	Toxic reaction[51]	1

different evaluation criteria would result in different outcomes and conclusions. Therefore, to ensure the reliability of the study results, the fatigue scales should be standardized and unified.

The proportion of quality-of-life scales is low and there is no consistent standard. The assessment of the quality-of-life is an essential step for cancer patients and is also crucial for the determination of clinical efficacy, while the current quality of life scale accounts for about 57%, and its proportion should be further escalated. There are four types of quality of life scales used in the study, and although it can be clearly recognized that most of the studies designated to adopt the Karlsberg score (KPS) there are still studies that use other types of scales to evaluate patients' quality-of-life, so there is a need for uniform standardization.

The proportion of objective indicators for assessment was not sufficient. Objective indicators were used in 56% of the 70 included studies, and the usage of objective indicators is expected to be further enhanced. Subjective scales such as fatigue scale and quality of life score can reflect patients' fatigue and other physical status, so most researchers made use of them as the main evaluation indexes. While fatigue is the primary symptom of cancer-related fatigue, objective indicators are always required to support the reliability of subjective indicators. Among the objective indices selected in the study, including blood, immune, inflammatory, and hormone levels, the proportion of immune and blood indices is relatively high, notwithstanding, there is still a problem of confusing indices and lack of specificity. The quality of life of cancer fatigue patients has been found to be closely linked to hemoglobin and albumin levels,[77] and also to immunity such as T-lymphocyte subsets and natural killer cells,[78] and traditional Chinese medicine is constructive in anti-tumor and regulating human immunity to relieve fatigue. However, because there is no clear pathogenesis of cancer-caused fatigue, the objective indexes are not standardized enough, so further research on the pathogenesis of cancer-caused fatigue is in need of improving the objective biochemical indexes.

Inadequate utilization of safety indicators, of the 70 included studies, only 41% used safety indicators as indicators of results. This study did not include the literature on the combination of herbal compounding with other external treatments limited to herbal treatment solely, and it was found that most of the studies that used safety indicators were dissertations, which proves that researchers did not pay enough attention to the safety of oral administration of herbal medicine. We should improve the use of security indicators and deal with them accordingly.

The selection criteria for control groups vary. The choice of a control group for a study protocol is a more important aspect and should follow the principle of equilibrium. On the other hand, cancer fatigue is different from ordinary illnesses, and any treatment has a big impact on the progression of cancer and the patient's condition. This study mainly aimed to take the advantage of allopathic treatment and chemotherapy as a control group, while other studies used non-pharmacological treatment or other beneficial and supportive medications as a control group. Although interventions are coherent within the treatment group, different control groups may lead to different study findings. Therefore, in order to ensure the effects of patient treatment and study balance, control groups in cancer fatigue studies should be standardized to come up with more reliable study results.

There is a high potential for bias in study results. About 6% of the 70 included studies reported the use of blinding, about 16% used concealing allowances, and only 10% of the studies documented the method of calculating the sample size. In addition, about 32% of the studies were grouped mostly by subjective decision of the investigator without specifying the randomization method of the study, all of which would lead to a high risk of selective bias. Therefore, the high risk of bias suggests that the test presents issues such as reporting positive results only and a lack of discussion and analysis of negative results.

Conclusion

In conclusion, there exist many outcome indicators categorized in the studies of cancer-caused fatigue in Chinese medicine, but it is uncomplicated to find that few of them are directly related to cancer-caused fatigue. Because fatigue is a subjective feeling in patients, most studies use fatigue, quality of life, and mood scales to more fully assess the overall fatigue state of patients. The objective indicators are very important to improve the reliability of the study, and the biochemical indicators currently used in clinical practice lack specificity and have reason to be standardized and unified, and insufficient attention is paid to safety indicators for cancer patients with poor overall physical status. The choice of control groups in the study was also unbalanced and inconsistent.

