Title: The effect of music on pain in the adult intensive care unit: A systematic review of randomized controlled trials

Authors:

Melissa Richard-Lalonde, MSc, RN, *McGill University, Montreal, QC, Canada*

Dr. Céline Gélinas, PhD, RN, *McGill University and Jewish General Hospital, Montreal, QC, Canada*

Dr. Madalina Boitor, PhD, *McGill University, Montreal, QC, Canada*

Dr. Emilie Gosselin, PhD, RN, *McGill University, Montreal, QC, Canada*

Dr. Nancy Feeley, PhD, RN, *McGill University and Jewish General Hospital, Montreal, QC, Canada*

Dr. Sylvie Cossette, PhD, RN, *Université de Montréal, and Montreal Heart Institute, Montreal, QC, Canada*

Dr. Linda L. Chlan, PhD, RN, ATSF, FAAN, *Mayo Clinic, Rochester, MN, USA*

Corresponding author.

Name: Melissa Richard-Lalonde

E-mail address: melissa.richard-lalonde@mail.mcgill.ca

Abstract

Context. Multimodal analgesic approaches are recommended for intensive care unit (ICU) pain management. Although music is known to reduce pain in acute and chronic care settings, less is known about its effectiveness in the adult ICU.

Objectives. Determine the effects of music interventions on pain in the adult ICU, compared with standard care or noise reduction.

Methods. This review was registered on PROSPERO (CRD42018106889). Databases were searched for randomized controlled trials of music interventions in the adult ICU, with the search terms [“music*” and (“critical care” or “intensive care”)]. Pain scores (i.e., self-report rating scales or behavioral scores) were the main outcomes of this review. Data were analyzed using a DerSimonian-Laird random effects method with standardized mean difference (SMD) of pain scores. Statistical heterogeneity was determined as I^2>50% and explored via subgroup analyses and meta-regression.

Results. Eighteen randomized controlled trials with a total of 1173 participants (60% males; mean age of 60 years) were identified. Ten of these studies were included in the meta-analysis based on risk of bias assessment (n = 706). Music was efficacious in reducing pain (SMD of -0.63 [95% CI -1.02, -0.24; n = 10]; I^2 = 87%). Music interventions of 20-30 minutes were associated with a larger decrease in pain scores (SMD -0.66 [-0.94, -0.37; n = 5]; I^2 = 30%) compared with interventions of less than 20 minutes (SMD 0.10 [95% CI -0.10, 0.29; n = 4]; I^2 = 0%). On a 0-10 scale, 20-30 minutes of music resulted in an average decrease in pain scores of 1.06 points [95% CI -1.56, -0.56].

Conclusion. Music interventions of 20-30 minutes are efficacious to reduce pain in adult ICU patients able to self-report.

Key Words

Systematic review, music, intensive care, critical care, adult, pain

Running Title: Systematic Review of Music Effect on ICU Pain

Introduction

Pain is a common symptom in the intensive care unit (ICU), occurring both at rest and during routine ICU procedures such as chest tube or drain removal, endotracheal suctioning and turning.[1] Clinical practice guidelines recommend a multimodal analgesic approach to minimize the amount of opioids administered,[2] which should include nonpharmacological interventions such as massage and music.[2-4] Although previous reviews have reported the positive effect of music in reducing pain, only five randomized controlled trials (RCTs) conducted in the adult ICU were included in these reviews.[4-10]

Previous systematic reviews in the adult ICU setting have reported the effects of music on anxiety, vital signs, stress or inflammatory markers.[11-13] An integrative review was published about the effects of music on the management of symptoms of anxiety, pain and insomnia in critically ill patients.[9] However, as their aim was to look at the most current evidence of music with adult critically ill patients, with their choice to only review literature published in English, the inclusion criteria were limited to studies published in English from 2010 to 2016.[9] Overall, there remains an important gap in the knowledge of the effects of music on pain in critically ill patients who are known to experience pain.[14,15] Therefore, a systematic review and meta-analysis is needed to help understand whether music is an efficacious intervention to reduce pain in the adult ICU, and if so, what features are efficacious, as well as to inform clinical practice guidelines for pain management in the adult ICU.

Research Question and Objectives

The research question was as follows: What is the effect of music, delivered in addition to standard ICU care, on pain scores, compared with standard care without music or noise reduction (two different types of comparators commonly used in music intervention RCTs) in the adult ICU?

A systematic review and a meta-analysis were conducted to evaluate the effect of music interventions on pain scores in the adult ICU. We also performed subgroup analyses based on music duration, selection (by participant vs. care providers), music provider (music therapist vs. nurse vs. research staff), timing of administration (during procedures vs. at rest), or presence vs. the absence of pharmacological coanalgesia.

Methods

Protocol and Registration

The protocol of this review was registered on PROSPERO in October 2018 (#CRD42018106889). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[16] The PRISMA steps include: identification of all relevant records, selection of eligible RCTs, risk of bias (ROB) assessment, data extraction, qualitative synthesis, and whenever possible, quantitative synthesis or meta-analysis (p. W-66).[16]

Eligibility Criteria

Eligibility criteria for studies were: 1) RCT primary findings; 2) conducted in the adult ICU regardless of specialty; 3) participants at least 18 years old regardless of diagnosis; 4) music as an intervention; and 5) reported pain scores as an outcome before and up to four hours after the music intervention, based on the usual duration of action of most common pain medications used in the ICU.[2,17] Music interventions were eligible if the music was delivered passively by earpiece, pillow, radio, or any other format; played continuously (without interruption);

prerecorded or live; played at any frequency, for any duration of time; delivered with or without medication for pain relief; tailored to the participant's preference or preselected by others; and any type of music including birdsongs or other nature-based sounds.

Music interventions were excluded if they were coadministered with any other nonpharmacological intervention (e.g., massage, aromatherapy, meditation, televised stimuli, or guided imagery).

The standard care comparator included any individually-prescribed pain management protocol, as part of the usual course of treatment for each patient. The noise reduction comparator included active (e.g., headphones emitting white noise) or passive (e.g., headphones emitting no sound) noise reducing methods, in addition to standard care.

For patients able to self-report, studies were included when pain was assessed using a self-report intensity scale such as the 0-100 Visual Analog Scale (VAS), the 0-10 Numeric Rating Scale (NRS), the 0-10 University of California, Los Angeles (UCLA) pain score, the 0-10 Faces Pain Scale or the pain thermometer. For all self-report pain scales, a higher score means a higher level of pain intensity.

For patients unable to self-report, studies were included when pain was assessed using the 0-8 Critical-Care Pain Observation Tool (CPOT) or the 3-12 Behavioral Pain Scale (BPS) for which cut-point scores greater than two and five, respectively, indicate the presence of pain.

Information Sources

Health sciences and music databases were accessed: MEDLINE, Cochrane CENTRAL, Embase, Web of Science, CINAHL, PsycINFO, Scopus, ProQuest Dissertations and Theses Full Text, Music Periodicals Database, JSTOR, Music Index, RILM, ViFaMusik, PubMed, and Google Scholar. Other sources included reference lists of selected articles, key journals, trial registers (ClinicalTrials.gov and the International Standard Randomised Controlled Trials Number: ISRCTN.com), conference proceedings, Internet resources, and contact with authors to attempt to identify any unpublished or otherwise inaccessible trials. No language restriction was applied. The databases were searched from their inception, covering periods as far back as 1800, until March 1, 2019.

Search

The search strategy, guided by an experienced music librarian, included the terms “music*” and (“critical care” or “intensive care”). Where applicable, the search filtered for controlled trials and adult participants (Supplementary Data 1). The search was also reviewed by an experienced healthcare research librarian.[18]

Study Selection

All the references were screened independently by two reviewers, starting with titles and abstracts, followed by full texts. A third reviewer was consulted for any disagreements in screening of full texts. The online systematic review software DistillerSR (Evidence Partners, Ottawa, Canada) was used for screening, data extraction, and ROB assessment.

Data collection process

A data extraction form adapted from the 2014 Cochrane “Data collection form for intervention reviews: RCTs only” was completed by two reviewers for independent data extraction using the DistillerSR software. The data extraction form was pilot tested using two randomly selected eligible articles, and minor modifications were made. For example, the word total was added next to percent participants to clarify that the percentage of all participants should be extracted (as opposed to the percentage of participants per arm). Disagreements were discussed between the reviewers and consensus was reached.

Data items

The following data was extracted: population description (age, sex and diagnosis), type of ICU, inclusion and exclusion criteria, comparator (standard care and noise reduction), type of outcome measure (pain assessment tools), outcomes (pain scores) and timing of measurement, intention to treat, power analysis, intervention description (type of music, duration, timing, frequency, mode of delivery, providers and any pharmacological cointervention), adverse events, funding and conflicts of interest.

To be consistent and have comparable data across RCTs, only data from one (the first) music session was extracted from studies that had multiple music sessions. Regarding RCTs that evaluated the effect of the music intervention for procedural pain, the first and second time points when data were collected in the study protocol were extracted. The baseline pain scores were extracted for all studies to evaluate the ROB because of baseline imbalances.

Risk of Bias

ROB was also assessed independently by two reviewers using the Cochrane ROB Tool for RCTs.[19] All discrepancies were discussed between all reviewers, and consensus was achieved. Studies with high risk of selection and attrition biases as well as studies deemed to have too much missing information were excluded from quantitative synthesis.

Summary Measures

Data on population characteristics, intervention characteristics and pain score outcomes were collected from the included RCTs and described.

