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Acoustic stimulation for relieving pain during venipuncture: a systematic review and network meta-analysis

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ABSTRACT

Objectives To assess whether acoustic stimulations relieve venipuncture pain and determine which stimulation is the most effective type.

Design Systematic review and network meta-analysis.

Data sources PubMed, Cochrane Central Register of Controlled Trials, Excerpta Medica dataBASE, Cumulative Index to Nursing and Allied Health Literature, ClinicalTrials.gov and the International Clinical Trials Registry Platform databases were systematically searched in September 2023.

Study selection Randomised controlled trials evaluating the efficacy of acoustic stimulations on patients undergoing venipuncture were eligible. Acoustic stimulations were classified into seven categories: five types of acoustic stimulations (music medicine (researcher selected), music medicine (patient selected), music therapy, sounds with linguistic meaning and sounds without linguistic meaning) and two controls (only wearing headphones and no treatment).

Primary and secondary outcome measures Primary outcomes included self-reported pain intensity assessed during venipuncture and treatment cost, and secondary outcomes were self-reported mental distress and adverse events.

Results Of 6406 citations, this network meta-analysis included 27 studies including 3416 participants; the mean age was 31.5 years, and 57% were men. Among the five types of acoustic stimulations, only musical interventions, such as music medicine (patient selected) (standardised mean difference (SMD) −0.44 (95% CI: −0.84 to −0.03); low confidence), music medicine (researcher selected) (SMD −0.76 (95% CI: −1.10 to −0.42); low confidence) and music therapy (SMD −0.79 (95% CI: −1.44 to −0.14); low confidence), were associated with improved pain relief during venipuncture compared with no treatment. No significant differences existed between the types of acoustic stimulations. Free-of-charge acoustic stimulations were provided to patients, and no specific adverse events were reported. In many studies, the risk of bias was rated high because of the difficulty of blinding the intervention to the participants and the self-reported pain outcome.

Conclusions Music interventions were associated with reduced venipuncture pain. Comparisons between types of acoustic stimulations revealed no significant differences. Therefore, music intervention could be a safe and inexpensive pain relief method for venipuncture.

PROSPERO registration number CRD42022303852.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Acoustic stimulations were classified into seven categories: five types of acoustic stimulations (music medicine (researcher selected), music medicine (patient selected), music therapy, sounds with linguistic meaning and sounds without linguistic meaning) and two controls (only wearing headphones and no treatment).
⇒ This study employs a network meta-analysis that allows comparisons not only between acoustic stimulation and control but also between types of acoustic stimulation.
⇒ We targeted venipuncture pain, which occurs frequently in clinical practice.
⇒ A limitation of the study is that the risk of bias ratings in most studies was high because the intervention was an acoustic stimulation, which makes it difficult to blind participants, and because pain is usually a self-reported outcome.

INTRODUCTION

Venipuncture is a common medical procedure in hospitals, clinics and during home care. Venipuncture is an essential procedure in modern medicine for testing blood and treatments, such as complete blood count, biochemistry tests, donations, intravenous fluids, drugs, and blood products.[1] A needle is used to penetrate the skin and blood vessels.

Almost all patients experience some pain when the needle penetrates the skin.[2] Some patients perceive more pain and may experience a vagal reflex during the procedure, resulting in hypotension and fainting.[3] Needle phobia or extreme fear of needles is a neurological disorder, with an estimated incidence of 3.5%–10%.[4] Avoiding hospital visits because of needle phobia can hinder early disease diagnosis, interfere with the initiation and continuation of treatment and increase the severity of illnesses. For example, pregnant women with severe needle phobia were 61% less likely to undergo prenatal testing than those with mild needle phobia.[5]

Although several pain relief methods have been tested to reduce venipuncture pain, a reliably effective method is yet to be established. Topical or oral analgesics have been used to reduce venipuncture pain. However, topical analgesics need to be prepared approximately 1–2 hours before the procedure[6]; thus, they can only be used for scheduled venipunctures. Moreover, topical analgesics may cause dermatitis.[7] Additionally, oral analgesics such as non-steroidal anti-inflammatory drugs and opioids could cause asthma, kidney damage and dependence as adverse effects[8 9]; as venipuncture is a frequently performed procedure, the use of drugs for each event becomes costly. Hence, it is usually performed without analgesics.

Besides being safe and inexpensive, several randomised controlled trials (RCTs) have reported that acoustic stimulation with music or other sounds is effective in relieving venipuncture pain.[10–13] However, a systematic review and meta-analysis of these studies have not yet been performed. When conducting a meta-analysis of acoustic stimulation, comparisons between acoustic stimulation and control and between the types of stimulation are important as the efficacy may vary depending on the stimulation's contents.[14–16] Therefore, evaluating the efficacy with a traditional meta-analysis that performs only direct comparisons is inadequate; a network meta-analysis is necessary to classify each acoustic stimulation and compare the effects of each stimulation directly and/or indirectly.[17] Herein, we performed a systematic review and network meta-analysis to assess whether acoustic stimulations relieve venipuncture pain and which type of acoustic stimulation is the most effective (online supplemental figure 1 shows a conceptual diagram of the research questions).

METHODS

This study followed the Preferred Reporting Items for Systematic Review and Meta-Analysis for Network Meta-Analyses (PRISMA-NMA) guidelines (online supplemental information 1).[18] The detailed study protocol was uploaded in Open Science Framework (osf.io/7syw6/) on 15 January 2022. The study was registered with PROSPERO, number CRD42022303852, on 14 February 2022.

Study selection

RCTs that investigated the efficacy of acoustic stimulation were selected; these included patients of any age receiving a venipuncture. Venipuncture refers to any procedure wherein the vein was punctured and/or a catheter was placed inside, for example, peripheral vascular puncture, central venous (CV) catheterisation or indwelling CV ports. The included RCTs addressed at least two of the following seven categories (five acoustic stimulations and two controls): (1) music therapy; (2) music medicine (patient selected); (3) music medicine (researcher selected); (4) sounds with linguistic meaning; (5) sounds without linguistic meaning; (6) 'only wearing headphones' (or earphones); and (7) no treatment. These seven categories were determined based on several previous reports.[14–16 19] Music was defined as an orderly arrangement of sounds consisting of melody, harmony, rhythm, tone and pitch.[20] Music therapy was defined as therapy implemented by trained music therapists, whereas music medicine was defined as music interventions administered by medical or healthcare professionals.[14] The flowchart illustrated in online supplemental figure 2 was used to classify the acoustic stimulations into five types (aforementioned categories 1–5).

We assessed the following four outcomes. Primary outcomes included self-reported pain intensity assessed during venipuncture and treatment cost. Secondary outcomes were self-reported mental distress and adverse events. Mental distress was broadly defined as any type of venipuncture-associated negative effect on mental status, such as anxiety, fear and stress. This study applied no restrictions on language, publication status or date of publication. We translated papers that were neither English nor Japanese using the translation software Google Translate.[21]

During study selection, an RCT conducted by Aghbolagh *et al*[22] reporting the Numerical Rating Scale score of pain as an outcome was found; however, the SD was uncharacteristically small. An SE may have been mistakenly reported as SD. Clarifications sought from the corresponding author regarding the possibility of this error did not receive any response. Moreover, although Arts *et al*[23] evaluated a pain scale as an outcome, its SD was not reported. We included these two studies in the meta-analysis by imputing their SDs with the pooled SDs of the other studies.[24] We also performed a sensitivity analysis excluding these studies.

Search strategy and information sources

The PubMed, Cochrane Central Register of Controlled Trials, Excerpta Medica dataBASE, Cumulative Index to Nursing and Allied Health Literature, ClinicalTrials.gov and International Clinical Trials Registry Platform databases were searched on 15 and 16 January 2022 and re-searched on 10 September 2023. Key search terms included intravenous injections, intravenous infusion, catheterisation, phlebotomy, acoustic stimulation, music, sound, noise and audiometry. The full search strategies are listed in online supplemental tables 1–4.

Data extraction and risk of bias assessment

The titles and abstracts of the selected studies were independently screened by two of the four authors (YY, EI, MKitamura and TI), and potentially relevant studies were selected for full-text screening. Disagreements were resolved through discussion with a third reviewer. Data were extracted from the included studies by independent reviewers using a prepared data extraction form. Two reviewers assessed the risk of bias independently using the Cochrane Risk of Bias Tool 2.[25] Each study was classified as having 'low', 'some concerns' or 'high risk of bias'.

Data analysis

The network geometry has been presented graphically, and the size of the nodes and thickness of the edges depend on the number of randomised participants and RCTs conducted, respectively. Frequentist network meta-analysis was performed with a version of the R package netmeta, implemented in MetaInsight.[26] For performing network meta-analysis, we assumed homogeneity within treatment arms, transitivity between treatment arms and consistency between direct and indirect evidence; in fact, the results of the current study did not suggest a violation of that assumption. Intertrial heterogeneity was anticipated; therefore, random effects models were used. For continuous outcomes, the effects were summarised using standardised mean difference (SMD) and CI, as the evaluation methods for the outcome differed in each study. We classified magnitudes of effect according to the following criteria: small or slight (SMD≥0.20 to <0.50), moderate (SMD≥0.50 to <0.80) or large (SMD≥0.80).[27]

We conducted two subgroup analyses: adults or children and the venipuncture technique. However, as for the venipuncture technique, network meta-analysis could not be performed for subgroups other than those who underwent peripheral vascular puncture owing to the small number of studies. Furthermore, sensitivity analyses were conducted excluding RCTs with a 'high risk of bias' and those RCTs whose SDs were imputed. Because of the large differences in the number of participants between studies, a post hoc sensitivity analysis was also performed, excluding patients with a small number of participants.

Confidence in evidence

The confidence in the evidence across trials was assessed using the Confidence in Network Meta-Analysis (CINeMA) approach,[28] which considers the following six domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity and incoherence. These domains are rated as 'no concerns', 'some concerns' or 'major concerns', except reporting bias, which was rated as 'low risk', 'some concerns' or 'high risk'. In the evaluation of incoherence, a global test for inconsistency was conducted using random effects design-by-treatment interaction model. Appraisals were then summarised across these six domains as 'very low', 'low', 'moderate' or 'high' confidence for comparing each treatment with no treatment (online supplemental information 2). The number of included studies was exceedingly limited for evaluating confidence with regard to the outcomes of treatment cost and adverse events.

Patient and public involvement

No patient or public involvement in the current study.

RESULTS

Study selection and trial population

The PRISMA flowchart for our study selection is illustrated in figure 1. We identified 8446 references, and after the duplicates were removed, 6406 were screened for eligibility by two reviewers. We attempted to collect 102 reports; however, 1 report was unavailable.[29] Thus, we obtained 101 full texts and identified 38 eligible full texts reporting on 27 RCTs.[22 23 30–63] We denote each study by the author's name and year of publication: Aydin 2017,[30] Tapar 2017,[31] Aghbolagh 2020,[22] Arts 1994,[23] Balan 2009,[32] Çelikol 2019,[33] Schaal 2021,[34 35] Jacobson 1999,[36 37] Hsieh 2017,[38] Karaca 2022,[39] Ikenoue 2020,[40–42] Shabandokht-Zarmi 2017,[43 44] Hoseini 2019,[45 46] Momenabadi 2021,[47] Raghibi 2018,[48] Mou 2020,[49] Hartling 2013,[50 51] Jacquier 2022 (52-54) (44, 50, 59), Gerçeker 2019,[55] Nouira 2020,[56] Sahiner 2016,[57] Shahabi 2007,[58] Press 2013,[59] Zengin 2013,[60] Kishida 2019,[61] Fleckenstein 2022[62] and Alemdar 2023.[63]

The detailed characteristics of the studies included in this review are presented in online supplemental tables 5 and 6. The 27 RCTs included 3416 participants. The mean age was 31.5 years and 57% were men. In total, 17 studies were on peripheral vessel puncture, 5 on haemodialysis vascular access cannulation, 1 on CV catheter insertion, 2 on CV port implantation and 1 on peripherally inserted CV catheter. The participants in one study were a mixture of those who underwent CV insertion, peripherally inserted CV catheter insertion and CV port insertion.

Classification of each intervention and network structure

Online supplemental table 7 presents the summary of each category of acoustic stimulations divided using the algorithm illustrated in online supplemental figure 2. The details of intervention were not available in most studies that employed music medicine (patient selected), music medicine (researcher selected) or music therapy, that is, 'music' or 'song' were the only descriptive words. Sounds with linguistic meaning included only radio news. Sounds without linguistic meaning included white noise, nature sounds and roller-coaster sounds. Regarding audio equipment, 60% (18/30) of acoustic stimulations used headphones or earphones, 20% (6/30) used a speaker and 17% did not report details. A total of 20% (6/30) of acoustic stimulations were accompanied by visual stimulation and were considered during the assessment of the indirectness domain of confidence. A detailed description of each intervention is listed in online supplemental table 8.

Figure 2 illustrates network plots for direct evidence between treatments. For the primary outcome of self-reported pain, the most common comparison was music medicine (researcher selected) versus no treatment, followed by music medicine (patient selected) versus no treatment. It was not possible to render a network plot on treatment cost. For self-reported mental distress, the most common comparison was music medicine (patient selected) versus no treatment. No loops were made for adverse events owing to the small number of available studies.

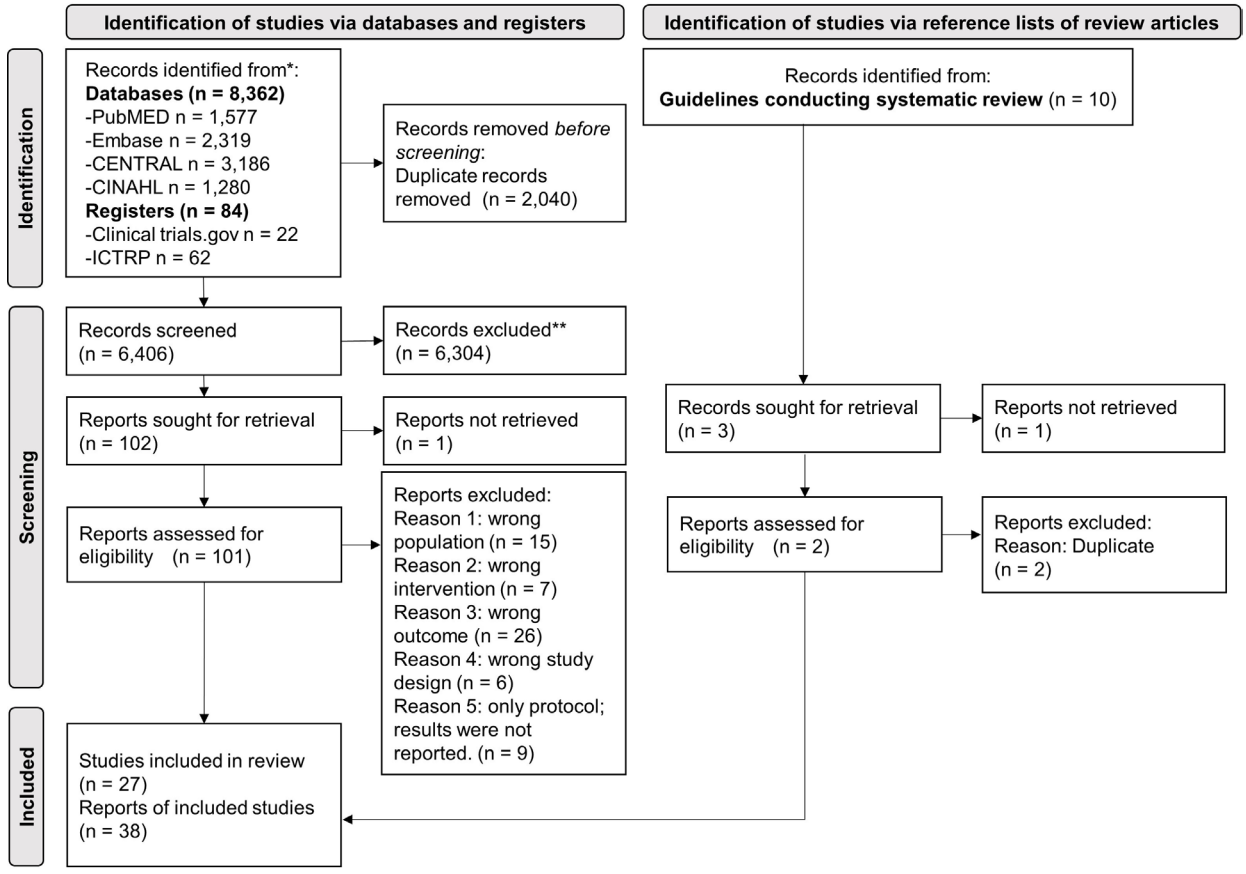

Figure 1 Preferred Reporting Items for Systematic Review and Meta-Analysis flowchart.

