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Research article

# The effectiveness of five-element music therapy for post-stroke depression: A systematic review and meta-analysis

Kelong Zhong [a], Xuemei An [b,*], Yun Kong [a]

[a] Chengdu University of Traditional Chinese Medicine, China
[b] Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, China

A R T I C L E I N F O

*Keywords:*
Five-element music
Post-stroke depression
Systematic review
Meta-analysis

A B S T R A C T

*Introduction:* Five-element music therapy is widely utilized as a complementary approach in stroke rehabilitation, particularly for addressing post-stroke depression (PSD). This study systematically evaluates the clinical impact of five-element music therapy on individuals experiencing PSD.
*Methods:* A comprehensive search of nine electronic databases, encompassing published and unpublished gray literature up to February 15, 2022, was conducted. Two investigators independently reviewed and extracted data, evaluating bias risk according to predefined criteria. Meta-analysis was performed using RevMan 5.4 software.
*Results:* Inclusive of 20 studies involving 1561 individuals with PSD, the meta-analysis revealed a significant difference in favor of five-element music therapy for relieving depression (standardized mean difference [SMD] = −1.07, 95% confidence interval [CI]: −1.34 to −0.81, $P < 0.00001$), improving daily living abilities (SMD = 2.49, 95% CI 1.00 to 3.98, $P < 0.00001$), and elevating serum 5-hydroxytryptamine(5-HT) levels (SMD = 0.87, 95% CI 0.56 to 1.17, $P < 0.00001$).
*Conclusion:* Five-element music therapy demonstrated efficacy in improving depressive symptoms, daily living skills, and serum 5-HT levels in individuals experiencing PSD.
The review was registered on International Prospective Register of Systematic Reviews (registration number CRD 42022332282).

## 1. Introduction

Stroke is the second leading cause of global mortality, constituting 11.8% of all deaths. It ranks third as a prevalent cause of disability, accounting for 4.5% of all disability-adjusted life years (DALYs) [1]. Post-stroke depression stands out as a prevalent complication following a stroke, presenting a dynamic course with occurrences at any post-stroke period. The highest risk manifests within the first year, resulting in a cumulative incidence of approximately 31% over 5 years [2,3]. The trajectory of post-stroke depression involves spontaneous alleviation in some patients, balanced by the emergence of new cases, maintaining a stable total incidence at approximately 30% [3] over an extended period.

Post-stroke depression amplifies the risk of mortality in stroke survivors by 50% [4], significantly impacting their quality of life. It hampers the recovery of limb function, social engagement, and cognitive abilities, consequently elevating disability rates. Stroke survivors with depression also face a 1.49 times higher risk of stroke recurrence compared to non-depressed counterparts [5], imposing

* Corresponding author.
*E-mail address:* 18981883967@163.com (X. An).

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a substantial healthcare burden on both individuals and society. Therefore, contemporary guidelines underscore the importance of heightened clinical vigilance, screening, and treatment for PSD [6].

Current clinical approaches to post-stroke depression predominantly involve antidepressant treatment, necessitating courses lasting 6 months to 1 year. However, this prolonged duration increases the likelihood of drug-related adverse reactions [6]. In contrast, five-element music therapy is a promising complementary treatment characterized by simplicity, safety, and effectiveness. It further demonstrates efficacy in enhancing language function and daily activities, and alleviating depression [7,8].

Five-element music therapy aligns with the principles of Chinese Traditional Medicine, utilizing the five musical tones of Jue, Zhi, Gong, Shang, and Yu to address various diseases [9]. Jue aligns with the "mi" sound, representing the essence of "wood" in the five-element system; it exudes a lively and cheerful style. Zhi, corresponding to the "So" sound, is associated with the "Fire" element, emanating warmth and cheerfulness. The Gong tone, tied to the "Do" sound and "Earth" element, carries a dignified style reminiscent of the solidity and richness of the land. Linked with the "re" sound and "metal" element, Shang possesses a powerful and majestic quality. Yu, harmonizing with the "la" sound and "water" element, embodies a soft, gentle, and flowing water-like essence [10]. Reports suggest that five-element music therapy plays a crucial role in ameliorating depressive states [11,12] and enhancing the daily life capabilities of individuals experiencing post-stroke depression [13,14]. However, the current literature lacks consistent and reliable evidence supporting the effectiveness of five-element music therapy in post-stroke depression (PSD) due to variations in quality. The efficacy and safety of this therapy in PSD remains uncertain. Therefore, this study aims to objectively analyze the clinical impact of five-element music therapy on patients with PSD, utilizing a rigorous systematic analysis methodology to establish credible evidence for clinical applications.

## 2. Materials and methods

### *2.1. Search strategy and eligibility criteria*

The meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [15], with a pre-established registered protocol (PROSPERO: CRD42022332282).

Two independent investigators conducted article retrieval from the following databases: PubMed, The Cochrane Library, Embase, Web of Science, Science Direct, Chinese National Knowledge Infrastructure (CNKI), WanFang Data Knowledge Service Platform (WanFang), Chinese BioMedical Database (CBM), and Weipu Information Chinese Periodical Service Platform (VIP). The search spanned from the inception of each database to February 15, 2022, considering only Chinese and English publications. MeSH terms and keywords were combined for the search. English terms included: (Stroke (MeSH) OR Apoplexy OR Cerebrovascular Accident × OR CVA*) AND (Five-element music OR Five lines music OR Five-tone therapy OR Five elements tonal OR Chinese traditional music) AND (Depressed OR Depression OR Psychology). For Chinese databases, the search terms were: (中风OR卒中OR脑梗*OR脑缺血OR脑血管意外) AND (五行音乐OR五音OR五行OR古琴音乐OR羽调OR角调OR宫调OR微调OR商调) AND (抑郁OR抑郁症OR忧郁OR情绪障碍). Additionally, we examined the reference lists of included literature for potential eligible trials. The PubMed search strategy was as follows:

#1 Stroke [Mesh] OR Apoplexy [Title/Abstract] OR Cerebrovascular Accident* [Title/Abstract] OR CVA* [Title/Abstract]
#2 Five-Element Music [Title/Abstract] OR Five lines music [Title/Abstract] OR Five tone therapy [Title/Abstract] OR Five elements tonal [Title/Abstract] OR Chinese traditional music [Title/Abstract]
#3 Depressed [Title/Abstract] OR Depression [Title/Abstract] OR Psychology [Title/Abstract]
#4 #1 AND #2 AND #3

## 3. Study inclusion and exclusion criteria

### *3.1. Inclusion criteria*

Participant types: Patients diagnosed with cerebrovascular disease or stroke through MRI or cranial CT, meeting the diagnostic criteria for PSD assessed by the Hamilton Rating Scale for Depression (HAMD) or the Self-Rating Depression Scale (SDS).