A meta-analysis was done for studies with a lower ROB (studies were excluded if they had a high ROB for random sequence generation, allocation concealment, and/or incomplete outcome data) and homogeneity was determined by an I^2 value inferior to 50%.[20] Data were analyzed using Review Manager (version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, The Netherlands).[21] The principal summary measures were standardized mean difference (SMD) of pain scores using a DerSimonian-Laird random effects model with a 95% CI. Publication bias was evaluated using funnel plot analyses of asymmetry.

Additional Analysis

Additional analyses were conducted to explore statistical heterogeneity ($I^2 > 50\%$) via subgroup analyses and meta-regression. Random effects meta-regression analyses were conducted for each prespecified potential effect modifier (music duration, selection, provider, timing of administration, and the presence of pharmacological analgesia) using STATA (Version 16.0; Stata-Corp LLC, College Station, TX).[22]

Results

Study Selection

The PRISMA flow diagram is illustrated in Fig. 1.[23] A total of 2907 references were retrieved from database searches, and five additional references were identified through reference lists of selected articles. Once duplicates were removed, 1618 references were screened for titles and abstracts and most (n = 947) were eliminated for not being RCTs. At the full-text phase, 149 articles were assessed. At this phase, most articles were excluded for not having pain as an outcome (n = 64). Eighteen studies were included for a qualitative synthesis, 10 of which were included in the meta-analysis based on ROB.

Study Characteristics

Studies were mostly in English, but some were also in German, Spanish, Portuguese, French, Greek, Turkish, and Chinese. For languages not understood by the reviewers, online translators were used, and multilingual colleagues were consulted to translate, and reviewers then determined the studies' eligibility. The 18 RCTs retained were in English, French, and Spanish, all languages understood by two of the reviewers. Table 1 presents the characteristics of the 18 RCTs conducted across seven countries (USA, n = 5; Iran, n = 5; France, n = 2; Spain, n = 2; Turkey, n = 2; China, n = 1; and Australia, n = 1), arranged chronologically from 1999 to 2018 (years of publication).[24-41] Sample sizes ranged from 17 to 156, totaling 1173 participants. Twelve RCTs (n = 744) compared the effect of a music intervention with standard care and seven RCTs (n = 533) compared the effect of a music intervention with noise reduction, with one RCT reporting both comparators. Two studies reported not having reached their planned sample sizes because of recruitment feasibility issues: Cooke et al.[24] enrolled 17 participants of their projected 50, and Shultis[25] had 20 participants instead of their required sample size of 106.[24,25] The main reason for recruitment issues was patients not meeting eligibility criteria (e.g., unplanned surgery, unable to answer questions).

The mean age of participants was 60 years with 60% males and 40% females. Eight studies solely included participants who had undergone cardiac surgeries, four included participants who had undergone various types of surgeries, and five included participants with a variety of medical diagnoses. Fifteen studies only included participants who were able to communicate (n = 978; 83.4% of included participants), whereas three studies included patients unable to communicate (n = 195; 16.6%). The pain assessment tools used in each study are presented in the last column of Table 1 and included 0-10 or 0-100 self-report scales (n = 14), as well as the 0-8 CPOT (n = 2) and the 3-12 BPS (n = 2). The CPOT was also used with participants who were able to self-report in one study, but no rationale for this was provided by the authors.[26]

None of the RCTs' mean baseline pain score was above six on a 0-10 self-reported scale. More specifically, eight RCTs[24,25,27-32] reported a low mean baseline pain score (zero to three of 10) and five RCTs[33-37] reported a moderate pain score (four to six of 10). For the trials that used behavioral scales, two RCTs[26,38] reported their participants' mean baseline behavioral pain scores to be below the cut-point score (i.e. CPOT <3 or BPS <5), and two RCTs[39,40] reported the scores to be above the cut-point scores (CPOT ≥3 or BPS ≥5). One RCT did not report baseline behavioral pain scores.[41]

Study Characteristics: Interventions

The characteristics of the music interventions varied widely across studies, as described in Table 2 and illustrated in Fig. 2. The music interventions varied in duration, ranging from 10 to 90 minutes, with most studies administering music for 30 minutes (n = 7). Eight RCTs[25,26,28,30,31,34,35,37] played prerecorded music with a pre-specified tempo, usually in the range of 60-80 beats per minute (bpm). Eight RCTs[24,26-28,30,32,37,39] reported music administration for procedural pain (e.g. caused by chest tube removal, endotracheal suction, turning or dressing change). In the other 10 studies, prerecorded or live music was administered while the patient was at rest, that is at a time when no predetermined standard ICU procedure was reported to occur.[25,29,31,33-36,38,40,41] A single music session was administered in 15 studies[24-30,32,34-39,41], and multiple sessions (three to eight) were administered in three studies.[31,33,40] Five studies reported that none of their participants received any pain medication during the music intervention (patients requiring analgesia at the time of the music delivery were excluded), whereas nine studies reported that their participants received opioids as needed, according to their pain management protocol. Three studies did not specify either way. None of the studies reported withholding standard ICU pain management interventions from the participants.

Providers involved in the delivery of the music intervention were usually not only research staff (n = 9), but also music therapists (n = 2), nurses (n = 2), nursing assistants (n = 1) and one musician (n = 1) (four studies did not specify who administered the music). Overall, music therapists were involved either in the production (e.g., MusiCure, Music Care), selection (e.g., harpist, music lecturer), and/or administration of the music intervention in 10 RCTs.[25-27,29,30,33,34,37,38,41]

In five studies one musical piece was used for all patients, whereas participants in the 13 other studies were offered a selection of at least two pieces. Despite this, eight participants across three studies reported not being satisfied with the music to the point of withdrawing from the study.[28,31,34]

Music was usually delivered by headphones (n = 11) or earphones (n = 4); in one study a music pillow was used, and in another, live harp music was played at the participant's bedside. The mode of delivery was not specified in one study.[25] The devices used for delivery were either cassette players (n = 2), compact disc players (n = 3), MP3 players (n = 7), harp (n = 1), or tablets (n = 1), with some not specified (n = 4).

Risk of Bias

Fig. 3 presents the ROB summary of all 18 RCTs (see Supplementary Data 2 for more details to support judgments).

In two studies, the randomization sequence was generated based on record number or on odd or even number.[26,41] These two studies were also considered high risk for allocation concealment. Because of the nature of music interventions, blinding of participants and/or personnel was deemed improbable for all studies, thus leading to a rating of high risk of performance bias for all studies. In the 14 studies where participants self-reported their pain intensity, blinding of outcome assessment was considered impossible, and group assignment was considered to have possibly influenced pain self-reports.[24,25,27,28-37,41] Of the four studies in which behavioral pain scores were obtained by nurses, only one reported blinding the outcome assessor to the group allocation.[38] In three studies, some participants withdrew from the study and intention to treat was not applied. The participants withdrew because of the emotional reaction to, or dislike of, the music or headphones: five of 35 (14.3%) participants in the study by Jaber et al.[34]; four of 35 (11.4%) participants in the study by Chan[28]; and two of 22 (9.1%) participants in the study by Sanjuan Navais et al.[31] In one crossover study, three participants withdrew due to discomfort or sudden instability, but it is unclear whether this was during the music or the noise reduction, so the risk of attrition bias was deemed unclear.[38] Otherwise, 12 studies had both low attrition and low reporting biases (Fig. 3). Finally, the funnel plot generated to determine reporting bias across all studies did not yield any conclusive results because of the lack of larger study sample sizes (Supplementary Data 3).

Eight studies were excluded from meta-analysis. One study was excluded because it reported compiled pain results from multiple music sessions instead of reporting results separately for each individual session.[31] Similarly, one study was excluded because it compiled data from a crossover study that did not have a washout period between the music intervention and the noise reduction period, leading to a risk of carryover effect from the music intervention into the control period.[38] Two studies were removed because of high risks of bias in random sequence generation and allocation concealment (see Supplementary Data 2 for more detail).[26,41] Two more studies were excluded because of high risk of attrition bias: in these studies, participants withdrew from the study (and analysis) because of disliking the music.[28,34] Finally, there was an insufficient quantity of studies (only one) reporting pain using behavioral scores from participants unable to self-report to include in the final analysis.[40] Therefore, only studies using self-reported pain intensity scores were included in the final meta-analysis.

Synthesis of Results

Overall, 12 out of the 18 (66.7%) RCTs reported that the music intervention resulted in a significant decrease in pain scores. Considering that the patients' self-reported pain scores and behavioral scores measure different components of pain, analyses were considered separately for both types of scales.[42] In patients able to self-report, data were sufficient to conduct a meta-analysis. The time points that were included in the meta-analysis are illustrated in Fig. 2 as T_{pre} and T_{post} for each study protocol.