Risk of bias

The results of the risk of bias are presented in online supplemental figures 3–5. Regarding self-reported pain and mental distress, most studies were evaluated as having a 'high risk of bias'. This was because Domain 4, 'Measurement of the outcome', was rated 'high' in most studies since the intervention was an acoustic stimulation, which makes it difficult to blind participants, and since pain and mental distress are self-reported outcomes. Domain 5, 'Selection of the reported results', was rated 'some concerns' in almost all studies because they did not disclose the statistical analysis plan. Regarding adverse events, almost all studies were evaluated as 'some concerns'. Treatment cost was unsuitable for the risk of bias evaluation because of the lack of suitable studies.

Trial results

Self-reported pain intensity

Among the included studies, 22 RCTs with 2276 participants reported self-reported pain as an outcome (online supplemental table 5). The study conducted by Aydin and Sahiner was a four-arm comparison study that includes

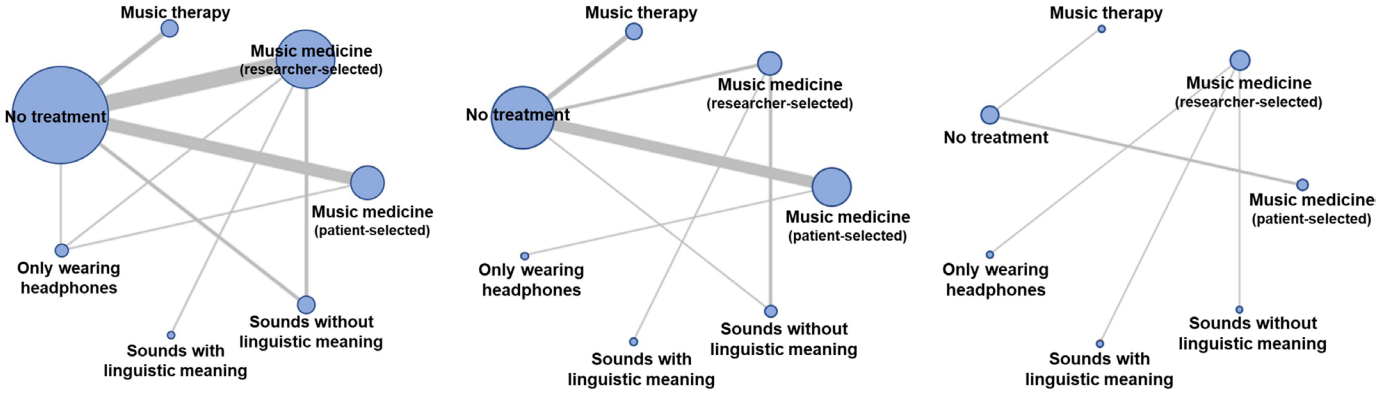

Figure 2 Network plot for each outcome. The size of the nodes and thickness of edges depends on the number of people randomised and trials conducted, respectively.

several targeted interventions, and the analytical treatment is shown in online supplemental information 2.[30] The results of the individual studies are presented in figure 3. In most studies, music-based interventions (music medicine (researcher selected), music medicine (patient selected) and music therapy) reduced pain compared with controls.

Figure 4 depicts the forest plot for all pooled network comparisons compared with no treatment. Compared with no treatment, music medicine (researcher selected) (SMD −0.76 (95% CI: −1.10 to −0.42); low confidence) and music therapy (SMD −0.79 (95% CI: −1.44 to −0.14); low confidence) may reduce self-reported pain. Music medicine (patient selected) possibly reduced pain slightly (SMD −0.44 (95% CI: −0.84 to −0.03); low confidence). Sounds with (SMD −0.67 (95% CI: −2.41 to 1.06); low confidence) and without (SMD −0.56 (95% CI: −1.17 to 0.05); low confidence) linguistic meaning tended to reduce pain; however, there was no significant difference. Conversely, wearing headphones may have increased pain (SMD 1.04 (95% CI: 0.27 to 1.81); very low confidence); however, the evidence is particularly uncertain.

Online supplemental table 9 exhibits the direct (in white) and pooled (in blue) SMD and 95% CIs for comparisons. Most of the five acoustic stimulations were associated with pain relief compared with no treatment and 'only wearing headphones'. The areas bordered by red lines in online supplemental table 9 show comparisons between the different acoustic stimulations and no significant differences were found between them for venipuncture pain relief. Treatments are ranked from best to worst along the leading diagonal; music medicine (researcher selected) was relatively more effective, followed by music therapy (marginal difference).

Treatment cost

Only three studies, Ikenoue *et al*,[40] Momenabadi *et al*[47] and Kishida *et al*[61] reported treatment costs (online supplemental table 5). Ikenoue *et al*[40] compared music medicine (researcher selected) versus sounds without linguistic meaning, whereas Kishida *et al*[61] compared music medicine (researcher selected) versus sounds with linguistic meaning. Both studies used free online music; only tablet computers and headphones/earphones purchased for research purposes were used for sound reproduction. No special labour costs were involved. Momenabadi *et al*[47] compared music medicine (patient selected) versus no treatment and reported that these interventions involved no patient expenses.

Self-reported mental distress

Self-reported mental distress was reported as an outcome in 15 studies that included 1516 patients (online supplemental table 5). The outcome results of the individual studies are exhibited in online supplemental figure 6. As illustrated in figure 4, music medicine (researcher selected) resulted in a reduction in mental distress when compared with no treatment (SMD −1.24 (95% CI: −2.34 to −0.15); low confidence). There were no significant differences between the five types of acoustic stimulations; however, music medicine (researcher selected) was relatively more effective in decreasing mental distress (online supplemental table 10).

Adverse events

Only six studies with 601 patients evaluated adverse events as an outcome (online supplemental table 5). The number of studies was limited; hence, we could not conduct a network meta-analysis. Hence, the results of each study are presented in online supplemental table 11. No adverse events were reported in four of the six studies (0/458 participants). Jacobson[37] reported canulation failure (20/72 participants), and Jacquire *et al*[52] (the study was performed in an intensive care unit setting) reported death (4/71 participants) as an adverse event. However, there were no significant differences between the groups in either study.

Subgroup and sensitivity analyses

We conducted subgroup analyses on the primary outcome of self-reported pain. The results of analyses that divided patients into adults or children (<18 years old) are illustrated in online supplemental figure 7. There were 10 studies for 896 adults and 10 studies for 1140 children. There were no significant differences between the subgroups in the efficacy of the five types of acoustic stimulations when compared with no treatment, although the effect of music medicine (patient selected) tended to be relatively stronger in adults, and the effect of sounds without linguistic meaning tended to be stronger in children. The efficacy of 'only wearing headphones' was different between the subgroups as follows: SMD −0.06 (95% CI: −0.82 to 0.71) for adults and SMD 2.47 (95% CI: 1.34 to 3.60) for children. The results of the subgroup of peripheral cannulation did not differ from those of the overall patient groups (online supplemental figure 8).

Results of sensitivity analysis excluding studies with 'high risk of bias' are exhibited in online supplemental figure 9. When evaluating the risk of bias, Domain 4 was rated as 'high' across most studies (online supplemental figure 3), and sensitivity analysis could not be performed in this case. Therefore, we defined Domain 4 as 'high' only for the study in which the SMD exceeded 2.00, and bias was highly suspected in the outcome measures for this analysis. We excluded six studies with 'high risk of bias'. In this analysis, the effect sizes for most interventions became smaller; regarding 'only wearing headphones', the difference was insignificant when compared with no treatment (SMD 0.12 (95% CI: −0.56 to 0.81)). The results of the two sensitivity analyses, excluding two studies that did not report SD and excluding five studies with a small number of participants, were similar to the overall results (online supplemental figures 10 and 11).

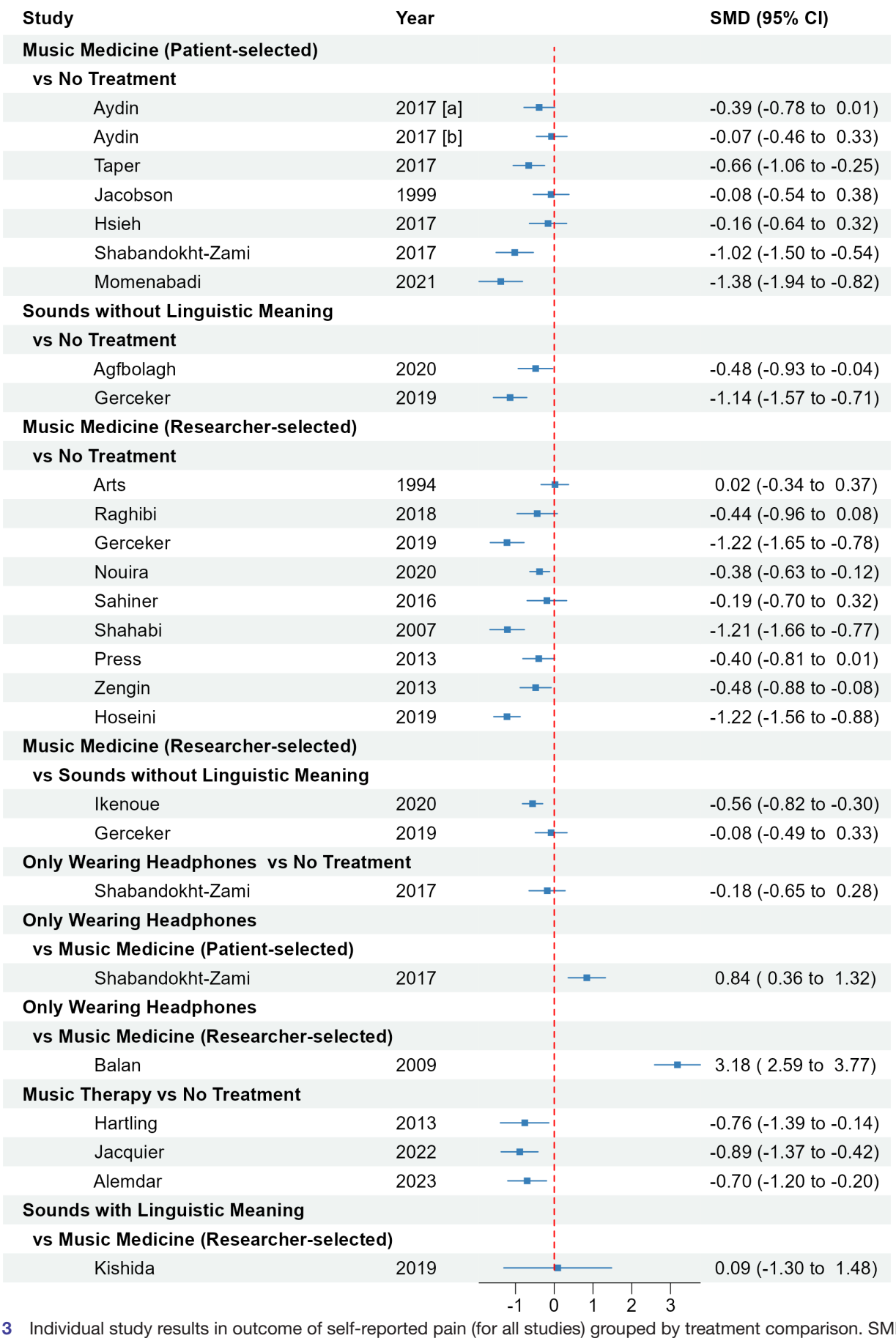

Figure 3 Individual study results in outcome of self-reported pain (for all studies) grouped by treatment comparison. SMD, standardised mean difference.

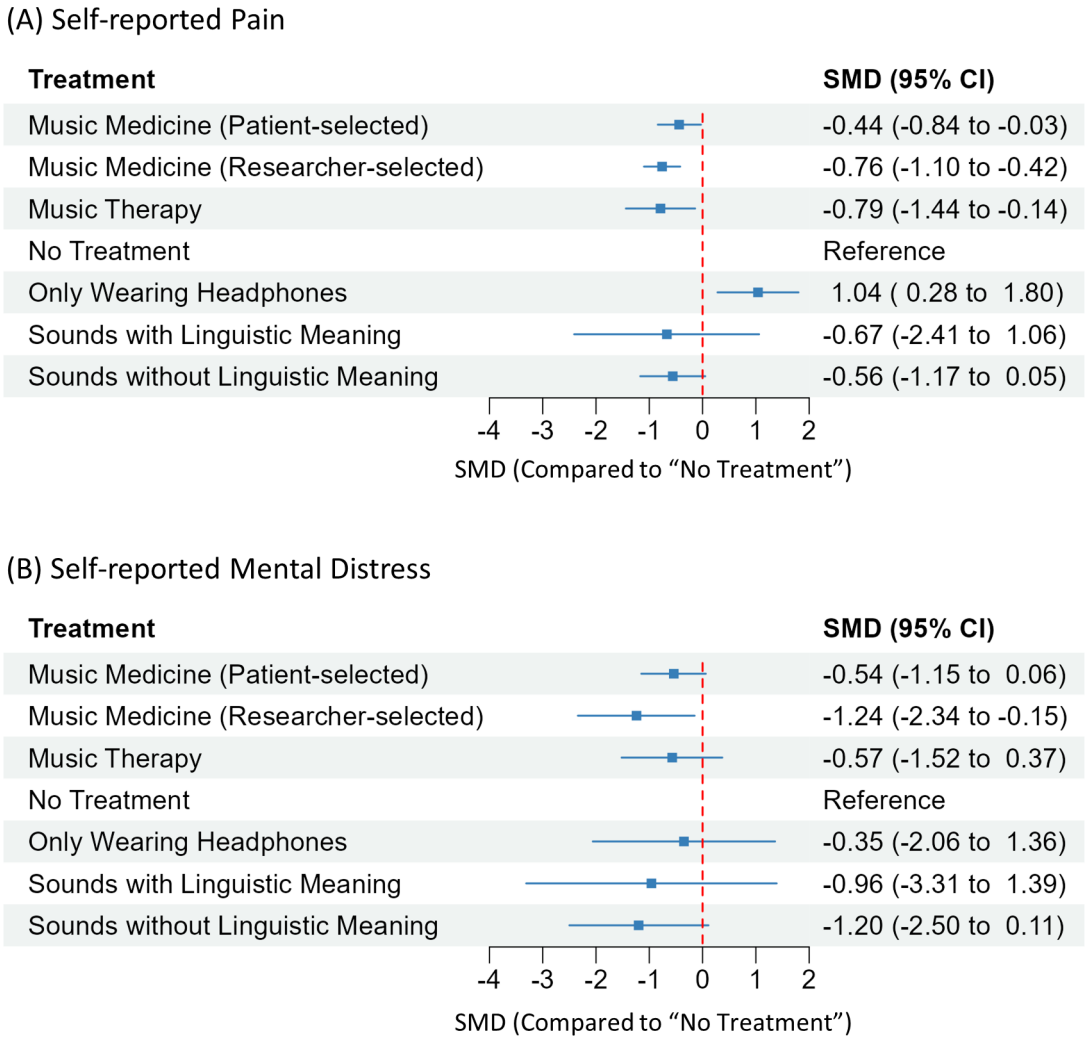

Figure 4 Forest plot for the outcomes of (A) self-reported pain and (B) self-reported mental distress. SMD, standardised mean difference.

Confidence in evidence

The confidence of the comparisons with CINeMA mainly demonstrated low ratings because most studies were rated as having a high risk of bias (online supplemental tables 12 and 13). We rated the confidence of no treatment versus 'only wearing headphones' for self-reported pain as 'very low' (online supplemental table 12). Incoherence occurred because the result of the direct comparison (SMD 0.18 (95% CI: −0.91 to 1.28)) differed from that of the pooled comparison (SMD −1.04 (95% CI: −1.80 to −0.28)). Therefore, global inconsistency was statistically significant for self-reported pain (online supplemental table 13). As the results obtained by Balan 2009,[32] which directly compared no treatment to 'only wearing headphones', exhibited potential heterogeneity, we excluded this study, resulting in a reduction of inconsistency to insignificance. A forest plot excluding Balan 2009 is depicted in online supplemental figure 12. The effect size of 'only wearing headphones' diminished (SMD for overall, 1.04 (95% CI 0.28 to 1.80); SMD after excluding Balan 2009, 0.06 (−0.74 to 0.87)), though there was not a substantial change for the other comparisons.

