

Music intervention affects the quality of life on Alzheimer's disease: a meta-analysis

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Research article

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Abstract

Background

Music intervention has been found to be beneficial for neurological diseases, especially in slowing down the progression of clinical symptom in patients. However, it remains unclear to what extent can music intervention may affect patients with Alzheimer's disease (AD). Questions remain on whether music intervention can improve the quality of life (QOL) of AD patients, who are usually with poor QOL owing to the burden of disease.

Methods

A search that compared the effectiveness of music intervention to improve the QOL of AD patients were carried out. PubMed, Cochrane library clinical trial database, and WANFANG database were searched to collect data from randomized controlled trials (RCTs). Two independent researchers extracted data from the selected eligible articles by using collection form and RevMan5.3 statistical software and applied for the meta-analysis.

Results

We included six RCTs in our meta-analysis. The results showed that compared to the control group, music intervention can significantly increase the score of the QOL-AD scale (MD=5.10, 95%CI: 2.95-7.24, P<0.001) and The World Health Organization QOL Rating Scale Short Form score (MD=5.76, 95%CI: 1.59-9.92, P=0.007).

Conclusions

Results suggested that music intervention could improve the QOL for the elderly patients with AD. Our findings indicated that music intervention might be considered as a non-pharmaceutical therapy for patients with AD in the future.

Background

Alzheimer's disease (AD) is a neurodegenerative disease which frequently occurs in the elderly population [1]. It accounts for most of dementia cases (~60-70%) worldwide [2]. AD-related pathologies include abnormal deposition of β -amyloid ($A\beta$), formation of senile plaques and neurofibrillary tangles in brain [3]. Its clinical manifestations are severe defects in cognition, such as memory, sensory and motor functions [4-6]. Motor dysfunction is characterized by slow walking, great gait variability, impaired balance and postural control, and deteriorated fine motor control in AD patients [7-9]. These symptoms have clearly reduced the quality of life of AD patients. So far there is no effective cure for the disease, however it is urgent needed to develop effective treatment methods, or prevention strategies to prolong the progression of AD [10]. The clinical situation of AD patient is one of the main factors affecting the quality of life. The World Health Organization (WHO) defined Quality of life as "individual's perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns" [11]. Improving the quality of life in AD is important for patients, caregivers and health care professions [12].

QOL mainly refers to the assessment of the status of an individual's physical, psychological, and social functions [13]. The QOL of patients can also be used as an important indicator of the effectiveness of the health care services they received [14]. Previous studies indicated that the cognitive impairment in elderly chronic diseases is a determinant of poor QOL [15, 16]. The relationship between quality of life and mortality is time dependent. A decrease in quality of life may increase the risk of mortality, therefore the quality of life would be used as a predictor of mortality [17]. The QOL has been accepted as an indicator for the evaluation for AD treatment because it can indicate the processing of AD, activities of daily living and achievement under treatment [18]. Reduced QOL, may have serious impacts on the psychological, physical, behavioral, and social levels of an individual.

Music intervention is a systematic intervention process [19]. The World Federation of Music Therapy (WFMT) defined it as "the professional use of music and its elements as an intervention in medical, educational, and everyday environments with individuals, groups, families, or communities who seek to optimize their quality of life and improve their physical, social, communicative, emotional, intellectual, and spiritual health and wellbeing". In the process, various type of music experience and the therapeutic relationship developed during the intervention process were used by therapists to help patients and improved their quality of life [20-24]. The music intervention has two main types: passive and active music intervention. Listening to music is believed as the predominant passive music intervention. In active music intervention, participants were encouraged to make music, to play instruments, to dance and so on. The latter mainly focuses on interaction and active learning [25]. Studies have demonstrated that listening to music increased the functional connectivity in corticocortical and corticocerebellar networks and can also increase memory and cognitive ability in AD patients by improving neural structure and neurophysiological characteristics [26, 27]. Playing instruments was significantly associated with less likelihood of dementia and cognitive impairment and may improve gross and fine motor coordination in individuals with motor impairments or neurological trauma [28, 29]. Singing blends language, music and instinctive human behavior to enhance neurological stimulation and regulate participants' mood [30]. Music intervention is a relative safer strategy than many other therapies such as medication and surgery, and it is great valuable for further study [31]. In summary, music intervention may potentially improve many aspects in patients with different degrees of dementia, including biological and physiological, behavioral and psychological, QOL, memory failure, cognitive level and so on [32]. However, it remains unclear whether music intervention could improve the QOL in AD patients, and therefore promote the effect of treatment.

