

# Evidence Map Analysis of Acupuncture for Chronic Fatigue Syndrome

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**Abstract:** This study analyzes the research status of randomized controlled trials (RCTs) on acupuncture treatment for chronic fatigue syndrome (CFS). We searched databases including CNKI, WanFang Data, CBM, VIP, PubMed, Embase, The Cochrane Library, and Web of Science. RCTs on acupuncture for CFS published from database inception to April 28, 2025, were collected. Basic characteristics, intervention methods, and outcome measures of the literature were extracted for categorization and visual statistical analysis. A total of 104 RCTs were included, involving 8,526 participants. They covered 57 outcome measures, used a cumulative total of 334 times. These outcome measures were summarized into 8 measurement domains: TCM syndromes, symptoms/signs, quality of life, mental health, laboratory tests, patient satisfaction, safety events, and long-term prognosis. Commonly used acupoint prescriptions for acupuncture treatment of CFS included ST36 (Zusanli), BL23 (Shenshu), SP6 (Sanyinjiao), BL20 (Pishu), GV4 (Guanyuan), and CV6 (Qihai). Current research exhibits issues such as non-standard methodological design, significant variations in scale usage, laboratory tests being limited mainly to immunological indices, unclear primary and secondary outcome measures, lack of economic evaluations, insufficient long-term follow-up, and a deficiency in highlighting TCM characteristics. Acupuncture is objectively effective for treating CFS. However, related RCTs urgently require standardization in methodological design and the selection of outcome measures. It is recommended to unify clinical evaluation criteria, standardize the setting of outcome measures, and enhance research and evidence quality.

**Keywords:** Chronic Fatigue Syndrome (CFS); Acupuncture and Moxibustion; Randomized Controlled Trial (RCT); Outcome Indicator; Evidence Map

## 1. Introduction

Chronic fatigue syndrome (CFS) is a complex disease characterized by multi-system dysfunction. Its core manifestation is persistent fatigue lasting  $\geq 6$  months that is not alleviated by rest, often accompanied by symptoms such as cognitive impairment, sleep problems, lymphadenopathy, and muscle/joint pain. The global prevalence is approximately 0.55%–1.67% [1-2]. In 2017, the number of patients in the United States alone reached 1.7–3.38 million [3], imposing a significant socioeconomic burden. The etiology and pathogenesis of CFS remain unclear. Multiple studies suggest an association between SARS-CoV-2 infection and the onset of CFS, with about 14.12% of patients potentially developing CFS post-infection [2,4], further highlighting the urgency and practical importance of intensifying CFS research.

Currently, there are no specific drugs for CFS. Clinical management primarily focuses on symptomatic treatment (e.g., analgesics, hypnotics, anti-anxiety/antidepressant drugs), but the efficacy is limited and often accompanied by side effects [5]. Acupuncture has shown significant efficacy in treating CFS [6] and can improve CFS-related symptoms through multiple pathways, such as regulating the immune, endocrine, and nervous systems [7].

The randomized controlled trial (RCT) is the gold standard for evaluating the efficacy and safety of interventions. Numerous RCTs have confirmed the clinical value of acupuncture in treating CFS, but a systematic summary and analysis of the related evidence is lacking. An evidence map is an emerging evidence synthesis and visualization technique that presents evidence from multiple perspectives using a combination of text and charts (citation) [8]. This article employs an evidence map format to visually present and synthesize RCTs on Traditional Chinese Medicine (TCM) for CFS, explores the current research status in this field, identifies promising research directions, and provides guidance and reference

for subsequent studies.

## 2. Methods

### 2.1. Study registration

This study has been registered on the PROSPERO platform (ID: CRD420251024495) and strictly adheres to the PRISMA reporting guidelines to ensure transparency and scientific rigor.

### 2.2. Literature search

This study systematically searched eight databases. Chinese databases: China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform (Wanfang), VIP Database (VIP), and SinoMed; English databases: PubMed, Web of Science, Embase, and the Cochrane Library. Following the PICO framework, the search covered RCTs on acupuncture interventions for CFS published from database inception to December 31, 2025. Search terms combined keywords related to chronic fatigue syndrome, acupuncture, randomized controlled trials, etc. The search strategy employed a combination of subject headings and free-text terms. Taking PubMed as an example, the specific search strategy is presented in Figure 1.

- #1 "Fatigue Syndrome, Chronic"[Mesh]
- #2 (Chronic Fatigue Syndromes[Title/Abstract]) OR (Fatigue Syndromes, Chronic[Title/Abstract]) OR (Chronic Fatigue-Fibromyalgia Syndrome[Title/Abstract]) OR (Chronic Fatigue Fibromyalgia Syndrome[Title/Abstract]) OR (Chronic Fatigue-Fibromyalgia Syndromes[Title/Abstract]) OR (Fatigue-Fibromyalgia Syndrome, Chronic[Title/Abstract]) OR (Fatigue-Fibromyalgia Syndromes, Chronic[Title/Abstract]) OR (Infectious Mononucleosis-Like Syndrome, Chronic[Title/Abstract]) OR (Infectious Mononucleosis Like Syndrome, Chronic[Title/Abstract]) OR (Royal Free Disease[Title/Abstract]) OR (Chronic Fatigue And Immune Dysfunction Syndrome[Title/Abstract]) OR (Chronic Fatigue Disorder[Title/Abstract]) OR (Chronic Fatigue Disorders[Title/Abstract]) OR (Fatigue Disorder, Chronic[Title/Abstract]) OR (Systemic Exertion Intolerance Disease[Title/Abstract]) OR (Myalgic Encephalomyelitis[Title/Abstract]) OR (Encephalomyelitis, Myalgic[Title/Abstract]) OR (Chronic Fatigue Syndrome[Title/Abstract]) OR (Postviral Fatigue Syndrome[Title/Abstract]) OR (Fatigue Syndrome, Postviral[Title/Abstract]) OR (Postviral Fatigue Syndromes[Title/Abstract]) OR (Syndrome, Postviral Fatigue[Title/Abstract])
- #3 #1 OR #2
- #4 "Acupuncture"[Mesh]
- #5 (Acupuncture Treatment[Title/Abstract]) OR (Acupuncture Treatments[Title/Abstract]) OR (Treatment, Acupuncture[Title/Abstract]) OR (Therapy, Acupuncture[Title/Abstract]) OR (Pharmacoacupuncture Treatment[Title/Abstract]) OR (Treatment, Pharmacoacupuncture[Title/Abstract]) OR (Pharmacoacupuncture Therapy[Title/Abstract]) OR (Therapy, Pharmacoacupuncture[Title/Abstract]) OR (Acupotomy[Title/Abstract]) OR (Acupotomies[Title/Abstract]) OR ("Acupuncture, Ear"[Title/Abstract]) OR ("Moxibustion"[Title/Abstract]) OR ("Needle Warming Therapy"[Title/Abstract])
- #6 #4 OR #5
- #7 ("Randomized Controlled Trial" [Publication Type]) OR ("Randomized Controlled Trials as Topic"[Mesh])
- #8 #3 AND #6 AND #7