The meta-analysis of all 10 studies is presented in Fig. 4. Music was found to significantly decrease pain scores, with a SMD of -0.63 [95% CI -1.02, -0.24; n = 10] when combining all studies regardless of comparator. Back-transforming the SMD to a 0-10 scale represents a decrease of 0.74 point [95% CI -1.10, -0.37] of 10.[22, 43]

Synthesis of Results: Music vs. Standard Care

In patients able to self-report, music was found to significantly decrease pain scores, with an SMD of -0.74 [95% CI -1.46, -0.02; n = 6] when compared with standard care (Fig. 5). Back-transforming the SMD to the 0-10 scale, this represents a decrease of 0.73 point [-1.36, -0.10] of 10.[21,43]

Synthesis of Results: Music vs. Noise Reduction

In patients able to self-report, music was found to be significantly efficacious in reducing pain scores with an SMD of -0.57 [-1.03, -0.12; n = 5] when compared to noise reduction (Fig. 6). Back-transforming the SMD to the 0-10 scale, this represents a decrease of 0.88 [-1.28, -0.47] of 10.[21,43]

Adverse and Undesired Effects

No adverse effect was reported in any of the 18 RCTs. However, there are some reports of undesired effects. In four studies, a total of nine participants of 107 participants who received music expressed dislike of the selected music.[28,31,33,34] In addition, four other participants expressed dislike of the headphones in two studies.[33,34] In post-RCT patient interviews conducted by Ames et al.,[33] some participants reported that the music interfered with their ability to communicate with others or with their self-dosing via patient-controlled analgesia because of falling asleep while the prerecorded music was playing.[33]

Additional Analysis

The meta-analysis of all 10 studies yielded high heterogeneity (Fig. 4; $I^2 = 87\%$). Studies of music vs. standard care (Fig. 5; $I^2 = 90\%$) and studies of music vs. noise reduction (Fig. 6, $I^2 = 83\%$) also produced high heterogeneity. To explore the heterogeneity, subgroup analyses were conducted based on preselected potential effect modifiers: music selection (participant vs. non-participant), timing of administration (at rest vs. during procedures), duration of music, provider of the music (nurses vs. music therapists vs. research staff), and coanalgesia (presence vs. absence). Meta-regression analyses revealed that none of the potential effect modifiers were significant (all *p*-values >0.05: $p_{\text{music selection}} = 0.139$; $p_{\text{music timing}} = 0.122$; $p_{\text{music provider}} = 0.347$; and $p_{\text{co-analgesia}} = 0.555$) to account for heterogeneity, with the exception of music duration ($p = 0.005$). The trend of increased music duration being associated with decrease in pain scores can be seen with all included studies compiled (Supplementary Data 4), as well as for studies of music with either type of control group: standard care (Supplementary Data 5) or noise reduction (Supplementary Data 6). Supplementary Data 7 illustrates that there is no significant difference in the efficacy of music interventions administered for pain at rest vs. procedural pain.

Subgroup analyses revealed that 10-15 minutes of music did not significantly decrease pain scores (SMD 0.10 [95% CI -0.10, 0.29; n = 4], $I^2 = 0\%$) whereas 20-30 minutes of music had a significant effect on self-reported pain scores (SMD -0.66 [95% CI -0.94, -0.37; n = 5]; $I^2 = 30\%$). On a 0-10 scale, 20-30 minutes of music resulted in an average decrease of 1.06 points [95% CI -1.56, -0.56].

Additional Analysis: Music vs. Standard Care

Subgroup analyses revealed that 10-15 minutes of music did not significantly decrease pain scores (SMD 0.07 [95% CI -0.16, 0.31; n = 3]; Fig. 7), whereas 20-30 minutes of music had a significant effect on self-reported pain scores (SMD -1.07 [95% CI -1.63, -0.52, n = 2]; Fig. 8). On a 0-10 scale, 20-30 minutes of music resulted in an average decrease of 1.75 points [95% CI -2.84, -0.66]. One study played prerecorded music for 50 minutes and had a significant effect on decreasing pain scores (SMD -3.13 [95% CI -4.12, -2.14]).

Additional Analysis: Music vs. Noise Reduction

Subgroup analyses revealed that 10-15 minutes of music did not have a significant decrease in pain scores (SMD 0.16 [95% CI -0.19, 0.51; n = 2]; Fig. 9), whereas 20-30 minutes of music had a significant decrease in pain scores (SMD -0.51 [95% CI -0.76, -0.26; n = 3]; Fig. 10). On a 0-10 scale, 20-30 minutes of music resulted in an average decrease of 0.82 point [95% CI -1.20, -0.44]. One study played prerecorded natural sounds (e.g., birdsongs) for 90 minutes and had a significant effect on pain reduction (mean difference [MD] -1.23 [95% CI -1.61, -0.79]). One study with the intervention duration of 90 minutes reported increasingly significant pain intensity reduction over time (30 min MD -0.76 [95% CI -1.26, -0.24] and 90 minutes MD -1.23 [95% CI -1.64, -0.82]).

Discussion

To our knowledge, this is the first systematic review and meta-analysis of RCTs to report the effect of music interventions on pain scores in adult ICU patients. Overall, 18 RCTs including 1173 participants were conducted in seven different countries across four continents, although none were from Canada. Music was found to be significantly efficacious in decreasing pain scores when compared with standard care and noise reduction. Subgroup analyses revealed that only duration (i.e., 20-30 minutes) was related to the efficacy of music. This is in line with previous systematic reviews and meta-analyses that have reported music to be efficacious in decreasing pain by 0.5-2.3 on 0-10 scales in acute and chronic care settings.[4-10]

Overall, in ICU adults able to self-report, music interventions were more favorable when compared with standard care. It is possible that noise reduction also has an effect on decreasing pain scores as it has been shown to significantly reduce anxiety in mechanically ventilated ICU patients.[44] If noise reduction has an effect on decreasing pain scores, the mechanism of action could be via the reduction of anxiety or stress because of the associations between anxiety, stress and pain.[45-48] However, in our review, both the noise reduction and the standard care comparators were found to have high heterogeneity. Thus, subgroup analyses were conducted, and heterogeneity was best explained by differences in music duration. Recently, a protocol was developed by Poulsen & Coto[49] for health care settings and nurses to use music in the context of postoperative pain. This protocol recommends the administration of music for at least 15-30 minutes twice daily both preoperatively and postoperatively.[49] This duration is also in line with the minimal duration recommended to reduce anxiety in mechanically ventilated ICU patients.[50] As a trend, it appears that the longer the duration of the first music session, the greater the decrease in pain score, although this may vary among individuals. Indeed, some benefits might attenuate over time as the novelty of the music stimulus wanes.

Although the effect of music on pain appears independent of the music tempo, recent nursing guidelines were proposed, as a protocol, for the use of music to reduce pain in the perioperative setting, and recommend that music be played at a prespecified tempo of 60-80 bpm in order "to match the recommended heart rate of 60-80 BPM" (p.175).[49] A recent systematic review combining studies conducted in acute and chronic care settings reported that music with a 60-80 bpm tempo was not associated with lower pain scores although the heterogeneity of the results was high ($I^2 = 93\%$), thus limiting the conclusions that can be drawn regarding the impact of tempo.[8] Moreover, in most studies, many characteristics of the music (e.g., tempo, the presence of lyrics) were not described, preventing us from conducting an in-depth analysis of their impact on pain. Furthermore, the guidelines by Poulsen and Coto[49] recommend that music be administered twice daily to be most effective. However, in this current review, there were only two studies with multiple sessions within the same day and these showed inconsistent results. Two of the three studies that tested the effect of multiple sessions (either separated by a minimum of four to six hours or by a minimum of eight hours) of music did not report a significant decrease in pain after multiple sessions.[31,33] On the other hand, one study that tested multiple sessions, each session separated by 24 hours, observed a significant decrease in pain scores in the group that received music on Day 2 and Day 3.[40] More trials should be conducted with multiple music sessions before firm conclusions can be drawn.

No adverse effect was reported, and less than 15% of participants who disliked the music withdrew before study completion in three[28,31,34] of the 18 RCTs. This finding highlights the importance of offering music to patients who like to listen to music, and the importance of selecting music based on their preferences. Although culture was beyond the scope of our review, these musical preferences could also include cultural considerations.[51,52] For patients unable to self-report, consulting with family members might be the most relevant strategy to determine whether music is an appropriate complementary approach and identify patient's music preferences. This is in line with previous research that has found that some family members are interested in being involved in the music selection process as well as participating in the pain management of their loved ones in the ICU.[53-56] For clinicians, family members can be a source of knowledge on the music preferences of the patient unable to self-report, which can help to direct any music selection made on their behalf. Although the body of literature pertaining to the social and cultural implications of music interventions is scarce, evidence supports that music is universally used for healing purposes, and that it varies more within societies than across them.[57] Thus, for safe and effective integration of music in culturally diverse critically ill patient populations, clinicians should be aware that all patients may benefit from music as long as the patient's preferences are considered. These preferences should be determined by discussing with patients (for those able to self-report) or family members (for those unable to self report). Streaming services with large collections of culturally diverse music could be a helpful resource but remains to be explored.

Based on findings from the meta-analysis, 20-30 minutes of music intervention can decrease pain by almost 2 points on a 0-10 scale for ICU adults able to self-report, when compared to standard care. This is clinically significant for patients with mild-to-moderate acute pain.[58] Moreover, because some patients reported not enjoying the music to the point of withdrawing from studies, efforts should be made to offer music tailored to patients' preferences. However, until there is enough cumulative evidence in the critically ill population, the administration of music at a tempo ranging from 60 to 80 bpm as recommended for postoperative pain management should be encouraged.[49] Otherwise, music appears to be safe and simple to deliver with evidence of reducing pain in ICU adult patients.

In addition, and as reported by participants in interviews post-RCT,[33] music may be less appropriate for patients self-administering analgesia (e.g. patient-controlled analgesia) if the music is a distraction or induces sleep to the point of causing the patient to skip an analgesic dose. Also, music might not be appropriate in patients who are able to self-report if it interferes with the patient's desire to communicate with others (i.e., by blocking auditory stimulus valued by the patient). Thus, delivery methods of music via headphones that also allow ambient sounds might be considered preferable in patients who desire such a function. In summary, it might be more beneficial to provide music based on the patients' preferences, in terms of not only music selection and timing of the intervention but also modes of delivery, for those who might dislike headphones.