For mental distress, the confidence of no treatment versus 'only wearing headphones' was rated 'very low' confidence, whereas the others were rated 'low' (online supplemental table 14).

DISCUSSION

We conducted the first network meta-analysis on the efficacy and safety of acoustic stimulation for relieving venipuncture pain. Among the five types of acoustic stimulations, only musical interventions, such as music medicine (patient selected), music medicine (researcher selected) and music therapy, were associated with improved pain relief during venipuncture compared with no treatment, although there were no significant differences between the types of acoustic stimulations.

Musical interventions could be useful in the reduction of venipuncture pain. From a psychological perspective, music reportedly alleviates pain by reducing anxiety through distraction.[64] Additionally, music elicits feelings of pleasure and activates the pain-inhibiting fibres in the central nervous system, thereby reducing pain.[65 66]

Moreover, the current meta-analysis revealed that music medicine (researcher selected) also reduced mental distress during venipuncture compared with no treatment. Conversely, animal experiments have shown that sound, even if not music, induces analgesia through corticothalamic circuits.[67] Herein, we could not detect any difference between the types of acoustic stimulations, although music medicine (researcher selected) and music therapy tended to have a larger effect size among the five types.

'Only wearing headphones' could amplify pain when compared with no treatment. The unusual condition of 'only wearing headphones' for research purposes may have caused a nocebo effect.[68] This enhancement effect was more pronounced in the subgroup of children (who are considered more prone to placebo and nocebo effects[69 70]) and smaller in sensitivity analysis, excluding the 'high risk of bias' studies, thereby supporting the aforementioned hypothesis. The direct comparison reported by Balan *et al*[32] of no treatment versus 'only wearing headphones' in children demonstrated a stronger nocebo effect. Hence, excluding Balan 2009 in the analysis resulted in an improvement in global consistency. Furthermore, the headphones could have deprived auditory sense and blocked stimulation by environmental sounds, thereby amplifying the pain.[71] These findings should be considered when designing future investigative studies on the efficacy of acoustic stimulation on pain reduction.

In addition, results of other outcomes revealed several notable findings. Regarding treatment cost, although under-reported, acoustic stimulation was revealed to be an inexpensive treatment. Moreover, most studies found no specific adverse events with acoustic stimulation, indicating that this is a safe pain relief method.

This review has several limitations. First, the current study found that the risk of bias ratings in most studies was high because the intervention was an acoustic stimulation, which makes it difficult to blind participants, and because pain and mental distress are usually self-reported outcomes. Therefore, there were some comparisons wherein the confidence was rated 'very low'. More high-quality results on this research question are expected in the future. Second, there was no significant pain reduction effect for sounds with and without linguistic meaning when compared with no treatment; this could be due to insufficient power owing to the limited number of studies. Third, although the acoustic stimulations were algorithmically classified into five categories, other classification methods may yield different results.

In conclusion, our study revealed that three types of music interventions were associated with reduced venipuncture pain. Comparisons between types of stimulations demonstrated no significant differences. Music medicine (researcher selected) could reduce self-reported procedure-related mental distress. Thus, music intervention may be a safe and inexpensive pain relief method for venipuncture. To further elucidate this research question, studies addressing the risk of bias introduced by the difficulty of blinding and usage of self-reported outcomes are required in the future.

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REFERENCES

1 Smoller BR, Kruskall MS. Phlebotomy for diagnostic laboratory tests in adults. *N Engl J Med* 1986;314:1233–5.
2 Welyczko N. Peripheral intravenous cannulation: reducing pain and local complications. *Br J Nurs* 2020;29:S12–9.
3 Ayala ES, Meuret AE, Ritz T. Treatments for blood-injury-injection phobia: a critical review of current evidence. *J Psychiatr Res* 2009;43:1235–42.
4 Jenkins K. Needle Phobia: a psychological perspective. *Br J Anaesth* 2014;113:4–6.
5 McAllister N, Elshtewi M, Badr L, *et al*. Pregnancy outcomes in women with severe needle phobia. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 2012;162:149–52.
6 Horikiri M, Ueda K, Sakaba T. Comparison of emla cream and topical lidocaine tape for pain relief of V-beam laser treatment. *J Plast Surg Hand Surg* 2018;52:94–6.
7 Çelik G, Özbek O, Yılmaz M, *et al*. Vapocoolant spray vs lidocaine/Prilocaine cream for reducing the pain of venipuncture in hemodialysis patients: a randomized, placebo-controlled, crossover study. *Int J Med Sci* 2011;8:623–7.
8 Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: a current perspective. *Biochem Pharmacol* 2020;180:114147.
9 Benich JJ. Opioid dependence. *Prim Care* 2011;38:59–70.
10 Hole J, Hirsch M, Ball E, *et al*. Music as an aid for postoperative recovery in adults: a systematic review and meta-analysis. *Lancet* 2015;386:1659–71.
11 Kyriakides R, Jones P, Geraghty R, *et al*. Effect of music on outpatient urological procedures: a systematic review and meta-analysis from the European association of urology section of uro-technology. *J Urol* 2018;199:1319–27.
12 Lee JH. The effects of music on pain: a meta-analysis. *J Music Ther* 2016;53:430–77.
13 Nguyen TN, Nilsson S, Hellström A-L, *et al*. Music therapy to reduce pain and anxiety in children with cancer undergoing lumbar puncture: a randomized clinical trial. *J Pediatr Oncol Nurs* 2010;27:146–55.
14 Bradt J, Dileo C, Shim M, *et al*. n.d. Music interventions for preoperative anxiety. *Cochrane Database Syst Rev*;2013.
15 Drzymalski DM, Lumbreras-Marquez MI, Tsen LC, *et al*. The effect of patient-selected or preselected music on anxiety during cesarean delivery: a randomized controlled trial. *J Matern Fetal Neonatal Med* 2020;33:4062–8.
16 Mitchell LA, MacDonald RAR. An experimental investigation of the effects of preferred and relaxing music listening on pain perception. *J Music Ther* 2006;43:295–316.
17 Caldwell DM, Ades AE, Higgins JPT. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;331:897–900.
18 Hutton B, Salanti G, Caldwell DM, *et al*. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med* 2015;162:777–84.
19 Karakoç A, Türker F. Effects of white noise and holding on pain perception in newborns. *Pain Manag Nurs* 2014;15:864–70.
20 Moss VA. Music and the surgical patient. The effect of music on anxiety. *AORN J* 1988;48:64–9.
21 Jackson JL, Kuriyama A, Anton A, *et al*. The accuracy of Google translate for abstracting data from non-English-language trials for systematic reviews. *Ann Intern Med* 2019;171:677–9.
22 Aghbolagh MG, Bahrami T, Rejeh N, *et al*. Comparison of the effects of visual and auditory distractions on fistula cannulation pain among older patients undergoing hemodialysis: a randomized controlled clinical trial. *Geriatrics (Basel)* 2020;5:53.
23 Arts SE, Abu-Saad HH, Champion GD, *et al*. Age-related response to lidocaine-prilocaine (EMLA) emulsion and effect of music distraction on the pain of intravenous cannulation. *Pediatrics* 1994;93:797–801.
24 Furukawa TA, Barbui C, Cipriani A, *et al*. Imputing missing standard deviations in meta-analyses can provide accurate results. *J Clin Epidemiol* 2006;59:7–10.
25 Sterne JAC, Savović J, Page MJ, *et al*. Rob 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
26 Owen RK, Bradbury N, Xin Y, *et al*. Metainsight: an interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. *Res Synth Methods* 2019;10:569–81.
27 Higgins JPT, Thomas J, Chandler J, *et al*. *Cochrane Handbook for Systematic Reviews of Interventions: Wiley*. 2019.
28 Papakonstantinou T, Nikolakopoulou A, Higgins JPT, *et al*. Cinema: software for semiautomated assessment of the confidence in the results of network meta-analysis. *Campbell Syst Rev* 2020;16:e1080.
29 Tan BL, Sin ACF, Ho SM, *et al*. Effect of music in reducing anxiety levels among patients who receive their first dose of chemotherapy treatment. *Singapore General Hospital Proceedings* 2008;17:46–56.
30 Aydin D, Sahiner NC. Effects of music therapy and distraction cards on pain relief during phlebotomy in children. *Appl Nurs Res* 2017;33:164–8.
31 Tapar H, Karaman T, Dogru S, *et al*. n.d. Evaluating the efficacy of Valsalva's maneuver and music therapy on peripheral venous Cannulation: a prospective study. Anaesth Pain Intensive Care;2018:219–23.
32 Balan R, Bavdekar SB, Jadhav S. Can Indian classical instrumental music reduce pain felt during venepuncture *Indian J Pediatr* 2009;76:469–73.
33 Çelikol Ş, Tural Büyük E, Yıldızlar O. Children's pain, fear, and anxiety during invasive procedures. *Nurs Sci Q* 2019;32:226–32.
34 Schaal NK, Brückner J, Wolf OT, *et al*. The effects of a music intervention during port catheter placement on anxiety and stress. *Sci Rep* 2021;11:5807.
35 Hepp P. Music intervention and its consequences during port placement and extraction on anxiety. 2015. Available: https://trialsearch.who.int/Trial2.aspx?TrialID=DRKS00009036 [Accessed 01 Jan 2015].
36 Jacobson A. *Effect of intradermal normal saline, listening to music, and insertion difficulty on pain of IV insertion*. Texas Woman's University, 1995.
37 Jacobson AF. Intradermal normal saline solution, self-selected music, and insertion difficulty effects on intravenous insertion pain. *Heart Lung* 1999;28:114–22.
38 Hsieh Y-C, Cheng S-F, Tsay P-K, *et al*. Effectiveness of cognitive-behavioral program on pain and fear in school-aged children undergoing intravenous placement. *Asian Nurs Res (Korean Soc Nurs Sci)* 2017;11:261–7.
39 Karaca TN, Cevik Guner U. The effect of music-moving toys to reduce fear and anxiety in preschool children undergoing intravenous insertion in a pediatric emergency department: a randomized clinical trial. *J Emerg Nurs* 2022;48:32–44.
40 Ikenoue T, Kishida M, Yamada Y, *et al*. Effectiveness of music for alleviating pain during Haemodialysis access cannulation: a multifacility, single-blind, randomised controlled trial. *Nephrol Dial Transplant* 2020;35:1646.
41 Inayama E, Yamada Y, Kishida M, *et al*. Effect of music in reducing pain during Hemodialysis access cannulation: a crossover randomized controlled trial. *Clin J Am Soc Nephrol* 2022;17:1337–45.
42 Kitamura M. The effectiveness of sound distraction for alleviation of pain during Cannulation of Hemodialysis patients. 2018. Available: https://trialsearch.who.int/Trial2.aspx?TrialID=JPRN-UMIN000032850 [Accessed 01 Jan 2018].
43 Nesami MB. The effect of self-selected calming music on pain intensity due to needle insertion in to a Fistula in Hemodialysis patients. 2016. Available: https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT201607297494N20)
44 Shabandokht-Zarmi H, Bagheri-Nesami M, Shorofi SA, *et al*. The effect of self-selected soothing music on fistula puncture-related pain in Hemodialysis patients. *Complement Ther Clin Pract* 2017;29:53–7.
45 Golaghaie F. Comparing the effect of music and riddle solving on pain of intravenous Cannulation. 2018. Available: https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20150818023670N3 [Accessed 01 Jan 2018].
46 Hoseini T, Golaghaie F, Khosravi S. Comparison of two distraction methods on venipuncture pain in children. AMUJ 2019;22:27–35.
47 Momenabadi A, Radmehr M, Sadeghi N. Effect of two methods of acupressure in hugo point and music on severity of pain during IV insertion in children. *AJMHS* 2021;14:697–700.
48 Raghibi A, Salar A, Askari H, *et al*. Investigating the effect of arnica ointment and distraction on the pain caused by fistula needle insertion in hemodialysis patients: a clinical trial. *Med Surg Nurs J* 2018;7.
49 Mou Q, Wang X, Xu H, *et al*. Effects of passive music therapy on anxiety and vital signs in lung cancer patients undergoing peripherally inserted central catheter placement procedure. *J Vasc Access* 2020;21:875–82.
50 Hartling L, Newton AS, Liang Y, *et al*. Music to reduce pain and distress in the pediatric emergency department: a randomized clinical trial. *JAMA Pediatr* 2013;167:826–35.
51 Hartling L. Music to reduce pain and anxiety in the pediatric emergency Department. 2008. Available: https://clinicaltrials.gov/show/NCT00761033 [Accessed 01 Jan 2018].
52 Jacquier S, Nay M-A, Muller G, *et al*. Effect of a musical intervention during the implantation of a central venous catheter or a dialysis catheter in the intensive care unit: a prospective randomized pilot study. *Anesth Analg* 2022;134:781–90.

53 Sophie Jacquier BS, Muller G, Boulain T, *et al*. Efect of a musical intervention during central venous catheterization in an intensive care unit: the MUSIC CAT prospective randomized pilot study. *Annals of Intensive Care Conference: French Intensive Care Society International Congress* 2020;10:16.
54 Nay M-A. MUSIC-CAT; Musical Intervention and Patient's Anxiety During Central Venous Catheter Insertion in the Intensive Care Unit, . 2018Available: https://clinicaltrials.gov/study/NCT03398525 [Accessed 01 Jan 2018].
55 Gerçeker GÖ. Effects of virtual reality on pain, fear and anxiety during blood draw in children aged 5-12 years old. 2019. Available: https://clinicaltrials.gov/study/NCT04040036 [Accessed 01 Jan 2018].
56 Chtourou D, Sfaxi S, Bahria W, *et al*. Music to reduce pain and distress due to emergency care: a randomized clinical trial. *Crit Care* 2020;24:87.
57 Sahiner NC, Bal MD. The effects of three different distraction methods on pain and anxiety in children. *J Child Health Care* 2016;20:277–85.
58 Shahabi M, Kalani- Tehrani D, Eghbal M, *et al*. Comparing the effects of EMLA ointment with a diversionary activity (music) on vein puncture pain at school-age children. *Advances in Nursing & Midwifery* 2007;17:13–20.
59 Press J, Gidron Y, Maimon M, *et al*. Effects of active distraction on pain of children undergoing Venipuncture: who benefits from it. *The Pain Clinic* 2003;15:261–9.
60 Zengin S, Kabul S, Al B, *et al*. Effects of music therapy on pain and anxiety in patients undergoing port catheter placement procedure. *Complement Ther Med* 2013;21:689–96.
61 Kishida M, Yamada Y, Inayama E, *et al*. Effectiveness of music therapy for alleviating pain during haemodialysis access cannulation for patients undergoing haemodialysis: a multi-facility, single-blind, randomised controlled trial. *Trials* 2019;20:631.
62 Fleckenstein FN, Böhm AK, Collettini F, *et al*. A prospective randomized controlled trial assessing the effect of music on patients' anxiety in venous catheter placement procedures. *Sci Rep* 2022;12:6922.
63 Küçük Alemdar D, Bulut A, Yilmaz G. Impact of music therapy and hand massage in the pediatric intensive care unit on pain, fear and stress: randomized controlled trial. *J Pediatr Nurs* 2023;71:95–103.
64 Villarreal EAG, Brattico E, Vase L, *et al*. Superior analgesic effect of an active distraction versus pleasant unfamiliar sounds and music: the influence of emotion and cognitive style. *PLoS One* 2012;7:e29397.
65 Lunde SJ, Vuust P, Garza-Villarreal EA, *et al*. Music-induced analgesia: how does music relieve pain *Pain* 2019;160:989–93.
66 Salimpoor VN, Benovoy M, Larcher K, *et al*. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. *Nat Neurosci* 2011;14:257–62.
67 Zhou W, Ye C, Wang H, *et al*. Sound induces analgesia through corticothalamic circuits. *Science* 2022;377:198–204.
68 Colloca L, Barsky AJ. Placebo and nocebo effects. *N Engl J Med* 2020;382:554–61.
69 Czerniak E, Oberlander TF, Weimer K, *et al*. "Placebo by proxy" and "nocebo by proxy" in children: a review of parents' role in treatment outcomes". *Front Psychiatry* 2020;11:169.
70 Gniß S, Kappesser J, Hermann C. Placebo effect in children: the role of expectation and learning. *PAIN* 2020;161:1191–201.
71 Domínguez Ugidos LJ, Rodríguez Morejón C, Vallés Varela H, *et al*. Auditory training with wide-band white noise: effects on the pain threshold and pure tone thresholds. *Acta Otorrinolaringol Esp* 2001;52:410–7.