*Figure 1 Retrieval strategy of PubMed database*

### 2.3. Inclusion criteria

(1) Study type: RCTs on acupuncture treatment for CFS; (2) Study population: Patients diagnosed with CFS according to authoritative criteria; (3) Interventions: The experimental group received various forms of acupuncture or moxibustion treatment, while the control group received non-acupuncture interventions, including Chinese or Western medication, sham acupuncture, etc.; (4) Outcome measures: Included literature must contain at least one outcome measure; (5) Language: Chinese or English.

#### 2.4. Exclusion criteria

(1) Literature for which the full text cannot be obtained even after contacting the authors; (2) Conference abstracts or dissertations; (3) Duplicate publications; (4) Literature with flawed experimental design or unmatched baseline data.

#### 2.5. Literature screening and data extraction

After importing the literature into EndNote X9 and removing duplicates, two researchers independently conducted the screening. First, based on titles and abstracts, they strictly adhered to the inclusion and exclusion criteria to cross-reference and screen the literature. For literature that passed the initial screening, they carefully read the full texts to determine whether to include it. In cases of disagreement between the two researchers, a third researcher was consulted for arbitration.

Information from the included literature was extracted using an Excel spreadsheet. The extraction content included: (1) Basic article information (title, first author, year, journal, language, sample size, baseline characteristics); (2) Study content (CFS diagnostic criteria, TCM syndrome types and reference standards, interventions, treatment course, follow-up); (3) Outcome measures (efficacy criteria, indicator names, measurement time points, safety assessment, economic evaluation).

#### 2.6. Literature Quality Assessment and Evidence Map Analysis

Two researchers independently conducted a bias analysis of the included RCTs using the Cochrane-recommended Risk of Bias 2.0 (ROB 2.0) tool. This assessment covered five domains: the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Any disagreements were resolved by a third researcher.

The collected outcome measures were organized in Excel. Following the classification system recommended by the COMET handbook <sup>[9]</sup>, they were categorized into eight outcome domains. A descriptive analysis of the recorded indicators was performed. Visualization and analysis were conducted using tools such as GraphPad Prism 9.5.1 and Gephi 0.9.2.

### 3. Result

#### 3.1. Literature screening process

The initial search retrieved 2,948 relevant articles (2,393 in Chinese and 555 in English). After removing duplicates, preliminary screening, and full-text review, 104 articles were finally included, consisting of 102 in Chinese and 2 in English. The literature screening process is illustrated in Figure 2.

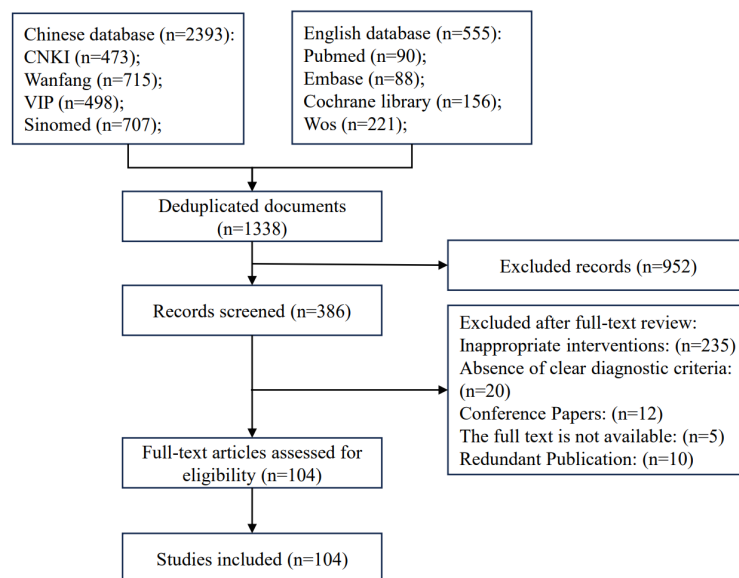


Figure 2: PRISMA Flowchart

3.2. Basic characteristics of included literature

3.2.1 Publication Trends of Literature on Acupuncture for CFS

From database inception to April 28, 2025, the number of RCTs on acupuncture for CFS showed a fluctuating but upward trend. The publication trend is presented in Figure 3.