To our best knowledge, there is no work conducted by systematic review and meta-analyses on the improvement of QOL by music intervention in AD patients previously. To clarify whether music intervention is an effective intervention contribute to improve the QOL of patients with AD, we employed a detailed search strategy to comprehensively summarize Chinese and internationally published literatures, and the impact of music intervention on the QOL in AD patients were analyzed.

Methods

1.1 Search strategy

PubMed, the Cochrane Library, and Wanfang Database, were systematically searched from January 1986 to March 2021. The search was performed parallel by author LYZ and FTZ. If not, sought a third person's opinion. Key words including "cognitive impairment", "mild cognitive impairment", "Alzheimer's disease", "music intervention", "music therapy", "music listening", "musical instrument", "music performance", "musical rhythms", "randomized controlled trial", "clinical trial" and "clinical study" were searched and an updated final repeat search was carried out on 24 March 2021. For data were not available online, we tried to contact corresponding authors.

1.2 Inclusion criteria

Inclusion criteria: population: 1) A randomized controlled study on the impact of music intervention on the QOL of patients with AD; 2) The participants in this study is patients with AD; 3) There is no significant difference among age, gender and education background in sorted groups before analysis which make these groups comparable; intervention: 1) Intervention Modality Music-based intervention; comparison: 1) All data were sorted into two groups: the music intervention group and the control group without any music intervention; outcome: 1) The indicators evaluated in the literature included the score of QOL-AD or WHOQOL-BERF scale, at least one of the two scales summarized in selected publications; language: 1) Only articles published in English and Chinese were considered.

1.3 Exclusion criteria

Exclusion criteria: 1) The participants were not diagnosed with AD; 2) Non-musical intervention; 3) Non-RCTs; 4) No specific values for outcome variables; 5) Articles lacking original data; 6) Repeat published reports; 7) Full text could not be obtained.

1.4 Quality rating of studies

The Cochrane's Risk of Bias tool was used to evaluate the quality of collected studies. A total of 7 domains were counted in these studies such as random sequence generation, allocation concealment, masking of participants and personal, masking of outcome assessment, incomplete outcome data, selective reporting, and other biases. These domains were classified as high, unclear, and low risk of bias. Low risk of bias means that it has little effect on the results of our study and high degree of risk of bias indicates that it will greatly affect the results in this study. Unclear-bias risk implies potential risks.

1.5 Data extraction and synthesis

A standardized template was used to extract data by two independent reviewers to show the population characteristics (The diagnosis was made according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria, Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria, International Classification of diseases (ICD-10) criteria and in combination with clinical symptoms, medical history, neurological physical examination, neuropsychological scale test results (CERAD) and pathological scoring scale (BEHAVE-AD); The AD patients included in the study (early-onset AD and late-onset AD) were elderly between 55 and 97 years of age) and the outcomes, and the name of the first author, region, year of publication, clinical study design, study participants, intervention modalities, intervention period, and outcome measurement were included. Meta-analysis was performed by using RevMan software (Version 5.3; Cochrane Collaboration, Oxford, England). Heterogeneity test was conducted for the filtration of collected studies and $P < 0.05$ was considered as heterogeneous. There was no significant statistical heterogeneity if $I^2 \leq 50\%$, and fixed effect model should be used; there was statistical heterogeneity among all studies if $I^2 > 50\%$ and random effect model should be used.

Results

2.1 Results of Literature Search

Our initial literature search yielded 298 unique recordings, 255 articles were extracted after duplicates were removed, and there were 32 records left after screening of the titles and abstracts. There are 6 studies (396 patients) with full text were eligible and included in these meta-analyses [33-38]. The detailed screening process is shown in the flow chart in Figure.1.

2.2 Characteristics of Included Studies

The sample size of the included RCTs ranged from 42 to 100 patients and the effect of music intervention on QOL in patients with AD were compared. The Study characteristics summarized the design of included RCTs, which focused on patient's characteristics, the intervention methods and the outcome assessment. Characterized studies are presented in [Table.1](#).