The HAMD and SDS, widely used in clinical settings and research for post-stroke depression evaluation, exhibit greater validity and sensitivity than the 9-item Patient Health Questionnaire (PHQ-9) [16]. A HAMD score >8 in the past week indicates depression [17]. The SDS, comprising 20 items with scores ranging from 25 to 100, categorizes scores as normal (50), mildly depressed (50–59), moderately depressed (60–69), and severely depressed (70) [18]. Patients included in this study had a HAMD score >8 or an SDS scale score >50.

Intervention types: The intervention group underwent five-element music therapy, possibly supplemented with other interventions, such as standard care. The control group received various comparator treatments, including routine care and psychological counseling.

Outcome types: Primary outcome: depression (including HAMD-17 and HAMD-24); secondary outcomes: daily living ability (including Activities of Daily Living, ADL; Barthel Index, BI). Additional outcome: 5-HT.

Study Design: Randomized controlled trials (RCTs) were included, with language restrictions on publication limited to Chinese and English.

### 3.1.1. *Exclusion criteria*

(i) Newspaper articles or conference papers.
(ii) Studies lacking sufficient data (untranslatable or unresponsive authors upon contact).

### 3.1.2. *Study selection and data extraction*

Two trained investigators independently conducted literature screening and quality evaluation, utilizing Endnote X9 software. Data extraction, aligned with predefined inclusion and exclusion criteria, underwent cross-verification. Extracted information encompassed the first author, publication country, publication year, participant characteristics (sex and age), sample size, intervention characteristics (type, duration, frequency, and assessment period), and outcomes. Discrepancies were resolved through discussion or consultation with a third investigator.

The risk of bias in the included literature was appraised based on the Cochrane Reviewer Handbook 5.3 quality assessment criteria [19]. Seven risk bias assessment items included sequence generation, allocation concealment, blinding of participants and outcome assessors, completeness of outcome data, selective reporting, and other biases. Each bias risk item was categorized as "low risk of bias," "high risk of bias," or "unclear risk of bias."

### 3.1.3. *Data synthesis and statistical analysis*

RevMan 5.4 software facilitated data analysis, deploying mean differences (MD) and 95% confidence intervals (CIs) for continuous