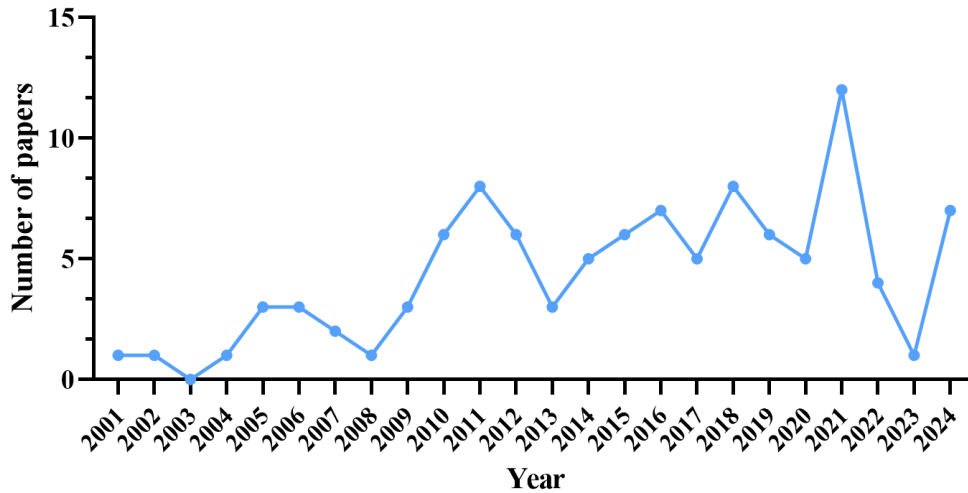


Figure 3: Number of RCTs published on acupuncture treatment of CFS

3.2.2 Basic contents of included literature

This study included a total of 104 RCTs, involving 8,526 patients (4,541 in the experimental groups and 3,985 in the control groups). The sample size of individual studies ranged from 30 to 200, with an average of 80 participants. Only 5 studies (4.81%) reported sample size calculations. Regarding participant characteristics, 101 articles (97.12%) reported age (18-65 years), 86 articles (82.69%) reported disease duration (3 months to 18 years), and 7 articles (6.73%) implemented follow-up (assessment time points: 1 or 3 months).

3.2.3 Interventions included in the literature

Among the interventions in the experimental groups, they were categorized into 8 types, including: acupuncture (41%), acupuncture plus moxibustion (16%), moxibustion (13%), acupuncture combined with Chinese herbal medicine (10%), moxibustion combined with other therapies (8%), acupuncture combined with other therapies (7%), electroacupuncture (3%), and electroacupuncture combined with other therapies (2%). The intervention measures of the included literature are shown in Figure 4.

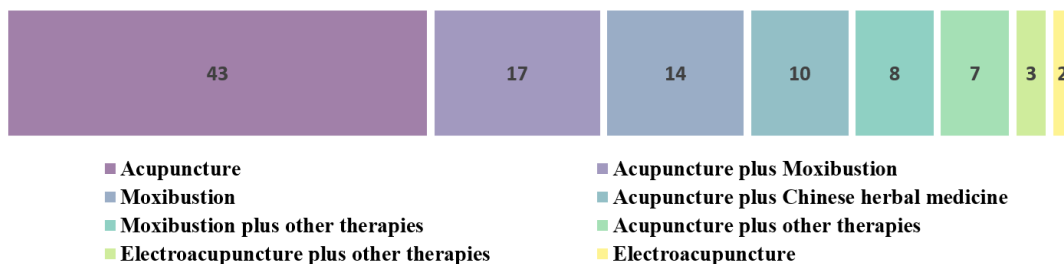


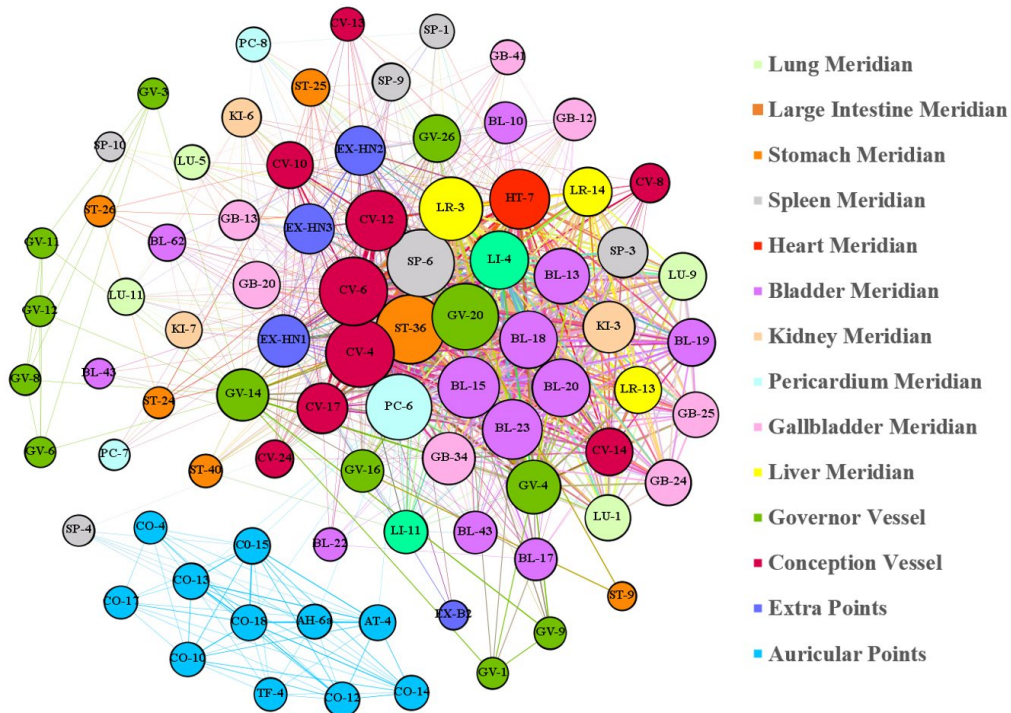
Figure 4: Intervention bar stacked chart

3.2.4 Core acupoint combination network of acupuncture intervention on CFS

Among the acupoints included in the RCT, Zusanli (ST36) is the most frequently used acupoint, followed by Shenshu (BL23) and Sanyinjiao (SP6). The acupoints with the highest frequency of use are shown in Table 1. Using gephi 0.9.2 to draw the node diagram of acupoint use combination, it can be concluded that "ST36+SP6", "bl20+BL23" and "BL23+bl18" are the acupoint combinations with high frequency. Bladder channel, Ren channel and Du channel are the most commonly used channels. The network of acupuncture point combinations is shown in Figure 5.