Table.1. Summary of study characteristics

Study author and year	Hee-Jin Kim (2015)	WANG Zhao (2018)	WANG Xiao-hong (2019)	FU Mei-hua (2016)	XIAO Jie-ping (2018)	MENG Shuang (2019)
Participants (N)	N=53	N=100	N=60	N=91	N=50	N=42
Patient's characteristics	All dementia with CDR=1, Probable AD, excluded (not meeting inclusion criteria; declined not want to participate)	Patients with AD, BEHAVE-AD score ≥ 8 points	Meets DSM-V diagnostic criteria for mild to moderate Alzheimer's disease	patients with AD, BEHAVE-AD score ≥ 8 points	patients with AD, BEHAVE-AD score ≥ 8 points	patients with AD, BEHAVE-AD score ≥ 8 points
Groups	MI (n =32) NMI(n= 21)	MI (n =50) NMI(n=50)	MI (n =30) NMI(n =30)	MI (n =45) NMI(n =46)	MI (n =25) NMI(n =25)	MI(n =21) NMI(n =21)
Intervention; music type	Interactive (playing melodies and/or accompanying chords for popular songs and participants were encouraged to develop musical expression and/or imitate musical rhythms)	Interactive (Music Listening/Music Performance)	Interactive (Chorus/Music Appreciation/Musical instrument)	Passive (musical backgrounds)	Interactive (Music Listening/Music recollection/Music singing)	Passive (Music Listening)
Intervention /Control (minutes/per week/ weeks)	I: Music therapy (60/5/24) C: cognitive intervention and pharmacotherapy	I: Music therapy (40~50/3/24) C: Conventional pharmacotherapy	I: Music therapy (60/5/48) C: Routine rehabilitation activities	I: Music therapy (30/3/4) C: pharmacotherapy	I: Music therapy (40/14/16) C: Cognitive training/ pharmacotherapy	I: Music therapy (30/14/8) C: pharmacotherapy
outcome assessment	QOL-AD	QOL-AD	QOL-AD	WHOQOL-BREF	WHOQOL-BREF	WHOQOL-BREF
conclusion	slightly improved QOL	improved QOL	improved QOL	improved QOL	improved QOL	improved QOL

Abbreviations: MI, music intervention; NMI non-music intervention; I, intervention group; C, control group; RCTs, randomized controlled trials

The evaluation on the studies included in the design is shown in [Table.1](#). These studies were generally divided into control group (non-musical intervention) and experimental (musical intervention) group, except one article due to it had 3 different types of musical intervention groups. Such studies commonly used interactive ways for musical intervention, which included music listening, chorus, music performance, music instruments and so on. The duration of treatment varies from 4 to 48 weeks. Quality of life in patients with Alzheimer's disease (AD) is often assessed using specific and validated instruments. We here adopted two scales as outcome measures: Quality of Life in Alzheimer's Disease (QoL-AD) and The World Health Organization Quality of Life (WHOQOL)-BREF. Given that many participants showed varying degrees of cognitive impairment or were at risk for dementia during the program, the QoL-AD scale is the best tool to assess participants' health-related quality of life. The scale consists of 13 items (health status, energy, mood, living conditions, memory, family, marriage, personal relationships, self-integrity, ability to do housework, ability to do things, money, and life integrity). And score four as excellent where total scores range from 13 to 52 [39]. WHOQOL-BREF is one of the most commonly used tools in clinical practice. Regarding the WHOQOL-BREF, it has 26 items and involves five domains, namely: overall, physical, psychological, social, and environmental, with a total score between 0 and 100, and a score indicating better [40].

2.3 Risk of Bias Assessment Results

The Cochrane's Risk of Bias tool was used to evaluate the quality of all selected studies and the 6 literatures included in this study had different degrees of bias, with moderate literature quality. All 6 papers were RCTs and concealment of allocation scheme was reported in 6 of them; blind method on outcome measurers were performed in four articles and all the six papers contain complete data results without any publication bias. The risk of bias assessment in selected and results were summarized in Figure.2 (high, low, and unclear risk of bias were marked with red, green, and yellow respectively).

2.4 Effects on cognitive function were shown by using different scales as outcome measurements following the intervention

2.4.1 QOL-AD score

There were 3 literatures of all 6 papers performed music intervention, and QOL-AD score in patients was evaluated before and post intervention [33-35]. The results showed that there was statistical heterogeneity among the 3 literatures ($I^2 = 81\%$, $P = 0.005$). A random-effects model was applied for the meta-analysis for selected results and showed that the QOL-AD scale score of the test group was higher than that of the control group (MD = 5.10, 95% CI:2.95-7.24, $P < 0.001$), as shown in Figure.3.