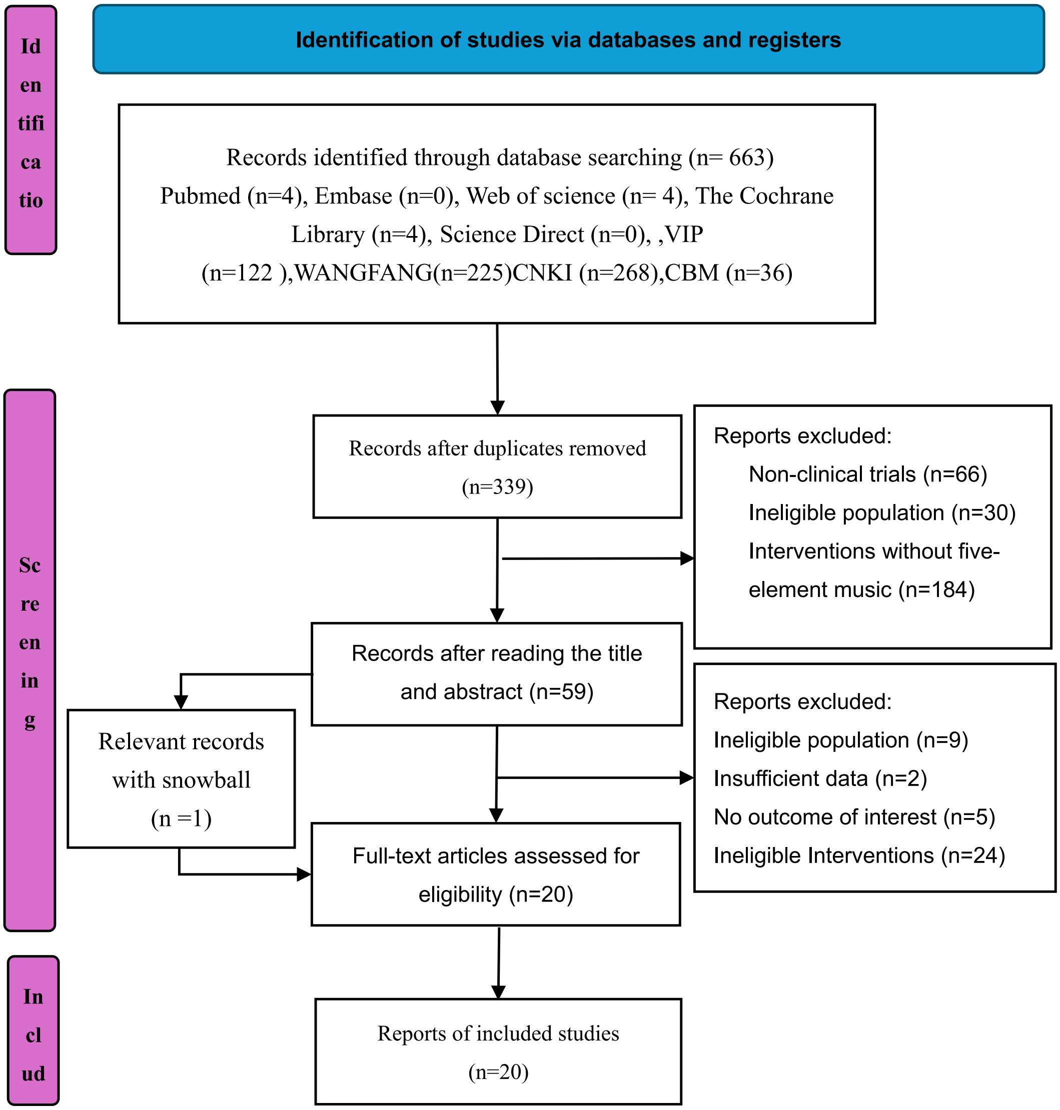


**Fig. 1.** Flow chart illustrating the study selection process.

**Table 1**
Overview of included studies.

| Author, year | Country | Sample size | Age (years) | Sex (M/F) | The course of disease (day) | Intervention | Frequency and duration | Evaluation of time | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Zhang Yao 2018 | China | C:21<br>E1:21<br>E2:21 | C:49.98 ± 7.60<br>E1:50.02 ± 7.87<br>E2:49.23 ± 8.14 | C:10/11<br>E1:13/8<br>E2:12/9 | C:14.02 ± 2.53<br>E1:14.18 ± 2.60<br>E2:13.93 ± 2.71 (weeks) | C: Acupuncture<br>E1: Five-element music therapy<br>E2: Acupuncture + Five-element music therapy | 30min/time,1time/d<br>6 times/W, 6 weeks | Before, after intervention | ①③ |
| Xie Hongzhi 2020 | China | C:50<br>E:50 | 72.67 ± 10.05 | C:28/22<br>E:28/22 | – | C: UC<br>E: UC + Five-element music therapy | 30min/time，2times/d<br>7 times/W, 8 weeks | Before, after intervention | ⑥ |
| Wang Ning 2019 | China | C:30<br>E1:30<br>E2:30 | C:48.56 ± 7.82<br>E1:50.05 ± 6.89<br>E2:49.53 ± 2.23 | C:12/18<br>E1:15/15<br>E2:13/17 | C:13.74 ± 1.79<br>E1:14.56 ± 2.40<br>E2:14.60 ± 2.23 (weeks) | C: Acupuncture<br>E1: Five-element music therapy<br>E2: Acupuncture + Five-element music therapy | 30min/time,1time/d<br>5 times/W, 4 weeks | Before, after intervention | ①③ |
| Wang Jingyi 2021 | China | C:40<br>E:40 | C:58.4 ± 7.2<br>E:60.1 ± 6.3 | C:22/18<br>E:24/16 | C:7.1 ± 1.9<br>E:6.3 ± 2.2 (months) | C: Sertraline Hydrochloride<br>E: Sertraline Hydrochloride + Five-element music therapy | 30min/time,2times/d<br>7 times/W, 12 weeks | Before, after intervention | ①⑥ |
| Pei Lei 2020 | China | C:60<br>E:60 | C:67.30 ± 5.73<br>E:67.33 ± 5.94 | C:33/27<br>E:35/25 | C:3.45 ± 4.38<br>E:3.62 ± 4.37 (months) | C: Flupentixol and Melitracen<br>E: Flupentixol and Melitracen + Five-element music therapy | 30min/time,1time/d<br>7 times/W, 8 weeks | Before, after intervention | ①④⑤ |
| Lin Yi 2018 | China | C:40<br>E:40 | C:64.40 ± 6.47<br>E:66.91 ± 7.50 | C:22/18<br>E:25/15 | C:33.07 ± 12.05<br>E:33.38 ± 11.00 | C: UC<br>E: UC + Five-element music therapy | 40–60min/time,1time/d<br>7 times/W, 4 weeks | Before, after intervention | ③⑥ |
| Li Zhuangmiao 2017 | China | C:35<br>E1:35<br>E2:35 | C:65.60 ± 14.45<br>E2:63.25 ± 14.45<br>E2:66.58 ± 13.13 | C:24/11<br>E1:25/10<br>E2:23/12 | C:69.22 ± 50.13<br>E1:71.03 ± 52.42<br>E2:68.18 ± 52.13 | C: UC<br>E1: UC + Western Music<br>E2: UC + Five-element music therapy | 60min/time,1time/d<br>7 times/W, 4 weeks | Before, after (2w,4w) | ①④ |
| Le Lizhen 2013 | China | C:75<br>E:75 | C:55.6 ± 11.2<br>E:56.8 ± 10.4 | C:39/36<br>E:37/38 | – | C: UC<br>E: UC + Five-element music therapy | 30min/time,1time/d<br>6 times/W, 4 weeks | Before, after intervention | ① |
| Lin Facai 2017 | China | C:30<br>E1:32<br>E2:30 | C:72.93 ± 10.37<br>E1:69.66 ± 10.41<br>E2:68.80 ± 11.53 | C:10/20<br>E1:17/15<br>E2:17/13 | – | C: Acupuncture<br>E1: Sertraline Hydrochloride<br>E2: Acupuncture + Five-element music therapy | 20min/time,2time/d<br>5 times/W, 3 weeks | Before, after intervention | ① |
| Hu Jing 2014 | China | C:30<br>E:30 | C:59.16 ± 6.68<br>E:59.43 ± 5.76 | C:22/8<br>E:20/10 | C:46.23 ± 11.41<br>E:45.36 ± 9.99 (weeks) | C: UC<br>E: UC + Five-element music therapy | 30min/time,1time/d<br>7 times/W, 4 weeks | Before, after intervention | ⑥ |
| Duan Xiaoyan 2016 | China | C:25<br>E:25 | C:56.3 ± 8.6<br>E:54.9 ± 9.3 | C:9/16<br>E:11/14 | C:30.1 ± 15.2<br>E:28.7 ± 17.5 | C: UC<br>E: UC + Five-element music therapy | 30min/time,1time/d<br>7 times/W, 3 weeks | Before, after intervention | ① |
| Tang Chenghua 2014 | China | C:30<br>E1:30<br>E2:30 | C:58.97 ± 7.09<br>E1:58.83 ± 7.34<br>E2:58.53 ± 6.77 | C:16/14<br>E1:18/12<br>E2:13/17 | – | C: TCM<br>E1: Fluoxetine<br>E2: TCM + Five-element music therapy | 30min/time,2time/d<br>7 times/W, 8 weeks | Before, after intervention | ①⑤ |

(*continued on next page*)

