Music Care, a personalized smartphone app for the relief of pain and anxiety: A Systematic Review of Randomized Controlled Trials

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Abstract

Background: Digital technologies and emerging innovations are increasingly being used to strengthen national health systems. Based on scientific recommendations, Music Care©, a web app-based personalized music intervention has been developed to provide a collection of culturally diverse original pieces composed and arranged following standardized specifications (U-Sequence). The Music Care app has been utilized in a broad variety of medical conditions and procedures to reduce anxiety and pain in patients with various diseases.

Objective: The aim of this report is to provide a review of the available evidence on the efficacy of Music Care app for the management of pain and anxiety. The specific medical context in which Music Care app has been tested is also examined to identify potential new applications and areas requiring more research.

Methods: Original English and French language randomized controlled trials (RCT) using the Music Care app were included and reviewed to summarize evidence on the effectiveness of a music intervention program in medicine. Ongoing RCT were also reported.

Results: A total of 17 RCTs were included. The majority of studies focused on chronic and acute pain conditions. Compared to the control interventions, Music Care was effective in reducing pain and anxiety in most medical contexts examined, including chronic pain, Alzheimer, and during surgeries or procedures. Significant improvements have also been found on cardio-respiratory activity, depressive symptoms, stress and burnout levels.

Conclusions: The Music Care app has proven effective in reducing pain, anxiety, depressive symptoms and stress and burnout symptoms in various medical conditions and procedures. Growing evidence suggests that the Music Care app could provide a useful digital, low-cost, portable and easy-to-implement tool as an adjuvant therapy in a broad scope of clinical situations. Potential new areas of application are discussed. Clinical Trial: Not applicable as this manuscript is a systematic litterature review

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Abstract

Background: Digital technologies and emerging innovations are increasingly being used to strengthen national health systems. Based on scientific recommendations, Music Care©, a web app-based personalized music intervention has been developed to provide a collection of culturally diverse original pieces composed and arranged following standardized specifications (U-Sequence). The *Music Care* app has been utilized in a broad variety of medical conditions and procedures to reduce anxiety and pain in patients with various diseases.

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Methods: Original English and French language randomized controlled trials (RCT) using the *Music Care* app were included and reviewed to summarize evidence on the effectiveness of a music intervention program in medicine. Ongoing RCT were also reported.

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Conclusion: The *Music Care* app has proven effective in reducing pain, anxiety, depressive symptoms and stress and burnout symptoms in various medical conditions and procedures. Growing evidence suggests that the *Music Care* app could provide a useful digital, low-cost, portable and easy-to-implement tool as an adjuvant therapy in a broad scope of clinical situations. Potential new areas of application are discussed.

Trial Registration: Not applicable

Keywords: Digital Therapeutics; Music Intervention; Music Care app; Pain; Anxiety; Depression; Neurocognitive Diseases

Introduction

Since prehistory, music has been integrated in the treatment of various diseases [1]. In the 1960s, music has been re-established with therapeutic purpose and music interventions have been used as a way of ameliorating pain and distress in patients with various medical issues [2] and particularly in the treatment of chronic and acute pain [3,4]. Effectiveness of music interventions in the treatment of pain has been reported in systematic reviews and meta-analysis. A recent meta-analysis showed that music interventions have beneficial effects on pain intensity, emotional distress, use of anesthetic and both opioid and non-opioid agents, heart rate, systolic and diastolic blood pressure and respiratory rate [2]. However, inconsistent results have been reported, possibly because of the high level of heterogeneity in music interventions between studies, with substantial differences in duration, frequency, style, genre, preparation, choice, rationale, personnel, equipment, and approach in the delivery of music intervention [2]. In order to overcome such a lack of consistency, recommendations for music interventions in clinical practice have been recently provided [5,6]. Today, three types of music interventions can be distinguished: *i)* music therapy, which uses live music (performed or created by the therapist and/or patient) and which is based on the relationship between the subject and the professional-trained music therapist; *ii)* music intervention, which consists of specific music programs proposed by caregivers; *iii)* music listening, in which patients listen to their own, self-selected music. The attention to personal musical preferences and cultural background is considered one of the main characteristics of a successful musical intervention [7], and it takes part to a broad process that includes assessment, treatment, and evaluation [5]. In music interventions using specific music programs, sessions should last between 20 and 60 minutes, music should be “slow and flowing”, approximately 60 to 80 beats per minute, and instrumental (non-lyrical), and it should consist primarily of harmonic variations. Patients should place themselves in a relaxed position (i.e., lying or recumbent) and use closed headphones combined with an eye mask

[8]. Finally, even if it is often nurses that apply music recordings, the consultation with or the supervision by a professional trained music therapist is strongly encouraged.

Based on such recommendations, a standardized web app-based music intervention has been developed at the University Hospital of Montpellier, France: the U-shape composing sequence. The musical sequence varies from 20 to 60 minutes and is divided into several stages that progressively enable the patient to relax according to the technique of a mounting U [9-12]. The downward phase of the U-sequence is based on the reduction of musical rhythm, orchestral complexity, frequency and volume, to induce increasing relaxation. A maximum relaxation phase (lower part of the "U") is followed by a re-energizing phase (ascending limb of the "U") (Figure 1).

Recent technological developments allow patient- and/or care- giver-controlled use of music-based interventions at bedside via hand-held devices. Based on the U sequence, the *Music Care* program is a smartphone-based application (app) that allows patients to listen to a variety of professionally pre-recorded music pieces of their choice. Previous studies have tested the efficacy of this app in reducing pain and/or anxiety in patients with various diseases, such as chronic and acute pain, Alzheimer’s type dementia, fibromyalgia or neurological pain [11-14].

Smartphone apps have advantages over traditional approaches, such as being low-cost, easily accessible and easy to implement on large and various populations. Digital therapeutic interventions are a new wave of smartphone apps which are rapidly growing [15]. However, their effectiveness has yet to be investigated in systematic reviews.

The aim of this review is to summarize evidence on the effectiveness of one digital therapeutic intervention, the *Music Care* app, for music interventions in medicine, and to standardize and evaluate the *Music Care* app as a useful digital tool to reduce pain and anxiety in patients. New clinical applications in surgeries and sleep disorders are also under investigation.

Methods

We conducted a comprehensive research in PubMed, Web of Science and PsycInfo databases according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2009 [16]. The keywords pain, anxiety, stress, Alzheimer Disease, neurocognitive diseases, music intervention, music therapy, *Music Care* app, web app-based music intervention, U sequence were used as appropriate. As an example, in PubMed, the following search string was applied: ((pain) OR (chronic pain) OR (surgery) OR (anxiety) OR (depression) OR (burnout) OR (stress) OR (caregivers) OR (Alzheimer disease) OR (neurocognitive diseases) OR (nursing home residents)) AND ((receptive music therapy) OR (Music Care) OR (smartphone-based music listening) OR (standardized music intervention) AND ((english[Filter] OR french[Filter]) AND (2002:2022[pdat])) AND ((y_5[Filter]) AND (humans[Filter]) AND (english[Filter] OR french[Filter])). Original studies in English and French conducted between 2003 and 2022 and related to the application of the *Music Care* app in medicine have been included. Studies were included if the *Music Care* app was implemented in any pathology, medical condition or medical procedure. Studies examining pain perception or pain modulation in healthy individuals using experimental methods were also included. Studies using any other music program were excluded. There was no limitation regarding age, gender, ethnicity, type of pain (chronic/acute) or pathology and medication use. Only randomized-controlled trials published in peer review journals have been included. Observational and pilot studies were excluded. Registered RCTs including a description of study design and preliminary results (when present) were explored to identify ongoing studies. A PRISMA flowchart presenting databases search and final selection of articles is presented in Figure 2. All members of the writing group had the opportunity to comment on the recommendations and approved the final version of this document. Following removal of duplicates, paper titles were scrutinized, those outside the scope of the review were rejected (Figure 2). The following descriptor variables were coded for each study: 1) Number of patients; 2) Age and sex; 3) Medical conditions;

4) Procedures; 5) Outcome (Table 1). The quality appraisal of studies was based on the PICOS approach (participants, interventions, control group, outcome and study design), according to PRISMA guidelines. Studies were critically analyzed to summarize existing evidence.

