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# Effect of music intervention during hemodialysis: a comprehensive meta-analysis

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**Abstract.** – **Aggravating disease and the accompanying increase in the frequency of hemodialysis interventions worsen the quality of life of patients leading to poor physical and psychological outcomes. Music-based interventions have been suggested to improve both the physical and psychological prognoses for patients undergoing hemodialysis. Two meta-analyses on the impact of music-based interventions on anxiety in patients undergoing hemodialysis failed to evaluate the impact of these interventions on other physiological outcomes. Therefore, in this study, we gather evidence on the effects of music-based interventions on physical and psychological outcomes in patients with chronic kidney disease undergoing hemodialysis. To determine the influence of music-based interventions on anxiety, pain, heart rate, and blood pressure (systolic, diastolic) in patients with chronic kidney disease undergoing hemodialysis, we performed a systematic literature search adhering to PRISMA guidelines on the EMBASE, CENTRAL, Scopus, and MEDLINE academic databases. We performed meta-analyses to consolidate the evidence on the influence of music-based interventions on the physical and psychological outcomes of patients with chronic kidney disease undergoing hemodialysis. From 1,402 studies, we found eight eligible studies with 597 (264 women, 287 men) patients with chronic kidney disease undergoing hemodialysis (mean age, 56.9 ± 10.8 years). Among these patients, 298 received the music-based intervention and 299 were included as controls. Our meta-analysis revealed a small-to-medium effect of the music-based intervention to reduce pain levels (Hedge's g, -0.75), anxiety (-0.16), heart rate (-0.15), and systolic (-0.14) and diastolic blood pressure (-0.11) in patients with chronic kidney disease receiving hemodialysis as compared to the values of the same variables in the control group. The evidence from our analyses supports the beneficial impact of music-based interventions to alleviate anxiety and pain, and to reduce heart rate and blood pressure in these patients.**

*Key Words:*

Chronic kidney disease, Anxiety, Hypertension, Heart rate.

## Introduction

Chronic kidney disease is one of the most common renal disorders in the world[1]. According to the National Kidney Foundation[2], chronic kidney disease is a pathological condition characterized by a reduced glomerular filtration rate (i.e., $\leq$ 60 ml/min/1.73 m$^2$). Epidemiological studies[1,3] have widely reported a high prevalence rate (i.e.,10.6% to 13.4%) of chronic kidney disease among general populations and the World Health Organization acknowledges that almost 1.1 million annual deaths worldwide are due to chronic kidney disease[4].

Chronic kidney disease progresses relentlessly in terms of severity due to the expansive nature of the interstitial renal-fibrosis[5,6]. Here, persistent levels of proteinuria, inflammatory markers, and the release of morphogenic cytokines that affect the nephrotic activity are thought to be the principal underlying mechanisms aggravating the disease[5,7]. Under severe circumstances with glomerular filtration rates lower than 15 ml/min/1.73 m$^2$, renal replacement therapy including hemodialysis is necessary[8]. Hemodialysis consists in the external filtration of blood through a dialyzer, thereby reducing the stress on the deficient nephrotic structures[9]. Despite enhancing the survival of patients with severe chronic kidney disease, hemodialysis causes psychological and physiological deficits in its patients[10,11]. Patients commonly exhibit signs of psychological distress in the form of heightened anxiety, depression, and stress due to the complex, long-term, and demanding nature of hemodialysis[12,13].

Furthermore, the restrictive nature of the management schedule[14], diet[15], and medications[16] imposed are additional factors contributing to the development of the psychological manifestations. Moreover, hemodialysis can instigate a range of physiological manifestations including pain, increased heart rate, hypotension, cramps, and



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fatigue[17,18]. Of note, Davison (2003)[19] reported that almost 55% of their cohort undergoing hemodialysis complained of severe pain. The administration of central catheters during hemodialysis can promote painful neuropathies of ischemic origin adding to the discomfort that arises due to the chronic kidney disease. Negative impacts on cardiovascular metabolic variables, such as heart rate and blood pressure, have also been documented for patients undergoing hemodialysis[20-22]. The accumulated negative impact of these manifestations has been associated with poor adherence rates to hemodialysis[23], eventually leading to morbidity- and mortality-related outcomes for these patients.