Through the results of the above statistical analysis, in the selection of fatigue scales, although the PFS was used most frequently in the included studies the PFS-R was more recommended by comparing the reliability of the fatigue scales and other aspects;[79] the KPS scale is widely used in cancer patients, and this scale can better reflect the patient's health status and is mostly used to judge cancer patients before chemotherapy,[80] without regard to the reliability, validity, and responsiveness of the QLQ-C30 are better and more frequently used, so the above two scales are recommended and support the selection of more relevant indicators in accordance with different cancer types and states. As for the selection of objective indicators, T-lymphocyte subsets, hemoglobin, leukocytes, and C-reactive protein are recommended for testing and assessment based on the frequency of use in the included studies. The effectiveness of Chinese medicine in the treatment of cancer-related fatigue must rest on an "evidence-based treatment", thus, a uniform Chinese medicine evidence scale should be adopted more often in the study, to analyze the patient's situation specifically and choose a more effective and reasonable treatment plan. In accordance with the risk of bias assessment, the risk of bias is a high-rise in most studies, so we should make an improvement on the design of the study protocols to provide more rigorous and reliable evidence-based clinical evidence.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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References

1. Bower JE. Cancer-related fatigue--mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol.* 2014;11:597–609.
2. Wu R, Xie C. Research progress on the pathogenesis and treatment of cancer-caused fatigue. *Zhongliuxue Zazhi.* 2020;26:240–244. doi:10.11735/j.issn.1671-170X.2020.03.B015
3. Zhang Y, Lou Y, Wang J, Yu C, Shen W. Research status and molecular mechanism of the traditional Chinese medicine and antitumor therapy combined strategy based on tumor microenvironment. *Front Immunol.* 2021;11:609705. doi:10.3389/fimmu.2020.609705
4. El-Seedi HR, Yosri N, Khalifa SAM, et al. Exploring natural products-based cancer therapeutics derived from Egyptian flora. *J Ethnopharmacol.* 2021;269:113626. doi:10.1016/j.jep.2020.113626

5. Zhang D, Zhang MY, Zheng WK. Construction of core index set of clinical trial of traditional Chinese medicine and implementation specification of Delphi method. *Zhongyi Zazhi*. 2017;58:20–22. doi:10.13288/j.11-2166/r.2017.01.006

6. Cao X, Gan L, Wang YF. Clinical observation of Sini plus Renshen Decoction in the treatment of cancer-related fatigue. *Zhonghua Zhongyiyao Xuekan*. 2022;40:58–60. doi:10.13193/j.issn.1673-7717.2022.01.015

7. Gao HL, Wu JF, Chen Y, Xie BY. Preventive and therapeutic effect of Xiaqi Decoction on cancer-related fatigue in advanced non-small cell lung cancer. *Guangzhou Zhongyiyao Daxue Xuebao*. 2022;39:769–775. doi:10.13359/j.cnki.gzxbtcm.2022.04.007

8. Zuo WY, Ding HJ, Pu BH, Hong QX. Effect of Jianpi Fuzheng Recipe on cancer-related fatigue in patients with mild to moderate anemia and tumor. *Shanghai Yiyao*. 2022;43:30–33. doi:10.3969/j.issn.1006-1533.2022.06.009

9. Dao R Clinical study of Bufei Jianzhong Decoction on improving cancer-related fatigue of lung deficiency and Qi deficiency syndrome in advanced lung cancer [M.Sc. Thesis]. Yunnan University of Traditional Chinese Medicine; 2021.

10. Gao KX, Wang XK, Li LX, Wang HT. Effect of Buzhong Yiqi Guben Decoction on adverse reactions and quality of life of cancer patients with spleen qi deficiency syndrome after chemotherapy. *Xinzhongyi*. 2021;53:109–113. doi:10.13457/j.cnki.jncm.2021.20.027

11. Du XL, Hu GS, Xu SJ, Wang YQ. Observation on the efficacy and safety of Feifukang formula in the treatment of cancer-related fatigue in advanced non-small cell lung cancer. *Zhongyiyao Daobao*. 2021;27(10):89–95.

12. Zhao F, Wang ZQ, Zhang QJ. Study on the preventive and therapeutic effect of Feiliu Xiaoji formula on cancer-related fatigue in patients with non-small cell lung cancer with phlegm and blood stasis. *Hebei Zhongyi*. 2021;43:922–925. doi:10.3969/j.issn.1002-2619.2021.06.010

13. Xu W. Clinical study on Fuzheng Jiedu Decoction in the treatment of cancer-related fatigue in patients with Spleen Qi weakness gastrointestinal malignant tumor after chemotherapy [M.Sc. Thesis]. Guangzhou University of Traditional Chinese Medicine; 2021.

14. Huang X Clinical observation and effect on immune function of Guilu Erxian Jiao Decoction in the treatment of cancer-related fatigue in patients with advanced colorectal cancer with deficiency of yin and Yang [M.Sc. Thesis]. Fujian University of Traditional Chinese Medicine; 2021.