Figure 1. The “U” sequence: music intervention technique used.

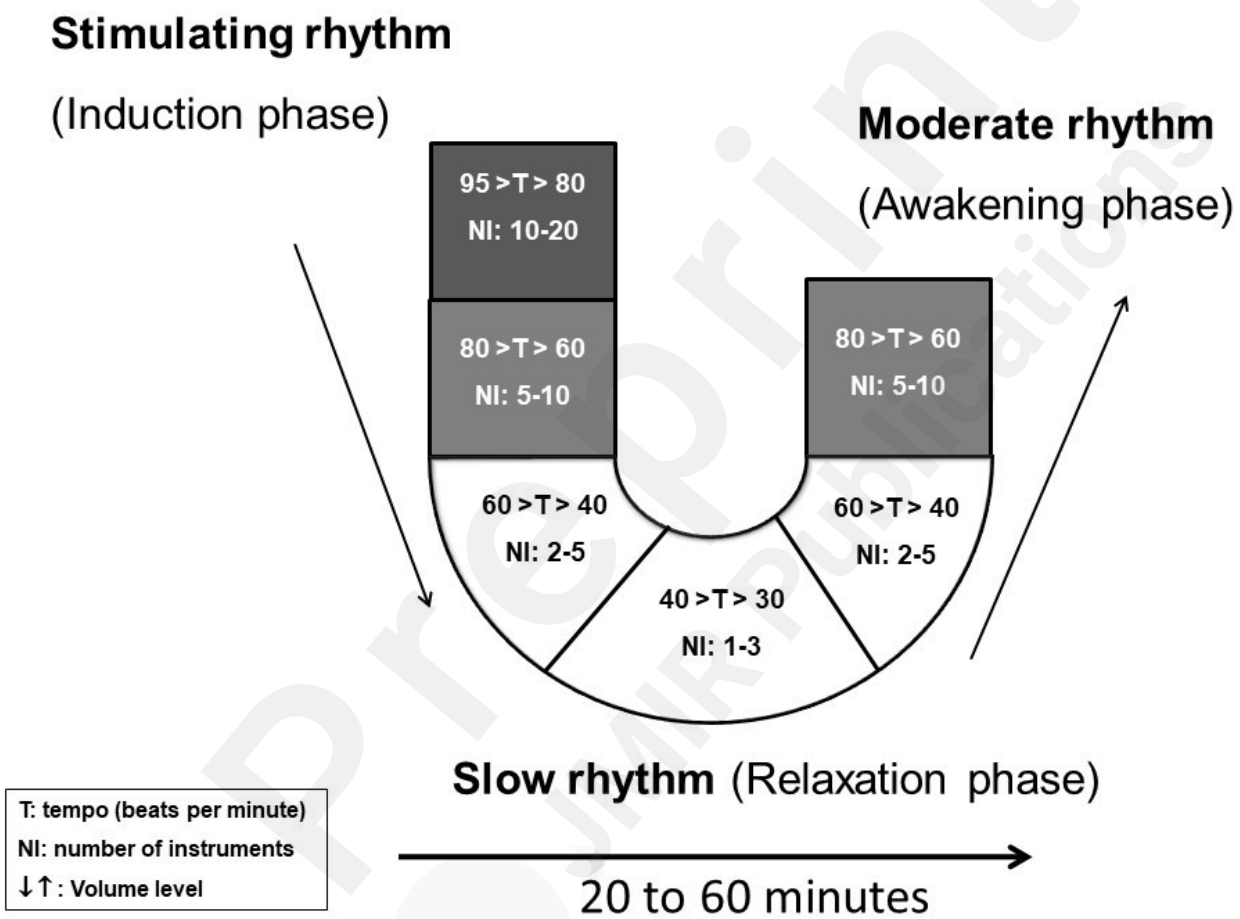
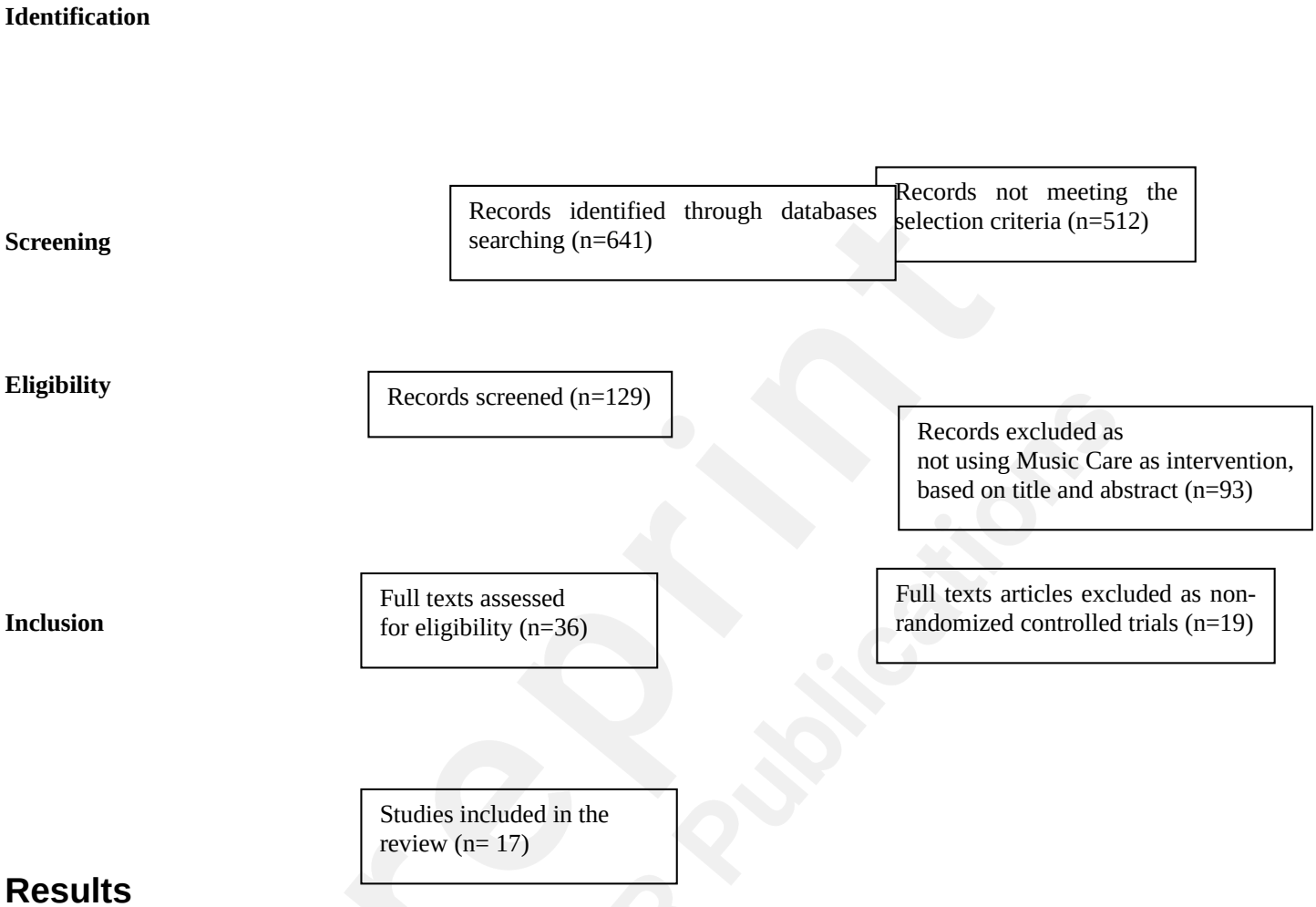


Figure 2. Flow diagram of the inclusion/exclusion process of the relevant literature with number of articles at each step.