2.4.2 WHOQOL-BERF score

There are three literatures in which the WHOQOL-BERF score is used to evaluate whether the QOL of AD patients is improved under music intervention [36-38]. The results showed that there was heterogeneity among the 3 included literatures ($I^2 = 85\%$, $P = 0.001$) and the random-effects model was selected for meta-analysis. The results showed that the WHOQOL-BERF score of the test group was higher than that of the control group without music intervention (MD = 5.76, 95% CI :1.59-9.92, $P = 0.007$), as shown in Figure.4.

2.5 Publication bias

In this study, 6 articles were evaluated and the scales of QOL as outcome measurement parameters were observed for publication bias analysis. Funnel plot for the meta-analysis of mean difference of quality of life changes between intervention groups and control groups (Figure 5). Each point in the figure represents a study, and the points are evenly distributed on both sides, indicating that there is no publication bias. The points were not concentrated at the top of the figure, indicating that the study sample size was small. There were also points that fell on the outside, suggesting possible heterogeneity. There are less than 10 literatures were included and this disadvantage might lead to publication bias potentially.

Discussion

3.1 Summary of results

This review evaluated the effectiveness of music intervention on QOL in AD patients. Six RCTs (three for QOL-AD and three for WHOQOL-BERF) were included in the meta-analysis. Music intervention as a non-pharmacological treatment for AD to improve QOL in patients has been concerned and studied.

3.2 Effect of music intervention on QOL in patients with AD

This Meta-analysis included 6 studies: participants aged 61–90, 55–66 were included in Wang Z and Fu's studies respectively, and they were all diagnosed with AD by ICD-10 as well as the presence of BPRS symptoms combined with BEHAVE-AD ≥ 8 points [36, 41]. The study participants of Xiao were 58-89 years old patients diagnosed as AD by clinical symptoms and BEHAVE-AD ≥ 8 points [37]. Participants aged 61.5–71.5, 58–97, and ≥ 60 were studied in Meng, Wang Xiaohong, and Hee-Kin Jim's research, and the diagnostic methods used were the NINCDS-ADRDA criteria, DSM-V manual, and CERAD test, respectively [33, 35, 38]. The six articles were selected in this meta-analysis have differences in the content and mode of music intervention including listening to music, music singing and instrument playing, and the main modes were interactive intervention, non-interactive intervention, short-term intervention and long-term intervention. The music intervention of all six articles included music listening, and for Meng's study different types of music comparison were performed indicating that Mozart and Liangzhu music could improve the quality of life of AD patients, while rock music had no significant effect. Music intervention such as music singing and instrument playing showed more effective intervention than therapy by just music listening. Interactive intervention showed more therapeutic effects than non-interactive intervention. The long-term intervention gave better intervention effect than short-term according to Xiao's study.

In summary, different music types showed different effects on QOL; and the exposure of time length of music intervention also has different levels of impact on the QOL in AD patients. Interactive (active) and receptive musical intervention involve different brain regions and may result in different clinical effects. In active music intervention, a higher percentage of patients showed improvements in cognitive deficits, behavioral symptoms, and functional status than in receptive listening, and passive music intervention had a stabilizing effect on neuropsychiatric symptoms [42]. Different music types and rhythms may determine the ability of music to induce arousal and evoke positive emotional responses that can activate the parasympathetic or sympathetic nervous system, thereby alleviating neuropsychological symptoms and enhancing encoding efforts [43]. Highly repetitive music and songs with a narrow range of tones, such as Mozart's music, it can improve reading comprehension; hip-hop music, UK during garage-style music, slow-tempo music by Bach, fast and loud music, familiar non-lyrical music and songs can decrease reading comprehension; and classical and dubstep music can affect cognitive performance, wave activity, and heart rate during reading comprehension [44].