The management of these psychophysiological manifestations during hemodialysis is usually resolved with pharmacological medications[24-26]. However, concerns about the adverse-effects, ineffectiveness, costs, and inability of drugs to resolve the underlying pathology have promoted the use of complementary non-pharmacological alternatives, such as music-based interventions[27]. The existing literature suggests that music-based interventions are one of the most efficient complementary therapies alleviating psychological and physiological manifestations associated with different diseases[28-31]. The neurologic influence of music-based interventions (including increased dopamine and endorphin production) may explain their beneficial effects, which include lowering levels of anxiety, pain, and heart rate[32-34].

However, a consensus on the influence of music-based interventions in patients with chronic kidney disease undergoing hemodialysis is still missing. Only two systematic reviews and meta-analyses[27,35] have reported the influence of music-based interventions on the psychological outcomes associated with anxiety. Both studies reported a *medium* standardized mean effect of music-based interventions to alleviate anxiety in patients with chronic kidney disease undergoing hemodialysis. But, as a limitation, these studies failed to evaluate the physiological influence of music-based interventions (especially on the cardiovascular outcomes of patients with chronic kidney disease undergoing hemodialysis). An updated systematic review and meta-analysis are strongly warranted.

Therefore, we synthesized the evidence regarding the influence of music-based interventions in patients with chronic kidney disease undergoing hemodialysis. In addition, we attempted to develop a state of evidence regarding the magnitude of the influence associated with music-based interventions on anxiety, pain, heart rate, and blood pressure (systolic, diastolic) in these patients. Our findings should be beneficial to nephrologists across the world to determine best practice guidelines for patients with chronic kidney disease undergoing hemodialysis.

## Materials and Methods

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to perform our systematic review and meta-analysis[36].

### Data Search Strategy

We searched the EMBASE, MEDLINE, CENTRAL, and Scopus scientific databases from inception until September 2020 using a combination of the following MeSH keywords: "Chronic kidney disease", "CKD", "Hemodialysis", "Anxiety", "Sleep", "Pain", "Heart rate", "Blood pressure", and "Cardiovascular". Moreover, we manually screened the bibliography section of the retrieved studies to identify further relevant studies. During the screening procedure, we adhered to the following inclusion criteria for our review:

- Studies evaluating the influence of music-based interventions on patients undergoing hemodialysis.
- Studies performed on the human population.
- Studies evaluating the influence of music-based interventions on anxiety, pain, heart rate, sleep, and blood pressure (systolic, diastolic) outcomes.
- The studies were either randomized-controlled trials, quasi-randomized controlled trials, or controlled-clinical trials.
- The studies were published in peer-reviewed scientific journals or conferences.
- The studies were published in the English.

Two reviewers independently performed the screening of the studies and held discussions with a third independent reviewer for arbitration in cases of disagreement. We extracted the following data from the included studies: author information, descriptive data, sample distribution, duration of music intervention, type of music intervention, evaluated parameters, and outcomes. Furthermore, we made attempts to contact the corresponding authors of publications missing quantitative values for gaining access to the data.

### Quality Assessment

We assessed the risk of bias of the included studies using the Cochrane risk of bias assessment tool for randomized controlled trials[37]. The tool considers inadequate randomization, selective reporting, concealed allocation, blinding of outcomes, and incomplete data as major bias threats. Two reviewers independently appraised the methodological quality of the studies and again held discussions with a third reviewer to conciliate disagreements.

### Data Analysis

We carried out a meta-analysis with the acquired data from the studies by using the Comprehensive Meta-analysis software version 2.0[38]. The within group meta-analysis was performed according to a random effects model[39]. We calculated the pooled weighted effect size as Hedge's *g* and assessed the heterogeneity among the studies by computing $I^2$ statistics (we considered values 0-25% as representing negligible heterogeneity, values of 25%-75% as representing moderate heterogeneity, and values higher than 75% as representing substantial heterogeneity)[40]. We distributed the data and performed analyses for the overall mortality and hospitalization outcomes. We reported rate ratios, 95% confidence intervals, levels of significance, and heterogeneity. Also, we assessed publication bias by using Duval and Tweedy's trim and fill procedure[41]. This method presents a nuanced perspective of the overall effect and predicts shifts in cases of apparent bias. The analysis can identify any unbiased effects by asserting studies from either side of the plotted graph. We set the alpha level of significance at 95%.

## Results

Our systematic search yielded 1375 studies. We also found 27 studies after screening the bibliography of articles (Figure 1). Eight studies met our inclusion criteria. All of them were randomized controlled trials[42-49]. We extracted and summarized the data of the included studies in detail (Table I).