Acoustic Stimulation for Relieving Pain During Venipuncture: A Systematic Review and Network Meta-analysis

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Supplementary materials

Supplemental Information 1. PRISMA NMA checklist of items to include when reporting a systematic review involving a network meta-analysis

Supplemental Information 2. Analytical treatment of the study by Aydin et al. and basis for the evaluation of confidence

Supplemental Table 1. Search strategy for PubMed used in the current study

Search number	Query
#1	"Infusions, Intravenous"[mh]
#2	"Injections, Intravenous"[mh]
#3	"Catheterization"[mh]
#4	"Catheterization, Peripheral"[mh]
#5	"Phlebotomy"[mh]
#6	"cannula*"[tiab] OR "catheter*"[tiab] OR "Phlebotom*"[tiab] OR "Venesection*"[tiab] OR "Venipuncture*"[tiab] OR ("pain*"[tiab] AND ("needl*"[tiab] OR "intravenous"[tiab])) OR ("needl*"[tiab] AND "procedure*"[tiab]) OR (("injection*"[tiab] OR "infusion*"[tiab] OR "punctur*"[tiab]) AND ("intravenous"[tiab] OR "vein*"[tiab] OR "Drip"[tiab] OR "blood vessel*"[tiab] OR "vascular"[tiab] OR "Arteriovenous Fistula*"[tiab])) OR ("intravenous"[tiab] AND "Drip"[tiab])
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8	"Acoustic Stimulation"[mh]
#9	"Music"[mh]
#10	"Music therapy"[mh]
#11	"Sound"[mh]
#12	"Noise"[mh]
#13	"Audiometry"[mh]
#14	"Acoustic"[tiab] OR "Auditory"[tiab] OR "Music*"[tiab] OR "rhythm*"[tiab] OR "melod*"[tiab] OR "singing"[tiab] OR "sing"[tiab] OR "song"[tiab] OR "songs"[tiab] OR "improvis*"[tiab] OR "sonic"[tiab] OR "sound*"[tiab] OR "noise*"[tiab] OR "Audiometr*"[tiab]
#15	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	("Randomized controlled trial"[pt] OR "controlled clinical trial"[pt] OR "Cross-Over Studies"[mh] OR "randomized"[tiab] OR "placebo"[tiab] OR "clinical trials as topic"[mh: noexp] OR "randomly"[tiab] OR "trial"[ti]) NOT ("animals"[mh] NOT "humans"[mh])
#17	#7 AND #15 AND #16

Search date: Jan 16th 2022（initial search) and Sep 10th 2023 (search again)

Search results: 1,577

Supplemental Table 2. Search strategy for EMBASE used in the current study

Set#	Searched for
S1	EMB.EXACT.EXPLODE("intravenous drug administration")
S2	EMB.EXACT.EXPLODE("catheterization")
S3	EMB.EXACT.EXPLODE("blood vessel catheterization")
S4	EMB.EXACT.EXPLODE("phlebotomy")
S5	ab(cannula* OR catheter* OR Phlebotom* OR Venesection* OR Venipuncture*) OR ti(cannula* OR catheter* OR Phlebotom* OR Venesection* OR Venipuncture*)
S6	ab(pain* AND (needl* OR intravenous)) OR ti(pain* AND (needl* OR intravenous))
S7	ab(needl* AND procedure*) OR ti(needl* AND procedure*)
S8	ab((injection* OR infusion* OR punctur*) AND (intravenous OR vein* OR Drip OR blood vessel* OR vascular OR Arteriovenous Fistula*)) OR ti((injection* OR infusion* OR punctur*) AND (intravenous OR vein* OR Drip OR blood vessel* OR vascular OR Arteriovenous Fistula*))
S9	ab(intravenous AND Drip) OR ti(intravenous AND Drip)
S10	S9 OR S8 OR S7 OR S6 OR S5 OR S4 OR S3 OR S2 OR S1
S11	EMB.EXACT.EXPLODE("auditory stimulation")
S12	EMB.EXACT.EXPLODE("music")
S13	EMB.EXACT.EXPLODE("music therapy")
S14	EMB.EXACT.EXPLODE("sound")
S15	EMB.EXACT.EXPLODE("noise")
S16	EMB.EXACT.EXPLODE("audiometry")
S17	ab(Acoustic OR Auditory OR Music* OR rhythm* OR melod* OR singing OR sing OR song OR songs OR improvis* OR sonic OR sound* OR noise* OR Audiometr*) OR ab(Acoustic OR Auditory OR Music* OR rhythm* OR melod* OR singing OR sing OR song OR songs OR improvis* OR sonic OR sound* OR noise* OR Audiometr*)
S18	S17 OR S16 OR S15 OR S14 OR S13 OR S12 OR S11
S19	S18 AND S10
S20	((ab(random*) OR ti(random*)) OR (ab(clinical NEAR/1 trial*) OR ti(clinical NEAR/1 trial*)) OR (EMB.EXACT("health care quality")))

S21	(EMB.EXACT("double blind procedure")) OR (ab(double NEAR/1 blind*) OR ti(double NEAR/1 blind*)) OR (ab(placebo*) OR ti(placebo*)) OR (ab(blind*) OR ti(blind*))
S22	S20 AND S19
S23	S21 AND S19

Search date: Jan 15th 2022 (initial search) and Sep 10th 2023 (search again)

Search results: 2,319

Supplemental Table 3. Search strategy for CENTRAL used in the current study

ID	Search
#1	MeSH descriptor: [Infusions, Intravenous] explode all trees
#2	MeSH descriptor: [Injections, Intravenous] explode all trees
#3	MeSH descriptor: [Catheterization] explode all trees
#4	MeSH descriptor: [Catheterization, Peripheral] explode all trees
#5	MeSH descriptor: [Phlebotomy] explode all trees
#6	(((cannula*) OR (catheter*) OR (Phlebotom*) OR (Venesection*) OR (Venipuncture*) OR ((pain*) AND ((needl*) OR (intravenous))) OR ((needl*) AND (procedure*)) OR (((injection*) OR (infusion*) OR (punctur*)) AND ((intravenous) OR (vein*) OR (Drip) OR (blood vessel*) OR (vascular) OR (Arteriovenous Fistula*))) OR ((intravenous) AND (Drip))):ti,ab,kw
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8	MeSH descriptor: [Acoustic Stimulation] explode all trees
#9	MeSH descriptor: [Music] explode all trees
#10	MeSH descriptor: [Music Therapy] explode all trees
#11	MeSH descriptor: [Sound] explode all trees
#12	MeSH descriptor: [Noise] explode all trees
#13	MeSH descriptor: [Audiometry] explode all trees
#14	((Acoustic) OR (Auditory) OR (Music*) OR (rhythm*) OR (melod*) OR (singing) OR (sing) OR (song) OR (songs) OR (improvis*) OR (sonic) OR (sound*) OR (noise*) OR (Audiometr*)):ti,ab,kw
#15	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	#7 AND #15

Search date: Jan 16th 2022 (initial search) and Sep 10th 2023 (search again)

Search results: 3,186

Supplemental Table 4. Search strategy for CINAHL used in the current study

Search number	Query
S1	MH infusions, intravenous
S2	MH injections, intravenous
S3	MH catheterization
S4	MH catheterization, peripheral
S5	MH phlebotomy
S6	(TI cannula* OR AB cannula*) OR (TI catheter* OR AB catheter*) OR (TI Phlebotom* OR AB Phlebotom*) OR (TI Venesection* OR AB Venesection*) OR (TI Venipuncture* OR AB Venipuncture*) OR ((TI pain* OR AB pain*) AND ((TI needl* OR AB needl*) OR (TI intravenous OR AB intravenous))) OR ((TI needl* OR AB needl*) AND (TI procedure* OR AB procedure*)) OR (((TI injection* OR AB injection*) OR (TI infusion* OR AB infusion*) OR (TI punctur* OR AB punctur*)) AND ((TI intravenous OR AB intravenous) OR (TI vein* OR AB vein*) OR (TI Drip OR AB Drip) OR (TI blood vessel* OR AB blood vessel*) OR (TI vascular OR AB vascular) OR (TI Arteriovenous Fistula* OR AB Arteriovenous Fistula*))) OR ((TI intravenous OR AB intravenous) AND (TI Drip OR AB Drip))
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6
S8	MH acoustic stimulation
S9	MH music
S10	MH music therapy
S11	MH sound
S12	MH noise
S13	MH audiometry
S14	(TI Acoustic OR AB Acoustic) OR (TI Auditory OR AB Auditory) OR (TI Music* OR AB Music*) OR (TI rhythm* OR AB rhythm*) OR (TI melod* OR AB melod*) OR (TI singing OR AB singing) OR (TI sing OR AB sing) OR (TI song OR AB song) OR (TI songs OR AB songs) OR (TI improvis* OR AB improvis*) OR (TI sonic OR AB sonic) OR (TI sound* OR AB sound*) OR (TI noise* OR AB noise*) OR (TI Audiometr* OR AB Audiometr*)
S15	S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16	(MH randomized controlled trials) OR (MH double-blind studies) OR (MH single-blind studies) OR (MH random assignment) OR (MH pretest‐posttest design) OR (MH cluster sample) OR (TI (randomised OR randomized)) OR (AB (random*)) OR (TI (trial)) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR (MH (placebos)) OR (PT (randomized controlled trial)) OR (AB (control W5 group)) OR (MH (crossover design) OR

	MH (comparative studies)) OR (AB (cluster W3 RCT)) NOT (((MH animals+) OR (MH (animal studies)) OR (TI (animal model*))) NOT (MH (human)))
S17	S7 AND S15 AND S16

Search date: 16th Jan 2022 (initial search) and Sep 10th 2023 (search again)

Search results: 1,280

Supplemental Table 5. Baseline characteristics of the 27 included studies

Publication	N randomized	Dropout (%)	Age (y)	Male (%)	Type of RCT	Type of cannulation	Interventions				Outcomes of interest
							Treatment A	Treatment B	Treatment C	Treatment D	
Aydin 2017	200	0	9	58	Parallel	Peripheral	Music medicine (patient-selected) + distraction card	Music medicine (patient-selected)	Distraction card	No treatment	Pain
Tapar 2017	153	2	45.7	NR	Parallel	Peripheral	Music medicine (patient-selected)	No treatment	Valsalva maneuver*		Pain, distress
Aghbolagh 2020	120	0	69.4	58	Parallel	Peripheral (HD access)	Sounds without linguistic meaning	No treatment	Visual distraction*		Pain
Art 1994	180	0	9.7	56	Parallel	Peripheral	Music medicine (researcher-selected)	No treatment	EMLA cream*		Pain
Balan 2009	150	0	8	59	Parallel	Peripheral	Music medicine (researcher-selected)	Only wearing headphones	EMLA cream*		Pain, AE
Çelikol 2019	200	0	9.7	50	Parallel	Peripheral	Music	No treatment	Video*		Distress

							medicine (patient-selected)				
Schaal 2021	107	21	56.6	0	Parallel	Port catheter	Music medicine (patient-selected)	Only wearing headphones			Distress
Jacobson 1999	110	0	53	53	Parallel	Peripheral	Music medicine (patient-selected)	No treatment	Intradermal injection of normal saline*		Pain, distress, AE
Hsieh 2017	68	0	8.1	53	Parallel	Peripheral	Music medicine (patient-selected)	No treatment			Pain, distress
Karaca 2022	60	0	4.9	48	Parallel	Peripheral	Music medicine (patient-selected)	No treatment			Distress
Ikenoue 2020	121	3	64	71	Crossover	Peripheral (HD access)	Music medicine (researcher-selected)	Sounds without linguistic meaning			Pain, cost, distress, AE
Shabandokht-Zarmi 2017	114	5	59	53	Parallel	Peripheral (HD access)	Music medicine (patient-selected)	Only wearing headphones	No treatment		Pain

Hoseini 2019	268	9	8.1	49	Parallel	Peripheral	Music medicine (researcher-selected)	No treatment	Riddle solving*		Pain
Momenabadi 2021	90	0	51	54	Parallel	Peripheral	Music medicine (patient-selected)	No treatment	Hugo point massage*		Pain, cost
Raghibi 2018	93	4	48.5	66	Parallel	Peripheral (HD access)	Music medicine (researcher-selected)	No treatment	Arnica ointment*		Pain
Mou 2020	300	0	57.3	80	Parallel	PICC	Music medicine (patient-selected)	No treatment			Distress
Hartling 2013	42	0	6.3	62	Parallel	Peripheral	Music therapy	No treatment			Pain, distress
Jacquier 2022	75	4	60.5	54	Parallel	CV catheter	Music therapy	No treatment			Pain, distress, AE
Gerçeker 2019	141	4	9.3*	54	Parallel	Peripheral	Music medicine (researcher-selected)	Sounds without linguistic meaning	No treatment		Pain, distress
Nouira 2020	240	0	NR	NR	Parallel	Peripheral	Music medicine (researcher-selected)	No treatment			Pain

Sahiner 2016	120	0	9.1	53	Parallel	Peripheral	Music medicine (researcher)	No treatment	Distraction cards*	Balloon inflation*	Pain
Shahabi 2007	46	0	9.1	52	Crossover	Peripheral	Music medicine (researcher-selected)	No treatment	EMLA cream*		Pain
Press 2013	94	0	10.7	61	Parallel	Peripheral	Music medicine (researcher-selected)	No treatment			Pain
Zengin 2013	100	0	49.9	52	Parallel	Port catheter	Music medicine (researcher-selected)	No treatment			Pain, distress
Kishida 2019	8	0	66.4	63	Parallel	Peripheral (HD access)	Music medicine (researcher-selected)	Sounds with linguistic meaning			Pain, cost, distress, AE
Fleckenstein 2022	117	43	60	53	Parallel	Port catheter or CV catheter or PICC	Music medicine (patient-selected)	No treatment			Distress, AE

Alemdar 2023	99	0	15.4	83	Parallel	Peripheral	Music therapy	No treatment	Hand massage*		Pain, distress

*These interventions were not included in the meta-analysis.

Abbreviations: RCT, randomized controlled trial; NR, not reported; HD, haemodialysis; EMLA, emulsion of lidocaine and prilocaine; AE, adverse events; PICC, peripherally inserted central venous catheter; CV, central venous

Supplemental Table 6. Characteristics, including eligibility criteria, of the 27 studies in this review

Publication	Study duration	Setting	Country	Inclusion criteria	Exclusion criteria	Funding
Aydin 2017	July 1st to September 20th, 2015	Single center	Turkey	Being aged 7−12 years and requiring blood tests.	If they were neuro-developmentally delayed, had verbal difficulties, hearing or visual impairments, used analgesics within the last 6 h, or if they had a history of syncope due to blood sampling and children who could not phlebotomy.	Unclear
Tapar 2017	April to July 2017	Single center	Turkey	Patients with an American Society of Anesthesiologists physical status score of I or II, aged between 18 and 65, and had given written informed consent were included.	Patients with a history of drug addiction, anxiety disorders, hearing problems, chronic consumption of analgesics, or peripheral neuropathy and patients with verbal communication problems were excluded. In addition, patients with failed first-attempt cannulation were excluded.	Unclear
Aghbolagh 2020	July to December 2017	Single center	Iran	Age over 60 years, at least two months passed from the installation of AVF, undergoing HD three sessions per week and each session lasting for 4 h, no history of verbal disturbances, no addiction or drug dependence to pain medications, no history of mental health diseases, and ability to pass the abbreviated mental test indicating their cognitive health.	Unwillingness to continue with the study, unsuccessful AVF cannulation at the first try, use of tranquilizers in the last 8 h, failure to attend more than two distraction sessions due to referral to another healthcare center, kidney transplantation and death, the presence of pain in other areas of the body based on the older patient's report, presence of infection and obstruction of fistula based on the nurse's inspection, and the presence of auditory and visual disturbances.	No
Arts 1994	Not reported	Not reported	Australia	Children aged 4 to 16 years who were to undergo surgery under general anesthesia via intravenous cannulation.	Children who required preanesthetic medication, who had major physical and mental handicaps and who refused intravenous cannulation.	Yes