Results

Among eligible articles and after removing the non-randomized controlled trials, a total of 17 RCTs on the application of the *Music Care* app in various medical conditions and diseases has been included. Table 1 summarizes RCTs on the application of the *Music Care* app in different medical conditions. Of 17 studies, 16 were conducted on chronic, acute procedural, or experimental pain or pain-related anxiety, and one on Alzheimer disease. Different pain conditions included chronic low-back pain, rheumatic disease, respiratory failure, pruritus, and sickle-cell disease; a number of studies were conducted on patients undergoing medical procedures such as coronary angiography, gynaecological surgery or cataract surgery, central venous catheter insertion or in intensive care unit. Depending on the study, the music intervention has been administered before, during or after the

medical procedure. In the majority of studies, the primary outcome was participants' self-reported level of pain intensity on 0-10 pain scales such as visual analog scales (VAS), numerical rating scales (NRS), and other validated pain scales. Other primary outcomes were participants' self-reported level of anxiety or discomfort intensity on 0-10 scales such as VAS, or other validated anxiety scales such as the State Trait Anxiety Inventory (STAI-Y) A scale; levels of anxiety and depressive symptoms were assessed with the Hospital Anxiety Depression scale (HAD). Levels of pain and/or anxiety were systematically evaluated before and after each intervention. In 3 studies, the consumption of medicaments or anxiolytic drugs has also been evaluated.

Effectiveness of music intervention on clinical pain

Ten RCTs evaluated the effect of the *Music Care* app on pain as the primary (n=8) or secondary (n=2) outcome, 6 of which reported a significant decrease in pain levels associated with the music intervention (see Table 1). A significant effect of music intervention on pain was reported in patients with chronic low-back pain, chronic pain, and fibromyalgia [12,13] and in adolescents with sickle-cell disease [18].

Similar results have been observed on procedural pain, in patients in reanimation [11], and in patients undergoing cataract surgery [23] and dental implant surgery [19]. The effect of the music intervention was not significant in one study on patients undergoing coronary angiography [20], in one study on patients undergoing central venous catheter insertion or dialysis [26] and in one study on critically ill patients [27]. Finally, reduced pain was reported in fibromyalgia patients following the music intervention, especially in a passive resting condition, but the improvement was generally comparable to the control condition involving listening to environmental sounds [17].

Effectiveness of music intervention on itch

A significant effect of music intervention compared to an emollient cream was reported one hour

after the intervention in patients with chronic pruritus [21].

Effectiveness of music intervention on anxiety and depressive symptoms

Levels of anxiety only or anxiety and depression were evaluated as the primary outcome in 4 studies and as a secondary outcome in 8 studies. Eight out of these 12 studies reported a significant decrease on anxiety and/or depression with the music intervention. Improvements were observed in patients with chronic pain [12,13], patients undergoing dental implant surgery [19] (trend at *P*=.07), coronary angiography, cataract surgery [19,20,22,23], and adolescents with sickle-cell disease [18]. One original study showed a significant improvement in anxiety and depression in resident of a nursing home suffering mild to moderate Alzheimer-type dementia [14]. No significant effect was found in patients with acute respiratory failure at a late measurement time, 90 days post-intervention [25], or in patients undergoing central venous catheter insertion [26]. In one study in women undergoing gynaecological surgery [24], Music Care was the control arm versus self-selected music. Anxiety significantly decreased in both arms with no significant difference in score reduction between groups. Similarly, the study on pruritus showed a small and comparable decrease in anxiety with the music intervention and the control emollient cream [21].

Effectiveness of music intervention on other outcomes

In three RCTs, a significant reduction in the consumption of anxiolytics and other drugs was found in the music group compared to the control group [13,20,22]. Reduction in agitation and improvements in several indices of cardio-respiratory activity and in the bispectral index (BIS) were also observed in patients at the ICU [11]. Similarly, improvements in heart-rate variability (Analgesia/Nociception Index; ANI) and discomfort intensity were observed in critically ill patients [27] (trend at *P*=.06 for discomfort). Similarly, a significant reduction in the incidence of hypertension related to anxiety and

a trend for a reduction of duration of cataract surgery were found in one RCT [22]. A reduction in fatigue was reported in fibromyalgia patients but similar effects were found with environmental sounds in the control condition [17].

Effectiveness of music intervention on pain induced by experimental tests

Two RCTs evaluated the effect of the Music Care app on pain induced by experimental thermal pain tests applied to the forearm in young healthy participants. One study examined nociceptive heat pain perception before, during, and after listening to the most liked music or the least liked music selected from the Music Care catalog [28]. The other examined heat and cold pain perception, temporal summation of heat pain, and conditioned pain modulation (CPM) of heat pain produced by the cold pressor test [29]. Both studies reported a significant decrease in pain during the music interventions. Soyeux and Marchand [28] also observed a significantly larger hypoalgesic effect while listening to the preferred music. Cabon et al. [29] further showed that music compared to silence produced a reduction in peak pain and in the temporal summation of pain. There was no direct interaction between the music intervention and conditioned hypoalgesia suggesting additive effects [29], but Soyeux and Marchand reported a weak but positive association between the magnitude music-induced hypoalgesia and the effect of CPM tested on a separate day without music [28].

Ongoing studies

Six RCTs are still ongoing (Table 2). These studies examine the effects of the music intervention in sickle-cell disease patients, dental, orthopedic and cataract surgeries, complex wound dressing care at home, and sleep disorders.

Table 1. Effectiveness of Music Care (MC) music intervention in chronic and acute pain.

