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# Alzheimer’s Disease

# Maladie d'Alzheimer

*Articles connexes*: - acupuncture expérimentale -

## 1. Systematic Reviews and Meta-Analysis

### 1.1. Huang 2026

Huang WL, Wang LL, Shi JR, Liu Q. Acupuncture for Alzheimer's disease: A systematic review and meta-analysis integrating traditional insights and scientific evidence. J Integr Med. 2026:S2095-4964(26)00097-X. https://doi.org/10.1016/j.joim.2026.08.002

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| **Background** | Alzheimer's disease (AD), a leading cause of dementia in the elderly, is characterized by progressive cognitive impairment, and still lacks effective therapeutic interventions. This systematic review synthesizes the classical theoretical foundations, clinical evidence, and modern mechanistic insights for the use of acupuncture to treat AD. |
| **Methods** | A meta-analysis was conducted based on a comprehensive literature search of PubMed, Embase, the Cochrane Library, CNKI, VIP information, and Wanfang Data, covering the period from inception until September 2025. Eligible randomized controlled trials (RCTs) compared acupuncture (manual or electroacupuncture) with control interventions, including sham acupuncture, donepezil, placebo, or no treatment. Data were extracted by two reviewers working independently and then analyzed using the meta and meta for packages in R (v4.3.2). Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated. |
| **Results** | A total of **21 RCTs comprising 1354 participants** met the inclusion criteria. Compared with no-treatment controls, acupuncture significantly improved cognitive performance, as measured by the Mini-Mental State Examination (MMSE) (WMD = 3.74, 95% CI: 1.34-6.14), and outperformed placebo controls (WMD = 2.13, 95% CI: 1.39-2.87). Acupuncture showed efficacy comparable to that of donepezil on MMSE and Activity of Daily Living (ADL), suggesting non-inferiority to standard pharmacotherapy. Frequently used acupoints included GV20, ST36, GB20, LR3, and ST40, often combining local (GV24, EX-HN1) and distal (SP10, KI3) points. Reported adverse events were mild and transient, with no significant difference from controls. Biomarker analyses indicated that acupuncture enhanced acetylcholine levels and reduced plasma Aβ1-40, Aβ1-42, and Tau levels, implying modulation of cholinergic transmission and AD-related pathology. |
| **Conclusion** | This review highlights acupuncture as a holistic, multi-targeted therapy with promising potential for managing AD. Future research should aim to standardize acupuncture protocols, integrate TCM syndrome differentiation, and adopt neurobiological and imaging techniques to explore mechanisms. |

#### 1.1.1. Wu J 2025

Wu J, Teng Y, Xie Y, Xing S, Zhi S. Comparing the efficacy of physical therapy interventions in Alzheimer's disease: a network meta-analysis. Front Aging Neurosci. 2025 Mar 5;17:1541287. https://doi.org/10.3389/fnagi.2025.1541287

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| **Backgroung** | Alzheimer's disease (AD) is a progressive and debilitating neurodegenerative disorder that significantly impairs cognitive function and daily living abilities, representing a major public health challenge. Given the multifactorial nature of AD, effective therapeutic interventions targeting both cognitive and functional decline are critical. |
| **Methods** | This study aimed to conduct a comprehensive comparison of the therapeutic effects of music therapy, acupuncture therapy, game therapy, cognitive training therapy, and exercise therapy on AD patients through a network meta-analysis. Randomized controlled trials (RCTs) published up until 2024 were systematically retrieved from multiple databases. Data were extracted, including the first author, publication year, country, total sample size, mean participant age, type and duration of intervention, and outcome measures such as the Mini-Mental State Examination, Activities of Daily Living, and Alzheimer's Disease Assessment Scale-Cognitive Subscale. Statistical analyses were performed using the RevMan 5.3 and Stata 17 software. The analysis included 52 RCTs with a total of 3,409 participants, offering a strong dataset. |
| **Results** | The results indicated that game therapy produced statistically significant improvements in mental state and daily living abilities, while acupuncture therapy yielded the most pronounced improvements in cognitive function among AD patients. Notably, the comparative efficacy of these interventions suggests that game therapy may offer short-term benefits, particularly for mental health and functional abilities, whereas **acupuncture therapy** demonstrated superior long-term cognitive enhancements. |
| **Conclusions** | In conclusion, tailored physical and cognitive interventions such as game therapy and **acupuncture therapy** may hold significant potential in optimizing treatment outcomes for AD patients, with implications for both clinical practice and future research. |

### 1.1.2. Wu Y 2025 (combined with donepezil)

Wu Y, Zhan Y, Zhu W, Pei J. Effectiveness of acupuncture combined with donepezil for Alzheimer's disease: A systematic review and meta-analysis. Medicine (Baltimore). 2025 Jun 6;104(23):e42651. https://doi.org/10.1097/MD.0000000000042651

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| **Backgound** | The incidence of Alzheimer's disease (AD) is gradually increasing in an aging society, imposing a heavy burden on society. Current studies have found that acupuncture therapy combined with donepezil has a good clinical effect in treating AD. We plan to conduct a systematic review and meta-analysis to evaluate the effectiveness of acupuncture combined with donepezil in AD patients. |
| **Methods** | Eight databases were searched for randomized controlled trials (RCTs) using acupuncture in combination with donepezil for the treatment of AD, from the establishment of the database to October 1st, 2023. The clinical efficacy rate, Mini-Mental State Examination, AD Assessment Scale for Cognitive Capacity, Skill Level on Activities of Daily Living, Montreal Cognitive Assessment, Behavioral Pathology in AD Rating Scale, and adverse events were mainly used to evaluate the outcomes. RevMan 5.4.1 software was used to evaluate the quality of the included studies and perform a meta-analysis. |

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| **Results** | A total of **12 RCTs** were included. Meta-analysis showed that acupuncture combined with donepezil seemed to be more effective than donepezil monotherapy for treatment of AD in improving the clinical efficacy rate (relative risk = 1.35; 95% confidence interval [CI]: 1.17-1.56; Z = 4.10; P < .0001), the Mini-Mental State Examination score (mean difference [MD] = 3.28; 95% CI: 1.81-4.75; Z = 4.37; P < .0001), and the Montreal Cognitive Assessment score (MD = 6.04; 95% CI: 4.76-7.32; Z = 9.23; P = .00001), while reducing the AD Assessment Scale for Cognitive Capacity score (MD = -3.57; 95% CI: -3.94 to -3.20; Z = 18.91; P < .00001), the Skill Level on Activities of Daily Living score (MD = -2.52; 95% CI: -4.05 to -0.99; Z = 3.23; P = .001), and the Behavioral Pathology in AD Rating Scale score (MD = -4.04; 95% CI: -4.58 to -3.50; Z = 14.64; P < .00001). |
| **Conclusions** | Acupuncture combined with donepezil is an effective treatment which can improve cognitive ability and quality of life for AD patients. However, it is imperative to conduct more large-scale and high-quality RCTs in order to establish more definitive conclusions regarding this therapeutic approach in the future. |

### 1.1.3. Guo 2024 (cognitive impairment)

Guo R, Shen X, Ealing J, Zhou J, Lu J, Ning Y. Efficacy and safety of acupuncture for cognitive impairment in Alzheimer's disease: a systematic review and meta-analysis. Front Dement. 2024 Jul 3;3:1380221. https://doi.org/10.3389/frdem.2024.1380221