### Participant Information

The eight studies included evaluated a total of 597 patients (264 women and 287 men) undergoing hemodialysis. One study failed to report the gender distribution[47]. The average age of the patients was 56.9 ± 10.8 years (three studies failed to report the average age in their sample)[43,47,49]. In the sub-groups, we evaluated data from 298

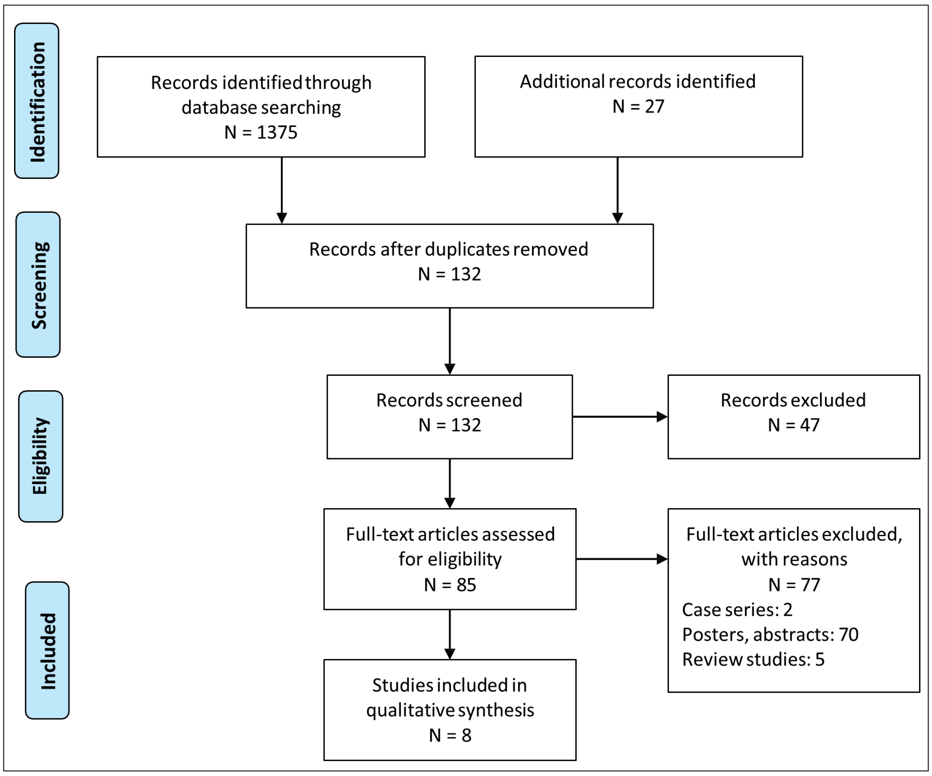


**Figure 1.** PRISMA flow-chart.

**Table I.** Details of the studies included.

| Study | Country | Study design | Sample size (women, men) | Overall age in years (mean ± S.D.) | Intervention Duration | Music type | Evaluated variables | Outcomes |
|---|---|---|---|---|---|---|---|---|
| Melo et al. (2018) | Brazil | Randomized controlled study | Exp: 30 (13 W, 17M) Ct: 30 (14W, 16M) | Exp: 42.1 ± 13.4 Ct: 44.3 ± 13.9 | Exp: 30 minutes Ct: - | Exp: Classical music Ct: - | State trait anxiety inventory, blood pressure (systolic and diastolic), and heart rate | Significantly reduced anxiety, blood pressure (systolic), heart rate, and respiratory rate in Exp as compared to Ct. Reduced blood pressure (diastolic) in Exp as compared to Ct. |
| Momennasab et al. (2018) | Iran | Randomized controlled study | Exp: 34 (14W, 20M) Ct: 35 (19W, 16M) | Exp: 49.8 ± 11.5 Ct: 48.8 ± 11.1 | Exp: 50-minutes Ct: - | Piano improvisation | Pittsburgh Sleep Quality Index | Significant improvement in Exp as compared to Ct. |
| Midilli et al. (2017) | Turkey | Randomized controlled study | Exp: 23 Ct: 23 | 59 ± 16 Exp: - Ct: - | Exp: 30-minutes Ct: - | Classical, pop and arabesque music | Blood pressure (systolic and diastolic), heart rate, and respiratory rate | Reduction in blood pressure (systolic and diastolic), heart rate, and respiratory rate in Exp as compared to Ct. |
| Burrai et al. (2014) | Italy | Randomized controlled study | Exp: 57 (32W, 25M) Ct: 57 (33W, 24M) | Exp: 68.9 ± 9.5 Ct: 67.4 ± 13.7 | Exp: 30-minutes Ct: - | Saxophone music | Blood pressure (systolic and diastolic), heart rate, visual analogue scale score | Significant reduction in visual analog scale score in Exp as compared to Ct. Reduction in blood pressure (systolic) in Exp as compared to Ct. No difference in heart rate, blood pressure (diastolic) between Exp and Ct. |