Reference	Publication	Aim of study	Study Design and interventions	N Participants reported	Outcomes	Main Results
Guétin et al. (2005) [12]	Annales de Réadaptation et de Médecine Physique	Evaluate the effect of music intervention on pain, anxiety and depression in hospitalized patients (functional rehabilitation unit) with chronic low back pain	Randomized Controlled Trial (RCT), (12-days follow-up) 2 parallel arms: intervention group (MC), control group (standardized physical therapy alone). 4 music sessions between day 1 and day 5 for music therapy group	65 patients (49% men) with low back pain (n=33 MC, n=32 control)	Level of pain (VAS); anxiety and depression score (HAD); scores for disability (Oswesrty index); Timepoints: D0, D5 and D12.	Pain was significantly decreased after each of the 4 music sessions (P<.001); no difference on pain between groups; MC significantly reduced disability, anxiety and depression compared to control (P<.01) from D1 to D5.
Jaber et al. (2007) [11]	Annales Françaises d'Anesthésie et de Réanimation	Evaluate the effect of 20-min music session on heart and respiratory rate, pain and agitation in intubated and non-intubated patients hospitalized in intensive care unit.	RCT, cross-over, uninterrupted rest and MC	30 patients (57% men) (n=15 intubated, n=15 non intubated)	Heart rate (HR), systolic blood pressure (SBP), respiratory rate (RespR), bispectral index (BIS), agitation/sedation state (Richmond-Agitation-Sedation-Scale, RASS) and pain (Numerical Rating Scale, NRS).	Music significantly reduced HR (P<.05), SBP (P<.05), RespR (P<.05), BIS (P<.01), RASS (P<.05) and NRS (P<.01) in both intubated and non-intubated groups.
Guétin et al. (2009) [14]	Dementia and Geriatric Cognitive Disorders	Assess the effect of music intervention on anxiety and depression in patients with mild to moderate Alzheimer-type dementia from a nursing home	RCT 2 parallel arms: intervention group (MC), control group (rest and reading). Weekly sessions between Day 0 (D0) and Week 16 (W16), (follow-up assessment at 24-weeks)	30 patients (27% men, 74-95 yrs) (n=15 MC, n=15 control)	Level of anxiety (Hamilton Scale); level of depression (Geriatric Depression Scale)	Significant improvements in anxiety and depression in the MC group compared to the control group (P<.01) at W16; the difference was still significant at W24.

Guétin et al. (2012) [13]	The Clinical Journal of Pain	Assess the effect of music intervention on patients with chronic pain hospitalized at Pain Assessment and Treatment Centre from Day 0 to Day 10.	RCT (90-days follow-up) 2 parallel arms: intervention group (MC + standard of care), control group (standard of care). At least 2 sessions per day between D0 and D60, at home from D10 to D60.	87 patients (22% men, 19-84 yrs.) with chronic pain (n=44 MC, n=43 control)	Level of pain (VAS); anxiety and depression (HAD); consumption of medication	MC significantly reduced pain, anxiety and depression (*P*<.001) at D60 and at D90 and reduced the consumption of anxiolytic agents, compared to control group.
Mercadie et al. (2015) [17]	Pain Management Nursing	Evaluate the effects of music intervention on patients with fibromyalgia at home evaluated in active (while carrying out a physical activity) or passive (at rest) situations.	RCT Free access of MC or environmental sounds (control intervention) for 28 days.	22 patients with fibromyalgia (100% women)	Level of pain (VAS); level of fatigue (VAS)	Decreases in pain and fatigue were generally observed after *both* the MC and control environmental sounds (*P*=.001), with the largest effect observed for MC on pain in the passive listening condition (-22%). A significant 3-way interaction was also found with the intervention (*P*=.03) but there was no clear indication that MC produced significantly larger effects than the control environmental sounds on pain or fatigue.

Messika et al. (2019) [25]	European Respiration Journal	Determine the effect of music intervention on respiratory discomfort during non-invasive ventilation (NIV) at ICU in patients with acute respiratory failure	RCT (90-days follow-up) 3 parallel arms: intervention group (MC), sensory deprivation group (headphones without any music), control group (nothing). Intervention once the NIV session was initiated, for all NIV session, until NIV discontinuation, day 28 or ICU discharge.	113 patients (55% men, 57-76 yrs) (n=36 MC, n=38 sensory deprivation group, n=39 control group)	Respiratory discomfort; anxiety and depression (HAD); Peri-traumatic Distress Inventory (PDI)	PDI was significantly reduced in MC versus controls at ICU discharge (*P*=.03); No significant difference in respiratory discomfort and anxiety and depression at follow-up (D90) between groups.
Demirtas et al. (2020) [21]	Journal of the European Academy of Dermatology and Venereology	Evaluate the effects of music intervention on pruritus at dermatology department of the University Hospital	RCT 2 parallel arms: intervention group (MC), control group (emollient). One music session.	50 patients (62% men, 20-93 yrs) with various chronic skin diseases (n=25 MC, n=25 emollient group)	Evolution of pruritus (NRS) before and one hour after intervention; anxiety (STAI-Y A Scale)	The intensity of pruritus decreased more in MC group compared to the emollient group (*P*<.05). A decrease in anxiety was found in both groups, with no statistically significant difference between groups.
Martin et al. (2020) [18]	Soins Pediatrie/ Puericulture	Evaluate the effect of a music intervention in adolescents with sickle-cell disease hospitalized for a vaso-occlusive crisis	RCT 2 parallel arms: intervention group (MC), control group (exercise of regular breathing). One music session.	20 sickle-cell adolescents (55% men) (n=10 MC, n=10 control group)	Level of pain (VAS); level of anxiety (STAI-Y A Scale)	Significant reduction in pain and anxiety in MC compared to the control group (*P*<.05).
Reynaud et al. (2021) [24]	Trials	Compare the effect of two music interventions in women before gynaecologic surgery	RCT 2 parallel arms: intervention group (personal music playlist), control group (MC). One music session 1h before surgery.	171 women (n=84 personal music playlist, n=84 MC)	Level of presurgical state anxiety (STAI)	Both interventions significantly reduced anxiety (*P*<.001). MC produced a larger mean effect (-19%) compared to self-selected playlist (-14%) but the difference was not statistically significant (*P*=.22).

Guerrier et al. (2021) [22]	JAMA Ophthalmology	Describe the effect of music intervention on the incidence of anxiety-related hypertension in patients during cataract surgery	RCT 2 parallel arms: intervention group (MC), control group (noise-cancelling headphones without music). One music session 20 min before surgery.	310 patients (43% men) (n=155 MC, n=155 control group)	Occurrence of anxiety-related hypertensive event during surgery; level of anxiety (VAS); mean number of anxiolytic drugs; duration of surgery	MC significantly reduced anxiety (*P*=.005), the incidence of hypertension related to anxiety (*P*<.001), and the mean number of sedative drug injections (*P*<.001) compared to control group. A trend in reduction of duration of surgery was found in MC compared to control group (*P*=.07).
Boccara et al. (2021) [20]	Music and Medicine	Assess the effect of music intervention on drug consumption level, pain and anxiety in patients undergoing coronary angiography	RCT 2 parallel arms: intervention group (MC), control group (standard of care). One music session during surgery.	76 patients (87% men, 40-86 yrs) (n=54 MC, n=22 control group)	Level of pain (VAS); level of anxiety (anxiety numeric scale, NRS, and Amsterdam Preoperative Anxiety Score, APAIS); consumption of medicaments during coronary angiography	Significant reduction on anxiety (*P*<.01) but not in pain score in MC compared to the control group; significant reduction on midazolam dose (*P*<.01) in MC compared to the control group.
Guerrier et al. (2021) [23]	Frontiers in Pharmacology	Assess the effect of music intervention on pain and anxiety in patients undergoing cataract surgery	RCT 2 parallel arms: intervention group (MC), control group (noise-cancelling headphones without music). One music session 20 min before surgery.	243 patients (47% men) (n=119 MC, n=124 control group) This is a subset of patients from Guerrier et al. (2021) [22].	Level of pain (numerical rating scale, NRS); level of anxiety (VAS)	Significant lower anxiety (*P*<.001) and pain score during surgical procedure and before discharge (respectively, *P*=.03 and *P*=.04) in MC compared to the control group.
Cabon et al. (2021) [28]	Music Perception	Assess the effect of music intervention on experimental thermal pain and on pain modulation produced by temporal summation and condition pain	RCT counterbalanced crossover design with two conditions, one with a self-selected music session (music condition M) and one in silence (no-music condition N)	27 healthy volunteers (52% men) (14 under MN sequence, 13 under NM)	Level of pain (VAS and VNS) produced by 120s of noxious contact heat on the right forearm before and after 120s of a cold pressor test (CPT) applied to the contralateral arm; peak of first heat pain (PP), temporal summation of heat pain (TS), and magnitude of conditioned pain	Mean pain ratings (VAS and VNS), PP and TS were significantly lower with music listening (*P*<.002); pain reduction by CPM was not affected by the music intervention (*P*=.88, ns) but results suggest additive effects