Implications for research

The effect of various duration and number of sessions of music should be further investigated to determine the efficacy of these intervention features on pain. Factorial study designs could be used to test multiple music durations and number of sessions simultaneously and more efficiently than multiple individual experiments.[59] The factorial study design also allows the evaluation of the main effect of each factor (duration and number of sessions) as well as all the interactions possible for each combination of factors. The participation of ICU patients, families and clinicians in decisions concerning duration and number of sessions would be advantageous to take into account the experience and expertise of all stakeholders. Indeed, the involvement of various professionals who have experience working with the critically ill population and/or with music interventions would most benefit future research.

Studies should also compare the costs for patients receiving music interventions for pain reduction with the costs for patients receiving standard ICU care, as patient-directed music intervention was found to be cost effective for reducing anxiety in mechanically ventilated ICU patients.[60]

Too few studies have been conducted with ICU adults unable to self-report to allow for a meta-analysis in this review (only one study had a low enough ROB to be included). Although three RCTs have reported a significant decrease in pain scores in this population, the effect size and clinical implications remain unknown. In future studies, families could be involved in the selection and/or administration of music interventions, based on their willingness to do so.[56] Furthermore, having less restrictive eligibility criteria (e.g., including all ICU patients, regardless of diagnosis or ability to communicate) would improve the feasibility of music studies in the adult ICU. Future studies should include not only surgical cases but also more medical and trauma cases as well as participants that are unable to communicate, as these are all representative of the general ICU population.

Future research steps to be explored include the use of music to reduce pain in nonsurgical ICU patients and those unable to self-report; the use of patient-selected music durations in those able to make such decisions while in the ICU; the interaction between noise reduction, anxiety and pain in the ICU; the examination of the mechanism of action of pain score reduction; and the development of strategies for the implementation of music in the adult ICU.

Limitations

Although it appears that longer music duration is associated with greater decrease in pain scores, no RCT has been conducted to compare various durations, and causality cannot be supported with subgroup analyses presented in this review. Furthermore, the sample sizes from the 20-30 minutes music vs. standard care subgroup meta-analysis were quite small; therefore, larger studies with lower ROB are needed to further understand the effect of music compared with standard care on pain scores.

The characteristics of the music interventions varied widely, which made it difficult to identify precisely the most relevant active components of these interventions. Finally, despite pain being a multidimensional experience, only pain intensity was reported in all studies included in this review, and therefore, the effect of music on other pain dimensions (e.g., distress, unpleasantness) remains unknown.

Conclusion

In conclusion, in the ICU adult population able to self-report, 20-30 minutes of music administration is efficacious in decreasing pain by one to two points on a 0-10 Numeric Rating Scale compared with noise reduction and standard care. Effective music interventions can be administered by research staff, nurses, or music therapists via headphones (for those who tolerate this mode of delivery) both at rest and during standard care procedures in the adult ICU based on available RCTs. Further research is needed with RCTs of lower ROB in order to draw firm conclusions, and there is an urgent need for more evidence on music effectiveness in ICU adults unable to self-report.

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Competing interests

The authors have declared that no competing interests exist. This review is being conducted to inform a music intervention pilot study in the adult intensive care unit.

Conflicts of interest

The authors declare that they have no known conflicts of interest.

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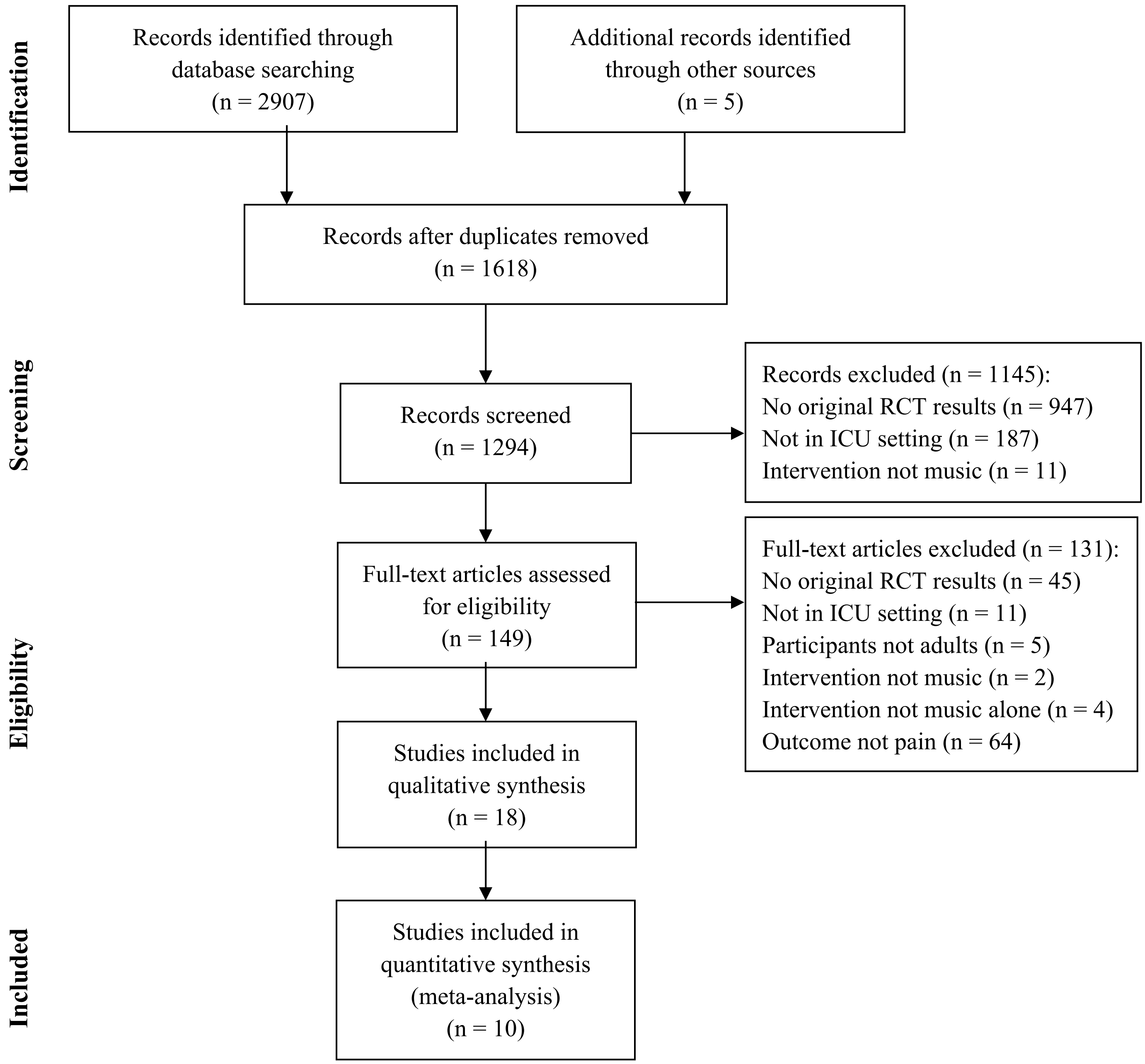


Fig. 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram of literature search and study selection. RCT = randomized controlled trial; ICU = intensive care unit.

Table 1. Description of Included Study Participants

First Author Name	Year	Country	Sample size	Age mean (SD or min-max)	Male/Female % distribution	Diagnoses included (%)	Ability to self-report	Pain Assessment Tool
Broscious[27]	1999	USA	156	66 (10)	69/31	Cardiac, postoperative (100)	Yes	NRS (0-10)
Voss et al.[37]	2004	USA	40	63 (13)	64/36	Cardiac, postoperative (100)	Yes	VAS (0-100)
Chan[28]	2007	China	66	≥35, most >75 (MNR)	73/27	Cardiac, post-PCI (100)	Yes	UCLA (0-10)
Jaber et al.[34]	2007	France	30	58 (13)	57/43	Postoperative (55.7), medical[a] (43.3)	Yes	NRS (0-10)
Cooke et al.[24]	2010	Australia	17	72[b] (19-87)	71/29	Postoperative[c] (100)	Yes	NRS (0-10)
Jafari et al.[35]	2012	Iran	60	58 (11)	43/57	Cardiac, postoperative (100)	Yes	NRS (0-10)
Shultis[25]	2012	USA	20	65 (37-83)	41/59	NR	Yes	VAS (0-10)
Chiasson et al.[29]	2013	USA	82	62 (17)	65/35	NR	Yes	TVPS (0-10)
Sanjuan Navais et al.[31]	2013	Spain	42	63 (3)	48/52	Medical (45.2), postoperative (54.8)	Yes	NRS (0-10)
Saadatmand et al.[36]	2015	Iran	60	44 (16)	57/43	Asthma (23.3), pneumonia (30), poisoning (20), pancreatitis (13.3), trauma (8.3), sepsis (5)	Yes	VAS (0-10)
Cigerci and Ozbayir[41]	2016	Turkey	68	62 (11)	76/24	Cardiac, postoperative (100)	Yes	VAS (0-10)
Kyavar et al.[39]	2016	Iran	60	60 (8)	77/23	Cardiac, postoperative: CABG (100)	No	CPOT (0-8)
Yaghoubinia et al.[40]	2016	Iran	60	50 (8)	50/50	Cardiac (21.7), neurologic (21.7), respiratory pathology (21.7), GI (21.7), renal (13.3)	No	BPS (3-12)
Yaman Aktas and Karabulut[26]	2016	Turkey	66	65 (12)	73/27	Cardiac, postoperative (100)	Yes	CPOT (0-8)
Ames et al.[33]	2017	USA	41	53 (14)	54/46	Postoperative[d] (100)	Yes	NRS (0-10)
Guilbaut[30]	2017	France	140	80 (49-96)	28/72	NR	Yes	NRS (0-10)
Mateu-Capell et al.[38]	2018	Spain	75	69 (14)	73/27	Infectious pathology (40), respiratory pathology (9.3), cardiac pathology (6.7), other (44)	No	BPS (3-12)
Yarahmadi et al.[32]	2018	Iran	90	58 (8)	67/33	Cardiac, postoperative[e] (100)	Yes	VAS (0-10)

NRS = Numeric Rating Scale; VAS = Visual Analog Scale; MNR = mean not reported; PCI = percutaneous coronary interventions; UCLA = University of California at Los Angeles universal pain score; NR = not reported; TVPS = Thermometer Visual Pain Scale; CABG = coronary artery bypass graft; CPOT = Critical-Care Pain Observation Tool; BPS = Behavioral Pain Scale; GI = gastrointestinal

[a] Medical = pancreatitis (13.3%), pneumopathy (16.7%), sepsis (13.3%).