Table 1: Acupoint application of acupuncture in the treatment of CFS

Acupoint	Frequency/time
ST36 (Zusanli)	54
BL23 (Shenshu)	47
SP6 (Sanyinjiao)	42
BL20 (Pishu)	40
CV4 (Guanyuan)	37
CV6 (Qihai)	36
GV20 (Baihui)	36
BL18 (Ganshu)	34
BL15 (Xinshu)	33
LR3 (Taichong)	25



Note: Colors represent the meridian(s) to which the acupoint belongs. The diameter of a node is proportional to the frequency of use of that acupoint. The thickness of the connecting lines between nodes indicates the frequency of co-occurrence of the acupoints.

Figure 5: Network diagram of core acupoint combination

### 3.2.5 Quality evaluation

All 104 included studies exhibited some degree of risk of bias. Overall, the risk of bias was judged as having "some concerns" in 96 studies and as "high risk" in 8 studies. The detailed assessment results are as follows:(1) Randomization process: 68 studies were rated as low risk due to appropriate methods and allocation concealment, 29 studies were rated as having some concerns due to lack of detailed description of randomization methods, and 7 studies were rated as high risk due to non-random methods or predictable sequences.(2) Deviations from intended interventions: None of the studies reported deviations from the intervention measures, all were rated as having some concerns.(3) Missing outcome data: 35 studies reported dropout rates of <5% and were rated as low risk, 68 studies did not report dropout or loss to follow-up data and were rated as having some concerns, and 1 study with a dropout rate >10% was rated as high risk.(4) Measurement of the outcome: 23 studies used blinding methods

such as sham acupuncture and were rated as low risk, while 81 studies did not use blinding and were rated as having some concerns.(5) Selection of the reported result: 8 studies were consistent with the registered protocol and were rated as low risk, while 96 studies did not mention study registration and were rated as having some concerns. The bias of the included literature is shown in Figure 6.

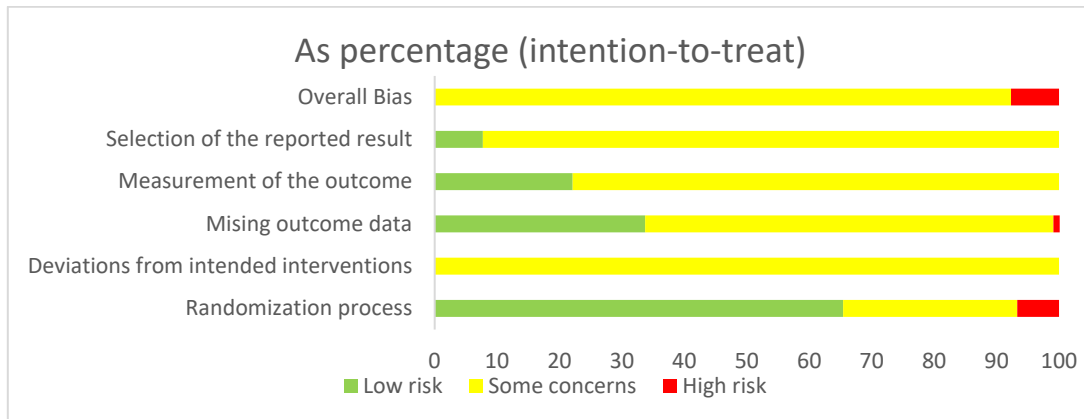


Figure 6: Bias risk assessment chart

### 3.2.6 Diagnostic criteria

All literatures reported the diagnostic criteria of CFS, of which 90.38% (94 articles) adopted the criteria revised by the Centers for Disease Control and prevention in 1994<sup>[10]</sup>, and the rest were detailed in Table 2.

Table 2: CFS diagnostic criteria

No.	Diagnostic Criteria	Frequency	Proportion
1	“The Chronic Fatigue Syndrome: A Comprehensive Approach to Its Definition and Study”(1994)	94	90.38%
2	“Chronic Fatigue Syndrome: A Working Case Definition”(1988)	3	2.88%
3	“The Doctor's Guide to Chronic Fatigue Syndrome: Understanding, Treating, and Living with CFIDs”(1995)	2	1.92%
4	“Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution”(2003)	1	0.96%
5	“Chronic fatigue syndrome”(2009)	1	0.96%
6	“Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution”(2005)	1	0.96%
7	“Determination of fatigue sub-health and identification of TCM Syndromes”(2020)	1	0.96%
8	“Guiding principles for clinical research of new drugs of traditional Chinese Medicine”(2002)	1	0.96%

### 3.3. Outcome index evaluation

#### 3.3.1 Index domain of acupuncture treatment for CFS

According to the technical specifications for the core outcome set of traditional Chinese medicine [8], the outcome measures were categorized into 8 domains based on their functional attributes: TCM syndrome/pattern, symptoms and signs, quality of life, mental health, laboratory and imaging examinations, patient satisfaction, safety events, and long-term prognosis. The indicator domain is shown in Figure 7.

