Effects of music therapy on anxiety and depression symptoms in adults diagnosed with mental disorders: a systematic review

Efeitos da musicoterapia sobre os sintomas de ansiedade e depressão em adultos com diagnóstico de transtornos mentais: revisão sistemática

Efectos de la musicoterapia sobre los síntomas de ansiedad y depresión en adultos con diagnóstico de trastornos mentales: revisión sistemática

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Abstract

Objective: To identify and synthesize evidence from randomized clinical trials that assessed the effects of music therapy on anxiety and depression symptoms in adults with mental disorders.

Methods: This is a systematic review guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis protocol. The search for articles in the MEDLINE, Embase, CENTRAL Cochrane, CINAHL, PsycINFO and LILACS databases, as well as manual search, selection of studies, data extraction and methodological assessment using the Jadad Scale and the Cochrane risk-of-bias, was performed by two reviewers independently.

Results: 1,649 studies were identified, eight of which were selected and analyzed. The findings showed a positive effect of music therapy on anxiety and depression symptoms in the adult population in different contexts. According to the Cochrane risk-of-bias, four studies were classified as low risk of bias, and the other four as high risk of bias. Adults who received music therapy showed physical and mental relaxation, reduced anxiety and depressive symptoms, promoting well-being in a conscious and healthy way.

Conclusion: Music therapy presents itself as a potential strategy to reduce anxiety and depression as well as to help maintain and recover the health of adults with mental disorders.

Resumo

Objetivo: Identificar e sintetizar as evidências oriundas de ensaios clínicos randomizados que avaliaram os efeitos da musicoterapia sobre os sintomas de ansiedade e de depressão em adultos com transtornos mentais.

Métodos: Revisão sistemática guiada pelo protocolo *Preferred Reporting Items for Systematic Reviews and Meta-Analysis*. A busca dos artigos nas bases de dados MEDLINE, Embase, CENTRAL Cochrane, CINAHL, PsycINFO e LILACS, bem como a busca manual, seleção dos estudos, extração dos dados e avaliação metodológica pela Escala de Jadad e pela ferramenta do Risco de Viés da Cochrane foram realizadas por dois revisores de forma independente.

Resultados: Foram identificados 1649 estudos, sendo oito selecionados e analisados. Os achados mostraram um efeito positivo da musicoterapia nos sintomas de ansiedade e depressão na população adulta em diferentes contextos. De acordo com a Risco de Viés da Cochrane, quatro estudos foram classificados como baixo risco de viés, e os outros quatro como alto risco de viés. Os adultos que receberam musicoterapia apresentaram relaxamento físico e mental, redução dos sintomas ansiosos e depressivos, promovendo o bem-estar de forma consciente e saudável.

Conclusão: A musicoterapia se apresenta como uma potencial estratégia para reduzir a ansiedade e a depressão bem como para auxiliar na manutenção e recuperação da saúde das pessoas adultas com transtornos mentais.

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Conflicts to interest: nothing to declare.

Resumen

Objetivo: Identificar y sintetizar las evidencias oriundas de ensayos clínicos aleatorizados que evaluaron los efectos de la musicoterapia sobre los síntomas de ansiedad y depresión en adultos con trastornos mentales.

Métodos: Revisión sistemática orientada por el protocolo *Preferred Reporting Items for Systematic Reviews and Meta-Analysis*. La búsqueda de los artículos en las bases de datos MEDLINE, Embase, CENTRAL Cochrane, CINAHL, PsycINFO y LILACS fue realizada por dos revisores de forma independiente, así como también la búsqueda manual, selección de los estudios, extracción de datos y evaluación metodológica a través de la Escala de Jadad y la herramienta de riesgo de sesgo de Cochrane.

Resultados: Se identificaron 1649 estudios, de los cuales ocho fueron seleccionados y analizados. Los resultados mostraron un efecto positivo de la musicoterapia en los síntomas de ansiedad y depresión en la población adulta en diferentes contextos. De acuerdo con el riesgo de sesgo de Cochrane, cuatro estudios fueron clasificados con bajo riesgo de sesgo y otros cuatro con alto riesgo de sesgo. Los adultos que recibieron musicoterapia presentaron relajamiento físico y mental, reducción de los síntomas ansiosos y depresivos, lo que promueve el bienestar de forma consciente y saludable.

Conclusión: La musicoterapia se presenta como una estrategia potencial para reducir la ansiedad y la depresión, así como para ayudar a mantener y recuperar la salud de las personas adultas con trastornos mentales.

Introduction

The World Health Organization (WHO) demonstrates significant concern with the growth of the population affected by mental disorders. This phenomenon affects about 700 million people worldwide and includes disorders such as anxiety and depression. Epidemiological data indicate that depression affects 4.4% of the global population, being higher among women than men (5.1% and 3.6%, respectively), and anxiety, with a prevalence of 3.6% of the population worldwide.[1]

Depression is marked by the presence of sadness, anhedonia, feelings of guilt, lack of self-esteem, changes in sleep and appetite, lack of concentration and tiredness. Anxiety is characterized by unpleasant feelings, worry and tension associated with physical symptoms such as agitation, palpitations, chills, sweating, nervousness. These mental disorders are chronic, recurrent and can be classified as mild, moderate, or severe.[1,2] Both disorders have a devastating effect on the lives of individuals undergoing long-term treatment, as they reduce the incentive to continue treatment, increase the frequency of hospitalizations, trigger lifestyle changes, and impair adherence to the therapeutic process.[3,4]

