

REVIEW ARTICLE

Comparative efficacy of non-pharmacological interventions on behavioural and psychological symptoms in elders with dementia: A network meta-analysis

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Email: huxiuying@scu.edu.cn**Abstract****Aim:** To explore the best non-pharmaceutical interventions for improving the behavioural and psychological symptoms in elders with dementia.**Design:** Bayesian network meta-analysis.**Methods:** A comprehensive electronic literature search was performed in five English databases and four Chinese databases to identify relevant randomized controlled trials (RCTs) that were published up to 31 October 2019.**Results:** A total of 41 RCTs were included in this network meta-analysis involving 5 different non-pharmacological interventions: therapeutic recreation (TC), reminiscence therapy (RT), behaviour therapy (BT), massage therapy (MT) and individualized nursing (IN). The results of network meta-analysis showed that individualized nursing was the best in improving depression, cognitive function, and activities of daily living of behavioural and psychological symptoms of dementia. Behaviour therapy was the best in improving anxiety symptoms. Reminiscence therapy was the best in improving neuropsychiatric symptoms.**KEYWORDS**

behavioural and psychological symptoms, dementia, network meta-analysis, non-pharmacological interventions

1 | INTRODUCTION

Dementia is a progressive neurodegenerative syndrome manifested by cognitive impairment, memory loss as well as behavioural and psychological disorders, which has posed a great burden on both human health and global economy. The global rising of life expectancy and an increasing proportion of elders in the population are the main reasons for worldwide population ageing (Heese, 2015). According to the World Alzheimer Report 2018, dementia affects about 50 million people and this number is expected to increase

to 152 million by 2050. Among patients with dementia, 60%–98% will develop behavioural and psychological symptoms of dementia (BPSD) (Finkel, 2000). BPSD is a wide spectrum of syndromes including mood disorders, depression, agitation, psychosis, sleep disturbances, anxiety, apathy, dysphoria, aberrant motor activity, hallucinations and delusions (Lyketsos et al., 2000).

The high incidence, poor prognosis, long course of the disease and serious adverse outcomes of BPSD have brought great burdens to patients with dementia and their families, particularly economic and social burdens (Beeri et al., 2002; Brodaty et al., 2014; Cerejeira

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et al., 2012; Savva et al., 2009; Wu et al., 2016). Given that the neuropathology and neurobiology of dementia remain indistinct, no consensus about aetiological treatments has been researched. Thus, alleviation of BPSD is the mainly medical intervention to improve the quality of patients' and caregivers' lives (Cumbo & Ligorì, 2014). Compared with the limitations and lack of safety of medications, non-pharmacological therapy is recommended as first-line treatment for BPSD.

Original research on non-pharmaceutical interventions for BPSD is diverse. The specific measures, implementation time and outcome indicators of each original research are different. It is impossible to know accurately whether different types of interventions are effective for BPSD. It is even more difficult to clarify the efficacy of various non-pharmaceutical interventions to improve BPSD. Due to the complication of broad interventions and the lack of head-to-head trials, it is impossible to synthesize present data on this issue depending on traditional pairwise meta-analysis method. Hence, we conducted this systematic review and hierarchical Bayesian Network meta-analysis, including only RCTs to provide comparative evidence and quantitative hierarchies on the efficacy of all available non-pharmacological therapies for elders with BPSD.

2 | METHODS

We conducted this network meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines extension statement for network meta-analysis (Hutton et al., 2015).

2.1 | Literature search strategy

We searched the following databases from inception until 31 October 2019: MEDLINE, EMBASE, EBM Reviews, Social Sciences Citation Index, Science Citation Index Expanded, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database, Wan Fang Data and Chinese Biomedical Literature Database. Further relevant publications were identified through the reference lists of the included publications. We also searched existing meta-analysis related to this topic and downloaded and read the original papers to avoid missing studies that met our inclusion criteria. Moreover, we contacted experts or communication authors in the field to obtain the documents found in the above search. For each database, the search strategy was personalized. The search used a combination of subject and free words for professional search. The search terms included dementia (dement*/Alzheimer*), intervention (arteriosclerotic encephalopathy*/binswanger*/horticultural therapy/behavior therapy/music/dance/sand play/environment* modif*/animal/pet/massag*/bodywork), BPSD (neuropsych*/behave*) and RCTs (RCT/trial).