*Continued*

**Table I** ***(Continued).*** Details of the studies included.

| Study | Country | Study design | Sample size (women, men) | Overall age in years (mean ± S.D.) | Intervention Duration | Music type | Evaluated variables | Outcomes |
|---|---|---|---|---|---|---|---|---|
| Koca Kutlu and Eren (2014) | Turkey | Randomized controlled study | Exp: 30 (10W, 20M) (13W, 17M) | Exp: 55.1 ± 9.6 Ct: 30 50.8 ± 11.1 | Exp: 30-minutes Ct: Ct: - | Violin and piano music for 12 sessions | Perception of levels of pain, cramp, vomiting nausea, and duration of dialysis | Significant reduction in pain, nausea level in Exp as compared to Ct after 12 sessions. Reduction in level of duration of dialysis, cramp, and vomiting in Exp as compared to Ct. |
| Cantekin and Tan (2013) | Turkey | Controlled clinical study | Exp: 50 (24W, 26M) Ct: 50 (23W, 27M) | Exp: - Ct: - | Exp: - Ct: - | Rast and Usak melody | State trait anxiety inventory | Significant reduction in anxiety levels in Exp as compared to Ct. |
| Lin et al. (2012) | China | Randomized | Exp: 44 controlled study | Exp: (22W, 22M) Ct: 44 (29W, 15M) | Exp: 69.1 ± 7.8 Ct: - 75.5 ± 9.1 | - 20 minutes for 3 times per week Ct: - | Heart rate and blood pressure (systolic and diastolic) | Reduction in heart rate and blood pressure (systolic and diastolic) in Exp as compared to Ct. |
| Pothoulaki et al. (2008) | Greece | Randomized controlled study | Exp: 30 (11W, 19M) | 52.9 Exp: - Ct: 30 (7W, 23M) | Exp: - Ct: - Ct: - | Greek folk music, ethnic music, jazz, and classical music | McGill pain questionnaire and state traii anxiety scale | Significant reduction in anxiety score in Exp as compared to Ct Reduction in percepti of pain in Exp as compared to Ct. |

Exp, experimental group; Ct, control group; W, women; M, men.

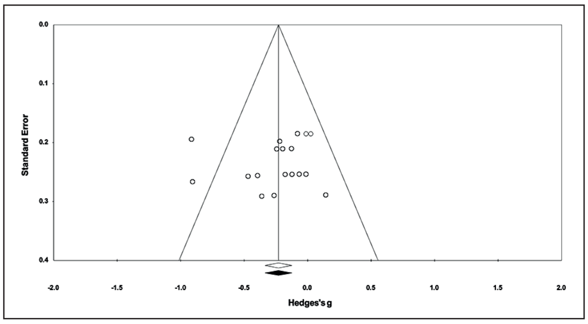


**Figure 2.** Publication bias by Duval & Tweedy's trim and fill method.

patients receiving music intervention. The gender distribution included a total of 126 women and 149 men. The average age in the experimental group was 57 ± 11.8 years. The control group had 299 patients (138 women and 138 men). The average age of the population in the control group was 57.3 ± 13.3 years.

### *Publication Bias*

We applied Duval and Tweedy's trim and fill method to identify any missing studies according to the random effects model on both sides of the funnel plot; the point estimates and the 95% confidence intervals for all the combined studies were -0.22 and (-0.33 to -0.12), respectively. After applying the trim and fill method, these values remained unchanged. Figure 2 shows the publication bias report details.

### *Quality Assessment for Randomized Controlled Trials*

Table II shows the results of our analysis of the risk of bias in the methodology of the randomized controlled trials. The overall risk was high. We observed a lack of random sequence generation, selecting reporting, and other biases. Figure 3 illustrates the overall risk of bias.