[b] Median.

[c] Post-op = abdominal (47%), vascular (18%), thoracic (18%), neurosx (6%), genitourinary (6%), neck (6%)

[d] Post-op = nephrectomy (42%), abdominal sx (27%), thoracotomy/lobectomy (22%), adrenalectomy (2%), other (7%).

[e] Cardiac surgeries: CABG (81.6%), valve surgery (18.4%).

Table 2. Music Intervention Characteristics

First author (Language)	Duration[a]	Tempo	Timing	Sessions	Coanalgesia	Provider	Music Selection	Delivery	Comparator
Broscious[27] (English)	10	NS	Procedure: CTR	1	Yes: opioids	NS	Participant chose from 10 categories of cassettes produced by music therapy students	Earphones, cassette player	WNH, SC
Voss[37] (English)	30	60-80	Procedure: chair rest	1	Yes: opioids	Researcher	Participant chose a tape from a collection of six types by listening to 30-second excerpts	Headphones, cassette player	SC
Chan[28] (English)	45	60	Procedure: C-clamp	1	NS	Researcher	Participant chose from three types	Earphones, MP3 player	SC
Jaber[34] (French)	20	U-shape	Rest	1	Music two hours postmedication	MT	U-shaped montage based on participant preferences	Headphones	SC
Cooke[24] (English)	15	NS	Procedure: turning	1	Yes: fentanyl/morphine	Researcher	Participant chose CD from home or from a selection of music provided by the researchers	Earphones, portable CD	NRE
Jafari[35] (English)	30	60-80	Rest	1	Yes	Researcher	Participant chose from a list provided by a music expert	Headphones, MP3 player	NRH
Shultis[25] (English)	22[b]	60-80	Rest	1	Not monitored	MT	Participant chose from five researcher-compiled CDs	CD player	SC
Chiasson[29] (English)	10	NS	Rest	1	None during music	Harpist	Music varied according to harpist's choice	Live harp	SC
Sanjuan Navais[31] (Spanish)	30	60-80	Rest	3-5[c]	Music one hour preanalgesics/ sedatives	NS	Participant chose from researchers' selection	Earphones	SC
Saadatmand[36] (English)	90	NS	Rest	1	Fentanyl boluses PRN but not during trial of two hours	Researcher, Nurse	Participant chose preferred sounds from CDs from the investigator's collection	Headphones, CD player	NRH
Cigerci[41] (English)	30	NS	Rest	One preoperatively and one in ICU	Opioids + NSAIDs	Researcher	Participant chose from two suggestions: folk vs. classical	Headphones, MP3 player	SC
Kyavar[39] (English)	30	NS	Procedure[d]	1	Yes: morphine	NS	Participant chose from selection	Headphones	NRH
Yaghoubinia[40] (English)	30	NS	Rest	One per day; three total	Fentanyl IV as per unit protocol	researcher	Researchers chose: instrumental music piece for all participants ("Beach Walk" by Arnd Stein)	Headphones, MP3 player	SC
Yaman Aktas[26] (English)	20 pre-ETS + 20 post-ETS	60-80	Procedure: ETS	1	NS	NS	Researcher and lecturer in music field chose: instrumental reed flute for all participants	Music pillow, MP3 player	SC
Ames[33] (English)	50	NS	Any time	4-8; every four to six hours	PCA and PRN	Nurse	Researchers chose one piece: MusiCure Dreams album by Grefion Records for all participants	Headphones	SC
Guilbaut[30] (French)	20	U-shape	Procedure[e]	1	Yes (41%), no (59%)	Nurse assistant	Participant chose from Music Care selection	Headphones, mobile tablet	NRH
Mateu-Capell[38] (English)	60	NS	Rest	1	NS	Researcher	Music therapist chose one piece for all participants (Reiki - Merlin's Magic by Andreas Mock)	Headphones, MP3 player	NCH
Yarahmadi[32] (English)	15 pre-CTR + 15 post-CTR	NS	Procedure: CTR	1	None one hour or more pre-CTR	Researcher	Participant chose from 15 pieces	Headphones, MP3 player	SC

NS = not specified; CTR = chest tube removal; WNH = white noise headphones; SC = standard care; MT = music therapist; CD = compact disc; NRE = noise reduction via earphones; NRH = noise reduction via headphones; PRN = pro re nata (as needed); ICU = intensive care unit; NSAIDs = nonsteroidal anti-inflammatory drugs; IV = intravenous; ETS = endotracheal suction; PCA = patient-controlled analgesia; NCH = noise-canceling headphones.

[a] In minutes.
[b] Mean duration.
[c] Minimum eight hours between each session.
[d] Dressing change.
[e] Dressing change, ETS, turning, and others.

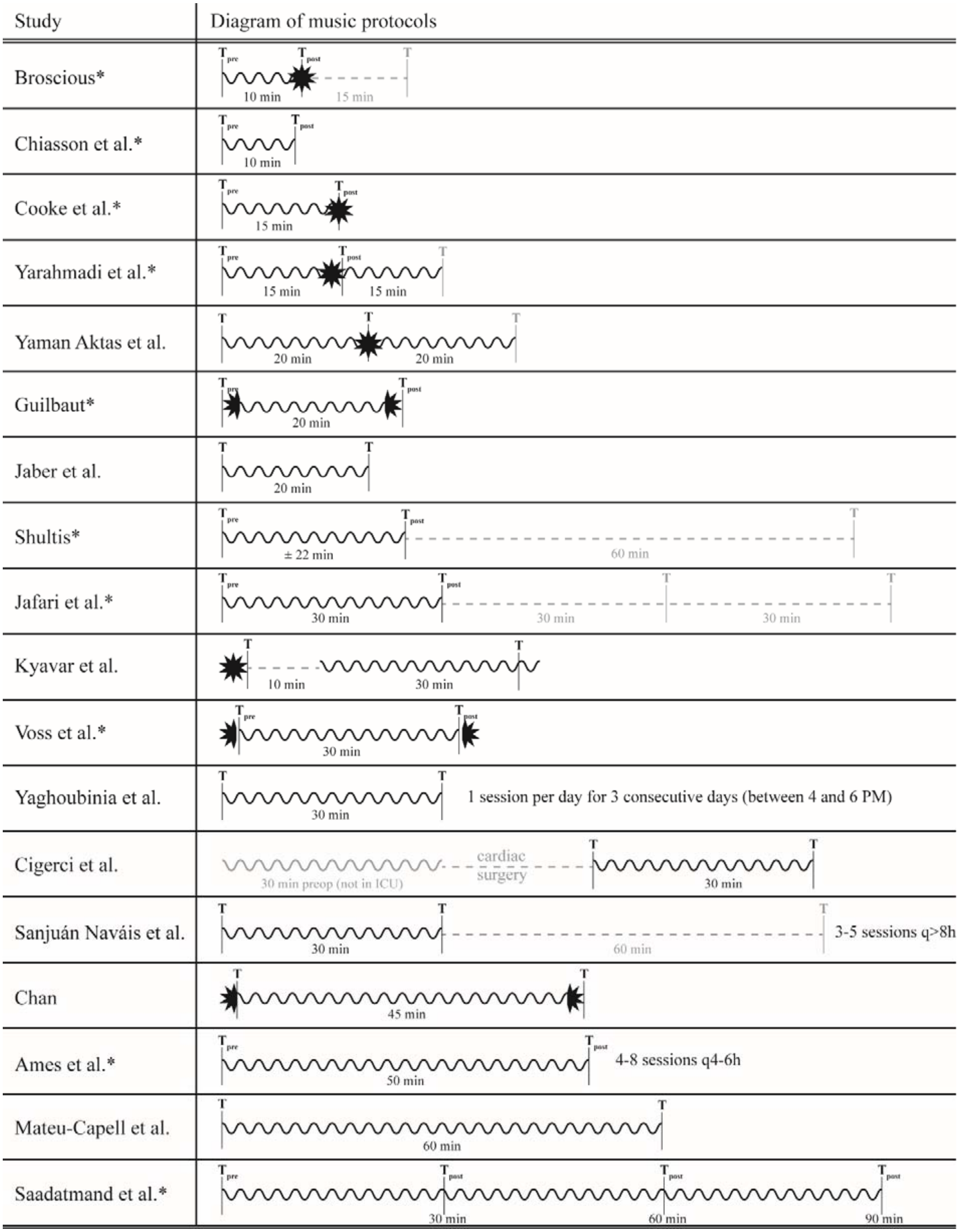


Fig. 2. Music protocol diagrams of included studies. *Studies included in meta-analysis.

music duration (five-minute length) time period without music

painful procedure in ICU **T_{pre} T_{post}** measurement points included in meta-analysis

Note. This figure was created by the first author.