In this context, patients suffering from mental disorders can benefit from complementary therapies, such as music therapy, to treat unpleasant symptoms.[5-8] Additionally, music therapy is also recommended by the Classification of Nursing Interventions (NIC) as an intervention that aids in behavioral changes, resulting in relief of these symptoms.[9] Music therapy works in areas where medications have no desired efficacy.[10] Research has shown that music therapy modulates immune responses in adults, evidenced by a significant increase in the number of lymphocytes, T cells, CD4s +, NK cells, as well as a decrease in pro-inflammatory cytokines such as IFN- and IL-6.[11-14] Furthermore, music therapy has been identified as a good strategy for treating disease symptoms, as well as for the nurse/patient relationship, making care closer.[10] It is a therapeutic approach of low cost and easy access that facilitates biopsychosocial and spiritual care, restores balance and well-being, favors individuals' communication and integration in the community.[5,6,15-17]

In Brazil, over time, the Ministry of Health has expanded the spectrum of integrative and complementary practices, including music therapy in the list of those belonging to the Brazilian National Policy for Integrative and Complementary Practices (PNPIC - *Política Nacional de Práticas Integrativas e Complementares*) within the scope of the Unified Health System (*Sistema Único de Saúde*). Through Ordinance 849 of March 27, 2017, the following were included: art therapy, ayurveda, biodanza, circular dance, meditation, music therapy, naturopathy, osteopathy, chiropractic care, reflex therapy, reiki, shantala, integrative community therapy, and yoga.[18] With Ordinance 702 of March 21, 2018, Consolidation Ordinance 2/GM/MS of September 28, 2017 was amended to include other new practices in PNPIC such as aromatherapy, apitherapy, bioenergetics, family constellation, color therapy, geotherapy, hypnotherapy, laying on of hands, anthroposophical medicine/anthroposophy applied

to health, ozone therapy, flower therapy, and social thermalism/crenotherapy. Thus, SUS currently authorizes 29 integrative and complementary practices, intensifying the challenge of training, implementing and offering these in public health in the country.

A recent systematic review with Cochrane meta-analysis on the topic that aimed to assess the effects of music therapy for depression in the general population compared to usual care found evidence of broad moderate-quality effects in favor of music therapy when compared with usual care alone, for both physician-rated depressive symptoms (SMD -0.98, 95% CI -1.69 to -0.27, n=219) and patient-reported depressive symptoms (SMD -0.85, 95% CI -1.37 to -0.34, n=142).[19] However, the effectiveness of music therapy, particularly, on symptoms of anxiety and depression in adults who have been diagnosed with mental disorders has not yet been elucidated. Therefore, a study that synthesizes evidence of the effects of music therapy, specifically, in adults - main group affected by the consequences of these symptoms of anxiety and depression, can help healthcare professionals in decision making and implementation of this complementary therapy in clinical practice. In this regard, the objective is to identify and synthesize evidence from randomized clinical trials that assessed the effects of music therapy on anxiety and depression symptoms in adults with mental disorders.

Methods

This is a systematic review study of randomized clinical trials (RCT) guided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[20] To formulate the objective and the review question, PICOS strategy was used (P - Population or Patients; I - Intervention; C - Comparison; O - Outcomes; S - Study design), where Population (P): adults affected by mental disorders; Intervention (I): music therapy; Comparison/Control (C): Standard Treatment and Outcome (O): Reduction of anxiety and depression symptoms; Study design (S): only randomized clin-

ical trials.[21] Thus, the following question was obtained from this review: What is the effect of music therapy on symptoms of anxiety and depression in adults suffering from mental disorders?

Primary studies whose design was an RCT, performed with adults (≥ 18 years), of both sexes, with diagnosis/assessment of symptoms of anxiety or depression, reporting the use of music therapy, active or passive, as an intervention were included. All gray literature, dissertations, theses, editorials, protocol studies, clinical guidelines, studies whose participants were children or elderly and studies that used more than one complementary therapy in combination were excluded.

The search for studies was performed on December 9, 2019, in the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, Embase (Excerpta Medica database), CENTRAL Cohcrane, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Caribbean Latin American Literature on Health Sciences (LILACS) and American Psychological Association (APA) PsycINFO. No publication temporality or language limits were applied.

Initially, the strategy for searching the studies consisted of a combination of controlled descriptors (indexers in the respective databases) and keywords, according to the indication offered in each electronic database. Thus, to search for articles in MEDLINE, controlled descriptors from the Medical Subject Headings (MeSH) were used; the PsycINFO Thesaurus was consulted for the PsycINFO base; Emtree terms for Embase; and the CINAHL subject headings for the CINAHL database. In order to expand the search strategy, a combination of controlled descriptors and keywords was performed using Boolean operators "AND" and "OR"[22-25] to obtain restrictive and additive combinations, respectively. In addition, the search was performed using identified descriptors and with a broader sense, without the use of database filters to preserve significant samples and ensure less risk of loss. This strategy justifies the small number of studies selected in view of the obtained sample, added to the fact that we established the RCT crite-

rion as a design to encompass the strongest evidence for decision-making in clinical practice. Chart 1 presents the final search strategy processed in the respective databases.