Balan 2009	Over 14 months.	Single center	India	Children aged 5-12 yrs requiring venipuncture for blood collection were enrolled, after obtaining informed consent from parents. In addition, children over 7 years of age were enrolled only if they provided assent for their participation.	Children with history of hypersensitivity to local anesthetics of theamide type or to one or more constituents of EMLA, those with history of congenital or idiopathic methemoglobinemia, glucose-6-phosphatase deficiency or severe hepatic disease were excluded. In addition, children with altered sensorium and those found to be having hearing impairment on clinical examination were excluded from the study. Children whose clinical condition warranted urgent administration of drugs, were also not included.	No
Çelikol 2019	July to September 2015	Single center	Turkey	Between 8 and 12 years of age, literate, no mental problems, able to communicate easily, and willing to participate.	Not reported	No
Schaal 2021	December 2015 to December 2019	Single center	Germany	Women had an indication for a planned placement of a port catheter under analgosedation to a degree that did not necessitate respiratory support, and adequate German language comprehension in order to answer the questionnaires.	Patients requiring general anaesthesia as well as known anxiety disorders or other severe psychiatric illnesses.	No
Jacobson 1999	Not reported	Multi centers	America	18 years or older, English speaking, capable of participating (vision and hearing intact, no obvious or reported cognitive, neurologic, or motor impairment), and medical orders for peripheral IV therapy.	Not reported	No
Hsieh 2017	June to November 2014	Single center	Taiwan	Hospitalized school-aged children between 6 and 12 years old.	If they had physical or mental disability; had a hearing or visual impairment; had not previously had an IV placement; or had received more than one IV placement concurrently during the procedure.	Unclear
Karaca 2022	July to November 2018	Single center	Turkey	Between the ages of 4 and 6 years, conscious, and with the ability to communicate.	The children had chronic and/or severe illness, mental/psychiatric illness, visual and/or hearing impairment, and inability to communicate verbally.	Unclear
Ikenoue 2020	August 27, 2018 to June 26, 2019	Multi centers	Japan	Across the five facilities, patients over the age of 20 years who are undergoing outpatient HD three times a week, who have received HD for more than 6 months, and who indicated	Not willing to participate; having a hearing, writing, or visual impairment; being paralysed; facing a difficulty communicating; having a psychiatric	No

				experiencing pain during cannulation based on a prior questionnaire.	disorder or dementia; undergoing HD therapy fewer than three times per week; and receiving HD through an indwelling catheter.	
Shabandokht-Zarmi 2017	October to December 2016	Multi centers	Iran	A desire to listen to the music, age of 18 years and older, not diagnosed with neuropathic disorders, no history of depression, treated with HD for at least 3 months, not administered tranquilizers, analgesics and sedatives 3 hours before the study, not recently taken antipsychotic medications and tranquilizers, not being cognitively impaired, no hearing and visual impairments, and not habitually listening to music during HD.	Acute pain in other parts of the body, more than one attempt for fistula puncturing, any changes in the physical status during the study, withdrawal from the study, and death	No
Hoseini 2019	January 2011 to January 2017	Single center	Iran	Age 7-9 years, clear consciousness, first venipuncture, no hearing and vision problems, able to communicate verbally, no mental retardation or cerebral palsy, no medication for diagnosed psychiatric disorder, no use of analgesics (oral and topical) and hypnotics within 48 hours, no painful illness before venipuncture.	Inability to obtain parental consent to participate, re-venipuncture in the same patient, epilepsy or other life-threatening emergency situations	No
Momenabadi 2021	Not reported	Single center	Iran	Children aged 3-6 years old who were admitted to pediatric section of Amiral-Momenin Hospital in Semnan and needed IV line insertion were selected by available sampling method. The conditions to enter the study were: not acute illness, first experience of IV insertion in hospital, absence of parents in the health and treatment group, not using sedative medications for 8 hours before IV insertion.	Children who needed IV insertion for second time.	No
Raghibi 2018	2017	Two centers	Iran	Above 18 years, consciousness, ability to communicate, need for HD at least twice a week, not receiving any analgesics or drugs six hours before HD, absence of severe pain in other organs, and no skin problems or numbness at the site of access to the veins of diabetic patients.	Lack of cooperation, kidney transplantation and termination of HD treatment, development of wound at the site of fistula at any stage of the disease, misplacement of the fistula needle at the first time, and death.	No

Mou 2020	May to December 2015	Single center	China	Having pathological proof of lung cancer, being hospitalized for chemotherapy and willing to accept PICC catheter, age above 18 years, with life expectancy more than three months, being able to understand, read, and Chinese.	Not the first time to receive PICC, diagnosed with mental illness, with symptoms of pain with hearing impairment does not like to listen to music and being in a critical condition.	No
Hartling 2013	January 1, 2009, to March 31, 2010	Single center	Canada	Children attending the pediatric emergency department were eligible if they were aged 3 to 11 years, undergoing an IV placement, conscious, and had sufficient knowledge of English to understand and follow instructions and complete the age appropriate pain	If they had hearing impairments, developmental disabilities, or sensory impairment to pain. Children were also excluded at the discretion of the attending staff (eg, child in critical condition; requiring urgent IV placement; or in an altered level of consciousness).	No
Jacquier 2021	from February 2018 to February 2019	Single center	France	Adults ≥18 years old who were hospitalized in the intensive care unit, and for whom insertion of a central venous catheter or a dialysis catheter was planned. Patients had to be able to hear and understand explanations and consent.	Severe hearing impairment, allergy to local anesthetic, pregnancy, previous participation, refusal to participate, and, according to the French law, absence of social security coverage number or patient under guardianship.	No
Gerceker 2019	September to November 2017	Single center	Turkey	Aged 5–12-year-old, underwent blood draw, had no chronic or genetic diseases, had no visual problem or eyeglasses. The informed consent was received form children and parents.	Patients who refused to participate, had chronic or genetic diseases, and had visual problem	Unclear
Nouira 2020	Not reported	Single center	Tunisia	Patients consulting the emergency department and needed venous sampling, peripheral venous catheter or arterial catheter.	not reported	Unclear
Sahiner 2016	not reported	Single center	Turkey	Children aged 6–12 years who requested blood tests.	not reported	No
Shahabi 2007	not reported	Single center	Iran	Children from 6 to 12 years old with Thalassemia	not reported	unclear
Press 2013	not reported	Single center	Israel	Age 6-16, conscious, Hebrew speaking, with no hearing problem, undergoing venipuncture	not reported	unclear

Zengin 2013	1 March to 30 September 2012	Single center	Turkey	Newly diagnosed oncology patients with ages ranging from 18 to 75 years, were enrolled in the study. Port catheters are placed to use chemotherapy and nutrition for the oncological patients in our medical center. Patients were included if they were undergoing port catheter placement for the first time; were aged at least 16 years; were Turkish-speaking and able to read at fifth-grade level; and were mentally competent to sign the consent form.	Auditory problems, hormonal dysfunction, steroid, anxiolytic and sedative use, cocaine abuse, an established diagnosis of severe anxiety disorder, active psychosis or dementia, and uncontrolled hypertension.	No
Kishida 2019	October to November 2016	Multi centers	Japan	Patients who are undergoing HD, and aged 20 and over. Patients who feel pain during AVF canulation (visual analog scale >30 mm in clinical practice)	Unable to obtain consent, hearing impairment, unable to write a self-assessment form, visual impairment, paralysis, communication difficulties, mental illness, cognition disease., patients who were not on HD more than 6 months, or patients with outpatient dialysis less than 3 times a week or more than 4 times a week	No
Fleckenstein 2022	November 2019 to June 2020	Not reported	Germany	Age of majority, hemodynamic stability, German speaking and ability to consent participation in the study.	Patients with hearing difficulties or dementia, emergency procedures and procedures under general anaesthesia were excluded. Moreover, specific exclusion criteria for port procedure comprised haemorrhagic diathesis, thrombosis of jugular and subclavian veins, bilateral or acute infectious disease (e.g. sepsis or local implantation site infection) with increased risk of early port infection.	No
Alemdar 2023	June 2019 to December 2020	Single center	Turkey	Being an adolescent aged 12–18 years, not being intubated and not receiving mechanical ventilator support, parents and child able to speak Turkish, and agreeing to participate in the research.	Cognitive dysfunction in the adolescent, surgical interventions being performed, receiving sedative or muscle-relaxant drugs, and hearing difficulty.	No

Abbreviations: AVF, arteriovenous fistula; HD, hemodialysis; EMLA, emulsion of lidocaine and prilocaine; IV, intravenous；PICC, peripherally inserted central venous catheter

Supplemental Table 7. Summary of acoustic stimulations assigned to each classification

Classification of stimulation	Study	Acoustic stimulation	Sound source and auditory device
Music medicine (patient-selected)	Jacobson 1999	Selected from 11 CDs including different type of music. (e.g., jazz, country music)	Portable CD player with headphones
	Hsieh 2017	Self-selected music video	Music video (auditory devise: NR)*
	Shabandokht-Zarmi 2017	Selected from pieces of familiar folklore/traditional/soothing music	MP4 player with headphones
	Momenabadi 2021	His/her favorite song	NR
	Aydin 2017	Selected from 20 Turkish pop fast songs	Tablet pc (probably with built-in speaker)
	Taper 2017	Their selected music	MP3 player with speaker
	Schaal 2021	Selected from 4 music lists with different types of music (jazz, classical, lounge, meditation music) without lyrics.	MP3 player with headphones
	Karaca 2022	Selected music (chosen 1 of 2 toys)	Toys with speaker*
	Mou 2020	Selected from 3 music libraries (classical, light, folk music)	Headphones (built-in sound source)
	Celikol 2019	Selected from 3 songs	Earphones (Sound source: NR)
	Fleckenstein 2022	Selected their desired style of music or artist	Smart speaker
Music medicine (researcher-selected)	Raghibi 2018	Nature alongside music	Laptop PC with headphones*
	Arts 1994	Appealing and distracting music (the same for all children-contemporary, up-beat music)	Earphones (Sound source: NR)
	Gerceker 2019	Slow music	Virtual reality headset*
	Nouira 2020	Music	Headphones (Sound source: NR)
	Sahiner 2016	Music of cartoon	NR
	Shahabi 2007	Music	NR
	Press 2013	Song	Headphones (Sound source: NR)

	Zengin 2013	Turkish classical music (‘Acemis¸ iran’ in Turkish)	Probably with speaker (Sound source NR)
	Hoseini 2019	Music	Music video (auditory devise: NR)*
	Balan 2009	Indian instrumental classical music (Hindustani classical music – instrumental – raaga-) ‘Todi’	Walkman with earphones
	Ikenoue 2020	Mozart’s “Sonata for two pianos in D major, K.448,”	Tablet PC with headphones
	Kishida 2019	Mozart music	Tablet PC with earphones
Music therapy	Hartling 2013	Music chosen by a music therapist	iPod with speaker
	Jacquier 2021	Music program composed by musicians, scientists, and music therapists	(Probably sound source: tablet PC) With headphones
	Alemdar 2023	Music selected by a classical music therapist	Music pillow
Sounds with linguistic meaning	Kishida 2019	Radio news	Tablet PC with earphones
Sounds without linguistic meaning	Ikenoue 2020	White noise	Tablet PC with headphones
	Aghbolagh 2020	Sounds from nature such as a flowing river, waterfall, walking through the forest, sea, and bird songs	MP3 player with headphones
	Gerceker 2019	Sound hearing in riding roller coaster	Virtual reality headset*

* Indirectness was downgraded by one rank when assessing confidence because visual stimuli were involved. Abbreviations: CD, compact disc; PC, personal computer; NR, not reported.

Supplemental Table 8. Intervention and outcome details for each study

Publication	Interventions in detail				Outcomes
	Treatment A	Treatment B	Treatment C	Treatment D	of interest
Aydin 2017	**Music medicine (patient)** **+ distraction card** During phlebotomy process, the children were asked to choose one of song stored in a tablet pc and music is playing, and the researcher asked the children about what they could see on the cards.	**Music medicine (patient)** During phlebotomy process, the children were asked to choose one of 20 Turkish pop fast songs stored in a tablet pc, which was then played throughout the phlebotomy process.	**Distraction card** The distraction cards consisted of 5 × 8 cm visual cards with various pictures and shapes. The children were given the opportunity to examine the cards, and then the researcher asked the children about what they could see on the cards. Distraction with the cards began immediately prior to phlebotomy and continued until the procedure had been completed.	**No treatment** The children in this group were allowed to keep their family nearby. The routine blood taking procedure was conducted.	**Pain:** Wong-Baker FACES pain rating scale
Tapar 2017	**Music medicine (patient)** Patients were asked about their music preferences before peripheral venous cannulation and listened to their selected music during the procedure (music was played for five minutes using speakers linked to an MP3 player.	**No treatment** No action was performed during peripheral venous cannulation.	**Valsalva maneuver** Patients were instructed to perform Valsalva maneuver just before peripheral venous cannulation: patients were asked to inhale deeply and then hold their breath after application of the tourniquet. cannulation was performed during this time. Patients were asked to resume breathing after cannulation.		**Pain:** VAS pain score **Distress:** VAS anxiety score
Aghbolagh 2020	**Sounds without linguistic meaning** Listening distraction was started five minutes prior to hemodialysis, and the older patient listened to the selected sounds from nature such as a flowing river, waterfall, walking through the forest, sea, and bird songs using headphones and an MP3-player considering a 25–50 dB sound volume calibrated by an audiologist. The	**No treatment** Received routine care during three consecutive hemodialysis sessions.	**Visual distraction** Initially five min before starting hemodialysis, natural and eye-catching images consisting of the images of sea, birds, and animals were broadcasted through a video display device on a laptop monitor in a manner that was easy for the older patient to watch while they were lying on the bed.		**Pain:** NRS

	distraction technique was continued for three consecutive hemodialysis sessions.				
Arts 1994	**Music medicine (researcher)** Appealing and distracting music (the same for all children-contemporary, up-beat music) via earphones. The music was begun just before the cannulation procedure.	**No treatment** The placebo cream which was indistinguishable from EMLA in appearance, smell and cosmetic characteristics, were applied according to the instructions (a thick layer under an occlusive permeable dressing) at least 1 hour before intravenous cannulation.	**EMLA cream** The EMLA creams were applied according to the EMLA cream instructions (a thick layer under an occlusive permeable dressing) at least 1 hour before intravenous cannulation.		**Pain:** Visual analogue toy
Balan 2009	**Music medicine (researcher)** Indian instrumental classical music (Type of music: Hindustani classical music – instrumental – raaga-) 'Todi': was played with the walkman.	**Only wearing headphones** RB applied placebo cream (2.5g) consisting of 100% petroleum jelly to the local body part with an occlusive dressing for 45 min. Earphones attached to a 'Walkman' was applied to the child's ears for 15 min before the procedure, through the procedure and for 5 min thereafter. However, no music was played.	**EMLA cream** EMLA cream (lidocaine 2.5% and prilocaine 2.5%) was applied. (placebo cream was not used for local application.)		**Pain:** VAS **AE**