2.2 | Eligibility criteria

The following inclusion criteria were observed: (a) Study subjects: Patients with BPSD, over 60 years old and regardless of sex; (b) Interventions: Patients in the intervention group underwent common non-pharmacological interventions for BPSD (therapeutic recreation [TC], reminiscence therapy [RT], behaviour therapy [BT], training of caregivers [TOC], physical environment modification [PEM], animal-assisted therapy [AAT], massage therapy [MT], therapeutic exercise [TE], individualized nursing [IN]). Definition of the interventions is shown in Table S2 (Xiaoxue & Dongmei, 2016; Corcoran & Gitlin, 1991; Cuevas et al., 2020; Dandan et al., 2017; Duisheng & Xiaoping, 2002; Goodarzi et al., 2016; Krasner, 1971; NHMRC, 2019; Shanshan & Jing, 2015; Viggo Hansen et al., 2006; Woods et al., 2018; Yakimicki et al., 2019); (c) Patients in the control group (CG) did not receive specific non-pharmacological interventions (blank controls); (d) Outcome indicators: main outcome indicator, neuropsychiatric inventory (NPI); secondary outcome indicators, neuropsychiatric inventory-questionnaire (NPI-Q), Hamilton Depression Scale (HAMD) and Mini-mental state examination (MMSE); and (e) Study design type: Published RCTs.

Exclusion criteria were interventions including two or more interventions or other factors that affect the effectiveness of the intervention, studies including dementia patients with other major diseases, such as severe organ failure.

2.3 | Study selection and data extraction

All of the searched records were imported into EndNote X7 to eliminate duplicate studies. Then, the two authors worked independently to identify RCTs that met the inclusion criteria and then extracted the data individually. To further evaluate the eligibility of potential studies, we obtained the full texts and discussed any disagreements with another author. From each included study, we extracted data including the author, year of publication, country, basic characteristics of participants, intervention details (e.g. type, duration, frequency and total sessions) and outcome measurement tools.

2.4 | Quality assessment

The quality of the included studies was assessed using the tool recommended by the Cochrane Handbook for systematic reviews of randomized trials (Higgins, 2011). This tool examined seven items (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting and other bias). All included studies were assessed independently by two authors, and the risk of bias for each item was categorized as "low risk," "unclear" or "high risk." Disagreements between the two authors were resolved by another author.

2.5 | Statistical analysis

We assessed network transitivity by visually inspecting tables containing the number of patients per treatment comparison; the number of studies per treatment comparison; and the following study characteristics: study duration, patient age, proportion of women ($\geq 50\%$ or $< 50\%$), study setting (for example, nursing home or clinic), dementia type, outcome measure reported, severity of dementia and 2 items from the risk-of-bias assessment (incomplete outcome data and blinding of outcome assessment).

We conducted Bayesian shared parameter random-effects NMA for each outcome. Informative prior distributions were implemented for all between-study heterogeneity parameters ($\log(2) - t[-3.85, 1.932, 5]$) (Rhodes et al., 2015). Vague prior distributions were implemented for trial baselines and treatment differences ($N[0, 1, 000]$). We ranked treatments by using surface under the cumulative ranking curve (SUCRA) values (Salanti et al., 2011), which were summarized across all treatments and outcomes in a rank-heat plot (Veroniki et al., 2016). The SUCRA value is the area under the cumulative ranking probability curve for an intervention. For positive indicators like MMSE, the SUCRA value ranges from 0% (indicating that the intervention has a low probability of being the best possible type) to 100% (indicating that the intervention has a high probability of being the best possible type). Continuous data used mean

difference (MD) and its 95% credibility interval (CrI) to describe the results.

We used RevMan for the quality assessment of the included literature. The GeMTC (Generate Mixed Treatment Comparisons) package of R software was used to draw the network map of this study. The Stata12.0 software Begg rank correlation method was used to make the funnel plot, and the $P > |z|$ value after continuous correction was used to evaluate whether there was publication bias.

3 | RESULTS

3.1 | Identification of relevant studies

A total of 5,370 articles were retrieved through professional literature search methods, including 3,212 Chinese articles and 2,158 English articles. Through reading and screening of each document, 41 articles were finally included in the review (Figure 1). A total of 3,368 people were included in the studies of non-pharmacological interventions for BPSD, with 1,712 in the observation group and 1,656 in the blank control group. The main characteristics of the included studies are shown in Table 1 and 2, and the details of non-pharmacological interventions are listed in Table S1.