		modulation (CPM)			modulation produced by the CPT on heat pain (difference between heat pain before vs after the CPT)	of music and CPM.
Bertacco et al. (2022) [19]	Journal of Dentistry	Evaluate the effect of music intervention on burden of care during dental implant surgery	RCT 2 parallel arms: intervention group (MC), control group (audiobook). One music session during surgery.	24 patients (33% men) (n=12 MC, n=12 control audiobook group)	Burden of care, a composite outcome including self-reported anxiety, pain, and dissatisfaction rated immediately and 1 week after the surgery (VAS), retrospectively; Affect (Self-Assessment Manikin)	Significant reduction on burden of care (*P*=.02); significant lower pain (*P*=.02) and a trend for reduced anxiety (*P*=.07) in MC compared to the audiobook group; positive affect reported after surgery in both groups (ns group effect) but music described as more relaxing (*P*=.002) and pleasant (*P*=.001).
Jacquier et al. (2022) [26]	Anesthesia and Analgesia	Assess the effect of music intervention on anxiety and pain in patients during central venous catheter insertion or a dialysis at ICU	RCT 2 parallel arms: intervention group (MC), control group (standard care). One music session during surgery.	72 patients (54% men) (n=37 MC, n=35 control group)	Level of anxiety (VAS); level of pain (VAS), after catheter insertion	No significant difference in anxiety and pain between groups
Merliot-Gailhoustet et al. (2022) [27]	Critical Care	Evaluate the effect of digital interventions music and including virtual reality on common stressful patient symptoms experienced in ICU	RCT Crossover design with four conditions, standard relaxation (TV/radio), music therapy (MC), and two virtual reality systems using either real motion pictures (DEEPSEN©) or synthetic motion pictures (HEALTHY-MIND©)	60 patients (67% men) (50 underwent the 4 sessions)	Discomfort intensity (NRS), level of pain, anxiety, dyspnea, thirst, lack of rest (NRS), ANI (electrophysiological measure of heart-rate variability indexing the balance between parasympathetic and sympathetic outflow related to the stress response)	Decrease on lack of rest symptom (*P*=.05) and improvement in ANI (*P*<.01) were observed after MC with no statistically significant difference with standard relaxation. A trend in reduction of dyspnea was found in MC compared to standard relaxation (*P*=.06). Adverse effects were documented (e.g. dizziness) but none involved MC.
Soyeux and	Frontiers in Pain	Assess the effect of	RCT;	33 healthy adults	Level of pain (VAS) produced by 120s	Overall, significant reduction in

Marchand (2023) [28]	Research	music intervention on experimental pain induced by thermal stimulation; compare the effects of music to the effect of conditioned pain modulation (CPM) to test possible shared mechanisms	Two experimental conditions; 20 minutes of listening to Most-Liked Music (MLM) and Least-Liked Music (LLM) on Day 2 and 3 (MLM and LLM crossover with order of MLM and LLM randomized across participant); CPM is tested separately on Day 1 with no music	(39% men, 18-34 yrs) (17 under MLM-LLM sequence, 16 under LLM-MLM)	of noxious contact heat applied to the non-dominant forearm at baseline, at 2.20 min after the music started; after the relaxation phase at 11.30 min and after the whole 20-min cycle; perception of time; magnitude of heat pain modulation produced by conditioned pain modulation induced by the cold pressor test to the contralateral arm	mean pain perceptions under LLM and MLM conditions compared to baseline pre-intervention (*P*=.009 and *P*<.001, respectively); Reduction was more important under MLM condition than under LLM condition at 2.20 min (*P*=.046) and at 11.30 min (*P*=.04). No difference between conditions at 20 min. Perception of time significantly shorter under MLM than LLM (*P*=.02). Music hypoalgesia at 2.20 min was modestly correlated to pain modulation by CPM in the LLM (r=.36, *P*=.047) and MLM (r=.35, *P*=.06, ns).

Table 2. Ongoing clinical trials using the *Music Care* app.

Reference	Aim of study	Study Completion Date	Type of study	N Participants	Parameters
NCT03639805	Test the effect of music intervention on pain in vaso-occlusive crises in sickle-cell disease patients	April 2020	RCT	40 patients	Daily mean morphine consumption during the first 3 days of hospitalization; level of anxiety (VAS); anxiety and depression (HAD)
NCT03925571	Assess the effect of music intervention on post-surgical pain in dental care and its effect on anxiety during surgery	April 2020	RCT	68 participants	Level of pain (VAS) after dental surgery; level of anxiety (STAI) during dental surgery
NCT04578860	Demonstrate effectiveness of music intervention on sleep disorders in general population	December 2020 (estimated)	RCT	120 participants	Sleep quality (Pittsburgh Sleep Quality Index, PSQI)
NCT04038593	Evaluate the feasibility of implementing *Music Care* app in the care of complex dressings at home	December 2022 (estimated)	RCT	250 patients	Level of pain (NRS) after the intervention; level of anxiety (NRS) before and after the intervention; time needed for the care.
NCT04781231	Assess the contribution of *MusicCare* app on patients' anxiety during cataract surgery with topical local anesthesia	May 2022 (estimated)	RCT	411 participants	Level of anxiety (VAS) before and after music intervention
NCT05015985	Assess the effect of this music therapy program delivered by application compared to usual playlist music on drug consumptions and physiological parameters, pain, anxiety levels in patients undergoing forearm orthopedic surgery under locoregional anesthesia	April 2023 (estimated)	RCT	80 participants	Sedative requirement during the intraoperative period, level of anxiety (VAS) and pain before and after music intervention, satisfaction score

Discussion

Principal Results

We aimed to summarize evidence on the effectiveness of the *Music Care* app in various medical conditions and procedures. Randomized Controlled Trials showed that *Music Care* app was primarily efficient in reducing levels of anxiety in a broad range of chronic and acute pain conditions. Anxiety is a core component of chronic pain conditions and recent evidence suggests a strong association between anxiety or depression, which commonly appear together, and chronic pain [30]. It is likely that pain may causes feelings of anxiety, which in turn can increase pain sensitivity, thus leading to a persistence of the pain experience [31]. Moreover, the presence of anxiety leads to a lower tolerance for pain which is more difficult to treat; similarly, pain has a negative impact on the prognosis of psychiatric diseases, with pain leading to more treatment resistance [32-35]. Interestingly, music interventions with the *Music Care* app significantly reduced self-reported levels of chronic and acute pain in the majority of studies. Such results are consistent with other reviews and meta-analysis reporting significant effects of music interventions on pain, emotional distress and the use of analgesic, opioid and non-opioid agents [2]. Follow-up assessments also reported a persistent significant effect at day 60 [13,25]. During medical surgery, the utilization of the *Music Care* app reduced the consumption of anxiolytics and analgesics and the duration of medical procedure [13,20,22]. Furthermore, studies demonstrated that *Music Care* app reduced pain and anxiety level before and during the procedure. Importantly, one study further demonstrated clinically meaningful improvement in cardio-respiratory activity in critically ill patients taken in charge in an ICU setting [11, 27], while another reported a reduced incidence of hypertension during cataract surgery [22]. These effects are consistent with the notion that the improvement produced by music on self-reports of anxiety and pain are mediated by basic neurophysiological mechanisms affecting emotions and nociceptive responses and may help reduce the risk of cardiovascular instability during invasive medical procedure.