Chart 1. Search expression in searched databases

Database	Search expression
MEDLINE*/ PubMed	("adult" [MeSH† Terms]) AND ("depressive disorder" [MeSH† Terms] OR ("depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive disorder"[All Fields] OR "depression"[All Fields] OR "depression"[MeSH† Terms]) AND ("anxiety"[MeSH† Terms] OR "anxiety"[All Fields]) AND ("music therapy"[MeSH † Terms] OR ("music"[All Fields] AND "therapy"[All Fields]) OR "music therapy"[All Fields])
‡Embase	adult AND depression OR anxiety OR 'music therapy'
§CENTRAL Cohcrane	("adult" [MeSH† Terms]) AND ("depressive disorder"[MeSH Terms] OR ("depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive disorder"[All Fields] OR "depression"[All Fields] OR "depression"[MeSH Terms]) AND ("anxiety"[MeSH Terms] OR "anxiety"[All Fields]) AND ("music therapy"[MeSH Terms] OR ("music"[All Fields] AND "therapy"[All Fields]) OR "music therapy"[All Fields])
‖PsycINFO	adult [Thesaurus] AND depression [Thesaurus] OR anxiety [Thesaurus] AND music therapy [Thesaurus]
**CINAHL	adult AND depression OR anxiety AND music therapy
‡‡LILACS	adulto OR adult OR adulto AND depressão OR depression OR depresión [Words] AND ansiedade OR anxiety OR ansiedad [Words] AND musicoterapia OR music therapy OR musicoterapia [Words]

*MEDLINE - Medical Literature Analysis and Retrieval System Online; †MeSH - Medical Subject Headings; ‡Embase - Excerpta Medica database; §CENTRAL - Cochrane Central Register of Controlled Trials; ‖PsycINFO - Psychology Information. **CINAHL – Cumulative Index to Nursing and Allied Health Literature; ‡‡LILACS – Latin American Caribbean Literature in Health Sciences. 12/09/2019 - Date on which the search strategy was carried out.

In addition to the electronic databases mentioned above, secondary searches were performed in other diverse sources, such as Clinical Trial Registry sites, such as ClinicalTrials.gov (National Institutes of Health, NIH, USA), The Brazilian Clinical Trials Registry (via ReBEC Platform) and Google Scholar. Additionally, the final reference list contained in the included primary studies was manually analyzed in order to find relevant studies to be added.[23,24] It is noteworthy that two researchers performed the search strategy independently. EndNote® bibliographic software (https://www.myendnoteweb.com/) was used to store, organize and manage all references and ensure a systematic and comprehensive search.

The sample was selected by two reviewers, independently and blindly. After this selection, a third reviewer was responsible for analyzing and deciding (along with the previous ones) on the inclusion or exclusion of each article, mainly in relation to those with a conflicting decision. Subsequently, after selecting a third reviewer, a manual search was carried out based on the references of selected articles.

Data were extracted based on pre-established tools[25-30] and included four domains: I) identification of the study, with data such as article title, journal impact factor, country of study authors, year of publication, host institution of the study (hospital; university; research center; multicenter study or study in a single institution); conflicts of interest; financing; II) methodological characteristics (study design; study objective or research question or hypotheses; sample characteristics), for example, sample size, age, baseline characteristics of experimental and control groups, recruitment method, losses, duration of follow-up, statistical analysis; III) main findings and implications for clinical practice; and IV) conclusions.

For data extraction, two charts were prepared using Microsoft Word® by two researchers independently to synthesize the data from the included studies. After this phase, the charts were compiled into a single one to proceed with the qualitative analysis.

The methodological quality of the RCTs was assessed using the Jadad Scale, with a score ranging from 0 to 5, with studies with a score < 3 considered of low quality and studies with a score of ≥ 3 classified as of high quality.[31] The internal validity and risk of bias for the RCTs were assessed using the Cochrane Risk of Bias tool from the Cochrane Collaboration Handbook for Systematic Reviews of Interventions, version 5.1.0 (RoB 1),[32] which assesses seven domains: I) Allocation of the randomization sequence (selection bias); II) Allocation secrecy (selection bias); III) Blinding of participants and staff involved (performance bias); IV) Blinding of outcome evaluators (detection bias); V) Incomplete outcomes (friction bias); VI) Selective outcome report (publication bias) and VII) Other sources of bias. Based on these assessed domains, studies are classified as low, high or uncertain risk of bias.

Since most of the studies assessed presented significant methodological differences, it was decided to carry out a qualitative synthesis of the data in this systematic review.

Results

The database survey resulted in 1,649 studies, and no additional studies were included after Google

Scholar searches, as well as clinical trial registries and selected primary article references. Search screening revealed 991 duplicates, resulting in 658 records after removing the duplicates. The first screening, based on the exclusion criteria, as well as through reading titles and abstracts, excluded most of studies (625). After eligibility/critical assessment of the full texts of 33 records, 8 records met all inclusion criteria and proceeded to the data extraction, exhaustive reading and qualitative synthesis phase. Figure 1 presents a flowchart of the search process according to the PRISMA flowchart.[20]
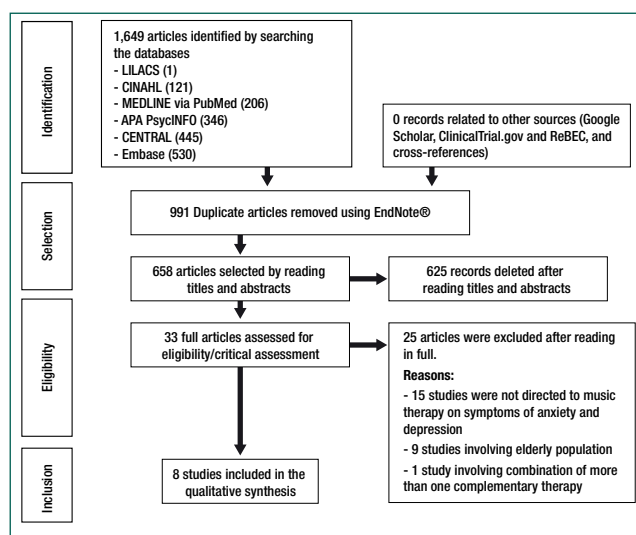

Figure 1. PRISMA[20] flowchart for study selection

Chart 2 summarizes the main characteristics of the studies included[33-40] in the qualitative synthesis in chronological order. The studies were carried out in eight different countries, including Brazil,[39] Canada,[40] Finland,[35] France,[36] Iran,[38] Norway,[37] South Korea,[34] and the USA.[33] All studies were performed at single centers and most included both sexes.[33-36,38-40] A single study included only men,[37] since the study population consisted of adults deprived of liberty. Most studies (n=7) included adults with mental disorders with different comorbidities.[33-36,38-40] The average number of participants who composed the samples in the studies was 75 (minimum value of 26 and maximum value of 113 participants).