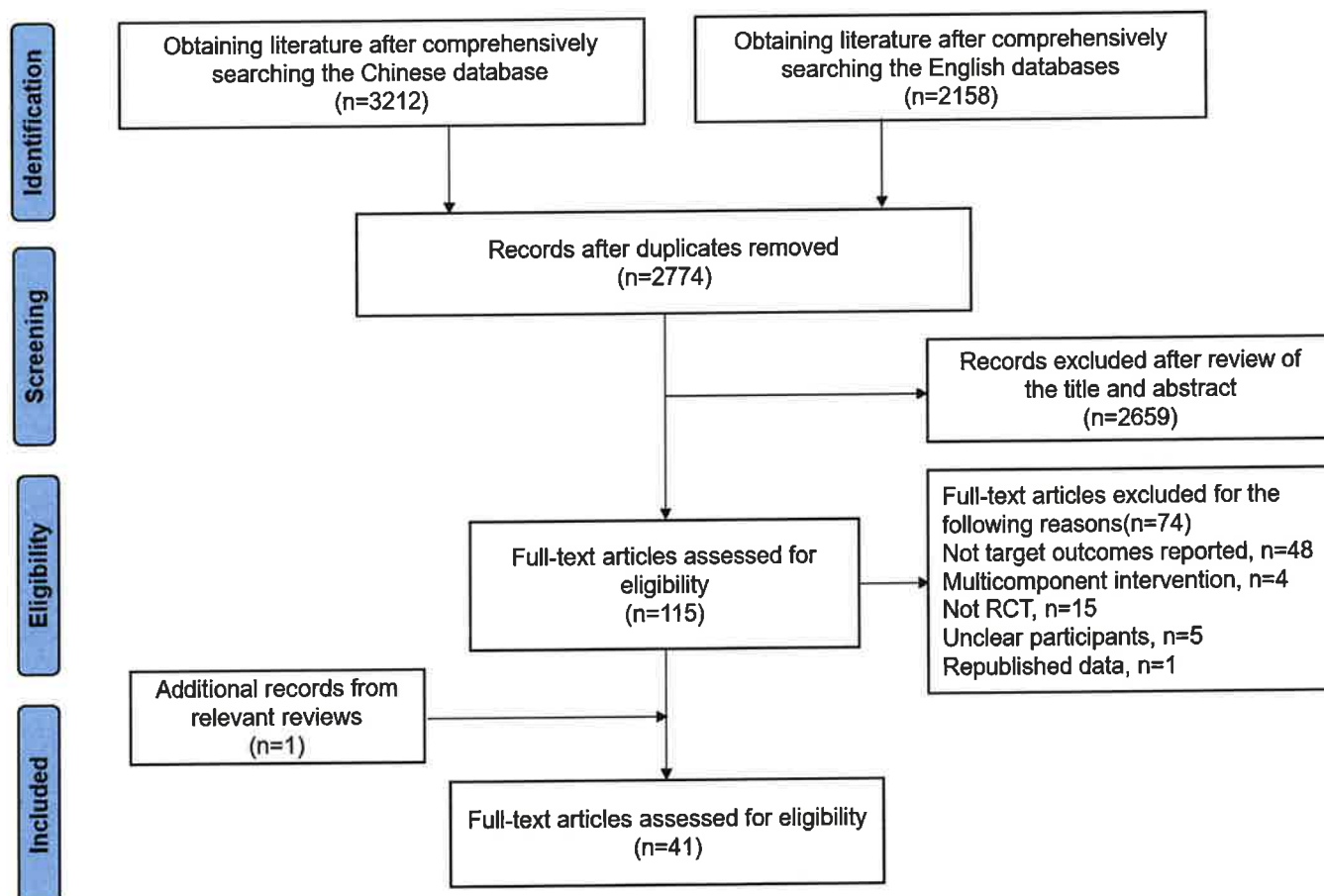


FIGURE 1 Study flow diagram

TABLE 1 Characteristics of 41 studies included in the systematic review

Characteristic	Studies, N (%)
Mean age of intervention group study participants	
<70 years	19(46.0.3)
70–79.9 years	11(26.8)
≥80 years	9(22)
Not reported	2 (4.9)
Women enrolled in study	
0%–49%	16 (39)
50%–100%	21 (51.2)
Not reported	4 (9.8)
Type of dementia in study participants	
Multiple (e.g. AD +VaD)	7 (17.1)
AD	11 (26.8)
PDD	16 (39)
Not reported	7 (17.1)
Dementia severity in study participants	
Mild	1 (2.4)
Mild/moderate	6 (14.6)
Moderate	1 (2.4)
Mild/moderate/severe	3 (7.3)
Moderate/severe	4 (9.8)
Not reported	26 (63.4)
Number of participants	
<50	14 (34.1)
50–99	18 (43.9)
≥100	9 (22)
Duration of study intervention	
<11 weeks	19 (46.3)
11–20 weeks	7 (17.1)
21–30 weeks	3 (7.3)
>30 weeks	2 (4.9)
Not reported	10 (24.4)
Study setting	
Clinic/community	5 (12.2)
Hospital	29 (70.7)
Nursing home/assisted living facility	5 (12.2)
Multiple settings	2 (4.9)