## Meta-Analysis Report

### *Anxiety Outcomes (State Trait Anxiety Inventory)*

Three studies in our meta-analysis reported overall anxiety outcomes as identified by the state trait anxiety inventory[43,46,49]. A small negative pooled weighted effect size as Hedge's $g$ was -0.16 (95% CI, -0.42 to 0.1; $p$=0.23) (Figure 4), without heterogeneity ($I^2$, 0%).

### *Pain*

Three studies reported the overall perceived level of pain[42,44,49]. The *medium* negative pooled weighted effect size as Hedge's $g$ was -0.75 (95% CI, -1.07 to -0.42; $p$<0.01) (Figure 5), with negligible heterogeneity ($I^2$, 1.2%).

### *Heart Rate*

Five studies reported the outcome for heart rate[42,45-47,49]. Overall a *small* negative effect size reported as Hedge's $g$ was -0.15 (95% CI, -0.35 to 0.05; $p$=0.14) (Figure 6), without heterogeneity ($I^2$, 0%).

### *Systolic Blood Pressure*

Four studies reported the outcome for systolic blood pressure[42,45-47]. The overall pooled weighted effect size as Hedge's $g$ was -0.14 (95% CI, -0.36 to 0.07; $p$=0.20) (Figure 7), without heterogeneity ($I^2$, 0%).

**Table II.** Risk of bias within studies according to Cochrane risk of bias tool for randomized controlled trials.

| | Random sequence generation | Concealment of allocation | Blinding of participant | Blinding of outcome | Incomplete outcome data | Threshold pre-specified | Selective reporting | Other biases |
|---|---|---|---|---|---|---|---|---|
| Melo et al (2018) | + | + | + | + | + | + | + | + |
| Momennasab et al (2018) | ? | + | + | + | + | + | + | + |
| Midilli et al (2017) | ? | + | + | + | - | + | ? | ? |
| Burrai et al (2014) | ? | + | + | + | + | + | + | + |
| Koca Kutlu and Eren (2014) | ? | + | + | + | + | + | + | ? |
| Cantekin and Tan (2013) | ? | + | + | + | - | + | ? | ? |
| Lin et al (2012) | ? | + | + | + | + | + | + | + |
| Pothoulaki et al (2008) | ? | + | + | + | - | + | ? | ? |

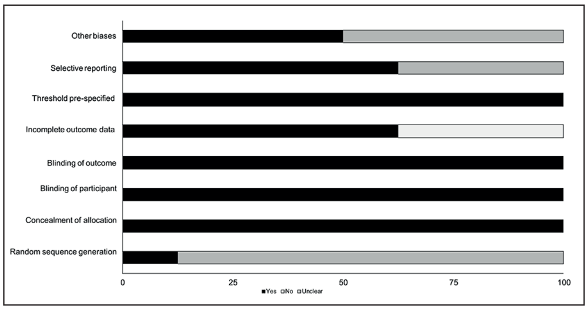


**Figure 3.** Risk of bias according to the Cochrane risk of bias assessment for the randomized controlled trials.

### *Diastolic Blood Pressure*

Four studies reported the outcome for diastolic blood pressure[42,45-47]. The overall pooled weighted effect size was *small* and in the negative direction as *g* -0.11 (95% CI, -0.33 to 0.11; *p*=0.32) (Figure 8), without heterogeneity ($I^2$, 0%).

## Discussion

This systematic review and meta-analysis provides a comprehensive state of the evidence on the influence of music-based interventions on the physiological and psychological outcomes of patients with chronic kidney disease undergoing hemodialysis. We found an overall beneficial influence of music-based interventions on the anxiety, pain, heart rate, and blood pressure (systolic, diastolic) outcomes of patients with chronic kidney disease undergoing hemodialysis when compared to the outcomes in control patients.