Anxiety and depression were the primary outcomes analyzed in most included studies (n=7).[33-35,37-40] Other outcomes assessed were pain;[36,39] mood,[33,39] quality of life,[35] social relationships,[34,37] inability, and disability.[40]

Three studies assessed anxiety using the State Trait Anxiety Inventory (STAI)[34,37,38] and three other studies assessed anxiety using the Hospital Anxiety and Depression Scale (HADS).[35,36,40] Depression was assessed using the Hospital Anxiety and Depression Scale (HADS) in five studies;[34-37,40] and only one study used the Beck Depression Inventory (BDI) to assess depressive symptoms.[38] Pain was assessed using the Visual Analog Scale (VAS).[36,39] Also, mood was assessed by the Profile of Mood States (POMS);[33,39] health-related quality of life by Health-related Quality of Life Survey – RAND-36,[35] social relations by Quality of Life Questionnaire Life and Appreciation and Satisfaction (Q-LES-Q)[37] or using the scale of change of relationship (RCS).[34] One study assessed disability as an outcome using the WHO Disability Assessment Program 2.0.[40]

Among the eight RCTs, (n=4; 50%) presented high methodological quality[35,36,39,40] according to the Jadad Scale (scores 3 or 4) (Chart 2).

Regarding the risk of bias according to RoB 1 for RCT, four studies[35,36,39,40] were classified as low risk of bias, and the other four[33,34,37,38] as high risk biased (Figure 2).[32] The main bias presented by all RCTs concerns the blinding of participants and staff (performance bias). In contrast, most studies had low risk of bias involving incomplete outcomes (friction bias), reporting of selective outcomes and other sources of bias.

Discussion

The results of this study contribute to the expansion of knowledge on the topic of the use of complementary therapies in healthcare. Overall, the studies analyzed showed a positive effect of music therapy on anxiety and depressive symptoms in the adult population with mental disorders in various settings. Adults who received music therapy showed physical and mental relaxation, reduced anxiety and depressive symptoms, promoting well-being in a conscious and healthy way. Furthermore, the results also re-

Chart 2. Characterization of the eight articles selected according to authors, country, objective, sample, intervention, variables, instruments, main results and score according to the Jadad Scale

Authors / Country	Objective	Sample	Intervention Experimental Group (EG)	Intervention Control Group (CG)	Variables/ Instruments	Main results	Jadad Score
Cassileth et al. 2003[33] USA	Determine the effects of music therapy on mood compared to standard care during hospitalizations for high-dose therapy with autologous stem cell transplantation	69 patients with hematologic malignancy admitted for high-dose therapy with autologous stem cell transplantation	(n=36) allocated to the music therapy group - Intervention: 20 to 30 minutes; sessions; 2-3 times/week; Follow-up: 6 months	(n=33) allocated to standard treatment without music therapy	Mood - POMS*	During hospitalization, patients in the EG (music therapy) had a 28% lower score on the Anxiety/Depression scale (p=0.065) and 37% lower (p=0.01) on the total score for mood disorders compared to patients of the CG	2
Choi et al. 2008[34] South Korea	Test the effectiveness of group music therapy to improve depression, anxiety and relationships in psychiatric patients	26 psychiatric patients	(n=13) allocated to the music therapy group - Intervention: 60 minutes; 15 sessions (once to twice a week); Follow-up: 15 weeks	(n=13) allocated to standard treatment without music therapy	Anxiety - STAI† Depression - HADS‡ Social relationships - RCS§	After 15 sessions, the group music therapy intervention significantly improved scores for depression (F [1.25]=257.7; p=0.001), anxiety (F [1.25]=202.7; p=0.001), and social relationships (F [1.25]=450.6; p=0.001) in psychiatric patients compared to the CG	1
Erkkilä et al. 2011[35] Finland	Determine the effectiveness of music therapy added to standard usual care compared to just standard usual care in depression treatment among people of working age	79 adults with unipolar depression	(n=33) patients allocated to receive music therapy and standard treatment - Intervention: 60 minutes; 20 sessions (twice a week); Follow-up: 6 months	(n=46) patients allocated only to standard treatment without music therapy	Anxiety and Depression - MADRS¶ - HADS‡ - GAF** Quality of Life - RAND36††	The EG showed higher rates of improvement in depressive symptoms than those who received only standard care (mean difference 4.65, 95%CI‡‡ 0.59 to 8.70, p=0.03) and anxiety symptoms (1.82, 95%CI‡‡ 0.09 to 3.55, p=0.04) in the three-month follow-up	3
Guétin et al. 2012[36] France	Assess the usefulness of music therapy in the treatment of patients with chronic pain	87 patients with low back pain, fibromyalgia, inflammatory disease or neurological disease	(n=44) allocated to the music therapy group - Intervention: 20 minutes; (twice a day); Follow-up: 3 months	(n=43) allocated to the standard treatment group without music therapy	Pain - VASǁ Anxiety and Depression - HADS‡	In the EG (music therapy), there was a more significant reduction in pain (p<0.001) when compared to the CG. Also, music therapy contributed to significantly reduce anxiety, depression and the consumption of anxiolytic agents	3
Gold et al. 2014[37] Norway	Examine the effects of music therapy on aspects of mental health, specifically depression, anxiety and social relationships in adults deprived of liberty	113 adult men deprived of liberty	(n=56) allocated to music therapy - Intervention: time not reported; sessions (2 to 3 times/week); Follow-up: 6 months	(n=57) allocated to standard treatment without music therapy	Anxiety - STAI† Depression - HADS‡ Social relationships - Q-LES-Q§§	Music therapy was well accepted by adults deprived of freedom. Post-hoc analysis of changes within the experimental group suggested a reduction in anxiety after 2 weeks of music therapy (d=0.33, p=0.025)	2
Salehi et al. 2016[38] Iran	Determine the effect of selected relaxing music on hospitalized patients with anxiety and depression during hemodialysis	102 patients in hemodialysis	(n=83) received music therapy - Intervention: 3 hours; 1 session; Follow-up: 1 day	(n=83) did not receive music therapy (standard care)	Anxiety -STAI† Depression - BDIǁǁ	There were no significant differences between groups before hemodialysis BDIǁǁ (p=0.253), t-anxiety (p=0.546) and s-anxiety (p=0.253), T-Anxiety (p=0.546) and S-Anxiety (p=0.776). There was also no significant difference in the BDIǁǁ (p=0.253) and T-anxiety (p=0.253) and T-Anxiety (p=0.546) between the two groups after hemodialysis	2
Dóro et al. 2017[39] Brazil	Assess the effect of music therapy about pain, mood and anxiety	100 patients undergoing allogeneic hematopoietic stem cell transplantation	(n=50) patients were selected for experimental music therapy - Intervention: 30 minutes; sessions based on clinical need (twice a week); Follow up: not reported	(n=50) patients who received only the standard treatment without music therapy	Pain, anxiety and mood - VASǁ	Significant differences were observed when comparing the groups, improving mood in the EG (p<0.001)	4
Trimmer et al. 2018[40] Canada	Test the feasibility of low-intensity music based cognitive-behavioral therapy for depression and anxiety symptoms	28 patients with symptoms of depression and anxiety attended at a community mental health service	(n=14) allocated to the intervention group with music therapy - Intervention: 90 minutes; 9 sessions; Follow-up: 9 weeks	(n=14) allocated to the standard treatment group without music therapy	Anxiety and Depression- - HADS‡ Disabilities - WHO¶¶ Disability Assessment Schedule 2.0	EG participants (music therapy) showed improvement in disability (p=0.027). Despite the reduction in depression and anxiety scores, these differences were not statistically significant.	3