Abbreviations: AD, Alzheimer disease; FTD, frontotemporal dementia; PDD, Parkinson disease dementia; VaD, vascular dementia.

3.2 | Risk-of-bias assessment

The quality of the 41 articles included in the systematic review was evaluated separately. Regarding methodological quality, one article was rated as having low bias risk; 34 articles, uncertain risk; and 6 articles, high bias risk (Figure S1).

3.3 | Meta-analysis results

This study included 10 outcome indicators, including psychological symptoms, behavioural symptoms, cognitive function and ADL. The network meta-analysis requires that an outcome indicator must have ≥2 interventions, and each intervention must have ≥2 articles. Combined with the requirements of network meta-analysis, the study finally included five outcome indicators: NPI, HAMD, HAMA, MMSE and BI.

3.3.1 | Network meta-analysis of NPI scores

Two articles compared MT and control group (CG) (no specific non-pharmacological intervention) (Bingbing, 2015; Mariko et al., 2015); two articles compared IN and CG (Kudoh et al., 2009; Lijian, 2016); two articles compared RT and CG (Hatakeyama et al., 2010; Mo et al., 2016); and four articles compared TC and CG (Giovagnoli et al., 2018; Haiyan et al., 2016; Huimin et al., 2017; Raglio et al., 2015). Transitivity was maintained across treatment comparisons for the outcomes of NPI Scores (Table S3a). Table S3a indicated most treatment comparisons were at low risk of bias because of missing data, used a subscale of the neuropsychiatric inventory as the outcome measure and involved mostly women with dementia who were aged 70 years or older and lived in long-term care facilities. The network plot was shown in Figure S2a. Compared with CG, a significant decrease in NPI was seen in RT, and the difference was statistically significant (MD = -10.42, 95% CI: -19.36--1.41) (Table 2).

The SUCRA results for MT, IN, RT, TC and CG for NPI are shown in Figure 2a. As NPI was a negative indicator, a greater value indicated worse mental and behaviour symptoms. MT, IN, RT, TC and CG had SUCRA values of 45.2, 28.2, 16.5, 68.8 and 91.2 respectively. Compared with the blank control, the non-pharmacological interventions for neuropsychiatric symptoms of BPSD were ranked in the decreasing order of RT, IN, MT and TC.

3.3.2 | Network meta-analysis of HAMD scores

Four articles compared BT and CG (Cao, 2016; Hongmei et al., 2017; Shaogang et al., 2013; Xiaoming et al., 2014); 13 articles compared IN and CG (Hongmei et al., 2016; Hongyan, 2015; Jiankun, 2010; Jun, 2013; Lijian, 2016; Qian et al., 2015; Qihua et al., 2014; Shihong, 2017; Wenjing, 2013; Xiaoning, 2016; Xiaoning et al., 2010; Yan, 2011; Yi & Zhahui, 2014). Transitivity was maintained across treatment comparisons for the outcomes of HAMD Scores (Table S3b). Most treatment comparisons were at low risk of bias because of missing data, used the Hamilton Depression Scale as the outcome measure and involved mostly men with dementia who were under 80 years old and living in hospitals. The network plot is shown in Figure S2b. Compared with the CG, a significant decrease in HAMD was seen in BT, and the difference was statistically

TABLE 2 Comparison of BPSD intervention effects between five non-pharmacological interventions measures and the blank control group