**Table 1** (*continued*)

| Author, year | Country | Sample size | Age (years) | Sex (M/F) | The course of disease (day) | Intervention | Frequency and duration | Evaluation of time | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Luo Jinfa 2020 | China | C:30<br>E:30 | C:51.55 ± 9.10<br>E:50.48 ± 7.15 | C:16/14<br>E:17/13 | C:12.64 ± 5.92<br>E:13.75 ± 6.95 (weeks) | C: Acupuncture<br>E: Acupuncture + Five-element music therapy | 30min/time,1time/d<br>7 times/W, 8 weeks | Before, after intervention | ①⑥ |
| Wang Min 2018 | China | C:40<br>E:40 | C:58.9<br>E:59.3 | C:24/16<br>E:23/17 | C:14~90<br>E:15-90 | C: Acupuncture<br>E: Acupuncture + Five-element music therapy | 30min/time,1time/d<br>5 times/W, 4 weeks | Before, after intervention | ①⑥ |
| Tao Chonghua 2015 | China | C:35<br>E:35 | – | C:29/6<br>E:23/12 | – | C: TCM<br>E: TCM + Five-element music therapy | 30min/time,1time/d<br>7 times/W, 6 weeks | Before, after intervention | ② |
| Sun Ruili 2020 | China | C:45<br>E:45 | C:53 ± 6<br>E:54 ± 5 | C:38/7<br>E:37/8 | C:5.5 ± 1.4<br>E:5.3 ± 1.6 (weeks) | C: UC<br>E: UC + Five-element music therapy | 30min/time,2time/d<br>7 times/W, 8 weeks | Before, after (4w,8w) | ①③ |
| Chen Yunfeng 2017 | China | C:36<br>E:36 | C:51.83 ± 4.87<br>E:52.21 ± 5.03 | C:21/15<br>E:19/17 | C:6.35 ± 1.69<br>E:5.83 ± 2.09 (months) | C: BaDuanJin<br>E: BaDuanJin + Five-element music therapy | 30min/time,2time/d<br>40 days | Before, after intervention | ② |
| Yang Jinmei 2019 | China | C:32<br>E1:32<br>E2:32 | 68 | 45/51 | – | C: Tongue Exercises of TCM<br>E1: Sertraline Hydrochloride<br>E2: Tongue Exercises of TCM + Five-element music therapy | 20min/time,2time/d<br>21 days | Before, after intervention | ①⑤ |
| Yang Hongyan 2016 | China | C:68<br>E:69 | C:61.91 ± 7.76<br>E:62.81 ± 6.99 | C:42/26<br>E:37/32 | – | C: UC<br>E: UC + Five-element music therapy | 30min/time,1time/d<br>5 times/W, 2 weeks | Before, after intervention | ① |
| Huang Weiling 2021 | China | C:30<br>E1:30<br>E2:30 | C:63.51 ± 6.09<br>E1:64.14 ± 5.47<br>E2:62.99 ± 6.49 | C:15/15<br>E1:17/13<br>E2:14/16 | C:67.71 ± 43.72<br>E1:65.13 ± 42.7<br>E2:68.77 ± 44.21 | C: Acupuncture<br>E1: Fluoxetine<br>E2: Acupuncture + Five-element music therapy | 30min/time,1time/d<br>6 times/W<br>, 8 weeks | Before, after intervention | ① ⑥ |

E: Experimental; C: Control; W: week; UC: Usual Care; TCM: Traditional Chinese Medicine.
① HAMD-17; ②HAMD-24; ③Barthel Index BI; ④Serum 5-HT; ⑤Activities of Daily Living ADL; ⑥Self-rating depression scale SDS.

variables. Standardized mean differences (SMD) were utilized when measurement means significantly differed or were on distinct scales. Meta-analyses were conducted for trials with similarities in participants, controls, interventions, outcomes, measures, and study designs. Quantitative synthesis of bulk data was achieved through descriptive counting, while qualitative analysis addressed data unsuitable for pooling analysis.

Statistical heterogeneity was assessed using I-square (I2), following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. An $I^2$ value > 50% indicated substantial heterogeneity [20]. In significant heterogeneity (I2 ≥ 50%), a random-effects model was employed for data pooling; otherwise, a fixed-effect model was applied.

When data were available, a sensitivity analysis was conducted to explore the impact of randomized trial type and quality. Subgroup analysis was performed as needed to investigate potential sources of heterogeneity. A funnel plot was generated to explore possible publication bias if more than ten trials were included in a meta-analysis. The significance level for all analyses was set at $P <$ 0.05.

## 4. Results

### 4.1. Search results

The PRISMA flow diagram depicts the detailed screening process (Fig. 1).

The initial search yielded 663 studies, with 324 excluded after removing duplicates. Careful screening of the titles and abstracts of the remaining 339 studies led to the selection of 59 of them based on inclusion criteria. Of these, 40 articles were excluded for the following reasons: ineligible population (n = 9), insufficient data (n = 2), no outcome of interest (n = 5), and ineligible interventions (n = 24). An additional article was identified by tracking the references included in the studies. In total, 20 studies [13,14,21–38] met the inclusion criteria and were utilized for the meta-analysis.

#### 4.1.1. Characteristics of the included studies

Table 1 summarizes the characteristics of the included studies.

All studies were conducted in China; 19 studies [13,14,21–26,28–38] were reported in Chinese-language journals, and one study [27] was reported in an English-language journal. A total of 1743 individuals with PSD participated, with 993 in the intervention group and 750 in the control group. Sample sizes ranged from 50 to 150, and interventions lasted between 2 and 12 weeks. Among the included studies, only seven explicitly stated that enrolled patients had mild to moderate depression. However, other studies did not provide such details, and therefore, the possibility of including patients with severe depression in the analysis cannot be ruled out. All sessions lasted between 20 and 60 min. Thirteen studies [13,21–23,25,28–33,35,36] used a two-arm parallel-group RCT design, whereas seven studies [14,24,26,27,34,37,38] used a three-arm RCT design. Homogeneous groupings constituted the sample populations, ensuring reduced bias throughout the review. The frequency of interventions varied, with once [13,22–26,28,29,31,33,34,36,38] or twice [14,27,30,32,35,37] a day. Most interventions were conducted seven times weekly, whereas some were conducted five or six times weekly. All studies assessed the effect of five-element music after the intervention, with only two studies examining the impact in the second [26] and fourth [30] weeks. The included studies did not have follow-ups to examine long-term outcomes.

No RCT reported any adverse effects of music therapy, suggesting its safety for PSD treatment.

## 5. Methodological quality

Figs. 2 and 3 illustrate the Cochrane risk of bias for the included studies.

By the Cochrane Reviewer's Handbook quality evaluation criteria, the quality of the literature was assessed based on seven factors. The results were summarized as follows: Six studies [22,25,31,33,35,37] utilized randomization without specifying the method,