*POMS - Profile of Mood States; †STAI - State Trait Anxiety Inventory; ‡HADS - Hospital Anxiety and Depression Scale; §RCS - Relationship Change Scale; ǁVAS - Visual Analog Scale; ¶MDARS - Montgomery–Asberg Depression Rating Scale; **GAF - Global Assessment of Functioning; ††REND-36 - Health-related quality of life survey; ‡‡95%CI - 95% confidence interval; §§Q-LES-Q - Quality of Life Enjoyment and Satisfaction Questionnaire; ǁǁBDI - Beck Depression Inventory; ¶¶WHO - World Health Organization

Studies	Random sequence generation (selection bias)	aAlocation secrecy (selection bias)	Blinding of participants/team involved (performance bias)	Blinding of outcome assessor (detection bias)	Incomplete outcomes (friction bias)	Selective outcome report (publication bias)	Other sources of bias	Risk of bias classification
			Risk of bias domain					
Cassileth et al. 2003[33]	+	–	–	–	?	+	?	High
Choi et al. 2008[34]	+	–	–	–	+	?	?	High
Erkkilä et al. 2011[35]	+	+	–	+	+	+	+	Low
Guétin et al. 2012[36]	+	+	–	+	+	+	+	Low
Gold et al. 2014[37]	+	+	–	?	–	?	?	High
Salehi et al. 2016[38]	–	?	–	–	+	+	?	High
Dóro et al. 2017[39]	+	+	–	+	+	?	+	Low
Trimmer et al. 2018[40]	+	+	–	+	+	+	+	Low

Source: Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1. Cochrane Collaboration; 2011. Available from: https://training.cochrane.org/handbooks[32]
*Assessment of internal validity and risk of bias of clinical trials included in the study according to the Cochrane Collaboration Tool (RoB 1) to assess the risk of bias of randomized clinical trials; †Percentage of risk of bias among clinical trials by domain of the Cochrane Collaboration Tool for Assessing the Risk of Bias of Randomized Clinical Trials. Plus symbol (+) indicates low risk of bias; negative symbol (-) indicates high risk of bias; question mark (?) indicates uncertain risk of bias

Figure 2. Risk of bias of eight randomized clinical trials included and assessed by the Cochrane Collaboration tool

vealed a significantly higher rate of adherence to music therapy, especially in adult hospitalized patients.

Well-conducted RCTs are the gold standard for assessing interventions, as their design allows controlling various systematic errors such as selection bias, measurement bias and confounding bias inherent to the design.[41,42] Regarding the internal validity of the studies included in our review, four studies (50%) were classified as low risk of bias. These findings are different from the results obtained in a recent systematic review and meta-analysis that aimed to determine the effectiveness of music therapy in depression treatment in older adults.[5] Based on the assessment of internal validity of studies using the Cochrane risk of bias tool (RoB 1), it was found that most studies were classified as high risk of bias due mainly to unclear randomization methods, blinding methods not appropriate and the presence of friction bias.[5] Performance bias is commonly presented as a limiting factor in clinical trials that use complementary therapies, either because of the difficulty of blinding participants due, for example, to the nature of the intervention as an integral part of the health service routine, and/or difficulties in the blinding of outcome assessors.