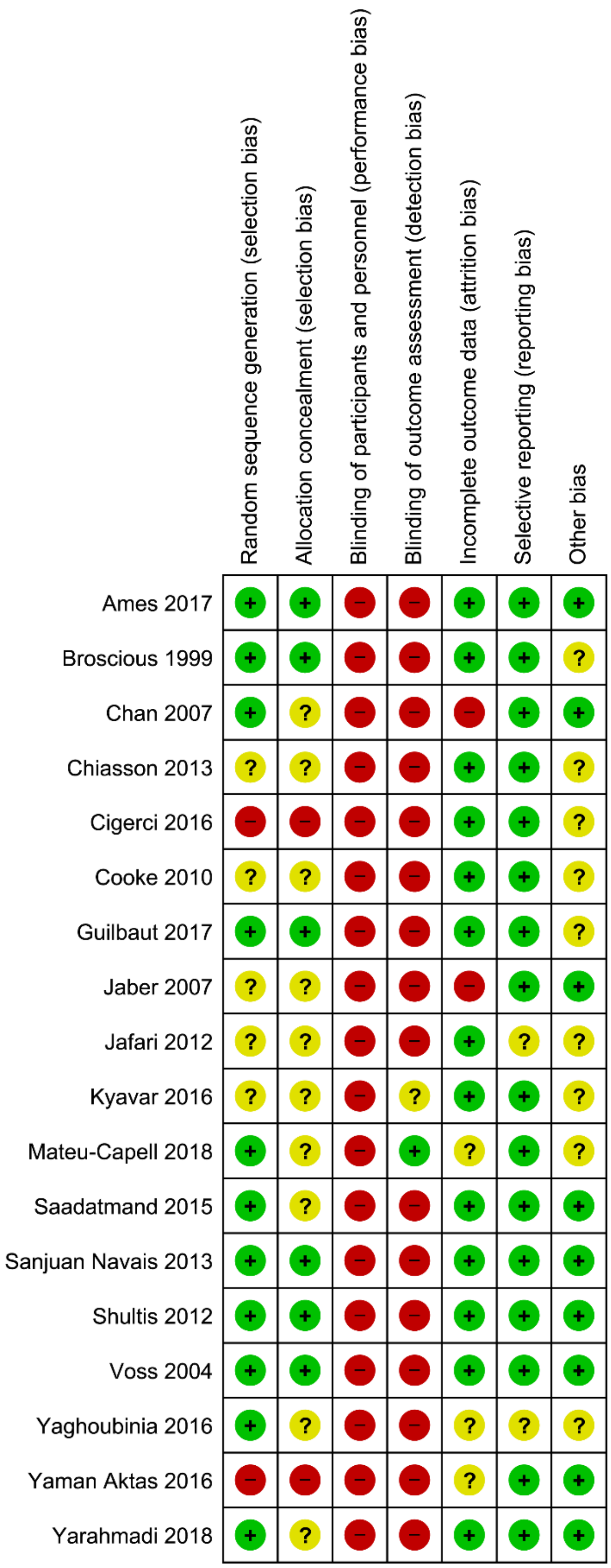


Fig. 3. Risk of bias summary: review of the authors' judgments about each risk of bias item for each included study.

Study or Subgroup	Music Mean	Music SD	Music Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Std. Mean Difference IV, Random, 95% CI
10min-Broscious 1999	5.8	2.8	68	5.6	2.9	36	8.5%	0.07 [-0.33, 0.47]
10min-Broscious 1999	5.8	2.8	68	5.43	2.63	47	8.6%	0.13 [-0.24, 0.51]
10min-Chiasson 2013	2.2	2.7	39	2.5	3	43	8.3%	-0.10 [-0.54, 0.33]
15min-Cooke 2010	0.9	3.7	17	-0.4	2.4	17	7.2%	0.41 [-0.27, 1.09]
15min-pre-Yarahmadi 2018	4.9	1.1	44	4.73	1.1	44	8.4%	0.15 [-0.27, 0.57]
20-25min-Shultis 2012	-0.89	1.12	13	-0.07	0.19	7	5.9%	-0.85 [-1.82, 0.11]
20min-Guilbaut 2017	1.8	2.2	70	2.5	1.8	70	8.7%	-0.35 [-0.68, -0.01]
30min-Jafari 2012	3.1	2.1	30	4.7	2.8	30	8.0%	-0.64 [-1.16, -0.12]
30min-Saadatmand 2015	3.9	1.02	30	4.66	0.95	30	8.0%	-0.76 [-1.29, -0.24]
30min-Voss 2004	19	13	19	45	27	21	7.3%	-1.18 [-1.86, -0.51]
50min-Ames 2017	-1.5	0.36	17	-0.4	0.3	20	5.7%	-3.27 [-4.29, -2.25]
60min-Saadatmand 2015	3.63	0.99	30	4.93	0.94	30	7.8%	-1.33 [-1.89, -0.77]
90min-Saadatmand 2015	3.6	0.89	30	4.8	0.74	30	7.7%	-1.45 [-2.02, -0.87]
Total (95% CI)			**475**			**425**	**100.0%**	**-0.63 [-1.02, -0.24]**

Heterogeneity: Tau² = 0.42; Chi² = 89.52, df = 12 (P < 0.00001); I² = 87%
Test for overall effect: Z = 3.17 (P = 0.002)

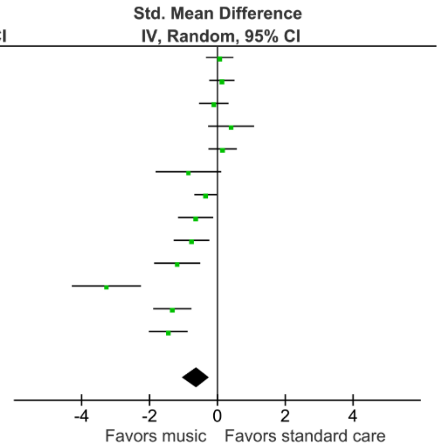


Fig. 4. The efficacy of music for self-reported pain scores of intensive care unit adults. IV = inverse variance.

Study or Subgroup	Music Mean	Music SD	Music Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Std. Mean Difference IV, Random, 95% CI
10min-Broscious 1999	5.8	2.8	68	5.43	2.63	47	18.5%	0.13 [-0.24, 0.51]
10min-Chiasson 2013	2.2	2.7	39	2.5	3	43	18.2%	-0.10 [-0.54, 0.33]
15min-pre-Yarahmadi 2018	4.9	1.1	44	4.73	1.1	44	18.3%	0.15 [-0.27, 0.57]
20-25min-Shultis 2012	-0.89	1.12	13	-0.07	0.19	7	14.4%	-0.85 [-1.82, 0.11]
30min-Voss 2004	19	13	19	45	27	21	16.6%	-1.18 [-1.86, -0.51]
50min-Ames 2017	-1.5	0.36	17	-0.4	0.3	20	14.0%	-3.27 [-4.29, -2.25]
Total (95% CI)			**200**			**182**	**100.0%**	**-0.74 [-1.46, -0.02]**

Heterogeneity: Tau² = 0.69; Chi² = 50.61, df = 5 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.02 (P = 0.04)

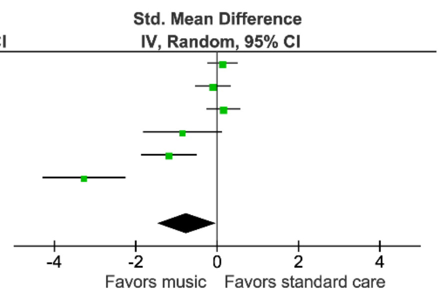


Fig. 5. The efficacy of music vs. standard care for self-reported pain scores of intensive care unit adults. IV = inverse variance.

Study or Subgroup	Favors music Mean	Favors music SD	Favors music Total	Noise reduction Mean	Noise reduction SD	Noise reduction Total	Weight	Std. Mean Difference IV, Random, 95% CI
10min-Broscious 1999	5.8	2.8	68	5.6	2.9	36	15.4%	0.07 [-0.33, 0.47]
15min-Cooke 2010	0.9	3.7	17	-0.4	2.4	17	12.6%	0.41 [-0.27, 1.09]
20min-Guilbaut 2017	1.8	2.2	70	2.5	1.8	70	16.0%	-0.35 [-0.68, -0.01]
30min-Jafari 2012	3.1	2.1	30	4.7	2.8	30	14.3%	-0.64 [-1.16, -0.12]
30min-Saadatmand 2015	3.9	1.02	30	4.66	0.95	30	14.2%	-0.76 [-1.29, -0.24]
60min-Saadatmand 2015	3.63	0.99	30	4.93	0.94	30	13.8%	-1.33 [-1.89, -0.77]
90min-Saadatmand 2015	3.6	0.89	30	4.8	0.74	30	13.7%	-1.45 [-2.02, -0.87]
Total (95% CI)			**275**			**243**	**100.0%**	**-0.57 [-1.03, -0.12]**

Heterogeneity: Tau² = 0.30; Chi² = 35.36, df = 6 (P < 0.00001); I² = 83%
Test for overall effect: Z = 2.49 (P = 0.01)

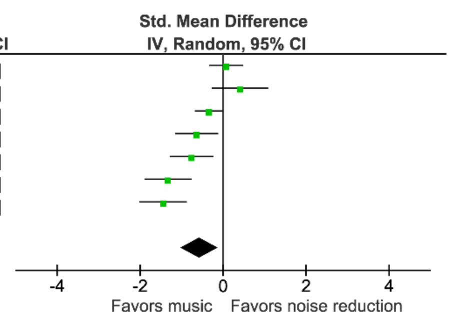


Fig. 6. The efficacy of music vs. noise reduction for self-reported pain scores of intensive care unit adults. IV = inverse variance.