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| **Objective** | To systematically evaluate the efficacy of acupuncture in the treatment of cognitive impairment in Alzheimer's disease (AD) by meta-analysis, in order to provide evidence-based evidence for the application of acupuncture therapy in the clinical process of AD. |
| **Methods** | From the establishment of the database to December 31, 2022, China Biomedical Literature Database (CBM), China National Knowledge Network (CNKI), VIP database, WanFang Database, Pubmed, Embase and Cochrane Library Database were systematically searched. To collect published randomized controlled clinical trials (RCTS) of acupuncture in the treatment of cognitive impairment in AD. The subjects in the intervention group were given acupuncture alone or combined with other treatments the same as the control group; the control group received conventional Western medicine treatment. The main outcome indicators of the study were cognitive function assessment of subjects, including: Simple Mental State Examination Scale (MMSE), Assessment of daily Living Ability Scale (ADL), Alzheimer's Disease Cognitive Function Assessment Scale (ADAS-Cog), TCM syndrome score (SDSD), Montreal Cognitive Test (MoCA), Secondary outcome indicators were the occurrence of adverse reactions. Literature screening, data extraction, and quality evaluation of the included literature were performed independently by two researchers, according to bias risk assessment tools recommended in the Cochrane manual. Data were analyzed by RevMan5.3 software. Dichotomous variables were represented by risk ratio (OR) and 95% CI, and continuity variables were represented by mean difference (MD) and 95% CI. For heterogeneity analysis, when P > 0.1 and I 2 ≤ 50%, fixed effect model was applied. When P ≤ 0.1 and I 2 > 50%, the random effects model is applied. |
| **Results** | A total of **1,172 eligible subjects were included in 18 RCTS**, including 595 in the intervention group and 577 in the control group. The results of meta-analysis are as follows: acupuncture intervention group improved MMSE [MD = 1.67, 95% CI (0.94, 2.41), P < 0.00001], ADL [MD = -1.18, 95% CI (-3.09, 0.72), P = 0.22], ADAS-Cog [MD = 3.31, 95% CI (5.84, 0.78), P = 0.01], SDSD [MD = 2.40, 95% CI (3.53, 1.26), P < 0.0001], MoCA [MD = 4.80, 95% CI (3.74, 5.86), P = 0.04] were better than the control group. No serious adverse reactions related to acupuncture were observed in the intervention group, and the incidence and severity of adverse reactions were lower than those in the control group, with statistical significance [OR = 0.17, 95% CI (0.04, 0.67), P = 0.01]. |

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| **Conclusion** | Existing data show that acupuncture therapy has certain advantages in improving cognitive dysfunction and improving self-care ability of patients with Alzheimer's disease. However, due to the small number of RCTS and cases evaluating the efficacy of acupuncture, and the possibility of measurement bias and selectivity bias in included studies, it is still unable to conduct high-intensity demonstration on its effectiveness. Further large-scale, high-quality randomized, double-blind controlled trials are needed to evaluate its efficacy. |

### 1.1.4. Lin 2022

Lin CJ, Yeh ML, Wu SF, Chung YC, Lee JC. Acupuncture-related treatments improve cognitive and physical functions in Alzheimer's disease: A systematic review and meta-analysis of randomized controlled trials. Clin Rehabil. 2022 May;36(5):609-635. https://doi.org/10.1177/02692155221079117

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| **Objective** | To determine acupuncture-related treatments' effects and duration on improving cognitive function, physical function, and quality of life in patients with Alzheimer's disease. |
| **Data sources** | Eight electronic databases were searched for eligible randomized controlled trials from database inception to January 2021, including Medline, PubMed, EBSCO, Embase, Cochrane, Airiti Library, China National Knowledge Infrastructure, and China Journal Full-text Database. |
| **Review methods** | A systematic review and meta-analysis were conducted on acupuncture types, cognitive function, activity of daily life, muscle strength and quality of life. |
| **Results** | **Sixty-six studies in total with 4191 participants**, the overall risk of bias was classified 60% as low and 24% as high. Acupuncture-related treatments for cognitive function and self-care ability revealed a moderate effect size, with a significant difference in noninvasive and invasive remedies ($p < 0.001$). Cognitive function showed significant differences in 6, 8, 12, and 24 weeks while self-care ability in the latter two weeks ($p < 0.001$). Meta-regression analysis showed cognitive function increased by 0.05 points ($p = 0.002$) and self-care ability decreased by 0.02 points ($p = 0.04$) after weekly treatment. There was a significant difference in muscle strength ($p = 0.0003$). |
| **Conclusion** | Acupuncture-related treatments effectively improved cognitive function with the treatment lasted 6 weeks at least, but self-care ability started showing effects after 12 weeks of treatment. The improvement of muscle strength was also confirmed. Acupuncture-related treatments, particularly noninvasive ones, have few complications and high safety, perhaps providing patients and caregivers diversified choices and clinical care guidelines for reference. |

### 1.1.5. Wang 2021 (Network Meta-Analysis)

Wang XS, Li JJ, Wang YS, Yu CC, He C, Huang ZS, Jiang T, Hao Q, Kong LH. Acupuncture and Related Therapies for the Cognitive Function of Alzheimer's Disease: A Network Meta-Analysis. Iran J Public Health. 2021 Dec;50(12):2411-2426. https://doi.org/10.18502/ijph.v50i12.7924

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| **Background** | Acupuncture and acupuncture-related therapies are effective for Alzheimer's disease (AD), therefore, we aimed to compare and rank the interventions that mainly focus on acupuncture-related therapies in the treatment of patients with mild to moderate AD. |
| **Methods** | We used network meta-analysis to evaluate the direct and indirect evidence shown in randomized controlled trials of AD. The data were analyzed using RavMan manager, Stata, and WinBUGS software after two researchers independently screened the literature, extracted the data, and assessed the risk of bias in the included studies. |

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| **Results** | We analyzed a total of 36 eligible studies, including 2712 patients, involving 14 types of acupuncture-related therapies and comprehensive therapies. For Mini-Mental State Examination (MMSE), acupuncture (ACU) combined with cognitive and memory training (Training) was more effective than ACU, ACU+Chinese herb (CH), ACU+Donepezil (DON), CH, DON, DON+Nimodipine (NIM), Music therapy (Music), NIM, Placebo, and Training ($P<0.05$), while ACU+CH was batter than CH ($P<0.05$), and ACU+DON+NIM was better than DON+NIM ($P<0.05$). For Alzheimer's Disease Assessment Scale-Cognitive section (ADAS-cog), ACU was more effective than DON and placebo ($P<0.05$). For Activities of Daily Living (ADL), ACU+DON was better than CH, DON, NIM, and Placebo ($P<0.05$). For the clinical effectiveness rate, ACU, ACU+CH, ACU+CH+DON, ACU+CH+DON+NIM, ACU+DON, CH, NIM were all more effective than DON+NIM ($P<0.05$), while ACU and ACU+CH were better than DON ($P<0.05$). The comprehensive ranking results show that ACU+training and ACU have the highest ranking probability. |
| **Conclusion** | ACU+Training and ACU may be the best therapies to improve the cognitive function of patients with mild to moderate AD, while the combination of acupuncture-related therapies and other therapies has a higher overall benefit. |

### 1.1.6. Jiao 2020

Jiao Lan, Ji-fei Miao, Shu-qi Ge, Tie-qu Chai, … Li-ming Lu. Acupuncture for cognitive impairment in vascular dementia, Alzheimer's disease and mild cognitive impairment: A systematic review and meta-analysis. European Journal of Integrative Medicine. 2020;35. [212068]. doi

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| **Introduction** | Cognitive impairment is a worldwide health problem. Numerous studies have been conducted to evaluate the effect of acupuncture on cognitive impairment. However, it is still unclear that if acupuncture shows the same efficacy on cognitive impairment caused by different diseases. Therefore, we conducted a systematic review and meta-analysis based on the current evidence to evaluate the efficacy and safety of acupuncture for cognitive impairment in vascular dementia (VD), Alzheimer's disease (AD) and mild cognitive impairment (MCI) patients. |
| **Methods** | Five databases were searched from their inception to December 2019. Randomized controlled trials (RCTs) involving VD, AD or MCI treated by acupuncture alone or as part of combination therapy were included. The primary outcomes were the Mini-Mental State Examination and the Hierarchic Dementia Scale. |
| **Results** | **Twenty-one RCTs (N = 2253)** were quantitatively analyzed. For VD, compared with Western medicine (WM), acupuncture showed better Hierarchic Dementia Scale scores ($P < 0.01$), and acupuncture plus WM also showed better Hierarchic Dementia Scale scores ($P < 0.01$). For MCI, acupuncture showed a significant improvement in Mini-Mental State Examination ($P < 0.01$) and picture recognition test scores compared with WM. For AD, WM resulted in better Hierarchic Dementia Scale scores than acupuncture ($P < 0.01$). Eight trials reported adverse events, 15 out of 2253 patients had adverse events related to acupuncture treatment, and 25 out of 2253 patients had adverse events related to WM treatment. |
| **Conclusion** | Acupuncture may be efficacious for improving cognitive function in patients with VD and MCI. However, the evidence is limited, and larger sample size and more rigorous RCTs should be conducted to verify the effectiveness and safety of acupuncture. |

### 1.1.7. Jin 2020

Jin Hyeon Shin, Hye Jeong Shin, Eui Byeol Kim, Yun Young An, Tae Han Yook, Yoo Min Choi, Beom Yong Song, Jong Uk Kim. The Effectiveness of Acupuncture Treatment for Patients with Alzheimer's Disease: A Meta-Analysis of Randomized Controlled Trials. J Acupunct Res. 2020;37(4):209-223. [219961]. doi