Depression and anxiety are disabling diseases that cause serious problems, with a consequent reduction in individuals' quality of life. In this sense, articulating music therapy with conventional treatment or standard care is seen as an opportunity to get in touch with emotions and promote interpersonality between healthcare professionals and patients.[10] This complementary therapy demonstrates that, in addition to providing distraction, it becomes a means of communication capable of overcoming barriers and limits of verbal expression.[8,15,40,43,44]

Depression is another emotional issue identified as a result of not adapting to correctional environments and programs. One of the studies analyzed in this review[37] pointed out that mental health problems are prevalent among adults deprived of freedom, specifically anxiety and depression. These findings are in line with a study in which adults deprived of liberty, with a minor criminal record, from a penitentiary unit in China, who had participated in music therapy with health education activities, care and individual counseling, showed a reduction in anxiety symptoms, depression and increased self-esteem. This practice favored impulse and an-

ger control. Furthermore, for adults deprived of liberty, who were not able to express or discuss their problems through verbal dialogue, music served as a means to help release emotions and thoughts in a positive way.[45]

In this review, studies were gathered that showed the effects of music therapy on anxiety and depression in adults with different chronic diseases with associated mental disorders, such as chronic kidney disease,[38] cancer,[33,39] depression[34,35], and chronic pain.[36] Individuals and caregivers in cancer treatment deal with isolation, emotional disturbances, anxiety, mood disorders, changes in cognition, and symptoms of depression.[4] Regarding the impact of music therapy on patients with chronic diseases including cancer, scientific results that show the psychological and physiological benefits in the adult and pediatric population.[7,15,23,46-51]

Music therapy also has a positive physiological and emotional impact on people who are undergoing trauma treatment, especially in the treatment of chronic pain. A study included in this review observed that participants with pain (mechanical, inflammatory, fibromyalgia and neurological) had reduced pain index in the experimental group compared to the control group. Pain reduction was significantly greater in the musical intervention group (-3.4 (± 2.3) and -1.6 (± 2.2), p <0.001), which corresponded to a relative improvement of 54% against 25.8% in the control group.[36] Another study showed that 69 patients hospitalized for autologous stem cell transplantation received music therapy, achieving a 28% reduction in the combined level of anxiety/depression (p=0.065) and a 37% lower (p=0.01) reduction in the total score of mood disorders compared to controls.[33] Studies have shown that the use of music combined with standard treatment generated greater peace of mind regarding chronic health problems in individuals.[33,34,38,39,52]

On the other hand, an RCT conducted in Canada with 28 participants, which aimed to test the feasibility of low-intensity music based on cognitive-behavioral therapy for depression and anxiety, showed that participants in the music therapy group who received intervention for 9 weeks showed no statistical differences when compared to participants in the control group, who received standard care.[40]

Furthermore, the present review highlighted the lack of intervention studies aimed at identifying the underlying effects of the molecular mechanisms involved and activated during music therapy on mental health outcomes. It should be emphasized that this is a promising and expanding area of nursing research, bringing patients to the center of care through translational research (from the laboratory bench to the patient side) in order to provide personalized care to patients.[53]

Further research to assess the impact of music therapy on symptom clusters in prolonged hospitalization in the adult population and to establish correlations with clinical outcomes should be encouraged in order to elucidate the mechanisms underlying the effect of this complementary therapy on health outcomes. Moreover, a more comprehensive assessment of the effect of music therapy on the adult population can be obtained by using larger samples with well-executed RCTs, also considering specific populations separately, with acute or chronic conditions, and using multivariate statistical analyzes to control for possible confounding variables.

Some limitations must be considered when interpreting the results of this systematic review. There was a great heterogeneity of studies, use of different musical styles, musical instruments and follow-up time. Therefore, these findings should be carefully analyzed with regard to generalization of results. The significant heterogeneity between the studies prevented the grouping of results, making it impossible to carry out a meta-analysis.

Conclusion

In summary, music therapy, as a complementary therapy, presents itself as a potential strategy to reduce anxiety and depression as well as to help maintain and recover the health of the adult population diagnosed with mental disorders. Furthermore, the data from this review offer a promising platform to support ongoing investigation of complementary

therapies for better psychological adjustment in the adult population suffering from mental disorders.

References

1. World Health Organization (WHO). Depression and Other Common Mental Disorders: Global Health Estimates. Geneva: WHO; 2017. [cited 2019 Jun 2]. Available from: http://www.who.int/mental_health/management/depression/prevalence_global_healthestimates/en/

2. Penninx BW. Depression and anxiety: their insidious dance. Lancet Psychiatry. 2015;2(6):479–80.

3. Barros MB, Lima MG, Azevedo RC, Medina LB, Lopes CS, Menezes PR, et al. Depression and health behaviors in Brazilian adults - PNS 2013. Rev Saude Publica. 2017;51 Suppl 1:8s.

4. Vitorino LM, Lopes-Júnior LC, de Oliveira GH, Tenaglia M, Brunheroto A, Cortez PJ, et al. Spiritual and religious coping and depression among family caregivers of pediatric cancer patients in Latin America. Psychooncology. 2018;27(8):1900–7.

5. Zhao K, Bai ZG, Bo A, Chi I. A systematic review and meta-analysis of music therapy for the older adults with depression. Int J Geriatr Psychiatry. 2016;31(11):1188–98.