Çelikol 2019	**Music medicine (patient)** The children were made to listen to one of the three songs intended to attract the children's attention through earphones, and the blood draw procedure was conducted when the children were busy listening. The children were made to listen to music or watch a video at least for 5 minutes before and during the procedure until the end of procedure.	**No treatment** Parents were allowed to accompany their children, but no pain-reducing intervention of any kind was applied in the blood testing room of the pediatric department. This was the usual procedure in the blood testing room.	**Video** The children were made to watch to a video they preferred among three different cartoons through 3D glasses, and the blood draw procedure was conducted when the children were busy watching.		**Distress:** Fear of Medical Procedures Scale
Schaal 2021	**Music medicine (patient)** Four music lists with different types of music (jazz music, classical music, lounge music, meditation music) were provided by the researchers for the intervention. Each patient selected one type of music genre she wanted to listen to during surgery. Music was carefully selected following recommendations described elsewhere. To prevent confounding effects caused by emotion-evoking texts, only instrumental music without lyrics was used. All participants wore noise-cancelling supra-aural headphones, connected to an mp3-player.	**Only wearing headphones** All participants wore noise-cancelling supra-aural headphones, connected to an mp3-player. In order to blind the medical staff, also the members of the control group wore headphones that were connected to the mp3-player.			**Distress:** VAS
Jacobson 1999	**Music medicine (patient)** Subject listened to music according to the technique of using music for distraction outlined by Mc Caffery. The subject selected one of 11 CDs that were representative of different musical styles. The type of music the CDs represented (eg, jazz, country) was explained to the	**No treatment** Subjects had the IV inserted by the usual method, without additional interventions.	**Intradermal injection of normal saline** An intradermal injection of normal saline solution		**Pain:** VAS **Distress:** VAS **AE:** Cannulation failure

	subject if needed. The subject chose a particular track from the CD, or played the beginning track, on a Craig portable compact disc player, with Sony Dynamic Stereo Headphones. The music treatment began after the subject signed the consent form and just before the investigator started the IV insertion. Subjects adjusted the volume to their liking, and listened to the music during the entire IV catheter insertion procedure.				
Hsieh 2017	**Music medicine (patient)** Children received the cognitive intervention before the placement procedure. The pre-placement intervention measures included providing the proposed educational photo book on IV placement (i.e.,Detective Conan) and explaining the contents of each page in the photo book within 10-15 minutes, thereby guiding the participants in comprehending the aims and procedure of IV placements. Allowing the children to watch or listen to their favorite music videos was an intervention measure used to divert their attention during the IV placement procedure, thereby mitigating their pain and fear. Before the IV placements were administered, the researchers discussed with the participants regarding their favorite songs, inviting their primary care providers to participate in the discussion. According to the children's selections, their preferred music videos were played from YouTube during the intervention. Immediately before the procedure, the children started to listen to the music	**No treatment** Children received routine care; specifically, before the IV placements were administered, the participants were verbally informed regarding the placement aims and procedure, and, after the placement, they were educated about care procedures.			**Pain:** NRS **Distress:** NRS

	videos that they had selected (total time: 5–10 minutes); the volume was controlled within a range of 40–60 dB.				
Karaca 2022	**Music medicine (patient)** Each child in the intervention group was given a choice to play with 1 of 2 toys with bee and rabbit figures. These toys appeal to all age groups, although they are attractive for the 4 to 6 age group. These toys dance to the music playing during the movement. They distract children with the music and lights flashing around them during the dance. The toys were introduced to the children by the researcher 5 to 10 minutes before the procedure. Children were asked to choose one, and they were allowed to play with the toy of their choice. The toy was	**No treatment** Standard care was maintained for the children in the control group. In many hospitals in Turkey, no pharmacological or non pharmacological methods are routinely used to reduce pain, fear, or anxiety during IV puncture procedure. Parents are allowed to stay with the child during the procedure. In this study, all parents stayed with their children during the IV insertion procedure.			**Distress:** Children's State Anxiety Scale

	placed on a hard surface in front of the bed or on the bed. After the child was asked to choose whether to perform the procedure lying down or sitting, the toy was placed in the child's line of sight to let them concentrate on the toy. The IV insertion procedure was carried out at least 5 to 10 minutes after the child concentrated on the toy. During the procedure, the child was allowed to take the toy and look at the lights and movements.				
Ikenoue 2020	**Music medicine (researcher)** During the music period, the participants started listening to music through the headphones eight minutes before the start of the cannulation procedure and underwent a puncture while listening to music. The music used was Mozart's "Sonata for two pianos in D major, K.448," which is known to have the "Mozart effect" as validated by multiple music therapy studies.	**Sounds without linguistic meaning** During the white noise period, participants similarly listened to white noise			**Pain:** VAS **Cost** **Distress:** VAS **AE**
Shabandokht-Zarmi 2017	**Music medicine (patient)** A few pieces of familiar Persian folklore/traditional/soothing music were initially selected by the experimenter on the basis of patients' social and cultural background, and were then offered to the music group during a session before the intervention. The music group listened to their self-selected and preferred music using an MP4 player through an headphone 6 minutes before needle insertion into a AVF until the end of venipuncture procedure. Each participant was asked to concentrate on the music and ignore everything else.	**Only wearing headphones** Subjects wore a headphone alone without listening to music 6 minutes before needle insertion into a AVF until the end of venipuncture procedure.	**No treatment** The control group did not receive any intervention from the research team during needle insertion into an AVF.		**Pain:** VAS

Hoseini 2019	**Music medicine (researcher)** Subjects listened to video music played using the same tablet computer from one minute before to one minute after the IV puncture procedure.	**No treatment** usual care	**Riddle solving** Video puzzle solving group		**Pain:** The Wong-Baker Scale
Momenabadi 2021	**Music medicine (patient)** Before playing the music, the child's parents were asked about favorite song in the area of approved songs and his/ her favorite song was played within the determined time limit.	**No treatment** Subjects did not receive any intervention and only the usual procedure of IV insertion was carried out.	**Hugo point massage** Subjects received a Hugo point massage before IV insertion.		**Pain:** Ocher's pain score **Cost**
Raghibi 2018	**Music medicine (researcher)** In order to distract the patients during insertion of AVF needle, images related to nature alongside music were presented using a laptop and headphone for 30 minutes. Specifically, the patients lied in a semi-seated position, the laptop was placed on the table ahead of the patients, and its monitor was opened towards them. Then, a headphone was provided to the patients, and music and images were presented to them. The music and images were presented for half an hour. Ten minutes after beginning the music, fistula needle insertion was performed.	**No treatment** Vaseline cream were employed by the researcher for 60 minutes before AVF insertion by as large as around 5 cm2 on the needle insertion site. A bandage was then placed on it. Next, Vaseline cream was cleared off the skin surface, the needle placement site was disinfected with Betadine, and then arterial needle insertion was performed.	**Arnica ointment** Arnica ointment were employed by the researcher for 60 minutes before fistula insertion by as large as around 5 cm2 on the needle insertion site. A bandage was then placed on it. Next, Arnica ointment was cleared off the skin surface, the needle placement site was disinfected with Betadine, and then arterial needle insertion was performed.		**Pain:** VAS
Mou 2020	**Music medicine (patient)** In addition to routine nursing care, music listening was performed during PICC placement procedure (generally 30min) and delivered by the researchers using wireless headphones with memory card slot. The music was selected by reviewing the literature about music therapy. A slow rhythm, low tone, soothing melody with 60-80	**No treatment** Routine nursing care			**Distress:** Numeric visual analog anxiety scale

	beats/min or less was chosen. Researcher set up three music libraries, including classical music, light music, and folk music; these belong to melodious music with pleasant rhythms, which has shown to yield a calming effect and a sense of well-being, and each music library consisted of 10 pieces of music. The patients selected their preferred music, a controlled volume (45-60dB) and listened through a wireless headphone.				
Hartling 2013	**Music therapy** Music was chosen by a music therapist and administered through an iPod dock. All participants listened to the same recordings via ambient speakers in the following order: The Planets Op. 32 Jupiter, Storms in Africa, Disco Beat, and Sunny Days. The volume of the music was set in advance and was the same for each child. Children listened to the music until the procedure was completed; in some cases, children did not listen to all 4 selections. Both groups received standard care. For both groups, there were no restrictions around whether the parent could be present or how they interacted with their child during the procedure.	**No treatment** Standard care (including topical anesthetics and techniques that staff would normally use to comfort the child such as talking to the child, explaining what is being done, and saying comforting and supportive things)			**Pain:** Faces Pain Scale–Revised **Distress:** STAI
Jacquier 2021	**Music therapy** Patients listened to music via headphones. The musical source we used was Music Care, a software commonly used in the intensive care unit and other medical fields.	**No treatment** The routine catheter insertion procedure			**Pain:** VAS **Distress:** VAS **AE**

Gerceker 2019	**Music medicine (researcher)** By wearing the virtual reality headsets, individuals can take an underwater tour with 12 different marine animals with slow music.	**Sounds without linguistic meaning** By wearing the virtual reality headsets, individuals feel as if they are getting on and riding a rollercoaster.	**No treatment** No additional procedure		**Pain:** VAS **Distress:** The Child Fear Scale
Nouira 2020	**Music medicine (researcher)** Ten minutes listening music by headphones	**No treatment** The same care without listening music.			**Pain:** VAS **Distress (**not reported) **AE (**not reported)
Sahiner 2016	**Music medicine (researcher)** The music of cartoons that are watched mostly by children aged 6–12 years. Fifteen cartoons in total were used in the room where blood was taken, and the kids were asked to which cartoon the music belonged. It was skipped to another song when the kids recognized the music. This process continued while blood was taken.	**No treatment** Routine blood taking procedure	**Distraction cards** The distraction cards consisted of visual cards of 5 x 8 cm2, covered with various pictures and shapes. In this method, the children carefully examined the cards, then the researcher asked some questions about those cards to be answered by the children, such as 'How many ladybugs are there in the picture?' and 'How many apes are there in the picture?' or 'Can you see the comet?' The distraction procedure via distraction cards began just before the phlebotomy and continued until the procedure was complete.	**Balloon inflation** The kids were given whatever color balloons they wanted. They were asked to inflate the balloon before process and kept on inflating after the process was concluded, at which time the kids were given the balloons they inflated.	**Pain:** Wong-Baker FACES pain rating scale
Shahabi 2007	**Music medicine (researcher)** Music from playing music with appropriate children's lyrics	**No treatment** Usual care	**EMLA cream** EMLA cream		**Pain:** Wong and Baker's self-report criteria
Press 2013	**Music medicine (researcher)** The experimental condition included uncertainty reduction together with active distraction. (1) Uncertainty reduction: one of the two attending nurses	**No treatment** Usual care			**Pain:** VAS

	participating in the study told the patient the following message: "Today you and I will do everything to make you feel good during the test. I'll show you can help yourself feel good". (2) Active distraction: the child was showed a pair of head-phones, was asked what they were, was offered to touch them, and instructed to put them on his/her ears. The child was then told: "I'll put a song on for you, listen to it until the end, and wait for a question about it". This was intended to produce active listening and more cognitive demands during the distraction. After hearing the song (and completing the venipuncture) the nurse asked the child a question about the song's content (the same question for all children in the experimental condition).				
Zengin 2013	**Music medicine (researcher)** All port catheter placement procedures were performed in the surgical intervention room of the emergency department, in which a music system had previously been established. Subjects listened to Turkish classical music (‘Acemisiran’ in Turkish) from the time when they were taken into the surgical intervention room until the procedures had been completed.	**No treatment** Usual care			**Pain:** VAS **Distress:** STAI
Kishida 2019	**Music medicine (researcher)** Wearing headphone and listening to Mozart music	**Sounds with linguistic meaning** Wearing headphone and listening to Radio News program			**Pain:** VAS **Distress:** VAS **AE**
Fleckenstein 2022	**Music medicine (patient-selected)** Patients were allowed to choose their desired style of music or artist. The music was played in the angio suite	**No treatment** No detailed description			**Distress:** STAI **AE**

	on a wireless stereo sound system established for that purpose exclusively (smart speaker). Sound volume was set to be around 50 dB.				
Alemdar 2023	**Music therapy** The music therapy application began 10 min before the painful procedure and continued during and after the procedure for a total of 20 min with a 'music pillow"(Creatone music pillow). The time, length, and frequency of the intervention were chosen based on the minimal data available. Classical music listened to by the study group in the research was a short piece chosen with nearly 60-beat tempo, without dramatic moments, disturbing chords and mismatched minors, and in a major key selected by a classical music therapist in line with expert opinion and the literature. The piece was slow and had soft movement. Additionally, acalm mental state was present in the piece.	**No treatment** Children did not have any non-pharmacological method applied. Adolescents received routine care practiced in the intensive care unit.	**Hand massage** the hand massage practice began 10 min before the painful procedure and continued during and after the procedure for a total of 20 min. The researcher was trained in the practice of massage. Massage began with the right hand and continued with the left hand. Classic massage techniques were used for hand massage. The massage began on the back of the hand and after effleurage 5 times for the whole back of the hand with the palm, effleurage was performed on each finger singly from the end joints to the bottom joints. Later palm massage began. For palm mas-sage, the researcher supported the patient's hand with their free hand and performed effleurage for the whole palm to the wrist with their other hand. After effleurage ended, surface friction was applied with the thumb to the finger joints and bottom joints. After friction, petrissage was performed for the tenar and hypotenar muscle groups with the fingers. Later general effleurage was performed for the hand and the massage was ended		**Pain:** Wong-Baker FACES Pain Rating Scale **Distress:** Children's Fear Scale **AE**

Abbreviation: VAS, visual analog scale; NRS, numerical rating scale; HD, hemodialysis; AE, adverse events; IV, intravenous; PICC, peripherally inserted central venous catheter; STAI, State-Trait Anxiety Inventory; EMLA, emulsion of lidocaine and prilocaine

Supplemental Table 9. Direct and pooled comparisons and rankings for self-reported pain

1. Music medicine (researcher-selected)	.	-0.09 [-1.79; 1.62]	-0.33 [-1.07; 0.41]	.	**-0.61 [-0.97; -0.26]**	**-3.18 [-4.33; -2.03]**
0.02 [-0.71; 0.76]	**2. Music therapy**	.	.	.	**-0.79 [-1.44; -0.14]**	.
-0.09 [-1.79; 1.62]	-0.11 [-1.97; 1.74]	**3. Sounds with linguistic meaning**	.	.	.	.
-0.20 [-0.81; 0.40]	-0.23 [-1.12; 0.66]	-0.12 [-1.92; 1.69]	**4. Sounds without linguistic meaning**	.	**-0.81 [-1.58; -0.04]**	.
-0.33 [-0.85; 0.20]	-0.35 [-1.12; 0.42]	-0.24 [-2.02; 1.55]	-0.12 [-0.85; 0.61]	**5. Music medicine (patient-selected)**	**-0.52 [-0.94; -0.11]**	-0.84 [-1.94; 0.26]
-0.76 [-1.10; -0.42]	**-0.79 [-1.44; -0.14]**	-0.67 [-2.41; 1.06]	-0.56 [-1.17; 0.05]	**-0.44 [-0.84; -0.03]**	**6. No treatment**	0.18 [-0.91; 1.28]
-1.80 [-2.57; -1.03]	**-1.82 [-2.82; -0.83]**	-1.71 [-3.58; 0.16]	**-1.60 [-2.54; -0.65]**	**-1.47 [-2.27; -0.68]**	**-1.04 [-1.80; -0.28]**	**7. Only wearing headphones**

Effect sizes are presented as standardized mean difference (SMD) and 95% confidence interval. Treatments are ranked from best to worst along the leading diagonal. Estimates from pairwise and network meta-analyses are depicted above and below the leading diagonal, respectively. In the network meta-analysis results, statistically significant differences are highlighted by underlining. The areas bordered by red lines show comparisons between different acoustic stimulations.

Supplemental Table 10. Direct and pooled comparisons and rankings for mental distress

1. Music medicine (researcher-selected)	-0.21 [-1.33; 0.91]	-0.28 [-2.36; 1.80]	.	.	.	-1.17 [-2.30; -0.04]
-0.04 [-1.13; 1.04]	**2. Sounds without linguistic meaning**	.	.	.	.	-1.70 [-3.31; -0.09]
-0.28 [-2.36; 1.80]	-0.23 [-2.58; 2.11]	**3. Sounds with linguistic meaning**	.	.	.	.
-0.67 [-2.12; 0.78]	-0.63 [-2.24; 0.99]	-0.39 [-2.92; 2.14]	**4. Music therapy**	.	.	-0.57 [-1.52; 0.37]
-0.70 [-1.95; 0.55]	-0.65 [-2.09; 0.78]	-0.42 [-2.85; 2.01]	-0.03 [-1.15; 1.09]	**5. Music medicine (patient-selected)**	-0.20 [-1.80; 1.41]	-0.54 [-1.15; 0.06]
-0.89 [-2.93; 1.14]	-0.85 [-3.00; 1.30]	-0.62 [-3.52; 2.29]	-0.22 [-2.18; 1.73]	-0.20 [-1.80; 1.41]	**6. Only wearing headphones**	.
-1.24 [-2.34; -0.15]	-1.20 [-2.50; 0.11]	-0.96 [-3.31; 1.39]	-0.57 [-1.52; 0.37]	-0.54 [-1.15; 0.06]	-0.35 [-2.06; 1.36]	**7. No treatment**

Effect sizes are presented as standardized mean difference (SMD) and 95% confidence interval. Treatments are ranked from best to worst along the leading diagonal. Estimates from pairwise and network meta-analyses are depicted above and below the leading diagonal, respectively. In the network meta-analysis results, statistically significant differences are highlighted by underlining. The areas bordered by red lines show comparisons between different acoustic stimulations.

Supplemental Table 11. Individual study results in outcome of adverse events (for all studies) grouped by treatment comparison

Study	Events	Total	Events	Total	Risk ratio [95%CI]
Music medicine (researcher-selected) vs Only wearing headphones					
Balan 2009	0	50	0	50	Not estimable
Music medicine (researcher-selected) vs Sounds without linguistic meaning					
Ikenoue 2020	0	117	0	117	Not estimable
Music medicine (patient-selected) vs No treatment					
Jacobson 1999	10	36	10	36	1.00 [0.47, 2.11]
Music therapy vs No treatment					
Jacquire 2021	3	36	1	35	2.92 [0.32, 26.72]
Music medicine (researcher-selected) vs Sounds with linguistic meaning					
Kishida 2019	0	4	0	4	Not estimable
Music medicine (patient-selected) vs No treatment					
Fleckenstein 2022	0	61	0	55	Not estimable

Supplemental Table 12. Report of confidence in network meta-analysis: self-reported pain.