Study or Subgroup	Music Mean	Music SD	Music Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Std. Mean Difference IV, Random, 95% CI
10min-Broscious 1999	5.8	2.8	68	5.43	2.63	47	39.6%	0.13 [-0.24, 0.51]
10min-Chiasson 2013	2.2	2.7	39	2.5	3	43	29.1%	-0.10 [-0.54, 0.33]
15min-pre-Yarahmadi 2018	4.9	1.1	44	4.73	1.1	44	31.3%	0.15 [-0.27, 0.57]
Total (95% CI)			**151**			**134**	**100.0%**	**0.07 [-0.16, 0.31]**

Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.59 (P = 0.55)

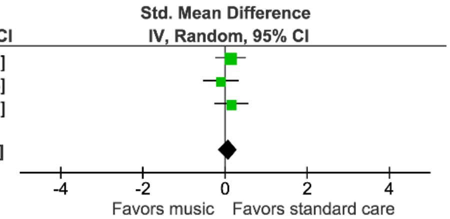


Fig. 7. The efficacy of music vs. standard care for self-reported pain scores of intensive care unit adults (10-15 minutes subgroup). IV = inverse variance.

Study or Subgroup	Music Mean	Music SD	Music Total	Standard care Mean	Standard care SD	Standard care Total	Weight	Std. Mean Difference IV, Random, 95% CI
20-25min-Shultis 2012	-0.89	1.12	13	-0.07	0.19	7	33.0%	-0.85 [-1.82, 0.11]
30min-Voss 2004	1.9	1.3	19	4.5	2.7	21	67.0%	-1.18 [-1.86, -0.51]
Total (95% CI)			**32**			**28**	**100.0%**	**-1.07 [-1.63, -0.52]**

Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 3.79 (P = 0.0001)

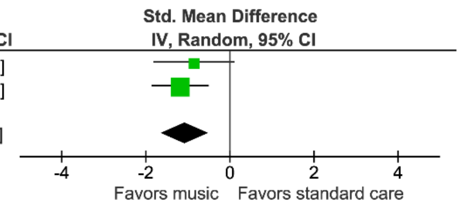


Fig. 8. The efficacy of music vs. standard care for self-reported pain scores of ICU adults (20-30 minutes subgroup)

Study or Subgroup	Music Mean	Music SD	Music Total	Noise reduction Mean	Noise reduction SD	Noise reduction Total	Weight	Std. Mean Difference IV, Random, 95% CI
10min-Broscious 1999	5.8	2.8	68	5.6	2.9	36	73.9%	0.07 [-0.33, 0.47]
15min-Cooke 2010	0.9	3.7	17	-0.4	2.4	17	26.1%	0.41 [-0.27, 1.09]
Total (95% CI)			**85**			**53**	**100.0%**	**0.16 [-0.19, 0.51]**

Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 1 (P = 0.40); I² = 0%
Test for overall effect: Z = 0.89 (P = 0.37)

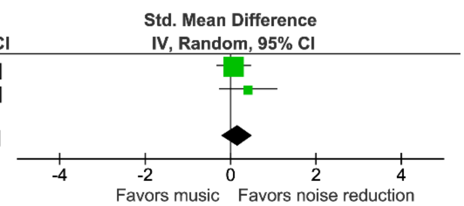


Fig. 9. The efficacy of music vs. noise reduction for self-reported pain scores of intensive care unit adults (10-15 minutes subgroup). IV = inverse variance.

Study or Subgroup	Music Mean	Music SD	Music Total	Noise reduction Mean	Noise reduction SD	Noise reduction Total	Weight	Std. Mean Difference IV, Random, 95% CI
20min-Guilbaut 2017	1.8	2.2	70	2.5	1.8	70	54.6%	-0.35 [-0.68, -0.01]
30min-Jafari 2012	3.1	2.1	30	4.7	2.8	30	22.9%	-0.64 [-1.16, -0.12]
30min-Saadatmand 2015	3.9	1.02	30	4.66	0.95	30	22.4%	-0.76 [-1.29, -0.24]
Total (95% CI)			**130**			**130**	**100.0%**	**-0.51 [-0.76, -0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 2.03, df = 2 (P = 0.36); I² = 2%
Test for overall effect: Z = 3.96 (P < 0.0001)

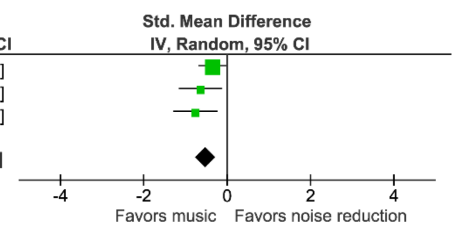


Fig. 10. The efficacy of music vs. noise reduction for self-reported pain scores of intensive care unit adults (20-30 minutes subgroup). IV = inverse variance.

Supplementary Data 1. Search Strategy for Medline (Ovid)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1996 to June 15, 2018

#	Searches	Results
1	MUSIC/ or music*.mp.	17595
2	intensive care.mp. or Critical Care/	137997
3	1 and 2	221

URL to search strategy: https://ovidsp-tx-ovid-com.proxy3.library.mcgill.ca/sp-3.30.0b/ovidweb.cgi

Supplementary Data 2. Risk of Bias Summary for Each Included Study

Ames 2017

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer-generated, permuted block randomization schema
Allocation concealment (selection bias)	Low risk	opaque, sealed envelopes prepared by the statistician
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	missing data balanced across groups
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported as per protocol
Other bias	Low risk	none identified

Broscious 1999

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	draw of a chip from a box containing 3 chips
Allocation concealment (selection bias)	Low risk	blind draw of chip by either primary investigator or research assistant
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	missing data balanced across groups
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear if baseline imbalance (large difference in n across three arms)

Chan 2007

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	random digit randomizer
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	High risk	missing data not balanced across groups; reasons likely related to outcome
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Chiasson 2013

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	general statement of random assignment
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	missing data balanced across groups
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear if baseline imbalance (too few sociodemographic characteristics reported)

Cigerci 2016

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	odd or even number
Allocation concealment (selection bias)	High risk	no concealment
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear if baseline imbalance (baseline pain values not reported)

Cooke 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	general statement of random assignment
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear if carry-over effect from cross-over design

Guilbaut 2017

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomization was done in blocks of four
Allocation concealment (selection bias)	Low risk	blinded envelope
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear if data was reported for individuals or for procedures

Jaber 2007

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	general statement of random assignment
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	High risk	missing data not balanced across groups; reasons likely related to outcome
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Jafari 2012

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	general statement of random selection
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Unclear risk	pre-specified and expected pain outcomes reported as per protocol
Other bias	Unclear risk	unclear if baseline imbalance (too few sociodemographic characteristics reported)

Kyavar 2016

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	samples were randomly divided into two groups
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	Unclear risk	pain was assessed using CPOT and it is unclear whether evaluators were blinded
Incomplete outcome data (attrition bias)	Low risk	missing data balanced across groups
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Unclear risk	unclear (missing information throughout article)

Mateu-Capell 2018

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer-generated random number sequence in blocks of eight
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	Low risk	pain was assessed using BPS and outcome assessors were blinded to group assignment
Incomplete outcome data (attrition bias)	Unclear risk	unclear if missing data is balanced across groups (when the participant dropout occurred in the crossover design)
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported as per protocol
Other bias	Unclear risk	unclear if carry-over effect from cross-over design

Saadatmand 2015

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	coin flip
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Sanjuan Navais 2013

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	simple random assignment
Allocation concealment (selection bias)	Low risk	distribution was carried out by means of sealed and numbered envelopes
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Shultis 2012

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	website randomizer
Allocation concealment (selection bias)	Low risk	blinded envelopes
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report were likely to be influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Voss 2004

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	varied block size prepared by the statistician
Allocation concealment (selection bias)	Low risk	sealed, blinded envelopes
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	reason for missing data not related to outcome
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Yaghoubinia 2016

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	permuted blocks, through random numbers table
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participants were unconscious but personnel were unlikely blinded as the control arm did not wear headphones
Blinding of outcome assessment (detection bias)	High risk	pain was assessed with BPS but outcome assessors were not blinded and could have influenced measurement
Incomplete outcome data (attrition bias)	Unclear risk	unclear if missing data is balanced across groups
Selective reporting (reporting bias)	Unclear risk	pre-specified and expected pain outcomes reported as per protocol
Other bias	Unclear risk	unclear (missing information throughout article)