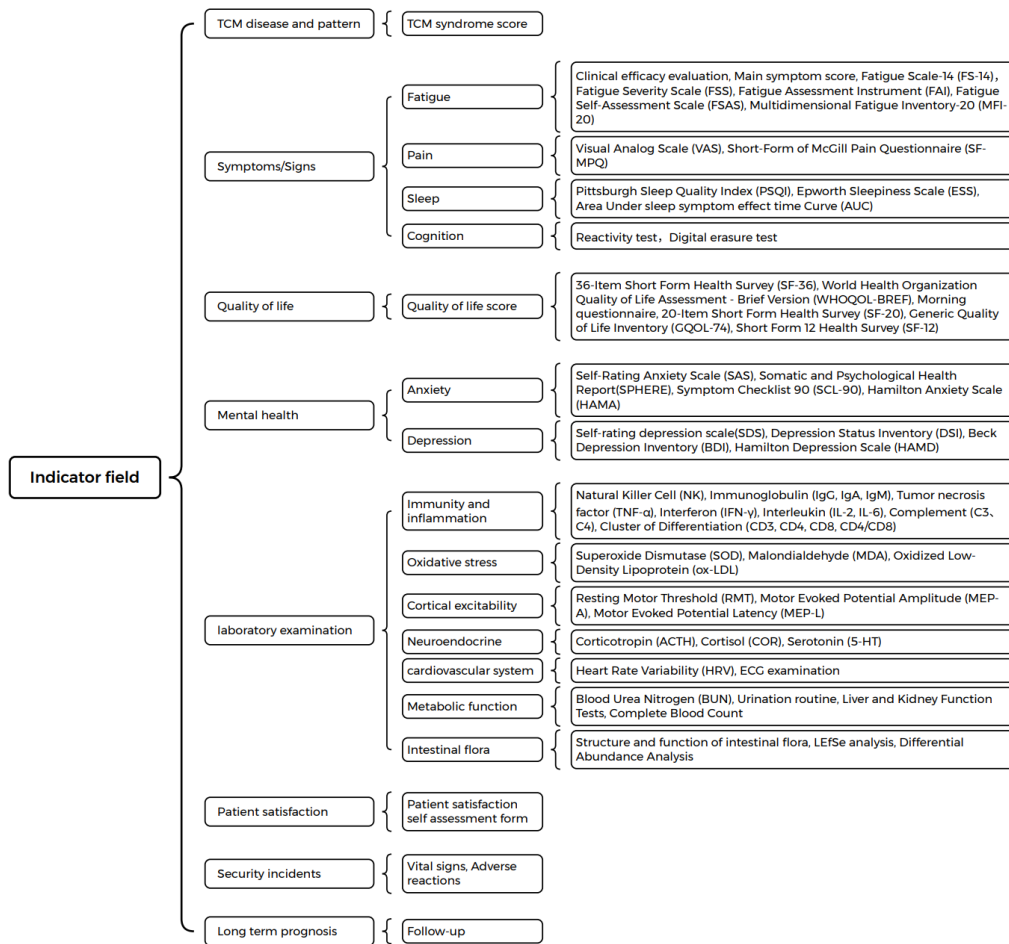


Figure 7: Outcome Domains in Randomized Controlled Trials of Acupuncture for CFS

3.3.2 Characteristics of outcome indicators

A total of 104 articles reported 57 outcome indicators, with a cumulative frequency of 334 times, and a maximum of 6 indicators were used in a single article. The most frequently used indicators were: clinical efficacy evaluation (symptoms/signs), SF-36 scale (quality of life), SAS scale (mental health), immunoglobulin (physical and chemical examination) and adverse reaction records (safety events).

Table 3: Utilization of Outcome Measures

Indicator field	Category	Label	Outcome indicators	Frequency	Proportion
TCM disease and pattern		1	TCM syndrome score	12	3.6%
	Symptoms/Signs	Fatigue	2	Clinical efficacy evaluation	72
3			Fatigue Scale-14 (FS-14)	42	12.6%
4			Main symptom score	17	5.1%
5			Fatigue Severity Scale (FSS)	6	1.8%
6			Fatigue Assessment Instrument (FAI)	6	1.8%
7			Fatigue Self-Assessment Scale (FSAS)	2	0.6%
8			Multidimensional Fatigue	1	0.3%