There are several reasons motivated us to address the study on the effect of music intervention on cognitive status in patients with AD. Firstly, music intervention has been approved to counteract to the development of dementia in recent days [45]. At the meanwhile, the music intervention itself can improve cognitive function, autobiographic and memory capacity, as well as patient's symptoms occur substantial alterations, with improvements referred to agitation, apathy, depression, anxiety, mood state, and relational skills. Secondly, music intervention presents significant therapeutic advantages in community situations, affecting QOL such as mood, cognition, social relations, functional activities, energy level, and volition. The chronic diseases of older adults improved remarkably, which has the characteristics of low cost, high benefit, simple and easy to carry out. Most importantly, music intervention is safe combined with no obvious harmful side effects, and easier to be well integrated with health education. It also indicated that music intervention could be great possibly be applied for AD patients' management and it is a potential important intervention in the dynamic and continuous health management process of the elderly. Due to aging worldwide, dementia has become killer of geriatric diseases. The physical and mental health of the elderly should be widely concerned. Therefore, more recreational activities in the elderly should be advocated, and strategies should also be considered to avoid or reduce the occurrence of mild cognitive impairments.

This study showed that music intervention can effectively improve the QOL for the elderly, and long-term treatment on the improvement of cognitive status is effective. The beneficial effects for physical and mental health of music intervention were supported by previous studies [46]. SantiváSantivnguage relieved pain and anxiety of AD patients [47]. Benedetto AR showed that music intervention improved mental health [48]. Further studies confirmed that music intervention did significantly improve cognitive function, ADL and mood in patients with mild to moderate AD [49]. These beneficial effects could be due to that music intervention could positively tap into the emotion and reward systems in the brain [50]. Therefore, it is undoubted that music intervention is an efficient protective factor for AD. At the meanwhile, in order to avoid the one-sidedness of outcomes caused by a single cognitive scale, two current mainstream scales for evaluating cognitive status were analyzed and studied. Results showed that no matter which scale was applied for the evaluation on QOL outcomes the intervention group performed better results than those in the control group without music intervention. This conclusion strongly supported that music intervention improves the QOL in AD patients.

The mechanisms by which music intervention improves the QOL in AD patients are far from known, and several hypothetic mechanisms is commonly accepted are listed: 1) listening to music stimulates neurological activities and coordinate the brainstem reticular formation by enhancing the brainstem reticular formation; 2) listening to music ameliorates the electromyogram (EMG) level of patients so that the myocardium is in a relative relaxed statuses, while playing hypnotic music before bedtime relieves the tension state of AD patients, so that patients quickly get into the sleep state deeply and obtain a good sleep quality [22, 51, 52]; 3) music intervention creates a good environment for AD patients, reduces the stress response of patients, achieves the effect of self-relaxation, promotes patient relaxation and relieves anxiety, reduces annoying disordered behavior, and improves the quality of life [53]; 4) music intervention stimulates the attention of AD patients, arouses the recall past experiences of patients, and promotes the recovery of patients' long-term memory; as well as the behaviors of AD patients are greatly and mildly enhanced under the music performance, which is conducive to the recovery of patients' orientation ability, enhances patients' language ability, and promotes self-expression and coordinated communication capability [54]; 5) music intervention does significantly improve the psycho-behavioral symptoms of AD patients, thereby effectively improving their agitation behavior [55]. In general, music intervention can improve the quality of life of patients, guide the conscious creation of a positive mentality in daily life, prevent adverse mentality, learn to adjust emotional distress and psychological pressure, active self-help, and improve social and mental health.

3.3 The limitations of this study

Although we confirmed that music intervention is beneficial to AD, there are still limitations in our study. Firstly, only published literatures were included in this study and there was a lack of gray literatures. Music intervention was tested as the intervention method and there were limited amount literatures using the QOL as the outcome assessment parameter. Thus, there might be publication bias caused by insufficient literatures filtration and selection; secondly, most studies included did not report blind method, which might lead to the selection bias and inaccuracy of the results; finally, the different trainers on the intervention measurement may affect the reliability of the results individually. Therefore, in the future, to avoid the limitations listed above, the design of rigorous, large-sample, high-quality randomized controlled trials should be considered to provide a reliable basis for clinical practice.

Conclusion

This meta-analysis was distinctive because it aimed to compare the efficacy of music intervention on QOL in AD patients. Preliminary evidence suggested that certain music intervention is effective in improving QOL in AD patients. There are various forms of music intervention, and it is believed that each individual would find a suitable music mode for their characterized treatment and this patient management strategy might great possibly contribute to improve the QOL in AD patients.