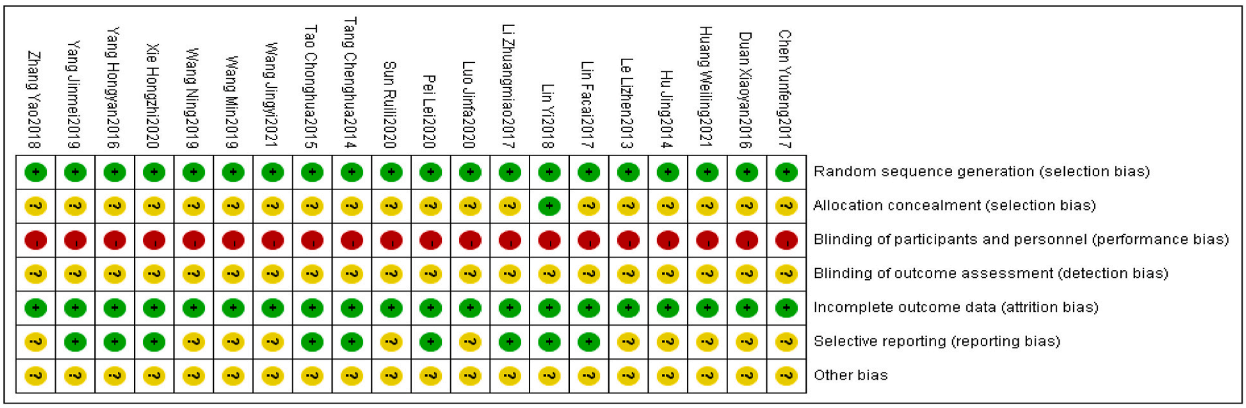


**Fig. 2.** Risk of bias summary.

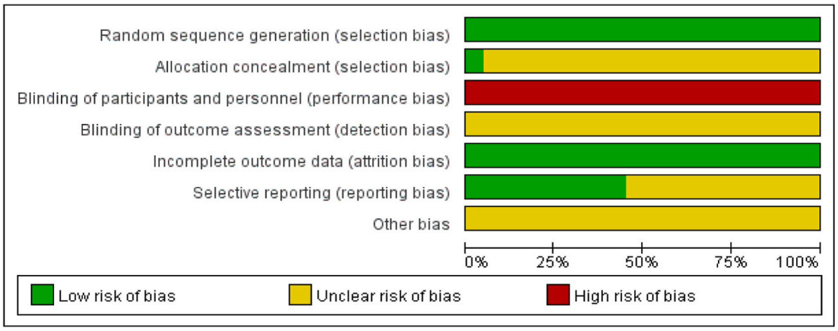


**Fig. 3.** Risk of bias summary.

raising concerns about its reliability. One study [23] employed a randomized lottery, while others used random number tables for generation; only one study [13] specified using opaque envelopes for concealment. The lack of assurance in assignment concealment make investigators aware of individual participant group assignments, potentially overestimating intervention effectiveness. Studies lacking allocation concealment may magnify the intervention's effect by 30%–40% [39]. Blinding was impractical due to the intervention's specificity, and none of the included studies implemented outcome assessor blinding. Given the unique nature of the intervention, five-element music therapy cannot employ blinding for patients or implementers; however, none of the studies used

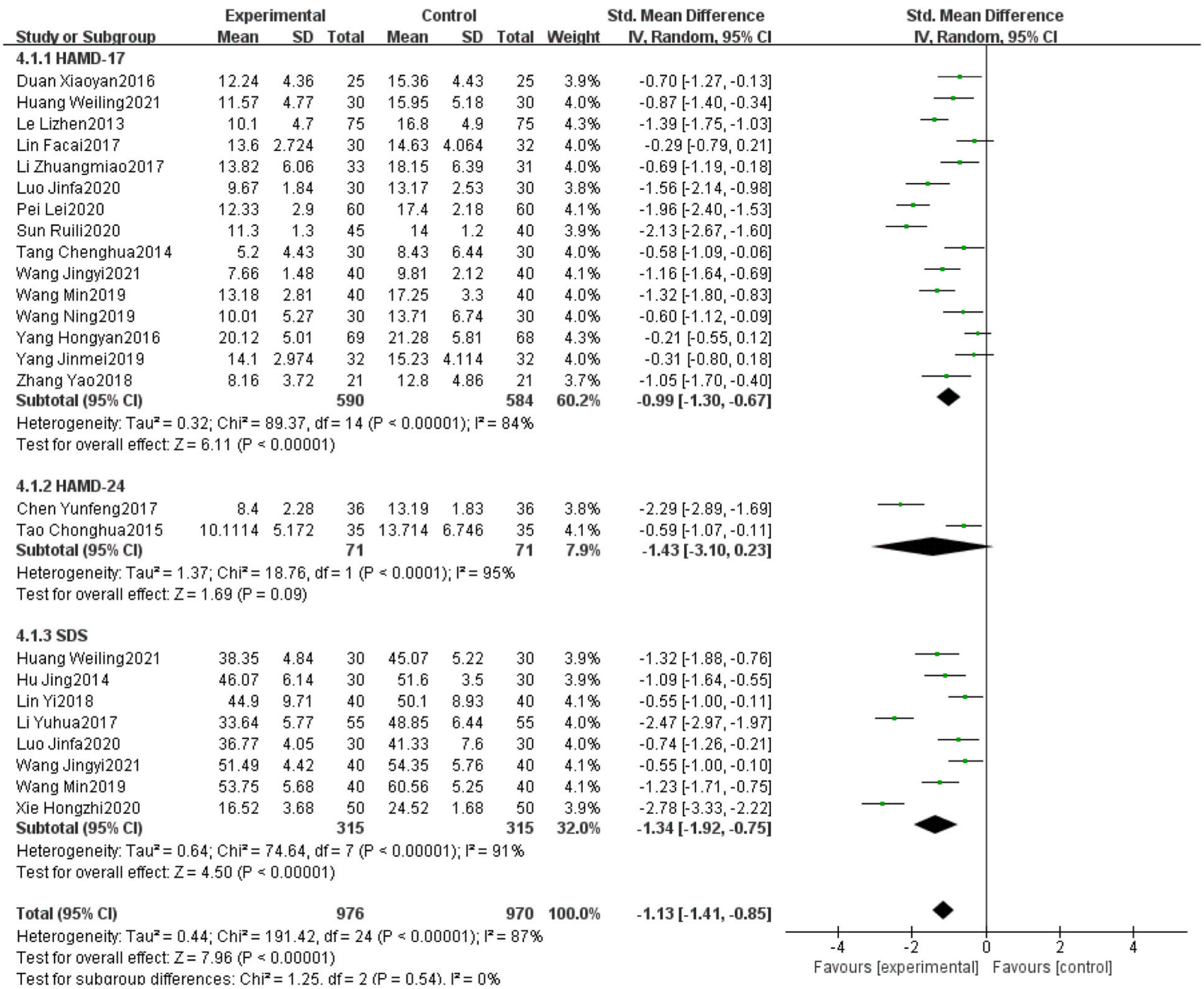


**Fig. 4.** Forest plot depicting the impact of five-element music therapy on depression.

blinding for evaluators, especially when the outcome primarily relates to subjective results, potentially introducing bias into the results. Nine studies [13,14,26,27,29,31,35–37] reported dropout and loss reasons during follow-up, while the remaining studies did not provide such information. Moreover, when participants dropped out, the researchers did not employ intention-to-treat analysis, which addresses missing data in both trials. Failure to use intention-to-treat analysis may significantly lead to overestimating the treatment effect if participants drop out due to dissatisfaction with the treatment results.