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| **Purpose** | The purpose of this study was to evaluate the effectiveness of acupuncture treatment for the symptoms of Alzheimer’s disease (AD). |
| **Methods** | There were 11 databases searched for randomized controlled trials using acupuncture treatment for AD. The risk-of-bias assessment tool of the Cochrane Library was used to evaluate the quality of each study. Using the Review Manager (RevMan), a meta-analysis was performed using risk ratio, mean difference, 95% confidence interval, and random effect model. |
| **Results** | There were **32 studies** selected, all of which were conducted in China. There were 16 studies where acupuncture was used as the intervention, and 23 studies used Donepezil as the control group. Acupoint GV20 was most frequently selected during the treatment. The Mini Mental State Examination (MMSE) was the most frequently used outcome variable. A period of 12 weeks was the most common treatment duration. As a result of meta-analysis (n = 25), acupuncture improved the MMSE and activities of daily living scores. Electroacupuncture improved the Alzheimer Disease Assessment Scale-Cognitive Subscale, and scalp acupuncture improved the MMSE score for AD. |
| **Conclusions** | Acupuncture alleviates the symptoms of AD. However, further research is necessary to provide a better level of evidence. |

### 1.1.8. Lai 2020 (Network Meta-Analysis)

Lai X, Wen H, Li Y, Lu L, Tang C. The Comparative Efficacy of Multiple Interventions for Mild Cognitive Impairment in Alzheimer's Disease: A Bayesian Network Meta-Analysis. Front Aging Neurosci. 2020. [210345]. doi

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| **Background** | Mild cognitive impairment (MCI) is the early phase of Alzheimer's disease (AD). The aim of early intervention for MCI is to decrease the rate of conversion from MCI to AD. However, the efficacy of multiple interventions in MCI, and the optimal methods of delivery, remain controversial. We aimed to compare and rank the treatment methods for MCI in AD, in order to find an optimal intervention for MCI and a way to prevent or delay the occurrence of AD. |
| **Methods** | Pair-wise and network meta-analysis were conducted to integrate the treatment effectiveness through direct and indirect evidence. Four English databases and three Chinese databases were searched for international registers of eligible published, single or double blind, randomized controlled trials up to September 31st 2019. We included nine comparative interventions: pharmacological therapies which incorporated cholinesterase inhibitors (ChEI), ginkgo, nimodipine, and Chinese medicine; non-pharmacological therapies comprising of acupuncture, music therapy, exercise therapy, and nutrition therapy; and a placebo group. The primary outcome was the Mini-Mental State Examination (MMSE) score. The secondary outcome was the AD Assessment Scale-cognitive subscale (ADAS-cog). |
| **Results** | Twenty-eight trials were eligible, including 6,863 participants. In the direct meta-analysis, as for the Mini-Mental State Examination scale, the ChEIs (MD: -0.38; 95% CI: -0.74, -0.01), Chinese medicine (MD: -0.31; 95% CI: -0.75, 0.13), exercise therapy (MD: -0.50; 95% CI: -0.65, -0.35), music therapy (MD: -1.71; 95% CI: -4.49, 1.07), were statistically more efficient than placebo. For AD Assessment Scalecognitive subscale outcome, ChEIs (MD: 1.20; 95% CI: 0.73, 1.68), Acupuncture (MD: 1.36; 95% CI: 1.28, 1.44), Chinese medicine (MD: 0.61; 95% CI: 0.49, 0.73) and exercise (MD: 0.61; 95% CI: 0.49, 0.73) were better than placebo. In the network meta-analysis, the MMSE outcome ranked music therapy (59%) as the best and Acupuncture (26%) as second. Nutrition and Ginkgo treatment had the lowest rank among all interventions. For ADAS-cog outcome, acupuncture (52) ranked the best. |

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| **Conclusion** | Among the nine treatments studied, music therapy appears to be the best treatment for MCI, followed by acupuncture. Our study provides new insights into potential clinical treatments for MCI due to AD, and may aid the development of guidelines for MCI in AD. |

### 1.1.9. Wang 2020

Wang YY, Yu SF, Xue HY, Li Y, Zhao C, Jin YH. Effectiveness and Safety of Acupuncture for the Treatment of Alzheimer's Disease: A Systematic Review and Meta-Analysis. Front Aging Neurosci. 2020. [209248]. doi/

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| **Background** | The effects of acupuncture on Alzheimer's disease (AD) outcomes remain controversial. The aim of this review was to evaluate the effectiveness and safety of acupuncture for the treatment of AD. |
| **Methods** | PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Chinese BioMedical Literature Database, VIP Database for Chinese Technical Periodicals, China National Knowledge Infrastructure, and Wanfang Data were searched to identify relevant randomized controlled trials from inception to January 19, 2019. Data were extracted and evaluated by two authors independently. The data analysis was conducted using R (version 3.6.0) and RStudio (version 1.2.1335) software. |
| **Results** | **Thirty trials involving 2,045 patients** were included. Acupuncture plus drug therapy may have been more beneficial for general cognitive function in AD patients than drug therapy alone (short-term treatment: MD, mean difference = 1.94, 95% CI: 1.11, 2.77; $p < 0.01$; medium-term treatment: MD = 4.41, 95% CI: 1.83, 7.00; $p < 0.01$). People who received acupuncture plus drug therapy attained higher ADL (Activities of Daily Living) scores than patients who received drug therapy alone for medium-term treatment duration (MD = -2.14; 95% CI: -3.69, -0.59; $p < 0.01$). However, there is no statistically significant difference in subgroup effect on MMSE (Mini-mental Status Examination) and ADLs ($p > 0.05$) when comparing acupuncture treatment with drug therapy (such as Donepezil hydrochloride, Nimodipine, or Yizhijiannao), or acupuncture plus drug therapy (such as Donepezil hydrochloride, Dangguishaoyaosan, or Jiannaosan) with drug therapy alone. There was also no significant difference in general cognitive function, ADLs, or incidence of adverse events between acupuncture treatment and drug therapy ($p > 0.05$). |
| **Conclusions** | This review indicates that acupuncture plus drug therapy may have a more beneficial effect for AD patients than drug therapy alone on general cognitive function in the short and medium term and on ADLs in the medium term. Acupuncture alone may not have superior effects compared with drug therapy on global cognitive function, ADLs, and incidence of adverse events. Duration of treatment may not modify the effect of acupuncture in comparison with drug therapy. Additional large-scale and high-quality clinical trials are needed. |

### 1.1.10. Huang 2019

Huang Q, Luo D, Chen L, Liang FX, Chen R. Effectiveness of Acupuncture for Alzheimer's Disease: An Updated Systematic Review and Meta-analysis. Curr Med Sci. 2019;39(3):500-511. [199649].

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| **Background** | Acupuncture has reportedly improved memory and cognitive impairment in both animal and clinical studies. It may be an effective treatment for Alzheimer's disease (AD). |
| **Objective** | The purpose of this meta-analysis was to review the effectiveness of acupuncture for the treatment of AD. |

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| **Methods** | Eight databases were searched for articles published up to and including July 2017, and **13 studies** fulfilling the inclusion criteria were identified. The main outcomes assessed were clinical efficacy rate, Mini-Mental State Examination score, Ability of Daily Living Scale score, Alzheimer's Disease Assessment Scale-Cognition score, Hasegawa's Dementia Scale (HDS) score, and adverse events. The methodological quality of the articles was assessed using Cochrane's risk of bias. All the studies compared the efficacy of acupuncture with that of medication, and were published in Chinese journals. |
| **Results** | Meta-analysis revealed that acupuncture yielded positive results as determined via all the indexes scored except the HDS (95% CI -0.26 to 0.90, Z=0.35, P=0.73). Only one of the studies reported adverse events associated with acupuncture and medication. The rate of adverse events in the medication group was 13%. In most of the studies assessed in the current meta-analysis, acupuncture alone was better than conventional western medicines for the treatment of AD. |

### 1.1.11. Wang 2019

Wang Yishen, Xu Jia, Fu Qinhui, Pei Jian. [Acupuncture combined with medicine for cognitive functions and life quality of patients with Alzheimer’s disease: a systematic review]. Shanghai Journal of Traditional Chinese Medicine. 2019;1:19-25. [201736].