Yaman Aktas 2016

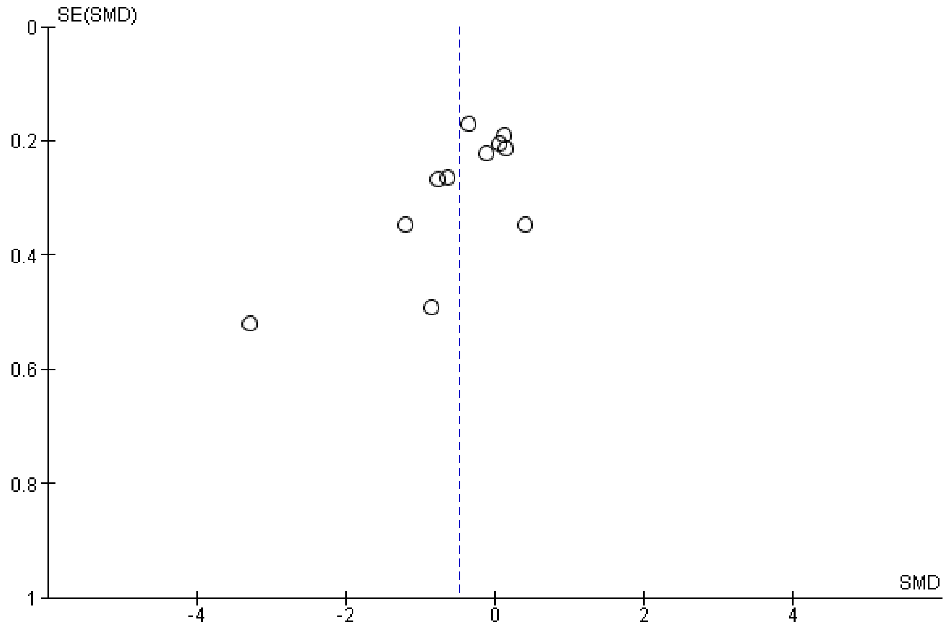
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	randomization using file numbers
Allocation concealment (selection bias)	High risk	no concealment
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was assessed with CPOT but outcome assessors were not blinded and could have influenced measurement
Incomplete outcome data (attrition bias)	Unclear risk	unclear if missing data is balanced across groups
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported
Other bias	Low risk	none identified

Yarahmadi 2018

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	using an eight-member block technique; factorial-controlled clinical trial
Allocation concealment (selection bias)	Unclear risk	not specified
Blinding of participants and personnel (performance bias)	High risk	participant blinding was not possible; participants could have been influenced by group assignment
Blinding of outcome assessment (detection bias)	High risk	pain was self-reported (no blinding) and self-report could have been influenced
Incomplete outcome data (attrition bias)	Low risk	no missing data reported
Selective reporting (reporting bias)	Low risk	pre-specified and expected pain outcomes reported as per protocol
Other bias	Low risk	none identified

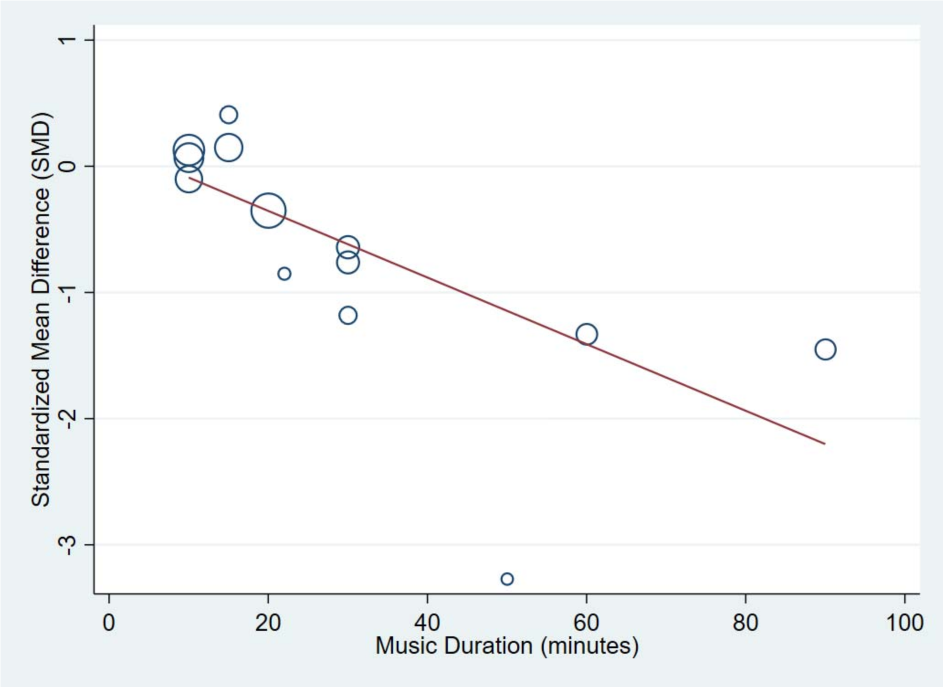
CPOT = Critical-Care Pain Observation Tool; BPS = Behavioral Pain Scale.

Supplementary Data 3. Funnel plot for all studies included in meta-analysis

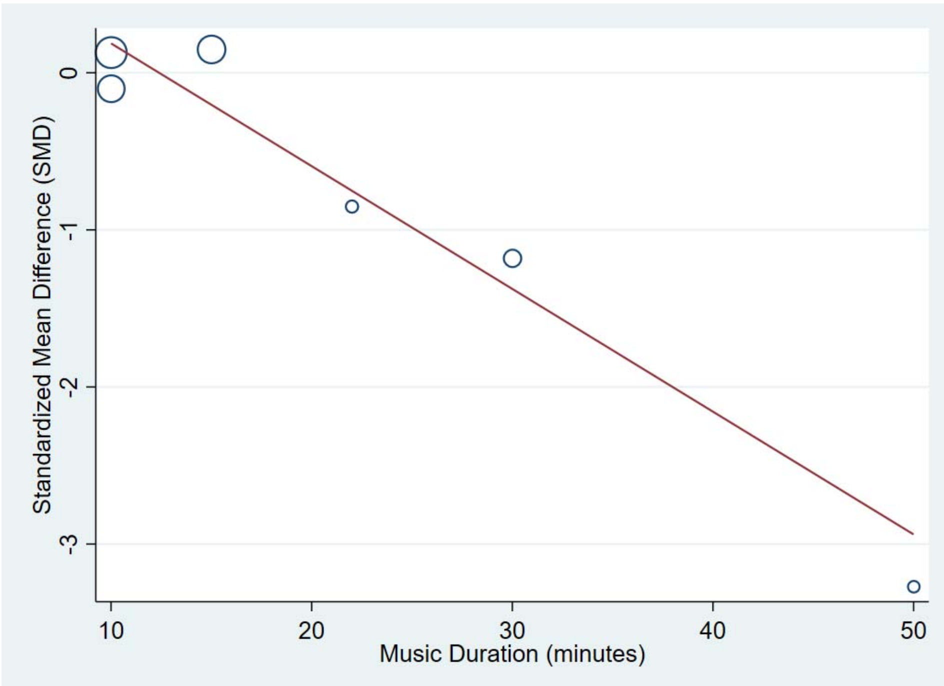


SMD = standardized mean difference.

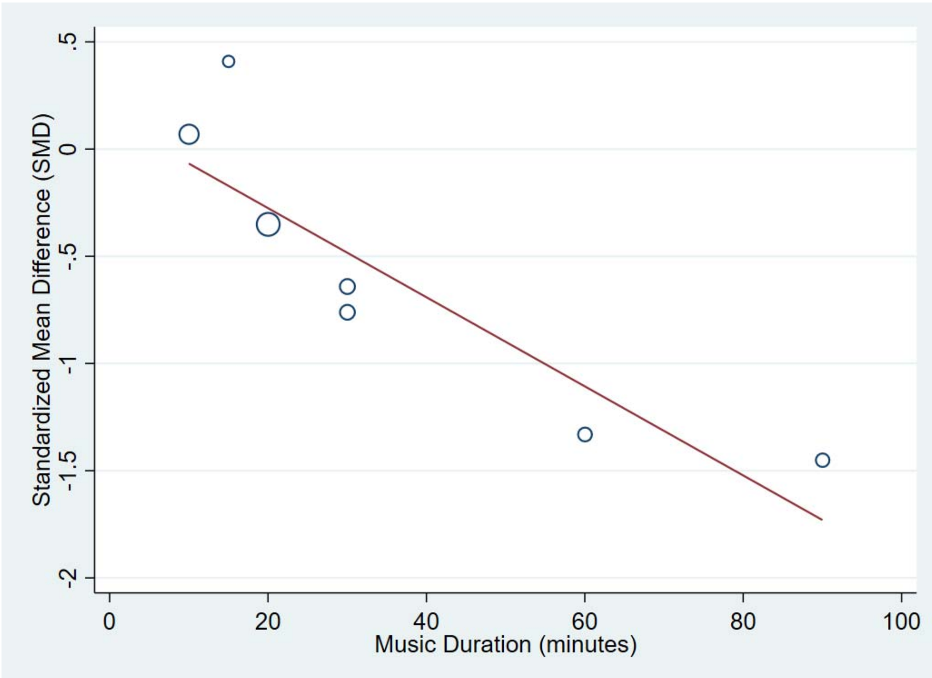
Supplementary Data 4. Meta-regression graph of the relationship between the standardized mean difference of pain and the duration of music interventions in all included studies (n = 10 studies)



Supplementary Data 5. Meta-regression graph of the relationship between the standardized mean difference of pain and the duration of music interventions in studies of music vs. standard care (n = 6 studies)



Supplementary Data 6. Meta-regression graph of the relationship between the standardized mean difference of pain and the duration of music interventions in studies of music vs. noise reduction (n = 5 studies)



Supplementary Data 7. Meta-regression graph of the relationship between the standardized mean difference of pain and music interventions given for pain at rest vs. procedural pain (n = 10 studies)