## 5.1. Effectiveness analysis

Impact of five-element music therapy on PSD patients' depressive status.

Twenty [13,14,21–38] RCTs involving 1556 patients with PSD examined patients' depression status using three measures, namely the HAMD-17 scale, the HAMD-24 scale, and the SDS scale. Due to scale variations, an SMD analysis was employed. The meta-analysis demonstrated a significant improvement in patients' depressive status with five-element music therapy utilizing a random-effects model analysis ($I^2 = 86\%$, $P < 0.00001$) (SMD = −1.07, 95% CI -1.34 to −0.81, $P < 0.00001$) (Fig. 4).

Subgroup analyses were conducted based on various measurement scales. Fifteen studies utilized the HAMD-17 scale [14,22,24–30,32–34,36–38] to assess the depressed status of 1174 patients with PSD, revealing heterogeneity among studies ($I^2 = 79\%$, $P < 0.00001$). The analysis demonstrated using a random-effects model that the intervention group exhibited significantly lower HAMD-17 ratings compared to the control group (MD = −3.34, 95% CI -4.15 to −2.35) ($P < 0.00001$).

Two studies [21,31] employed the HAMD-24 scale to measure the depressive status of 142 patients with PSD, finding no heterogeneity between studies ($I^2 = 0\%$, $P = 0.43$). Using a fixed-effects model, the findings indicated significantly lower HAMD-24 scores in the intervention group compared to the control group (MD = −4.67, 95% CI -5.57 to −3.76) ($P < 0.00001$).

Seven studies [13,23,24,28,32,33,35] employed SDS scores to measure the depressive status of 520 patients with PSD and showed heterogeneity ($I^2 = 69\%$, $P = 0.003$). The results of the random-effects model revealed a significant difference in SDS scores compared to controls (MD = −5.82, 95% CI -7.42 to −4.23, $P < 0.00001$).

### 5.1.1. The impact of five-element music therapy on PSD patients' daily life

Six studies [13,14,29,30,34,37,38] used the BI and ADL measures to evaluate the activities of daily living ability of 516 patients with PSD. A random-effects model analysis was performed ($I^2 = 97\%$, $P < 0.00001$); the meta-analysis demonstrated a significant improvement in the activities of daily living ability (SMD = 2.49, 95% CI 1.00 to 3.98) with five-element music therapy ($P < 0.00001$) (Fig. 5).

Subgroup analyses based on various measurement scales revealed that two studies [14,29] employed ADL scores to measure daily living capacity in 244 patients with PSD, showing inter-study heterogeneity ($I^2 = 95$ %, $P < 0.00001$). The results indicated a significant difference in ADL scores compared to the control group (MD = 14.38, 95% CI 3.02 to 25.73, $P = 0.01$).

Four studies [13,30,34,38] employed the BI to assess daily living capacity in 271 patients with PSD, revealing inter-study heterogeneity ($I^2 = 84$ %, $P = 0.0003$) using a random-effects model. The results demonstrated a significant difference in the BI compared to the control group (MD = 9.69, 95% CI 5.87 to 13.52, $P < 0.00001$).

### 5.1.2. The impact of five-element music therapy on serum 5-HT in patients with PSD

Two studies [25,29] comprising 184 patients with PSD who were evaluated for serum 5-HT levels were analyzed, and the results indicated heterogeneity among studies ($I^2 = 39\%$, $P = 0.20$) using a fixed-effects model. The results revealed a significant improvement in the PSD patients' serum 5-HT levels (SMD = 0.87, 95% CI 0.56 to 1.17) with five-element music therapy ($P < 0.00001$) (Fig. 6).

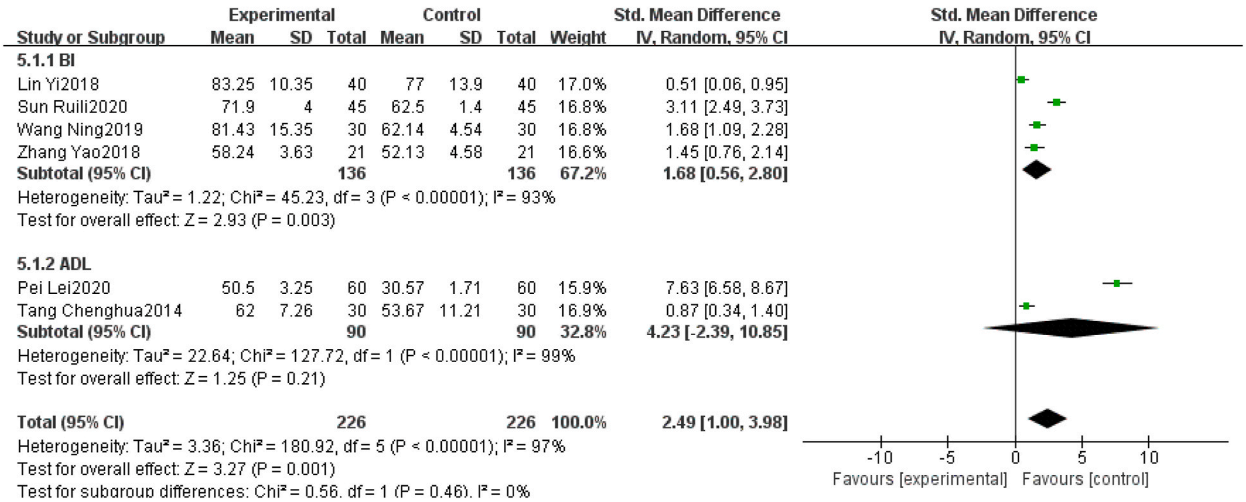


**Fig. 5.** Forest plot depicting the impact of five-element music therapy on activities of daily living.

## 6. Sensitivity analysis and publication bias

### 6.1. Sensitivity analysis

The Cochrane Handbook categorizes meta-analysis heterogeneity into: clinical, methodological, and statistical heterogeneity. Clinical heterogeneity involves variation due to differences in participants, interventions, and study endpoints. Methodological heterogeneity relates to variations in trial design and quality, such as differences in blinding and allocation concealment or inconsistencies in the definition and measurement of outcomes during the trial [19].