Outcome indicators	(IN) MD (95% CrI) Studies (patients)	(RT) MD (95% CrI) Studies (patients)	(TC) MD (95% CrI) Studies (patients)	(MT) MD (95% CrI) Studies (patients)	(BT) MD (95% CrI) Studies (patients)
Neuropsychiatric inventory (NPI)	-8.35 (-17.87, 1.35) 2 (106)	-10.42 (-19.36, -1.41) 2 (79)	-2.22 (-7.48, 3.15) 4 (209)	-5.54 (-14.63, 3.56) 2 (59)	/
Hamilton Depression Scale (HAMD)	-6.24 (-8.49, -4.04) 13 (1, 202)	/	/	/	-5.87 (-9.64, -2.10) 4 (305)
Hamilton Anxiety Scale (HAMA)	-4.77 (-8.47, -1.46) 3 (239)	/	/	/	-7.56 (-11.82, -4.17) 2 (167)
Mini-mental state examination (MMSE)	3.43 (1.87, 5.06) 6 (612)	/	0.09 (-2.63, 2.74) 4 (147)	1.72 (-2.60, 5.97) 2 (59)	2.93 (-0.16, 6.06) 2 (110)
Barthel Index (BI)	8.82 (2.27, 15.70) 3 (267)	/	/	5.32 (-13.95, 23.91) 2 (59)	/

Note: "/" means that the non-pharmaceutical intervention has no corresponding outcome indicators included. Significant results are in bold.

Abbreviations: BT, behaviour therapy; CrI, credible interval; IN, individualized nursing; MD, mean difference; MT, massage therapy; RT, reminiscence therapy; TC, therapeutic recreation.

significant ($MD=-5.87$, 95% $CrI=-9.64$ ~-2.10). Compared with the CG, a significant decrease in HAMD was seen in IN, and the difference was statistically significant ($MD=-6.24$, 95% $CrI=-8.49$ ~-4.04). There was no statistically significant difference in HAMD between IN and BT ($MD=-0.36$, 95% $CrI=-4.82$ ~ 4.00) (Table 2).

The SUCRA results for BT, IN and CG for HAMD are shown in Figure 2a. As HAMD was a negative indicator, a greater value indicated worse depressive symptoms. BT, IN and CG had SUCRA values of 28.6, 21.5 and 99.9 respectively. Compared with the blank control, the non-pharmacological interventions for depressive symptoms of BPSD were ranked in the decreasing order of IN and BT.

3.3.3 | Network meta-analysis of HAMA scores

Two articles compared BT and CG (Shaogang et al., 2013; Xiaoming et al., 2014); and three articles compared IN and CG (Jiankun, 2010; Shihong, 2017; Xiaoning, 2016). Transitivity was maintained across treatment comparisons for the outcomes of HAMA Scores (Table S3c). Most treatment comparisons were at low risk of bias because of missing data, used the Hamilton Anxiety Scale as the outcome measure and involved mostly men with dementia who were under 80 years old and living in hospitals. The network plot is shown in Figure S2c. Compared with the CG, the IN showed a decrease in the HAMA index, and the difference was statistically significant ($MD=-4.77$, 95% $CrI=-8.47$ ~-1.46). Compared with the CG, a significant decrease in HAMA was seen in BT, and the difference was statistically significant ($MD=-7.56$, 95% $CrI=-11.82$ ~-4.17).

However, there was no statistically significant difference in improving patients' anxiety symptoms between IN and BT ($MD=-2.85$, 95% $CrI=-8.13$ ~ 2.16) (Table 2).

The SUCRA results for BT, IN and CG for HAMA are shown in Figure 2a. As HAMA was a negative indicator, a greater value indicated worse anxiety symptoms. BT, IN and CG had SUCRA values of 3.9, 46.7 and 99.4 respectively. Compared with the blank control, the non-pharmacological interventions for anxiety symptoms of BPSD were ranked in the decreasing order of BT and IN.

3.3.4 | Network meta-analysis of MMSE scores

Two articles compared BT and CG (Map elli et al., 2013; Xiaoming et al., 2014); two articles compared MT and CG (Bingbing, 2015; Mariko et al., 2015); six articles compared IN and CG (Guilin et al., 2013; Longju, 2017; Meiling et al., 2017; Mossello et al., 2008; Shihong, 2017; Xiling et al., 2017); and four articles compared TC and CG (Giovagnoli et al., 2018; Haiyan et al., 2016; Huimin et al., 2017; Silber, 1999). Transitivity was maintained across treatment comparisons for the outcomes of MMSE Scores (Table S3d). Most treatment comparisons were at low risk of bias because of missing data, used the Mini-mental State Examination Scale as the outcome measure and involved mostly women with dementia who were under 80 years old and living in hospitals. The network plot is shown in Figure S2d. Compared with the CG, a significant increase in MMSE was seen in IN, and the difference was statistically significant ($MD=3.43$, 95% $CrI=1.87$ ~ 5.06). The difference between TC and IN was statistically significant ($MD=-3.43$, 95% $CrI=-6.55$ ~-0.28) (Table 2).