15. Zheng Q, Yao DJ, Cai Y. Effect of Huoxue Fuyuan decoction on severe cancer-related fatigue and serum CRP, IL-6, ACTH and cortisol levels in patients with lung cancer. *Sichuan Zhongyi*. 2021;39:61–64.

16. Du C Effect of Jianpi Bushen Recipe on cancer-related fatigue in patients with colorectal cancer [M.Sc. Thesis]. Nanjing University of Traditional Chinese Medicine; 2021. doi:10.16448/j.cjtcm.2020.0133.

17. Xin T. Clinical effect of Jianpi Xiaoji Decoction on cancer-related fatigue of patients with liver cancer. *Zhongguo Yiyao Zhinan*. 2021;9:136–137.

18. Li TM, Li S, Mi S, Yu J. A randomized controlled study of Jianpi Yiqi recipe in the treatment of cancer-related fatigue in patients with lung spleen qi deficiency non-small cell lung cancer after chemotherapy. *Liaoning Zhongyi Zazhi*. 2021;48:126–129. doi:10.13192/j.issn.1000-1719.2021.08.038

19. Guo S Clinical study of neibuhuangqi Decoction on cancer-related fatigue of lung cancer with Qi and blood deficiency [M.Sc. Thesis]. Shandong University of Traditional Chinese Medicine; 2021.

20. Cao W Clinical observation of Qiyan Liujun Decoction in the treatment of digestive tract related cancer-related fatigue (spleen stomach weakness type) [M.Sc. Thesis]. Shanxi University of Traditional Chinese Medicine; 2021.

21. Gao Y Clinical observation of Shengyang Yiwei decoction combined with Sanxian Decoction in the treatment of cancer-related fatigue of qi deficiency type [M.Sc. Thesis]. Tianjin University of Traditional Chinese Medicine; 2021.

22. Cao X, Wang YF, Wu Y, Gu BL. Effects of Sini Decoction on cancer-related fatigue and serum CEA, CYFRA21-1 and CA125 Levels in patients with advanced non-small cell lung cancer. *Guangming Zhongyi*. 2021;36:1081–1083.

23. Xu Y Clinical observation of Weining formula in the treatment of cancer-related fatigue in patients with advanced gastric cancer [M.Sc. Thesis]. Guangxi University of Traditional Chinese Medicine; 2021.

24. Chen KW, Chen BY, He SX, Nie XZ. Effect analysis of YangZheng Jiefan Decoction in the treatment of cancer-related fatigue with deficiency of Qi and Yin. *Shenzhen Zhongxiyi Jiehe Zazhi*. 2021;31:76–78. doi:10.16458/j.cnki.1007-0893.2021.20.028

25. Hu J, Li X, Fang Y, Peng J. Efficacy and safety of Buzhong Yiqi Decoction in improving cancer-related fatigue and immunity of cervical carcinoma patients: a protocol of randomized controlled trial. *Medicine*. 2021;100:e27938. doi:10.1097/MD.0000000000027938

26. Lee JY, Kim EH, Yoon JH, Eo W, Yoon SW. Traditional Herbal Medicine, Sipjeondaebo-Tang, for Cancer-Related Fatigue: a Randomized, Placebo-Controlled, Preliminary Study. *Integr Cancer Ther*. 2021;20:15347354211040830. doi:10.1177/15347354211040830

27. Li Y, Yang RY, Li MQ. Clinical study on self-made Fuzheng Jiedu formula in the treatment of cancer-related fatigue in patients with gastric cancer after chemotherapy. *Nanjing Zhongyiyao Daxue Xuebao*. 2021;37:366–370. doi:10.14148/j.issn.1672-0482.2021.0366

28. Jiang H Clinical study on the treatment of cancer-related fatigue (Qi and blood deficiency syndrome) by supplementing qi and nourishing blood [M.Sc. Thesis]. Changchun University of Traditional Chinese Medicine; 2020.

29. Qin C Clinical observation of Bazhen Decoction in the treatment of postoperative cancer-related fatigue of breast cancer of Qi and blood deficiency type [M.Sc. Thesis]. Shandong University of Traditional Chinese Medicine; 2020.

30. Zhang H. Therapeutic effect of Shenling Baizhu powder on cancer-related fatigue and spleen stomach weakness syndrome. *Zhongguo Yejin Gongye Yixue Zazhi*. 2021;38:245.

31. Zhang X Clinical study on Shenqi Dihuang Decoction in the treatment of cancer-related fatigue of lung cancer [M.Sc. Thesis]. Shandong University of Traditional Chinese Medicine; 2020.