The management of chronic kidney disease is challenging for nephrologists due to its atypical pathophysiological mechanisms, co-existing morbidities, and clinical manifestations[50,51]. The management of severely progressive cases by means of renal replacement therapy (i.e., hemodialysis), although necessary, leads to unwanted physiological and psychological outcomes that can promote the morbidity and mortality of patients[12,52-55]. Different mechanisms could be behind the aggravating manifestations, such as pain, fatigue, cramps, and nausea in patients undergoing hemodialysis[56]. Sabitha et al (2008)[57] mentioned cannulation of arterial and venous fistulas during hemodialysis as a major underlying cause of pain and discomfort; the cannulation procedures largely take place in the absence of local anesthetic agents because of concerns for latent vasoconstriction, infection, and scarring. Moreover, the negative implications of hemodialysis in terms of psychological outcomes (i.e., anxiety, stress, and depression) have also been widely documented. Murray et al (2006)[58] reported that patients undergoing hemodialysis exhibit higher levels of cognitive deficits, of fatigue, and of sleep disorders[59,60], and the restrictive nature of the treatment in terms of independence and diet also promotes the onset of psychological disorders. Together, these changes eventually worsen the treatment adherence, morbidity, and mortality outcomes in these patients[61,62].

Complementary therapies, such as music-based interventions, have been implemented in the past decade to manage these psychological and physiological deficits[27,35]. Music-based interventions

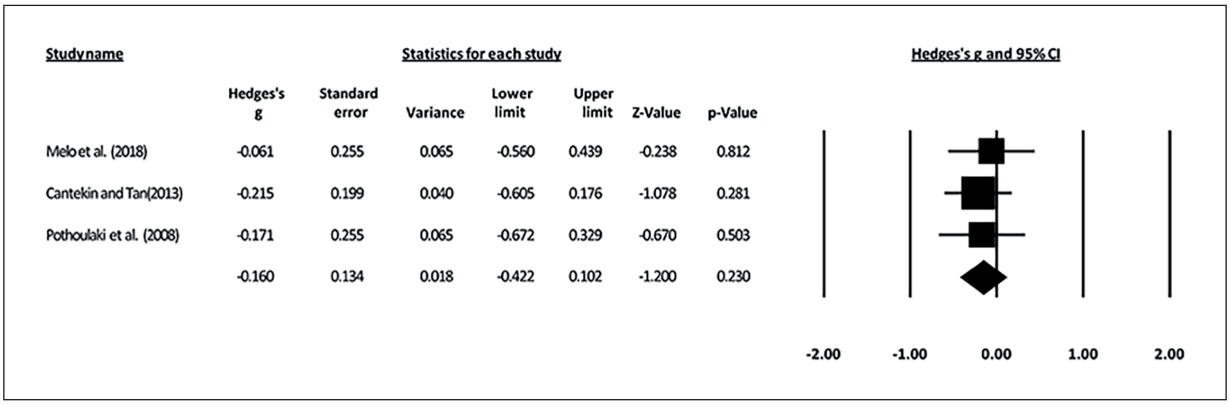


**Figure 4.** Forest plot for studies evaluating the influence of music-based interventions on anxiety in patients with chronic kidney disease undergoing hemodialysis. Adjusted hazard ratios are presented as black boxes and 95% confidence intervals as whiskers. A negative effect size represents reduced anxiety levels for the experimental group, whereas the positive rate ratio represents a reduced anxiety level for the control group.

| Study name | Hedges's g | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|
| Burrai, Micheluzzi, Zito, Pietro, and Sisti (2014) | -0.909 | 0.196 | 0.038 | -1.292 | -0.526 | -4.649 | 0.000 |
| Koca Kutlu and Eren (2014) | -0.901 | 0.268 | 0.072 | -1.426 | -0.376 | -3.364 | 0.001 |
| Pothoulaki et al. (2008) | -0.389 | 0.257 | 0.066 | -0.893 | 0.115 | -1.512 | 0.131 |
| | -0.753 | 0.166 | 0.028 | -1.078 | -0.428 | -4.539 | 0.000 |

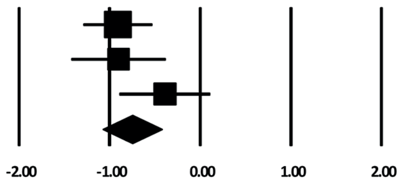


**Figure 5.** Forest plot for studies evaluating the pain perception in patients with chronic kidney disease undergoing hemodialysis Adjusted hazard ratios are presented as black boxes and 95% confidence intervals as whiskers. A negative effect size represents reduced pain levels for the experimental group, whereas the positive rate ratio represents a reduced pain level for the control group.