6. Zhang Y, Cai J, An L, Hui F, Ren T, Ma H, et al. Does music therapy enhance behavioral and cognitive function in elderly dementia patients? A systematic review and meta-analysis. Ageing Res Rev. 2017;35:1–11.

7. Lopes-Júnior LC, Bomfim EO, Nascimento LC, Nunes MD, Pereira-da-Silva G, Lima RA. Non-pharmacological interventions to manage fatigue and psychological stress in children and adolescents with cancer: an integrative review. Eur J Cancer Care (Engl). 2016;25(6):921–35.

8. van der Steen JT, van Soest-Poortvliet MC, van der Wouden JC, Bruinsma MS, Scholten RJ, Vink AC. Music-based therapeutic interventions for people with dementia. Cochrane Database Syst Rev. 2017;5(5):CD003477.

9. Bulechek GM, Butcher HK, Dochterman JM. Classification of Nursing Interventions - NIC. 6th ed. Rio de Janeiro: Elsevier; 2016.

10. Pauwels EK, Volterrani D, Mariani G, Kostkiewics M. Mozart, music and medicine. Med Princ Pract. 2014;23(5):403–12.

11. Abrahão CA, Bomfim E, Lopes-Júnior LC, Pereira-da-Silva G. Complementary therapies as a strategy to reduce stress and stimulate immunity of women with breast cancer. J Evid Based Integr Med. 2019;24:2515690X19834169.

12. Koyama M, Wachi M, Utsuyama M, Bittman B, Hirokawa K, Kitagawa M. Recreational music-making modulates immunological responses and mood states in older adults. J Med Dent Sci. 2009;56(2):79–90.

13. Wachi M, Koyama M, Utsuyama M, Bittman BB, Kitagawa M, Hirokawa K. Recreational music-making modulates natural killer cell activity, cytokines, and mood states in corporate employees. Med Sci Monit. 2007;13(2):CR57–70.

14. Bittman B, Croft DT Jr, Brinker J, van Laar R, Vernalis MN, Ellsworth DL. Recreational Music-Making alters gene expression pathways in patients with coronary heart disease. Med Sci Monit. 2013;19:139–47.

15. Bradt J, Dileo C, Magill L, Teague A. Music interventions for improving psychological and physical outcomes in cancer patients. Cochrane Database Syst Rev. 2016;15(8):CD006911.

16. Melo GA, Rodrigues AB, Firmeza MA, Grangeiro AS, Oliveira PP, Caetano JA. Musical intervention on anxiety and vital parameters of chronic renal patients: a randomized clinical trial. Rev Lat Am Enfermagem. 2018;26(0):e2978.

17. Batt-Rawden K. The role of music in a salutogenic approach to health. Int J Ment Health Promot. 2010;12(2):11–8.

18. Brrasil. Ministério da Saúde. Portaria n. 849, de 27 de março 2017. Inclui a Arteterapia, Ayurveda, Biodança, Dança Circular, Meditação, Musicoterapia, Naturopatia, Osteopatia, Quiropraxia, Reflexoterapia, Reiki, Shantala, Terapia Comunitária Integrativa e Yoga à Política Nacional de Práticas Integrativas e Complementares. Diário Oficial da União. 2017 Mar. 28; Sec. 1:68. [citado 2021 Mai 26]. Disponível em:http://189.28.128.100/dab/docs/portaldab/documentos/prt_849_27_3_2017.pdf

19. Aalbers S, Fusar-Poli L, Freeman RE, Spreen M, Ket JC, Vink AC, et al. Music therapy for depression. Cochrane Database Syst Rev. 2017;11(11):CD004517.

20. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;(7):e1000097.

21. Methley AM, Campbell S, Chew-Graham C, McNally R, Cheraghi-Sohi S. PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC Health Serv Res. 2014;14(1):579.

22. Lopes-Júnior CL, Cruz LA, Leopoldo VC, Campos FR, Almeida AM, Silveira RC. Effectiveness of traditional chinese acupuncture versus sham acupuncture: a systematic review. Rev Lat Am Enfermagem. 2016;24(0):e2762.

23. Nunes MD, Bomfim E, Olson K, Lopes-Junior LC, Silva-Rodrigues FM, Garcia de Lima RA, et al. Interventions minimizing fatigue in children/adolescents with cancer: an integrative review. J Child Health Care. 2018;22(2):186–204.

24. Gonçalves CA, Lopes-Júnior LC, Nampo FK, Zilly A, Mayer PC, Pereira-da-Silva G. Safety, efficacy and immunogenicity of therapeutic vaccines in the treatment of patients with high-grade cervical intraepithelial neoplasia associated with human papillomavirus: a systematic review protocol. BMJ Open. 2019;9(7):e026975.

25. Lopes-Júnior LC, Bomfim E, Olson K, Neves ET, Silveira DS, Nunes MD, et al. Effectiveness of hospital clowns for symptom management in paediatrics: systematic review of randomised and non-randomised controlled trials. BMJ. 2020;371:m4290.

26. Galvão CM, Sawada NO, Trevizan MA. Revisão sistemática: recurso que proporciona a incorporação das evidências na prática da enfermagem. Rev Lat Am Enfermagem. 2004;12(3):549-56.

27. Silva Junior FJ, Sales JC, Monteiro CF, Costa AP, Campos LR, Miranda PI, et al. Impact of COVID-19 pandemic on mental health of young people and adults: a systematic review protocol of observational studies. BMJ Open. 2020;10(7):e039426.

28. Lopes-Júnior LC, Rosa GS, Pessanha RM, Schuab SI, Nunes KZ, Amorim MH. Efficacy of the complementary therapies in the management of cancer pain in palliative care: A systematic review. Rev Lat Am Enfermagem. 2020;28:e3377.