Declarations

Funding

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Author's contributions

Xin Yu, Hongyan Shuai conceived the idea and revised the manuscript; Linyan Zuo and Fengting Zhu wrote the manuscript; Rui Wang analyzed the data revised the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors have no competing of interests which are directly relevant to the content of this manuscript.

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Figures

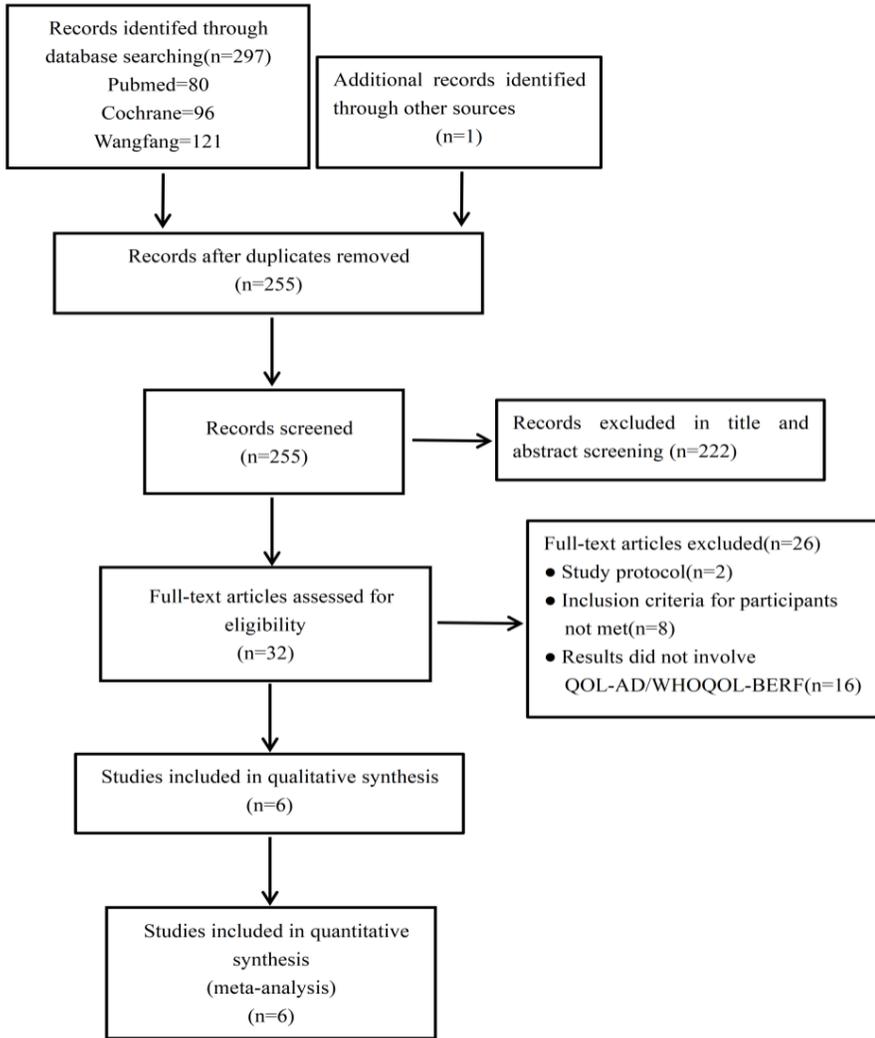


Figure 1

Process of study selection – Flow chart of studies included and excluded.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
FU Mei-hua 2016	+	+	+	+	+	+	+
Hee-Jin Kim 2015	+	+	+	?	+	+	+
MENG Shuang 2019	+	+	+	?	+	+	+
WANG Xiao-hong 2019	+	+	+	+	+	+	+
WANG Zhao 2018	+	+	+	?	+	+	+
XIAO Jie-ping 2018	+	+	+	+	+	+	+

Figure 2

Risk of bias summary: review authors' judgments on the risk bias of included studies.