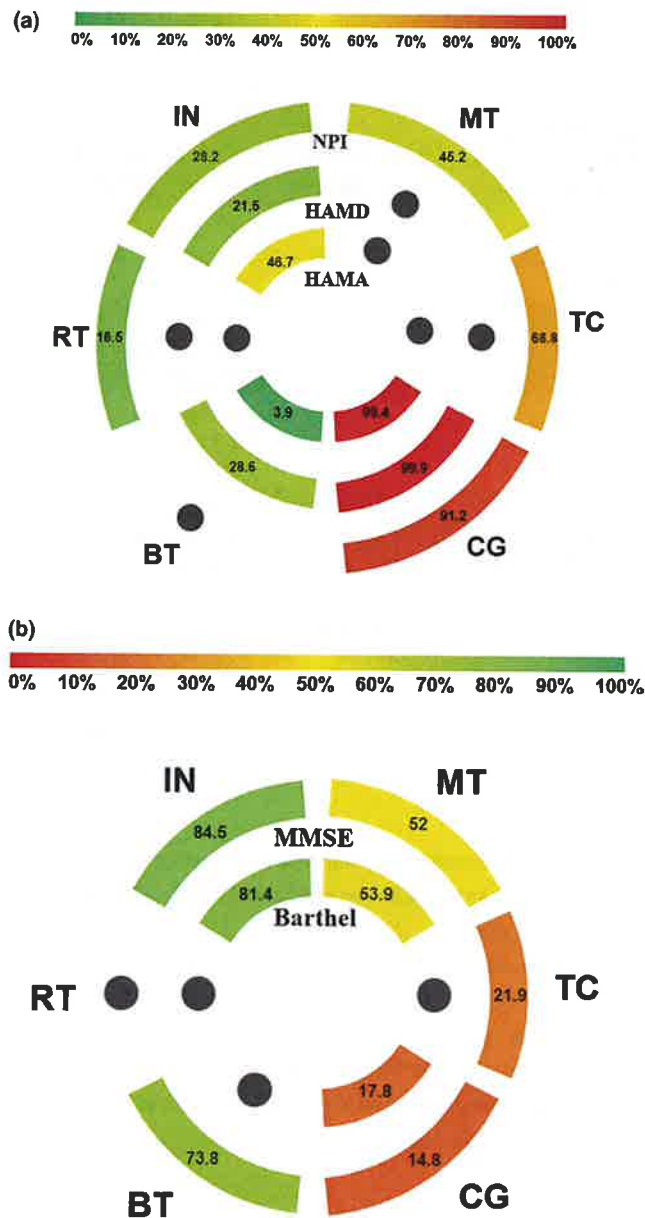


FIGURE 2 (a) Rank-heat plot of SUCRA values for non-pharmacological interventions targeting NPI, HAMD and HAMA in elders with dementia. The scale bar represents the SUCRA value for each intervention, with red indicating the highest values (worst/least efficacious treatments) and green indicating the lowest values (best/most efficacious treatments). IN, individualized nursing; MT, massage therapy; TC, therapeutic exercise; BT, behaviour therapy; RT, reminiscence therapy; CG, control group; NPI, neuropsychiatric inventory; HAMD, Hamilton depression scale; HAMA, Hamilton anxiety scale. * Treatment without data on the outcome within the circle. (b) Rank-heat plot of SUCRA values for non-pharmacological interventions targeting MMSE and BI in elders with dementia. The scale bar represents the SUCRA value for each intervention, with red indicating the highest values (worst/least efficacious treatments) and green indicating the lowest values (best/most efficacious treatments). IN, individualized nursing; MT, massage therapy; TC, therapeutic exercise; BT, behaviour therapy; RT, reminiscence therapy; CG, control group; MMSE, Mini-mental state examination; BI, Barthel index. * Treatment without data on the outcome within the circle

The SUCRA results for IN, BT, MT, TC and CG for MMSE are shown in Figure 2b. As MMSE was a positive indicator, a lower value indicated worse cognitive dysfunction. BT, MT, IN, TC and CG had SUCRA values of 73.8, 52.0, 84.5, 21.9 and 17.8 respectively. Compared with the blank control, the non-pharmacological interventions for cognitive dysfunction of BPSD were ranked in the decreasing order of IN, BT, MT and TC.