29. de Campos Pereira Silveira RC, Dos Reis PE, Ferreira EB, Braga FT, Galvão CM, Clark AM. Dressings for the central venous catheter to prevent infection in patients undergoing hematopoietic stem cell transplantation: a systematic review and meta-analysis. Support Care Cancer. 2020;28(2):425–38.

30. Lopes-Júnior LC, Rosa MA, Lima RA. Psychological and psychiatric outcomes following picu admission: a systematic review of cohort studies. Pediatr Crit Care Med. 2018;19(1):e58–67.

31. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17(1):1–12.

32. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1. Cochrane Collaboration; 2011.

33. Cassileth BR, Vickers AJ, Magill LA. Music therapy for mood disturbance during hospitalization for autologous stem cell transplantation: a randomized controlled trial. Cancer. 2003;98(12):2723–9.

34. Choi AN, Lee MS, Lim HJ. Effects of group music intervention on depression, anxiety, and relationships in psychiatric patients: a pilot study. J Altern Complement Med. 2008;14(5):567–70.

35. Erkkilä J, Punkanen M, Fachner J, Ala-Ruona E, Pöntiö I, Tervaniemi M, et al. Individual music therapy for depression: randomised controlled trial. Br J Psychiatry. 2011;199(2):132–9.

36. Guétin S, Giniès P, Siou DK, Picot MC, Pommié C, Guldner E, et al. The effects of music intervention in the management of chronic pain: a single-blind, randomized, controlled trial. Clin J Pain. 2012;28(4):329–37.

37. Gold C, Assmus J, Hjørnevik K, Qvale LG, Brown FK, Hansen AL, et al. Music therapy for prisoners: pilot randomised controlled trial and implications for evaluating psychosocial interventions. Int J Offender Ther Comp Criminol. 2014;58(12):1520–39.

38. Salehi B, Salehi M, Nsirnia K, Soltani P, Adalatnaghad M, Kalantari N, et al. The effects of selected relaxing music on anxiety and depression during hemodialysis: A randomized crossover controlled clinical trial study. Arts Psychother. 2016;48:76–80.

39. Dóro CA, Neto JZ, Cunha R, Dóro MP. Music therapy improves the mood of patients undergoing hematopoietic stem cells transplantation (controlled randomized study). Support Care Cancer. 2017;25(3):1013–8.

40. Trimmer C, Tyo R, Pikard J, McKenna C, Naeem F. Low-intensity cognitive behavioural therapy-based music group (CBT-music) for the treatment of symptoms of anxiety and depression: a feasibility study. Behav Cogn Psychother. 2018;46(2):168–81.

41. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". Lancet. 2005;365(9453):82–93.

42. Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. JAMA. 2007;297(11):1233–40.

43. Gallagher LM, Lagman R, Rybicki L. Outcomes of music therapy interventions on symptom management in palliative medicine patients. Am J Hosp Palliat Care. 2018;35(2):250–7.

44. Keenan A, Keithley JK. Integrative review: effects of music on cancer pain in adults. Oncol Nurs Forum. 2015;42(6):E368–75.

45. Chen XJ, Hannibal N, Xu K, Gold C. Group music therapy for prisoners: protocol for a randomised controlled trial. Nord J Music Ther. 2014;23(3):224–41.

46. Nunes MD, Jacob E, Bomfim EO, Lopes-Junior LC, de Lima RA, Floria-Santos M, et al. Fatigue and health related quality of life in children and adolescents with cancer. Eur J Oncol Nurs. 2017;29:39–46.

47. Xavier WS, Pacheco ST, Silva LF, Nascimento LC, Lopes-Junior LC, Araújo BB, et al. Intervenções não farmacológicas na melhoria da qualidade de vida de crianças/adolescentes oncológicos. Acta Paul Enferm 2020;33:e-APE-20190022.

48. Hyacinth O, Machado Silva-Rodrigues F, Darezzo Rodrigues Nunes M, Carlos Lopes L Jr, Fernandes A, Castanheira Nascimento L, et al. Pain experience, physical function, pain coping, and catastrophizing in children with sickle cell disease who had normal and abnormal sensory patterns. J Pain Symptom Manage. 2020;60(6):1079–91.

49. Lopes-Júnior LC, Pereira-da-Silva G, Silveira DS, Veronez LC, Santos JC, Alonso JB, et al. The effect of clown intervention on self-report and biomarker measures of stress and fatigue in pediatric osteosarcoma inpatients: a pilot study. Integr Cancer Ther. 2018;17(3):928–40.

50. Tuinmann G, Preissler P, Böhmer H, Suling A, Bokemeyer C. The effects of music therapy in patients with high-dose chemotherapy and stem cell support: a randomized pilot study. Psychooncology. 2017;26(3):377–84.

51. Lopes-Júnior LC, Silveira DS, Olson K, Bomfim EO, Veronez LC, Santos JC, et al. Clown intervention on psychological stress and fatigue in pediatric patients with cancer undergoing chemotherapy. Cancer Nurs. 2020;43(4):290–9.

52. Messika J, Hajage D, Panneckoucke N, Villard S, Martin Y, Renard E, et al. Effect of a musical intervention on tolerance and efficacy of non-invasive ventilation in the ICU: study protocol for a randomized controlled trial. Trials. 2016;17(1):450.

53. Lopes-Júnior LC, Olson K, de Omena Bomfim E, Pereira-da-Silva G, Nascimento LC, de Lima RA. Translational research and symptom management in oncology nursing. Br J Nurs. 2016;25(10):S12, S14, S16 passim.