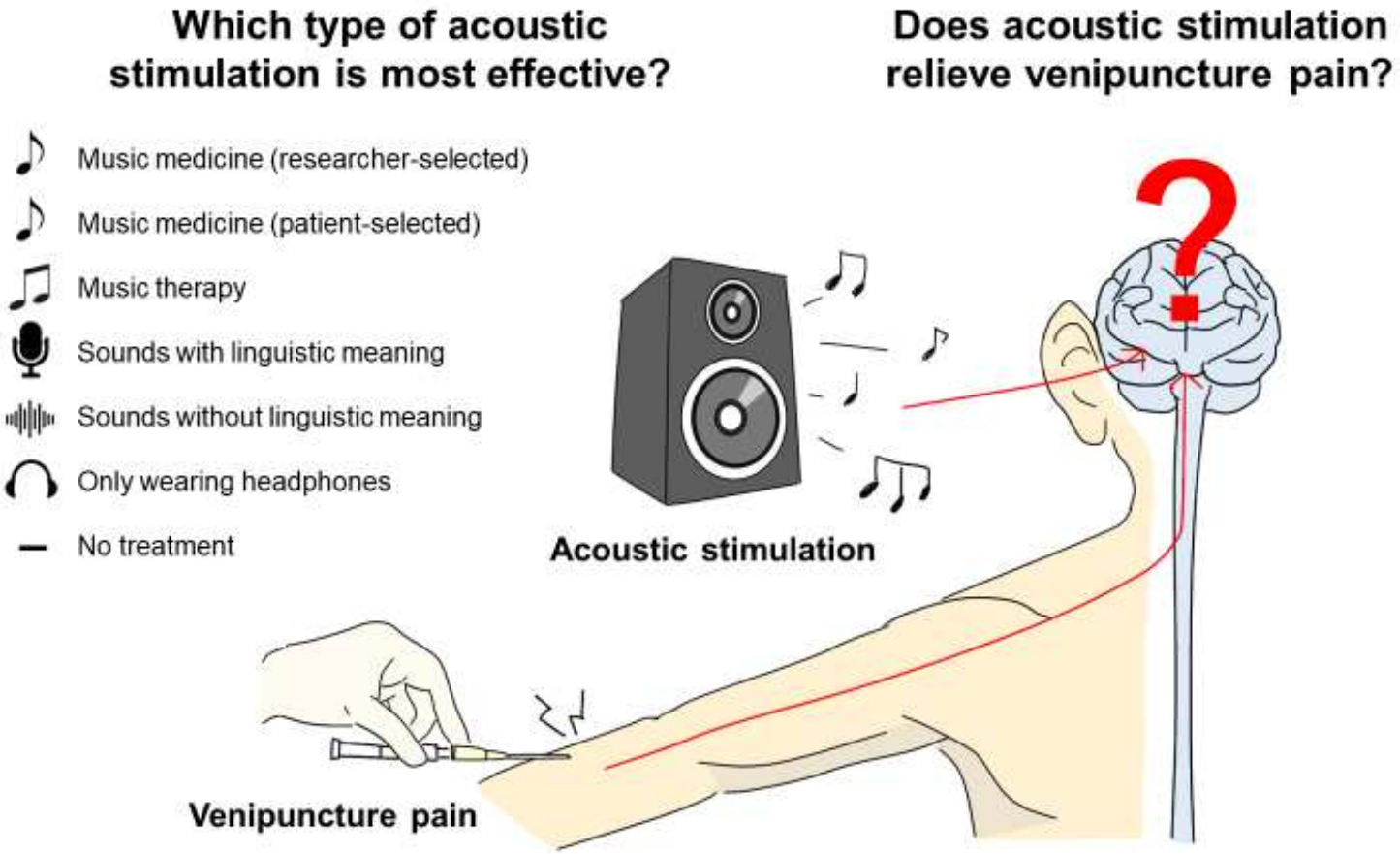
Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Music medicine patient-selected:No treatment	7	Major concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	Low
Music medicine researcher-selected:No treatment	8	Major concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Low
Music therapy:No treatment	3	Major concerns	Low risk	No concerns	No concerns	No concerns	Some concerns	Low
No treatment:Only wearing headphones	1	Major concerns	Low risk	No concerns	No concerns	No concerns	Major concerns	Very low
No treatment:Sounds without linguistic meaning	1	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
No treatment:Sounds with linguistic meaning	0	No concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	Low

Supplemental table 13. Global test based on a random-effects design-by-treatment interaction model

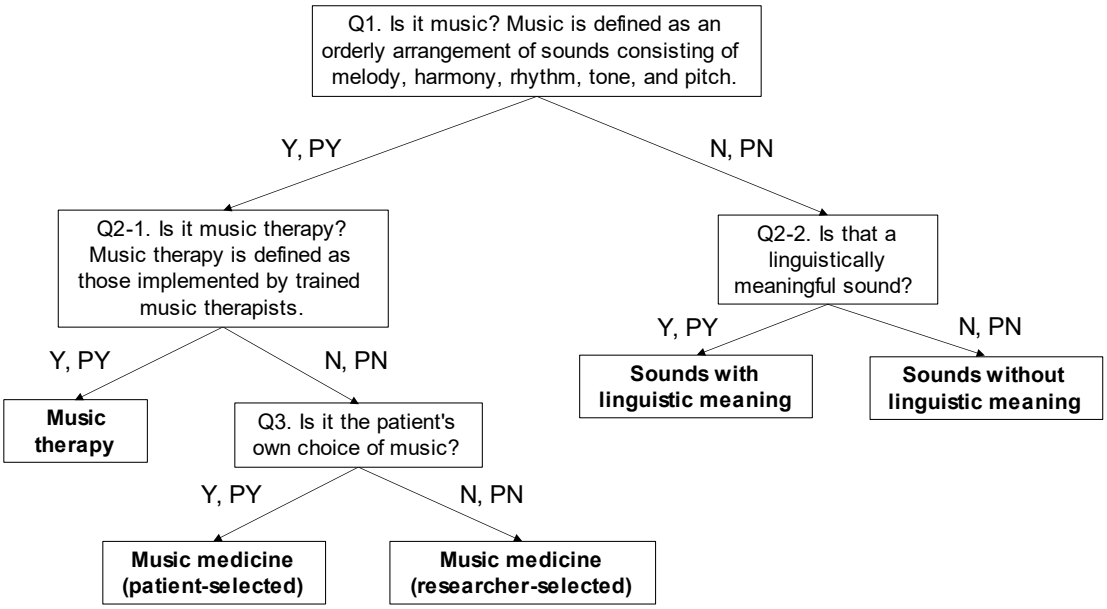
Outcome	$\chi 2$ statistic	P value
Self-reported pain	20.945 (5 degrees of freedom)	0.001
Self-reported pain (Balan 2009 excluded)	5.637 (4 degrees of freedom)	0.228
Self-reported distress	1.073 (2 degrees of freedom)	0.585

Supplemental Table 14. Report of confidence in network meta-analysis: self-reported distress

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Music medicine (patient-selected):No treatment	7	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Music medicine (researcher-selected):No treatment	2	Major concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Low
Music therapy:No treatment	3	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
No treatment:Sounds without linguistic meaning	1	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
No treatment:Only wearing headphones	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
No treatment:Sounds with linguistic meaning	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

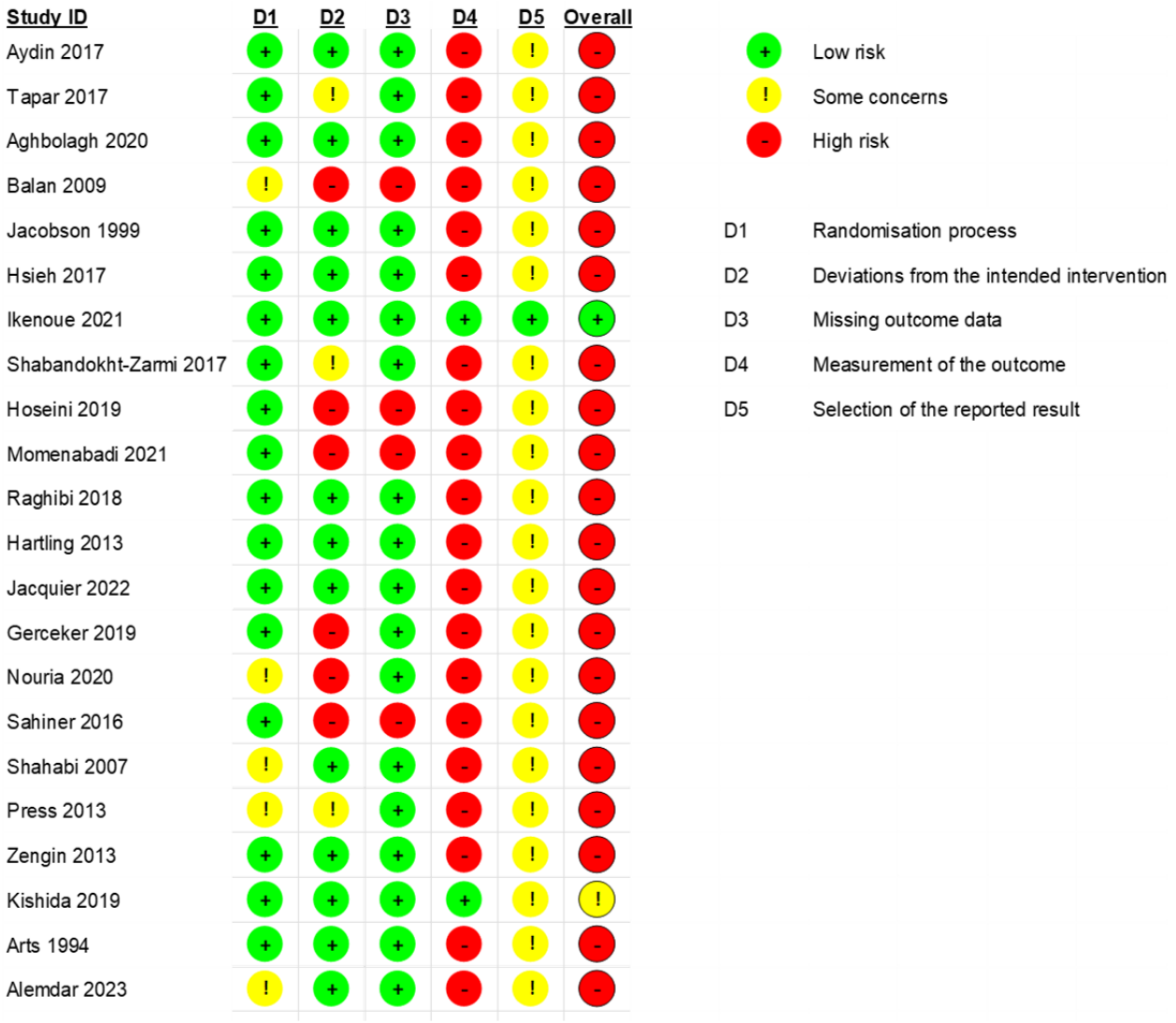


Supplemental Figure 1. Conceptual diagram of the research questions for this study.



Supplemental Figure 2. Flow chart to classifying the acoustic stimulations into 5 groups

Abbreviations: Y, yes; PY, probably yes; N, no; PN, probably no.

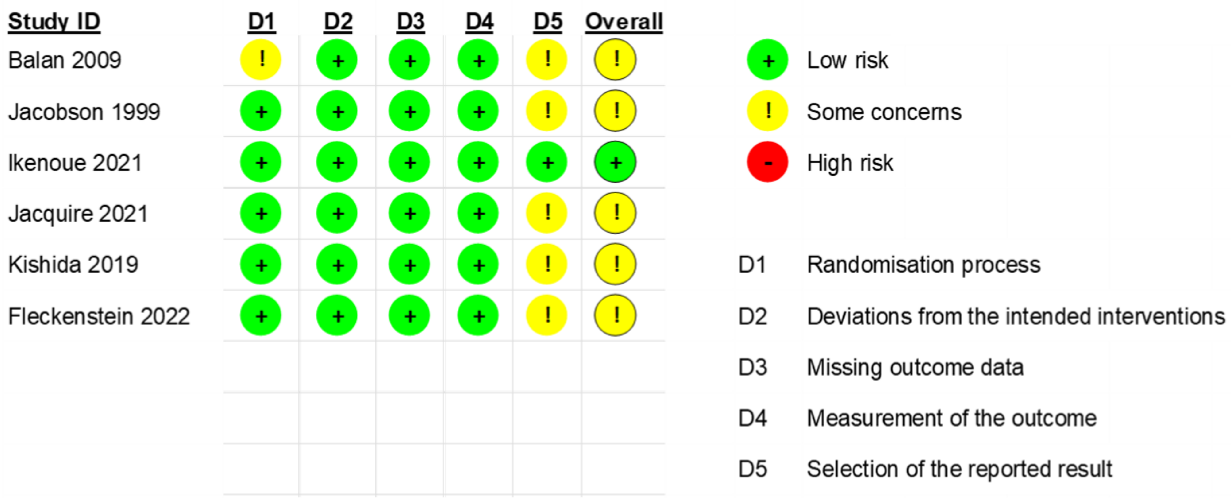


Supplemental Figure 3. Risk of bias for outcome of self-reported pain

"D" denotes "Domain".

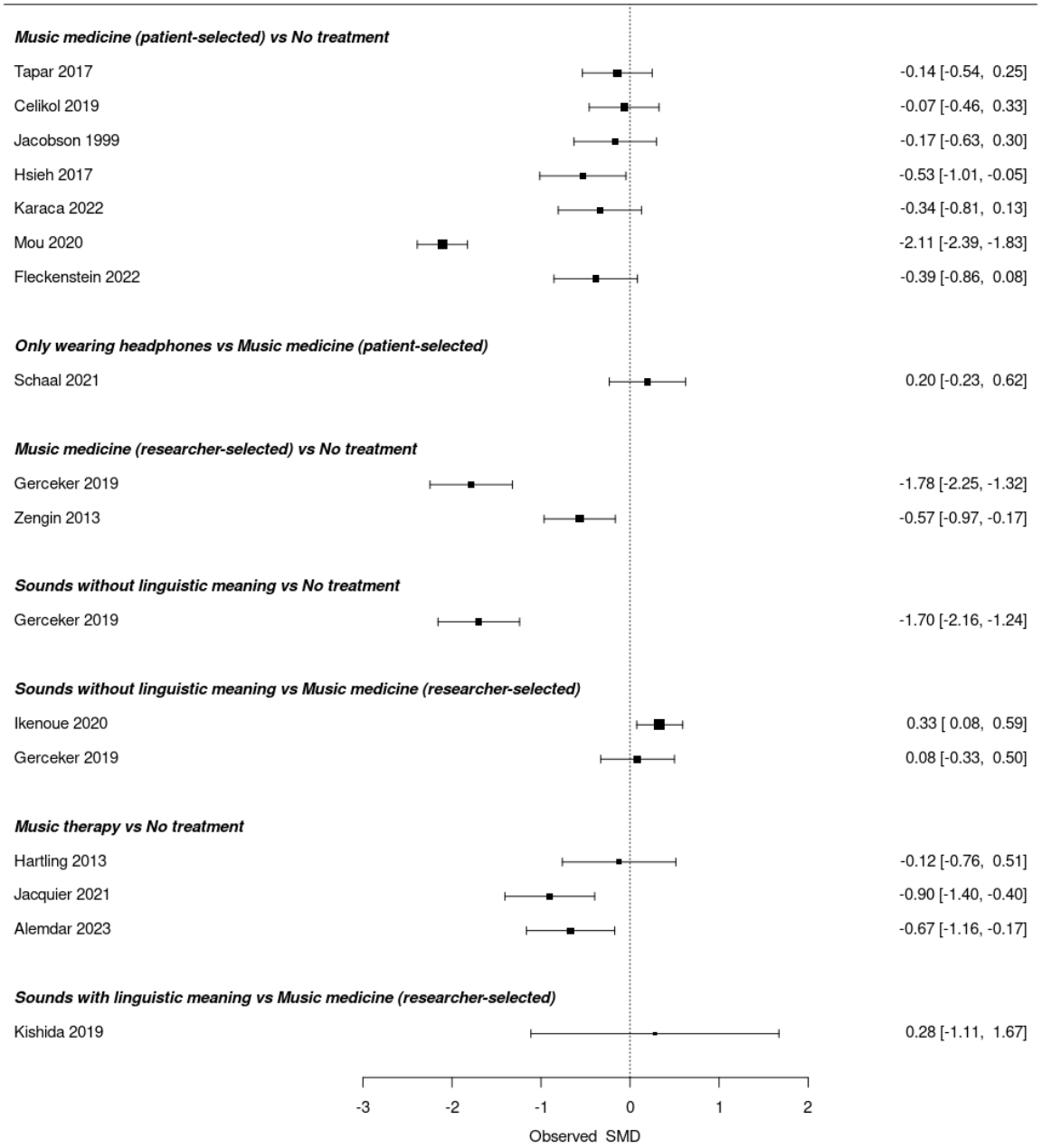
Supplemental Figure 4. Risk of bias for outcome of self-reported mental distress

"D" denotes "Domain".