| Study name | Hedges's g | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|
| Meloet al. (2018) | -0.463 | 0.258 | 0.067 | -0.970 | 0.043 | -1.794 | 0.073 |
| Midilli, Ergin, andY?lmaz(2017) | 0.148 | 0.290 | 0.084 | -0.421 | 0.717 | 0.511 | 0.609 |
| Burrai, Micheluzzi, Zito, Pietro, and Sisti (2014) | -0.008 | 0.186 | 0.035 | -0.372 | 0.357 | -0.042 | 0.967 |
| Lin, Lu, Chen, and Chang (2012) | -0.121 | 0.212 | 0.045 | -0.536 | 0.293 | -0.574 | 0.566 |
| Pothoulaki et al. (2008) | -0.389 | 0.257 | 0.066 | -0.893 | 0.115 | -1.512 | 0.131 |
| | -0.150 | 0.104 | 0.011 | -0.353 | 0.053 | -1.450 | 0.147 |

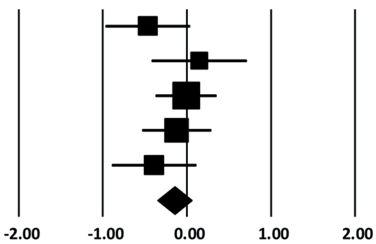


**Figure 6.** Forest plot for studies evaluating the outcome for heart rate in patients with chronic kidney disease undergoing hemodialysis. The adjusted hazard ratios are presented as black boxes whereas 95% confidence intervals as whiskers. A negative effect size represents reduced heart rate levels for the experimental group, whereas the positive rate ratio represents reduced heart rate levels for the control group.

are favored because they have been considered effective in alleviating psychophysiological deficits in patients undergoing hemodialysis, while avoiding the adverse effects of pharmacological medications[63,64]. In our review, we observed a range of studies reporting the predominant influence of music-based interventions to reduce the pain-related outcomes in these patients. Pothoulaki et al (2008)[49] reported beneficial effects of music-based intervention on perceived levels of pain (1.2 ± 2.2) in 30 patients with chronic kidney disease undergoing hemodialysis as compared

| Study name | Hedges's g | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|
| Meloet al. (2018) | -0.117 | 0.255 | 0.065 | -0.617 | 0.383 | -0.458 | 0.647 |
| Midilli, Ergin, andY?lmaz(2017) | -0.259 | 0.291 | 0.085 | -0.829 | 0.312 | -0.889 | 0.374 |
| Burrai, Micheluzzi, Zito, Pietro, and Sisti (2014) | -0.075 | 0.186 | 0.035 | -0.440 | 0.290 | -0.402 | 0.687 |
| Lin, Lu, Chen, and Chang (2012) | -0.191 | 0.212 | 0.045 | -0.606 | 0.224 | -0.901 | 0.368 |
| | -0.144 | 0.113 | 0.013 | -0.365 | 0.078 | -1.273 | 0.203 |

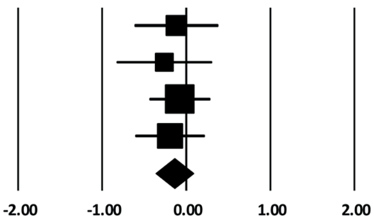


**Figure 7.** Forest plot for studies evaluating the outcome for systolic blood pressure in patients with chronic kidney disease undergoing hemodialysis. Adjusted hazard ratios are presented as black boxes and 95% confidence intervals as whiskers. A negative effect size represents reduced systolic blood pressure levels for the experimental group, whereas the positive rate ratio represents reduced systolic blood pressure levels for the control group.

| Study name | Hedges's g | Standard error | Variance | Lower limit | Upper limit | Z-Value | p-Value |
|---|---|---|---|---|---|---|---|
| Meloetal. (2018) | -0.007 | 0.255 | 0.065 | -0.507 | 0.492 | -0.029 | 0.977 |
| Midilli, Ergin, andY?lmaz(2017) | -0.356 | 0.292 | 0.085 | -0.929 | 0.217 | -1.219 | 0.223 |
| Burrai, Micheluzzi, Zito, Pietro, andSisti (2014) | 0.030 | 0.186 | 0.035 | -0.335 | 0.395 | 0.160 | 0.873 |
| Lin, Lu, Chen, andChang (2012) | -0.237 | 0.212 | 0.045 | -0.653 | 0.178 | -1.120 | 0.263 |
| | -0.111 | 0.113 | 0.013 | -0.333 | 0.110 | -0.984 | 0.325 |