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| **Objective** | To systematically evaluate the efficacy and safety of acupuncture combined with medicine for cognitive functions and life quality of the patients with Alzheimer’s Disease ( AD). |
| **Methods** | The randomized controlled trials ( RCTs) regarding acupuncture combined with medicine for AD published from January 1st of 2008 to August 31th of 2018 were researched in China National Knowledge Infrastructure, VIP medicine information system, Wan Fang database, Chinese Biomedical Database, PubMed, Medline, Springer Link and Cochrane Library. The quality assessment was performed based on the guidance of the Cochrane Reviewers’ Handbook, and Meta-analyses was performed by using Rev Man 5. 3 software. |
| **Results** | Totally **8 RCTs** were included, Involving **472 AD patients**. The results of Meta-analyses showed that the treatment group was superior to the control group in improving the mini-mental state examination (MMSE)MD = 0.76,95%CI [0.42,1.10], P<0.000 01), Alzheimer’s disease assessment scale-cognitive section ( ADAS-cog) ( MD =-0.32,95%CI [-0.61,-0.03],P = 0.03), activities of daily living (ADL)( MD =-0.66,95%CI [-1.06,-0.27],P = 0.001). |
| **Conclusion** | Acupuncture combined with medicine for cognitive functions and life quality of AD patients is effective. However, the included studies were with risk of bias and with clinical heterogeneity. So more RCTs of high quality are needed to further confirm its efficacy and safety. |

### 1.1.12. Zou 2016 ~

Zou Jingfeng, Xie Ke, Guo Peiyan, Dong Xushuai, Zhao Fei. [Meta-analysis of randomized controlled clinical trial about acupuncture in treating Alzheimer's disease]. Gansu Journal of Traditional Chinese Medicine. 2016;1:80-84. [186969].

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| **Objectives** | To systematically assess the differences between traditional acupuncture and western medicine in treating alzheimer's disease. |

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| **Methods** | Randomized controlled trials (RCTs) about acupuncture compared with western medicine in treating alzheimer's disease were chosen by searching PubMed, Embase, Cochrane library, CNKI, VIP and Wanfang, the quality of the literature which met the included standard were assessed and meta-analysis was performed by using RevMan 5. 2 software. |
| **Results** | **Eight articles and 349 patients** were included. The results of Meta-analysis showed that the difference had no statistical meaning between both groups, while clinical effects of acupuncture in treating alzheimer's disease [OR=1. 15, 95%CI (0. 69, 1. 91)], MMSE scaling [MD=0. 40, 95%CI (-2. 18, 2. 97)], ADL scaling [MD=0. 60, 95%CI (-0. 54, 1. 74)], HDS scaling [MD=-0. 20, 95%CI (-1. 19, 0. 80)] were equivalent to these indexes of western medicine. |
| **Conclusions** | The advantages of acupuncture in treating alzheimer's disease compared with western medicine are unsure, more large samples and high quality RCTs are needed to further validate the results. |

### 1.1.13. Xu 2015 (combined with western medicine) ☆☆

Xu Xiaotai, Xie Wei. [Meta-analysis on acupuncture combined with western medicine for treatment of Alzheimer’s disease]. World Science and Technology-Modernization of Traditional Chinese Medicine. 2015;4:836-840. [187068].

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| **Objectives** | This study was aimed to evaluate efficacy of acupuncture combined with western medicine in treatment of Alzheimer’s disease (AD) with meta-analysis of data came from randomized controlled trials (RCTs). |
| **Methods** | Databases both at home and abroad were comprehensively searched to collect efficacy data of acupuncture combined with western medicine versus western medicine in RCTs. The data was extracted from each study to conduct a meta-analysis with Rev Man 5. 2. |
| **Results** | The results showed that **10 studies** measured up to standard. Seven studies reported effective cases were carried out by meta-analysis. The total RR was 1. 25 [1. 14, 1. 38]. The funnel plot was approximately symmetry. It was suggested that effect of the therapy group was better than the control group (Z = 4. 66, P<0. 01). Four studies reported mini-mental state examination (MMSE) scores were carried out by meta-analysis. The total MD was 2. 87 [0. 64, 5. 10]. The funnel plot was approximately symmetry. It was suggested that the therapy group was better than the control group on AD treatment in cognitive function improvement (Z = 2. 52, P= 0. 01). |
| **Conclusions** | It was concluded that from current study, **acupuncture combined with western medicine in AD treatment was definitely effective**. However, it still required further study. |

### 1.1.14. Zhou 2015 ☆☆

Zhou J, Peng W, Xu M, Li W, Liu Z. The Effectiveness and Safety of Acupuncture for Patients with Alzheimer Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Medicine (Baltimore). 2015;94(22). [183449].

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| **Objectives** | The use of acupuncture for treating Alzheimer disease (AD) has been increasing in frequency over recent years. As more studies are conducted on the use of acupuncture for treating AD, it is necessary to re-assess the effectiveness and safety of this practice. The objective of this study was to assess the effectiveness and safety of acupuncture for treating AD. |

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| **Methods** | Central Register of Controlled Trials (CENTRAL), PubMed, MEDLINE, Embase, PsycINFO, Chinese Biomedicine Literature (CBM), Chinese Medical Current Content (CMCC) and China National Knowledge Infrastructure (CNKI) were searched from their inception to June 2014. Randomized controlled trials (RCTs) with AD treated by acupuncture or by acupuncture combined with 1 kind of drugs were included. Two authors extracted data independently. The continuous data were expressed as mean differences (MD) with 95% confidence intervals (Cis). Weighted MD (WMD) was used instead of standardized MD (SMD) when the same scales were used. Adverse reactions related to acupuncture were also investigated. |
| **Results** | **Ten randomized controlled trials with a total of 585 participants** were included in the meta-analysis. The combined results of 6 trials showed that acupuncture was better than drugs at improving scores on the Mini Mental State Examination (MMSE) scale (MD 1.05, 95% CI 0.16-1.93). Evidence from the pooled results of 3 trials showed that acupuncture plus donepezil was more effective than donepezil alone at improving the MMSE scale score (MD 2.37, 95% CI 1.53-3.21). Out of 141 clinical trials, 2 trials reported the incidence of adverse reactions related to acupuncture. Seven out of 3416 patients had adverse reactions related to acupuncture during or after treatment; the reactions were described as tolerable and not severe |
| **Conclusions** | **Acupuncture may be more effective than drugs and may enhance the effect of drugs for treating AD in terms of improving cognitive function**. Acupuncture may also be more effective than drugs at improving AD patients' ability to carry out their daily lives. Moreover, acupuncture is safe for treating people with AD |

### 1.1.15. Cao 2014 Ø

Cao Fei, Pan Xiao-Ling, Li Xuan-Chao, Chen Bao, Jin Yuan, Huang Peng. [Systematic review and meta-analysis on acupuncture for Alzheimer disease in chinese population]. Acta Academiae Medicinae Jiangxi. 2014;9:59-61, 6. [186901].

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| **Objectives** | To assess the therapeutic effect of acupuncture on Alzheimer disease (AD)in Chinese population, and to provide more reliable information for the treatment of AD. |
| **Methods** | The literature published from January 1979 to December 2013 on the acupuncture for treatment of Alzheimer disease in Chinese population was collected, and the effects of acupuncture on mini-mental state examination (MMSE) and activity of daily living (ADL) were assessed. The meta-analysis was conducted by using RevMan5. 0. |
| **Results** | A total of **5 randomized controlled trials** were identified and all controls were oral medications. In the aspect of cognitive function, the weighted mean difference (WMD)was -0. 61 (- 1. 34, 0. 13). In the aspect of ADL, the WMD was -0. 48 (-0. 72, 0. 76). |
| **Conclusions** | **Compared with oral medications, the acupuncture can not improve the MMSE and ADL scores in patients with AD**. Furthermore, the quality of literature is poor. Therefore, more observations are needed to verify the effect of acupuncture on AD. |

### 1.1.16. Lee 2009

Lee MS, Shin BC, Ernst E. Acupuncture for Alzheimer's disease: a systematic review. Int J Clin Pract. 2009;63(6):874-9. [153322].