Sensitivity analysis was conducted on the included studies through item-by-item exclusion. Lin FC et al. [27], Yang JM et al. [37], Yang HY et al. [36], Wang JY et al. [32], Pei L et al. [29], and Le LZ et al. [25] were identified as sources of heterogeneity in HAMD-17 scores, with no heterogeneity among studies after exclusion ($I^2 = 0$ %, $P = 0.46$). The results of a fixed-effects model indicated significantly lower HAMD-17 scores in the experimental group than in the control group (MD = −3.11, 95% CI -3.53 to −2.70, $P <$ 0.00001) (Appendix A, Fig. 1). The difference in interventions could have contributed to the heterogeneity in these studies. Most of the included literature adopted once-a-day interventions, whereas these two researchers used twice-a-day interventions, potentially explaining the source of heterogeneity. The heterogeneity in Pei L et al. [29] study may be associated with the chosen intervention time. In comparison, the variance in the Yang HY et al. [36] study could be linked to the intervention duration. Yang HY et al. study has a shorter intervention period of only 2 weeks. In the study by Le LZ et al., no significant clinical heterogeneity was identified. Therefore, this observation was attributed to the relatively early publication date of the study.

In the SDS score subgroup, a sensitivity analysis identified the studies by Xie HZ et al. [35] and Wang JY et al. [32] as sources of heterogeneity. No heterogeneity was observed after excluding two studies ($I^2 = 0\%$, $P = 0.76$). The results of the fixed-effects model indicated a significant decrease in SDS scores compared to the control group (MD = −5.97, 90% CI -7.21 to −4.73, $P < 0.00001$) (Appendix A, Fig. 2). In Xie HZ et al. [35] study, the source of heterogeneity could be related to the age of the participants, with an average age of 72.67 ± 10.05 years old, which was significantly higher than in other studies. The average age of the patients included in Wang N's [34] study was 48.56 ± 7.82 years. The source of heterogeneity in Wang JY et al. [32] study may be linked to the course of stroke included in the patients, as the disease duration in Wang JY et al. study was approximately 7 months. In contrast, other studies had patients with a stroke duration of approximately 1–3 months.

In the BI subgroup, a sensitivity analysis revealed that the studies by Wang N et al. [34] and Sun RL et al. [30] were the sources of heterogeneity. No heterogeneity was observed after excluding these two studies ($I^2 = 0\%$, $P = 0.96$). The fixed-effects model showed a considerable elevation in the BI compared to the control group (MD = 6.13,95% CI 3.87 to 8.40, $P < 0.00001$) (Appendix A, Fig. 3). In Sun RL et al. [30] study, the use of twice-a-day interventions, unlike the once-a-day interventions in most included literature, could be the source of heterogeneity. In Wang N et al. [34] study, despite speculation that heterogeneity might arise from methodological and statistical differences, the exact source of this variance could not be precisely identified.

Due to the limited number of studies in both the ADL and 5-HT subgroups, a sensitivity analysis using the one-by-one exclusion method could not be conducted.

After excluding the literature with substantial heterogeneity, the results remained consistent with the previous findings, indicating the stability of the meta-analysis results.

#### 6.1.1. Publication bias

A funnel plot analysis of the gathered literature on the impact of five-element music therapy on depressive status in patients with PSD indicated publication bias, as most studies clustered in the upper-middle region and displayed asymmetry to the left and right (Fig. 7).

## 7. Discussion

### 7.1. Five-element music therapy demonstrates efficacy in alleviating depression and enhancing daily living abilities

The HAMD is available in three versions: HAMD-17, HAMD-21, and HAMD-24. The HAMD-17 is commonly used to assess the intensity of depressive symptoms, whereas the HAMD-21 and HAMD-24 evaluate the pathological symptoms of depression [40]. The study revealed significant reductions in patients' HAMD-17, HAMD-24, and SDS scale scores with five-element music therapy, suggesting its effectiveness in alleviating the depressive state and pathological symptoms in patients with PSD.

Contemporary medicine posits that music reduces unpleasant emotions by increasing the volume of gray matter in the brain's

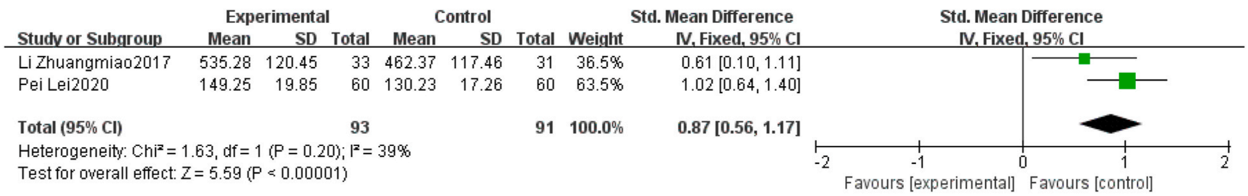


**Fig. 6.** Forest plot showing the effect of five-element music therapy on 5-HT.

limbic region [12] and triggering the release of catecholamines and cytokines. It further activates the dopaminergic midbrain limbic system [41], influencing the nucleus accumbens, which regulates emotions. This activation increases extracellular dopamine, resulting in positive emotions in patients [41].

The BI and ADL scales are standard tools for evaluating daily living abilities in patients with PSD, with higher scores indicating a more remarkable ability to perform everyday tasks. The study demonstrated that the five-element music therapy significantly enhances the everyday life abilities of patients with PSD. According to modern medicine, music's autoregulatory impact induces broad activation of various brain networks, increasing blood flow to the medial cerebral arteries and enhancing patient mobility. Furthermore, music promotes neuroplasticity, with mechanisms including neuronal hypertrophy, increased neuronal cell volume, and alterations in vascular or glial compartments. Stimulation of the dopaminergic midbrain limbic system by music may improve patients' executive function and motivation [41].

Five-element music therapy represents a fusion of contemporary music and traditional Chinese medicine, embodying a distinctive therapeutic approach within traditional Chinese medicine that addresses ailments through syndrome distinction and promotes overall well-being based on the principles of the principles of the five elements, five internal organs, five sounds, and five spirits. Post-stroke depression, attributed to deficiencies in liver dispersion, spleen transportation, heart assistance, and spirit loss [11], aligns with the traditional Chinese medicine's perspective of visceral Yin and Yang imbalance—a consequence of various pathogenic factors disrupting the body's equilibrium and leading to pathological changes [40].

According to the Yellow Emperor's Classic of Internal Medicine, the interplay of five elements, five tones (Jue, Zhi, Gong, Shang, and Yu), five seasons, five changes, five organs (liver, heart, spleen, lungs, and kidneys), and five emotions (anger, happiness, anxiety, sadness, and fear), intricately connects with the five-element theory [9]. For instance, the Jue tone, associated with wood properties, regulates liver function, promoting Qi circulation, liver drainage, and prevention of Qi obstruction [42].