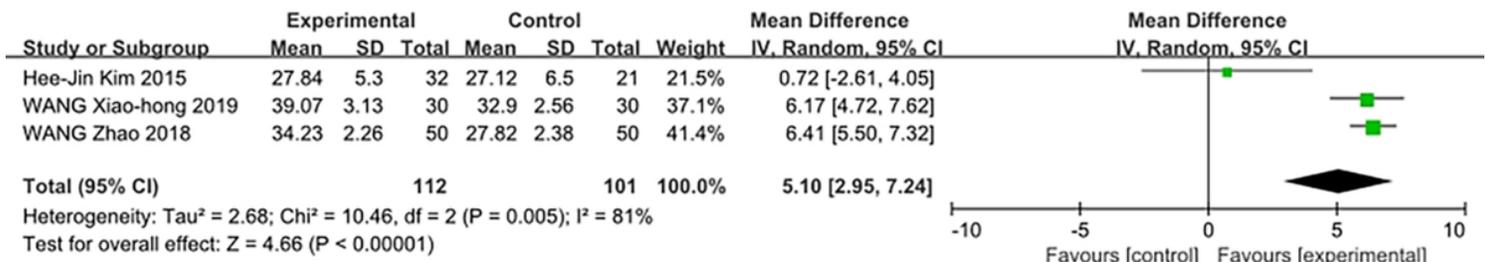


Figure 3

Forest plot for meta-analysis of QOL-AD in patients with AD under music intervention.

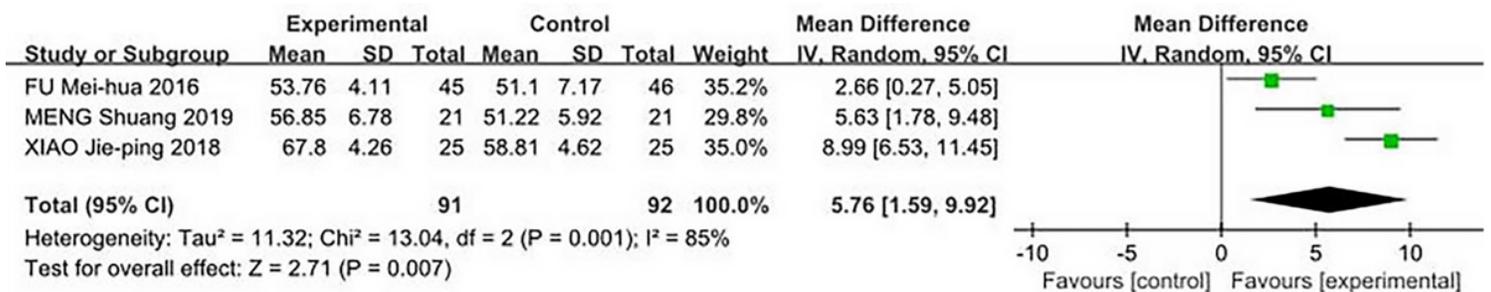


Figure 4

Forest plot for meta-analysis of WHOQOL-BERF in patients with AD with music intervention.

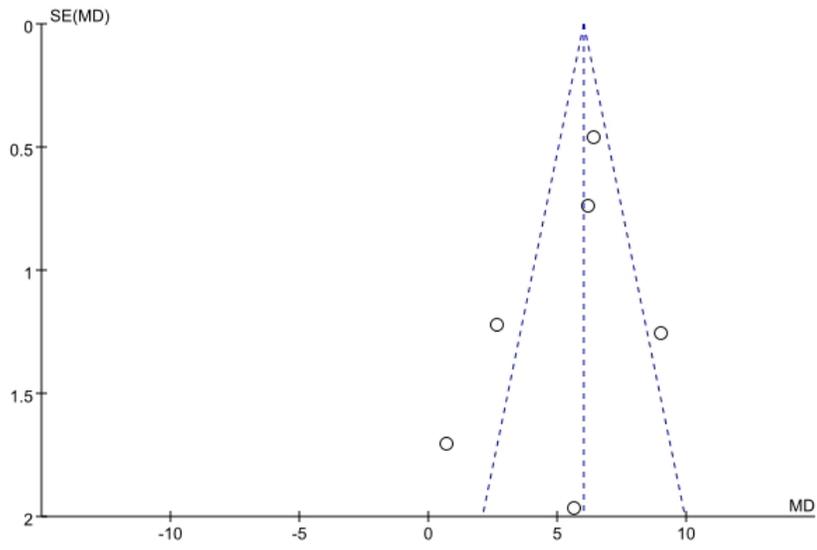


Figure 5

Funnel plot for the meta-analysis of mean difference of QOL change between the groups of music intervention and control groups.