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| **Background** | Acupuncture is often used as a treatment for dementia and is claimed to be effective in improving intelligence. |
| **Aims** | The objective of this review is to assess the clinical evidence for or against acupuncture as a treatment for Alzheimer's disease (AD). |

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| **methods** | We searched the literature using 17 databases from their inception to August 2008, without language restrictions. We included all randomised clinical trials (RCTs) of needle acupuncture to treat human patients suffering from AD. Methodological quality was assessed using the Jadad score. |
| **Results** | Three RCTs met all inclusion criteria. Two RCTs assessed the effectiveness of acupuncture on cognitive function compared with drug therapy. Their results suggested no significant effect in favour of acupuncture [n = 72, weight mean difference (WMDs), -0.55; 95% confidence intervals (CIs) -1.31 to 0.21, p = 0.15, heterogeneity: tau(2) = 0, chi(2) = 0.048, p = 0.49, I(2) = 0%]. Two RCTs tested acupuncture for activities of daily living (ADL). One RCT reported favourable effects of drug therapy compared with acupuncture for ADL, while the other failed to so. The meta-analysis of these data showed significant effects of drug therapy compared with acupuncture (n = 72, WMD, -1.29; 95% CIs: -1.77 to -0.80, p < 0.001, heterogeneity: tau(2) = 0, chi(2) = 0.17, p = 0.68, I(2) = 0%). |
| **Conclusion** | Even though the number of studies is small, the existing evidence does not demonstrate the effectiveness of acupuncture for AD. |

## 1.2. Special outcome

### 1.2.1. Neuroimaging studies

#### 1.2.1.1. Wang 2026

Wang K, Shao B, Ye LF, Wen JZ, Chen Y, Fang C, Luo X. Effects of acupuncture on brain functional networks in patients with mild cognitive impairment and Alzheimer's disease: a systematic review and activation likelihood estimation meta-analysis of neuroimaging studies. Quant Imaging Med Surg. 2026 Jan 1;16(1):29. https://doi.org/10.21037/qims-2025-1047

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| **Background** | The increasing prevalence of Alzheimer's disease (AD) and mild cognitive impairment (MCI) presents a significant societal and familial burden. Acupuncture has shown promise in modulating brain function; however, systematic evidence on its effects on brain functional networks in individuals with AD and MCI remains limited. This study aimed to quantitatively synthesize neuroimaging findings using activation likelihood estimation (ALE) meta-analyses. |
| **Methods** | We systematically searched PubMed, PsycINFO, Google Scholar, SinoMed, and China National Knowledge Infrastructure (CNKI) for neuroimaging studies on acupuncture in AD and MCI. Activation coordinates were analyzed using GingerALE software. Separate ALE meta-analyses were conducted for AD and MCI with family-wise error (FWE) correction (P<0.05) and a cluster-forming threshold of P<0.001 (5,000 permutations), achieving >80% post hoc power. Contrast analyses used P<0.01, a minimum cluster size of 200 mm3 (10,000 permutations), and 95% confidence intervals from permutation distributions. |

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| **Results** | **Thirteen studies (702 participants: 105 with AD, 312 with MCI, and 285 controls)** with 303 activation foci (153 increased and 150 decreased) were included in the analysis. In patients with AD, acupuncture enhanced activation in the right superior frontal gyrus (BA10), left cerebellar regions, and right inferior occipital gyrus (BA19), while reducing activation in the right middle frontal gyrus (BA6). In an individual with MCI, increased activation was found in the right superior and middle temporal gyri (BA38 and BA21), parahippocampal gyrus (BA28), bilateral posterior cerebellar lobes, and left superior parietal lobe (BA7), which was accompanied by decreased activity in the right superior frontal gyrus (BA6) and cerebellar regions. Combined analyses revealed convergent activation in the bilateral cerebellar tonsils, parahippocampal gyrus, right middle temporal gyrus, left superior parietal lobe, and right superior frontal gyrus, indicating shared modulatory effects across both disorders. |
| **Conclusion** | Acupuncture consistently activates the frontal, temporal, parietal, and cerebellar regions linked to cognitive and sensorimotor functions. Stronger effects in individuals with MCI suggest greater neuroplastic responsiveness. These findings provide quantitative evidence supporting acupuncture as a potential adjunctive therapy for cognitive impairment in neurodegenerative diseases. |

#### 1.2.1.2. Zhu 2026

Zhu W, Li H, Wang K, Sun M, Xiang K, Shan S, Ke C. Evidence integration of acupuncture for prevention and treatment of Alzheimer's disease and mild cognitive impairment from a neuroimaging perspective. Review J Alzheimers Dis. 2026 Mar 20;13872877261420235. https://doi.org/10.1177/13872877261420235

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| **Background** | Acupuncture has clinical potential in treating Alzheimer's disease (AD) and mild cognitive impairment (MCI), but there is a lack of systematic review and presentation of clinical evidence from the perspective of neuroimaging in this field. |
| **Objective** | To conduct a systematic review of clinical studies on acupuncture for AD and MCI from the perspective of neuroimaging, and to comprehend the evidence distribution of relevant research. |
| **Methods** | This article retrieved all the neuroimaging clinical studies on acupuncture treatment for AD and MCI that were published and included in the seven databases from their establishment until February 22, 2025. It analyzed and organized the data based on the PICOS (Population, Intervention, Comparison, Outcome, Study design) principle, and presented the quality and distribution of evidence. |
| **Results** | A total of 58 studies were included. The diagnostic criteria for the research subjects mainly refer to the standards of Western medicine. The task design was mostly two-arm before-and-after comparisons and single-group immediate studies, with the intervention measures mainly including hand acupuncture and electroacupuncture. The study employed 8 neuroimaging techniques and 29 outcome measures, with a primary focus on brain functional activation regions and brain functional connectivity. Included studies had high bias risk in blinding design/implementation; overall evidence quality was acceptable. |
| **Conclusion** | Acupuncture for AD and MCI demonstrates clear efficacy, which is supported by imaging evidence. In the future, more large-sample, multi-center joint clinical studies using neuroimaging methods will be needed to further investigate AD and MCI, providing more high-quality evidence-based medical evidence in this field. |

## 1.3. Special Acupuncture Techniques

### 1.3.1. Comparison of acupuncture techniques

#### 1.3.1.1. Hu 2026

Hu JX, Wen Q, Zhou H, Hui Q, Yuan QX, Cai H, Cheng X, Liu J, Lin L. Summary of the evidence on TCM nonpharmacological interventions for cognitive impairment in patients with Alzheimer's disease. Geriatr Nurs. 2026;71:104096. https://doi.org/10.1016/j.gerinurse.2026.104096

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| **Objective** | To systematically synthesize the best available evidence on nonpharmacological interventions in traditional Chinese medicine (TCM) for cognitive impairment in patients with Alzheimer's disease (AD). |
| **Methods** | Guided by the “6S” evidence pyramid model, a comprehensive search was conducted across multiple databases from their inception to March 2025. Two researchers independently assessed the quality of the literature, while four researchers extracted the evidence using a standardized form. The best available evidence was ultimately identified through group discussion. |
| **Results** | A total of ten articles were included, comprising two guidelines, one expert consensus statement, and seven systematic reviews. Eighteen evidence items were summarized across five areas: acupuncture, acupuncture combined with Chinese herbal medicine (CHM), five-element music therapy, Baduanjin exercise, and Tai Chi. |
| **Conclusion** | Evidence regarding TCM nonpharmacological interventions for AD-related cognitive impairment is both scientific and comprehensive. However, further high-quality, large-scale clinical trials are still warranted. |

#### 1.3.1.2. Li 2026

Li Z, Bai X, Li J, Geng W, Xing X, Liang J, Li J, Li J. Network meta-analysis of different traditional Chinese medicine therapies as adjuvant treatments for Alzheimer's disease. Complement Ther Clin Pract. 2026;64:102075. https://doi.org/10.1016/j.ctcp.2026.102075

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| **Background and purpose** | This network meta-analysis aimed to compare and rank different traditional Chinese medicine (TCM) therapies used as adjuncts to conventional Western medicine (CWM) for Alzheimer's disease (AD), in order to inform evidence-based clinical decision-making. |
| **Methods** | Randomized controlled trials evaluating TCM therapies as adjuncts to CWM for AD were searched in eight databases from inception to January 1, 2025. Two reviewers independently performed study selection, data extraction, and risk-of-bias assessment (RoB 2.0). Network meta-analysis was conducted using RevMan 5.4 and Stata 16.0. |

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| **Results** | Thirty-one randomized controlled trials involving 3,221 patients were included. Seven interventions were compared: CWM alone, CWM plus Chinese herbal medicine (CHM), **acupuncture (Acup)**, Chinese patent medicine (CPM), **acupuncture plus acupoint application (AA)**, **acupuncture plus CPM**, and **acupuncture plus CHM**. CWM+Acup+AA ranked first for overall clinical effectiveness [odds ratio (OR)=10.71, 95% CI: 3.44-33.33; SUCRA=94.5%] and activities of daily living (ADL) [standardized mean difference (SMD)=4.10, 95% CI: 1.18-7.02; SUCRA=99.2%]. CWM+CHM+Acup ranked first for Mini-Mental State Examination (MMSE) score (SMD=3.01, 95% CI: 1.65-4.37; SUCRA=97.2%), Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) score (SMD=2.43, 95% CI: 0.43-4.43; SUCRA=89.3%), and serum superoxide dismutase (SOD) (SMD=2.78, 95% CI: 0.87-4.69; SUCRA=94.1%). CWM+CPM ranked first for inflammatory biomarkers IL-1β, IL-6, and TNF-α. |
| **Conclusions** | Current evidence suggests that Chinese patent medicine added to conventional Western medicine may be advantageous for inflammatory biomarkers, whereas acupuncture-based combinations may provide greater benefits for selected clinical and functional outcomes. However, because most comparisons were supported by few studies and the certainty of evidence was low to very low, these findings require confirmation in rigorously designed randomized controlled trials. |