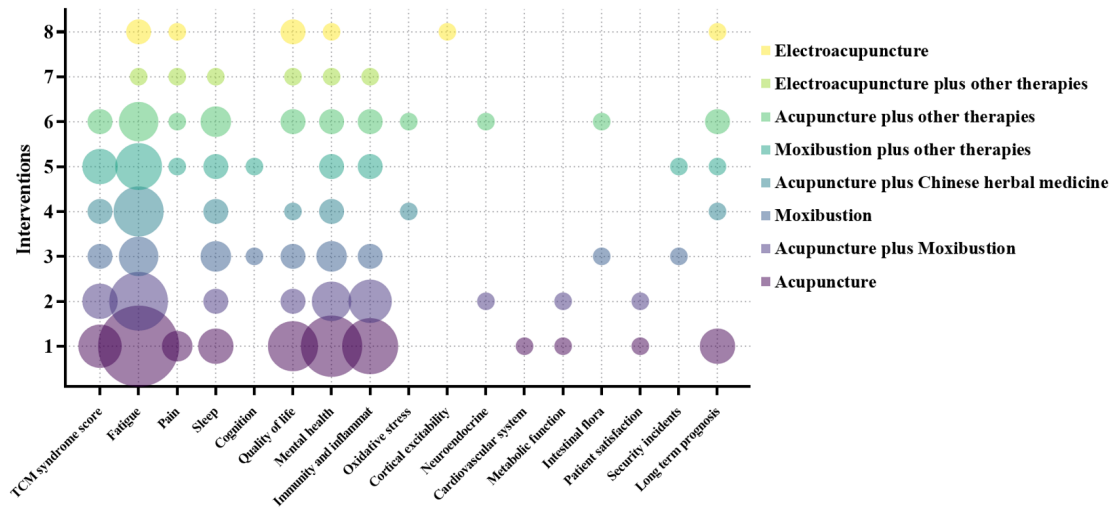
		Inventory-20 (MFI-20)			
	Pain	9	Visual Analog Scale (VAS)	6	1.8%
		10	Short-Form of McGill Pain Questionnaire (SF-MPQ)	1	0.3%
	Sleep	11	Pittsburgh Sleep Quality Index (PSQI)	13	3.9%
		12	Epworth Sleepiness Scale (ESS)	1	0.3%
		13	Area Under sleep symptom effect time Curve(AUC)	1	0.3%
		14	Reactivity test	1	0.3%
Quality of life	Cognition	15	Digital erasure test	1	0.3%
		16	36-Item Short Form Health Survey (SF-36)	12	3.6%
	17	Generic Quality of Life Inventory (GQOL-74)	1	0.3%	
	18	World Health Organization Quality of Life Assessment - Brief Version(WHOQOL-BREF)	2	0.6%	
	19	Morning questionnaire	1	0.3%	
	20	20-Item Short Form Health Survey (SF-20)	1	0.3%	
	21	Short Form 12 Health Survey (SF-12)	1	0.3%	
	Anxiety	22	Self-Rating Anxiety Scale (SAS)	12	3.6%
		23	Somatic and Psychological Health Report (SPHERE)	5	1.5%
		24	Symptom Checklist 90(SCL-90)	4	1.2%
25		Hamilton Anxiety Scale (HAMA)	1	0.3%	
Mental health	Depression	26	Self-rating depression scale (SDS)	9	2.7%
		27	Depression Status Inventory (DSI)	3	0.9%
		28	Hamilton Depression Scale (HAMD)	1	0.3%
		29	Beck Depression Inventory (BDI)	1	0.3%
		30	Immunoglobulin (IgG、 IgA、 IgM)	9	2.7%
laboratory examination	Immunity and inflammation	31	Interleukin (IL-6)	8	2.4%
		32	Interferon- $\gamma$ (IFN- $\gamma$ )	5	1.5%

	33	Interleukin (IL-2)	5	1.5%
	34	Natural Killer Cell (NK)	4	1.2%
	35	Tumor necrosis factor (TNF- $\alpha$ )	4	1.2%
	36	Cluster of Differentiation (CD3、 CD4、CD8、CD4/CD8)	4	1.2%
	37	Complement (C3、C4)	2	0.6%
	38	Superoxide Dismutase (SOD)	3	0.9%
Oxidative stress	39	Malondialdehyde (MDA)	3	0.9%
	40	Oxidized Low-Density Lipoprotein (ox-LDL)	1	0.3%
	41	Resting Motor Threshold (RMT)	1	0.3%
Cortical excitability	42	Motor Evoked Potential Amplitude (MEP-A)	1	0.3%
	43	Motor Evoked Potential Latency (MEP-L)	1	0.3%
	44	Serotonin (5-HT)	2	0.6%
Neuroendocrine	45	Cortisol (COR)	1	0.3%
	46	Corticotropin (ACTH)	1	0.3%
cardiovascular system	47	ECG examination	2	0.6%
	48	Heart Rate Variability (HRV)	1	0.3%
Metabolic function	49	Urination routine	2	0.6%
	50	Liver and Kidney Function Tests	2	0.6%
	51	Complete Blood Count	2	0.6%
	52	Blood Urea Nitrogen (BUN)	1	0.3%
	53	Distribution of intestinal flora (Structure and function of intestinal flora, LEfSe analysis, Differential Abundance Analysis)	2	0.6%
Patient satisfaction	54	Patient satisfaction self assessment form	2	0.6%
Security incidents	55	Vital signs	18	5.4%
	56	Adverse reactions	2	0.6%
Long term prognosis	57	Follow-up	9	2.7%

### 3.3.3 Distribution of outcome indicators in acupuncture treatment of CFS

The bubble chart depicting the utilization frequency of outcome measures across different

interventions revealed that the types of outcome measures selected in the included studies were relatively consistent. High-frequency measures included fatigue (30.3%), mental health (14.1%), immunity and inflammation (11.6%), and TCM syndrome scores (10.1%). The distribution of outcome indicators is shown in Figure 8.

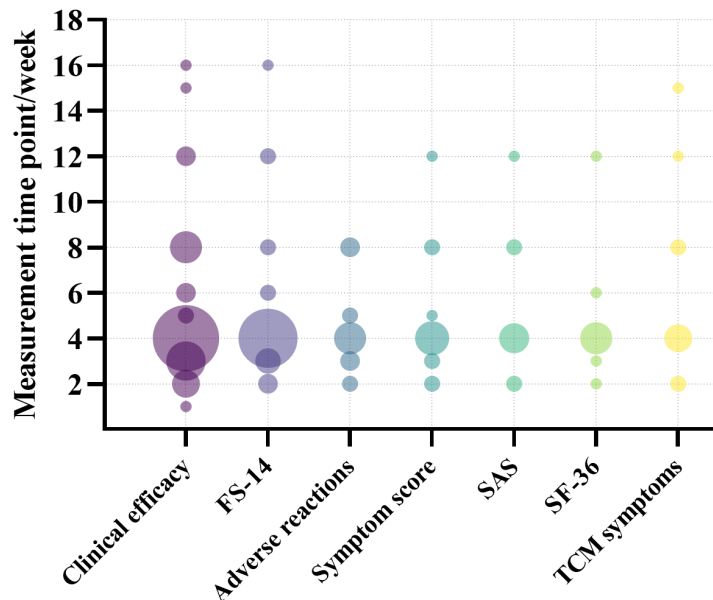


Note: Different colors represent different interventions. The diameter of each node is proportional to the frequency of use of that outcome measure.