Music Care app has also been evaluated on pain induced by experimental tests to assess endogenous pain control mechanisms. The advantage of this approach is the precise control of the pain stimuli, the possibility to calibrate stimuli to control for individual differences in pain sensitivity, and the possibility to assess the effect of music on endogenous pain modulation processes. Results suggested that music listening reduced pain perception and the temporal summation of pain, a phenomenon operating at the dorsal spinal cord level [29]. This is consistent with the involvement of inhibitory/facilitatory descending pain modulatory mechanisms previously shown to be associated with the positive/negative emotional valence of music [36,37] or visual stimuli [38-40]. Notably, one previous study using emotional pictures also indicated that pain and nociceptive spinal responses were modulated in the same direction by emotional valence (i.e. less pain and nociception under pleasant vs unpleasant condition), but that visual distraction decrease pain and may *increase* the spinal response [41]. This valence effect is consistent with the larger hypoalgesic effect observed in response to the most liked music [28]. Interestingly, music-induced hypoalgesia produced additive effects with the CPM [29] and was weakly but positively associated with the magnitude of the CPM effect [28]. Taken together, these effects are consistent with the possible activation of descending inhibitory control mechanisms by pleasant music. These emotion-related effects demonstrate that music is not merely a distractor and may further reduce other negative affective states beyond pain.

In Alzheimer Disease, music intervention with the *Music Care* app successfully reduced anxiety and depressive levels. The majority of individuals suffering from neurodegenerative diseases also presents anxiety and depressive symptoms [42,43], which are often the first signs of cognitive disorders and are correlated with faster progression to dementia [42,44,45]. Anxiety is a modifiable risk factor for AD and dementia in longitudinal studies [46] and it has been associated with

disability in social functioning [47] and resistance to treatment [48]. However, anxiety is particularly difficult to treat in the cognitively impaired and older population, because of comorbid medical problems, important side effects of medication and reduced self-expression in the elderly, so that the presence of “quiet” anxiety often remains undetected. According to the literature, symptomatic treatments have limited evidence for use in anxiety, and non-pharmacological treatments such as environmental approaches are highly encouraged [48]. Among them, the utilization of music interventions in the elderly with neurocognitive diseases is recommended [49,50], with specific music programs required for nursing homes. Consistent with this recommendation, a pilot cross-over RCT conducted in elderly residents of a nursing home with mild to moderate cognitive impairments compared MC to a no music condition and to an active control condition involving music from the 1960s to the 1990s played on a national radio station [51]. MC significantly reduced refusal of care and pain and increased the residents’ satisfaction. Duration of toileting was also significantly reduced (median duration of 12 min) compared to music control (20 min) and no music (18 min). Therefore, an implementation of the *Music Care* app for nursing homes may constitute a simple and cost-effective intervention to improve the resident’s well-being. This application deserves more attention in future research.

Methodological considerations and limitations

Across the studies detailed in this article, multiple designs and control intervention have been evaluated. With few exceptions (e.g. [27]), the most frequent design in clinical studies was parallel arms which is the easiest to put in place whatever the pathology and does not need to control for possible carry-over and order effects that complicates the interpretation of cross-over trials. Regarding the control arm, Music Care has been compared with standard of care, self-selected playlist, audiobook, environmental sounds, or rest. The superiority of Music Care + Standard care vs Standard care alone has been demonstrated in chronic pain conditions [13]. The results of

Bertacco [19] indicate that Music Care is also superior to an audiobook intervention, which is consistent with the notion that music provides more than auditory distraction. However, other types of audio stimulation used as control might provide some benefits. Interestingly, Music Care was used as a control condition in one study on presurgical anxiety and produced significant improvement, with a slightly larger effect (ns) compared to a self-selected playlist [24]. Similarly, environmental sounds produced comparable decrease in pain and fatigue in fibromyalgia [17], a finding that should be further investigated to specify how different kinds of environmental sounds may compare to music, and whether their integration with music may improve the overall benefits. Taken together, the results confirm the improvements provided by Music Care and suggest that other forms of auditory stimulation might also provide some benefits.

Limitations include the heterogeneity in study designs (e.g. control condition), populations, and clinical conditions, which did not allow performing a meta-analysis. Many other observational studies and pilot studies on the application of the *Music Care* app exist, which were not included in this review because they did not meet the inclusion criteria. For future research, more RCTs are required to increase the methodological rigor of studies and the reliability of results. Studies including physiological measurements provide promising results in the context of medical procedures, but such studies generally require large samples to detect a reduction in the risk of hemodynamic instability (e.g. n=310 in Guerrier et al., 2021 [22]) because these adverse events generally have a low rate of occurrence in well-controlled surgical contexts using standard care. Systematic follow-up assessment is also indicated especially in chronic conditions to determine long-term benefits. Furthermore, given the observed benefits on anxiety, the utilization of the *Music Care* app in other medical conditions involving mental health challenges may constitute an interesting avenue for future research.

Another aspect that appears neglected in the assessment of music interventions is the rate of individuals who might dislike or be indifferent to musical interventions, and the occurrence of

possible adverse effects. Documenting the reasons for refusal to participate in studies on music interventions might provide some insight on the absolute rate of potential patients that might benefit from such intervention. The appreciation of music is also highly variable between individual with congenita amusia affecting up to 1.5% of the population [52], and music anhedonia, or the lack of music rewarding effects, reported in about 5% of the population [53]. Furthermore, some patients report anecdotally a strong association created between the specific pieces and the clinical context in which it was used, such that listening to the piece later evokes the vivid recall of the medical episode; some authors have therefore argued that original and health-care dedicated music might be favored over patients' preferred music [54]. Similarly, a panel of expert consulted on a music intervention for end-of-life care has raised similar concerns that patients' own selected music might spontaneously evoke strong negative emotions that might need to be addressed by the attending caretaker [55]. These effects should be documented more systematically, especially when the patients' preferred music is used and might evoke strong emotional experiences or be embedded in associative memories evoking the stressful medical context. MC provides a valuable solution to overcome these issues by the inclusion of a variety of choice allowing for a person-centered approach considering individual preferences of music style and dedicated use of the musical pieces in clinical context, protected from broad diffusion and thereby unlikely to evoke inopportune recall.

Conclusion

Evidence from the available RCTs shows that the *Music Care* app is effective in reducing anxiety and pain intensity in many medical conditions and procedures. The effects of the *Music Care* app on depressive symptoms and on the consumption of medicaments have also been confirmed by a number of studies. Improvements in physiological activity are particularly meaningful clinically in the ICU, critical care, and surgical contexts, and measuring these outcomes must be encouraged in future studies with large enough samples. Moreover, even if most studies focus on chronic and

acute pain in young and middle-aged adults, results show that the *Music Care* app may be suitable for adolescents, and older adults with different medical issues (various chronic pathologies, surgery, neurodegenerative diseases). MC was not superior to active listening conditions involving self-preferred music or environmental sounds, but these findings likely reflect the benefits of both MC and these control conditions. Ongoing RCTs will provide more results on some of the previously studied conditions, including cataract surgery, dental surgery, and sickle-cell disease. Furthermore, other medical conditions including sleep disorders and dressing care, are currently under investigation.