#### 1.3.1.3. Yu 2026

Yu Z, Li H, Wang Y, Shen F, Wang Y. Aerobic exercise versus acupuncture as adjuncts to acetylcholinesterase inhibitors in Alzheimer's disease: a systematic review and Bayesian network meta-analysis. Am J Clin Exp Immunol. 2026;15(2):37-49. https://doi.org/10.62347/FDDF9443

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| **Background** | Acetylcholinesterase inhibitors (AChEIs) remain the standard therapy for Alzheimer's disease (AD), yet their cognitive and functional benefits are limited, creating a strong need for effective adjunctive treatments. Aerobic exercise and acupuncture have been proposed as promising complements to AChEIs because of their potentially synergistic neurotrophic and cholinergic effects. |
| **Methods** | To compare these treatment combinations, we carried out a Bayesian network meta-analysis (BNMA) of randomized controlled trials (RCTs). These studies were sourced from major English and Chinese databases and examined cognitive and functional outcomes. In total, 37 RCTs were included, covering 2,188 participants. |
| **Results** | Among all, combined acupuncture (SUCRA = 78.92%) and fire needle therapy (SUCRA = 78%) demonstrated the highest probability of improving Mini Mental State Examination scores, while moderate intensity aerobic exercise ranked best for the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog, SUCRA = 23.3%) and the Barthel Index (SUCRA = 71.1%). Combined acupuncture was ranked highest for the Alzheimer's Disease Assessment Scale-Activities of Daily Living (ADAS-ADL, SUCRA = 94.3%), although its effects did not reach statistical significance. Across analyses, heterogeneity was minimal ($I2 \leq 4\%$), model convergence was stable, and no publication bias was detected. |
| **Conclusion** | Overall, this BNMA suggests that combined or thermal acupuncture offers the strongest cognitive gains alongside AChEIs, whereas moderate-intensity aerobic exercise provides the most reliable functional support. Because overall functional improvements were modest and evidence for some interventions remains limited, the benefits appear selective rather than broad. Larger, standardized trials are needed to clarify these patterns and guide their use in practice. |

#### 1.3.1.4. Yin 2023 (Network Meta-Analysis)

Yin W, Chen Y, Xu A, Tang Y, Zeng Q, Wang X, Li Z. Acupuncture May Be a Potential Complementary Therapy for Alzheimer's Disease: A Network Meta-Analysis. Evid Based Complement Alternat Med. 2022 Nov 23;2022:6970751. https://doi.org/10.1155/2022/6970751

With Alzheimer's disease (AD) becoming a worldwide problem, traditional Chinese medicine (TCM), especially acupuncture, stands out as a complementary therapy because of its feature-"treatment based on syndrome differentiation". This systematic review and network meta-analysis (NMA) confirms the complement effect of acupuncture and explores the best combination of therapy for AD based on the total effect and activity of daily living scale (ADL). We searched relevant randomized controlled trials (RCTs) that applied acupuncture for treating AD. **58 studies with 4334 patients** were included in accordance with PRISMA guidelines. The results showed that for the total effect, the order of probability for the effect: acupuncture + western medicine > acupuncture + herbal medicine > acupuncture > acupuncture + western medicine + herbal medicine. For the ADL score, the order of probability for the effect: acupuncture + western medicine > acupuncture > acupuncture + western medicine + herbal medicine > acupuncture + herbal medicine. The combination of acupuncture and medicine has a better clinical effect than acupuncture only in a way. Acupuncture + western medicine has an obvious and exact improvement in the curative effect from both total effect and ADL score, but further higher quality studies, which can detail the classification of these interventions, are still needed to verify it.

#### 1.3.1.5. Yin 2022 (Network Meta-Analysis)

Yin Z, Li X, Wang L, Sun M, Zhao L, Liang F. The Comparative Efficacy of Multiple Acupuncture for Alzheimer's Disease: A Bayesian Network Meta-Analysis. Evid Based Complement Alternat Med. 2022 May 17;2022:3288948. https://doi.org/10.1155/2022/3288948



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| **Background** | Alzheimer's disease (AD) is a progressive neurodegenerative disease. Numerous cases have illustrated that the acupuncture method could improve AD patients' cognitive function and daily living ability. However, the optimal acupuncture treatments remain controversial. Therefore, we aimed to conduct a systematic review to compare the efficacy of multiple acupuncture therapies for AD and identify the optimal acupuncture intervention for delaying AD progression. |
| **Methods** | To select potentially concerned randomized controlled trials (RCTs), we searched four English databases, four Chinese databases, and additional sources from 1 May 2021. Two independent reviewers conducted study screening, data extraction, and methodological quality assessment. The primary outcome was global cognitive function improvement. Pairwise and Bayesian network meta-analyses were performed using STATA v15.0 and ADDIS v1.16.8. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool was used to assess the quality of evidence. |
| **Results** | This study included **34 RCTs with 2,071 participants**. Regarding global cognitive function improvement, the pairwise meta-analysis confirmed that electronic acupuncture (EA) plus conventional medicine (CM) and manual acupuncture (MA) plus CM were statistically significantly different from CM, and EA plus CM was ranked as the best combination in the network meta-analysis. In terms of response rate, MA outperformed CM statistically significantly; warm acupuncture (WA) was ranked as the best in the network meta-analysis. Regarding activity of daily living improvement, EA plus CM, MA plus CM, and fire acupuncture plus CM, MA, and scalp acupuncture were statistically significantly different from CM, and EA plus CM was ranked as the best combination in the network meta-analysis. However, the evidences were ranked as low to critically low. |

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| **Conclusions** | Acupuncture, as a monotherapy or an adjuvant therapy, may have a beneficial effect on efficacy for AD. EA plus CM may be the optimal acupuncture therapy for AD and should be administered to AD patients. It may aid and support patient, operative, and societal decision-making. Due to the dearth of high-quality evidence, additional high-quality studies should be conducted to ensure these findings in the future. This study is registered with PROSPERO (CRD42021252305). |

### 1.3.2. Combined with Traditional Chinese Medicine

#### 1.3.2.1. Wang 2023 (combined with tonifying kidney decoction)

Wang XC, Chu CL, Lu K, Chen X, Jin XQ, Quan SJ. The role of tonifying kidney decoction and acupuncture in the treatment of Alzheimer's disease: A network meta-analysis. Medicine (Baltimore). 2022 Nov 18;101(46):e31243. https://doi.org/10.1097/MD.0000000000031243.

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| **Importance** | As one of the chronic neurological degenerative diseases with the highest incidence of amnesia and dementia, Alzheimer's disease (AD) carried out the clinical treatment based on the 2 traditional Chinese medicine (TCM) of Chinese herbal compound and acupuncture (AP). With the vigorous development of TCM, doctors are facing the problem of choosing TCM or western medicine in clinical work. Hence there is an urge to make pairwise comparisons among these interventions to provide evidence for clinical practice. |
| **Objective** | The used efficacy of the 2 TCM methods and combined with donepeziline were compared to compile the best treatment through network meta-analysis. |
| **Methods** | Patients diagnosed with AD were included in the randomized clinical trial, who were treated with tonifying kidney decoction (TKD) or AP combined with donepezil hydrochloride (DH) as an intervention measure, while the control group was treated with DH. The total effective rate was the primary outcome, and mini-mental state examination (MMSE) score and activities of daily living (ADCS-ADL) scores were the secondary indicators. |
| **Results** | Eventually **30 studies reporting 2236 patients** underwent TKD or AP combined with DH were enrolled. In terms of total efficiency, compared with TKD and DH, TKD + DH was significantly preferable. In addition, TKD were classified into 2 categories, namely tonifying kidney with reducing phlegm formulas (TKRP) and tonifying kidney with filling lean marrow (TKFLM). Regarding to MMSE score of TKD, of the 3 interventions, only TKRP + DH (standard mean difference [SMD] = 4.84, 95% confidence interval [CI]: 0.86-8.82) and TKFLM + DH (SMD = 3.93, 95% CI: 1.06-6.80) had significant efficacy over TKFLM (SMD = 4.25, 95%CI: -2.58 to 11.08). Although no difference between TKRP and other groups, its effectiveness was higher than TKFLM + DH and TKFLM (surface under the cumulative ranking curve (SUCRA) = 61.5%). For the ADL score, compared with TKFLM + DH and DH, TKRP + DH had more effective (SUCRA = 70.2%). Regarding to the total effective rates, AP + DH was more statistically better than AP, and AP was statistically better than DH. |
| **Conclusion** | TKD or AP in combination with DH are significantly superior in treating AD. |

#### 1.3.2.2. Jiao 2020

Jiao Li. [Systematic Review of Acupuncture Combined with Traditional Chinese Medicine in Treatment of Alzheimer's Disease ]. Journal of Hubei Minzu University (Medical Edition). 2020. [212897].