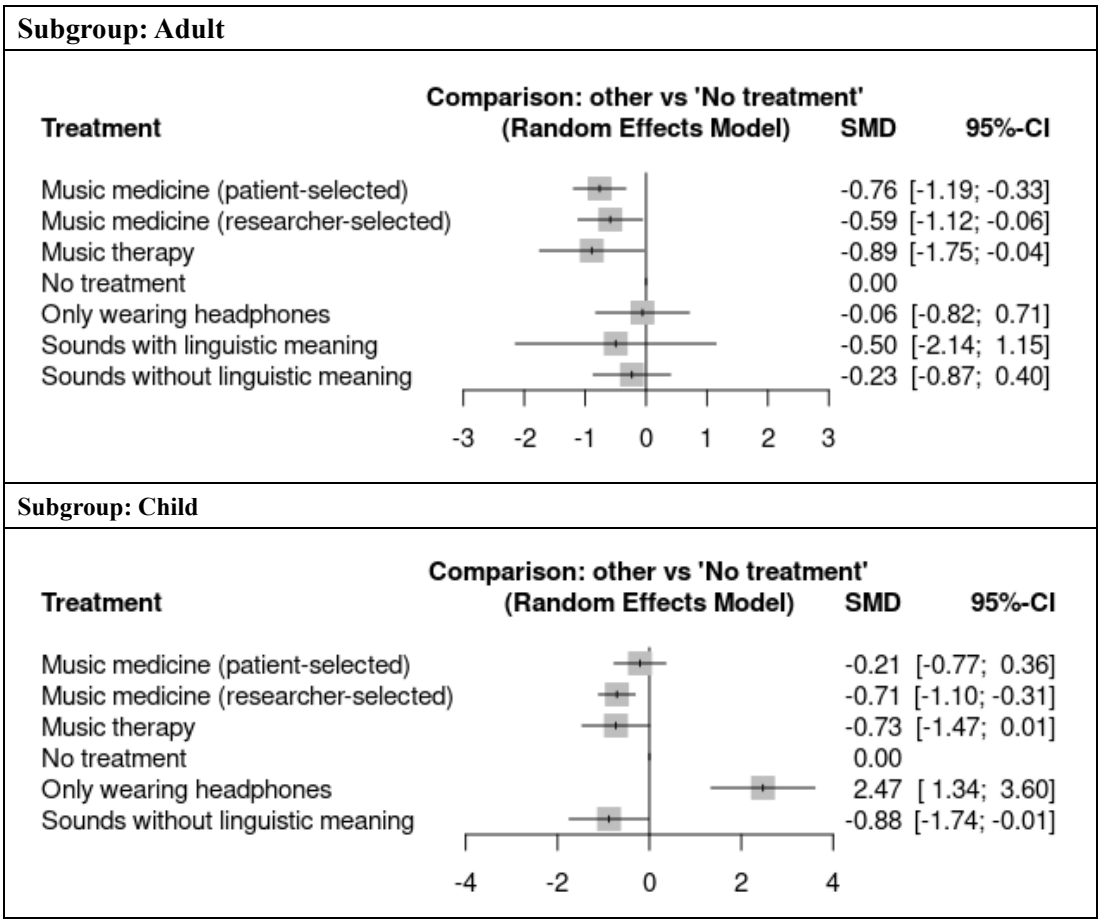


Supplemental Figure 5. Risk of bias for outcome of adverse events

"D" denotes "Domain".

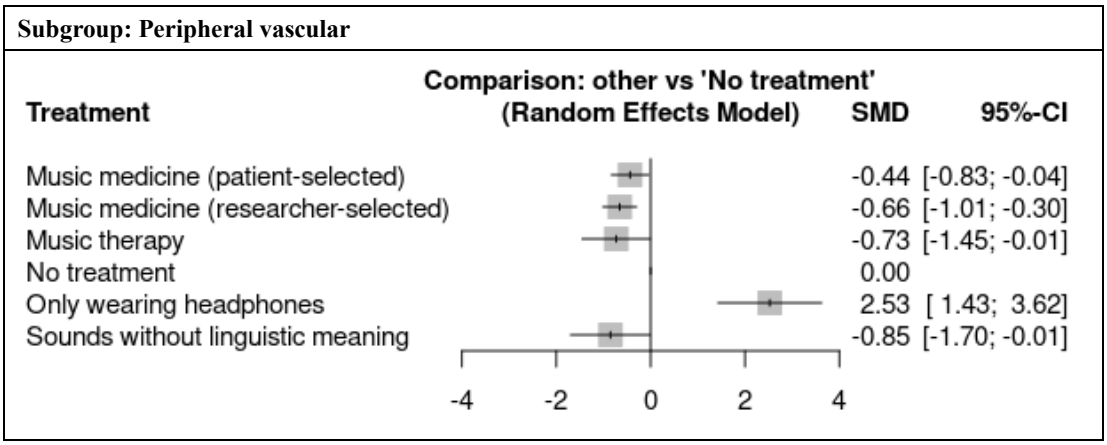


Supplemental Figure 6. Individual study results in outcome of self-reported mental distress (for all studies) grouped by treatment comparison



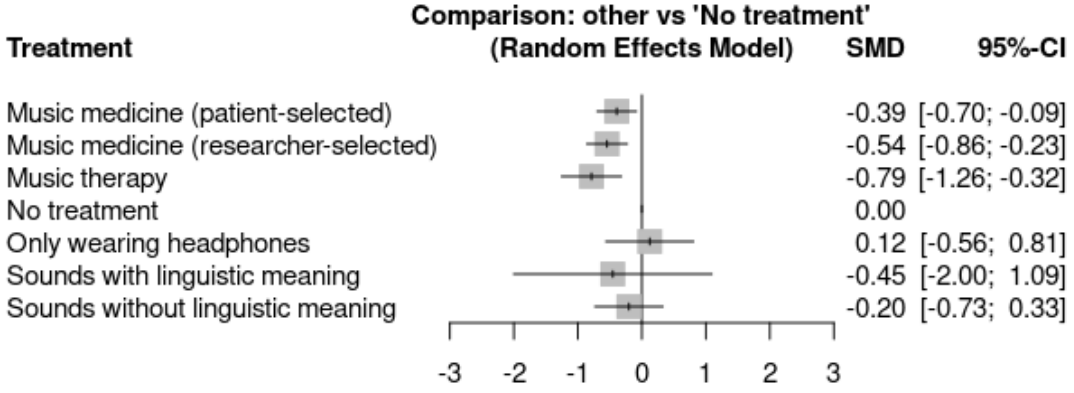
Supplemental Figure 7. Results of subgroup analysis divided into adults or children

There were 10 studies for 896 adults, and 10 studies for 1140 children, defined as < 18 years old. Outcome: self-reported pain.



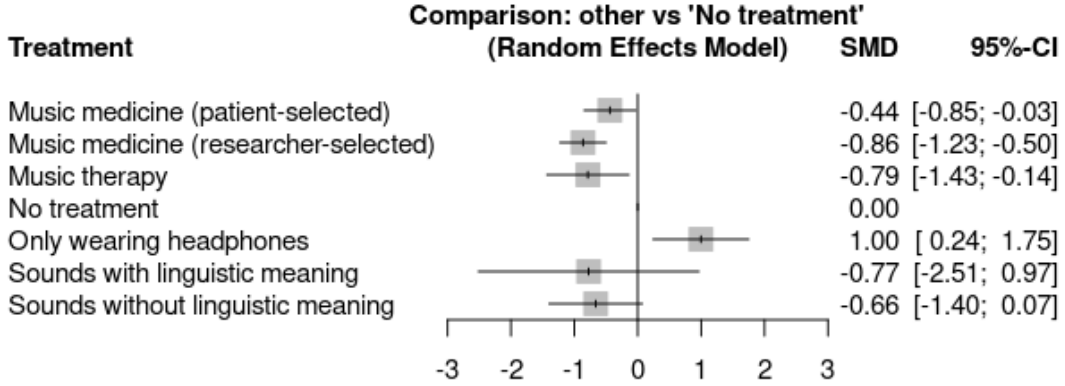
Supplemental Figure 8. Results of subgroup analysis by type of venipuncture technique

There were 15 studies for 1,612 peripheral cannulation. There were 5 studies for 489 dialysis access cannulation. Subgroups of dialysis vascular access and indwelling CV catheter were difficult to consider due to small number of studies. Outcome: self-reported pain.



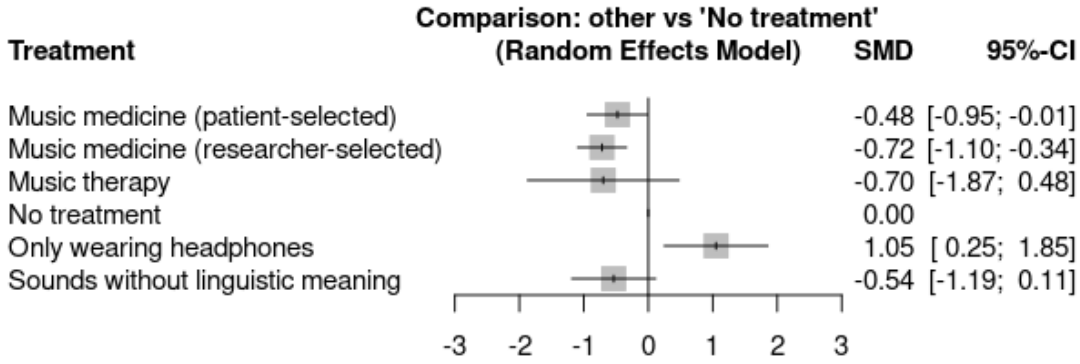
Supplemental Figure 9. Sensitivity analysis excluding high risk of bias study

For D4 in risk of bias evaluation, only studies with SMD > 2 (suspected to have a particularly high risk of bias) were defined as High and calculated; 6 studies (Balan 2009, Hoseini 2019, Momenabadi 2020, Gerceker 2020, Nouira 2020, Sahiner 2016) were excluded.



Supplemental Figure 10. Sensitivity analysis excluding studies that did not report the standard deviation of self-reported pain

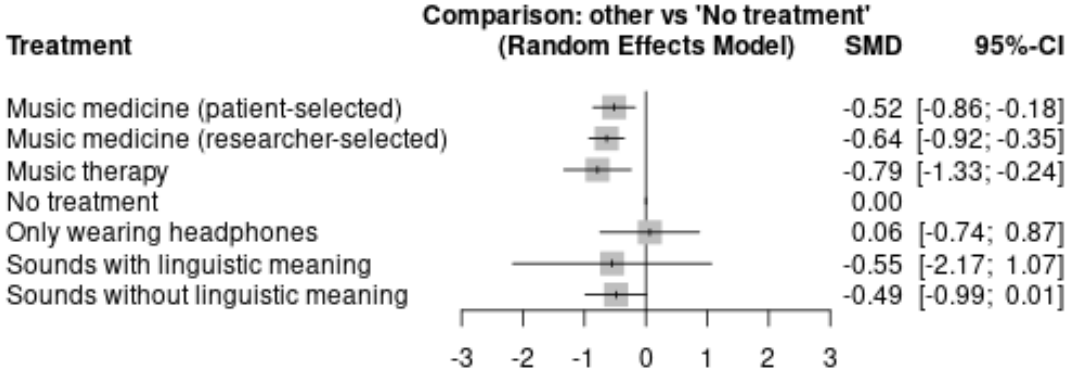
Two studies whose SD were imputed (Aghbolagh 2020 and Arts 1994) were excluded.



Supplemental Figure 11. Post-hoc sensitivity analysis excluding studies with small number of subjects

Five studies with fewer than 25th percentile patients (Hsieh 2017, Hartling 2013, Jacquier 2022, Shahabi 2007, and Kishida 2019) were excluded.

Supplemental Figure 12. Forest plot for self-reported pain (Balan 2009 excluded)



Supplemental Information 1. PRISMA NMA checklist of items to include when reporting a systematic review involving a network meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	Page 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	Page 3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.*	Page 6
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 7
METHODS			

Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	Page 8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	Page 8-9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 9-10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 10
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 10
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 9
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	Page 10-11
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	Page 10-11
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	Page 10-11

Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	Page 11
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Page 11
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	Page 11
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 13
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	Figure 2
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	Figure 2, Supplemental Table 5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Supplemental Table 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Page 22

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	Page 23, Figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	Page 23-25
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	Page 26-27
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	Page 26-27
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	Page 26
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	Page 28-29
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	Page 29
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 30
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that	Page 31

	could affect use of treatments in the network.	

PICOS = population, intervention, comparators, outcomes, study design.

* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Supplemental Information 2. Analytical treatment of the study by Aydin et al. and basis for the evaluation of confidence

- **Analytical treatment of the study by Aydin et al.**

Aydin study included four interventions below:

1. music medicine (patient-selected) + distraction card group
2. music medicine (patient-selected) group
3. distraction card group
4. no treatment group

In order to extract the effect of music medicine (patient-selected), The study was divided into below 2 pairs in the analysis:

1. music medicine (patient-selected) group vs No treatment group (Aydin 2017[a])
2. music medicine (patient-selected) + distraction card group vs distraction group (Aydin 2017[b])

- **Basis for the evaluation of confidence**

Outcome: Self-reported pain

- ✓ Within-study bias: The within-study bias of each comparison was evaluated based on the mean score of the results of the overall bias of the ROB for each study, with score 1 for low risk, score 2 for moderate, and score 3 for high risk. For “No treatment vs Sounds with linguistic meaning”, only Kishida 2019 is involved. Although the results of the ROB evaluation of that study are some concerns, the reason is a non-significant reason that the statistical protocols are not publicly available. Therefore. we rated it as Low concerns.
- ✓ For the reporting bias, funnel plots were difficult to evaluate due to the small number of studies (less than 10). However, when the studies included in this review were evaluated individually, reporting bias was considered low risk for all comparisons because many of them assessed outcomes predetermined in the protocols and because all statistical analysis methods were simple and there was no doubt that multiple analyses were performed.
- ✓ For indirectness, the intervention was downgraded one level if it involved visual stimuli such as video as well as acoustic stimulation. However, the proportion was small, and it was considered low risk.
- ✓ For imprecision, we defined clinically important size of effect: 0.8. The Cochrane guidebook was used as reference to establish the value.
- ✓ Heterogeneity was considered as some concerns in the comparison of music medicine

(researcher-selected) vs no treatment.

- ✓ For incoherence, no treatment vs only wearing headphones was rated as very low based on point estimate of the effect size of direct and indirect comparisons.
- ✓ For the comparison of no treatment vs only wearing headphones, we rated its confidence rating as very low because there were two major concerns. For the other comparisons, its confidence rating was set to low since there was a major concern. None of the items rated as some concerns were considered to be significant in the confidence rating evaluation.

Outcome: Self-reported distress

- ✓ Within-study bias: The within-study bias of each comparison was evaluated based on the mean score of the results of the overall bias of the ROB for each study, with score 1 for low, score 2 for some concerns, and score 3 for high. For "No treatment vs Sounds with linguistic meaning", only Kishida 2019 is involved. Although the results of the ROB evaluation of that study are some concerns, the reason is a non-significant reason that the statistical protocols are not publicly available. Therefore, we rated it as low concerns.
- ✓ For the reporting bias, funnel plots were difficult to evaluate due to the small number of studies (less than 10). However, when the studies included in this review were evaluated individually, reporting bias was considered low risk for all comparisons because many of them assessed outcomes predetermined in the protocols and because all analysis methods were simple and there was no doubt that multiple analyses were performed.
- ✓ For indirectness, the intervention was downgraded one level if it involved visual stimuli such as video as well as acoustic stimulation. However, the proportion was small, and it was considered low risk.
- ✓ For imprecision, we defined clinically important size of effect: 0.8. The Cochrane guidebook was used as reference to establish the value.
- ✓ Heterogeneity was determined to be of no significant concern because the studies included in each comparison had the same positive or negative direction of effect sizes.
- ✓ For incoherence, there was no significant difference between the results of direct and indirect comparisons.
- ✓ For the comparison of no treatment vs only wearing headphones, we rated its confidence rating as very low because there were two major concerns. For the other comparisons, its confidence rating was set to low since there was a major concern. None of the items rated as some concerns were considered to be significant in the confidence rating evaluation.