32. Jiang JW, Zhang H, Zhu FT. Effect of Chaihu Pingwei Powder on prevention and treatment of cancer-related fatigue related to tumor chemotherapy. *Zhongguo Yiyao Daobao*. 2020;17:86–90.

33. Sun M Clinical observation of Bufei Huaji Decoction in improving cancer-related fatigue in patients with advanced NSCLC [M.Sc. Thesis]. Changchun University of Traditional Chinese Medicine; 2020.

34. Wang L Clinical study on tiaoganyangxue recipe in the treatment of cancer-related fatigue of liver depression and blood deficiency type [M.Sc. Thesis]. Beijing University of Traditional Chinese Medicine; 2020.

35. Lin H Clinical observation of Fuzheng anticancer formula in the treatment of cancer-related fatigue of advanced lung cancer [M.Sc. Thesis]. Guangzhou University of Traditional Chinese Medicine; 2020.

36. Gan JW, Yue SB, Cai JY. Clinical efficacy of Fuzheng Xiaoliu Decoction in the treatment of carcinogenic fatigue caused by radiotherapy and chemotherapy for breast cancer. *Shenzhen Zhongxiyi Jiehe Zazhi*. 2020;30:1–5. doi:10.16458/j.cnki.1007-0893.2020.22.001

37. Zhao Y Clinical observation of Fuzheng Yangrong recipe in the treatment of cancer-related fatigue in breast cancer [M.Sc. Thesis]. Shandong University of Traditional Chinese Medicine; 2020.

38. Liu T Observation on the clinical efficacy of modified Gancao Xiexin Decoction in the treatment of cancer-related fatigue of deficiency in middle and damp heat block type [M.Sc. Thesis]. Chengdu University of Traditional Chinese Medicine; 2020.

39. Dai Y Clinical study on Jianpi Yangwei recipe in the treatment of cancer-related fatigue of advanced gastric cancer based on immune regulation mechanism [M.Sc. Thesis]. Nanjing University of Traditional Chinese Medicine; 2020.

40. Ning B Clinical study on modified Buzhong Yiqi Decoction in the treatment of cancer-related fatigue after colorectal cancer surgery [M.Sc. Thesis]. Shanxi University of Traditional Chinese Medicine; 2020.

41. Xu W. Effects of Bu Xu Yi Shi Fang on cancer-related fatigue, nutritional status and quality of life in patients with advanced lung cancer after chemotherapy. *Zhongguo Zhongyiyao Keji*. 2021;28:1013–1015.

42. He SQ, Wang RX, Yang T. Clinical observation on the treatment of cancer-related fatigue by Invigorating the spleen and kidney. *Zhongyiyao Linchuang Zazhi*. 2020;32:128–130. doi:10.16448/j.cjtcm.2020.0133

43. Xie YH, Li LC, Miao WH. Effect of Buzhong Yiqi Decoction on cancer-related fatigue and quality of life in patients with advanced gastric cancer. *Jianyan Linchuangyu Yixue*. 2020;17:3455–3458. doi:10.3969/j.issn.1672-9455.2020.23.018

44. Han T A randomized controlled trial of modified Dioscorea pill in the treatment of chemotherapy-induced fatigue of lung cancer with deficiency of Qi and blood [M.Sc. Thesis]. Xinjiang Medical University; 2020.

45. Xu Y, Wang XS, Chen Y, Shi Q, Chen TH, Li P. A Phase II Randomized Controlled Trial of Renshen Yangrong Tang Herbal Extract Granules for Fatigue Reduction in Cancer Survivors. *J Pain Symptom Manage*. 2020;59:966–973. doi:10.1016/j.jpainsymman.2019.10.018

46. Xiao Z, Hu L, Lin J, et al. Efficacy and safety of Jianpishengsui for chemotherapy-related fatigue in patients with non-small cell lung cancer: study protocol for a randomized placebo-controlled clinical trial. *Trials*. 2020;21:94. doi:10.1186/s13063-019-3982-3

47. Liu C, Zhao XZ, Wang ZQ, Deng HB. Clinical study on the effect of Feiyanning formula combined with anti-tumor synergistic formula on cancer-related fatigue, immune function and tumor markers in patients with advanced lung adenocarcinoma after chemotherapy. *Shanghai Zhongyiyao Zazhi*. 2019;53:49–53. doi:10.16305/j.1007-1334.2019.06.013

48. Lu HQ, Xia LM, Zhu YF. Clinical study on compound Shougong powder in the treatment of cancer-related fatigue. *Zhongyiyao Linchuang Zazhi*. 2019;31:532–534. doi:10.16448/j.cjtcm.2019.0155

49. Bao W Clinical study of Jiawei Zhenqi Fuzheng Recipe on cancer-related fatigue of Qi Yin deficiency syndrome caused by radiotherapy and chemotherapy [M.Sc. Thesis]. Beijing University of Traditional Chinese Medicine; 2019.