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| **Objective** | The aim of the study is to comprehensively evaluate the clinical efficacy of acupuncture combined with Traditional Chinese Medicine in the treatment of a Alzheimer disease. |
| **Methods** | We performed online searches of the CNKI, Wanfang, VIP, PubMed, web of Science (SCI), Medline until July 2019 to find randomized controlled trials about acupuncture combined with Traditional Chinese Medicine in the treatment of Alzheimer disease. Two reviewers independently screened and extracted data according to inclusion and exclusion criteria. Review Manager5. 3 was used to perform the meta-analysis. |
| **Results** | Totally 12 RCTs involving 737 patients were included eventually. The results of Meta-analysis showed that compared with Western medicine, acupuncture combined with Traditional Chinese Medicine had better efficacy in improving effective rate [RR=1. 29, 95%CI (1. 16, 1. 44)] and MMSE score [WMD=1. 87, 95%CI (0. 76, 2. 98)] (P<0. 01). |
| **Conclusion** | Current RCTs clinical evidence indicated that acupuncture combined with Traditional Chinese Medicine was better than Western medicine in the treatment of Alzheimer disease, and there was no serious adverse reaction. Due to the small sample size and the generally low quality of included studies, this conclusion still needs support from large sample, multi-center, high-quality randomized controlled research. |

#### 1.3.2.3. Zhou 2017

Zhou S, Dong L, He Y, Xiao H. Acupuncture plus Herbal Medicine for Alzheimer's Disease: A Systematic Review and Meta-Analysis Am J Chin Med. 2017;45(7):1327-1344. [52387].

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| **Background** | Alzheimer's disease (AD) is associated with the unprecedented aging tendency in our world population and has become a significant health issue. The use of Traditional Chinese Medicine to treat AD has been increasing in recent years. |
| **Objective** | The objective of this meta-analysis is to evaluate the effectiveness of combining acupuncture with herbal medicine to treat AD. |
| **Methods** | Randomized controlled trials (RCTs) of acupuncture plus herbals versus treatment with western drugs for AD were retrieved from 11 databases. The data were extracted by two authors; dichotomous data were expressed as odds ratio (Ors) and 95% confidence intervals (Cis), while continuous data were calculated by mean differences (MDs) with 95% Cis. |
| **Results** | Although the combined analysis of the score of Activity of Daily Life (ADL) scale MD was [Formula: see text]3.59 (95% CI [Formula: see text]7.18-0.01, [Formula: see text]), which indicates there was no statistically significant difference between the two treatments at reducing the ADL scale score, the pooled results of 12 trials indicated that acupuncture plus Chinese herbal medicine was better than western drugs at improving the effectiveness rate (OR 2.24, 95% CI 1.40-3.56), the combined evidence of 11 articles showed that acupuncture plus Chinese herbal medicine was more effective than western drugs at improving the scores for the Mini Mental State Examination (MMSE) scale (2.10, 95% CI 0.69-3.51, [Formula: see text]) and the traditional Chinese medicine symptom (MD 5.07, 95% CI 3.90-6.25, [Formula: see text]). |
| **Conclusions** | From the current research results, acupuncture plus herbal medicine may have advantages over western drugs for treating AD. Nevertheless, well-designed RCTs with a larger sample size are required in the future. |

#### 1.3.2.4. Zou 2016 ☆

Zou Jingfeng, Guo Peiyan, Xie Ke, Dong Xushuai, Zhao Fei. [Meta-analysis of the effectiveness of acupuncture treatment combined with traditional chinese medicine treatment of Alzheimer disease]. China Journal of Chinese Medicine. 2016;1:138-143. [186905].

目的：比较针刺联合中药与单用中药治疗阿尔茨海默病的疗效差异. 方法：通过检索PubMed□Embase□CNKI等中外论文数据库，筛选出针药对照单用中药治疗阿尔茨海默病的随机临床对照试验. 对符合标准的文献评价质量，并应用RevMan Manager 5. 2软件进行Meta分析. 结果：纳入共包括335例患者的6篇文献. Meta分析结果显示，针药结合、单用中药治疗阿尔茨海默病后的有效率分别为76. 96%和65. 28%，合并效应量的比值比OR=1. 89, (95□ CI=1. 11, 3. 21), P=0. 02 □0. 05, 提示差异有统计学意义;针药与单用中药治疗阿尔茨海默病后的MMSE□ADL量表评分的分析结果分别为MD=1. 55, (95□CI=0. 98, 2. 12), P□0. 000 01□WMD=0. 36, (95□ CI=0. 14, 0. 59), P=0. 002, 以上结果P均<0. 05，提示治疗前后量表评分改变上针药与单用中药的疗效比较，差异有统计学意义. 结论：针药结合比单用中药治疗阿尔茨海默病更具优势，但仍需更多大样本高质量的随机临床对照试验进一步验证.

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| **Objectives** | to compare the Alzheimer's disease treated by acupuncture combined with traditional Chinese medicine and traditional Chinese medicine efficacy. |
| **Methods** | Search PubMed, Embase, CNKI database and foreign papers, filter out acupuncture controlled randomized controlled clinical trials of traditional Chinese medicine for treatment of Alzheimer's disease alone. To meet the standard of quality of literature evaluation, and using RevMan Manager 5. 2 software Meta analysis. |
| **Results** | included in total including 335 cases 6 references. Meta analysis shows that acupuncture and using traditional Chinese medicine for treatment of Alzheimer's disease, the effective rate was 76. 96% and 65. 28%, the combined effect of the ratio of OR=1. 89, (95% CI=1. 11, 3. 21), P=0. 02 <0. 05, indicating there was a statistically significant difference; acupuncture and using traditional Chinese medicine in the treatment of Alzheimer's disease after the MMSE, ADL scale scores results for MD=1. 55, (95%CI=0. 98, 2. 12), P<0. 000 01□WMD=0. 36, (95% CI=0. 14, 0. 59), P=0. 002, results above all <0. 05, scores on the changes before and after treatment of acupuncture and medicine with comparison of the curative effect of traditional Chinese medicine alone, there was a statistically significant difference. |
| **Conclusions** | **acupuncture has an advantage over using traditional Chinese medicine** in the treatment of Alzheimer's disease, but still needs more large scale high quality randomized controlled trials for further verification. |

### 1.3.3. Warm needle

#### 1.3.3.1. Chen 2022

Chen X, Liu F, Lin N, Lin Q, Lyu Z, Xiu H, Nie P. Warming needle moxibustion for Alzheimer's disease: A systematic review of randomized controlled trials. Geriatr Nurs. 2022 Jan-Feb;43:219-226. https://doi.org/10.1016/j.gerinurse.2021

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| **Objective** | To systematically research the impact of warming needle moxibustion (WNM) for Alzheimer's Disease (AD). |
| **Methods** | Four Chinese databases and six English databases were systematically searched. Randomized controlled trials (RCTs) involving the use of WNM to intervene in AD patients were included. Data were extracted from the included studies and methodological quality was evaluated according to the Cochrane Handbook for Systematic Reviews of Intervention 5.1.0. Meta-analysis was performed using RevMan 5.4 software. |

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| **Results** | **8 RCTs comprising 524 patients** were included. Most studies had no significant bias. The study showed that WNM was more effective in the treatment of AD than acupuncture or pharmacotherapy. The findings were as follows: MMSE (MD = 1.01, 95%CI: 0.13, 1.90, P = 0.03) and CDR (MD = -0.73, 95%CI: -0.84, -0.61, P < 0.00001) for global cognitive function, ADL (MD = -1.84, 95%CI: -2.47, -1.22, P < 0.00001) for activities of daily living, Syndrome Differentiation Scale of Dementia (SDSD) (MD = -2.67, 95%CI: -3.62, -1.72, P < 0.00001), and the total effective rate of patients (OR = 3.20, 95%CI: 1.90 to 5.38, P < 0.0001). The differences in all indicators were statistically significant. |
| **Conclusion** | WNM might have a significant effect on improving cognitive function and daily living ability, reducing the symptoms of AD, and increase the total effective rate. WNM is an effective non-pharmacological therapy for patients with AD. |