Five-element music therapy employs dialectical treatment to harmonize the Qi and blood, facilitating their transmission and maintaining dynamic organ balance. This approach alleviates depression and enhances daily activities [11].

From a modern scientific standpoint, each organ resonates at specific frequencies aligned with the five-element music theory [9], a concept well-established in physical acoustics with international measurement standards.

Furthermore, scientific studies indicate that music therapy, including the five-element approach, reduces serum cortisol levels and inhibits cardiovascular stress [43]. Given the link between elevated cortisol levels in patients with stroke and increased infarct volume, incorporating the five-element music therapy may contribute to reducing depressive states, lowering the risk of adverse outcomes, and improving overall prognosis [44].

#### *7.1.1. The impact of five-element music therapy on serum 5-HT levels remains debatable*

5- HT, a crucial neurotransmitter in the central nervous system, is strongly linked to various physiopathological functions, including mood regulation, sleep, appetite, pituitary endocrine function, intuitive impairment, somatic movement, and cardiovascular regulation. It plays a role in neuronal remodeling through cortico-hippocampal synaptic connections and contributes to increased neuron numbers in significant brain locations, including the dentate gyrus of the hippocampus [45]. Changes in 5-HT levels are strongly associated with depressive symptoms, with studies indicating lower plasma and cerebrospinal fluid 5-HT levels in individuals with PSD compared to those with stroke alone. This observation may be attributed to infarct lesions obstructing the central 5-HT pathway [46]. Neuronal cell bodies of 5-HT in the lower brainstem, innervated by limbic and prefrontal cortices, influence mood regulation. Infarct lesions impairing monoamine neurons in the midbrain and brainstem may decrease the bioavailability of monoamine neurotransmitters such as 5-HT, norepinephrine (NE), and dopamine (DA), potentially leading to depression [47]. Furthermore, overexpression of 5-HT1A self-receptors in the presynaptic membrane, causing decreased 5-HT levels in the synaptic gap, is recognized as a contributing factor in depression [48].

The studies in this research employed serum 5-HT levels to assess the depressive state of patients, revealing a significant elevation in serum 5-HT levels with the application of five-element music therapy. This observation suggests that five-element music therapy effectively enhances serum 5-HT content among patients with PSD, thereby alleviating their depression symptoms.

## 8. Limitation

Limitations of this study include substantial variations in the types of control, the number and frequency of interventions, and the types of five-element music utilized across the included studies. Some studies employed TCM dialectic-based five-element music [21,24,25,27,29,30,32,33,37,38], while others used music based on patient preference [23] or predetermined tunings [14,26,28,31,35,36]. The diverse nature of interventions makes it challenging to evaluate their impact on clinical outcomes systematically. Due to this diversity, there is currently insufficient evidence to determine the effects of different types, numbers, and frequencies of interventions. Further research is warranted to identify the optimal intervention type, frequency, and quantity.

Secondly, this review exclusively incorporated Chinese and English literature, and despite comprehensive searching, incomplete literature retrieval remains possible. The publication bias, as indicated by the funnel plot, is a limitation of this study. Including 20 randomized controlled trials, characterized by varying intervention durations, modest sample sizes in certain studies, and a reliance on scales as outcome measures, underscores the need for larger sample sizes and more objective indicators.

## 9. Conclusions

In conclusion, five-element music therapy exhibits the potential to mitigate depression severity, alleviate pathological symptoms,

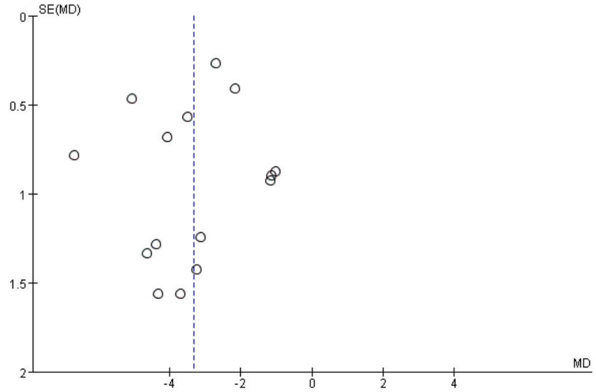


**Fig. 7.** Funnel plot assessing depression.

and enhance daily living skills in patients with PSD. However, the effectiveness of 5-HT as a precise measure of five-element music therapy's impact on the depressive status of patients with PSD requires further validation through high-quality studies.

While this review demonstrated the efficacy of five-element music therapy in improving depression and daily living abilities in PSD, its integration into clinical practice necessitates collaborative efforts from medical practitioners and researchers. Several unresolved issues merit attention.

Firstly, the effectiveness of five-element music therapy in diverse countries and its variation across cultural backgrounds remain uncertain. The absence of relevant data from foreign populations in this review hinders a reliable interpretation of this uncertainty. Therefore, future large-sample, multi-center clinical trials encompassing different population and cultural backgrounds are recommended to validate the effects of five-element music therapy on patients with PSD.

Secondly, systematic evaluation uncovered issues in some studies related to selecting five-element music, including varied repertoire modalities, a wide overall style range, and incomplete correspondence between repertoire style and modality, leading to a perplexing clinical classification of repertoire. In recent years, the absence of a standardized repertoire for five-element music, coupled with a limited number of compositions and the diverse age range of clinical patients, has impeded this therapeutic approach's broader application and development. Therefore, collaboration between professional musicians and medical practitioners is crucial to establishing a comprehensive and systematic music database. Keeping pace with societal advancements and evolving patient needs necessitates ongoing efforts to create new music that aligns with contemporary sensibilities, ensuring meaningful therapeutic outcomes for a diverse patient population. Establishing authoritative standards for classifying five-element music and including popular music in the repertoire is vital for the continued growth of this therapeutic modality.

Throughout this systematic review, it became evident that most studies relied on assessment scales as outcome indicators. While the reliability of these scales was verified, the potential for measurement bias remains. Leveraging modern technology to incorporate objective indicators, such as the impact of different music repertoires on patients, can enhance the application of five-element music in clinical settings and better serve the public.

## Author disclosure statement

The authors declare no personal or financial conflicts of interest. We thank the participating nurses and authors who provided original data for the meta-analysis.

## Data availability statement

All data supporting the findings of this study are available within the paper and its Supplementary Information.

## CRediT authorship contribution statement

**Zhong Kelong:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Xuemei An:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization. **Yun Kong:** Writing – review & editing, Visualization, Validation, Software, Methodology, Data curation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e26603.

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