The *Music Care* app has many advantages such as being digital, low-cost, portable, and easy to implement as part of a routine intervention in clinical practice. It may be implemented at bedside, during medical surgery, in nursing homes as well as in individual session for hospital's staff members. Moreover, the utilization of a visual analogical scale integrated to the app allows patients to rate pain and anxiety intensity independently, thus partially overcoming the lack of time and the surcharge of medical staff members. Finally, it constitutes a standardized tool that may allow overcoming the heterogeneity in procedures, type and duration of music and equipment reported in other reviews and meta-analysis [2], thus potentially improving the consistency in results.

In conclusion, this review supports the effectiveness of the *Music Care* app in various medical conditions and in different populations, thus extending knowledge on the effects of a standardized web app-based music intervention to improve the effective co-management of pain, anxiety, and depression. Because of the growing incidence of such issues in the general population, this app may constitute a substantial help as an adjuvant therapy in a large variety of clinical situations. The available results should motivate rigorous clinical assessments in new populations and clinical contexts involving various medical procedure, in-patients general care, including long-term care of the cognitively impaired persons, as well as homecare, to enrich the co-management strategies to

improve pain, anxiety, and sleep.

Conflicts of Interest

JT, PG and PR act as volunteer members of the scientific counsel of Music Care© but have no financial interest. The authors declare no conflict of interest.

Abbreviations

AD- Alzheimer Disease

APIS- Amsterdam Preoperative Anxiety Score

ANI- Analgesia/Nociception Index

BIS- Bispectral index

CPM- Conditioned Pain Modulation

CPT- Cold Pressor Test

D- Day

HAD- Hospital Anxiety Depression

HR- Heart Rate

ICU- Intensive care unit

LLM- Least-Liked Music

MC- Music Care©

MLM- Most-Liked Music

NIV- Non-Invasive Ventilation

NRS- Numerical Rating Scale

ns- non-significant

PDI- Peri-traumatic Distress Inventory

PICOS- Participants, Interventions, Control group, Outcome and Study design

PP- Peak of first heat Pain

PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSQI- Pittsburgh Sleep Quality Index

RASS- Richmond-Agitation-Sedation-Scale

RCT- Randomized Controlled Trial

RespR- Respiratory Rate

SBP- Systolic Blood Pressure

STAY- State Trait Anxiety Inventory

TS- Temporal Summation of heat pain

VAS- Visual Analog Scale

VNS- Visual Numeric Scale

W- Week

References

1. Marwick C. Music therapists chime in with data on medical results. JAMA; 2000 Feb; 283(6): 731–733.

2. Lee JH. The effects of music on pain: A Meta-Analysis. Journal of Music Therapy; 2016 Dec; 53(4): 430–477.

3. Brandes V, Terris DD, Fischer C, Loerbroks A, Jarczok MN, Ottowitz G, Titscher G, Fischer JE, Thayer JF. Receptive music therapy for the treatment of depression: a proof-of-concept study and prospective controlled clinical trial of efficacy. Psychotherapy and Psychosomatics; 2010 Aug; 79(5): 321–322.

4. Dileo C. Effects of music and music therapy on medical patients: A meta-analysis of the research and implications for the future. Journal of the Society for Integrative Oncology; 2006 Jan; 4(2): 67–70.

5. Kamioka H, Tsutani K, Yamada M, Park H, Okuizumi H, Tsuruoka K et al. Effectiveness of music therapy: A summary of systematic reviews based on randomized controlled trials of music interventions. Patient Preference and Adherence; 2014 May; 8: 727–754.

6. Nilsson U. The anxiety- and pain-reducing effects of music interventions: a systematic review. AORN Journal; 2008 Apr; 87(4): 780–807.

7. Good M, Picot BL, Salem SG, Chin C-C, Picot SF, Lane D. Cultural differences in music chosen for pain relief. Journal of Holistic Nursing; 2000 Sep; 18(3): 245–260.

8. White JM. State of the science of music interventions: critical care and perioperative practice. Perioperative Critical Care; 2000 Jun; 12(2): 219–225.

9. Guétin S, Touchon J. Musique et douleur : la séquence en « U », une solution thérapeutique standardisée et validée. Douleur et analgésie; 2017 Jul.

10. Guétin S, Soua B, Voiriot G, Picot M-C, Hérisson C. The effect of music therapy on mood and anxiety–depression: an observational study in institutionalised patients with traumatic brain injury.

Annals of Physical and Rehabilitation Medicine; 2009 Feb; 52(1): 30–40.

11. Jaber S, Bahloul H, Guétin S, Chanques G, Sebbane M, Eledjam J-J. Effects of music therapy in intensive care unit without sedation in weaning patients versus non-ventilated patients. Annales Françaises d'Anesthésie et de Réanimation; 2007 Jan; 26(1): 30–38.

12. Guétin S, Coudeyre E, Picot MC, Ginies P, Graber-Duvernay B, Ratsimba D, Vanbiervliet W, Blayac JP, Hérisson C. Effect of music therapy among hospitalized patients with chronic low-back pain: a controlled, randomized trial. Annales de Réadaptation et de Médecine Physique; 2005 Jun; 48(5): 217–224.

13. Guétin S, Giniès P, Siou DKA, Picot M-C, Pommié C, Guldner E et al. The Effects of music intervention in the management of chronic pain: a single-blind, randomized, controlled trial. The Clinical Journal of Pain; 2012 May; 28(4): 329-337.

14. Guétin S, Portet F, Picot MC, Pommié C, Messaoudi M, Djabelkir L et al. Effect of music therapy on anxiety and depression in patients with Alzheimer's type dementia: randomised, controlled study. Dementia and Geriatric Cognitive Disorders; 2009 Aug; 28(1): 36–46.

15. Webb J, Peerbux S, Smittenaar P, Siddiqui S, Sherwani Y, Ahmed M et al. A reliminary outcomes of a digital therapeutic intervention for smoking cessation in adult smokers: randomized controlled trial. JMIR Ment Health; 2020 Oct;7(10):e22833. .

16. Liberati A, Altman DG, Tetzlaff J, Murlow C, Gotzsche PC, Ioannidis JPA et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ; 2009 Jul; 21: 339.

17. Mercadíe L, Mick G, Guétin S, Bigand E. Effects of listening to music versus environmental sounds in passive and active situations on levels of pain and fatigue in fibromyalgia. Pain Manag Nurs; 2015 Oct;16(5):664-71.

18. Martin J, Le Faucheur L, Pondarré C, Carlier-Gonod A, Baeza-Velasco C. Effects of a standardized musical intervention on the management of pain and anxiety-state of sickle-cell adolescents. Soins Pédiatrie/Puériculture; 2020 Jun; 6850(314): 1.

19. Bertacco M, Soyeux O, Durand R, Boudrias P, Wiseman L, Rompre P, Rainville P, Emani E, Gosselin N. Effect of personalized musical intervention on burden of care in dental implant surgery: A pilot randomized controlled trial. J Dent; 2022 May; 120:104091.

20. Boccara G, Mazeraud A, Cassagnol D, Tarragano F. A web app based-music intervention (MUSIC-CARE) reduces sedative requirement and anxiety during coronary angioplasty. Music & Medicine; 2021; 13(4): 265-271.

21. Demirtas S, Houssais C, Tanniou J, Misery L, & Brenaut E. Effectiveness of a music intervention on pruritus: an open randomized prospective study. Journal of the European Academy of Dermatology and Venereology; 2020 Dec; 34(6): 1280–1285.

22. Guerrier G, Abdoul H, Jilet L, Rothschild P-R, Baillard C. Efficacy of a web app-based music intervention during cataract surgery: a randomized controlled clinical trial. JAMA Ophthalmology; 2021 Sep 1;139(9):1007-1013.