Figure 8: Distribution of Outcome Measures in Acupuncture Treatment for CFS

### 3.3.4 Evaluation time point

The evaluation of outcome measures involved a total of 10 assessment time points, spanning a period from 1 to 16 weeks, with the post-4-week treatment assessment being the most frequently used. By tallying the frequency of use at each evaluation time point, a bubble chart of assessment time points was generated, where the size of each bubble is proportional to its frequency of use. The distribution of usage frequencies across the different time points is shown in Figure 9.



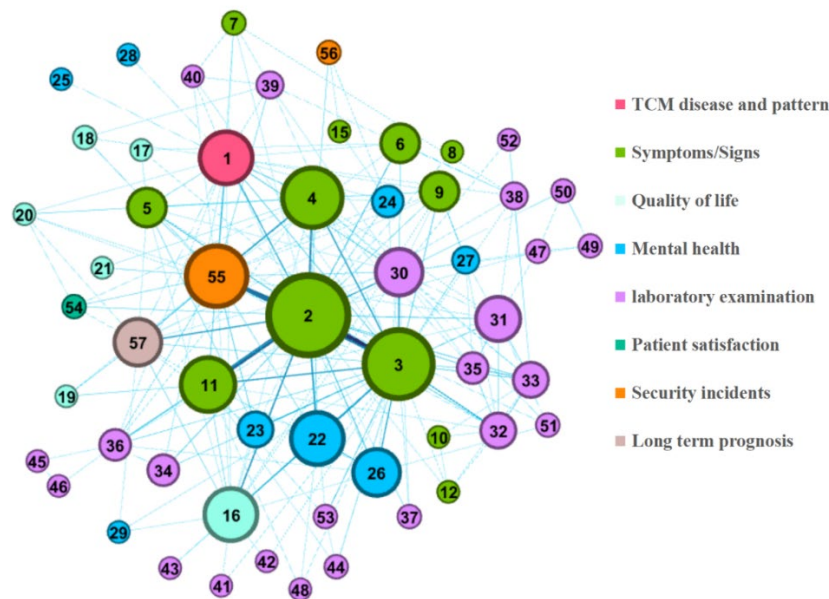
Note: The color represents the type of intervention. The diameter of a node is proportional to the frequency of use of that outcome measure.

Figure 9 Outcome index evaluation time point

### 3.3.5 Combined use of outcome indicators

To analyze the combined use of outcome measures, this study constructed a co-occurrence network of outcome measures, as shown in Figure 10. The node size is proportional to the frequency of use of

each measure; the color depth and width of the edges are proportional to the co-occurrence frequency between measures. The results showed that the three pairs of measures with the highest co-occurrence frequency were "FS-14 and Clinical Efficacy Evaluation," "PSQI and Clinical Efficacy Evaluation," and "Adverse Events and Clinical Efficacy Evaluation." The numbering of outcome measures is provided in Table 3.



*Note: Each node represents an outcome measure, with the corresponding numbers provided in Table 3. The color indicates the category of the outcome measure. The diameter of a node is proportional to the frequency of use of that outcome measure. The thickness of the connecting lines between nodes indicates the frequency of co-occurrence of the outcome measures.*

Figure 10 Combination diagram of outcome indicators

## 4. Discussion

### 4.1. Methodological quality of randomized controlled trials and risk of bias assessment of included studies

According to the assessment using the ROB 2.0 tool, all 104 included studies were identified as having a risk of bias. The main issues are as follows: (1) Unclear randomization process. Twenty-nine studies did not provide a detailed description of their randomization procedure, and 7 studies employed inappropriate randomization methods, such as alternating allocation based on the order of patient visits. (2) Lack of blinding design. Although the nature of acupuncture treatment makes double-blinding difficult, single-blinding methods such as sham acupuncture or placebo needles could still have been applied. Eighty-one studies did not implement any form of blinding, which increases the risk of performance bias and measurement bias. (3) Incomplete reporting of dropout data. Sixty-eight studies did not specify dropout data or clearly define dropout criteria, which may lead to selection bias and reporting bias.

### 4.2. Utilization of Assessment Scales

Symptom network analysis indicates that the clinical manifestations of CFS exhibit significant individual differences and diversity<sup>[11]</sup>. This characteristic makes assessment scales a core basis for its diagnosis and efficacy evaluation. This study involved a total of 23 scales, with fatigue assessment scales being the most frequently used. The fatigue assessment tools included in this study are the Fatigue Scale-14 (FS-14), the Fatigue Severity Scale (FSS), the Fatigue Assessment Instrument (FAI), the Fatigue Self-Assessment Scale (FSAS), and the Multidimensional Fatigue Inventory-20 (MFI-20). These scales differ in structure and assessment focus (specific characteristics of each scale are detailed in Table 4). In practical selection, it is recommended to consider factors such as the assessment purpose, population characteristics, dimensions of fatigue, and time constraints. Specific recommendations are as follows:

- (1) For rapid screening or group comparisons, the FS-14 or FSS are suitable.
- (2) To assess the impact of fatigue on daily functioning, the FSS is the preferred choice.
- (3) For comprehensive, in-depth research or complex clinical assessments, the MFI-20 or FAI are recommended.
- (4) When emphasizing localization context and patients' subjective experience, the combined use of the FSAS can be considered.