50. Zhan PP, Yu L, Lin JT. Clinical observation of Jianpi Shengsui ointment in the treatment of cancer-related fatigue after chemotherapy. *Zhongguo Quanke Yixue*. 2019;22:1855–1859.

51. Li Z. Effects of Jianpi Yishen Buqi Decoction on immune function and cancer-related fatigue in postoperative patients with colorectal cancer. *Jiangxi Zhongyiyao Daxue Xuebao*. 2019;31:43–45.

52. Tao Z Clinical study on Jianpi Yishen Yangxue recipe in the treatment of cancer-related fatigue of stage III-IV tumor (deficiency of spleen and kidney and deficiency of Qi and blood) [M.Sc. Thesis]. Hunan University of Traditional Chinese Medicine; 2019.

53. Cai Y. Study on the improvement of cancer-related fatigue and immune function of modified Sanju Decoction in patients with cervical cancer after radiotherapy and chemotherapy. *Tianjin Zhongyiyao*. 2019;36:1069–1072. doi:10.11656/j.issn.1672-1519.2019.11.09

54. Li Y Clinical study on modified Shashen Maidong Decoction in the treatment of cancer-related fatigue of lung cancer with deficiency of Qi and Yin [M.Sc. Thesis]. Anhui University of Traditional Chinese Medicine; 2019.

55. Han X, Chi W, Pang X. Effect and mechanism of Shiquan Dabu Decoction on cancer-related fatigue in patients with lung cancer after chemotherapy. *Liaoning Zhongyiyao Daxue Xuebao*. 2019;21:139–142. doi:10.13194/j.issn.1673-842x.2019.05.037

56. He G Clinical study of warming spleen and tonifying kidney in the treatment of cancer-related fatigue of colorectal cancer during chemotherapy [M.Sc. Thesis]. Nanjing University of Traditional Chinese Medicine; 2019.

57. Lin ZR, Pan P. Clinical observation of Buzhong Yiqi Decoction in the treatment of cancer-related fatigue. *Guangming Zhongyi*. 2018;33:2039–2041. doi:10.3969/j.issn.1003-8914.2018.14.023

58. Shi YL, Zhang ZW, Yin Y. Effects of changyijian combined with oxaliplatin on immune function, cancer-related fatigue and quality of life in postoperative patients with colorectal cancer. *HebeiYixue*. 2018;40:2766–2769. doi:10.3969/j.issn.1002-7386.2018.18.010

59. Ning WM, Deng LE, He SD. Clinical study on Fuzheng Sanjie Jiedu recipe in the treatment of cancer-related fatigue in patients with colorectal cancer after postoperative chemotherapy. *Zhongguo Zhongyiyao Xinxi Zazhi*. 2018;25:24–27. doi:10.3969/j.issn.1005-5304.2018.12.007

60. Liu D Clinical study on modified Guipi Decoction in the treatment of cancer-related fatigue caused by breast cancer [M.Sc. Thesis]. Heilongjiang University of Traditional Chinese Medicine; 2018.

61. Liu WW. Clinical observation of Guipi Decoction in the treatment of cancer-related fatigue of digestive tract tumor. *Quanke Kouqiang Yixue Zazhi*. 2018;5:187–188. doi:10.3969/j.issn.2095-7882.2018.36.124

62. Li JC, Jian XY, Lai X. Effect of modified Shiquan Dabu Decoction on cancer-related fatigue in patients with lung cancer during palliative treatment. *Sichuan Zhongyi*. 2018;36:121–123.