23. Guerrier G, Bernabei F, Lehmann M, Pellegrini M, Giannaccare G, Rothschild P-R. Efficacy of preoperative music intervention on pain and anxiety in patients undergoing cataract surgery. Front Pharmacol; 2021; 12: 748296.

24. Reynaud D, Bouscaren N, Lenclume V, Boukerrou M. Comparing the effects of self-selected MUsic versus predetermined music on patient ANXiety prior to gynaecological surgery: the MUANX randomized controlled trial. Trials; 2021 Aug 13;22(1):535.

25. Messika J, Martin Y, Maquigneau N, Puechberty C, Henry-Lagarrigue M, Stoclin A et al. A musical intervention for respiratory comfort during noninvasive ventilation in the ICU. European Respiratory Journal; 2019 Sep; 53(1): 1801873.

26. Jacquier S, Nay MA, Muller G, Muller L. 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. Anesthesia and Analgesia; 2022; 134(4): 781-790.

27. Merliot-Gailhoustet L, Raimbert C, Garnier O, Carr J, De Jong A, Molinari N, Jaber S, Chanques G. Discomfort improvement for critically ill patients using electronic relaxation devices:

results of the cross-over randomized controlled trial E-CHOISIR (Electronic-CHOIce of a System for Intensive care Relaxation). Crit Care; 2022 Sep 26;26(1): 291.

28. Marchand S, Soyeux O. A web app-based music intervention reduces experimental thermal pain: a randomized trial on preferred versus least-liked music style. Front. Pain Res; 2023 Jan 16;3.

29. Cabon M, Le Fur-Bonnabesse A, Genestet S, Quinio B, Misery L, Woda A et al. Impact of Music on First Pain and Temporal Summation of Second Pain: A Psychophysical Pilot Study. Music Perception; 2021; 38 (3): 267–281.

30. de Heer EW, Gerrits MMJG, Beekman ATF, Dekker J, van Marwijk HWJ, de Waal, MWM et al. The association of depression and anxiety with pain: A study from NESDA. PloS One; 2014 Oct; 9(10): e106907.

31. Vlaeyen JWS, & Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. Pain; 2000 Apr; 85(3): 317-332.

32. Gerrits MMJG, Vogelzangs N, van Oppen P, van Marwijk HWJ., van der Horst H, Penninx BWJH. Impact of pain on the course of depressive and anxiety disorders. Pain; 2012 Feb; 153(2): 429-436.

33. Demyttenaere K, Bruffaerts R, Lee S, Posada-Villa J, Kovess V, Angermeyer MC et al. Mental disorders among persons with chronic back or neck pain: results from the world mental health surveys. Pain; 2007 Jun; 129(3): 332-342.

34. Papakostas GI, Petersen T, Denninger J, Sonawalla SB, Mahal Y, Alpert JE et al. Somatic symptoms in treatment-resistant depression. Psychiatry Research; 2003 May; 118(1): 39—45.

35. Teh CF, Morone NE, Karp JF, Belnap BH, Zhu F, Weiner DK, & Rollman BL. Pain interference impacts response to treatment for anxiety disorders. Depression and Anxiety; 2009 Jan; 26(3): 222–228.

36. Roy M, Lebuis A, Hugueville L, Peretz I, Rainville P. Spinal modulation of nociception by music. Eur J Pain; 2012 Jul;16(6): 870-7.

37. Roy M, Peretz I, Rainville P. Emotional valence contributes to music-induced analgesia. Pain;

2008 Jan;134(1-2): 140-7.

38. Rhudy JL, Williams AE, McCabe KM, Russell JL, Maynard LJ. Emotional control of nociceptive reactions (ECON): do affective valence and arousal play a role? Pain; 2008 Jun; 136(3): 250-261.

39. Rhudy JL, Bartley EJ, Williams AE. Habituation, sensitization, and emotional valence modulation of pain responses. Pain; 2010 Feb;148(2): 320-327.

40. Roy M, Piché M, Chen JI, Peretz I, Rainville P. Cerebral and spinal modulation of pain by emotions. Proc Natl Acad Sci U S A; 2009 Dec 8;106(49): 20900-5.

41. Roy M, Lebuis A, Peretz I, Rainville P. The modulation of pain by attention and emotion: a dissociation of perceptual and spinal nociceptive processes. Eur J Pain; 2011 Jul;15(6): 641.

42. Gulpers B, Ramakers I, Hamel R, Köhler S, Oude Voshaar R, Verhey F. Anxiety as a predictor for cognitive decline and dementia: a systematic review and meta-analysis. The American Journal of Geriatric Psychiatry; 2016 Oct; 24(10): 823–842.

43. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment. JAMA; 2002 Sep; 288(12): 1475–1483.

44. Dillon C, Serrano CM, Castro D, Leguizamón PP, Heisecke SL, Taragano FE. Behavioral symptoms related to cognitive impairment. Neuropsychiatric Disease and Treatment; 2013 Sep; 9: 1443–1455.

45. Taragano FE, Allegri RF, Krupitzki H, Sarasola DR, Serrano CM, Loñ L et al. Mild behavioral impairment and risk of dementia: a prospective cohort study of 358 patients. The Journal of Clinical Psychiatry; 2009 Apr; 70(4): 584–592.

46. Becker E, Orellana Rios CL, Lahmann C, Rücker G, Bauer J, Boeker M. Anxiety as a risk factor of Alzheimer's disease and vascular dementia. The British Journal of Psychiatry; 2018 Nov; 213(5): 654–660.

47. Porter VR, Buxton WG, Fairbanks LA, Strickland T, O'Connor SM, Rosenberg-Thompson S et

al. Frequency and characteristics of anxiety among patients with Alzheimer's disease and related dementias. The Journal of Neuropsychiatry and Clinical Neurosciences; 2003 May; 15(2): 180–186.

48. Gomoll BP, Kumar A. Managing anxiety associated with neurodegenerative disorders. F1000prime Reports; 2015 Jan; 7: 05.

49. Ray KD, & Götell E. The use of music and music therapy in ameliorating depression symptoms and improving well-being in nursing home residents with dementia. Frontiers in Medicine; 2018 Oct; 5: 287–287.

50. Werner J, Wosch T, & Gold C. Effectiveness of group music therapy versus recreational group singing for depressive symptoms of elderly nursing home residents: Pragmatic trial. Aging & Mental Health; 2017 Feb; 21(2): 147–155.

51. Loko A, Coudeyre E, Guétin S, Jarzebowski W, Belmin J. Effects of standardized musical intervention on refusal of care and aggression during toileting in people with institutionalized neurocognitive disorders. Ann Phys Rehabil Med; 2018 Nov;61(6): 421-423.

52. Peretz I, Vuvan DT. Prevalence of congenital amusia. Eur J Hum Genet; 2017 May;25(5):625-630.

53. Zatorre RJ. Musical pleasure and reward: mechanisms and dysfunction. Ann N Y Acad Sci; 2015 Mar;1337: 202-11.

54. Messika J, Kalfon P, Ricard JD. Adjuvant therapies in critical care: music therapy. Intensive Care Med; 2018 Nov;44(11): 1929-1931.

55. Bissonnette J, Pierre S, Duong ATJ, Pinard AM, Rainville P, Ogez D. Development of a Mixed Hypnosis and Music Intervention Program for the Management of Pain, Anxiety, and Wellbeing in End-of-Life Palliative Care. Front Pain Res (Lausanne); 2022 Jul 6;3: 926584.