**4.3. Insufficient assessment of the cognitive domain**

Although multiple studies and international clinical guidelines indicate that cognitive dysfunction is one of the core clinical manifestations of CFS [10,12], involving dimensions such as information processing speed, attention, and memory [13-14], its assessment was severely inadequate in the literature included in this study. Only two measures—the Digit Cancellation Test and reaction ability tests—were used for related assessments, with a total frequency of merely two occurrences, which is insufficient to comprehensively reflect the extent of cognitive impairment. Future research urgently needs to introduce systematic and standardized cognitive assessment tools and develop CFS-specific cognitive assessment scales to provide a reliable basis for mechanistic exploration and clinical intervention.

**4.4. Laboratory indicators were predominantly immunological and inflammatory indicators.**

It is widely recognized that CFS involves imbalances across multiple systems, including the neurological, endocrine, immune, metabolic, and gut microbiota systems [15-17]. However, existing clinical research has been overly focused on immunological and inflammatory indicators. Among the 20 types of laboratory indicators included, immunological indicators were used a cumulative total of 41 times, while 15 other indicators were used no more than twice. Although immune modulation is considered one of the important mechanisms of acupuncture in treating CFS [18-19], the variety of laboratory indicators selected in the included studies was relatively limited, making it difficult to comprehensively elucidate the pathological mechanisms from multi-system and multi-target perspectives. It is recommended that future research expand the scope of testing and strengthen multi-index combined analysis to systematically elucidate the mechanisms of acupuncture in treating CFS.

*Table 4: Summary of fatigue assessment scale*

Scale	Number of Items	Main Assessment Dimensions	Advantages	Disadvantages	Applicable Scenarios
FS-14	14	Two dimensions: Physical fatigue, Mental fatigue.	Brief and quick, with clear dimensions (physical/mental), able to distinguish types of fatigue, good reliability and validity, available in multiple languages.	Shallow assessment of the depth and impact of fatigue (such as impact on quality of life).	Can quickly distinguish types of fatigue, suitable for clinical screening, large-scale epidemiological surveys, and preliminary evaluation of treatment efficacy.
FSS	9	Single dimension: Impact of fatigue on daily functioning.	Very concise, high reliability, most widely used clinically. Particularly focuses on the impact of fatigue on behavioral and psychological functions rather than the feeling of fatigue	Single-dimension limitation, lacks evaluation of cognitive/emotional dimensions and symptom specificity; not sensitive to mild to moderate fatigue.	Quickly assess fatigue severity and functional impairment, suitable for evaluating interference of fatigue with quality of life.

		itself.			
FAI	29	4 dimensions: Fatigue severity, Situational specificity, Psychological/behavioral impact, and Response to sleep.	Reflects fatigue over the past 2 weeks, comprehensive content with broad coverage, assesses not only fatigue intensity but also situational changes and consequences, provides reliable information.	Many items, time-consuming, poor clinical feasibility.	Comprehensively detail causes, severity, and characteristics of fatigue. Suitable for in-depth clinical research on fatigue.
FSAS	23	2 dimensions: Types and severity of fatigue (physical and mental fatigue and consequences of fatigue); Characteristics of fatigue (response to sleep/rest, emotional aspects of fatigue, diurnal variation).	Developed/ revised for Chinese populations, item wording is close to local context, good internal consistency.	Weak international comparability, limited comparative data with mainstream international scales, restricted cross-study comparability.	Subjective fatigue self-assessment with broad dimensional coverage. Suitable for domestic clinical research.
MFI-20	20	5 dimensions: General fatigue, Physical fatigue, Psychological fatigue, Reduced activity, Reduced motivation.	Reflects fatigue over the past 2 weeks, multidimensional detailed assessment, clear dimension division, clear structure, sensitive to changes before and after intervention.	Relatively many items, complex scoring, prone to errors, requires some time to complete.	Evaluate patient fatigue levels through multiple dimensions, suitable for populations with complex fatigue manifestations, conducting multidimensional analysis and subtype classification. Helpful for developing more targeted interventions.

**4.5. Others**

The included studies also shared the following common issues: (1)Unclear distinction between primary and secondary outcomes: Among the 88 studies that used multiple outcome measures, only 3 clearly differentiated between primary and secondary outcomes. This may increase the risk of false-positive findings due to multiple comparisons [20]. (2)Lack of economic evaluations: None of the studies conducted an economic evaluation. The treatment cycle for CFS is long, and the societal burden is heavy, with annual treatment costs for patients ranging from €979 to €1,140 [5,21]. Current research fails to demonstrate the economic advantages of acupuncture in treating high-burden diseases. (3)Inadequate

long-term follow-up: Only 5 studies reported follow-up data (with follow-up periods concentrated between 1 and 3 months), resulting in a lack of evidence for long-term efficacy. (4) Deficiency in TCM-specific evaluation systems: Only 12 studies employed TCM syndrome scores, and most studies failed to reflect the principle of syndrome differentiation and treatment in acupoint selection and efficacy assessment.

## 5. Conclusion

In summary, this study systematically analyzed the current application of outcome measures in randomized controlled trials (RCTs) of acupuncture for CFS, revealing significant shortcomings in methodological design, indicator selection, and evaluation systems. Optimization is recommended focusing on the following three aspects: (1) Establish a standardized set of assessment scales to enhance comparability across different studies; (2) Expand the scope of laboratory indicators to provide more comprehensive evidence for elucidating the pathogenesis of CFS; (3) Standardize the clinical efficacy evaluation system to facilitate future evidence integration and analysis. Building on this, it is urged to promptly establish a Core Outcome Set (COS) for acupuncture in treating CFS to guide researchers in the appropriate selection of outcome measures, standardize study design and reporting procedures, improve evidence quality, and promote the scientific application and dissemination of acupuncture in CFS clinical practice.

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