63. Jia L, Zhang YQ. Effects of self-made Jianpi Yishen Jiedu Recipe on cancer-related fatigue and immune function in patients with colorectal cancer. *Zhongguo Laonian Yixue*. 2018;16:49–51. doi:10.3969/j.issn.1672-2671.2018.02.018

64. Lee JY, Oh HK, Ryu HS, Yoon SS, Eo W, Yoon SW. Efficacy and Safety of the Traditional Herbal Medicine, Gamiguibi-tang, in Patients With Cancer-Related Sleep Disturbance: a Prospective, Randomized, Wait-List-Controlled, Pilot Study. *Integr Cancer Ther*. 2018;17:524–530. doi:10.1177/1534735417734914

65. Zhang J, Zhang Y, Zhou F, Hu JH. Bazhen decoction regulates the immune function of cancer-related fatigue after colorectal cancer surgery. *Zhongguo Shiyan Fangjixue Zazhi*. 2017;23:196–201. doi:10.13422/j.cnki.syfjx.2017110196

66. Nian J Clinical study of Shugan Jianpi Granule in the treatment of cancer-related fatigue in breast cancer [M.Sc. Thesis]. Beijing University of Traditional Chinese Medicine; 2017.

67. Li HZ, Huang ZF, Zhang ZJ, Chen C, Tan ZQ, Chen W. Clinical effect of Jianpi Xiaoji Decoction on cancer-related fatigue of liver cancer. *Zhongyi Linchuang Yanjiu*. 2016;8:18–20.

68. Liu Y, Han T, Zhang SH. Clinical observation of Buzhong Yiqi Decoction in the treatment of cancer-related fatigue in patients with advanced cancer. *Linchuang Wuzhen Wuzhi*. 2016;29:88–91.

69. Li Z. Therapeutic effect and mechanism analysis of invigorating spleen and kidney on cancer-related fatigue in patients with advanced colorectal cancer. *Zhongguo Shiyan Fangjixue Zazhi*. 2016;22:148–152. doi:10.13422/j.cnki.syfjx.2016090148

70. Xu J Analysis of clinical characteristics of cancer-related fatigue in digestive tract and observation on the intervention effect of Yiqi Jianpi Bushen recipe [M.Sc. Thesis]. Beijing University of Traditional Chinese Medicine; 2016.

71. Zhao G Clinical study on Jinshui Fuyuan formula in the treatment of cancer-related fatigue with deficiency of lung and kidney Yin [M.Sc. Thesis]. Beijing University of Traditional Chinese Medicine; 2016.

72. Li Z. Effect of invigorating the spleen and kidney on cancer-related fatigue, syndrome score and survival status of patients with advanced colorectal cancer undergoing FOLFOX6 chemotherapy. *Zhongguo Quanke Yixue*. 2015;18:4492–4495. doi:10.3969/j.issn.1007-9572.2015.36.019

73. Ji J Clinical study of Shiquan Dabu Decoction in the treatment of cancer-related fatigue [M.Sc. Thesis]. Shandong University of Traditional Chinese Medicine; 2015.

74. Ma T, Wang Y, Wang JB. Effect of Xingjian Decoction on quality of life and fatigue state of cancer-related fatigue patients. *Henan Zhongyi*. 2015;35:3025–3027. doi:10.16367/j.issn.1003-5028.2015.12.1299

75. Tan X, Chen X, Chen Z, You J. Effect of syndrome differentiation of Jianpi yiqiatan Recipe on cancer fatigue in patients with lung cancer undergoing chemotherapy. *Zhongyi Zazhi*. 2012;53:1301–1304.

76. Zhang H. Therapeutic effect of Shenling Baizhu powder on cancer-related fatigue and spleen stomach weakness syndrome. *Zhongguo Yejin Gongye Yixue Zazhi*. 2021;38:245.

77. Kersten K, Salvagno C. Exploiting the immunomodulatory properties of chemotherapeutic drugs to improve the success of cancer immunotherapy. *Front Immunol*. 2015;6:516. doi:10.3389/fimmu.2015.00516

78. Xue XJ, Xu CP, Yang XY. Research Progress on evaluation tools and indicators of cancer-related fatigue. *Zhonghua Huli Zazhi*. 2012;47:859–861. doi:10.3761/j.issn.0254-1769.2012.09.036

79. Liu M, Zhang L, Sun LH, Bo L. Analysis of KPS score of tumor chemotherapy patients in Liaoning Province. *Zhongguo Zhongliu*. 2013;22:635–637. doi:10.11735/j.issn.1004-0242.2013.08.A007

80. Zhang C, Guo W, Yao X, et al. Database mining and animal experiment-based validation of the efficacy and mechanism of Radix Astragali (Huangqi) and Rhizoma Atractylodis Macrocephalae (Baizhu) as core drugs of Traditional Chinese medicine in cancer-related fatigue. *J Ethnopharmacol*. 2022;285:114892. doi:10.1016/j.jep.2021.114892