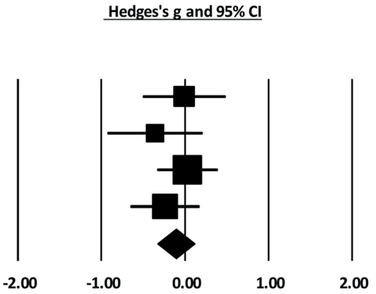


**Figure 8.** Forest plot for studies evaluating the outcome for diastolic blood pressure in patients with chronic kidney disease undergoing hemodialysis. Adjusted hazard ratios are presented as black boxes and 95% confidence intervals as whiskers. A negative effect size represents reduced diastolic blood pressure levels for the experimental group, whereas the positive rate ratio represents reduced diastolic blood pressure levels for the control group.

with the levels in the control group (2.3 ± 2.0). Similarly, Koca Kutlu and Eren (2014)[44] reported the beneficial influence of music-based interventions for reducing the perceived levels of pain and other complications associated with hemodialysis like nausea, vomiting, and muscle cramps. Burrai et al (2014)[42] speculated that music-based interventions may alleviate the perception of pain by inhibiting the interneurons that transmit the nociceptive signals to the brain[65]. Based on our meta-analysis findings, we confirm a *medium* negative overall effect of the music-based intervention for reducing the perceived level of pain in patients with chronic kidney disease undergoing hemodialysis (Hedge's *g*, -0.75; 95% CI, 1.07 to -0.42).

We also attempted to synthesize the data on the influence of music-based interventions on cardiovascular metabolic outcomes, including heart rate and blood pressure in patients with chronic kidney disease undergoing hemodialysis. Patients undergoing hemodialysis usually exhibit a transient increase in heart rate and blood pressure[17,66,67]. However, most studies in our systematic review reported an overall reduction in cardiovascular metabolic outcomes in their patients. Melo et al (2018)[46] found a significant ($p<0.01$) reduction from the baseline values in heart rate and blood pressure (systolic, diastolic) in the patients of the interventional group in their study and interpreted this as a sign of relaxation in the patients undergoing hemodialysis. This interpretation was based on correlative findings of a reduction in anxiety-related outcomes in patients with chronic kidney disease undergoing hemodialysis while receiving music-based interventions (State trait anxiety score, 32.8 ± 9.6 in the interventional group and 33.3 ± 6.3 in the control group). Similarly, Lin et al (2012)[45] also associated the significant reduction in cardiovascular metabolic outcomes in patients receiving music-based interventions with reduced levels of anxiety, basing their hypothesis on the prospective influence of music-based interventions on the autonomic nervous system[68-70], which may reduce cardiovascular metabolic outcomes while simultaneously improving the psychological outcomes[71]. Our meta-analysis findings support those in the literature reporting a negative *small* effect of music-based interventions on the heart rate (*g*, -0.15; 95% CI, -0.35 to 0.05), systolic blood pressure (g, -0.14; 95% CI, -0.36 to 0.07), and diastolic blood pressure (g, -0.11; 95% CI, -0.33 to 0.11) in the interventional group patients. We also found a *small* reduction effect in state trait anxiety scores (g, -0.16; 95% CI, -0.42 to 0.1) in the same group.

We are aware of the limitations of our systematic review and meta-analysis. Mainly, we did not register our systematic review and meta-analysis on the PROSPERO repository, and we know this may raise concerns regarding the validity of our review[72]. However, the current pandemic crisis meant that our registration at PROSPERO would have taken more than a year to complete due to extended waiting times. Secondly, we could not evaluate sleep quality outcomes due to the scarcity of data (only one study in our analysis included this evaluation)[48]. Therefore, high-quality studies evaluating the influence of music-based interventions on sleep-related outcomes of patients undergoing hemodialysis are needed. The evaluation of these outcomes would help medical practitioners and patients alike to understand the overall influence of music-based interventions on the psychological outcomes of patients undergoing hemodialysis.

## Conclusions

Briefly, our analysis confirms the beneficial influence of music-based interventions on alleviating physiological and psychological manifestations associated with hemodialysis in patients with chronic kidney disease. We also found evidence supporting the effects of the intervention for reducing pain perception, heart rate, anxiety, and blood pressure. Our findings should be considered when developing best practice guidelines for the management of physical and psychological manifestations in patients with chronic kidney disease undergoing hemodialysis.

#### Conflict of Interest

The Authors declare that they have no conflict of interests.

#### Availability of Data and Materials

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


#### Disclosure of Grants or Other Funding

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