3.3.5 | Network meta-analysis of BI scores

Three articles compared IN and CG (Longju, 2017; Qihua et al., 2014; Shihong, 2017); two articles compared MT and CG (Bingbing, 2015; Mariko et al., 2015). Transitivity was maintained across treatment comparisons for the outcomes of MMSE Scores (Table S3e). Most treatment comparisons were at low risk of bias because of missing data, used the Barthel Index Scale as the outcome measure and involved mostly women with dementia who were under 80 years old and living in hospitals. The network plot is shown in Figure S2e. Compared with the CG, a significant increase in BI was seen in RT, and the difference was statistically significant ($MD=8.82$, 95% $CrI=2.27 \sim 15.70$) (Table 2).

The SUCRA results for IN, MT and CG for BI comparison are shown in Figure 2b. As BI was a positive indicator, a lower value indicated worse ADL. MT, IN and CG had SUCRA values of 53.9, 81.4 and 14.8 respectively. Compared with the blank control, the non-pharmacological interventions for ADL of BPSD were ranked in the decreasing order of IN and MT.

3.4 | Publication bias

The publication bias of the study with the outcome index of NPI, HAMD and MMSE was evaluated. The funnel plots, with their corresponding continuous corrected $Pr>|z|>0.05$, were shown in Figure S4a,b,c, indicating that the publication bias of the included literature was not obvious. The funnel plot requires more than 5 independent studies (He et al., 2007). The number of articles included in HAMA and BI was not enough to make a funnel plot; therefore, no publication bias analysis was performed.

4 | DISCUSSION

Behavioural and psychological symptoms of dementia is a broad term encompassing the behavioural and neuropsychiatric symptoms that patients with dementia may experience, including mood disorders, depression, agitation, psychosis, sleep disorders, anxiety, apathy, irritability, motor abnormalities, hallucinations and delusions (Lyketsos et al., 2000). This study explored the effectiveness, advantages and disadvantages of common non-pharmacological interventions of BPSD from the perspective of non-pharmaceutical interventions.

4.1 | Summary and interpretation of findings

The NPI includes 10 mental and behaviour symptom assessment items, including delusions, hallucinations and agitation, to assess the severity of symptoms in BPSD (Siette et al., 2013). The NMA in this study showed that compared with the blank control, although TC, MT, IN and RT could all reduce the NPI score of BPSD, only RT could significantly reduce the NPI score and improve the neuropsychiatric symptoms of older adults with dementia. Results of the NMA also showed that the best intervention for improving neuropsychiatric symptoms in BPSD was RT, followed by IN, MT and TC. Reminiscence work can be seen to have a cognitive rationale. People with dementia often could recall events from their childhood, but not from more recent times, even earlier the same day. Drawing on the apparently preserved store of remote memories appears a sensible strategy, when dementia is typically accompanied by great difficulty in new learning. By linking with the person's cognitive strengths in this way, communication might be enhanced, allowing the person to talk confidently of their earlier life and experiences (Woods et al., 2018).

In terms of psychological symptoms, patients with dementia are prone to depression and anxiety (Orgeta et al., 2015). The present results showed that both BT and IN significantly reduced the patients' depression score and improved depressive symptoms in patients with dementia with mental and behavioural symptoms compared with those receiving no non-pharmaceutical interventions. The NMA based on the Bayesian random-effects model showed that IN was the best non-pharmacological intervention for improving the depressive symptoms of BPSD, with its effect being better than those of BT. This outcome could be because compared with BT, scientific nursing activities, patient nursing guidance and harmonious nurse-patient relationship could better relieve patients' depression and help patients gradually resolve symptoms, overcome negative psychological feelings and recover from depression. American practice has also proposed that personalized nursing care programmes be recommended to improve depressive symptoms in patients with dementia (NHMRC, 2019). Therefore, targeted IN can be used to assess the emotional and psychological status of patients with BPSD and implement appropriate nursing measures for patients with depressive symptoms. It can also help alleviate patients' depression and improve adverse psychological symptoms (Mo et al., 2014).

Regarding the anxiety symptoms in patients with BPSD, IN and BT can significantly reduce the anxiety score of patients compared with patients who do not receive non-pharmaceutical interventions. The NMA results showed that BT was the best in improving anxiety symptoms in BPSD. It is estimated that the prevalence of depression in dementia is approximately 25% with anxiety occurring in up to 75%. Persons experiencing neurologic disorders, such as dementia or Parkinson's disease (PD), and depressive or anxiety disorders have poorer outcomes with reduced quality of life, poor functional status and worsened cognition (Goodarzi et al., 2016). Although the NMA showed that BT was better than IN in improving anxiety in BPSD, BT is known to be not as extensive as IN. Therefore, further research on the treatment of BPSD with BT is needed to confirm its effect on BPSD.