### 1.4. Mechanistic systematic reviews

#### 1.4.1. Yang 2026

Yang M, Tong L, Guo Z, Tan Z, Holmes TC, Yu Z, Xu X. Evaluating the potential of acupuncture for Alzheimer's disease treatment: A meta-analysis and systematic review of mouse model studies. Transl Psychiatry. 2026 Mar 17. https://doi.org/10.1038/s41398-026-03923-9

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| **Background** | Acupuncture is an ancient practice that was developed within the framework of traditional Chinese medicine. While acupuncture has been recently proposed as a therapy for Alzheimer's disease (AD), acupuncture effects are not well understood in terms of neural mechanisms. |
| **Objective** | Here, we review and examine the studies that used AD mouse models and analyze the experiments where researchers administered electroacupuncture (EA) to AD mice to assess the potential therapeutic impact of acupuncture on disease pathology and cognitive function in controlled laboratory settings. |
| **Methods** | We analyzed 29 relevant PubMed articles published between January 2014 and July 2025. |
| **Results** | Our results reveal that EA significantly reduces both amyloid-beta (Aβ) and phosphorylated tau (p-tau) levels and neuroinflammatory biomarkers, including molecular signatures for activated microglia and astrocytes in the brain. EA also enhances cognitive functions. While no study directly compared acupoint strategies, the indirect comparisons in our network analysis suggest that GV20 has potential as a therapeutic target for AD. |
| **Conclusion** | Our present meta-analysis and review of literature add to the evidence of integrative health practices for acupuncture-based Alzheimer's disease treatment. |

## 2. Overviews of systematic reviews

### 2.1. Ke 2024

Ke C, Shan S, Yu J, Wei X, Pan J, Zhang W. Acupuncture for patients with Alzheimer's disease: An evidence map of randomized controlled trials, systematic reviews, and meta-analysis. J Alzheimers Dis. 2024 Dec;102(4):924-942. https://doi.org/10.1177/13872877241295400

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| **Backgound** | Acupuncture is an effective complementary treatment for Alzheimer's disease (AD). This review aims to summarize the available evidence provided by randomized controlled trials (RCTs) and systematic reviews (SRs) or meta-analyses (MAs) on the effect of acupuncture on AD. |
| **Objective** | To systematically summarize and combine clinical research evidence on AD distribution. |
| **Methods** | We conducted a comprehensive search of various databases, including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wan Fang Data, Chinese BioMedical Literature Database (CBM) and Chonqing VIP (CQVIP), from their inception to September 2023. Relevant literature about acupuncture for AD was included, and the characteristics of the evidence map were presented through charts and textual analyses. |
| **Results** | In total, **117 RCTs and 17 SRs or MAs** were included. The results were divided into three categories: basic characteristics of the included literature, clinical characteristics and quality assessment of the included RCTs, and clinical characteristics and quality assessment of the included SRs and MAs. |
| **Conclusions** | Acupuncture as a therapeutic measure for AD has some advantages in improving cognition and quality of life; thus, it is imperative to conduct multi-center, large-scale RCTs to enhance the evidence supporting the use of acupuncture in AD. This is the first evidence map exploring acupuncture treatment for AD, providing insights into the current clinical research landscape on acupuncture treatment for AD. Furthermore, the findings of this study highlight research gaps in this field and serve as a valuable reference for guiding the planning and selection of topics for future research. |

# 3. Evidence Map

## 3.1. Wang 2026

Wang N, Dang L, Chang W, Qi H, Ban J, Guo H, et al. Non-pharmacological interventions for cognitive function improvement in patients with Alzheimer's disease: a best evidence summary. Front Neurol. 2026;17:1888519. https://doi.org/10.3389/fneur.2026.1888519

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| **Background** | Non-pharmacological interventions are widely used to address cognitive impairment in Alzheimer's disease (AD), but the available evidence spans multiple intervention types and evidence sources. This review aimed to systematically retrieve, appraise, and synthesize evidence on interventions intended to improve overall cognitive function in patients with AD. |
| **Methods** | The review followed PRISMA-ScR guidance and the JBI scoping review framework. The evidence-based question was developed using the PIPOST framework. Databases and professional platforms were searched from inception to January 30, 2026, using the “5S” evidence model. Included studies were quality-appraised, and eligible evidence was extracted, synthesized, graded, and assigned recommendation levels. |
| **Results** | Fifteen studies were included: 1 guideline, 7 expert consensus reports, 6 systematic reviews, and 1 randomized controlled trial. Eighteen best-evidence items were identified and grouped into six categories: cognitive training and digital therapy; neuromodulation techniques; exercise interventions; lifestyle and reminiscence therapy; music and sensory stimulation; and **acupuncture** and combined interventions. |
| **Conclusion** | This best-evidence summary identified multiple non-pharmacological approaches that may be considered for improving overall cognitive function in patients with Alzheimer's disease. Intervention selection should be adapted to clinical context and individual patient characteristics, with attention to implementation quality and quality control. |

### 3.1.1. Cui 2025

Cui S, Zhao Y, Wang X, Huang Y, Ye J, Deng Z, Li Y, Qin H, Wang L, Li Y, Wang K, Zheng G, Qin Q. Evaluating the clinical evidence of TCM in Alzheimer's disease: an evidence map perspective. Front Neurol. 2025 Aug 29;16:1571361. https://doi.org/10.3389/fneur.2025.1571361

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| **Objective** | This systematic review aimed to synthesize current clinical evidence from randomized controlled trial (RCT) and meta-analyses on the efficacy and safety of TCM in the treatment of Alzheimer's Disease (AD). |
| **Methods** | Systematic searches across eight biomedical databases (PubMed, Embase, Web of Science, Cochrane Library, CNKI, Wanfang, VIP, SinoMed) through October 26, 2024 yielded an evidence matrix, which was analyzed through integrated narrative-graphic synthesis. |
| **Results** | Our analysis encompassed 187 studies (**141 RCTs and 46 systematic reviews/meta-analyses**), demonstrating cyclical publication growth with recent contraction. Study characteristics included sample sizes of 50-100 participants and intervention durations of 4-24 weeks. Interventions included acupuncture, herbal decoctions, and proprietary medicines. Outcomes focused on clinical efficacy, scale scores, TCM syndrome scores, and safety. While TCM demonstrated therapeutic potential, prescription heterogeneity and diagnostic ambiguity constrained specificity. Methodological quality was generally low, with few high-quality systematic reviews or meta-analyses. |
| **Conclusion** | While TCM shows therapeutic potential in Alzheimer's disease, methodological limitations persist. Subsequent research requires enhanced trial designs with standardized outcome metrics and rigorous bias control protocols. |

# 4. Clinical Practice Guidelines

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| ⊕ positive recommendation (regardless of the level of evidence reported)<br>Ø negative recommendation (or lack of evidence) |

## 4.1. US-based practitioner’s guide (USA) 2025 ⊕

Grossberg GT, Sanford A, Montano CB, Porsteinsson AP, Scanland S, Worz C, McMillian S, Atri A. A US-based practitioner's guide to diagnosis, evaluation, and evidence-based treatment of agitation in Alzheimer's dementia - recommendations of an expert, multispecialty advisory panel. Postgrad Med. 2025 Aug;137(6):469-485. https://doi.org/10.1080/00325481.2025.2517535

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| 3.4. Treatment: nonpharmacologic interventions. Key Recommendation: Individualize nonpharmacologic interventions based on the patient’s psychosocial and cultural background, personality, and interests considering the patient’s current level of functioning to provide a structured routine that includes engaging and meaningful activities.<br>Examples of nonpharmacologic interventions with published evidence supporting efficacy of treatment for agitation include aromatherapy [Citation10], music therapy [Citation11], **acupressure**/therapeutic touch [Citation12,Citation13], robot-assisted activity [Citation14], animal-assisted therapy [Citation15], and doll therapy [Citation16]. |

## 4.2. National Institute for Health and Care Excellence (NICE, UK) 2018 Ø

Dementia: assessment, management and support for people living with dementia and their carers (NG97). Evidence-based recommendations on diagnosing and managing dementia (including Alzheimer’s disease) . London (UK): National Institute for Health and Care Excellence (NICE).

2018;:43P. [174901]. Annexes realtives à l'acupuncture [174901-b].

*1.4 Interventions to promote cognition, independence and wellbeing.* 1.4.5 Do not offer acupuncture to treat dementia.

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