Moreover, the study showed that IN, BT, MT and TC increased the MMSE score of older adults with dementia, but only IN could significantly increase MMSE scores and improve cognitive function in BPSD. The difference was statistically significant. NMA showed that the best non-pharmacological intervention for improving cognitive function was IN, followed by BT, MT and TC. Dementia is a progressive disease with a long course and slow progression, and the cognitive function of patients will inevitably decline, gradually (Dyer et al., 2018). The interventions selected here are short-termed and one cycled, and MMSE is well known for continuously declining indicator in AD. Therefore, future clinical trials of non-pharmacological interventions should have longer terms and more cycles in order to confirm their efficacy on the cognitive function of elders with dementia.

This study showed that compared with the control group, IN could significantly increase patients' BI score and improve the ADL of older adults with BPSD, with the difference being statistically significant. The best non-pharmacological intervention for improving the ADL in older adults with BPSD was IN, followed by MT. For older adults with dementia, the nursing staff can assess and determine whether the former have a disability or the appropriate self-care ability and then formulate and implement corresponding nursing plans (Qingqing et al., 2016). As the best non-pharmaceutical intervention for improving the ADL of older adults with dementia, IN's comprehensive nursing procedures, targeted nursing plans, and active and effective nursing evaluation have positive effects on the maintenance and recovery of physical function in BPSD.

4.2 | Strengths and limitations

There were some strengths in our network meta-analysis: (a) we performed an exhaustive comparison of the efficacy of 5 different non-pharmacological interventions on the behavioural and psychological symptoms in elders with dementia based on Bayesian network meta-analysis. And the differences among different interventions were distinguished according to the SUCRA values; and (b) only RCTs were included, which implies that the included studies had a rigorous study design.

Admittedly, this study has several limitations that should be recognized. This study included 41 RCTs, but only three studies had sample sizes exceeding 100. Most of the other studies had relatively small sample sizes ($N < 100$ people), which could increase the sampling error and reduce the test efficiency of the present study. Some of the included RCTs did not use a blind method; only a small number of studies used a single- or double-blind method. This could have affected the intervention effect. We did not directly compare each intervention, but directly compared different interventions with the control group, so as to indirectly obtain the intervention effects of different interventions. Therefore, the heterogeneity of the two methodologies cannot be tested. Moreover, we presented a section on "publication bias," yet there is no mention on potential bias to unpublished papers. It may be worthwhile adding this as a potential.

4.3 | Implication for practice and research

The NMA results will facilitate informed decision-making by patients, caregivers, clinicians and policymakers. The implementation of appropriate non-pharmaceutical interventions by healthcare professionals in elders with dementia can help alleviate the behavioural and psychological symptoms. Therefore, healthcare professionals should be encouraged to apply appropriate non-pharmacological interventions for elders with dementia. Furthermore, most non-pharmacological interventions, easy to apply, might be useful strategies to be used by family caregivers. Healthcare professionals should strengthen the training of family caregivers about non-pharmacological interventions and promote their use of non-pharmacological interventions. Policymakers should consider instituting and promoting policies to facilitate use of non-pharmacological interventions. Future clinical trials of non-pharmacological interventions with greater sample sizes, multi-arm design, longer terms and more cycles are needed.

5 | CONCLUSIONS

We performed an exhaustive comparison of the effects of 5 different non-pharmacological interventions on the behavioural and psychological symptoms in elders with dementia. In summary, the five non-pharmacological interventions included in the NMA were superior to the different symptoms of BPSD compared with the blank control. Both BT and IN significantly improved patients' depression; the latter worked best. RT showed a significant improvement in patients' neuropsychiatric symptoms and was the best intervention for this aspect. Therefore, healthcare professionals should develop and apply cautious and personalized intervention programmes based on participants' life backgrounds and preferences, so as to alleviate the behavioural and psychological symptoms in elders with dementia and reduce the burden on caregivers.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

Hu Xiuying: Study concept, design and guide. Li Wenjie and Xu Xiaofeng: Manuscript draft, data collection and equal contribution. Wu Fen: Data analysis. All authors: Final approval of the manuscript.

ETHICAL APPROVAL

This study was approved by the Sub-Committee on Biomedical Ethics of West China Hospital, Sichuan University (No. 2017269).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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